POC 2020 DATA ACQUISITION MANUAL

BREAST CANCER

COLON/RECTUM CANCER

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1. STUDY OVERVIEW

1.1. The Patterns of Care Study funded in fiscal year 2022 will examine the diagnosis, demographic and tumor characteristics, biomarkers, and therapies offered to patients diagnosed in 2020 with breast cancer (AJCC stage 0 - IV) and colon/rectum cancer (AJCC stage II - IV). The study will also collect data on documentation of the effects of the COVID-19 pandemic on screening, diagnosis, treatment, and palliative care for these cancers from the medical record. The National Cancer Institute has a Congressional Mandate to report on the dissemination of state-of-the-art therapy into community practice.

1.2. BREAST CANCER

Estimated new cases and deaths from breast cancer in the United States in 2022 are:

- New cases: 290,560
- Deaths: 43,780

Breast cancer is the most common non-cutaneous cancer in U.S. women. Fewer than one in six women diagnosed with breast cancer die of the disease. Men account for 1% of breast cancer cases and breast cancer deaths. Widespread adoption of screening increases breast cancer incidence in a given population and changes the characteristics of cancers detected, with increased incidence of lower-risk cancers, premalignant lesions, and ductal carcinoma in situ (DCIS). Population studies from the United States and the United Kingdom demonstrate an increase in DCIS and invasive breast cancer incidence since the 1970s, attributable to the widespread adoption of both postmenopausal hormone therapy and screening mammography. In the last decade, women have refrained from using postmenopausal hormones, and breast cancer incidence has declined, but not to the levels seen before the widespread use of screening mammography.

Staging Information for Breast Cancer

The American Joint Committee on Cancer (AJCC) staging system provides a strategy for grouping patients with respect to prognosis. Therapeutic decisions are formulated in part according to staging categories but also according to other clinical factors such as the following, some of which are included in the determination of stage:

- Tumor size.
- Lymph node status.
- Estrogen-receptor and progesterone-receptor levels in the tumor tissue.
- Human epidermal growth factor receptor 2 (HER2/neu) status in the tumor.
- Tumor grade.

- Menopausal status.
- General health of the patient.

The standards used to define biomarker status are described as follows:

- Estrogen receptor (ER) expression: ER expression is measured primarily by immunohistochemistry (IHC). Any staining of 1% of cells or more is considered positive for ER.
- Progesterone receptor (PR) expression: PR expression is measured primarily by IHC. Any staining of 1% of cells or more is considered positive for PR.
- HER2 expression: HER2 is measured primarily by either IHC to assess expression of the HER2 protein or by in situ hybridization (ISH) to assess gene copy number. The American Society of Clinical Oncology/College of American Pathologists consensus panel has published guidelines for cases when either IHC or ISH testing is equivocal.

IHC:

- Negative: 0 or 1+ staining
- Equivocal: 2+ staining
- Positive: 3+ staining

ISH (dual probe):

- Possible negative results:
    - HER2/chromosome enumeration probe (CEP17) ratio <2.0 AND HER2 copy number <4
- Possible equivocal results: (requires performing alternative ISH test to confirm equivocal or IHC if not previously performed)
    - HER2/CEP17 ratio <2.0 AND HER2 copy number ≥4 but <6
- Possible positive results:
    - HER2/CEP17 ratio ≥2.0 by ISH
    - HER2 copy number ≥6 regardless of ratio by ISH

ISH (single probe):

- Negative: <4 HER2 copies

- Equivocal: ≥4 HER2 copies but <6 HER2 copies
- Positive: ≥6 HER2 copies

TNM Definitions and AJCC Stage Groupings

The AJCC has designated staging by TNM (tumor, node, metastasis) classification to define breast cancer. The grade of the tumor is determined by its morphologic features, such as tubule formation, nuclear pleomorphism, and mitotic count. Tables presenting AJCC definitions for T, N, and M classification; histologic grade; DCIS nuclear grade and AJCC Anatomic and Prognostic Stage Groups are available at https://www.cancer.gov/types/breast/hp/breast-treatment-pdq. In the United States, cancer registries and clinicians must use the Clinical and Pathological Prognostic Stage Group tables for reporting. It is expected that testing is performed for grade, HER2, ER, and PR status and that results are reported for all cases of invasive cancer in the United States.

Treatment

Treatment Option Overview for Early/Localized/Operable Breast Cancer

Standard treatment options for early, localized, or operable breast cancer may include the following:

Surgery:

- Breast-conserving surgery (lumpectomy) and sentinel lymph node (SLN) biopsy with or without axillary lymph node dissection for positive SLNs.
- Modified radical mastectomy (removal of the entire breast with axillary dissection of levels I and II) with or without breast reconstruction and sentinel node biopsy with or without axillary lymph node dissection for positive SLNs.

Postoperative radiation therapy:

- Axillary node–negative breast cancer (postmastectomy):
    - No additional therapy.
    - Radiation therapy.
- Axillary node–positive breast cancer (postmastectomy):

    - For one to three nodes, the role of regional radiation therapy to the infra/supraclavicular nodes, internal mammary nodes, axillary nodes, and chest wall is unclear.
    - For four or more nodes or extranodal involvement, regional radiation therapy is advised.
- Axillary node–negative or positive breast cancer (post–breast-conserving therapy):
    - Whole-breast radiation therapy.

Postoperative systemic therapy:

- Therapy depends on many factors including stage, grade, molecular status of the tumor (e.g., estrogen receptor [ER], progesterone receptor [PR], human epidermal growth factor receptor 2 [HER2/neu], or triple-negative [ER-negative, PR-negative, and HER2/neu-negative] status). Adjuvant treatment options may include the following:
    - Tamoxifen.
    - Aromatase inhibitor (AI) therapy.
    - Ovarian function suppression.
    - Chemotherapy.

Preoperative systemic therapy:

- Chemotherapy.
- HER2-targeted therapy.
- Endocrine therapy.

Surgery

Stages I, II, IIIA, and operable IIIC breast cancer often require a multimodal approach to treatment. The diagnostic biopsy and surgical procedure that will be used as primary treatment should be performed as two separate procedures:

- Biopsy. In many cases, the diagnosis of breast carcinoma is made by core needle biopsy.

- Surgical procedure. After the presence of a malignancy is confirmed by biopsy, the following surgical treatment options can be discussed with the patient before a therapeutic procedure is selected:
    - Breast-conserving surgery.
    - Modified radical mastectomy (removal of the entire breast with axillary dissection of levels I and II) with or without breast reconstruction.

To guide the selection of adjuvant therapy, many factors including stage, grade, and molecular status of the tumor (e.g., ER, PR, HER2/neu, or triple-negative status) are considered.

Locoregional treatment

Selection of a local therapeutic approach depends on the following:

- Location and size of the lesion.
- Analysis of the mammogram.
- Breast size.
- Patient's desire to preserve the breast.

Options for surgical management of the primary tumor include the following:

- Breast-conserving surgery plus radiation therapy. All histologic types of invasive breast cancer may be treated with breast-conserving surgery plus radiation therapy. However, the presence of inflammatory breast cancer, regardless of histologic subtype, is a contraindication to breast-conserving therapy. The presence of multifocal disease in the breast and a history of collagen vascular disease are relative contraindications to breast-conserving therapy.
- Mastectomy with or without breast reconstruction.

Surgical staging of the axilla should also be performed.

Survival is equivalent with any of these options, as documented in the trial of the European Organization for Research and Treatment of Cancer (EORTC) (EORTC-10801) and other prospective randomized trials.

The rate of local recurrence in the breast after conservative treatment is low and varies slightly with the surgical technique used (e.g., lumpectomy, quadrantectomy, segmental mastectomy, and others). Whether completely clear microscopic margins

are necessary has been debated. For patients undergoing partial mastectomy, margins may be positive after primary surgery, often leading to re- excision.

Axillary lymph node management

Axillary node status remains the most important predictor of outcome in breast cancer patients. Evidence is insufficient to recommend that lymph node staging can be omitted in most patients with invasive breast cancer. Several groups have attempted to define a population of women in whom the probability of nodal metastasis is low enough to preclude axillary node biopsy. In these single-institution case series, the prevalence of positive nodes in patients with T1a tumors ranged from 9% to 16%. Another series reported the incidence of axillary node relapse in patients with T1a tumors treated without axillary lymph node dissection (ALND) was 2%.

The axillary lymph nodes are staged to aid in determining prognosis and therapy. SLN biopsy is the initial standard axillary staging procedure performed in women with invasive breast cancer. The SLN is defined as any node that receives drainage directly from the primary tumor; therefore, allowing for more than one SLN, which is often the case. Studies have shown that the injection of technetium Tc 99m-labeled sulfur colloid, vital blue dye, or both around the tumor or biopsy cavity, or in the subareolar area, and subsequent drainage of these compounds to the axilla results in the identification of the SLN in 92% to 98% of patients. These reports demonstrate a 97.5% to 100% concordance between SLN biopsy and complete ALND.

Because of the following body of evidence, SLN biopsy is the standard initial surgical staging procedure of the axilla for women with invasive breast cancer. SLN biopsy alone is associated with less morbidity than axillary lymphadenectomy.

For patients who require an ALND, the standard evaluation usually involves only a level I and II dissection, thereby removing a satisfactory number of nodes for evaluation (i.e., at least 6–10), while reducing morbidity from the procedure.

Breast reconstruction

For patients who opt for a total mastectomy, reconstructive surgery may be performed at the time of the mastectomy (i.e., immediate reconstruction) or at some subsequent time (i.e., delayed reconstruction).[36-39]

Breast contour can be restored by the following:

- Submuscular insertion of an artificial implant (silicone or saline filled). If an immediate implant cannot technically be performed, a tissue expander can be inserted beneath the pectoral muscle. Saline is injected into the expander to

stretch the tissues for a period of weeks or months until the desired volume is obtained. The tissue expander is then replaced by a permanent implant.

- Rectus muscle or other lap. Muscle flaps require a considerably more complicated and prolonged operative procedure, and blood transfusions may be required.

After breast reconstruction, radiation therapy can be delivered to the chest wall and regional nodes in either the adjuvant or local recurrent disease setting. Radiation therapy after reconstruction with a breast prosthesis may affect cosmesis, and the incidence of capsular fibrosis, pain, or the need for implant removal may be increased.]

Postoperative Radiation Therapy

Radiation therapy is regularly employed after breast-conserving surgery. Radiation therapy is also indicated for high-risk postmastectomy patients. The main goal of adjuvant radiation therapy is to eradicate residual disease thus reducing local recurrence

Post–breast-conserving surgery

For women who are treated with breast-conserving surgery without radiation therapy, the risk of recurrence in the conserved breast is substantial (>20%) even in confirmed axillary lymph node–negative women. Although all trials assessing the role of radiation therapy in breast-conserving therapy have shown highly statistically significant reductions in local recurrence rate, no single trial has demonstrated a statistically significant reduction in mortality. However, a large meta-analysis demonstrated a significant reduction in risk of recurrence and breast cancer death. Thus, evidence supports the use of whole-breast radiation therapy after breast-conserving surgery.

Additional studies are needed to determine whether shorter fractionation is appropriate for women with higher nodal disease burden.

Regional nodal irradiation

Regional nodal irradiation is routinely given postmastectomy to patients with involved lymph nodes; however, its role in patients who have breast-conserving surgery and whole-breast irradiation has been less clear.

Postmastectomy

Postoperative chest wall and regional lymph node adjuvant radiation therapy has traditionally been given to selected patients considered at high risk of locoregional failure after mastectomy. Patients at highest risk of local recurrence have one or more of the following:

- Four or more positive axillary nodes.
- Grossly evident extracapsular nodal extension.
- Large primary tumors.
- Very close or positive deep margins of resection of the primary tumor.

In this high-risk group, radiation therapy can decrease locoregional recurrence, even among those patients who receive adjuvant chemotherapy.

Patients with one to three involved nodes without any of the high-risk factors are at low risk of local recurrence, and the value of routine use of adjuvant radiation therapy in this setting is unclear.

Timing of postoperative radiation therapy

The optimal sequence of adjuvant chemotherapy and radiation therapy after breast-conserving surgery has been studied. Based on the following studies, delaying radiation therapy for several months after breast- conserving surgery until the completion of adjuvant chemotherapy does not appear to have a negative impact on overall outcome. Additionally, initiating chemotherapy soon after breast-conserving surgery may be preferable for patients at high risk of distant dissemination.

Late toxic effects of radiation

Late toxic effects of radiation therapy are uncommon and can be minimized with current radiation delivery techniques and with careful delineation of the target volume.

Postoperative Systemic Therapy

Stage and molecular features determine the need for adjuvant systemic therapy and the choice of modalities used. The selection of therapy is most appropriately based on knowledge of an individual’s risk of tumor recurrence balanced against the short-term and long-term risks of adjuvant treatment. This approach allows clinicians to help individuals determine if the gains anticipated from treatment are reasonable for their situation.

Many of the studies that support the use of chemotherapy after surgery were conducted before the widespread practice of testing for HER2. In general, their results are still applicable to the management of patients with all three subtypes of breast cancer.

Pertuzumab

Pertuzumab is a humanized monoclonal antibody that binds to a distinct epitope on the extracellular domain of the HER2 receptor and inhibits dimerization. Its use, in combination with trastuzumab, has been evaluated in a randomized trial in the postoperative setting.

Endocrine therapy for hormone receptor–positive breast cancer

Much of the evidence presented in the following sections on therapy for women with hormone receptor–positive disease has been considered in an American Society of Clinical Oncology guideline that describes several options for the management of these patients. Five years of adjuvant endocrine therapy has been shown to substantially reduce the risks of locoregional and distant recurrence, contralateral breast cancer, and death from breast cancer.

The optimal duration of endocrine therapy is unclear, with the preponderance of evidence supporting at least 5 years of endocrine therapy.

Tamoxifen

Tamoxifen has been shown to be of benefit to women with hormone receptor–positive breast cancer.

Ovarian ablation, tamoxifen, and chemotherapy

Evidence suggests ovarian ablation alone is not an effective substitute for other systemic therapies. Further, the addition of ovarian ablation to chemotherapy and/or tamoxifen has not been found to significantly improve outcomes

Aromatase inhibitors (AIs)

Premenopausal women

AIs have been compared with tamoxifen in premenopausal women in whom ovarian function was suppressed or ablated. The results of these studies have been conflicting.

Postmenopausal women

In postmenopausal women, the use of AIs in sequence with or as a substitute for tamoxifen has been the subject of multiple studies, the results of which have been summarized in an individual patient-level meta- analysis.

Duration of AI therapy

The optimal duration of AI therapy is uncertain, and multiple trials have evaluated courses longer than 5 years.

Endocrine therapy and cyclin-dependent kinase (CDK) inhibitor therapy

CDK4 and CDK6 have been implicated in the continued proliferation of hormone receptor–positive breast cancer that is resistant to endocrine therapy. CDK inhibitors, in combination with endocrine therapy, have been approved by the FDA in both first-line and later-line treatment of patients with advanced hormone receptor– positive HER2-negative breast cancer and are now being studied in the adjuvant setting.

Bone-modifying therapy

Both bisphosphonates and denosumab have been evaluated as adjuvant therapies for early-stage breast cancer; however, the role of these agents as adjuvant therapy for early-stage breast cancer is unclear. Compared with denosumab, the amount of evidence supporting bisphosphonates is greater, and there is evidence supporting breast cancer mortality—an endpoint that is more clinically relevant.

Neoadjuvant therapy is particularly favored in patients with triple-negative or HER2-positive disease, when pathologic response is used as a guide in choosing the optimal adjuvant therapy after surgery.

Omission of postoperative radiation therapy to the regional nodes in patients who initially present as node positive and become node negative after neoadjuvant therapy is currently being evaluated.

Patient selection, staging, treatment, and follow-up

Multidisciplinary management of patients undergoing preoperative therapy by an experienced team is essential to optimize the following:

- Patient selection.
- Choice of systemic therapy.

- Management of the axilla and surgical approach.
- Decision to administer adjuvant radiation therapy.

The tumor histology, grade, and receptor status are carefully evaluated before preoperative therapy is initiated. Patients whose tumors have a pure lobular histology, low grade, or high hormone-receptor expression and HER2-negative status are less likely to respond to chemotherapy and should be considered for primary surgery, especially when the nodes are clinically negative. Even if adjuvant chemotherapy is administered after surgery in these cases, a third-generation regimen (anthracycline/taxane based) may be avoided.

Before beginning preoperative therapy, the extent of the disease within the breast and regional lymph nodes should be assessed. Staging of systemic disease may include the following:

- CT scan of the chest and abdomen and a bone scan.
- Positron-emission tomography.

Baseline breast imaging is performed when breast-conserving therapy is desired to identify the tumor location and exclude multicentric disease. Suspicious abnormalities are usually biopsied before beginning treatment and a marker placed at the center of the breast tumor(s). When possible, suspicious axillary nodes should be biopsied before initiation of systemic treatment.

In patients with clinically negative nodes who receive neoadjuvant chemotherapy, an SLN biopsy is typically performed at the time of surgery. In patients presenting with positive lymph nodes, detected by either clinical examination or imaging, SLN biopsy may be performed in a patient who becomes clinically node negative after preoperative therapy. The use of dual mapping with both radiocolloid and blue dye and retrieval of at least three negative lymph nodes was associated with a lower false-negative rate and ALND may be omitted in these patients.

When considering preoperative therapy, treatment options include the following:

- For HER2-negative breast tumors, an anthracycline/taxane-based chemotherapy regimen.
- For HER2-positive disease, chemotherapy and HER2-targeted therapy.
- Ideally, the entire treatment regimen is administered before surgery.
- For postmenopausal women with hormone receptor–positive breast cancer, chemotherapy is an option. For those who cannot be given chemotherapy, preoperative endocrine therapy may be an option.

- For premenopausal women with hormone-responsive cancer, the use of preoperative endocrine therapy is under investigation.

Regular clinical assessment of response to therapy is necessary after beginning preoperative therapy. Repeat radiographic assessment is also required if breast conservation is the surgical goal. Patients with progressive disease during preoperative therapy may either transition to a non–cross-resistant regimen or proceed to surgery, if feasible. Although switching to a non–cross-resistant regimen results in a higher pCR rate than continuing the same therapy, there is no clear evidence that other breast cancer outcomes are improved with this approach.

HER2/neu-negative breast cancer

Early trials examined whether anthracycline-based regimens used in the adjuvant setting would prolong DFS and OS when used in the preoperative setting. The evidence supports higher rates of breast-conserving therapy with the use of a preoperative anthracycline chemotherapy regimen than with postoperative use, but no improvement in survival was noted with the preoperative strategy.

Typically, an anthracycline-and-taxane–based regimen is used if chemotherapy is administered in the neoadjuvant setting for patients with HER2/neu-negative breast cancer.

Triple-negative breast cancer

Promising results have been observed with the addition of carboplatin to anthracycline/taxane combination chemotherapy regimens in patients with triple-negative breast cancer (TNBC). Future definitive studies evaluating survival endpoints and the identification of biomarkers of response or resistance are necessary before the addition of carboplatin to standard preoperative chemotherapy can be considered a new standard of care.

Longer term follow-up with regard to survival outcomes and toxicity will inform the use of immunotherapy in the neoadjuvant treatment of TNBC. Key issues that remain to be clarified include identification of a predictive biomarker, the optimal chemotherapy backbone, and the role of adjuvant immunotherapy after neoadjuvant chemotherapy plus immunotherapy.

HER2/neu-positive breast cancer

After the success in the adjuvant setting, initial reports from phase II studies indicated improved pCR rates when trastuzumab, a monoclonal antibody that binds the

extracellular domain of HER2, was added to preoperative anthracycline/taxane–based regimens. This has been confirmed in phase III studies.

Trastuzumab

Newer HER2-targeted therapies (lapatinib, pertuzumab) have also been investigated. It appears that dual targeting of the HER2 receptor results in an increase in pCR rate; however, no survival advantage has been demonstrated to date with this approach.

Pertuzumab

Pertuzumab is a humanized monoclonal antibody that binds to a distinct epitope on the extracellular domain of the HER2 receptor and inhibits dimerization. Pertuzumab, in combination with trastuzumab with or without chemotherapy, has been evaluated in two preoperative clinical trials to improve on the pCR rates observed with trastuzumab and chemotherapy.

Lapatinib

Lapatinib is a small-molecule kinase inhibitor that is capable of dual receptor inhibition of both epidermal growth factor receptor and HER2. Study results do not support the use of lapatinib in the preoperative setting.

Preoperative endocrine therapy

Preoperative endocrine therapy may be an option for postmenopausal women with hormone receptor-positive breast cancer when chemotherapy is not a suitable option because of comorbidities or performance status.

Although the toxicity profile of preoperative hormonal therapy over the course of 3 to 6 months is favorable, the pCR rates obtained (1%–8%) are far lower than have been reported with chemotherapy in unselected populations.

The use of preoperative endocrine therapy in premenopausal women with hormone-responsive breast cancer remains investigational.

Postoperative therapy

Capecitabine

One clinical trial suggested that there is a benefit to using capecitabine as adjuvant therapy in patients who did not obtain a pCR after preoperative chemotherapy.

Trastuzumab emtansine (T-DM1)

Radiation therapy is administered after breast conservation in most women who have received preoperative therapy to reduce the risk of locoregional recurrence. Baseline clinical and subsequent pathologic staging should be considered in deciding whether to administer postmastectomy radiation.

Other adjuvant systemic treatments may be administered either postoperatively, during, or after completion of adjuvant radiation, including adjuvant hormonal therapy for patients with hormone receptor-positive disease and adjuvant trastuzumab for those with HER2-positive disease.

Posttherapy Surveillance

The frequency of follow-up and the appropriateness of screening tests after the completion of primary treatment for stage I, stage II, or stage III breast cancer remain controversial.

Evidence from randomized trials indicates that periodic follow-up with bone scans, liver sonography, chest x- rays, and blood tests of liver function does not improve survival or quality of life when compared with routine physical examinations. Even when these tests permit earlier detection of recurrent disease, patient survival is unaffected. On the basis of these data, acceptable follow-up can be limited to the following for asymptomatic patients who complete treatment for stages I to III breast cancer:

- Physical examination.
- Annual mammography.

Locally Advanced or Inflammatory Breast Cancer

Treatment Option Overview for Locally Advanced or Inflammatory Breast Cancer

On the basis of the available evidence, multimodality therapy delivered with curative intent is the standard of care for patients with locally advanced or inflammatory breast cancer.

The standard treatment options for locally advanced or inflammatory breast cancer may include the following:

- Breast-conserving surgery or total mastectomy with axillary lymph node dissection.
- Chemotherapy.
- Radiation therapy.

- Hormone therapy.

Initial surgery is generally limited to biopsy to permit the determination of histology, estrogen receptor (ER) and progesterone receptor levels, and human epidermal growth factor receptor 2 (HER2/neu) overexpression.

The standard chemotherapy regimen for initial treatment is the same as that used in the adjuvant setting, although trials done solely in patients with locally advanced disease have not shown a statistically significant advantage to dose- dense chemotherapy.

For patients who respond to preoperative chemotherapy, local therapy may consist of total mastectomy with axillary lymph node dissection followed by postoperative radiation therapy to the chest wall and regional lymphatics. Breast-conserving therapy can be considered for patients with a good partial or complete response to preoperative chemotherapy. Subsequent systemic therapy may consist of further chemotherapy. Hormone therapy is administered to patients with ER-positive or ER-unknown tumors.

Although the evidence described below has not been replicated, it suggests patients with locally advanced or inflammatory breast cancer should be treated with curative intent.

All patients are considered candidates for clinical trials to evaluate the most appropriate way to administer the various components of new multimodality regimens.

Locoregional Recurrent Breast Cancer

Recurrent breast cancer is often responsive to therapy, although treatment is rarely curative at this stage of disease. Patients with locoregional breast cancer recurrence may become long-term survivors with appropriate therapy.

The rates of locoregional recurrence have been reduced over time, and a meta-analysis suggests a recurrence rate of less than 3% in patients treated with breast-conserving surgery and radiation therapy. The rates are somewhat higher (up to 10%) for those treated with mastectomy. Nine percent to 25% of patients with locoregional recurrence will have distant metastases or locally extensive disease at the time of recurrence.

Before treatment for recurrent breast cancer, restaging to evaluate the extent of disease is indicated. Cytologic or histologic documentation of recurrent disease is obtained whenever possible. When therapy is selected, the estrogen-receptor (ER) status, progesterone-receptor (PR) status, and human epidermal growth factor

receptor 2 (HER2/neu) status at the time of recurrence and previous treatment are considered, if known.

ER status may change at the time of recurrence. Treatment options for locoregional recurrent breast cancer include the following:

- Chemotherapy.
- Hormone therapy.
- Radiation therapy.
- Surgery.
- Targeted therapy (e.g., trastuzumab).

Patients with locoregional recurrence should be considered for further local treatment (e.g., mastectomy).

Metastatic Breast Cancer

Treatment of metastatic disease is palliative in intent. Goals of treatment include prolonging life and improving quality of life. Although median survival has been reported to be 18 to 24 months overall, survival varies according to subtype. The longest median outcomes have been observed in patients with human epidermal growth factor receptor 2 (HER2)-positive and hormone receptor–positive metastatic breast cancer, and less favorable outcomes have been observed in patients with triple-negative metastatic breast cancer.

Treatment options for metastatic breast cancer include the following:

- Hormone therapy (tamoxifen, aromatase inhibitors).
- HER2-targeted therapy.
- CDK4/6 inhibitors.
- mTOR inhibitors.
- PIK3CA inhibitors.
- Chemotherapy.
- Immunotherapy.
- Surgery, for patients with limited symptomatic metastases.
- Radiation therapy, for patients with limited symptomatic metastases.
- Bone-modifying therapy, for patients with bone metastases.

In many cases, these therapies are given in sequence and used in various combinations.

Cytologic or histologic documentation of metastatic disease, with testing of estrogen receptor (ER), progesterone receptor, and HER2 status, should be obtained whenever possible.

All patients with metastatic breast cancer are considered candidates for ongoing clinical trials.

Hormone Receptor–Positive Breast Cancer

Endocrine therapy and cyclin-dependent kinase (CDK) inhibitor therapy

CDK4 and CDK6 have been implicated in the continued proliferation of hormone receptor–positive breast cancer resistant to endocrine therapy. CDK inhibitors have been approved by the U.S. Food and Drug Administration (FDA) in combination with endocrine therapy in both first-line and later-line treatment of advanced hormone receptor–positive HER2-negative breast cancer. Three oral CDK4/6 inhibitors are currently available: palbociclib, ribociclib, and abemaciclib.

Overall, the addition of CDK4/6 inhibitors to endocrine therapy is associated with improved breast cancer outcomes and, in general, either maintained or improved quality of life. This benefit was observed across multiple clinicopathological subgroups of breast cancer.

First-line palbociclib and endocrine therapy

First-line ribociclib and endocrine therapy

Ribociclib, another CDK4/6 inhibitor, has also been tested in the first-line setting for postmenopausal patients and premenopausal patients with hormone receptor–positive and HER2-negative recurrent or metastatic breast cancer.

First-line abemaciclib and endocrine therapy

Abemaciclib, another CDK4/6 inhibitor, has also been tested in the first-line setting for postmenopausal patients with hormone receptor–positive and HER2-negative recurrent or metastatic breast cancer.

Second-line palbociclib and endocrine therapy

Second-line ribociclib and endocrine therapy

Second-line abemaciclib and endocrine therapy

Single-agent CDK inhibitor therapy

Mammalian target of rapamycin (mTOR) inhibitor therapy plus endocrine therapy

Preclinical models and clinical studies suggest that mTOR inhibitors might overcome endocrine resistance.

Alpelisib plus endocrine therapy

Activating mutations in PIK3CA are identified in approximately 40% of hormone receptor–positive and HER2- negative breast cancers. Alpelisib is an alpha-specific PI3K inhibitor.

Endocrine therapy alone

With the PFS and OS advantages associated with combination therapy with targeted agents and endocrine therapy as discussed above, single-agent endocrine therapy is less frequently used, especially in the first-line setting. However, its use remains appropriate in select cases as first-line therapy and in later-line therapy after progression on targeted therapies and before the use of chemotherapy in cases in which endocrine-sensitive disease is still thought to be present.

Commonly used single-agent endocrine therapies include tamoxifen, nonsteroidal AI (letrozole, anastrozole), the steroidal AI exemestane, and fulvestrant. In general, premenopausal women with metastatic breast cancer undergo ovarian suppression or ablation and are treated in the same manner as postmenopausal women.

Tamoxifen and AI therapy

While tamoxifen has been used for many years in treating postmenopausal women with newly metastatic disease that is ER positive, PR positive, or ER/PR unknown, several randomized trials suggest equivalent or superior response rates and PFS for the AI compared with tamoxifen.

Fulvestrant

Fulvestrant is a selective estrogen receptor degrader that has been studied in the first-line and second-line setting in women with advanced or metastatic breast cancer.

Combination endocrine therapy with an AI and fulvestrant

Conflicting results were found in two trials that compared the combination of the antiestrogen fulvestrant and anastrozole with anastrozole alone in the first-line treatment of hormone receptor–positive postmenopausal patients with recurrent or metastatic disease.

Sequencing Therapy for Hormone Receptor–Positive Metastatic Breast Cancer

The optimal sequence of therapies for hormone receptor–positive metastatic breast cancer is not known. In general, in the absence of a visceral crisis, most patients receive sequential endocrine-based regimens before transitioning to chemotherapy. On the basis of the PFS and OS improvements mentioned above, a combination of a CDK4/6 inhibitor therapy and endocrine therapy in the first line is an appropriate choice.

Hormone Receptor–Negative Breast Cancer

The treatment for hormone receptor–negative breast cancer is chemotherapy.

HER2/neu-Positive Breast Cancer

Antibody therapy targeting the HER2 pathway has been used since the 1990s and has revolutionized the treatment of HER2-positive metastatic breast cancer. Several HER2-targeted agents (e.g., trastuzumab, pertuzumab, ado-trastuzumab emtansine, lapatinib) have been approved for treatment of this disease.

Monoclonal antibody therapy

Trastuzumab

Approximately 20% to 25% of patients with breast cancer have tumors that overexpress HER2/neu. Trastuzumab is a humanized monoclonal antibody that binds to the HER2/neu receptor. In patients previously treated with cytotoxic chemotherapy whose tumors overexpress HER2/neu, administration of trastuzumab as a single agent resulted in a response rate of 21%. Clinical trials comparing multiagent chemotherapy plus trastuzumab with single-agent chemotherapy have yielded conflicting results. Outside of a clinical trial, standard first-line treatment for metastatic HER2-overexpressing breast cancer is single-agent chemotherapy plus trastuzumab.

Pertuzumab

Pertuzumab is a humanized monoclonal antibody that binds to a different epitope at the HER2 extracellular domain than does trastuzumab. The binding of pertuzumab to HER2 prevents dimerization with other ligand- activated HER receptors, most notably HER3.

Ado-trastuzumab emtansine

Ado-trastuzumab emtansine (T-DM1) is an antibody-drug conjugate that incorporates the HER2-targeted antitumor properties of trastuzumab with the cytotoxic activity of the microtubule-inhibitory agent DM1. T-DM1 allows specific intracellular drug delivery to HER2-overexpressing cells, potentially improving the therapeutic index and minimizing exposure of normal tissue.

Trastuzumab deruxtecan

Trastuzumab deruxtecan is an antibody-drug conjugate that combines trastuzumab with a topoisomerase inhibitor. A phase I study demonstrated antitumor activity in patients with advanced HER2-positive breast cancer who received the drug conjugate

Tyrosine kinase inhibitor therapy

There are currently three FDA-approved tyrosine kinase inhibitors for metastatic HER2-positive breast cancer.

Tucatinib

Tucatinib is an oral tyrosine kinase inhibitor highly selective for the kinase domain of HER2 that minimally inhibits the epidermal growth factor receptor. A phase Ib trial in pretreated patients demonstrated activity when tucatinib was combined with trastuzumab and capecitabine.

Neratinib

Neratinib is an irreversible pan-HER tyrosine kinase inhibitor (HER1, HER2, and HER4), which is approved in combination with capecitabine for the treatment of patients with advanced or metastatic HER2-positive breast cancer after two or more prior anti–HER2-based regimens in the metastatic set.

Lapatinib

Lapatinib is an orally administered tyrosine kinase inhibitor of both HER2/neu and the epidermal growth factor receptor. Lapatinib plus capecitabine has shown activity

in patients who have HER2-positive metastatic breast cancer that progressed after treatment with trastuzumab.

Germline BRCA Mutation

For patients with metastatic breast cancer who carry a germline BRCA mutation, the oral inhibitor of poly (ADP- ribose) polymerase (PARP) has shown activity. BRCA1 and BRCA2 are tumor suppressor genes that encode proteins involved in DNA repair through the homologous recombination repair pathway. PARP plays a critical role in DNA repair and has been studied as therapy for patients with breast cancer who harbor a germline BRCA mutation.

Olaparib

Talazoparib

Chemotherapy

Patients receiving hormone therapy whose tumors have progressed are candidates for cytotoxic chemotherapy. There are no data suggesting that combination therapy results in an OS benefit over single-agent therapy.

Patients with hormone receptor–negative tumors and those with visceral metastases or symptomatic disease are also candidates for cytotoxic agents. Single agents that have shown activity in metastatic breast cancer include the following:

- Anthracyclines.
    - Doxorubicin.
    - Epirubicin.
    - Liposomal doxorubicin.
    - Mitoxantrone.
- Taxanes.
    - Paclitaxel.
    - Docetaxel.
    - Albumin-bound nanoparticle paclitaxel (ABI-007 or Abraxane).
- Alkylating agents.
    - Cyclophosphamide.
- Fluoropyrimidines.
    - Capecitabine.

    - Fluorouracil (5-FU).
- Antimetabolites.
    - Methotrexate.
- Vinca alkaloids.
    - Vinorelbine.
    - Vinblastine.
    - Vincristine.
- Platinum.
    - Carboplatin.
    - Cisplatin.
- Other.
    - Gemcitabine.
    - Mitomycin C.
    - Eribulin mesylate.
    - Ixabepilone.

Combination regimens that have shown activity in metastatic breast cancer include the following:

- AC: Doxorubicin and cyclophosphamide.
- EC: Epirubicin and cyclophosphamide.
- Docetaxel and doxorubicin.
- CAF: Cyclophosphamide, doxorubicin, and 5-FU.[
- CMF: Cyclophosphamide, methotrexate, and 5-FU.
- Doxorubicin and paclitaxel.
- Docetaxel and capecitabine.
- Vinorelbine and epirubicin.
- Capecitabine and ixabepilone.
- Carboplatin and gemcitabine.
- Gemcitabine and paclitaxel.

There are no data suggesting that combination therapy results in an OS benefit over single-agent therapy.

The selection of therapy in individual patients is influenced by the following:

- Rate of disease progression.
- Presence or absence of comorbid medical conditions.
- Physician/patient preference.

Currently, no data support the superiority of any particular regimen. Sequential use of single agents or combinations can be used for patients who relapse with metastatic disease. Combination chemotherapy is often given if there is evidence of rapidly progressive disease or visceral crisis. Combinations of chemotherapy and hormone therapy have not shown an OS advantage over the sequential use of these agents.

Decisions regarding the duration of chemotherapy may consider the following:

- Patient preference and goals of treatment.
- Presence of toxicities from previous therapies.
- Availability of alternative treatment options.

Chemotherapy plus immunotherapy

Sacituzumab govitecan

Cardiac toxic effects with anthracyclines

The potential for anthracycline-induced cardiac toxic effects should be considered in the selection of chemotherapeutic regimens for selected patients. Recognized risk factors for cardiac toxicity include the following:

- Advanced age.
- Previous chest-wall radiation therapy.
- Previous anthracycline exposure.
- Hypertension and known underlying heart disease.
- Diabetes.

The cardioprotective drug dexrazoxane has been shown to decrease the risk of doxorubicin-induced cardiac toxicity in patients in controlled studies. The use of this agent has permitted patients to receive higher cumulative doses of doxorubicin and has allowed patients with cardiac risk factors to receive doxorubicin. The risk of cardiac toxicity may also be reduced by administering doxorubicin as a continuous intravenous infusion. The American Society of Clinical Oncology guidelines suggest the use of dexrazoxane in patients with metastatic cancer who have received a

cumulative dose of doxorubicin of 300 mg/m2 or more when further treatment with an anthracycline is likely to be of benefit. Dexrazoxane has a similar protective effect in patients receiving epirubicin.

Surgery

Surgery may be indicated for select patients. For example, patients may need surgery if the following issues occur:

- Fungating/painful breast lesions (mastectomy).
- Parenchymal brain or vertebral metastases with spinal cord compression.
- Isolated lung metastases.
- Pathologic (or impending) fractures.
- Pleural or pericardial effusions.

Radiation Therapy

Radiation therapy has a major role in the palliation of localized symptomatic metastases.[114] Indications for external-beam radiation therapy include the following:

- Painful bony metastases.
- Unresectable central nervous system metastases (i.e., brain, meninges, and spinal cord).
- Bronchial obstruction.
- Fungating/painful breast or chest wall lesions.
- After surgery for decompression of intracranial or spinal cord metastases.
- After fixation of pathologic fractures.

Strontium chloride Sr 89, a systemically administered radionuclide, can be administered for palliation of diffuse bony metastases.

Bone-Modifying Therapy

The use of bone-modifying therapy to reduce skeletal morbidity in patients with bone metastases should be considered.

Ductal Carcinoma In Situ

Introduction

Ductal carcinoma in situ (DCIS) is a noninvasive condition. DCIS can progress to invasive cancer, but estimates of the probability of this vary widely. Some reports include DCIS in breast cancer statistics. In 2022, DCIS is expected to account for about 15% of all newly diagnosed invasive plus noninvasive breast tumors in the United States. For invasive and noninvasive tumors detected by screening, DCIS accounts for approximately 25% of all cases.

The frequency of a DCIS diagnosis has increased markedly in the United States since the use of screening mammography became widespread. Very few cases of DCIS present as a palpable mass, with more than 90% being diagnosed by mammography alone.

DCIS comprises a heterogeneous group of histopathologic lesions that have been classified into the following subtypes primarily because of architectural pattern:

- Micropapillary.
- Papillary.
- Solid.
- Cribriform.
- Comedo.

Comedo-type DCIS consists of cells that appear cytologically malignant, with the presence of high-grade nuclei, pleomorphism, and abundant central luminal necrosis. Comedo-type DCIS appears to be more aggressive, with a higher probability of associated invasive ductal carcinoma.

Treatment Options for Patients With DCIS

Treatment options for DCIS include the following:

- Breast-conserving surgery or mastectomy plus radiation therapy with or without tamoxifen.
- Total mastectomy with or without tamoxifen.

In the past, the customary treatment for DCIS was mastectomy. The rationale for mastectomy included a 30% incidence of multicentric disease, a 40% prevalence of residual tumor at mastectomy after wide excision alone, and a 25% to 50% incidence of in-breast recurrence after limited surgery for palpable tumor, with 50% of those recurrences being invasive carcinoma. The combined local and distant recurrence rate after mastectomy is 1% to 2%. No randomized comparisons of mastectomy versus breast-conserving surgery plus breast radiation therapy are available.

Because breast-conserving surgery combined with breast radiation therapy is successful for invasive carcinoma, this conservative approach was extended to DCIS. To determine whether breast-conserving surgery plus radiation therapy was a reasonable approach to the management of DCIS, the National Surgical Adjuvant Breast and Bowel Project (NSABP) and the European Organisation for Research and Treatment of Cancer (EORTC) have each completed prospective randomized trials in which women with localized DCIS and negative surgical margins after excisional biopsy were randomly assigned to receive either breast radiation therapy (50 Gy) or no further therapy.

The decision to prescribe endocrine therapy after a diagnosis of DCIS often involves a discussion with the patient about the potential benefits and side effects of each agent.

1.3. COLORECTAL CANCER

COLON CANCER

Estimated new cases and deaths from rectal and colon cancer in the United States in 2022:

- New cases of colon cancer: 106,180.
- New cases of rectal cancer: 44,850.
- Deaths: 52,580 (rectal and colon cancers combined).

Colorectal cancer affects men and women almost equally. Among all racial groups in the United States, Black individuals have the highest sporadic colorectal cancer incidence and mortality rates.

Cancer of the colon is a highly treatable and often curable disease when localized to the bowel. Surgery is the primary form of treatment and results in cure in approximately 50% of the patients. Recurrence following surgery is a major problem and is often the ultimate cause of death.

Cellular Classification of Colon Cancer

Histologic types of colon cancer include the following:

- Adenocarcinoma (most colon cancers).
    - Mucinous (colloid) adenocarcinoma.

    - Signet ring adenocarcinoma.
- Scirrhous tumors.
- Neuroendocrine. Tumors with neuroendocrine differentiation typically have a poorer prognosis than pure adenocarcinoma variants.

Stage Information for Colon Cancer

Treatment decisions can be made with reference to the TNM (tumor, node, metastasis) classification rather than to the older Dukes or the Modified Astler-Coller classification schema.

The AJCC and a National Cancer Institute–sponsored panel recommended that at least 12 lymph nodes be examined in patients with colon and rectal cancer to confirm the absence of nodal involvement by tumor. This recommendation takes into consideration that the number of lymph nodes examined is a reflection of the aggressiveness of lymphovascular mesenteric dissection at the time of surgical resection and the pathologic identification of nodes in the specimen. Retrospective studies demonstrated that the number of lymph nodes examined in colon and rectal surgery may be associated with patient outcome.

AJCC Stage Groupings and TNM Definitions

The AJCC has designated staging by TNM classification to define colon cancer. The same classification is used for both clinical and pathologic staging. Tables presenting AJCC TNM stage definitions for colon cancer are available at https://www.cancer.gov/types/colorectal/hp/colon-treatment-pdq#_39.

Treatment Option Overview for Colon Cancer

Table 6. Standard Treatment Options for Stages 0–III Colon Cancer

Stage (TNM Staging Criteria)	**Standard Treatment Options**
Stage 0 Colon Cancer	Surgery
Stage I Colon Cancer	Surgery
Stage II Colon Cancer	Surgery
Stage III Colon Cancer	Surgery Adjuvant chemotherapy

Table 7. Treatment Options for Stage IV and Recurrent Colon Cancer

Stage (TNM Staging Criteria)	Treatment Options
Treatment of Liver Metastasis	Surgery
	Neoadjuvant chemotherapy
	Local ablation
	Adjuvant chemotherapy
	Intra-arterial chemotherapy
Treatment of Stage IV and Recurrent Colon Cancer	Surgery
	Systemic therapy
	Immunotherapy

Primary Surgical Therapy

Standard treatment for patients with colon cancer has been open surgical resection of the primary and regional lymph nodes for localized disease.

Surgery is curative in 25% to 40% of highly selected patients who develop resectable metastases in the liver and lung. Improved surgical techniques and advances in preoperative imaging have allowed for better patient selection for resection.

Adjuvant Chemotherapy

The potential value of adjuvant chemotherapy for patients with stage II colon cancer is controversial. Pooled analyses and meta-analyses have suggested a 2% to 4% improvement in OS for patients treated with adjuvant fluorouracil (5-FU)–based therapy compared with observation.

Before 2000, 5-FU was the only useful cytotoxic chemotherapy in the adjuvant setting for patients with stage III colon cancer. Since 2000, capecitabine has been established as an equivalent alternative to 5-FU and leucovorin (5-FU/LV). The addition of oxaliplatin to 5-FU/LV has been shown to improve OS compared with 5-FU/LV alone.

Chemotherapy regimens

Table 8 describes the chemotherapy regimens used to treat colon cancer.

Table 8. Drug Combinations Used to Treat Colon Cancer

Regimen Name	Drug Combination	Dose
AIO or German AIO	Folic acid, 5-FU, and irinotecan	Irinotecan (100 mg/m^2) and LV (500 mg/m^2) administered as 2-hour infusions on d 1, followed by 5-FU (2,000 mg/m^2) IV bolus administered via ambulatory pump weekly over 24 h, 4 times a y (52 wk).
CAPOX	Capecitabine and oxaliplatin	Capecitabine (1,000 mg/m^2) bid on d 1–14, plus oxaliplatin (70 mg/m^2) on d 1 and 8 every 3 wk.
Douillard	Folic acid, 5-FU, and irinotecan	Irinotecan (180 mg/m^2) administered as a 2-h infusion on d 1, LV (200 mg/m^2) administered as a 2-h infusion on d 1 and 2, followed by a loading dose of 5-FU (400 mg/m^2) IV bolus, then 5-FU (600 mg/m^2) administered via ambulatory pump over 22 h every 2 wk on d 1 and 2.
FOLFIRI	LV, 5-FU, and irinotecan	Irinotecan (180 mg/m^2) and LV (400 mg/m^2) administered as 2-h infusions on d 1, followed by a loading dose of 5-FU (400 mg/m^2) IV bolus administered on d 1, then 5-FU (2,400–3,000 mg/m^2) administered via ambulatory pump over 46 h every 2 wk.
FOLFOX-4	Oxaliplatin, LV, and 5-FU	Oxaliplatin (85 mg/m^2) administered as a 2-h infusion on d 1, LV (200 mg/m^2) administered as a 2-h infusion on d 1 and 2, followed by a loading dose of 5-FU (400 mg/m^2) IV bolus, then 5-FU (600 mg/m^2) administered via ambulatory pump over 22 h every 2 wk on d 1 and 2.
FOLFOX-6	Oxaliplatin, LV, and 5-FU	Oxaliplatin (85–100 mg/m^2) and LV (400 mg/m^2) administered as 2-h infusions on d 1, followed by a loading dose of 5-FU (400 mg/m^2) IV bolus on d 1, then 5-FU (2,400–3,000 mg/m^2) administered via ambulatory

Regimen Name	Drug Combination	Dose
		pump over 46 h every 2 wk.
FOLFOXIRI	Irinotecan, oxaliplatin, LV, 5-FU	Irinotecan (165 mg/m^2) administered as a 60-min infusion, then concomitant infusion of oxaliplatin (85 mg/m^2) and LV (200 mg/m^2) over 120 min, followed by 5-FU (3,200 mg/m^2) administered as a 48-h continuous infusion.
FUFOX	5-FU, LV, and oxaliplatin	Oxaliplatin (50 mg/m^2) plus LV (500 mg/m2) plus 5-FU (2,000 mg/m2) administered as a 22-h continuous infusion on d 1, 8, 22, and 29 every 36 d.
FUOX	5-FU plus oxaliplatin	5-FU (2,250 mg/m^2) administered as a continuous infusion over 48 h on d 1, 8, 15, 22, 29, and 36 plus oxaliplatin (85 mg/m^2) on d 1, 15, and 29 every 6 wk.
IFL (or Saltz)	Irinotecan, 5-FU, and LV	Irinotecan (125 mg/m^2) plus 5-FU (500 mg/m^2) IV bolus and LV (20 mg/m^2) IV bolus administered weekly for 4 out of 6 wk.
XELOX	Capecitabine plus oxaliplatin	Oral capecitabine (1,000 mg/m^2) administered bid for 14 d plus oxaliplatin (130 mg/m^2) on d 1 every 3 wk.
5-FU = fluorouracil; AIO = Arbeitsgemeinschaft Internistische Onkologie; bid = twice a day; IV = intravenous; LV = leucovorin.		

Adjuvant Radiation Therapy

While combined modality therapy with chemotherapy and radiation therapy has a significant role in the management of patients with rectal cancer (below the peritoneal reflection), the role of adjuvant radiation therapy for patients with colon cancer (above the peritoneal reflection) is not well defined. Patterns-of-care analyses and single-institution retrospective reviews suggest a role for radiation therapy in certain high-risk subsets of colon cancer patients (e.g., T4, tumor location in immobile sites, local perforation, obstruction, and residual disease postresection).

Adjuvant radiation therapy has no current standard role in the management of patients with colon cancer following curative resection, although it may have a role for patients with residual disease.

Stage 0 Colon Cancer Treatment

Stage 0 colon cancer is the most superficial of all the lesions and is limited to the mucosa without invasion of the lamina propria. Because of its superficial nature, the surgical procedure may be limited.

Standard Treatment Options for Stage 0 Colon Cancer

Surgery

Standard treatment options for stage 0 colon cancer include the following:

- Local excision or simple polypectomy with clear margins.
- Colon resection for larger lesions not amenable to local excision.

Stage I Colon Cancer Treatment

Because of its localized nature, stage I colon cancer has a high cure rate.

Standard Treatment Options for Stage I Colon Cancer

Surgery

Standard treatment options for stage I colon cancer include the following:

- Wide surgical resection and anastomosis.

Stage II Colon Cancer Treatment

Standard Treatment Options for Stage II Colon Cancer

Surgery

Standard treatment options for stage II colon cancer include the following:

- Wide surgical resection and anastomosis.

Treatment Options Under Clinical Evaluation

Adjuvant chemotherapy

The potential value of adjuvant chemotherapy for patients with stage II colon cancer remains controversial. Although subgroups of patients with stage II colon cancer may be at higher-than-average risk for recurrence (including those with anatomic features such as tumor adherence to adjacent structures, perforation, and complete obstruction), evidence is inconsistent that adjuvant fluorouracil (5-FU)–based chemotherapy is associated with an improved OS compared with surgery alone.

Features in patients with stage II colon cancer that are associated with an increased risk of recurrence include the following:

- Inadequate lymph node sampling.
- T4 disease.
- Involvement of the visceral peritoneum.
- A poorly differentiated histology.

The decision to use adjuvant chemotherapy for patients with stage II colon cancer is complicated and requires thoughtful consideration by both patients and their physicians. Adjuvant therapy is not indicated for most patients unless they are entered into a clinical trial.

Stage III Colon Cancer Treatment

Stage III colon cancer denotes lymph node involvement. Studies have indicated that the number of lymph nodes involved affects prognosis; patients with one to three involved nodes have a significantly better survival than those with four or more involved nodes.

Standard Treatment Options for Stage III Colon Cancer

Standard treatment options for stage III colon cancer include the following:

- Surgery.
- Adjuvant chemotherapy.

Surgery

Surgery for stage III colon cancer is wide surgical resection and anastomosis.

Adjuvant chemotherapy

Chemotherapy regimens before 2000

Before 2000, fluorouracil (5-FU) was the only useful cytotoxic chemotherapy in the adjuvant setting for patients with stage III colon cancer. Many of the early randomized studies of 5-FU in the adjuvant setting failed to show a significant improvement in survival for patients.[6-9] These trials employed 5-FU alone or 5-FU/semustine.

Chemotherapy regimens after 2000

Capecitabine

Capecitabine is an oral fluoropyrimidine that undergoes a three-step enzymatic conversion to 5-FU with the last step occurring in the tumor cell. For patients with metastatic colon cancer, two studies have demonstrated the equivalence of capecitabine to 5-FU/LV. For patients with stage III colon cancer, capecitabine provides equivalent outcome to intravenous 5-FU/LV.

Oxaliplatin

Oxaliplatin has significant activity when combined with 5-FU/LV in patients with metastatic colorectal cancer.

Most physicians have adopted FOLFOX as the standard of care because of toxicity concerns with weekly FLOX. FOLFOX has become the reference standard for the next generation of clinical trials for patients with stage III colon cancer.

Capecitabine and oxaliplatin

The combination of capecitabine and oxaliplatin (CAPOX) is an accepted standard therapy in patients with metastatic colorectal cancer.

Oxaliplatin length of therapy

Given the high rate of disabling neuropathy, the duration of oxaliplatin adjuvant therapy became an open question. CAPOX appears to be slightly more active than FOLFOX in the adjuvant setting.

Treatment Options Under Clinical Evaluation

Eligible patients can be considered for entry into carefully controlled clinical trials comparing various postoperative chemotherapy regimens.

Stage IV and Recurrent Colon Cancer Treatment

Stage IV colon cancer denotes distant metastatic disease. Treatment of recurrent colon cancer depends on the sites of recurrent disease demonstrable by physical examination and/or radiographic studies. In addition to standard radiographic procedures, radioimmunoscintography may add clinical information that may affect management.[1] Such approaches have not led to improvements in long-term outcome measures such as survival.

Treatment Options for Stage IV and Recurrent Colon Cancer

Treatment options for stage IV and recurrent colon cancer include the following:

- Surgical resection of locally recurrent cancer.
- Surgical resection and anastomosis or bypass of obstructing or bleeding primary lesions in selected metastatic cases.
- Resection of liver metastases in selected metastatic patients (5-year cure rate for resection of solitary or combination metastases exceeds 20%) or ablation in selected patients.[2-11]
- Resection of isolated pulmonary or ovarian metastases in selected patients.[12]
- Palliative radiation therapy.
- Palliative chemotherapy.
- Targeted therapy.
- Clinical trials evaluating new drugs and biological therapy.
- Clinical trials comparing various chemotherapy regimens or biological therapy, alone or in combination.

Treatment of Liver Metastasis

Approximately 50% of colon cancer patients will be diagnosed with hepatic metastases, either at the time of initial presentation or because of disease recurrence. Although only a small proportion of patients with hepatic metastases are candidates for surgical

resection, advances in tumor ablation techniques and in both regional and systemic chemotherapy administration provide for several treatment options. These include the following:

- Surgery.
- Neoadjuvant chemotherapy.
- Local ablation.
- Adjuvant chemotherapy.
- Intra-arterial chemotherapy.

Surgery

Hepatic metastasis may be considered to be resectable based on the following factors:

- Limited number of lesions.
- Intrahepatic locations of lesions.
- Lack of major vascular involvement.
- Absent or limited extrahepatic disease.
- Enough functional hepatic reserve.

For patients with hepatic metastasis that is considered to be resectable, a negative margin resection resulted in 5-year survival rates of 25% to 40% in mostly nonrandomized studies, such as the North Central Cancer Treatment Group trial (NCCTG-934653 [NCT00002575]). Improved surgical techniques and advances in preoperative imaging have improved patient selection for resection. In addition, multiple studies with multiagent chemotherapy have demonstrated that patients with metastatic disease isolated to the liver, which historically would be considered unresectable, can occasionally be made resectable after the administration of chemotherapy.

Neoadjuvant chemotherapy for unresectable liver metastases

Patients with hepatic metastases that are deemed unresectable will occasionally become candidates for resection if they have a good response to chemotherapy. These patients have 5-year survival rates similar to patients who initially had resectable disease. There is no consensus on the best regimen to use to convert unresectable isolated liver metastases to resectable liver metastases.

Local ablation

Radiofrequency ablation has emerged as a safe technique (2% major morbidity and <1% mortality rate) that may provide for long-term tumor control. Radiofrequency ablation and cryosurgical ablation remain options for patients with tumors that cannot be resected and for patients who are not candidates for liver resection.

Other local ablative techniques that have been used to manage liver metastases include embolization and interstitial radiation therapy. Patients with limited pulmonary metastases, and patients with both pulmonary and hepatic metastases, may also be considered for surgical resection, with 5-year survival possible in highly-selected patients.

Adjuvant or neoadjuvant chemotherapy for resectable liver metastases

The role of adjuvant chemotherapy after potentially curative resection of liver metastases is uncertain. There is no level 1 evidence to demonstrate that perioperative or postoperative chemotherapy improves OS for patients undergoing resection of liver metastases. Nevertheless, on the basis of post hoc subset analyses of the EORTC study, some physicians feel perioperative or postoperative therapy is reasonable in this setting.

Intra-arterial chemotherapy after liver resection

Hepatic intra-arterial chemotherapy with floxuridine for liver metastases has produced higher overall response rates but no consistent improvement in survival when compared with systemic chemotherapy. A meta- analysis of the randomized studies, which were all done in the era when only fluoropyrimidines were available for systemic therapy, did not demonstrate a survival advantage.

Further studies are required to evaluate this treatment approach and to determine whether more effective systemic combination chemotherapy alone may provide similar results compared with hepatic intra-arterial therapy plus systemic treatment.

Several studies show increased local toxic effects with hepatic infusional therapy, including liver function abnormalities and fatal biliary sclerosis.

Treatment of Stage IV and Recurrent Colon Cancer

- Surgery.
- Systemic therapy.
- Immunotherapy.

Surgery

Treatment of patients with recurrent or advanced colon cancer depends on the location of the disease. For patients with locally recurrent and/or liver-only and/or lung-only metastatic disease, surgical resection, if feasible, is the only potentially curative treatment.

Systemic therapy

The following are U.S. Food and Drug Administration (FDA)-approved drugs that are used alone and in combination with other drugs for patients with metastatic colorectal cancer:

- 5-FU.
- Capecitabine.
- Irinotecan.
- Oxaliplatin.
- Bevacizumab.
- FOLFOXIRI (irinotecan, oxaliplatin, LV, and 5-FU).
- Cetuximab.
- Aflibercept.
- Ramucirumab.
- Panitumumab.
- Anti-epidermal growth factor receptor (EGFR) antibody versus anti-vascular endothelial growth factor (VEGF) antibody with first-line chemotherapy.
- Regorafenib.
- TAS-102.
- Encorafenib with cetuximab for patients with BRAF V600E mutations.

5-FU

When 5-FU was the only active chemotherapy drug, trials in patients with locally advanced, unresectable, or metastatic disease demonstrated partial responses and prolongation of the time-to-progression (TTP) of disease, and improved survival and quality of life for patients who received chemotherapy versus best supportive care. Several trials have analyzed the activity and toxic effects of various 5-FU/LV regimens

using different doses and administration schedules and showed essentially equivalent results with a median survival time in the 12-month range.

Capecitabine

Before the advent of multiagent chemotherapy, two randomized studies demonstrated that capecitabine was associated with equivalent efficacy when compared with the Mayo Clinic regimen of 5-FU/LV.

Irinotecan

Three randomized studies demonstrated improved response rates, PFS, and OS when irinotecan or oxaliplatin was combined with 5-FU/LV. Since the publication of these studies, the use of either FOLFOX or FOLFIRI is considered acceptable for first-line treatment of patients with metastatic colorectal cancer. When using an irinotecan-based regimen as first-line treatment of metastatic colorectal cancer, FOLFIRI is preferred.

Oxaliplatin

Randomized phase III trials have addressed the equivalence of substituting capecitabine for infusional 5-FU. Two phase III studies have evaluated 5-FU/oxaliplatin (FUOX) versus capecitabine/oxaliplatin (CAPOX). When using an oxaliplatin-based regimen as first-line treatment of metastatic colorectal cancer, a CAPOX regimen is not inferior to a FUOX regimen.

Before the availability of cetuximab, panitumumab, bevacizumab, and aflibercept as second-line therapy, second-line chemotherapy with irinotecan in patients treated with 5-FU/LV as first-line therapy demonstrated improved OS when compared with either infusional 5-FU or supportive care.

Bevacizumab

Bevacizumab is a partially humanized monoclonal antibody that binds to VEGF. Bevacizumab can reasonably be added to either FOLFIRI or FOLFOX for patients undergoing first-line treatment of metastatic colorectal cancer.

FOLFOXIRI

Cetuximab

Cetuximab is a partially humanized monoclonal antibody against EGFR. Because cetuximab affects tyrosine kinase signaling at the surface of the cell membrane, tumors with mutations causing activation of the pathway downstream of the EGFR, such as KRAS mutations, are not sensitive to its effects. The addition of cetuximab to multiagent chemotherapy improves survival in patients with colon cancers that lack a KRAS mutation (i.e., KRAS wild type). Importantly, patients with mutant KRAS tumors may experience worse outcome when cetuximab is added to multiagent chemotherapy regimens containing bevacizumab.

Aflibercept

Aflibercept is a novel anti-VEGF molecule and has been evaluated as a component of second-line therapy in patients with metastatic colorectal cancer. On the basis of these results, the use of aflibercept/FOLFIRI is an acceptable second-line regimen for patients previously treated with FOLFOX-based chemotherapy. Whether to continue bevacizumab or initiate aflibercept in second-line therapy has not been addressed yet in any clinical trial, and there are no data available.

Ramucirumab

Ramucirumab is a fully humanized monoclonal antibody that binds to vascular endothelial growth factor receptor-2. On the basis of these data, FOLFIRI/ramucirumab is an acceptable second-line regimen for patients previously treated with FOLFOX/bevacizumab. Whether to continue bevacizumab in second-line chemotherapy or use ramucirumab in second-line chemotherapy has not yet been addressed in a clinical trial.

Panitumumab

Panitumumab is a fully humanized antibody against the EGFR. The FDA approved panitumumab for use in patients with metastatic colorectal cancer refractory to chemotherapy. In clinical trials, panitumumab demonstrated efficacy as a single agent or in combination therapy, which was consistent with the effects on PFS and OS with cetuximab. There appears to be a consistent class effect.

Anti-EGFR antibody versus anti-VEGF antibody with first-line chemotherapy

In the management of patients with stage IV colorectal cancer, it is unknown whether patients with KRAS wild- type cancer should receive an anti-EGFR antibody with chemotherapy or an anti-VEGF antibody with chemotherapy.

Regorafenib

Regorafenib is an inhibitor of multiple tyrosine kinase pathways including VEGF. In September 2012, the FDA granted approval for the use of regorafenib in patients who had progressed on previous therapy.

TAS-102

TAS-102 (Lonsurf) is an orally administered combination of a thymidine-based nucleic acid analog, trifluridine, and a thymidine phosphorylase inhibitor, tipiracil hydrochloride. Trifluridine, in its triphosphate form, inhibits thymidylate synthase; therefore, trifluridine, in this form, has an anti-tumor effect. Tipiracil hydrochloride is a potent inhibitor of thymidine phosphorylase, which actively degrades trifluridine. The combination of trifluridine and tipiracil allows for adequate plasma levels of trifluridine.

Encorafenib with cetuximab in patients with BRAF V600E mutations

BRAF V600E mutations occur in about 10% of metastatic colorectal cancers and are an indicator of poor prognosis. Unlike in melanoma, BRAF inhibitor monotherapy has not shown a benefit in colorectal cancer, and multiple studies have evaluated concurrent targeting of the EGFR-MAPK pathway.

Immunotherapy

Approximately 4% of patients with stage IV colorectal cancer have tumors that are mismatch repair deficient (dMMR) or microsatellite unstable/microsatellite instability-high (MSI-H). The MSI-H phenotype is associated with germline defects in the MLH1, MSH2, MSH6, and PMS2 genes and is the primary phenotype observed in tumors from patients with hereditary nonpolyposis colorectal cancer (HNPCC) or Lynch syndrome. Patients can also have the MSI-H phenotype because one of these genes was silenced via DNA methylation. Testing for microsatellite instability can be done with molecular genetic tests, which look for microsatellite instability in the tumor tissue, or with immunohistochemistry, which looks for the loss of mismatch repair proteins. MSI-H status has historically been prognostic of increased survival for patients with earlier-stage disease and since 2015, has also been found to predict tumor response to checkpoint inhibition.

The FDA approved pembrolizumab for use in patients with treatment-naïve, metastatic, dMMR/MSI-H colorectal cancer in June 2020. Studies regarding first-line treatment with dual checkpoint inhibitors are ongoing. The FDA approved the anti-programmed cell death protein 1 (PD-1) antibodies pembrolizumab in May 2017 and nivolumab in July 2017 for the treatment of patients with microsatellite-unstable tumors who had

previously received 5-FU, oxaliplatin, and irinotecan-based therapy. In July 2018, the FDA granted accelerated approval for the combination of nivolumab with ipilimumab (a CTLA-4 inhibitor) to treat MSI-H colorectal cancers that progressed on prior 5-FU, oxaliplatin, and irinotecan-based therapies.

First-line immunotherapy

Pembrolizumab monotherapy

Nivolumab and ipilimumab

Second-line immunotherapy

Pembrolizumab monotherapy

Nivolumab monotherapy

Nivolumab and ipilimumab

Treatment Options Under Clinical Evaluation

Treatment options under clinical evaluation for stage IV and recurrent colon cancer include the following:

- Clinical trials evaluating new drugs and biological therapy.
- Clinical trials comparing various chemotherapy regimens or biological therapy, alone or in combination.

RECTAL CANCER

It is difficult to separate epidemiological considerations of rectal cancer from those of colon cancer because studies often consider colon and rectal cancer together (i.e., colorectal cancer).

Cellular Classification and Pathology of Rectal Cancer

Adenocarcinomas account for the vast majority of rectal tumors in the United States. Other histologic types account for an estimated 2% to 5% of colorectal tumors.

The World Health Organization classification of tumors of the colon and rectum includes the following:

Epithelial Tumors

Adenoma

- Tubular.
- Villous.
- Tubulovillous.
- Serrated.

Carcinoma

- Adenocarcinoma.
- Mucinous adenocarcinoma.
- Signet-ring cell carcinoma.
- Small cell carcinoma.
- Adenosquamous carcinoma.
- Medullary carcinoma.
- Undifferentiated carcinoma.

Carcinoid (well-differentiated neuroendocrine neoplasm)

- Enterochromaffn-cell, serotonin-producing neoplasm.
- L-cell, glucagon-like peptide and pancreatic polypeptide/peptide YY–producing tumor.
- Others.

Intraepithelial neoplasia (dysplasia) associated with chronic inflammatory diseases

- Low-grade glandular intraepithelial neoplasia.
- High-grade glandular intraepithelial neoplasia.

Mixed carcinoma-adenocarcinoma

- Others.

Nonepithelial Tumors

- Lipoma.
- Leiomyoma.

- Gastrointestinal stromal tumor.
- Leiomyosarcoma.
- Angiosarcoma.
- Kaposi sarcoma.
- Melanoma.
- Others.

Malignant lymphomas

- Marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue type.
- Mantle cell lymphoma.
- Diffuse large B-cell lymphoma.
- Burkitt lymphoma.
- Burkitt-like/atypical Burkitt lymphoma.

Stage Information for Rectal Cancer

Accurate staging provides crucial information about the location and size of the primary tumor in the rectum, and, if present, the size, number, and location of any metastases. Accurate initial staging can influence therapy by helping to determine the type of surgical intervention and the choice of neoadjuvant therapy to maximize the likelihood of resection with clear margins. In primary rectal cancer, pelvic imaging helps determine the following:

- The depth of tumor invasion.
- The distance from the sphincter complex.
- The potential for achieving negative circumferential (radial) margins.
- The involvement of locoregional lymph nodes or adjacent organs.

Staging Evaluation

Clinical evaluation and staging procedures may include the following:

- Digital-rectal examination (DRE): DRE and/or rectovaginal exam and rigid proctoscopy to determine if sphincter-saving surgery is possible.
- Colonoscopy: Complete colonoscopy to rule out cancers elsewhere in the bowel.
- Computed tomography (CT): Pan-body CT scan to rule out metastatic disease.
- Magnetic resonance imaging (MRI): MRI of the abdomen and pelvis to determine the depth of penetration and the potential for achieving negative circumferential (radial) margins and to identify locoregional nodal metastases and distant metastatic disease. MRI may be particularly helpful in determining sacral involvement in local recurrence.

- Endorectal ultrasound: Endorectal ultrasound with a rigid probe or a flexible scope for stenotic lesions to determine the depth of penetration and identify locoregional nodal metastases.
- Positron emission tomography (PET): PET to image distant metastatic disease.
- Carcinoembryonic antigen (CEA): Measurement of the serum CEA level for prognostic assessment and the determination of response to therapy.

In patients with rectal cancer, the circumferential resection margin is an important pathological staging parameter. Measured in millimeters, it is defined as the retroperitoneal or peritoneal adventitial soft-tissue margin closest to the deepest penetration of tumor.

AJCC Stage Groupings and TNM Definitions

The AJCC has designated staging by TNM (tumor, node, metastasis) classification to define rectal cancer. The same classification is used for both clinical and pathologic staging. Treatment decisions are made with reference to the TNM classification system, rather than the older Dukes or Modified Astler-Coller classification schema.

Cancers staged using this staging system include adenocarcinomas, high-grade neuroendocrine carcinomas, and squamous carcinomas of the colon and rectum. Cancers not staged using this staging system include these histopathologic types of cancer: appendiceal carcinomas, anal carcinomas, well-differentiated neuroendocrine tumors (carcinoids).

Lymph node status

The AJCC and a National Cancer Institute-sponsored panel suggested that at least 10 to 14 lymph nodes be examined in radical colon and rectum resections in patients who did not receive neoadjuvant therapy. In cases in which a tumor is resected for palliation or in patients who have received preoperative radiation therapy, fewer lymph nodes may be present. This takes into consideration that the number of lymph nodes examined is a reflection of both the aggressiveness of lymphovascular mesenteric dissection at the time of surgical resection and the pathologic identification of nodes in the specimen.

Retrospective studies, such as Intergroup trial INT-0089 (NCT00201331), have demonstrated that the number of lymph nodes examined during colon and rectal surgery may be associated with patient outcome.

A new tumor-metastasis staging strategy for node-positive rectal cancer has been proposed.

Tables presenting AJCC TNM stage definitions for colon cancer are available at https://www.cancer.gov/types/colorectal/hp/rectal-treatment-pdq#_19

Treatment Option Overview for Rectal Cancer

The management of rectal cancer varies somewhat from that of colon cancer because of the increased risk of local recurrence and a poorer overall prognosis. Differences include surgical technique, the use of radiation therapy, and the method of chemotherapy administration. In addition to determining the intent of rectal cancer surgery (i.e., curative or palliative), it is important to consider therapeutic issues related to the maintenance or restoration of normal anal sphincter, genitourinary function, and sexual function.

The approach to the management of rectal cancer is multimodal and involves a multidisciplinary team of cancer specialists with expertise in gastroenterology, medical oncology, surgical oncology, radiation oncology, and radiology.

Table 6. Standard Treatment Options for Stages 0–III Rectal Cancer

Stage (TNM Definitions)	Standard Treatment Options
Stage 0 Rectal Cancer	Polypectomy or surgery
Stage I Rectal Cancer	Surgery with or without chemoradiation therapy
Stages II and III Rectal Cancer	Surgery
	Preoperative chemoradiation therapy
	Short-course preoperative radiation therapy followed by surgery and chemotherapy
	Postoperative chemoradiation therapy
	Primary chemoradiation therapy followed by intensive surveillance for complete clinical

	responders

Table 7. Treatment Options for Stage IV and Recurrent Rectal Cancer

Stage (TNM Definitions)	Treatment Options
Stage IV and Recurrent Rectal Cancer	Surgery with or without chemotherapy or radiation therapy
	Systemic therapy
	Second-line chemotherapy
	Immunotherapy
	Palliative therapy
Liver Metastases	Surgery
	Neoadjuvant chemotherapy
	Local ablation
	Adjuvant chemotherapy
	Intra-arterial chemotherapy after liver resection

Primary Surgical Therapy

The primary treatment for patients with rectal cancer is surgical resection of the primary tumor. The surgical approach to treatment varies according to the following:

- Tumor location.
- Stage of disease.
- Presence or absence of high-risk features (i.e., positive margins, lymphovascular invasion, perineural invasion, and poorly differentiated histology).

Types of surgical resection include the following:

- Polypectomy for select T1 cancers.
- Transanal local excision and transanal endoscopic microsurgery for select clinically staged T1/T2 N0 rectal cancers.

- Total mesorectal excision with autonomic nerve preservation techniques via low-anterior resection.
- Total mesorectal excision via abdominoperineal resection for patients who are not candidates for sphincter- preservation, leaving patients with a permanent end-colostomy.

Polypectomy alone may be used in certain instances (T1) in which polyps with invasive cancer can be completely resected with clear margins and have favorable histologic features.

Local excision of clinical T1 tumors is an acceptable surgical technique for appropriately selected patients. For all other tumors, a mesorectal excision is the treatment of choice. Very select patients with T2 tumors may be candidates for local excision. Local failure rates in the range of 4% to 8% after rectal resection with appropriate mesorectal excision (total mesorectal excision for low/middle rectal tumors and mesorectal excision at least 5 cm below the tumor for high rectal tumors) have been reported.

For patients with advanced cancers of the mid- to upper rectum, low-anterior resection followed by the creation of a colorectal anastomosis may be the treatment of choice. For locally advanced rectal cancers for which radical resection is indicated, however, total mesorectal excision with autonomic nerve preservation techniques via low- anterior resection is preferable to abdominoperineal resection.

The low incidence of local relapse after meticulous mesorectal excision has led some investigators to question the routine use of adjuvant radiation therapy. Because of an increased tendency for first failure in locoregional sites only, the impact of perioperative radiation therapy is greater in rectal cancer than in colon cancer.

Chemoradiation Therapy

Preoperative chemoradiation therapy

Neoadjuvant therapy for rectal cancer, using preoperative chemoradiation therapy, is the preferred treatment option for patients with stages II and III disease. However, postoperative chemoradiation therapy for patients with stage II or III rectal cancer remains an acceptable option.

Multiple phase II and III studies examined the benefits of preoperative chemoradiation therapy, which include the following:

- Tumor regression and downstaging of the tumor.
- Improved tumor resectability.
- Higher rate of local control.
- Improved toxicity profile of chemoradiation therapy.
- Higher rate of sphincter preservation.

Complete pathologic response rates of 10% to 25% may be achieved with preoperative chemoradiation therapy. However, preoperative radiation therapy is associated with increased complications compared with surgery alone; some patients with cancers at a lower risk of local recurrence might be adequately treated with surgery and adjuvant chemotherapy.

Postoperative chemoradiation therapy

Preoperative chemoradiation therapy is the current standard of care for stages II and III rectal cancer.

Fluorouracil (5-FU)

Acceptable postoperative chemoradiation therapy for patients with stage II or III rectal cancer not enrolled in clinical trials includes continuous-infusion 5-FU during 45 Gy to 55 Gy pelvic radiation and four cycles of adjuvant maintenance chemotherapy with bolus 5-FU with or without modulation with leucovorin (LV).

Chemotherapy regimens

Table 8 describes the chemotherapy regimens used to treat rectal cancer.

Table 8. Drug Combinations Used to Treat Rectal Cancer

Regimen Name	Drug Combination	Dose
AIO or German AIO	Folic acid, also known as LV, 5-FU, and irinotecan	Irinotecan (100 mg/m^2) and LV (500 mg/m^2) administered as 2-h infusions on d 1, followed by 5-FU (2,000 mg/m^2) IV bolus administered via ambulatory pump weekly over 24 h, 4 times a y (52 wk).
CAPOX	Capecitabine and	Capecitabine (1,000 mg/m^2) bid on d 1–14, plus

Regimen Name	Drug Combination	Dose
	oxaliplatin	oxaliplatin (70 mg/m^2) on d 1 and 8 every 3 wk.
Douillard	Folic acid, 5-FU, and irinotecan	Irinotecan (180 mg/m^2) administered as a 2-h infusion on d 1, LV (200 mg/m^2) administered as a 2-h infusion on d 1 and 2, followed by a loading dose of 5-FU (400 mg/m^2) IV bolus, then 5-FU (600 mg/m^2) administered via ambulatory pump over 22 h every 2 wk on d 1 and 2.
FOLFIRI	LV, 5-FU, and irinotecan	Irinotecan (180 mg/m^2) and LV (400 mg/m^2) administered as 2-h infusions on d 1, followed by a loading dose of 5-FU (400 mg/m^2) IV bolus administered on d 1, then 5-FU (2,400–3,000 mg/m^2) administered via ambulatory pump over 46 h every 2 wk.
FOLFOX4	Oxaliplatin, LV, and 5-FU	Oxaliplatin (85 mg/m^2) administered as a 2-h infusion on day 1, LV (200 mg/m^2) administered as a 2-h infusion on d 1 and 2, followed by a loading dose of 5-FU (400 mg/m^2) IV bolus, then 5-FU (600 mg/m^2) administered via ambulatory pump over 22 h every 2 wk on d 1 and 2.
FOLFOX6	Oxaliplatin, LV, and 5-FU	Oxaliplatin (85–100 mg/m^2) and LV (400 mg/m^2) administered as 2-h infusions on d 1, followed by a loading dose of 5-FU (400 mg/m^2) IV bolus on d 1, then 5-FU (2,400– 3,000 mg/m^2) administered via ambulatory pump over 46 h every 2 wk.
FOLFOXIRI	Irinotecan, oxaliplatin, LV, 5-FU	Irinotecan (165 mg/m^2) administered as a 60-min infusion, then concomitant infusion of oxaliplatin (85 mg/m^2) and LV (200 mg/m^2) over 120 min, followed by 5-FU (3,200 mg/m^2) administered as a 48-h continuous infusion.
FUFOX	5-FU, LV, and oxaliplatin	Oxaliplatin (50 mg/m^2) plus LV (500 mg/m2) plus 5-FU (2,000 mg/m2) administered as a 22-h continuous infusion on d 1, 8, 22, and 29 every

Regimen Name	Drug Combination	Dose
		36 d.
FUOX	5-FU plus oxaliplatin	5-FU (2,250 mg/m^2) administered as a continuous infusion over 48 h on d 1, 8, 15, 22, 29, and 36 plus oxaliplatin (85 mg/m^2) on d 1, 15, and 29 every 6 wk.
IFL (or Saltz)	Irinotecan, 5-FU, and LV	Irinotecan (125 mg/m^2) plus 5-FU (500 mg/m^2) IV bolus and LV (20 mg/m^2) IV bolus administered weekly for 4 out of 6 wk.
XELOX	Capecitabine plus oxaliplatin	Oral capecitabine (1,000 mg/m^2) administered bid for 14 d plus oxaliplatin (130 mg/m^2) on d 1 every 3 wk.
5-FU = fluorouracil; AIO = Arbeitsgemeinschaft Internistische Onkologie; bid = twice a day; IV = intravenous; LV = leucovorin.		

Treatment toxicity

The acute side effects of pelvic radiation therapy for rectal cancer are mainly the result of gastrointestinal toxicity, are self-limiting, and usually resolve within 4 to 6 weeks of completing treatment.

Of greater concern is the potential for late morbidity after rectal cancer treatment. Patients who undergo aggressive surgical procedures for rectal cancer can have chronic symptoms, particularly if there is impairment of the anal sphincter. Patients treated with radiation therapy appear to have increased chronic bowel dysfunction, anorectal sphincter dysfunction (if the sphincter was surgically preserved), and sexual dysfunction than do patients who undergo surgical resection alone.

An analysis of patients treated with postoperative chemotherapy and radiation therapy suggests that these patients may have more chronic bowel dysfunction than do patients who undergo surgical resection alone. A Cochrane review highlights the risks of increased surgical morbidity as well as late rectal and sexual function in association with radiation therapy.

Improved radiation therapy planning and techniques may minimize these acute and late treatment-related complications. These techniques include the following:

- The use of high-energy radiation machines.
- The use of multiple pelvic radiation fields.
- Prone patient positioning.
- Customized patient molds (belly boards) to exclude as much small bowel as possible from the radiation fields and immobilize patients during treatment.
- Bladder distention during radiation therapy to exclude as much small bowel as possible from the radiation fields.
- Visualization of the small bowel through oral contrast during treatment planning so that when possible, the small bowel can be excluded from the radiation field.
- The use of 3-dimensional or other advanced radiation planning techniques.

In Europe, it is common to deliver preoperative radiation therapy alone in one week (5 Gy × five daily treatments) followed by surgery one week later, rather than the long-course chemoradiation approach used in the United States. One reason for this difference is the concern in the United States for heightened late effects when high radiation doses per fraction are given.

Ongoing clinical trials comparing preoperative and postoperative adjuvant chemoradiation therapy should further clarify the impact of either approach on bowel function and other important quality-of-life issues (e.g., sphincter preservation) in addition to the more conventional endpoints of DFS and OS.

Stage 0 Rectal Cancer Treatment

Standard Treatment Options for Stage 0 Rectal Cancer

Stage 0 rectal cancer or carcinoma in situ is the most superficial of all rectal lesions and is limited to the mucosa without invasion of the lamina propria.

Standard treatment options for stage 0 rectal cancer include the following:

- Polypectomy or surgery.

Polypectomy or surgery

Local excision or simple polypectomy may be indicated for stage 0 rectal cancer tumors. Because of its localized nature at presentation, stage 0 rectal cancer has a high cure rate.

For large lesions not amenable to local excision, full-thickness rectal resection by the transanal or transcoccygeal route may be performed.

Stage I Rectal Cancer Treatment

Standard Treatment Options for Stage I Rectal Cancer

Stage I tumors extend beneath the mucosa into the submucosa (T1) or into, but not through, the bowel muscle wall (T2). Because of its localized nature at presentation, stage I rectal cancer has a high cure rate.

Standard treatment options for stage I rectal cancer include the following:

- Surgery with or without chemoradiation therapy.

Surgery with or without chemoradiation therapy

There are three potential options for surgical resection in stage I rectal cancer:

- Local excision. Local excision is restricted to tumors that are confined to the rectal wall and that do not, on rectal ultrasound or magnetic resonance imaging, involve the full thickness of the rectum (i.e., are not T3 tumors). The ideal candidate for local excision has a T1 tumor with well-to-moderate differentiation that occupies less than one-third of the circumference of the bowel wall. Local excision is associated with a higher risk of local and systemic failure and is applicable only to select patients with T2 tumors. Local transanal or other resection [1,2] with or without perioperative external-beam radiation therapy (EBRT) plus fluorouracil (5-FU) may be indicated.
- Low-anterior resection. Wide surgical resection and anastomosis are options when an adequate low- anterior resection can be performed with sufficient distal rectum to allow a conventional anastomosis or coloanal anastomosis.
- Abdominoperineal resection. Wide surgical resection with abdominoperineal resection is used for lesions too distal to permit low-anterior resection.

Patients with tumors that are pathologically T1 may not need postoperative therapy. Patients with tumors that are T2 or greater have lymph node involvement about 20% of the time. Patients may want to consider additional therapy, such as radiation therapy and chemotherapy, or wide surgical resection of the rectum.[3] Patients with poor histologic features or positive margins after local excision may consider low-anterior resection or

abdominoperineal resection and postoperative treatment as dictated by full surgical staging.

For patients with T1 and T2 tumors, no randomized trials are available to compare local excision with or without postoperative chemoradiation therapy to wide surgical resection (low-anterior resection and abdominoperineal resection).

Stages II and III Rectal Cancer Treatment

Standard Treatment Options for Stages II and III Rectal Cancer

Standard treatment options for stages II and III rectal cancer include the following:

- Surgery.
- Preoperative chemoradiation therapy.
- Short-course preoperative radiation therapy followed by surgery and chemotherapy.
- Postoperative chemoradiation therapy.
- Primary chemoradiation therapy followed by intensive surveillance for complete clinical responders.

Surgery

Total mesorectal excision with either low anterior resection or abdominoperineal resection is usually performed for stages II and III rectal cancer before or after chemoradiation therapy.

Retrospective studies have demonstrated that some patients with pathological T3, N0 disease treated with surgery and no additional therapy have a very low risk of local and systemic recurrence.

Preoperative chemoradiation therapy

Preoperative chemoradiation therapy has become the standard of care for patients with clinically staged T3 or T4 or node-positive disease, based on the results of several studies.

Short-course preoperative radiation therapy followed by surgery and chemotherapy

The use of short-course radiation therapy before surgery has been a standard approach in parts of Europe and Australia.

Postoperative chemoradiation therapy

Progress in the development of postoperative treatment regimens relates to the integration of systemic chemotherapy and radiation therapy, as well as redefining the techniques for both modalities. The efficacy of postoperative radiation therapy and 5-FU-based chemotherapy for stages II and III rectal cancer was established by a series of prospective, randomized clinical trials, including the following:

- Gastrointestinal Tumor Study Group (GITSG-7175).
- Mayo/North Central Cancer Treatment Group (NCCTG-794751).
- National Surgical Adjuvant Breast and Bowel Project (NSABP-R-01).

These studies demonstrated an increase in DFS interval and OS when radiation therapy was combined with chemotherapy after surgical resection. After the publication in 1990 of the results of these trials, experts at a National Cancer Institute-sponsored Consensus Development Conference recommended postoperative combined-modality treatment for patients with stages II and III rectal carcinoma. Since that time, preoperative chemoradiation therapy has become the standard of care, although postoperative chemoradiation therapy is still an acceptable alternative.

Chemotherapy Regimens

Many academic oncologists suggest that LV/5-FU/oxaliplatin (FOLFOX) be considered the standard for adjuvant chemotherapy in rectal cancer. However, there are no data about rectal cancer to support this consideration.

Preoperative oxaliplatin with chemoradiation therapy

Oxaliplatin has also been shown to have radiosensitizing properties in preclinical models. Phase II studies that combined oxaliplatin with fluoropyrimidine-based chemoradiation therapy have reported pathologic complete response rates ranging from 14% to 30%. Data from multiple studies have demonstrated a correlation between rates of pathologic complete response and endpoints including distant metastasis-free survival, DFS, and OS.

There is no current role for off-trial use of concurrent oxaliplatin and radiation therapy in the treatment of patients with rectal cancer.

Postoperative oxaliplatin-containing regimens

On the basis of results of several studies, oxaliplatin as a radiation sensitizer does not appear to add any benefit in terms of primary tumor response, and it has been associated with increased acute treatment-related toxicity. The question of whether oxaliplatin should be added to adjuvant 5-FU/LV for postoperative management of stages II and III rectal cancer is an ongoing debate. There are no randomized phase III studies to support the use of oxaliplatin for the adjuvant treatment of rectal cancer. However, the addition of oxaliplatin to 5-FU/LV for the adjuvant treatment of colon cancer is now considered standard care.

Primary chemoradiation therapy followed by intensive surveillance for complete clinical responders

Since the advent of preoperative chemoradiation therapy in rectal cancer, the standard approach has been to recommend definitive surgical resection by either abdominoperineal resection or laparoscopic-assisted resection. In most series, after long-course chemoradiation therapy, 10% to 20% of patients will have a complete clinical response in which there is no sign of persistent cancer by imaging, rectal exam, or direct visualization during sigmoidoscopy. It was a long-held belief that most patients who did not undergo surgery for personal or medical reasons would experience a local and/or systemic recurrence. However, it became clear that patients with a pathologic complete response to preoperative chemoradiation therapy followed by definitive surgery had a better DFS than did patients who did not have a pathologic clinical response.

Several single-institution studies have challenged this standard of care by demonstrating that most patients with complete clinical response will be cured of rectal cancer without surgery and that many patients who experience a local recurrence can be treated with surgical resection (abdominoperineal resection or laparoscopic-assisted resection) at the time of their recurrence. These institutional series were hampered by their small size and inherent selection bias.

Patients managed by watch and wait underwent a more intensive follow-up protocol consisting of outpatient digital rectal examination; MRI (every 4–6 months in the first 2 years); examination under anesthesia or endoscopy; computed tomography scan of the chest, abdomen, and pelvis; and at least two carcinoembryonic antigen measurements in the first 2 years. The optimal follow-up has not been determined.

For patients who have a complete clinical response to therapy, it is reasonable to consider a watch-and- wait approach with intensive surveillance instead of immediate surgical resection.

Stage IV and Recurrent Rectal Cancer Treatment

Treatment of patients with advanced or recurrent rectal cancer depends on the location of the disease.

Metastatic and Recurrent Rectal Cancer

Standard treatment options for stage IV and recurrent rectal cancer include the following:

- Surgery with or without chemotherapy or radiation therapy.
- Systemic therapy.
- Second-line chemotherapy.
- Immunotherapy.
- Palliative therapy.

Surgery with or without chemotherapy or radiation therapy

For patients with locally recurrent, liver-only, or lung-only metastatic disease, surgical resection, if feasible, is the only potentially curative treatment. Patients with limited pulmonary metastasis, and patients with both pulmonary and hepatic metastasis, may also be considered for surgical resection, with 5-year survival possible in highly selected patients. The presence of hydronephrosis associated with recurrence appears to be a contraindication to surgery with curative intent.

Locally recurrent rectal cancer may be resectable, particularly if an inadequate prior operation was performed. For patients with local recurrence alone after an initial, attempted curative resection, aggressive local therapy with repeat low anterior resection and coloanal anastomosis, abdominoperineal resection, or posterior or total pelvic exenteration can lead to long-term disease-free survival.

The use of induction chemoradiation therapy for previously nonirradiated patients with locally advanced pelvic recurrence (pelvic side-wall, sacral, and/or adjacent organ involvement) may increase resectability and allow for sphincter preservation. Intraoperative radiation therapy in patients who underwent previous external- beam

radiation therapy may improve local control in patients with locally recurrent disease, with acceptable morbidity.

Systemic therapy

The following are U.S. Food and Drug Administration (FDA)-approved drugs that are used alone and in combination with other drugs for patients with metastatic colorectal cancer:

- Fluorouracil (5-FU).
- Irinotecan.
- Oxaliplatin.
- Capecitabine.
- Bevacizumab.
- FOLFOXIRI (irinotecan, oxaliplatin, leucovorin [LV], and 5-FU).
- Cetuximab.
- Aflibercept.
- Ramucirumab.
- Panitumumab.
- Anti-epidermal growth factor receptor (EGFR) antibody versus anti-vascular endothelial growth factor (VEGF) antibody with first-line chemotherapy.
- Regorafenib.
- TAS-102.
- Encorafenib with cetuximab for patients with BRAF V600E mutations.

5-FU

When 5-FU was the only active chemotherapy drug, trials in patients with locally advanced, unresectable, or metastatic disease demonstrated partial responses and prolongation of the time-to-progression (TTP) of disease, and improved survival and quality of life in patients who received chemotherapy versus best supportive care. Several trials have analyzed the activity and toxic effects of various 5-FU/LV regimens using different doses and administration schedules and showed essentially equivalent results with a median survival time in the approximately 12-month range.

Irinotecan and oxaliplatin

Three randomized studies in patients with metastatic colorectal cancer demonstrated improved response rates, progression-free survival (PFS), and overall survival (OS) when irinotecan or oxaliplatin was combined with 5- FU/LV.

Since the publication of these studies, the use of either FOLFOX or FOLFIRI is considered acceptable for first-line treatment of patients with metastatic colorectal cancer. However, when using an irinotecan-based regimen as first-line treatment of metastatic colorectal cancer, FOLFIRI is preferred.

Capecitabine

Before the advent of multiagent chemotherapy, two randomized studies demonstrated that capecitabine was associated with equivalent efficacy when compared with the Mayo Clinic regimen of 5-FU/LV.

Randomized phase III trials have addressed the equivalence of substituting capecitabine for infusional 5-FU. Two phase III studies have evaluated capecitabine/oxaliplatin (CAPOX) versus 5-FU/oxaliplatin regimens (FUOX or FUFOX).

When using an oxaliplatin-based regimen as first-line treatment of metastatic colorectal cancer, a CAPOX regimen is not inferior to a 5-FU/oxaliplatin regimen.

Bevacizumab

Bevacizumab can reasonably be added to either FOLFIRI or FOLFOX for patients undergoing first-line treatment of metastatic colorectal cancer. There are currently no completed randomized controlled studies evaluating whether continued use of bevacizumab in second-line or third-line treatment after progressing on a first-line bevacizumab regimen extends survival.

FOLFOXIRI

Cetuximab

Cetuximab is a partially humanized monoclonal antibody against EGFR. Importantly, patients with mutant KRAS tumors may experience worse outcome when cetuximab is added to multiagent chemotherapy regimens containing bevacizumab.

Aflibercept

Aflibercept is a novel anti-VEGF molecule and has been evaluated as a component of second-line therapy in patients with metastatic colorectal cancer.

Ramucirumab

Ramucirumab is a fully humanized monoclonal antibody that binds to vascular endothelial growth factor receptor-2 (VEGFR-2).

Panitumumab

Panitumumab is a fully humanized antibody against the EGFR. The FDA approved panitumumab for use in patients with metastatic colorectal cancer refractory to chemotherapy.[41] In clinical trials, panitumumab demonstrated efficacy as a single agent or in combination therapy, which was consistent with the effects on PFS and OS with cetuximab. There appears to be a consistent class effect.

Anti-EGFR antibody versus anti-VEGF antibody with first-line chemotherapy

In the management of patients with stage IV colorectal cancer, it is unknown whether patients with KRAS wild- type cancer should receive an anti-EGFR antibody with chemotherapy or an anti-VEGF antibody with chemotherapy.

Regorafenib

Regorafenib is an inhibitor of multiple tyrosine kinase pathways including VEGF. In September 2012, the FDA granted approval for the use of regorafenib in patients who had progressed on previous therapy.

TAS-102

TAS-102 (Lonsurf) is an orally administered combination of a thymidine-based nucleic acid analog, trifluridine, and a thymidine phosphorylase inhibitor, tipiracil hydrochloride. Trifluridine, in its triphosphate form, inhibits thymidylate synthase; therefore, trifluridine, in this form, has an anti-tumor effect. Tipiracil hydrochloride is a potent inhibitor of thymidine phosphorylase, which actively degrades trifluridine. The combination of trifluridine and tipiracil allows for adequate plasma levels of trifluridine.

Encorafenib with cetuximab for patients with BRAF V600E mutations

BRAF V600E mutations occur in about 10% of metastatic colorectal cancers and are an indicator of poor prognosis. Unlike in melanoma, BRAF inhibitor monotherapy has not shown a benefit in colorectal cancer, and multiple studies have evaluated concurrent targeting of the EGFR-MAPK pathway.

Second-line chemotherapy

Second-line chemotherapy with irinotecan in patients treated with 5-FU/LV as first-line therapy demonstrated improved OS when compared with either infusional 5-FU or supportive care.

Similarly, a phase III trial randomly assigned patients who progressed on irinotecan and 5-FU/LV to bolus and infusional 5-FU/LV, single-agent oxaliplatin, or FOLFOX4. The median TTP for FOLFOX4 versus 5-FU/LV was 4.6 months versus 2.7 months (stratified log-rank test, 2-sided $P < .001$).

Immunotherapy

Approximately 4% of patients with stage IV colorectal cancer have tumors that are mismatch repair deficient (dMMR) or microsatellite unstable/microsatellite instability-high (MSI-H). The MSI-H phenotype is associated with germline defects in the MLH1, MSH2, MSH6, and PMS2 genes and is the primary phenotype observed in tumors from patients with hereditary nonpolyposis colorectal cancer (HNPCC) or Lynch syndrome. Patients can also have the MSI-H phenotype because one of these genes was silenced via DNA methylation. Testing for microsatellite instability can be done with molecular genetic tests, which look for microsatellite instability in the tumor tissue, or with immunohistochemistry, which looks for the loss of mismatch repair proteins. MSI-H status has historically been prognostic of increased survival for patients with earlier-stage disease and since 2015, has also been found to predict tumor response to checkpoint inhibition.

The FDA approved pembrolizumab for use in patients with treatment-naïve, metastatic, dMMR/MSI-H colorectal cancer in June 2020. Studies regarding first-line treatment with dual checkpoint inhibitors are ongoing. The FDA approved the anti-programmed cell death protein 1 (PD-1) antibodies pembrolizumab in May 2017 and nivolumab in July 2017 for the treatment of patients with microsatellite-unstable tumors who had previously received 5-FU, oxaliplatin, and irinotecan-based therapy. In July 2018, the FDA granted accelerated approval for the combination of nivolumab with ipilimumab (a CTLA-4 inhibitor) to treat MSI-H colorectal cancers that progressed after prior 5-FU, oxaliplatin, and irinotecan-based therapies.

First-line immunotherapy

Pembrolizumab monotherapy

Nivolumab and ipilimumab

Second-line immunotherapy

Pembrolizumab monotherapy

Nivolumab monotherapy

Nivolumab and ipilimumab

Palliative therapy

Palliative radiation therapy, chemotherapy, and chemoradiation therapy may be indicated. Palliative, endoscopically-placed stents may be used to relieve obstruction.

Treatment of Liver Metastasis

Approximately 15% to 25% of colorectal cancer patients will present with liver metastases at diagnosis, and another 25% to 50% will develop metachronous hepatic metastasis after resection of the primary tumor. Although only a small proportion of patients with liver metastasis are candidates for surgical resection, advances in tumor ablation techniques and in both regional and systemic chemotherapy administration provide a number of treatment options. These include the following:

- Surgery.
- Neoadjuvant chemotherapy.
- Local ablation.
- Adjuvant chemotherapy.
- Intra-arterial chemotherapy after liver resection.

Surgery

Hepatic metastasis may be considered to be resectable on the basis of the following factors:

- Limited number of lesions.
- Intrahepatic locations of lesions.
- Lack of major vascular involvement.

- Absent or limited extrahepatic disease.
- Sufficient functional hepatic reserve.

For patients with hepatic metastasis that is considered to be resectable, a negative margin resection has been associated with 5-year survival rates of 25% to 40% in mostly nonrandomized studies, such as the North Central Cancer Treatment Group trial NCCTG-934653 (NCT00002575). Improved surgical techniques and advances in preoperative imaging have improved patient selection for resection. In addition, multiple studies with multiagent chemotherapy have demonstrated that patients with metastatic disease isolated to the liver, which historically would be considered unresectable, can occasionally be made resectable after the administration of neoadjuvant chemotherapy.

Neoadjuvant chemotherapy

Patients with hepatic metastases that are deemed unresectable will occasionally become candidates for resection if they have a good response to chemotherapy. These patients have 5-year survival rates similar to patients who initially had resectable disease.

Local ablation

Radiofrequency ablation has emerged as a safe technique (2% major morbidity and <1% mortality rate) that may provide long-term tumor control. Radiofrequency ablation and cryosurgical ablation remain options for patients with tumors that cannot be resected and for patients who are not candidates for liver resection.

Adjuvant chemotherapy

The role of adjuvant chemotherapy after potentially curative resection of liver metastases is uncertain.

Additional studies are required to evaluate this treatment approach and to determine whether more effective systemic combination chemotherapy alone would provide results similar to hepatic intra-arterial therapy plus systemic treatment.

Intra-arterial chemotherapy after liver resection

Hepatic intra-arterial chemotherapy with floxuridine for liver metastases has produced higher overall response rates but no consistent improvement in survival when compared with systemic chemotherapy. Controversy regarding the efficacy of regional chemotherapy was the basis of a large, multicenter, phase III trial (Leuk-9481)

(NCT00002716) of hepatic arterial infusion versus systemic chemotherapy. The use of combination intra-arterial chemotherapy with hepatic radiation therapy, especially employing focal radiation of metastatic lesions, is under evaluation.

Several studies show increased local toxic effects after hepatic infusional therapy, including liver function abnormalities and fatal biliary sclerosis.

2. OBJECTIVES

The objectives of the 2020 Diagnosis Year Patterns of Care Study are to:

2.1. Describe the use of recommended biomarker tests which shall be verified with the treating physician/physician office staff or with unified medical record (record with all inpatient and outpatient records in a single file) or complete medical records (inpatient and outpatient medical records from multiple hospitals/healthcare systems/medical practices that include all records of cancer treatment);

2.2. Describe the use of targeted therapy which shall be verified with the treating physician/physician office staff or with unified/complete medical records;

2.3. Describe the use of adjuvant therapy, which shall be verified with the treating physician/physician office staff or with unified/complete medical record;

2.4. Characterize the practice patterns in different communities;

2.5. Compare the patterns of treatment (surgery, radiation therapy, systemic therapy [chemotherapy, immunotherapy, hormonal therapy, targeted therapy]) over time and by age, sex, race/ethnicity, and insurance status;

2.6. Describe comorbidities and the effect of co-morbid conditions on treatment;

2.7. Describe treatment by hospital characteristics (i.e., for profit vs. not for profit, teaching vs. non-teaching, bed size, etc.);

2.8. Describe the use of diagnostic tests and compare their use by demographic variables and geographic region;

2.9. Describe the medical record documentation of discussions about palliative care; and

2.10. Describe the effects of the COVID-19 pandemic on cancer care and patient outcomes.

3. STUDY PLAN

3.1. Data collection will be of breast cancer cases (stage 0 – IV) diagnosed between January 1, 2020 and December 31, 2020 and colon or rectal cancer cases (stage II – IV) diagnosed between January 1, 2020 and December 31, 2020.

3.2. All stage coding will be based on the AJCC 8th Edition Staging Manual and on the SEER 2018 Coding and Staging Manual.

3.3. To obtain more stable estimates, Blacks, Hispanics Asian/Pacific Islanders, and Native American/Alaskan Natives will be oversampled. Hispanic cases can be of any race. If a case has Hispanic ethnicity, the case should be in a Hispanic stratum rather than the stratum based on the case's race. Due to the small numbers, all American Indians and Native Alaskans will be sampled. Women diagnosed with breast cancer at age younger than 50 years and/or diagnosed with stage IV triple negative breast cancer will also be oversampled. Women and men diagnosed with colorectal cancer at age younger than 35 years will also be oversampled.

3.4. Data collection will include:

Re-abstraction from the medical record of all variables on the data abstraction form:

- Insurance status
- Co-morbid conditions
- Characteristics of the hospital providing treatment
    - Bed size
    - Approved residency training program
    - Ownership
        - Not-for-profit; For profit
        - Federal government
        - Government-nonfederal
- Biomarker tests/assays completed and biomarkers identified
- Type of biopsy/cytology
- Surgery and pathologic margins
- Tumor characteristics
- Radiation therapy and systemic therapy (targeted therapy, chemotherapy, immunotherapy, hormonal therapy)

Abstraction from the medical record of specific pilot study variables on the data abstraction form:

- Effects of the COVID-19 pandemic on cancer care and patient outcomes

Verification with the treating physician or physician's office staff or with unified/complete medical records

- Participation in clinical trials
- Specific treatments given or refusal of treatments
- Specific agents given
- Tumor mutation testing
- Receipt of and type of palliative care

4. TIMETABLE

4.1. Data collection can begin as soon as the 2020 case samples can be drawn.

4.2. Quality control activities will be conducted AS DATA ABSTRACTING PROGRESSES BUT **NOT** SIMULTANEOUSLY WITH CASE ABSTRACTION. That is, QC should not be performed for a particular case until the case has already been abstracted and it has been found to meet inclusion criteria for POC. A different registrar should complete the QC abstract. QC abstracts should be compared to the non-QC abstract in real-time by the registry to identify coding issues and discrepancies. QC data should be evaluated by the registry PRIOR to data submission.

4.3. All data must be submitted to Information Management Services by Dec. 23, 2023.

5. SUBMISSION OF DATA

5.1. The data file from the electronic data abstracting tool should be uploaded to NCI DCCPS' Biomedical Computing Contractor via the SEER*DMS portal or via file transfer protocol (FTP) for those registries not on SEER*DMS.

6. QUALITY CONTROL

6.1. A blind re-abstraction of data on a random 5% sample of the cases is to be included for each cancer site.

6.2. The 5% sample of cases to be re-abstracted should be selected by the registry. The procedure used by each registry for selecting the sample should be available if questions should arise. Quality control activities will be conducted **AS DATA ABSTRACTING PROGRESSES**, but individual cases should not be QC abstracted until the original abstract is complete. The re-abstracted data shall be reviewed by the supervisor, marked "QC=1" in the QC Data Item, and uploaded with the other abstracts. Retraining of the abstracting staff shall occur as needed as the QC is performed. Submission of the quality control (duplicate abstracting of 5% of the abstracts) to Information Management Services, Inc. will be done with the Dec. 2023 submission of the POC data.

6.3. The entire data acquisition form should be completed by a second abstractor without referring to the original data abstract. Data sources to be re-abstracted include the hospital records and the information obtained from the physician verification form (do not re-contact the physician).

6.4. Prior to submitting the quality control and the original data abstract, any discrepancies between abstracts should be reconciled. The corrected data will then appear on both the QC and the study abstract form. The QC record is coded "1" in the Quality Control Data Item, while the original is coded "0". Every record that is coded "1" will have a corresponding "0" (non-QC) record, but only 5% of non-QC records (0) will have a QC record (1).

7. CONFIDENTIALITY

7.1. For all cancer patients in the sample, the name will be known only to the registry and communication about cases will be through the registry identification number.

7.2. Hospital characteristics will be assigned at the registry. Names of the hospitals will not be provided to the National Cancer Institute nor to Information Management Services. This will ensure the confidentiality of all hospitals.

7.3. Data analysis will be done by individuals who agree to maintain confidentiality.

7.4. In scientific publications, only aggregate statistics, which will preserve the confidentiality, will be presented

7.5. Registries participating in POC agree that NCI personnel and registry PI's participating in POC will have access to these data for research purposes and will be able to link geographic variables to POC data using patients' state, county, zip code, or census tract. Unencrypted geographic characteristics (e.g., state, county, zip code, and census tract of residence) will remain at IMS and will not be shared with NCI or other researchers using these data. No attempts will be made to identify patients with linking of geographic-level information.

References

https://www.cancer.gov/types/breast/hp/breast-treatment-pdq

https://www.cancer.gov/types/colorectal/hp/colon-treatment-pdq

https://www.cancer.gov/types/colorectal/hp/rectal-treatment-pdq

POC DATA ACQUISITION MANUAL

SECTION II

PATIENT ELIGIBILITY

SECTION II - PATIENT ELIGIBILITY

CONTENTS

PATIENT ELIGIBILITY

In addition to using a common set of data items and codes, it is important that the registries involved in this study adopt a uniform policy by which patients are selected for inclusion. This will ensure that the patient populations are comparable across registries and over time.

1. PATIENT SELECTION

1.1. The sampling procedures and the proportion of cases to be sampled are outlined below.

1.2. Women diagnosed with Stage 0-IV breast cancer between January 1, 2020 and December 31, 2020 will be sampled by age group, race/ethnicity, and stage (defined below).

1.3. Men and women diagnosed with Stage II-IV colon and rectal cancers between January 1, 2020 and December 31, 2020 will be sampled by age group and race/ethnicity (defined below).

2. SAMPLING

2.1. Each registry will select cases from their database according to the sampling plan below. Cases will be sampled proportionately to the registry size. Non-Hispanic blacks, Hispanics, Asian/Pacific Islander and Native Alaskan/American Indians will be over-sampled to provide more stable estimates. Women diagnosed with breast cancer at age younger than 50 years and/or diagnosed with stage IV triple negative breast cancer will also be oversampled. Women and men diagnosed with colorectal cancer at age younger than 35 years will also be oversampled.

2.2. For registries using SEER*DMS, algorithms will be implemented within SEER*DMS to identify cases for the POC study. Registry staff will be able to review the cases identified by the POC algorithms in SEER*DMS; and registry staff will use extracts in SEER*Abs to identify cases for abstracting.

2.3. For registries not using SEER*DMS to sample cases, assign a random number between 0 and 1 to all eligible cases of breast cancer in your registry diagnosed from January 1, 2020 through December 31, 2020 and separately for all eligible cases of colon or rectal cancer in your registry diagnosed from January 1, 2020 through December 31, 2020. The number of cases to be sampled divided by the total number of eligible cases will be your sampling fraction. If the case has a number less than or equal to your sampling fraction, X, the case will be included in the study. If the random number assigned is greater than your sampling fraction, the case will not be abstracted for the Patterns of Care study. For example, all breast cancer cases eligible for inclusion in the study would have a random number between 0 and 1 assigned. If the sampling fraction for breast cancer is 0.63 and case 10100001 were given the random number of 0.594, it would be included in the study. Its number is less than the sampling fraction number of

0.63. If case 10100001 were assigned the random number of 0.654, it would not be abstracted for this study because its number is greater than the 0.63 sampling fraction.

2.4. At some point during the study, it is likely that cases will be added to the registry's database after sampling has already been completed. To give these additional cases an opportunity to be included in the study, the registries should identify such patients. Registries using SEER*DMS can re-run the sampling extract. Registries not using SEER*DMS can add them to the appropriate Sampling File, and assign them random numbers between 0 and 1. All cases found after the initial sampling **MUST** be sampled in this way. These additional cases will not modify the sampling fractions already obtained for a given time interval. The basis for selection of these cases into the study will be the sampling fractions (i.e., if the fraction for a cancer site group or subgroup is 0.49, a case will be added to the appropriate Patterns of Care file if the assigned random number is 0.49 or less). **If one or more of these additional cases is found to be ineligible after selection into the study, do not replace them with another case. If there are more than 9 cases found to be ineligible, please discuss with NCI whether additional cases should be sampled.**

3. REPORTABLE CASES

3.1. Reportable cases are to be drawn from all cancer patients who are in the registry who meet study criteria (described below).

3.2. A reportable case is one that meets the following criteria:

3.2.1. Patient must have a microscopically confirmed invasive colon cancer or rectal cancer or microscopically confirmed in situ or invasive breast cancer.

3.2.2. Patients must be age 20 or older.

3.2.3. Patient must have been diagnosed between January 1, 2020 and December 31, 2020 (including those diagnosed on Jan. 1 and Dec. 31).

3.2.4. Malignant neoplasms arising in the ICD-O Topography sites listed below are reportable to the POC study. See SEER Program Coding and Staging Manual 2018 for a list of reportable terms.

3.2.5. For breast, colon, and rectal cancer patients, this must be the first cancer diagnosed for this patient except for basal cell or squamous cell carcinoma of the skin.

3.2.6. Patients are excluded if there are simultaneously diagnosed cancers of more than one site (e.g., a patient diagnosed with primary breast and primary lung cancer simultaneously) or simultaneously diagnosed cancers in the same site (i.e., two or more different primary cancers in the same site).

3.2.7. Site-specific inclusion criteria are listed below.

4. BREAST CANCER CASES

4.1. Include breast cases meeting the following criteria:

ICD-O	Term
C500	Nipple
C501	Central portion of breast
C502	Upper-inner quadrant of breast (UIQ)
C503	Lower-inner quadrant of breast (LIQ)
C504	Upper-outer quadrant of breast (UOQ)
C505	Lower-outer quadrant of breast (LOQ)
C506	Axillary tail of breast
C508	Overlapping lesion of breast
C509	Breast, NOS (excludes Skin of breast C445); multi-focal neoplasm in more than one quadrant of the breast

- Histology codes 8000-8530, 8550-8576 – NOTE: Excludes Paget Disease (8540-8543)
- Behavior code 2 (carcinoma in situ), 3 (malignant)
- Diagnostic Confirmation codes 1, 2, 4
- AJCC Stage 0, I, II, III, IV (2018 8th edition)

4.2. Exclude breast cancer cases with the following specifications:

- Males
- Paget's disease with no underlying tumor (ICD O-3 code 8540-8543)
- Simultaneously diagnosed separate primary cancers
- Histology codes: All other histologies
- Stage: All unknown stage or unstaged cases

4.3. Patients diagnosed with breast cancer at age <50 years and those diagnosed with stage IV triple negative breast cancer (i.e., negative for ER, PR and HER-2) will be oversampled. Therefore, patients will be sampled separately by age group (<50 vs. 50 and older), race/ethnicity, and stage (0-III, IV not triple negative vs. IV triple negative).

4.4. Details of Sampling: Eligibility

Site	Race/Ethnicity	Age Group	Stage
Breast	NH-White NH-Black Hispanic Asian/Pacific Islander AI/AN	<50 50 or older	0-III (no hormone selection) and IV not triple negative IV triple negative

5. COLON AND RECTUM CANCER CASES

5.1. Include Colon/Rectum cases with the following criteria:

C18.0	Cecum
	Ileocecal valve
	Ileocecal junction
C18.2	Ascending colon
	Right colon
C18.3	Hepatic flexure of colon
C18.4	Transverse colon
C18.5	Splenic flexure of colon
C18.6	Descending colon
	Left colon
C18.7	Sigmoid colon
	Sigmoid flexure
	Sigmoid, NOS
	Pelvic colon
C18.8	Overlapping lesion of the colon
C18.9	Colon, NOS
	Large intestine
	Large bowel, NOS
C19.9	Rectosigmoid junction
	Rectosigmoid colon
	Rectosigmoid, NOS
	Colon and rectum
	Pelvirectal junction
C20.9	Rectum, NOS
	Rectal ampulla

- Histology codes: adenocarcinoma only, 8140-8490
- Behavior code: 3 only
- Diagnostic Confirmation codes 1, 2, 4

- AJCC Stage II, III, IV (2018 8th edition)

5.2. Exclude Colon/Rectum cases with the following criteria:

- C18.1 (appendix)
- Simultaneously diagnosed separate primary cancers
- AJCC stage 0, I
- Histology Codes: All other histologies
- Unknown stage or unstaged patients

5.3. Patients diagnosed with colon or rectal cancer at age <35 years will be oversampled. Therefore, patients will be sampled separately by age group (<35 vs. 35 and older) and race/ethnicity.

5.4. Details of sampling; Eligibility

Site	Derived AJCC Stage Group	Age Group	Race/Ethnicity
Colon and Rectum	II-IV	<35 35 and older	NH-White NH-Black Hispanic Asian/Pacific Islander AI/AN

6. GENERAL NON-REPORTABLE CASES AND MALIGNANCIES

6.1. Cases which are not reportable to the POC study are those with:

6.1.1. Exclusion criteria applied to the selection process:

- Neuroendocrine tumor (NET) histologies
- Lymphoma/hematopoietic histology M-9590/3-9993/3
- Unknown stage or unstaged cases
- Death certificate only diagnosis
- Autopsy only diagnosis
- Previous malignancies (except basal cell or squamous cell carcinoma of the skin)
- Simultaneously diagnosed cancers 60 days or less apart of the same site or of two different sites. Examples:
  - A patient simultaneously diagnosed with primary breast cancer and primary lung cancer within 60 days.
  - A patient diagnosed with two breast primaries within 60 days
  - A patient diagnosed with multiple simultaneous colon primaries in different segments of the colon
- Non-histologically proven diagnosis (clinical diagnosis only)
- Cases with age at diagnosis less than 20 years old

6.1.2 Exclusion criteria identified during the case abstraction process

- Cases with previously diagnosed neoplasms of uncertain or unknown behavior
- Cases previously diagnosed with GIST of malignant or unknown behavior
- Cases that are identified for POC but upon abstraction are found to be improperly coded such that when corrected do not meet POC criteria
- Cases that were reported via out-of-state data exchange and for which there are no local (in-state) providers to contact and no medical records to access; cases reported via out-of-state data exchange but for which medical records are available should be included.
- Cases for which the registry has only a record of the cancer diagnosis or only pathology information and does not have any information on subsequent treatment or outcomes

7. REPORTABILITY SUMMARY BY SITE

7.1. Breast cancer

- Include primary sites ICD-O-3 C50.0-C50.6, C50.8-C50.9
- Include histology codes: 8000-8530, 8550-8576
- Include behavior code: 2 and 3 only
- Include Diagnostic Confirmation codes 1, 2, 4
- Include AJCC 8th Edition Stage 0, I, II, III, IV

7.2. Colorectal cancer

- Include primary sites ICD-O-3 C18.0, C18.2-C18.9, C19.9, C20.9
- Include histology codes: adenocarcinoma only, 8140-8490
- Include behavior code: 3 only
- Include Diagnostic Confirmation codes 1, 2, 4
- Include AJCC 8th Edition Stage II, III, IV

POC DATA ACQUISITION MANUAL

SECTION III

COMMON DATA SET

SECTION III – COMMON DATA SET

CONTENTS

SEER REGISTRY PARTICIPANT NUMBER

ITEM A-1

1. **Code:** 2 digits

2. **Description:**

   2.1. The SEER Institution Number consists of the 2-digit SEER PARTICIPANT Code used for annual submissions to NCI.

   2.2. See below for a list of participating Registries and their Participant Numbers.

Registry	Participant Number
Connecticut	02
Greater California	41
Hawaii	21
Iowa	22
Kentucky	42
Louisiana	43
New Jersey	44
New Mexico	23
Seattle	25
Utah	26

CASE NUMBER

ITEM A-2

1. **Code:** 8 digits

2. **Description:**

   2.1. The CASE NUMBER is the registry-specific patient identification number used on the files submitted to the National Cancer Institute.

   2.2. The CASE NUMBER is used for administrative purposes by NCI and for communication with the Registry concerning the case. Patient name and number assignment lists will be available only at the Registry.

   2.3. If you do not have a full eight digits, please code this exactly as you would for other data submissions.

QUALITY CONTROL (QC)

ITEM A-3

1. **Code:** 0 = No
   1 = Yes

2. **Description:**

   2.1. For each cancer site, a random 5% sample of cases to be re-abstracted should be selected by the registry. The procedure used by each registry for selecting this sample should be available if questions arise. QC activities should be conducted as data abstracting progresses, rather than waiting until the end of the data collection.

   2.2. The QC abstraction of a particular case must be performed ***after*** the original abstract is completed, to ensure the case is appropriate for inclusion in POC.

   2.3. Code "0" if this is **not** a re-abstracted QC case. Code "1" if it is a re-abstracted QC case.

   2.4. QC is to be done as the abstracting proceeds. **The goal of QC is to correct mistakes being made as the study progresses rather than waiting until all of the data have been incorrectly collected.** Therefore, a comparison between the original abstract and the QC abstract should be made at the time of completion of the QC form by the QC expert. Any discrepancies should be immediately addressed with the abstractor and it should be determined whether the abstractor or the QC person is correct. Once discrepancies are addressed the appropriate correction should be made to the abstract or to the QC form and a full discussion should take place to be certain that the data is being accurately abstracted and coded. The abstract and the QC form should be reconciled before submission to IMS. The form with the incorrect data, whether it is the study abstract or the QC form, should be corrected so that both forms contain the same data.

   2.5. Steps to be taken:

      1. Original abstract completed
      2. QC abstract completed
      3. Immediate comparison of the original and QC forms
      4. Identification of differences between the original and QC
      5. Determination of correct item or code
      6. Discussion of correct abstracting or coding
      7. Correction of original or QC abstract
      8. Submit finalized QC and original abstracts

TUMOR RECORD NUMBER

ITEM A-4

1. **Code:** 2-digit code
   - 01 First record for a case
   - 02 Second record for a case
   - ..
   - ..
   - nn Last of nn records for a case

2. **Description:**

   2.1. This is the unique sequential number as assigned to the case being abstracted.

   2.2. This is the number that refers to the order in which the cancer was registered by the participating registry. This data item will not be edited. It is for registry use only and can be blank if it is not needed.

SEQUENCE NUMBER

ITEM A-5

1. **Code:** 2-digits

2. **Description**:

   2.1. The SEQUENCE NUMBER is the number of this primary in the life history of the patient. This is the SEQUENCE NUMBER as assigned for SEER submissions.

   2.2. For breast, colon, and rectum cancer cases, only “00” and “01” will be eligible since these cancers will be first primary cancers for all cases included in POC.

PRIMARY SITE

ITEM A-6

1. **Code**: 3 digits

2. **Description**:

   2.1. The Topography section of the International Classification of Disease for Oncology, Third edition (ICD-O-3, 2001) is used for coding the primary site of all solid tumors.

   2.2. The coding of primary site is to be completed as described in *The SEER Program Coding and Staging Manual 2018* Section IV, Primary Site.

   2.3. The 'C' should not be coded and the decimal point should be disregarded.

GRADE

ITEM A-7

1. **Code:** 3 digits

Clinical Grade	1digit
Pathological Grade	1 digit
Post-therapy Grade	1 digit

2. **Description**:

2.1. All pathology reports related to this cancer for the case should be examined.

2.2. Clinical Grade records the grade of a tumor before any treatment (surgical resection or initiation of any treatment including neoadjuvant). Clinical Grade must not be blank. Assign the highest grade from the primary tumor assessed during the clinical time frame.

2.3. Code Clinical Grade as 9 when the grade from the primary site is not documented; clinical workup is not done (for example, cancer is an incidental finding during surgery for another condition); or grade checked "not applicable" on CAP Protocol (if available) and no other grade information is available. If there is only one grade available and it cannot be determined if it is clinical or pathological, assume it is a clinical grade and code appropriately. Then code unknown (9) for pathological grade and blank for post therapy grade.

2.4. Pathological Grade records the grade of a solid primary tumor that has been resected and for which no neoadjuvant therapy was administered. If AJCC staging is being assigned, the tumor must have met the surgical resection requirements in the AJCC manual. This may include the grade from the clinical workup. Record the highest grade documented from any microscopic specimen of the primary site whether from the clinical workup or the surgical resection. Pathological grade must not be blank. If the clinical grade is the highest grade identified, use the grade that was identified during the clinical time frame for both the clinical grade and the pathological grade. If a resection is done of a primary tumor and there is no grade documented from the surgical resection, use the grade from the clinical workup. If a resection is done of a primary tumor and there is no residual cancer, use the grade from the clinical workup. Pathological Grade code 4 includes anaplastic.

GRADE (cont)

2.5. Code Pathological Grade as 9 when grade from primary site is not documented; there was no resection of the primary site; neo-adjuvant therapy is followed by a resection (see Post Therapy Grade); this is a clinical case only (see clinical grade); there is only one grade available and it cannot be determined if it is clinical, pathological, or after neo-adjuvant therapy; or grade checked "not applicable" on CAP Protocol (if available) and no other grade information is available.

2.6. Post Therapy Grade records the grade of a solid primary tumor that has been resected following neoadjuvant therapy. If AJCC staging is being assigned, the tumor must have met the surgical resection requirements in the AJCC manual. Record the highest grade documented from the surgical treatment resection specimen of the primary site following neoadjuvant therapy. Leave Post Therapy Grade blank when there is no neoadjuvant therapy; this is a clinical or pathological case only; or there is only one grade available and it cannot be determined if it is clinical, pathological or post therapy. Assign the highest grade from the resected primary tumor assessed after the completion of neoadjuvant therapy. Post Therapy Grade 4 includes anaplastic. Code Post Therapy Grade as 9 when surgical resection is done after neoadjuvant therapy and grade from the primary site is not documented; surgical resection is done after neoadjuvant therapy and there is no residual cancer; or grade is checked "not applicable" on CAP Protocol (if available) and no other grade information is available.

HOSPITAL CODE

ITEM A-8

1. **Code:** 5 digits

2. **Description**:

2.1. This item will be assigned by the participating registry to the hospital of most definitive surgery or, if no surgery, the most definitive therapy in hierarchical order of radiation then systemic therapy. The codes are used to describe the hospital characteristics. Bed size, residency training program (Teaching Status), hospital classification (Type of Control), Patient Experience Rating (star rating), and average length of stay for oncology patients are provided by the American Hospital Directory at https://www.ahd.com/search.php

2.2. On the American Hospital Directory webpage (https://www.ahd.com/search.php), enter the Hospital Name, State, or Zip Code for the hospital and click Submit. If more than one hospital is listed in the Table of Search Results, select the relevant Hospital Name.

2.3. At the top of the Free Profile for each hospital, the Type of Control (hospital ownership, coded in POC as "Hospital Classification code"), Total Staffed Beds, and Patient Experience Rating are listed under "Identification and Characteristics". Approved Residency Training (yes/no) is listed further down the Free Profile page under "Teaching Status". Average length of stay for oncology patients is listed below "Teaching Status" in the "Inpatient Utilization Statistics by Medical Service" table. Please make sure to select the Oncology row from this table. If Oncology is not listed in this table, code average length of stay for oncology patients as 9 = Unknown.

2.4. A patient seen in more than one institution/hospital should be assigned only one HOSPITAL CODE, that of the hospital providing the most definitive treatment as described above.

2.5. The HOSPITAL CODE is used to describe the characteristics of the hospitals/institutions while maintaining the confidentiality of each.

2.6. The HOSPITAL CODE is comprised of the five components below. All components are listed on the American Hospital Directory entry for a hospital. If no information on any of the five components of the HOSPITAL CODE is available, code that component as 9 = Unknown. If a hospital is not listed in the American Hospital Directory, code the hospital as

9 9 9 9 9

Digit 1: Bed size code:

1 = 1 - 49 beds

2 = 50 - 99 beds

3 = 100 - 199 beds

4 = 200 - 299 beds

5 = 300 - 399 beds

6 = 400 - 499 beds

7 = 500 or more beds

8 = OPD, including doctor's office or other non-hospital outpatient setting, including facilities with zero beds

9 = Unknown

Digit 2: Approved Residency training

0 = No

1 = Yes (MD or DO training program)

9 = Unknown

Residency training approval by the Accreditation Council for Graduate Medical Education. A physician's office should be coded "0- No."

Digit 3: Hospital Classification code:

1 = Government, nonfederal (state, county, city, city/county, hospital district/hospital authority)

2 = Non-government, not-for-profit (church-operated, other not-for-profit)

3 = Non-government, for-profit (individual, partnership, corporation); physician office

4 = Government, Federal (Air force, Army, Navy, Public Health Service, Veterans Administration, Public Health Service Indian Service, Department of Justice, other Federal facilities)

9 = Unknown

Digit 4: Patient Experience Rating:
1 = 1 star
2 = 2 stars
3 = 3 stars
4 = 4 stars
5 = 5 stars
9 = Unknown

Digit 5: Oncology Average Length of Stay:
1 = 0 - 3.16
2= >3.16 - 5.25
3 = >5.25 – 8.48
4 = >8.48
9 = Unknown

2.7. Each hospital will have a five-digit code that will include one code for each of these items above. These codes will be assigned by the registry. For example, a 300 bed hospital with an approved residency program that is a not-for-profit, State University Hospital and has a 3-star Patient Experience Rating, and an average length of stay for oncology of 4.62 days would be coded as:

5 1 1 3 2

2.8. There will be one code for each hospital/institution. However, these codes will not necessarily be unique. Your registry area may have several hospitals with the same characteristics. It is possible that there may be several 100-199 beds hospitals with no residency training program that are non-government/not-for- profit, have 4-star ratings, and have average length of stay for oncology between 5.25 and 8.48 days. The 5-digit code for all of these hospitals would be:

3 0 2 4 3

2.9. If a patient is seen only in a physician’s office and is never treated in a hospital as an inpatient or outpatient, code the bed size as 8, OPD. The code would be:

8 0 3 9 9

INSURANCE STATUS

ITEM A-9

1. **Code**: 0 = No

   1 = Yes

   2 = Patient died within 30 days of diagnosis (response option for >30 days after diagnosis only)

   3 = Yes, but coverage dates unknown

   9 = Unknown

   Code separately for:

   - At or within 30 days of diagnosis (≤ 30 days)
   - More than 30 days after diagnosis (> 30 days)

   - ☐ No insurance/Self pay
   - ☐ Medicare fee-for-service (FFS), which may be listed as Part A, Part A/B, or Medicare unspecified
   - ☐ Medicare HMO, which may be listed as Medicare Advantage, Medicare managed care, or Medicare Part C
   - ☐ Medicare Part D or Medicare prescription drug plan (PDP)
   - ☐ Supplemental private insurance with Medicare plan, which may be listed as Medigap insurance (select only if patient also has Medicare coverage)
   - ☐ Medicaid
   - ☐ Medicaid Pending
   - ☐ Private Insurance/IPA Plan/HMO or Managed Care Plan Not Including Medicare or Medicaid
   - ☐ Tricare/Other Military Not Including Veterans Affairs (VA)
   - ☐ Veterans Affairs (VA)
   - ☐ IHS (Indian Health Service)
   - ☐ Other (specify)_____

2. **Description**:

   2.1. This item is used to code information on all insurance coverage reported by the patient and has two parts; all insurance coverage reported **at or within 30 days** of diagnosis, and separately all insurance coverage reported **more than 30 days after** diagnosis. Cases may have more than one types of insurance. Code all appropriate insurance carriers on the abstract form. Please try to determine insurance status as accurately as possible because insurance status influences selection of therapy for cancer patients.

INSURANCE STATUS (continued)

2.2. Patients may have codes of "1 – Yes" for multiple types of insurance. For example, a patient with both Medicare and Medicaid insurance would be coded as having "1 – Yes" for both their specific type(s) of Medicare insurance and for Medicaid insurance. If a patient has the same insurance at diagnosis and >30 days after diagnosis, it should be coded as "1 = Yes" for both the "at or within 30 days" as well as the "More than 30 days" fields.

2.3. If a patient is listed as having a specific type or types of insurance (e.g., Medicaid), please code all other types of insurance as "0 = No". If a patient is listed as being insured but the type of insurance is not specified or is unknown, please code "No insurance/Self pay" as "0 = No", each other type of insurance as "9 = Unknown", and specify "insured, type unknown" under "Other (specify)".

2.4. Code "1 – Yes" for No Insurance when it is stated in the medical record that a patient has no insurance coverage or is a self-pay. If the medical record states that a patient subsequently has insurance during the same time period (30 days or less after diagnosis vs. more than 30 days after diagnosis), the type(s) of insurance specified should also be indicated by "1 – Yes". If a patient has insurance at diagnosis and subsequently loses all insurance, code "1 – Yes" for No Insurance in addition to coding "1 – Yes" for other insurance that the patient previously had during the time period.

2.5. For patients with Medicare insurance, code "1 – Yes" for Medicare HMO if they are listed as having Medicare Advantage insurance (which is also called Medicare managed care or Medicare Part C). If patients are listed as having Medicare insurance or the type of Medicare plan is not specified, code "1 – Yes" for Medicare fee-for-service (FFS).

2.6. Medicare patients may also have a separate Medicare prescription drug plan, which is also known as Medicare Part D. For these patients, both their main Medicare insurance and Medicare Part D should be coded "1 – Yes".

2.7. For patients with Medicare insurance and private insurance (sometimes called Medigap insurance), both their main Medicare insurance the "Supplemental private insurance with Medicare plan" should be coded "1 – Yes". "Supplemental private insurance with Medicare plan" should be coded "1 – Yes" only for patients who also have another type of Medicare insurance.

INSURANCE STATUS (continued)

2.8. Code “1 – Yes” for Medicaid if the patients is listed as having Medicaid (not otherwise specified) or any type of Medicaid coverage (e.g., Medicaid HMO or Medicaid managed care). Code “1 – Yes” for Medicaid Pending if the patient is listed as having applied for Medicaid or that Medicaid coverage is pending. Do not code “1 – Yes” for Medicaid Pending if the patient is uninsured and there is no mention of applying for Medicaid coverage or Medicaid coverage being pending.

2.9. Code “1 – Yes” for private insurance when the patient is reported to have a private insurance carrier such as Blue Cross, Travelers, Aetna, whether or not this is an HMO or managed care program, including an IPA. As stated in (2.6), individuals with Medicare and private insurance should have codes of “1 – Yes” for both their main type of Medicare insurance and Supplemental private insurance with Medicare plan”. Individuals with “Supplemental private insurance with Medicare plan” should not also have private insurance coded as “1 – Yes” unless their insurance changed from private insurance to Medicare coverage.

2.10. A small number of patients may utilize services provided by the Indian Health Service (IHS). Code “1 – Yes” when the patient has information in the medical record of receiving services provided by IHS.

2.11. If a patient died within 30 days of diagnosis, code all insurance types for more than 30 days after diagnosis (> 30 days) as “2 = Patient died within 30 days of diagnosis”.

2.12. If it is known that the patient had a specific type of insurance, but the coverage dates are unknown, code “3” in both time periods.

2.13. Code "9 - Unknown, not stated" to all when there is no insurance carrier information in the patient's medical record.

Specifics:

2.14. Medicaid is insurance provided by the state and supplemented by the federal government for those who are low-income, on welfare, or are medically indigent (i.e., cannot afford to pay their medical bills although they are not on welfare). Some states may use a term other than Medicaid for their program: e.g., California has a program called "MediCal." Please verify the name of the Medicaid program in your state. If the hospital has noted that “Medicaid is pending,” code Medicaid as “1 – Yes.” Patients with Medicaid do not usually have any other insurance except for some patients on Medicare. If Medicaid is coded “1 – Yes,” then all other insurance variables will most likely be coded “0 – No.”

INSURANCE STATUS (continued)

2.15. Blue Cross/Blue Shield is one of the most common non-governmental insurance carriers. There are many other similar companies, such as Aetna, Prudential, Travelers, UnitedHealthcare, Cigna, Humana, etc. These companies offer a variety of insurance plans including HMOs (Health Maintenance Organizations, also referred to as managed care), IPAs (Independent Practice Associations), and other plan types. These companies may also provide Medicare or Medicaid coverage. Therefore, having Blue Cross/Blue Shield or a similar company listed does not necessarily mean private insurance. Determine the type of insurance (private, Medicare, or Medicaid) provided for the patient and code appropriately.

2.16. Tricare/Other Military vs. VA: Tricare is a comprehensive insurance plan provided by the federal government for retired military and diplomatic personnel and their dependents. This form of health insurance was previously known as CHAMPUS. VA (Veterans Affairs) is different from Tricare; this coverage entitles patients to treatment at no cost at VA hospitals. Code Tricare/Other Military as "1 – Yes" if the patient has this type of insurance; code VA as "1 – Yes" if the patient received care at a VA facility.

Examples:

2.17. Patient with Medicare and supplemental Blue Cross/Blue Shield private insurance: Code "1 – Yes" to both Medicare and Supplemental private insurance. Patients who have only Medicare managed care/HMO insurance that is administered by Blue Cross/Blue Shield should have "1- Yes" coded ONLY for "Medicare HMO".

2.18. Patient who has documentation in the record that no insurance coverage is available: Code "1 – Yes" to no insurance and code all others "0 – No."

2.19. Patient who has no information available in the record regarding insurance coverage: Code "9 – Unknown" to all types of insurance.

2.20. If Medicaid pending is coded as "1 – Yes". It is unlikely that the patient has any other type of insurance, although they may be pending for enrollment in a Medicaid managed care program.

TREATMENT PROTOCOL REGISTRATION

ITEM A-10

1. **Code**: 0 = Not registered on treatment protocol
   1 = Registered on treatment protocol during first course of therapy
   2 = Registered on treatment protocol during after course of therapy
   3 = Registered on treatment protocol during and after first course of therapy
   7 = Patient or patient's guardian refused treatment protocol
   8 = Treatment protocol participation recommended, unknown if registered
   9 = Unknown, not stated

2. **Description**:

   2.1. Code whether the patient was registered on a treatment protocol at any time following cancer diagnosis. This includes treatment protocols sponsored by cooperative groups, clinical cancer centers, comprehensive cancer centers, and drug companies. This includes registration in protocols to treat cancer or to treat cancer-related symptoms (e.g. fatigue).

   2.2. If a patient is registered on a non-therapeutic protocol (pain control, for instance, cancer control, or other protocol), but is not participating in a treatment protocol, code this item as "0 - Not registered on treatment protocol."

   2.3. Code "0 - Not registered on a treatment protocol" when it is known that the patient was not registered on a treatment protocol during the first course of therapy.

   2.4. Code "1 - Registered on treatment protocol during first course of therapy" when the patient was registered on a treatment protocol during the first course of therapy. Code "2 - Registered on treatment protocol after the first course of therapy" when the patient was registered on a treatment protocol after the first course of therapy. Code "3 - Registered on treatment protocol during and after first course of therapy" when the patient was registered on two or more different treatment protocol, at least one during the first course of therapy and at least one after the first course of therapy.

   2.5. Code "7 - Patient or patient's guardian refused protocol" when registration on a treatment protocol was recommended, but the patient was never registered because of patient/guardian refusal.

   2.6. Code "8 - Treatment protocol participation recommended, unknown if registered" when a treatment protocol was recommended, but it is unknown whether the patient was actually registered.

   2.7. Code "9 - Unknown, not stated" when there is no documentation regarding registration on a treatment protocol.

TREATMENT PROTOCOL SPONSOR AND NUMBER

ITEM A-11

1. **Code**: 1 to 12 characters representing the Treatment Protocol Sponsor such as cooperative group, research base, Clinical Cancer Center, or Comprehensive Cancer Center and the Protocol Number.

2. **Description**:

2.1. "Treatment Protocol Sponsor" identifies the research base or cooperative group that is conducting the first clinical trial in which the patient was enrolled. When the patient was entered through an intermediate research base, the actual sponsoring group should be recorded. "Treatment Protocol Number" identifies the specific treatment protocol. If the patient was enrolled in more than one treatment protocol, code only the first.

2.2. **Code letters and digits only**, eliminating all punctuation such as hyphens, slashes, periods, and spaces.

2.3. If a patient was not registered on a treatment protocol, record "9" in the first (left) code box on the form. If A-10 is coded “0”, “7”, “8”, or “9”, then A-11 should be coded with a single “9” in the left most box and the other boxes in A-11 should be left blank.

2.4. The Treatment Protocol Sponsor and Number should be left-justified and the remaining code spaces left blank.

2.5. If a patient is registered on a local treatment protocol, record "LOCAL."

2.6. If a patient is registered on a drug company treatment protocol, record the name of the drug company.

2.7. If the protocol sponsor and number are unknown, then A-11 should be coded with a single “9” in the left most box and the other boxes in A-11 should be left blank.

2.8. **For this item record the protocol sponsor and number not the clinical trial registration number.**

TREATMENT PROTOCOL SPONSOR AND NUMBER (continued)

Examples:

SWOG 8711 is coded:

S W O G 8 7 1 1 _ _ _ _

Sponsor: SWOG Number: 8711

Local protocol is coded:

L O C A L _ _ _ _ _ _ _

Drug company protocol is coded:

ASTRAZENECA _

Sponsor: AstraZeneca

CASE INFORMATION VERIFIED WITH PHYSICIAN OR OFFICE STAFF

ITEM A-12

1. **Code**: 0 = No outpatient verification and unified/complete medical record not available
   1 = Yes, physician or office staff
   2 = Unified or complete (inpatient and outpatient) records reviewed
   3 = Death prior to discharge from hospitalization for initial cancer treatment
   4 = Discharge from hospitalization for initial cancer treatment to hospice

2. **Description**:

   2.1. This item will allow investigators to determine whether the case information recorded has been **verified by a source other than only the hospital medical record.**

   2.2. Unified medical record refers to record with all inpatient **and** outpatient records in a single file. Complete medical records refers to inpatient **and** outpatient medical records from multiple hospitals/healthcare systems/medical practices that include all records of cancer treatment. If you have reviewed unified/complete medical records, there is no need to send a physician verification form. Code "2 = Unified or complete records review" should take priority. That is, if unified/complete medical records are reviewed, code "2 = Unified or complete records review" should always be indicated for this item.

   2.3. In the case of facilities such as HMOs or hospitals with both inpatient and outpatient records documenting all cancer treatment, reviewing this record would be equivalent to reviewing the physician's office records. Code these cases as "2 –Unified or complete records review."

   2.4. For cases that were not treated at facilities with unified medical records (i.e., both inpatient and outpatient records including all cancer treatment the patient received for a single facility or healthcare system), **but inpatient and outpatient records are available for all facilities/healthcare systems where any cancer treatment occurred, also code these cases as "2 – Unified or complete records review."**

   2.5. If unified/complete medical records are not available **and** the medical record indicates the patient was hospitalized prior to initiation of cancer therapy and died during this hospitalization, code this Item as "3 = Death prior to discharge from hospitalization for initial cancer treatment ".

CASE INFORMATION VERIFIED WITH PHYSICIAN OR OFFICE STAFF (cont)

2.6. If unified/complete medicals record are not available **and** the patient was not hospitalized and died prior to initiation of cancer therapy (code "3") **and** the medical record indicates that the patient was hospitalized prior to initiation of cancer therapy and was then discharged to hospice, code this item as "4 = Discharge from hospitalization for initial cancer treatment to hospice". For codes "3" or "4", physician verification is not required and the abstraction is in the same category as if unified/complete medical records were used.

2.7. If a case is not verified with unified/complete medical records, death prior to hospital discharge, or discharge to hospice (codes "2", "3", or "4") and the patient was diagnosed and/or treated at more than one hospital or outpatient facility, attempts should be made to obtain medical records from all treating hospitals/outpatient facilities regardless of location (i.e., both in-state and out-of-state). If a patient was diagnosed at one hospital and treated at another hospital, the treating hospital may have copies of the diagnosis records; therefore, it may not be necessary to obtain these records from the diagnosing hospital.

2.8. If the case information was verified through contact with a physician or physician office staff, code "1 – Yes, physician or office staff." **The contact may be the physician's response to a letter or a telephone contact with the physician or office staff, or a review of the physician's office records by a POC abstractor.**

2.9. If a case is not verified with unified/complete medical records, death prior to hospital discharge, or discharge to hospice (i.e., options 2, 3, or 4 do not apply) and the patient was treated by more than one oncologist, verification forms should be sent to all treating oncologists regardless of location (i.e., both in-state and out-of-state). If at least one of the treating oncologists completes and returns the verification form, this item can be coded as being verified "1= Yes, physician or office staff", and a comment should be included with the item (in the comment field that goes to NCI) indicating the number of treating oncologists/oncology practices and the number of oncologists/oncology practices who provided verification information.

2.10. If the case information was not verified by the physician or office staff, there was no review of the patient's unified/complete medical records, and the patient neither died during an initial treatment hospitalization prior to discharge nor was discharged to hospice after an initial hospitalization, then code this item as "0 – No outpatient verification and unified/complete records not available." This might be the case if the hospital medical records cannot be found. Also use code "0" if the individual was a "VA patient only" and access to the medical records has been denied by the VA. (Some registries are allowed access while other VA systems will not provide information to the registry.) Please document in the "comment" column of the POC abstracting software if you were not allowed access to medical records.

HEIGHT / WEIGHT

ITEM A-13

1. **Code**: Height

030-998 = Actual height
999 = Unknown/not recorded

Units

1 = Inches (in)
2 = Centimeters (cm)
3 = Other specify
9 = Unknown/not stated

Weight

010-998 = Actual body weight
999 = Unknown/not recorded

Units

1 = Pounds (lbs)
2 = Kilograms (kg)
3 = Other specify
9 = Unknown/not stated

PLEASE BE CERTAIN TO RECORD THE UNITS OF ALL OF THESE MEASURES.

2. **Description**:

2.1. Body mass, overweight and obesity have been associated with certain types of cancer. Of particular concern is whether those who are overweight or obese are receiving appropriate therapy which will decrease the disparity in survival rates. ASCO reports that as many as 40% of obese patients do not receive systemic therapy based on their weight. The ASCO has established guidelines for physicians to consider actual weight rather than ideal weight to determine dose.

HEIGHT / WEIGHT (continued)

2.2. Record the height of the patient. Round height to the nearest whole number if a decimal point has been recorded. Record the unit of measure, inches or cm. If it is unknown or not stated which unit of measure is used, then record "9 = unknown."

2.3. Record the patient weight from the medical record. This is a difficult variable to find in the record. Please record weight closest to the time of treatment, if possible, since the concern is the appropriate dose of chemotherapy. If weight at diagnosis is not available, then record "usual" weight if stated. Round weight to the nearest whole number if a decimal point has been recorded.

2.4. Record the units of measure for each item. They are extremely important in calculating body mass or obesity. Do not convert from one unit of measure to another, i.e. kilograms to pounds.

DATE OF FIRST ONCOLOGIST CONSULTATION

ITEM A-14

1. **Code**: Date of FIRST oncologist appointment or consultation following cancer diagnosis

   MM-DD-YYYY

   00-00-0000 – Patient did not have an appointment or consultation with an oncologist following cancer diagnosis

   99-99-9999 – Date not available in medical record for first oncologist appointment or consultation

2. **Description**:

   2.1. Record the date specified in the medical record for the patients first appointment or consultation with an oncologist following cancer diagnosis. This could be any meeting with a medical oncologist, surgical oncologist/cancer surgeon, or radiation oncologist on or after the date of definitive cancer diagnosis. The appointment or consultation could be inpatient or outpatient. If the patient did not have any appointments or consultations with an oncologist following cancer diagnosis, record the date as 00-00-0000. If the patient did have an appointment or consultation with an oncologist following cancer diagnosis but the date of this is not specified, code the date as 99-99-9999.

IMPACT OF COVID-19 PANDEMIC ON CANCER CARE

ITEM A-15

1. **Code**: 1 digit each

A. Patient diagnosed with COVID-19 following cancer diagnosis

0 No diagnosis of COVID-19 following cancer diagnosis listed in medical record (Code dates below as 00-00-0000)
1 COVID-19 diagnosis following cancer diagnosis listed in medical record

B. Date of FIRST positive COVID-19 diagnosis following cancer diagnosis

MM-DD-YYYY
00-00-0000 – COVID-19 diagnosis not listed in medical record
99-99-9999 – Date not available for first COVID-19 diagnosis in medical record

C. Date of FIRST hospital admission for COVID-19 following cancer diagnosis

MM-DD-YYYY
00-00-0000 – COVID-19 diagnosis not listed in medical record
88-88-8888 – Patient diagnosed with COVID-19 but no hospital admission for COVID-19 listed in medical record
99-99-9999 – Date not available for first hospital admission for COVID-19

D. Impact of COVID-19 pandemic on patient's definitive cancer diagnosis

0 No impact of COVID-19 on definitive cancer diagnosis specified in medical record
1 Cancer diagnosis delayed due to COVID-19
8 Other impact to cancer diagnosis due to COVID-19 (specify) _____

E. Impact of COVID-19 pandemic on patient's first cancer surgery to the primary site

0 No impact of COVID-19 on first cancer surgery to the primary site specified in medical record
1 First surgery to the primary site was delayed
2 First surgery to the primary site was altered
3 First surgery to the primary site was canceled
4 Patient refused first cancer surgery to the primary site due to COVID-19
8 Other impact to surgery due to COVID-19 (specify) _____
9 Patient did not receive surgery to the primary cancer site for reasons other than COVID-19

IMPACT OF COVID-19 PANDEMIC ON CANCER CARE (cont)

F. Impact of COVID-19 pandemic on patient's first course of radiation therapy to the primary site

0 No impact of COVID-19 on first course of radiation therapy to the primary site specified in medical record
1 First course of radiation therapy to the primary site was delayed
2 First course of radiation therapy to the primary site was altered
3 First course of radiation therapy to the primary site was canceled
4 Patient refused first course of radiation therapy due to COVID-19
8 Other impact to radiation due to COVID-19 (specify) _____
9 Patient did not receive radiation therapy to the primary cancer site for reasons other than COVID-19

G. Impact of COVID-19 pandemic on patient's first course of systemic therapy

0 No impact of COVID-19 on first course of systemic therapy specified in medical record
1 First course of systemic therapy to the primary site was delayed
2 First course of systemic therapy to the primary site was altered
3 First course of systemic therapy to the primary site was canceled
4 Patient refused first course of systemic therapy due to COVID-19
8 Other impact to systemic therapy due to COVID-19 (specify) _____
9 Patient did not receive systemic therapy for reasons other than COVID-19

H. Impact of COVID-19 pandemic on patient's palliative care

0 No impact of COVID-19 on palliative care specified in medical record
1 Palliative care was delayed
2 Palliative care was altered
3 Palliative care was canceled
4 Patient refused palliative care due to COVID-19
8 Other impact to palliative care due to COVID-19 (specify) _____
9 Patient did not receive palliative care for reasons other than COVID-19

IMPACT OF COVID-19 PANDEMIC ON CANCER CARE (cont)

2. **Description**:

2.1. This item collects information on impact of the COVID-19 pandemic on the patient's cancer care specified in the medical record. This could include mention in the medical record of "COVID" or "coronavirus". To complete this section, review the following sections of the medical record (when present): assessment and plan from oncology and palliative care clinician notes; oncology history from any clinician notes; palliative care notes; and chemotherapy and radiation therapy flow sheets

2.2. In **Item A**, record whether the medical record indicates that the patient was diagnosed with COVID-19 after the date of cancer diagnosis. In **Item B**, record the date of COVID-19 diagnosis. If the patient was not diagnosed with COVID-19 following cancer diagnosis, record the date as 00-00-0000. If the patient was diagnosed with COVID-19 after cancer diagnosis but the date of COVID-19 diagnosis is not specified, code the date as 99-99-9999.

2.3. In **Item C**, record the date of the first hospital admission due to COVID-19 after the date of cancer diagnosis. If the patient was not diagnosed with COVID-19 following cancer diagnosis, record the date as 00-00-0000. If the patient was diagnosed with COVID-19 after cancer diagnosis but there is no hospital admission due to COVID-19 specified in the medical record, code the date as 88-88-8888. If the patient had a hospital admission due COVID-19 after cancer diagnosis but the date of the hospital admission is not specified, code the date as 99-99-9999.

2.4. In **Item D**, record whether the medical record specifies an impact of COVID-19 on the definitive diagnosis. This is the medical procedure, usually involving examination of a biopsy, aspiration, or other tissue by a pathologist that confirms a diagnosis of cancer. Only record information specifically indicating effects of COVID-19 or coronavirus. If the medical record does not indicate an impact of COVID-19 on the definitive diagnosis, code Item D as "0". If the medical record indicates that the definitive diagnosis was delayed due to COVID-19, code Item D as "1". If the medical record indicates an impact on the definitive diagnosis due to COVID-19 other than delay, code Item D as "8" and enter the appropriate text in the "Other Specify" field.

IMPACT OF COVID-19 PANDEMIC ON CANCER CARE (cont)

2.5. **Items E-H** collect information on impacts of COVID-19 on different aspects of cancer care specified in the medical record. Only record information specifically indicating effects of COVID or coronavirus.

2.6. In **Item E**, record whether the medical record specifies an impact of COVID-19 on the patient's first cancer surgery to the primary site. This can be potentially curative surgery or palliative surgery (e.g., surgery of a colonic obstruction for a patient with metastatic colon cancer). If the medical record does not indicate an impact of COVID-19 on the first cancer surgery to the primary site, code Item E as "0". If the medical record indicates that the first cancer surgery to the primary site was delayed due to COVID-19, code Item E as "1". If the medical record indicates that the first cancer surgery to the primary site was altered other than a delay due to COVID-19 (e.g., change in the facility where the surgery was performed, change from inpatient to outpatient procedure, or change in the type of surgical procedure performed), code Item E as "2". If the medical record indicates that the first cancer surgery to the primary site was canceled by health care personnel (not by the patient) due to COVID-19, whether or not the surgery was subsequently rescheduled, code Item E as "3". If the medical record indicates that the patient refused the first cancer surgery to the primary site due to COVID-19, whether or not the surgery was subsequently rescheduled, code Item E as "4". If the medical record indicates some other impact on the patient's surgery due to COVID-19, code as "8" and enter the appropriate text in the "Other Specify" field. If the patient did not receive cancer surgery to the primary site for reasons other than COVID-19, for unknown/unspecified reasons, or surgery was not planned first course, code Item E as "9".

2.7. In **Item F**, record whether the medical record specifies an impact of COVID-19 on the patient's first course of radiation therapy to the primary site. This can be a potentially curative radiation therapy or palliative radiation therapy. If the medical record does not indicate an impact of COVID-19 on the first course of radiation therapy to the primary site, code Item F as "0". If the medical record indicates that the first course of radiation therapy to the primary site was delayed due to COVID-19, code Item F as` "1". If the medical record indicates that the first course of radiation therapy to the primary site was altered other than a delay due to COVID-19 (e.g., change in the facility where the radiation therapy was administered or change in the type, duration, or frequency of radiation therapy treatments), code Item F as "2". If the medical record indicates that the first course of radiation therapy to the primary site was canceled by health care personnel (not by the patient) due to COVID-19, whether or not the radiation therapy was subsequently rescheduled, code Item F as "3". If the medical record indicates that the patient refused first course of radiation therapy to the primary site due to COVID-19, whether or not the radiation

IMPACT OF COVID-19 PANDEMIC ON CANCER CARE (cont)

therapy was subsequently rescheduled, code Item F as "4". If the medical record indicates some other impact on radiation due to COVID-19, code as "8" and enter the appropriate text in the "Other Specify" field. If the patient did not receive radiation therapy to the primary site for reasons other than COVID-19, for unknown/unspecified reasons, or radiation was not planned first course, code Item F as "9".

2.8. In **Item G**, record whether the medical record specifies an impact of COVID-19 on the patient's first course of systemic therapy. This can be a potentially curative systemic therapy or palliative systemic therapy. If the medical record does not indicate an impact of COVID-19 on the first course of systemic therapy, code Item G as "0". If the medical record indicates that the first course of systemic therapy was delayed due to COVID-19, code Item G as "1". If the medical record indicates that the first course of systemic therapy altered other than a delay due to COVID-19 (e.g., change in the facility where the systemic therapy was administered or change in the type, duration, or frequency of systemic therapy treatments, including a change from parenteral to oral systemic therapy), code Item G as "2". If the medical record indicates that the first course of systemic therapy was canceled by health care personnel (not by the patient) due to COVID-19, whether or not the systemic therapy was subsequently rescheduled, code Item G as "3". If the medical record indicates that the patient refused first course of systemic therapy due to COVID-19, whether or not the systemic therapy was subsequently rescheduled, code Item G as "4". If the medical record indicates some other impact on systemic therapy due to COVID-19, code as "8" and enter the appropriate text in the "Other Specify" field. If the patient did not receive systemic therapy for reasons other than COVID-19, for unknown/unspecified reasons, or systemic therapy was not planned first course, code Item G as "9".

2.9. In **Item H**, record whether the medical record specifies an impact of COVID-19 on palliative therapy. This can include pain management, rehabilitative services (e.g., physical therapy), or treatment of other systems associated with cancer or cancer treatment, as well as surgery, radiation therapy, or systemic therapy that is specifically designated as palliative. If the medical record does not indicate an impact of COVID-19 on the palliative therapy, code Item H as "0". If the medical record indicates that the palliative therapy was delayed due to COVID-19, code Item H as` "1". If the medical record indicates that the palliative therapy altered other than a delay due to COVID-19 (e.g., change in the facility where palliative therapy was administered or change in the type, duration, or frequency of palliative therapy treatments, including a change from in-person to virtual palliative therapy), code Item H as "2". If the medical record indicates that the palliative therapy was canceled by

IMPACT OF COVID-19 PANDEMIC ON CANCER CARE (cont)

health care personnel (not by the patient) due to COVID-19, whether or not palliative therapy was subsequently rescheduled, code Item H as “3”. If the medical record indicates that the patient refused palliative therapy due to COVID-19, whether or not palliative therapy was subsequently rescheduled, code Item H as “4”. If the medical record indicates some other impact on palliative therapy due to COVID-19, code as “8” and enter the appropriate text in the “Other Specify” field. If the patient did not receive palliative therapy for reasons other than COVID-19, for unknown/unspecified reasons, or palliative care was not planned first course, code Item H as “9”.

IMPACT OF COVID-19 PANDEMIC ON FINANCES/INSURANCE

ITEM A-16

1. **Code**: 1 digit each

A. Impact of COVID-19 pandemic on patient's finances following cancer diagnosis

0 No impact of COVID-19 on patient's finances specified in medical record
1 Medical record specifies impact of COVID-19 on patient's finances

B. Impact of COVID-19 pandemic on patient's employment following cancer diagnosis

0 No impact of COVID-19 on patient's employment in medical record
1 Medical record specifies impact of COVID-19 on patient's employment

C. Impact of COVID-19 pandemic on patient's health insurance following cancer diagnosis

0 No impact of COVID-19 on patient's health insurances in medical record
1 Medical record specifies impact of COVID-19 on patient's health insurance

2. **Description**:

2.1. In **Items A-C**, record whether the medical record states there was any impact of the COVID-19 pandemic on the patient's finances, employment, or health insurance following cancer diagnosis. Only record information specifically indicating effects of COVID-19 or coronavirus.

2.2. To complete **Items A-C**, review the following sections of the medical record (when present): assessment and plan from oncology and palliative care clinician notes; oncology history from any clinician notes; palliative care notes; and chemotherapy and radiation therapy flow sheets

2.3. In **Item A** include any mention of the impact of COVID-19 pandemic on patient's finances, including mention of financial hardship, debt, or loss of income following cancer diagnosis

2.4. In **Item B** includes any mention of the impact of COVID-19 pandemic on patient's employment, including loss or change of job/employment following cancer diagnosis

2.5. In **Item C** includes any mention of the impact of COVID-19 pandemic on patient's health insurance, including loss or change of health insurance following cancer diagnosis.

PALLIATIVE CARE

ITEM A-17

1. **Code**: 1 digit each

A. Receipt of palliative care after cancer diagnosis

0 No palliative care provided (Code date as 00-00-0000)
1 Surgery (which may involve a bypass procedure) to alleviate symptoms, but no attempt to diagnose, stage, or treat the primary tumor is made.
2 Radiation therapy to alleviate symptoms, but no attempt to diagnose, stage, or treat the primary tumor is made.
3 Chemotherapy, hormone therapy, or other systemic drugs to alleviate symptoms, but no attempt to diagnose, stage, or treat the primary tumor is made.
4 Patient received or was referred for pain management therapy with no other palliative care.
5 Any combination of codes 1, 2, and/or 3 without code 4.
6 Any combination of codes 1, 2, and/or 3 with code 4.
7 Palliative care was performed or referred, but no information on the type of procedure is available in the patient record.
8 Palliative care was provided that does not fit the descriptions for codes 1–6.
9 It is unknown if palliative care was performed or referred; not stated in patient record (Code date as 00-00-0000).

B. Date palliative care FIRST appears in medical record after cancer diagnosis

MM-DD-YYYY
00-00-0000 – Palliative care not listed in medical record or not given.
99-99-9999 – Date not available for first listing of palliative care in medical record

C. Receipt of counseling/mental health services after cancer diagnosis

0 No counseling/mental health services
1 Counseling/mental health services received, related to cancer diagnosis or symptoms
2 Counseling/mental health services received, unrelated to cancer diagnosis or symptoms
3 Counseling/mental health services received, unknown if related to cancer diagnosis or symptoms
9 Unknown if counseling/mental health services received

PALLIATIVE CARE (cont)

D. Date counseling/mental health care services FIRST appears in medical record after cancer diagnosis

MM-DD-YYYY

00-00-0000 – Counseling/mental health care services not listed in medical record or not given.

99-99-9999 – Date not available for first listing of counseling/mental health care services in medical record

E. Receipt of hospice services/admission after cancer diagnosis

0 No hospice services/admission

1 Hospice services/admission received

9 Unknown if hospice services/admission received

F. Date hospice services/admission FIRST appears in medical record after cancer diagnosis

MM-DD-YYYY

00-00-0000 – Hospice services/admission not listed in medical record

99-99-9999 – Date not available for first listing of hospice services/admission in medical record

2. **Description**:

2.1. In **Item A**, record the type of palliative care provided. Only services provided on or after the date of cancer diagnosis should be included, no matter how long after diagnosis. This does not need to be first course. This item is based on NAACCR Item #3280. For this item, only record treatment that is specified in the medical record as palliative, non-curative, or performed/administered to address symptoms or make the patient more comfortable.

2.2. Surgical procedures, radiation therapy, or systemic therapy provided to prolong the patient's life by controlling symptoms, to alleviate pain, or to make the patient comfortable should be coded as palliative care. Palliative care including surgery, radiation therapy, or systemic therapy can be received in addition to potentially curative surgery, radiation therapy, or systemic therapy. Palliative care should be coded in Item A regardless of whether or not curative therapy is also received.

2.3. Palliative care is not used to diagnose or stage the primary tumor or for potentially curative treatment.

PALLIATIVE CARE (cont)

2.4. Do **not** code routine **pain management** following surgery or other treatment; **DO** code first course pain management for persistent pain.

2.5. Do not code **hospice** care in Item A. Hospice care should be coded in **Item E**. If the patient did not receive any care listed as palliative (as specified in 2.1, above) but was admitted to hospice, code Item A as 0.

2.6. In **Item B**, specify the date that palliative care was first mentioned in the medical record. If palliative care was not mentioned or not received, (i.e., Item A is coded 0 or 9), then code as the date as 00-00-0000.

2.7. In **Item C**, record whether counseling, psychotherapy, or other mental health care services were received on or after the date of cancer diagnosis. This includes pastoral care, chaplains, or any type of therapist. If any of these services are specified as related to cancer diagnosis, cancer treatment, or symptoms resulting from the cancer diagnosis (e.g., anxiety or depression associated with cancer, cancer treatment, or effects of cancer or cancer treatment), code this as "1". If all counseling/mental health services are specified as related to causes other than cancer diagnosis, treatment, or associated symptoms (e.g., counseling for a mental health condition that was present prior to the cancer diagnosis), code this as "2". If it is unknown whether these services are or are not associated with cancer diagnosis, treatment, or associated symptoms, code this as "3". If it is unknown whether any counseling or mental health care services were received, code this as "9". Do not code receipt of counseling/mental health services if these services were discussed or recommended but the patient did not receive this care. If the patient was referred for counseling/mental health services but it is unknown whether these services were received, code Item C as 9.

2.8. In **Item D**, specify the date that counseling/mental health care services were first mentioned in the medical record, whether or not they were specifically related to cancer diagnosis, treatment, or symptoms. If counseling/mental health care services were not mentioned or not done, (i.e., coded 9 or 0 in Item C), then code as 00-00-0000.

PALLIATIVE CARE (cont)

2.9. In **Item E**, code whether the hospice services or admission to hospice were received on or after the date of cancer diagnosis. Hospice services can be inpatient or outpatient and does not need to be first course. Only record as hospice services/admission medical care that is specifically identified as hospice. Do not code other palliative or end-of-life care as hospice if it is not identified as hospice. Do not code receipt of hospice services/admission if hospice services/admission were discussed or recommended but the patient did not receive this care. If the patient was referred to hospice care but it is unknown whether hospice services/admission were received, code Item E as 9.

2.10. In **Item F**, specify the date that hospice services/admission were first mentioned in the medical record. If hospice services/admission were not mentioned or not done, (i.e., coded 9 or 0 in Item E), then code as 00-00-0000.

NEXTGEN SEQUENCING (NGS)

ITEM A-18

1. **Code**: 0 – Not performed
   1 – Performed, no positive findings
   2 – Performed, only positive finding is variants of unknown significance (VUS)
   3 – Performed, only positive finding is high tumor mutation burden (TMB) OR VUS and TMB in combination
   4 – Performed, positive finding(s) other than variants of unknown significance (VUS) or high tumor mutation burden (TMB)
   5 – Performed, findings unknown
   9 – Unknown if performed/no mention

2. **Description**:

   2.1. Next-generation sequencing (NGS) is a method used to determine a portion of the nucleotide sequence of a tumor's genome. This technique utilizes DNA sequencing technologies that are capable of processing multiple DNA sequences in parallel. Examples of NGS tests include Foundation One, MSK IMPACT, Oncomine, Caris Molecular Intelligence, Trusight Oncology, Guandant360, and Myriad MYCHOICE. The type of NGS test used does not matter for this item, only whether or not NGS was performed.

   2.2. Code "0 – Not performed" if it was stated that the NGS test was not performed.

   2.3. Code "1 – Performed, no positive findings" when the NGS test was performed and there were not positive findings

   2.4. Code "2 – Performed, only positive finding is variants of unknown significance (VUS)" if the NGS test was performed and the only positive findings were "variants of unknown significance" (VUS)

   2.5. Code "3 – Performed, only positive finding is high tumor mutation burden (TMB) OR VUS and TMB in combination" if the NGS test was performed and the only positive findings were high tumor mutation burden (TMB) or **both** high tumor mutation burden (TMB) **and** variants of unknown significance (VUS)

NEXTGEN SEQUENCING (NGS) (cont)

2.6. Code "4 – Performed, positive finding(s) other than variants of unknown significance (VUS) or high tumor mutation burden (TMB)" if the NGS test was performed and there were positive findings other than high tumor mutation burden (TMB) and/or variants of unknown significance (VUS). This may include high TMB and/or VUS findings in addition to other findings.

2.7. Code "5 – Performed, findings unknown" when the NGS test was performed and the findings are unknown or not reported in the medical record.

2.8. Code "9 – Unknown if performed/no mention" if it is unknown whether the NGS test was performed, or there is no mention of it in the records.

SMOKING/TOBACCO USE

ITEM A-19

1. **Code**:

A. Number of cigarette packs per day

00.0 – Never smoked cigarettes
00.5 – Half a pack or less per day (≤0.5 ppd)
00.9 – More than half a pack to less than 1 pack per day (>0.5 to <1 ppd)
01.0 – 1 pack per day
02.0 – 2 packs per day
03.0 – 3 packs per day
...
...
55.5 – Light or occasional smoker
66.6 – Moderate smoker
77.7 – Heavy smoker
88.8 – Smoked, number of packs unknown
99.9 – Unknown, not stated whether patient smoked cigarettes

B. Non-cigarette tobacco use

0 – Never used non-cigarette tobacco products
1 – Reported use of e-cigarettes/vaping
2 – Reported use of cigars, pipes, and/or waterpipe tobacco/hookahs
3 – Reported use of smokeless tobacco products (chewing tobacco or snuff)
4 – Reported use of other non-cigarette tobacco products not listed above
5 – Reported use of multiple types of non-cigarette tobacco products
9 – Unknown, not stated whether patient ever used non-cigarette tobacco products

C. Number of years smoked or used other tobacco products

00 – Never smoked/used other tobacco products
01 – Smoked/used other tobacco products for one year
02 – Smoked/used other tobacco products for two years
...
...
88 – Smoked/used other tobacco products, number of years unknown
99 – Unknown, not stated whether patient smoked/used other tobacco products

SMOKING/TOBACCO USE (cont)

D. Pack Years

00 – Never smoked cigarettes and never used other tobacco products

01 – One pack-year history of cigarette smoking

02 – Two pack-year history of cigarette smoking

...

...

88 – Smoked cigarettes, pack years unknown

89 – >88 pack years

90 – Never smoked cigarettes but reported use of non-cigarette tobacco products (e-cigarettes, cigars, pipes, waterpipe, chewing tobacco, snuff, or other)

99 – Unknown, not stated whether patient smoked cigarettes or used non-cigarette tobacco products

E. Smoking/Tobacco Use Status at Diagnosis (applies to cigarette smoking and use of non-cigarette tobacco products)

0 – Never smoked/used any non-cigarette tobacco products

1 – Current smoker/non-cigarette tobacco user

2 – Former smoker/ non-cigarette tobacco user

9 – Unknown if ever used any form of tobacco

2. **Description**:

2.1. This item is to be coded for any information known about the patient's smoking/tobacco use status. Code the number of packs per day, non-cigarette tobacco use, the number of years smoked and/or the pack years smoked as well as smoking/tobacco use status at diagnosis. If the patient never smoked cigarettes or used other forms of tobacco, code "00.0" in Packs Per Day; "0" in Non-cigarette tobacco use; code the Number of Years Smoked and Pack Years as "00"; and code Smoking Status at Diagnosis as "0". When multiple values for years, packs, or pack-years of smoking history are listed, record the lowest value presented.

2.2. If the patient smoked "half a pack or less per day," then code "00.5" in packs per day. If the record notes the patient smoked "less than a pack per day," then code "00.9" in packs per day.

SMOKING/TOBACCO USE (cont)

2.3. There are 20 cigarettes per pack. If the record states that the individual smoked 40 cigarettes per day for 10 years, then code 02.0 packs in the packs per day and 10 in number of years smoked; not 40.0 in the packs per day and 10 in the number of years smoked. Do not calculate pack years; code "88 – smoked pack years unknown" if number of pack-years smoked is not provided in the medical record. Record pack years only if it is given in the medical record.

2.4. If the patient is known to have smoked, but the number of packs is unknown, code "88.8- Smoked, number of packs unknown."

2.5. If the record does not give the number of cigarettes smoked, but instead states that the person was a heavy smoker, code "77.7 – Heavy smoker". A moderate smoker would be coded as "66.6" and a light smoker would be coded as "55.5".

2.6. If it is unclear or if it is not mentioned in the record whether the patient smoked, then code "99.9 - Unknown, not stated whether patient smoked" in packs, "99" in years and pack years, and "9" in Smoking Status at Diagnosis.

2.7. If the patient used non-cigarette tobacco product (either by themselves or in addition to cigarette smoking), code the appropriate information in Item B. If the patient used e-cigarettes vaping product, code as 1. If the patient used cigars, pipes, and/or waterpipes/hookahs, code as 2. If the patient used smokeless tobacco products including chewing tobacco or snuff, code as 3. If the patient used other non-cigarette tobacco products not listed, code as 4. If the patient used multiple types of non-cigarette tobacco products, code as 5. If it is unknown whether the patient used non-cigarette tobacco products, code as 9.

2.8. In **Item C**, "Number of years smoked or used other tobacco products", code as "00" if the patient never smoked or used other tobacco products. If the patient is known to have smoked cigarettes, code the number of years smoked if known; if the number of years he/she smoked is unknown, then code "88 - Smoked, number of years unknown". If the patient only used non-cigarette tobacco products, record the number of years non-cigarette tobacco products were used or code "88" if the number of years used is unknown. If the patient smoked cigarettes and used non-cigarette tobacco products, record only the number of years smoked cigarettes or code "88" if the number of years smoked cigarettes is unknown. If it is unknown whether the patient ever smoked/used non-cigarette tobacco products, code this item as "99".

2.9. If the record states, "The patient has been a heavy smoker for many years," without additional details, then code "77.7 – Heavy smoker" in packs (Item A), and "88 – Smoked cigarettes, number of years unknown" in years (Item C).

SMOKING/TOBACCO USE (cont)

2.10. If the record states number of pack years smoked, code this number in the "Pack Years" item (**Item D**). Code this item as "88 – Smoked cigarettes, number of pack years unknown" if the number of pack years is not specified. If the number of pack years smoked is 88 or more, code this item as "89 – >88 pack years." If the patient never smoked cigarettes but used other tobacco products, code Item D as "90". If it is unknown whether the patient ever smoked cigarettes or used other tobacco products, code Item D as "99". If the patient never smoked or used other tobacco products, code Item D as "00".

2.11. Under "Smoking/Tobacco Use Status at Diagnosis" (**Item E**), code whether the patient never smoked cigarettes/used any non-cigarette tobacco products; was currently using cigarettes/ non-cigarette tobacco products at cancer diagnosis; or had previously used cigarettes/ non-cigarette tobacco products but was no longer doing so at cancer diagnosis. Code this item as "9" if it is unknown whether the patient ever smoked cigarettes or used non-cigarette tobacco products.

SECONDHAND SMOKE EXPOSURE

ITEM A-20

1. **Code**: 0 – Not exposed to secondhand smoke
   1 – Exposed to secondhand smoke
   9 – Unknown/not mentioned whether exposed to secondhand smoke

2. **Description**:

   2.1. Secondhand smoke exposure (also known as passive smoke exposure or passive smoking) is a risk for developing several serious diseases. Secondhand smoking occurs when one or more individuals in the patient's environment smokes. Whether or not the patient smokes, (s)he is forced to inhale the secondhand smoke when (s)he breathes. Patients may be exposed to secondhand smoke in their home, workplace, or in public places.

   2.2. Secondhand smoke exposure is coded separately from "active" smoking/tobacco use history (Item A-19). That is, even when a patient is listed as a current smoker, if they are also described as having secondhand smoke exposure, that should be recorded separately. However, do not code a current smoker/tobacco user as having secondhand smoke exposure only because they are exposed to their own smoking. Patients should be coded as having secondhand smoke exposure only if exposed to someone else's smoking, whether or not they themselves smoke.

   2.3. Code "0 – Not exposed to secondhand smoke" if the record indicates that the individual was not exposed to secondhand smoke.

   2.4. The patient would be considered "exposed" if (s)he reports working in an environment that permits smoking, such as a casino or bar that permits smoking. This should be coded as "1 – Exposed to secondhand smoke".

   2.5. A statement such as, "Husband/wife is a smoker" is **not** sufficient to indicate that the patient was exposed to secondhand smoke. Only if there is information stating that another individual smokes in the presence of the patient should this be coded as "1 – Exposed to secondhand smoke".

   2.6. If it is unclear or not mentioned whether the patient was exposed to secondhand smoke, then code "9 – Unknown, not mentioned whether exposed to secondhand smoke".

FAMILY HISTORY OF CANCER OF THE SAME SITE

ITEM A-21

1. **Code**: 0 – No cancer of the same site reported among first-degree relatives
   1 – Cancer of the same site reported among first-degree relatives
   9 – Unknown/not mentioned whether cancer of the same site reported among first-degree relatives

2. **Description**:

   2.1. A family history cancer of the same site (i.e., breast cancer among individuals with breast cancer or colorectal cancer among individuals with colorectal cancer) may be a risk factor for hereditary syndromes or genetic markers associated with increased risk of cancer. A patient's FAP diagnosis is not enough to code this item as "1".

   2.2. Code "0 – No cancer of the same site reported among first-degree relatives" if the medical record indicates that there is no history (i.e., previous diagnosis) of cancer of the same site among the patient's first-degree relative (parents, siblings, or children).

   2.3. Code "1 – Cancer of the same site reported among first-degree relatives" if the medical record indicates that there is a history (i.e., previous diagnosis) of cancer of the same site among the patient's first-degree relative (parents, siblings, or children).

   2.4. Code "9 – Unknown/not mentioned whether cancer of the same site among first-degree relatives" if the medical record indicates that it is unknown whether there is a history (i.e., previous diagnosis) of cancer of the same site among the patient's first-degree relative (parents, siblings, or children). Also code as "9" if the medical record does not state whether or not there is a history of cancer of the same site among the patient's first-degree relatives.

CO-MORBID CONDITIONS

ITEM C

1. **Code**: List all co-morbid conditions noted on the record at the time of initial diagnosis and during first course of treatment. These may be noted on the face sheet, discharge summary, nurse's notes, physician notes and/or the history and physical. **Please check the entire record.** Symptoms due to cancer or side-effects from cancer treatment are not considered co-morbid conditions. Comorbidities are conditions that were present **prior to the diagnosis** of cancer or are not related to cancer or cancer therapy.

2. **Description**:

   2.1. Co-morbid conditions: List all medical conditions, including histories of disease or health problems.

   2.2. If you run out of room in the co-morbid fields in POC SEER*Abs, list the others in the abstractor's comments.

   2.3. If the condition was reported as a history of, be certain that "HISTORY" is recorded with the condition.

   2.4. **This item is to record co-morbidities, not side effects of treatment.** A medical condition that is related to the cancer or cancer therapy should not be included.

   2.5. If there are no comorbidities, enter "**None**" in the first field only and **leave the remaining fields blank.** Do not enter "None" in any of the fields except the first comorbidity.

ABSTRACTOR ID

1. **Code**: Provide the assigned abstractor ID.

2. **Description**:

   2.1. Please code the 5-digit coder identification number provided to the individuals coding the abstract.

   2.2. If there are multiple abstractors, please include the identification of the individual consolidating the abstracts.

DATE ABSTRACTED

1. **Code**: mmddyyyy

2. **Description:**

   2.1. Code the month, day and year that the final abstracting was completed. This might be the final abstracting of the hospital medical record, or it might be the date the physician verification form was completed.

   2.2. We are collecting treatment data, so it is important to know how long the patient was followed. For example, we are much less likely to find much treatment information for a patient whose DATE ABSTRACTED was 1 month following diagnosis. Compare this to an individual whose abstract was completed 18 months following diagnosis. This patient is much more likely to have been treated, perhaps with several regimens - e.g., chemotherapy and radiation.

   2.3. This is NOT the last date specified in the medical record. It is the date when the abstraction form was completed, which may involve review of medical records from multiple sources, or the date the physician verification form was received or the office visited.

POC DATA ACQUISITION MANUAL

SECTION IV

BREAST CANCER DATA SET

SECTION IV – BREAST CANCER DATA SET

CONTENTS

DATE OF FIRST POSITIVE BIOPSY/ASPIRATION PROCEDURE

ITEM B-1

1. **Code** MM-DD-YYYY
00-00-0000-No biopsy/aspiration done.

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
.	.	
12 - December	31	
77	77	7777-Patient or guardian refused
95	95	9595-Recommended, not performed
96	96	9696-Recomm., unknown if performed
97	97	9797-Unknown if performed
99 - Month Unk	99 - Day Unk	9999-Year Unknown

2. Description

2.1. This item refers to the date of the first positive biopsy or aspiration procedure. This may be a biopsy/aspiration of the primary site, lymph node or metastatic site that confirmed the diagnosis of breast cancer. Code the date the specimen was obtained (NOT the date of the pathology/cytology report).

2.2. If the biopsy/aspiration was performed on the same day as definitive surgery, the biopsy date and the Date of Cancer Directed Surgery to Primary Site (Item B-3) will be the same. The first positive biopsy/aspiration may have been done as an outpatient procedure but must be no later than the Date of First Cancer-Directed Surgery to Primary Site.

2.3. If there was no biopsy/aspiration done prior to the time of surgical resection, code "00- 00-0000".

2.4. Code “99-99-9999” if it is **KNOWN** that the patient had a biopsy/aspiration but the day, month and/or year given cannot be determined. If the exact date of the first positive biopsy/aspiration is unknown, code an estimate (e.g., if in history and physical, the physician states the patient had a biopsy two weeks ago, code date of biopsy as 14 days prior to date of admission). Coding closest approximation is preferable to coding unknown.

DATE OF FIRST POSITIVE BIOPSY/ASPIRATION PROCEDURE (cont)

2.5. Code “77-77-7777” if patient or the patient’s guardian refused biopsy/aspiration.

2.6. Code “95-95-9595 – Recommended, not performed” when the records indicate that biopsy/aspiration was recommended but was not performed for a reason other than refusal.

2.7. Code “96-96-9696 – Recommended, unknown if performed” if the records indicate that the biopsy/aspiration was recommended but it is unclear whether the patient had the biopsy.

2.8. If it is unknown whether or not a biopsy/aspiration was performed, code “97-97-9797”.

2.9. Histologic diagnoses are based upon microscopic examination of tissue specimens, frozen section, and surgical specimens. Cytologic diagnoses are based upon microscopic examination of cells instead of tissues. Examples are breast aspiration cytology and cytologic examination of breast secretions.

DATE OF PATHOLOGIC CONFIRMATION REPORT

ITEM B-2

1. **Code** MM-DD-YYYY
00-00-0000-No biopsy/aspiration done.

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
12 - December	31	
77	77	7777-Patient or guardian refused
95	95	9595-Recommended, not performed
96	96	9696-Recomm., unknown if performed
97	97	9797-Unknown if performed
99 - Month Unk	99 - Day Unk	9999-Year Unknown

2. Description

2.1. This item refers to the date of the REPORT of the pathologic confirmation of breast cancer by the biopsy or aspiration coded in Item B-1. This is NOT the date the specimen was obtained. This is NOT the date the breast cancer was suspected. If the pathology department has "real-time" reporting (the reports are sent electronically as they are completed to the physicians' offices), then the date of the report may be the same as the date of pathologic confirmation.

2.2. If the patient or guardian refused the biopsy, code "77-77-7777- Patient/guardian refused." This is unlikely for these patients because the diagnosis must be pathologically confirmed.

2.3. If the biopsy/aspiration was recommended but it is unknown if it was performed, code "96-96-9696 – Recommended, unknown if performed." This is unlikely for these patients because the diagnosis must be pathologically confirmed.

2.4. If it is unknown if biopsy/aspiration was offered or performed, code "97-97-9797 – Unknown if offered or performed." This is unlikely for these patients because the diagnosis must be pathologically confirmed.

2.5. If the exact date of the first positive biopsy/aspiration is unknown, then estimate. For example, if in history and physical, the physician states the patient had a biopsy two weeks ago, then code the date of biopsy as 14 days prior to date of admission. Coding closest approximation is preferable to coding unknown. If an estimate cannot be made, then code "99-99-9999". If the pathology department has real-time reporting, record the date the report was received.

PRIMARY SITE SURGERY AND DATE

ITEM B-3

1. Code **Surgery Code**: 00-99
Refer to *SEER Program Coding and Staging Manual 2018, Appendix C.*

Surgery Date: MM-DD-YYYY
00-00-0000 -- No Surgery

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
12 - December	31	
77	77	7777-Patient or guardian refused
95	95	9595-Recommended, not performed
96	96	9696-Recomm., unknown if performed
97	97	9797-Unknown if performed
99 - Month Unk	99 - Day Unk	9999-Year Unknown

2. **Description**:

2.1. Enter the site-specific surgery code as defined in SEER Program Coding and Staging Manual 2018, Appendix C. This is only for the initial (first course) surgery to the primary site.

2.2. Enter the date on which the most definitive surgery of the primary site was performed. Code "00-00-0000" if no surgery to the primary site was performed.

2.3. If the patient or patient's guardian refused surgery to the primary site, then code "77-77- 7777 – Patient/guardian refused".

2.4. Code "95-95-9595 – Recommended, not performed" when the records indicate that surgery was recommended, but was not performed for a reason other than refusal.

2.5. If surgery to the primary site was recommended, but it is unknown if it was performed, then code "96-96-9696 – Recommended, unknown if given".

2.6. If it is unknown whether or not the patient had surgery to the primary site, then code "97-97-9797-Unknown if performed".

PRIMARY SITE SURGERY AND DATE (cont)

2.7. Code “99-99-9999” if it is **KNOWN** that the patient had surgery to the primary site, but the day, month and/or year given cannot be determined. If the exact date of the surgery is unknown, then code an estimate. For example, if in history and physical, the physician states the patient had surgery two weeks ago, then code the date of surgery as 14 days prior. Coding the closest approximation is preferable to coding unknown.

PATHOLOGICAL MARGINS

ITEM B-4

1. **Code** 0 – No resection/surgery performed or only biopsy performed
   1 – Margins of resection pathologically free of tumor
   2 – Tumor at margins of resection, or residual tumor in area of primary
   3 – Margins not stated in pathology report--surgeon indicates no residual tumor
   8 – Resection recommended unknown if performed
   9 – Unknown, not stated

2. **Description**:

   2.1. This item records the pathological margin status following the most definitive surgery performed after diagnosis (Item B-3). This refers to pathological margins only for the initial surgery at the primary site.

   2.2. Code "0 – No resection/surgery performed" when no cancer-directed surgery or only a biopsy was performed.

   2.3. Code "1 – Margins of resection pathologically free of tumor" when the pathologist reported no residual tumor in the area of the primary site.

   2.4. Code "2 – Tumor at margins of resection, or residual tumor in area of primary" when the pathologist reported involvement of the surgical resection margins.

   2.5. Code "3 – Margins not stated in pathology report--surgeon indicates no residual tumor" when the pathology report does not document the pathologic margin status, but the surgeon states in the operative report that no tumor was left in the area of the primary site.

   2.6. Code “8 – Resection recommended unknown if performed” if the physician recommended surgery, but it is unknown whether it was performed.

   2.7. Code "9 – Unknown, not stated" when there is no information in the pathology report regarding pathologic margins and the surgeon does not document margin status in the operative report.

SIZE OF PRIMARY TUMOR

ITEM B-5

1. Code

000 – No mass/tumor found

001 – 1 mm or described as less than 1 mm

002-988 – Exact size in millimeters (2 mm to 988 mm)

989 – 989 millimeters or larger

990 – Microscopic focus or foci only and no size of focus is given

996 – Mammographic/xerographic diagnosis only, no size given; clinically not palpable

998 – Diffuse

999 – Unknown; size not stated/not documented in patient record; Size of tumor cannot be assessed; Not applicable

Type of Staging (see notes below for further guidance)

Clinical – size of primary tumor **before** any treatment

Pathologic – size of primary tumor that has been resected

2. Description:

2.1. Refer to the 2018 SEER Program Coding and Staging Manual for complete details. **Code information about both clinical and pathologic tumor size for each patient.** Code the tumor size recorded prior to initiation of therapy. This information should not be taken from autopsy records. When multiple masses are present, code the longest diameter. Code the exact value from 001 (00.1 cm) through 989 (98.9 cm) if available. Be certain that the units are correctly recorded. Do not confuse mm and cm; 5 mm and 5 cm are markedly different and have different therapies.

2.2. For clinical tumor size, record the largest measurement of the primary tumor from the priority list below before any form of treatment. Use information available within four months of the date of diagnosis, in the absence of disease progression when no treatment is administered.

Record largest size according to the following priority order:

1. Operative report from surgical exploration without resection
2. Imaging-guided tissue biopsy (i.e., incisional biopsy done under imaging)
3. Diagnostic imaging
4. Physical exam

SIZE OF PRIMARY TUMOR (cont)

Note 1: Tumor size noted in a resection operative report is a clinical tumor size, and not a pathologic tumor size.

Note 2: Check the Clinical History/Clinical Impression/Clinical Information section of the pathology report for information on the clinical size of the tumor.

Note 3: A smaller size from a higher priority source should be coded.

2.3. For pathologic tumor size, code the size as recorded from the surgical resection specimen as noted in the pathology report or the synoptic/CAP protocol before adjuvant treatment. Code the largest size of the primary tumor (invasive portion) measured on the surgical resection specimen when **surgery is administered as part of the first course treatment.**

a. Code the size from the synoptic report (also known as CAP protocol or pathology report checklist) when there is a discrepancy among tumor size measurements in the various sections of the pathology report.

b. Use final diagnosis, microscopic, or gross examination, in that order, when only a pathology report is not available.

Example 1: CT shows 3.5 cm mass; the pathology report from the surgery states that the same mass is malignant and measures 2.8 cm. Record tumor size as 028 (28 mm).

Example 2: Pathology report states tumor is 2.1 cm x 3.2 cm x 1.4 cm. Record tumor size as 032 (32 mm).

Note: The pathologic tumor size is recorded from the surgical resection specimen when surgery (including after neoadjuvant therapy) is administered as part of the first course treatment.

2.4. If the tumor was palpable, but no size is documented, then code "999 - Not stated".

2.5. When there was a biopsy followed by a more extensive resection with residual tumor removed, code the largest tumor size recorded. Do not add the dimensions of the individually excised tumor tissue together.

2.6. If the tumor was only diagnosed by mammography/xerography with no size given and is not clinically palpable, code “996-Mammography/xerography diagnosis only with no size given (clinically not palpable)”.

SIZE OF PRIMARY TUMOR (cont)

2.7. When the tumor is multi-focal or when multiple tumors are reported as a single primary, code the size of the largest invasive tumor, or the largest in situ tumor if all tumors are in situ. Code the exact value in millimeters from 001 (00.1 cm) through 988 (98.8 cm).

2.8. Code only the size of the primary tumor. Do not code the size of other structures like cysts.

2.9. If there is no tumor or mass found after neoadjuvant therapy code pathologic tumor size "000 - No mass/tumor found."

2.10. Refer to the 2018 SEER Program Coding and Staging Manual for rules on rounding measurements, less than/greater than statements, priority order of reports and discrepancies between reports.

3. **Examples**:

A tumor of 0.9 cm (9 mm) in size is coded "009".

A tumor of 5.5 cm (55 mm) in size is coded "055".

A tumor of 8.3 cm (83 mm) in size is coded "083".

A tumor of 10.0 cm (100 mm) in size is coded "100".

METHOD OF MEASUREMENT OF PRIMARY TUMOR SIZE

ITEM B-6

1. **Code**
   0 - No mass; no tumor found
   1 - Microscopic focus or foci only
   2 - Mammography/xerography measurement
   3 - Ultrasound
   4 - Pathological specimen
   5 - Other (specify _____)
   9 - Size unknown/not stated

2. Description:

2.1. Code the method used to determine the tumor size coded in Item B-5. This will most often be the pathological specimen; method of measurement of pathologic tumor size is preferred for this item. However, if this is unavailable, other methods of measurement may be available. Use the CS Tumor Size coding hierarchy in the SEER Program Coding and Staging Manual 2018, Appendix C. https://seer.cancer.gov/archive/manuals/2018/appendixc.html

2.2. Code "0" when no mass or tumor is found. Item B-5 (Tumor Size) should be coded as "000".

2.3. Code "1" when only microscopic foci are found. Item B-5 (Tumor Size) should be coded as "990".

2.4. Code "2" when the measurement is from a mammogram or xerographic measurement. Item B-5 (Tumor Size) should be coded as the exact tumor size when a size is given or "996" when the tumor size is not given.

2.5. Code "3" when the measurement is taken at the time of an ultrasound.

2.6. The preferred measurement is one taken from the specimen obtained when the tumor is removed. This can usually be found in the path report. This measurement is preferred over others. Use the SEER coding hierarchy.

2.7. Code "9" when the size is unknown or not stated for palpable tumors. Item B-5 (Tumor Size) should be coded as "999".

METHOD OF TUMOR DETECTION

ITEM B-7

1. **Code**: 1 – Signs/symptoms
   2 – Physician's physical exam
   3 – Self-discovered
   4 – Screening Mammography
   5 – Spouse or partner
   6 – Other, specify_____
   9 – Unknown/Not specified

2. **Description**:

   2.1. Code the method by which the tumor was initially detected. This refers to the first notice of a breast tumor, NOT the diagnostic procedures that followed.

   2.2. Code "1 – Signs/symptoms" when the patient had signs/symptoms such as changes in appearance (color, shape, or size) of the breast or nipple, nipple discharge other than breast milk, breast pain/discomfort.

   2.3. Code "2 – Physician's physical exam" when the patient's breast abnormality was initially detected by a routine breast exam performed by her physician.

   2.4. Code "3 – Self-discovered" when the patient found a breast abnormality herself while doing a breast self-exam or while in the shower.

   2.5. Code "4 – Screening Mammography" when the tumor was first seen on a routine screening mammogram.

   2.6. Code "5 – Spouse or Partner" if the woman's spouse or partner discovered a mass.

   2.7. Code "6 – Other, specify" when the tumor was discovered by some other means. Specify the method of discovery.

   2.8. Code "9 – Unknown/Not specified" when it cannot be determined from the records how the tumor was initially detected.

REGIONAL NODE DISSECTION

ITEM B-8

1. **Code**: 0 – No nodal dissection
   1 – Axillary nodal dissection only
   2 – Sentinel node biopsy only
   3 – Sentinel node biopsy followed by axillary node biopsy and/or dissection
   4 – Internal mammary node biopsy or excision only
   5 – Both axillary and internal mammary node biopsy or excision
   6 – Other, specify_____
   8 – Node dissection performed, type unknown
   9 – Unknown/Not stated

NOTE: THESE ARE NOT THE SEER CODES.

2. **Description**:

2.1. Code "0 – No nodal dissection" when the woman did not have her nodes dissected/biopsied. If this item is coded as "0", then Item B-9 (Number of Regional Nodes Positive) should be coded as "98" and Item B-10 (Nodes Examined) should be coded "00".

2.2. Code "1 – Axillary nodal dissection only" when the surgeon performed the traditional axillary lymph node dissection.

2.3. Code "2 – Sentinel node biopsy only" when the surgeon injected dye or radioactive material into the tumor and removed the node(s) that took up the dye or radioactive material.

2.4. Code "3 – Sentinel node biopsy followed by axillary node biopsy and/or dissection" when the surgeon performed a sentinel node biopsy, but followed it with an axillary node biopsy or dissection. If the nodes were positive on frozen section, additional nodes might be removed through an axillary node dissection.

2.5. Code "6 – Other, specify" when a different type of nodal dissection is performed. Specify the type of nodal dissection.

2.6. Code "9 – Unknown/Not stated" if it cannot be determined whether a nodal dissection/biopsy was performed. If this item is coded as unknown, then B-9 (Number of Regional Nodes Positive) & Item B-10 (Nodes Examined) would also be unknown.

NUMBER OF REGIONAL LYMPH NODES POSITIVE and EXAMINED

ITEM B-9
ITEM B-10

1. **Code:** **B-9 – Number of positive regional lymph nodes**
   00 – All examined nodes negative
   01 – One positive node
   02 – Two positive nodes
   ...
   ...
   90 – 90 or more positive nodes
   95 – Positive aspiration or core biopsy of lymph node(s) performed
   97 – Positive nodes documented – number unspecified
   98 – No nodes examined
   99 – Unknown, not stated

   B-10 – Number of regional lymph nodes examined
   00 – No nodes examined (no nodal dissection performed)
   01 – One node examined
   02 – Two nodes examined
   ...
   ...
   90 – 90 or more examined
   95 – No regional nodes removed, but aspiration or core biopsy of regional nodes performed
   96 – Regional lymph node removal documented as sampling and number of nodes unknown/not stated
   97 – Regional lymph node removal documented as dissection and number of nodes unknown/not stated
   98 – Regional lymph nodes surgically removed but number of nodes unknown/not stated and not documented as sampling or dissection; nodes examined but number unknown
   99 – Unknown/not stated whether nodes examined

2. **Description**:

   2.1. For information on which nodes are considered regional, refer to the AJCC Staging Manual 8th Edition.

NUMBER OF REGIONAL LYMPH NODES POSITIVE & EXAMINED (cont)

2.2. Record the number of regional nodes examined by a pathologist and found to contain metastasis. These should be coded based only on data from lymph nodes that are pathologically examined, not from lymph nodes that are clinically examined or examined using imaging procedures.

2.3. Code the number of regional lymph nodes positive in Item B-9 and the number of regional lymph nodes examined in Item B-10. Include all node dissections done during the first course of therapy.

2.4. If more than one dissection was done during the first course of treatment, code the total number of lymph nodes positive and examined.

2.5. If the number of nodes positive was 90 or greater, code Item B-9 as "90". If the number of nodes examined was 90 or greater, code Item B-10 as "90".

2.6. If lymph nodes were known to be positive, but the exact number positive is unknown, code Item B-6 as "97".

2.7. If lymph nodes were known to be positive, but the exact number positive is unknown and the exact number examined is unknown, code Item B-9 as "97" and Item B-10 as "96", "97", or "98".

2.8. If no regional lymph nodes were positive, and the number examined is at least one, but the total is unknown, code Item B-9 "00" and B-10 "96", "97" or "98".

2.9. If no regional node dissection was done or no regional lymph nodes were removed/examined, code Item B-9 "98" and B-10 "00".

2.10. If it is unknown or not stated whether any nodes were either positive or examined, then code "99" in Items B-9 and B-10.

2.11. If regional lymph nodes were aspirated, code Item B-9 either "00" for negative or "95" if positive and code Item B-10 as "95".

2.12. When there is a difference in the number of nodes positive and/or examined between the body of the pathology report and the final medical report, code the information from the final medical report.

PROPHYLACTIC CONTRALATERAL MASTECTOMY / OOPHORECTOMY

ITEM B-11

1. **Code**: Prophylactic Contralateral Mastectomy

   0 – No prophylactic contralateral mastectomy

   1 – Prophylactic contralateral mastectomy

   9 – Unknown/no mention whether prophylactic contralateral mastectomy was performed

   Prophylactic Oophorectomy or Prophylactic Salpingo-oophorectomy

   0 – No prophylactic oophorectomy or prophylactic salpingo-oophorectomy

   1 – Prophylactic oophorectomy or prophylactic salpingo-oophorectomy

   9 – Unknown/no mention whether oophorectomy or prophylactic salpingo-oophorectomy was performed

2. **Description**:

   2.1. A prophylactic contralateral mastectomy is a mastectomy on the contralateral (opposite) breast although there is no indication that there is cancer in that breast. If a patient had a mastectomy on the contralateral (opposite) breast because the contralateral (opposite) breast had cancer, this would not be prophylactic and the patient would be ineligible for the POC study due to simultaneous diagnosis. Similarly, if the patient received a contralateral mastectomy but it is not clear if there was cancer in the removed breast (i.e., it is unknown whether the patient had simultaneously diagnosed primary cancers in both breasts), the patient would be ineligible for the POC study. Prophylactic contralateral mastectomy should be recorded for a procedure that occurred at any time following the initial cancer diagnosis. However, if there is a new cancer diagnosed in the contralateral breast after the initial cancer diagnosis (either a new primary breast cancer or a metastasis of the original breast cancer), this should **not** be coded as a prophylactic contralateral mastectomy.

   2.2. Prophylactic oophorectomy is surgery to remove the ovaries and sometimes fallopian tubes (salpingo-oophorectomy) before disease develops in the ovaries. Removing the ovaries lowers the amount of estrogen in the body, which may slow the growth of some types of breast cancer. It is also called risk-reducing oophorectomy. Prophylactic oophorectomy or prophylactic salpingo-oophorectomy should be recorded for a procedure that occurred at any time following the initial breast cancer diagnosis. However, if there is a new cancer diagnosed in the ovaries or fallopian tubes after the initial breast cancer diagnosis (either a new primary cancer or a metastasis of the original breast cancer), this should not be coded as a prophylactic oophorectomy. Code “0” is used when there was no prophylactic procedure performed (code separately for each data item).

PROPHYLACTIC CONTRALATERAL MASTECTOMY / OOPHORECTOMY (cont)

2.3. Code “1” is used when the patient received the prophylactic procedure (code separately for each data item)

2.4. Code “9- Unknown/no mention” if it is unknown whether the prophylactic procedure was performed or it was not mentioned.

METASTASIS AT DIAGNOSIS

ITEM B-12

1. **Code**: 0 – No evidence of metastasis at the site
   1 – Yes, only pathologic confirmation of metastasis at the site
   2 – Yes, only clinical confirmation of metastasis at the site
   3 – Yes, both clinical and pathologic confirmation of metastasis at the site
   9 – Unknown if metastasis at the site

   Sites
   Lung
   Distant lymph node(s)
   Bone
   Liver
   Brain/nervous system
   Peritoneal cavity (pelvis and abdomen)
   Other (Specify pathologic) _____
   Other (Specify clinical) _____
   Other (Specify clinical and pathologic) _____

2. **Description**:

   2.1. Refer to the 2018 SEER Program Coding and Staging Manual for complete details. Code information about metastasis identified at the time of diagnosis. Information about metastatic involvement may be clinical or pathologic. These codes are NOT the codes from the SEER Manual—the POC codes are expanded to capture clinical and pathologic information. This information should not be taken from autopsy records.

   2.2. Code "0 – No" if there is no evidence of distant metastasis in the medical record or imaging reports.

   2.3. Code "1 – Yes, only pathologic confirmation of metastasis at the site" when there is pathologic but no clinical evidence of distant metastasis. Pathologic confirmation requires a biopsy positive for cancer at the metastatic site and may be reported in a pathology report or surgical records.

   2.4. Code "2 – Yes, only clinical confirmation of metastasis at the site" when there is clinical but no pathologic evidence of distant metastasis. Clinical confirmation can be derived from documentation in patient history or physical examination and imaging reports. However, imaging of distant organs is not required.

METASTASIS AT DIAGNOSIS (cont)

2.5. Code "3 – Yes, both clinical and pathologic confirmation of metastasis at the site" when there is clinical and pathologic confirmation of distant metastasis.

2.6. Code "9 - Unknown" if it is unknown whether there is metastasis at the site. If there is no information about whether the patient had any metastatic disease, all sites should be coded "9 – Unknown."

2.7. There are three "Other (Specify)" text fields. It is possible there may be multiple sites of metastasis to record. Enter all sites confirmed pathologically in "Other (Specify pathologic)". Enter all sites confirmed clinically in "Other (Specify clinical)". Enter all sites with both pathologic and clinical confirmation in "Other (Specify clinical and pathologic)".

2.8. If the record indicates that there is "metastatic disease" but does not provide any information on the site of metastasis, code all sites as "9 – unknown" and code Other (Specify) as "1 – Yes." Enter "other site" in the text field. Choose the appropriate Other Specify field for clinical only, pathologic only, or both clinical and pathologic.

2.9. If there is no evidence of metastases at any site, all sites should be coded as "0 – No."

2.10. Refer to the 2018 SEER Program Coding and Staging Manual for interpretation of ambiguous terminology.

3. Specifics

3.1. Metastasis to all sites may be a single metastatic lesion or multiple in the same site.

3.2. Bone involvement does **NOT** include bone marrow involvement.

3.3. Distant lymph node involvement does **NOT** include regional lymph nodes.

HER-2 (c-erbB-2, her2/neu): IHC

ITEM B-13

1. **Code**: 00 – Negative
   01 – 1+
   02 – 2+
   03 – 3+
   92 – Equivocal IHC, value not reported
   93 – Equivocal, value not reported, type IHC or in situ hybridization (ISH) test unknown
   94 – Positive IHC, specific value not reported
   95 – Positive test, type IHC or ISH test unknown, specific value not reported
   96 – Negative IHC, specific value not reported
   97 – Negative test, type IHC or ISH test unknown, specific value not reported
   98 – Not Done
   99 – Unknown/No mention

2. Description

2.1. HER-2 (also called her2/neu, c-erbB-2, human EGF receptor 2, and human epidermal growth factor receptor 2) is a protein involved in normal cell growth. HER-2 may be made in larger than normal amounts by some types of cancer cells; this may cause cancer cells to grow more quickly. Determining the amount of HER-2 may help plan treatment.

2.2. Record the results of the measurement of HER-2. When testing for HER-2, the immunohistochemical (IHC) test may be used alone or followed by an ISH test including FISH (fluorescence in situ hybridization), SPoT-Light HER2 CISH (subtraction probe technology chromogenic in situ hybridization), or Inform HER2 Dual ISH (inform dual in situ hybridization) test. Please record the IHC in Item B-13 and the ISH in Item B-14. (It is possible that the HER-2 value may be entered into the record as 'Herceptest').

2.3. Code "00 - Negative" when the record indicates the test for her2/neu results were negative with the value given.

2.4. Code "01" when the IHC test value was reported as 1+.

2.5. Code "02" when the IHC test value was reported as 2+.

2.6. Code "03" when the IHC test value was reported as 3+.

HER-2 (c-erbB-2, her2/neu): IHC (cont)

2.7. Code “92” when the results of the her2/neu by IHC were stated as being equivocal and no value is given.

2.8. Code “93” when the results of the HER-2 value is equivocal, but the type of test (IHC or ISH) is unknown. Item B-14 should also be coded “93”.

2.9. Code “94” when the HER-2 test is reported as positive by IHC, but the value is not reported.

2.10. Code “95” when the record indicates that the test for her2/neu was positive, but the type of test (IHC or ISH test) is unknown and the test result value is not reported. Item B-14 should also be coded “95”.

2.11. Code “96” when the report states only that the IHC test was negative and does not provide the actual value.

2.12. Code “97” when the test is reported as negative, but the type of test (IHC or ISH) is unknown and the test result value is not reported. Item B-14 should also be coded “97”.

2.13. If the test was not done, then code “98 - not done”.

2.14. If it is unknown whether the test was ordered or there is no mention, then code “99 – Unknown/no mention”.

HER-2 (c-erbB-2, her2/neu): *IN SITU* HYBRIDIZATION (ISH)

ITEM B-14

1. **Code**: 0.1…9.0 – Actual value
   9.1 – 9.1 or higher
   92 – Equivocal by ISH, value not reported
   93 – Equivocal, value not reported, type IHC or ISH unknown
   94 – Positive by ISH, value not reported
   95 – Positive test, type IHC or ISH unknown, value not reported
   96 – Negative ISH, value not reported
   97 – Negative test, type IHC or ISH unknown, value not reported
   98 – Not Done
   99 – Unknown/no mention

   ISH Tests:

   - Fluorescence *in situ* hybridization (FISH)
   - Subtraction probe technology chromogenic *in situ* hybridization (SPoT-Light HER2 CISH or CISH)
   - Inform dual *in situ* hybridization (Inform HER2 Dual ISH or DISH)

2. **Description**:

   2.1. Record the results of the measurement of HER-2 as reported when performed by in situ hybridization (ISH). These are more sensitive tests and a patient may have the IHC first, followed by ISH, or may have an ISH test alone. IHC should be reported in Item B-13. For ISH, code the actual value given which will be a 2-digit number. The decimal point between the two numbers need not be recorded because it is already written on the abstract form and in the abstracting utility. For example, the value of 0.5 should be recorded as “05”.

   2.2. Record the actual value from the laboratory test. The data are reported as a ratio of the number of her2 signals to 17 centromere signals. For ISH tests, a ratio >2.0 is consistent with amplification of HER-2 gene sequences or a positive test, a ratio of 1.8-2.0 is an equivocal finding and requires further testing and a ratio of <1.8 is within the normal limits (negative).

   2.3. Code “92” when the record indicates that the test for HER-2 is equivocal by ISH, but the value is not reported.

HER-2 (c-erbB-2,her2/neu): *IN SITU* HYBRIDIZATION (ISH) (cont)

2.4. Code “93” when the record indicates that the test for HER-2 was equivocal, but does not indicate the value nor the type of test (IHC or ISH). Item B-13 should also be coded “93”.

2.5. Code “94” when the record indicates that the test for HER-2 is positive by ISH, but the value is not reported.

2.6. Code “95” when the record indicates that the test for HER-2 is positive, but the type of test (IHC or ISH) is unknown and the test result value is not reported. Item B-13 should also be coded “95”.

2.7. Code “96” when the record indicates only that the ISH test was negative and does not provide the actual value.

2.8. Code “97” when the record indicates that the test for HER-2 was negative, but the type of test (IHC or ISH) is unknown and the test result value is not reported. Item B-13 should also be coded “97”.

2.9. If the test was not done, then code “98 - Not done”.

2.10. Code “99 – Unknown/no mention” if it is unknown whether the test was ordered or there is no mention.

GENE ASSAYS

ITEM B-15

1. **Code**: *Test type*
   0 – No mention, not performed
   1 – Oncotype DX™
   2 – ProsignaTM (PAM 50)
   3 – MammaPrint
   4 – PreludeDx™

   Score
   000-100 – Recurrence Score™ or DCIsion score (do not include decimal point)
   200 – Low Risk
   300 – Intermediate Risk
   400 – High Risk
   555 – Not performed
   977 – Ordered, Results unknown
   999 – Unknown/no mention

2. **Description**:

FOR EACH TEST THE RECURRENCE SCORE IS PREFERRED TO THE RISK LEVEL

2.1. Oncotype DX™ is an FDA-approved 21-gene assay that is reported to provide an assessment of the likelihood of distant breast cancer recurrence. The company that developed the assay, Genomic Health (which was subsequently purchased by Exact Sciences), states that the test will "assist physicians in optimizing treatment plans." The assay was initially intended for use in newly diagnosed breast cancer patients with stage I or II, node negative, estrogen receptor-positive cancer, and who will be treated with tamoxifen. The assay uses formalin-fixed, paraffin-embedded tumor tissue. The use of the assay has now been expanded to other stages and ER status.

2.2. The results are expressed as a Recurrence Score™ (0-100). The Recurrence Score™ (RS) is supposed to correlate with the probability of distant recurrence at 10 years. The likelihood of distant recurrence at 10 years increases continuously with increase in RS, with RS risk groups defined as low-risk (RS < 18), intermediate-risk (RS 18-30), and high-risk (RS ≥ 31). Although an RS falls into a risk group, each RS score is specific to each patient. For example, within the intermediate-risk category, an RS of 18 is different from an RS of 30.1 Genomic Health developed this assay and they run the ONLY laboratory that performs the assay. Record the value provided by Genomic Health, between 0 and 100. If you are unable to locate the assay or the exact value is unknown and there are written comments about the results, such as "RS is high," then code "400 – High".

GENE ASSAYS (cont)

2.3. ProsignaTM (PAM 50) is an FDA approved assay similar to Oncotype DX™ and reports similar risk categories (low, intermediate, high) and a numerical score (0-100). The assay is used to assess the probability of distant recurrence of disease at 10 years for post-menopausal women with early stage, hormone-receptor positive, invasive breast cancer.

2.4. A third FDA approved assay is MammaPrint. It assays 70 genes and also is used to predict the risk of recurrence at 10 years. The results are presented as either low or high risk; it does not record intermediate risk. They do report probability in percentages, of recurrence with and without systemic therapy.

2.5. PreludeDX is a test which quantifies the risk of DCIS recurrence as well as enables personalized treatment (surgery alone or surgery with radiation therapy). The result is expressed as a DCISionScore™, from 00.1 to 10.0. When coding the result for PreludeDx in the Score field, include the leading zeroes and do not include the decimal point. For example, a score of 1.5 would be coded as 015, and a result of 10.0 would be coded as 100.

2.6. These gene assays may be found in the hospital record. However, if it is ordered by the medical oncologist, it might be in the office record only.

2.7. If the test was ordered, but there is no record of the results, then code “977 – Ordered, Results unknown”. If there are comments about whether the test was high, intermediate or low, then record those as appropriate instead of recording “Results unknown”.

2.8. Code “555 – Not Performed” when it is known that the test was not performed.

2.9. If it cannot be determined whether the test was ordered or there is no mention in the record, record “999 – Unknown/no mention”.

PD-L1 TESTING

ITEM B-16

1. **Code**: *Test Type*
   0 – No mention if performed or not performed
   1 – Merck/Dako Assay (including Combined Positive Score (CPS) or IHC 22C3 pharmDx kit)
   2 – Ventana PD-L1 Assay
   3 – Other/Unknown Assay

   Score
   000-100 – Percent (%) PD-L1 positive
   555 – Not performed
   977 – Ordered, results unknown
   999 – Unknown/no mention

2. **Description**:

   2.1. Programmed death-ligand 1 (PD-L1) is a tumor cell marker used to select patients for anti-PD-1/PD-L1 treatment agents. PD-L1 tests report on the proportion of tumor cells that are PD-L1 positive. Several tests are used to assess PD-L1 status.

   2.2. Code the type of test used to assess PD-L1 level of the breast cancer. If no PD-L1 testing is listed, code Test Type as "0". If the test is listed as the Merck or Dako assay, a Combine Positive Score (CPS) is reported, or the test is performed using the IHC 22C3 pharmDx kit, code as "1". If the test is listed as the Ventana assay, code as "2". If PD-L1 testing was performed but the test type is unknown (not specified) or a type other than those listed, code as "3"

   2.3. Code the PD-L1 test score (i.e., the proportion of tumor cells that are PD-L1 positive). If a test was not performed (i.e., Test Type coded as "0"), code the score "555". If a test was indicated as ordered but results are unknown, code the score as "977". If a PD-L1 test was specified but there is no information as to whether it was ordered and no test score listed, code score as "999". Also use code "999" if there was no mention.

BREAST CANCER INDEX (BCI) SCORE

ITEM B-17

1. **Code**: *Score*
   xxx.xx% – Breast cancer index (BCI) score
   55555 – Test not performed
   88888 – Ordered, results unknown
   99999 – Unknown if test performed/no mention

2. **Description**:

   2.1. The Breast Cancer Index (BCI) test analyzes the expression of multiple genes to help predict the risk of recurrence of hormone-receptor-positive breast cancer.

   2.2. Code the BCI test score (i.e., the disease recurrence). If a test was not performed, code the score "55555". If a test was indicated as ordered but results are unknown, code the score as "88888". If a BCI test was specified but there is no information as to whether it was ordered and no test score listed, code score as "99999". Also use code "99999" if there is no mention.

OTHER MUTATIONS AND TESTING

ITEM B-18

1. Code:
   0 – Test not performed
   1 – One or more of specified test performed, all positive
   2 – One or more of specified test performed, all negative
   3 – More than one of specified test performed, initially positive and subsequently negative
   4 – More than one of specified test performed, initially negative and subsequently positive
   8 – Test performed, result unknown
   9 – Unknown if test performed/no mention

   Code separately for each of the following tests
   MSI/Microsatellite instability
   MMR deficiency/Mismatch repair deficiency
   Circulating tumor DNA (ctDNA)

2. **Description**:

   2.1. Molecular marker or mutations status information can come from either the primary tumor or from metastases; if tests are performed using either, the specified marker/mutation should be coded using the values indicated.

   2.2. Microsatellites are short, repeated sequences of DNA. Microsatellite instability-high (MSI-H) cancer cells may have a defect in the ability to correct mistakes that occur when DNA is copied in the cell.

   2.3. Mismatch repair (MMR) deficiency describes cells that have mutations (changes) in certain genes that are involved in correcting mistakes made when DNA is copied in a cell. MMR deficient cells usually have many DNA mutations, which may lead to cancer. Knowing if a tumor is MMR deficient may help plan treatment or predict how well the tumor will respond to treatment.

   2.4. Circulating tumor DNA (ctDNA) are small pieces of DNA that are released into a person's blood by tumor cells as they die. A sample of blood can be used to look for and measure the amount of circulating tumor DNA and identify specific mutations. Circulating tumor DNA is being used as a biomarker to help diagnose some types of cancer, to help plan treatment, or to find out how well treatment is working or if cancer has come back.

   2.5. If the test was not performed, then code "0 – Test not performed".

OTHER MUTATIONS AND TESTING (cont)

2.6. If a test was performed one or more times and all test results were positive, code that test as “1 – One or more of specified test performed, all positive”.

2.7. If a test was performed one or more times and all test results were negative, code that test as “2 – One or more of specified test performed, all negative”.

2.8. If a test was performed more than one time and the test results were positive the first time but were negative for any subsequent test, code that test as “3 – More than one of specified test performed, initially positive and subsequently negative”.

2.9. If a test was performed more than one time and the test results were negative the first time but were positive for any subsequent test, code that test as “4 – More than one of specified test performed, initially negative and subsequently positive”.

2.10. If there is mention of the test being performed in the record but no results, then code “8 – Test performed, results unknown”.

2.11. If a patient received a panel of multiple tests (also called a “gene panel”) and the specified mutation is listed as being part of the panel, assume that it was tested for. However, if the result is not listed, don’t assume the test result was negative. If the specified test result is not listed, coded this as “8 – One or more test performed, result unknown”.

2.12. If MSI or MMR results were recorded in the NGS data item (Common section), then do not code the results again in this data item.

2.13. If it is unknown if the test was performed, or there is no mention, then code “9 – Unknown/no mention if test performed”.

EOD OF PRIMARY TUMOR

ITEM B-19

1. Code: Breast

Code	Description	SS2018 T
000	In situ: noninfiltrating; intraepithelial Intraductal WITHOUT infiltration Lobular neoplasia, grade 3 (LIN 3)	IS
100	Any size tumor Confined to breast tissue and fat including nipple and/or areola Localized, NOS EXCLUDES: skin invasion of breast, nipple and areola (see code 200)	L
200	Any size tumor Attachment or fixation to pectoral muscle(s) or underlying tumor Deep fixation Invasion of • Pectoral fascia or muscle(s) • Subcutaneous tissue Local infiltration of dermal lymphatics adjacent to primary tumor involving skin by direct extension Skin infiltration of primary breast including skin of nipple and/or areola	RE
300	Invasion of (or fixation to) • Chest wall • Intercostal or serratus anterior muscle(s) • Rib(s)	RE

Code	Description	SS2018 T
400	Extensive skin involvement WITHOUT a stated diagnosis of inflammatory carcinoma WITH or WITHOUT dermal lymphatic filtration • Edema of skin • En cuirasse • Erythema • Inflammation of skin • Lenticular nodule(s) • Peau d'orange ("pigskin") • Satellite nodule(s) • Skin edema • Ulceration of skin of breast	RE
450	Diagnosis of inflammatory carcinoma WITH a clinical description of inflammation, erythema, edema, peau d'orange, etc., involving less than or equal to one-third (33%) of the skin of the breast or percentage not stated WITH or WITHOUT dermal lymphatic infiltration • En cuirasse • Satellite nodule(s) • Skin edema • Ulceration of skin of breast	RE
500	300 + (400 OR 450)	RE
600	Diagnosis of inflammatory carcinoma WITH a clinical description of inflammation, erythema, edema, peau d'orange, etc., involving greater than one-third (33%) or more of the skin of the breast WITH or WITHOUT dermal lymphatic infiltration • En cuirasse • Lenticular nodule(s) • Satellite nodule(s) • Ulceration of skin of breast	RE
700	Stated as "Inflammatory carcinoma" with no other information	RE
800	No evidence of primary tumor	U

Code	Description	SS2018 T
999	Unknown; extension not stated Primary tumor cannot be assessed Not documented in patient record Death Certificate Only	U

Note 1: Changes such as dimpling of the skin, tethering, and nipple retraction are caused by tension on Cooper's ligament(s), not by actual skin involvement. They do not alter the classification.

Note 2: Adherence, attachment, fixation, induration, and thickening are clinical evidence of extension to skin or subcutaneous tissue; assign code 200.

Note 3: "Fixation, NOS" is involvement of pectoralis muscle; assign code 200.

Note 4: For a clinical description of inflammation, erythema, edema, peau d'orange, or other terms describing skin changes without a stated diagnosis of inflammatory carcinoma, assign code 400.

2. **Description**:

2.1. USE 2018 SEER CODING RULES – see EOD Breast Data on SEER*RSA.

DATE RADIATION TO PRIMARY SITE BEGAN AND COMPLETION STATUS

ITEM B-20

1. **Code**: MM-DD-YYYY
   00-00-0000-No radiation

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
.	.	
12 - December	31	
77	77	7777-Patient or guardian refused
95	95	9595-Recommended, not given
96	96	9696-Recomm., unknown if given
97	97	9797-Unknown if given/no mention
99 - Month Unk	99 - Day Unk	9999-Year Unknown

Radiation course completion status

0 – No, not completed
1 – Yes, completed
2 – No radiation given to primary site
3 – Radiation given, unknown if completed
9 – Unknown/no mention whether radiation was given or completed

2. **Description**:

2.1. Enter the date the patient first received radiation **TO THE PRIMARY SITE** (breast/chest wall) at any time after diagnosis.

2.2. Code "00-00-0000" if there was no radiation given or recommended.

2.3. Code “77-77-7777 – Patient/guardian refused radiation” if the patient or the guardian refused radiation.

2.4. Code “95-95-9595 – Recommended, not given” when the records indicate that radiation was recommended, but was not given for a reason other than refusal.

2.5. Code “96-96-9696 – Recommended, unknown if given" if it is unknown whether the recommended radiation was performed.

2.6. If it is unknown or it is not mentioned whether the patient had radiation therapy, code “97-97-9797 – Unknown if radiation given/no mention”.

DATE RADIATION TO PRIMARY SITE BEGAN AND COMPLETION STATUS (cont)

2.7. Code "99-99-9999" if it is KNOWN that the patient had radiation therapy, but the day, month and/or year given cannot be determined. If the exact date of the first therapy is unknown, code an estimate. For example, if in history and physical, the physician states the patient had radiation therapy beginning two weeks ago, code date of radiation as 14 days prior to that date. If the record states that radiation was given recently, code the month and year, but not the day. Code the day as "99." Coding the closest approximation is preferable to coding unknown.

2.8. Code whether the full course of radiation was completed (Code 1– Yes, completed) or if the patient received less than a full course of radiation (Code 0 – No, not completed).

2.9. If the patient did not receive radiation to the primary site (breast/chest wall), code date as "00-00-0000" and completion as "2 – No radiation given to primary site."

2.10. If the patient did receive radiation to the primary site (breast/chest wall), but it is unknown if the radiation therapy was completed, code date as specified above and completion as "3 – Radiation given, unknown if completed"

2.11. If it is unknown whether radiation to the primary site (breast/chest wall) was given or completed, then code completion as "9 - unknown."

RADIATION THERAPY RECEIVED

ITEM B-21

1. **Code**: 0 – No radiation received
   1 – Received whole breast radiation
   2 – Received chest wall radiation
   3 – Received accelerated partial breast irradiation (Brachytherapy)
   4 – Received breast and regional nodal radiation
   5 – Received chest wall and regional nodal radiation
   6 – Other, Specify _____
   8 – Received radiation, type unknown
   9 – Unknown/no mention whether radiation received

2. **Description**:

   2.1. Code "0 – No radiation received" if the patient did not receive radiation in Item B-15.

   2.2. Code "1 – Whole breast radiation" when the patient received traditional external beam radiation to the entire breast region.

   2.3. Code "2 – Chest wall radiation" when the patient received radiation to the chest wall, the mastectomy scar and the drain sites (when present).

   2.4. Code "3 – Accelerated partial breast irradiation" when the patient received radiation therapy targeted just to the tumor site. This is often referred to as conformal, 3-D radiation, or brachytherapy

   2.5. Code "4 – Breast and regional nodal radiation" When the patient received external beam radiation to the breast AND to lymph nodes including the paraclavicular, axillary, and internal mammary nodes.

   2.6. Code "5 – Chest wall and regional nodal radiation" when the patient received radiation to the chest wall, the mastectomy scar and the drain sites (when present) to lymph nodes including the paraclavicular, axillary, and internal mammary nodes.

   2.7. Code "6 – Other, specify" when the patient received a different kind of radiation or radiation to a different site. Specify the type of radiation and site.

   2.8. Code "8 – Received radiation, type unknown" when the woman received radiation but the type of radiation is not specified.

   2.9. Code "9 – Unknown/no mention" when it is unknown or not mentioned whether the woman received radiation.

METASTASIS OR LOCAL RECURRENCE AFTER DIAGNOSIS

ITEM B-22

1. **Code** *i) Metastasis or local recurrence after diagnosis*

0 – Patient had metastatic disease at diagnosis
1 – No evidence of metastasis or local recurrence after diagnosis/no mention
2 – Yes, metastasis at a distant site identified after diagnosis
3 – Yes, local recurrence at primary tumor site identified after diagnosis
4 – Yes, both metastasis and local recurrence identified after diagnosis
9 – Unknown if metastasis or local recurrence after diagnosis

ii) Date first metastasis or local recurrence identified after diagnosis

MM-DD-YYYY

00-00-0000-No evidence/no mention of metastasis or local recurrence; Patient had metastatic disease at diagnosis; or Unknown if metastasis or local recurrence after diagnosis

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
.	.	
12 - December	31	
99 - Month Unk	99 - Day Unk	9999-Year Unknown

2. **Description**:

2.1. This item collects information on whether a cancer metastasis or local recurrence is identified **after** the initial tumor diagnostic work-up. Metastasis refers to the presence of the same cancer at a site distant from the primary tumor. Local recurrence refers to the presence of the same cancer at the primary tumor site **after** the primary tumor has been removed. If the primary tumor is not removed, there cannot be a local recurrence.

2.2. For item (i), Code "0 - Patient had metastatic disease at diagnosis" if at initial diagnosis the patient was diagnosed with metastatic disease (M-stage M1 or coded as "Yes" in the data item "METASTASIS AT DIAGNOSIS").

METASTASIS OR LOCAL RECURRENCE AFTER DIAGNOSIS (cont)

2.3. Code "1 – No" if there is no evidence or no mention of metastasis or local recurrence in the medical record or imaging reports after the initial tumor diagnosis work-up. The initial tumor diagnostic work-up is not just the initial biopsy but also includes subsequent imaging studies to determine the initial stage of the patient's cancer. **This option should be selected only if the patient did not have metastatic disease at diagnosis.** If the patient had metastatic disease at diagnosis (M-stage M1 or coded as "Yes" in METASTASIS AT DIAGNOSIS), instead use code "0 - Patient had metastatic disease at diagnosis".

2.4. Code "2 – Yes, metastasis at a distant site identified after diagnosis" when there is clinical or pathologic evidence of distant metastasis **after** diagnosis for patients who did not have an initial diagnosis of metastatic cancer.

2.5. Code "3 – Yes, local recurrence at primary tumor site identified after diagnosis" when there was surgery to completely remove the primary tumor and after the surgery there is clinical or pathologic evidence of a new cancer of the same type at the site of the primary tumor. If local and regional lymph nodes were reported to be negative at diagnosis but were subsequently found to be positive for cancer, please code this as a recurrence. If local or regional lymph nodes were reported as positive at diagnosis or the status of these lymph nodes was not reported at diagnosis, later findings of positive local or regional lymph nodes should NOT be considered recurrence or metastasis.

2.6. Code "4 – Yes, both metastasis and local recurrence identified after diagnosis" when there is clinical and pathologic evidence of distant metastasis after diagnosis **AND** clinical or pathologic evidence of local recurrence at the primary tumor site (including the lymph node involvement described above).

2.7. Code "9 - Unknown" if it is unknown whether there is metastasis or local recurrence after diagnosis.

2.8. For item (ii), code the first date that the metastasis or local recurrence after initial diagnosis listed in the medical record. If the patient had metastatic disease at diagnosis (item (i) coded "0"), no evidence/no mention of metastasis or local recurrence (item (i) coded "1"), or unknown whether there is metastasis or local recurrence after diagnosis (item (i) coded "9"), code item (ii) "00-00-0000".

SYSTEMIC THERAPY AGENTS

ITEMS B23-B42

1. **Code** i) Date of start of therapy
MM-DD-YYYY
00-00-0000-No systemic therapy given

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
.	.	
12 - December	31	
77	77	7777-Patient or guardian refused
95	95	9595-Recommended, not given
96	96	9696-Recomm., unknown if given
97	97	9797-Unknown if given
99 - Month Unk	99 - Day Unk	9999-Year Unknown

ii) Mode of administration:
Oral (O)
Parenteral (P)
Both Oral and Parenteral (B)
Unknown (U)
N/A (N)

B-23 Ado-trastuzumab emtansine (Kadcyla)

B-24 Capecitabine (Xeloda)

B-25 Carboplatin

B-26 Cyclophosphamide

B-27 Docetaxel (Taxotere, Docefrez)

B-28 Doxorubicin (Adriamycin)

B-29 Eribulin (Halaven)

B-30 Fluorouracil (5-FU)

B-31 Gemcitabine (Gemzar)

B-32 Lapatinib (Tykerb)

B-33 Nab-Paclitaxel (Abraxane)

SYSTEMIC THERAPY AGENTS (cont)

B-34 Paclitaxel (Taxol, Onxol)

B-35 Pembrolizumab (Keytruda)

B-36 Pertuzumab (Perjeta)

B-37 Tamoxifen (Nolvadex)

B-38 Trastuzumab (Herceptin)

B-39 Vinorelbine (Navelbine)

B-40 Aromatase Inhibitors [anastrozole (Arimidex), exemestane (Aromasin), letrozole (Femara)]

B-41 GnRH analogs [buserelin (Suprefact), goserelin acetate (Zoladex), leuprolide (Lupron, Lupron Depot), nafarelin (Synarel), degarelix (Firmagon), histrelin acetate (Vantas; Supprelin LA), triptorelin pamoate (Trelstar, Trelstar LA, Trelstar Depot), Gonadorelin (Factrel)]

B-42 Other Specify_____

Examples of other chemotherapeutic agents which might have been given are:

Topotecan, Vinblastine (Velban), Mitoxantrone (Novantrone)

This list is by no means complete and if other systemic therapeutic agents are found, please list them as well. Please be sure to record only systemic therapeutic agents.

Please be sure to record all systemic therapy agents. SEER*Rx is useful for looking up chemotherapy, immunotherapy, and other agents used to treat cancer.

2. **Description**:

2.1. Enter information for each agent separately. If therapy agents are present in the medical record that are not included in this list, please include these in the "Other Specify" field. Please record information on all systemic therapy, from diagnosis to end of available medical records, not just the first course of systemic therapy. This item also includes ovarian suppression drugs.

2.2. Code the date therapy started for each systemic therapy agent given at any time following diagnosis.

SYSTEMIC THERAPY AGENTS (cont)

2.3. Code "00-00-0000-Not given" when the patient did not receive systemic therapy, even when it was recommended. Also, use this code when the agent was considered or recommended, and it is known that the patient did not receive it. (See also “77-77-7777-Refused”.) If no systemic therapy agent was given, then all agents should be coded as "00-00-0000", unless the patient or the patient's guardian refused the systemic therapy. (See also code “7777-Patient/guardian refused").

2.4. Code “77-77-7777” if an agent was recommended but was not administered because of patient or guardian refusal. If the patient refuses therapy, but it is not known which specific drug was refused, all agents known to have been recommended should be coded "77-77-7777”.

2.5. Code “95-95-9595 – Recommended, not given” when the records indicate that systemic therapy was recommended but was not given for a reason other than refusal.

2.6. Code “96-96-9696 - Recommended, unknown if given” when a patient was recommended to receive an agent, but it is unknown if it was actually received. When therapy was recommended, but the agents used were not documented, all agents must be coded “96-96-9696 – Recommended, unknown if given”.

2.7. Code “97-97-9797 - Unknown" when there is no documentation regarding therapy in the medical records reviewed and there is no information about the therapy from the treating physician.

2.8. Code “99-99-9999” if it is **KNOWN** that the patient had a particular agent, but the date given cannot be determined. If the exact date of the first administration is unknown, code an estimate. For example, if in history and physical, the physician states the patient had Bevacizumab beginning two weeks ago, code date of first Bevacizumab as 14 days prior to that date. If the record states that the Bevacizumab was given recently, code the month and year, but not the day. Code the day as “99”. Coding the closest approximation is preferable to coding unknown.

2.9. When a systemic therapy is administered as one or more arms of a clinical trial and it is not known whether the patient was in that arm, this therapy should be coded as “Unknown if given” (97-97-9797). For example, if a patient were in a trial of new investigational agent vs. bevacizumab, bevacizumab should be coded as “Unknown if given”. The new investigational agent should also be listed as “Unknown if given”. However, if a patient was in a trial of bevacizumab plus new investigational agent in one arm vs. bevacizumab plus placebo in the other arm, bevacizumab should be coded as given since it is part of both arms. Do not include “placebo” as part of systemic therapies.

SYSTEMIC THERAPY AGENTS (cont)

2.10. Even if a systemic therapy agent is listed as being administered only for palliative therapy, record the name and date of first administration of that agent in this item.

2.11. For item (ii), code the mode of administration for each therapy administered. This can be coded as O = Oral (by mouth), P = Parenteral, administration, B = Both Oral and Parenteral, U = Unknown/not specified, or N = N/A. Parenteral administration is general intravenous (IV), but can also include intramuscular (IM), subcutaneous (SC or SQ), or administration via an angiocatheter; Broviac, Groshong, or Hickman catheter; PICC line; or port-a-cath. If a therapy was not administered (date of administration in item (i) coded as 00-00-0000, 77-77-7777, or 95-95-9595), code mode of administration as N = N/A. If it is unknown if a therapy was administered (date of administration in item (i) coded as 96-96-9696 or 97-97-9797) or a therapy was administered but date of administration is unknown (date of administration in item (i) coded as 99-99-9999), code mode of administration using any available information in the medical chart, including specified recommendations regarding mode of administration.

2.12. The code for both oral and parenteral administration (B) should be used for drug regimens that include both orally administered and parenterally administered systemic therapy agents.

2.13. For item (ii), code the mode of administration for each therapy administered. This can be coded as O = Oral (by mouth), P = Parenteral, U = Unknown/not specified, or N = N/A. Parenteral administration is general intravenous (IV), but can also include intramuscular (IM), subcutaneous (SC or SQ), or administration via an angiocatheter; Broviac, Groshong, or Hickman catheter; PICC line; or port-a-cath. If a therapy was not administered (date of administration in item (i) coded as 00-00-0000, 77-77-7777, or 95-95-9595), code model of administration as N = N/A. If it is unknown if a therapy was administered (date of administration in item (i) coded as 96-96-9696 or 97-97-9797) or a therapy was administered but date of administration is unknown (date of administration in item (i) coded as 99-99-9999), code mode of administration using any available information in the medical chart, including specified recommendations regarding mode of administration.

Common Data Items

A1. SEER Participant ☐☐

A2. Case Number ☐☐☐☐☐☐☐☐

A3. Quality Control ☐

A4. Tumor Record Number ☐☐

A5. Sequence Number ☐☐

A6. Primary Site ☐☐☐

A7. Grade ☐ Clin ☐ Path ☐ Post-Th

A8. Hospital Code ☐☐☐☐☐

A9. Insurance Status

	≤ 30 days	> 30 days
No ins/ Self Pay……	☐	☐
Medicare FFS……	☐	☐
Medicare HMO……..	☐	☐
Medicare Part D/PDP…….	☐	☐
Medicare + Private (supp)..	☐	☐
Medicaid……..	☐	☐
Medicaid pending……	☐	☐
Private/IPA/HMO……	☐	☐
Tricare/Other military……..	☐	☐
Veterans Affairs……..	☐	☐
Indian Health Service……	☐	☐
Other (enter text below)….	☐	☐

≤ 30 days _____

> 30 days _____

A10. Treatment Protocol Registration ☐

A11. Protocol Sponsor and Number

☐☐☐☐☐☐☐☐☐☐☐☐

A12. Case Information Verified ☐

A13. Height/Weight

Ht ☐☐☐ Ht Units ☐_____

Wt ☐☐☐ Wt Units ☐_____

A14. Date of First Onco Consul ___ /___ /_____ (mm dd yyyy)

A15. Impact of COVID-19 on Cancer Care **AFTER cancer dx**

A. Patient Dx'd with C-19 ☐

B. Date of 1st Pos C-19 Dx ___ /___ /_____ (mm dd yyyy)

C. Date of 1st hosp adm for C-19 ___ /___ /_____ (mm dd yyyy)

A15. Impact of COVID-19 on:

		Other, specify
D. Cancer Diagnosis	☐	_____
E. Surgery to primary site	☐	_____
F. Radiation to primary site	☐	_____
G. Systemic Therapy	☐	_____
H. Palliative Care	☐	_____

A16. Impact of COVID-19 on Finances/Insurance:

Only code info in A-15 through A-17 **for after cancer dx**

A. Patient's finances ☐

B. Patient's Employment ☐

C. Patient's Insurance ☐

A17. Palliative Care **AFTER cancer dx**

A. Palliative Care Received ☐

B. Date of 1st Pall Care ___ /___ /_____ (mm dd yyyy)

C. Counseling/mental health Received ☐

D. Date of 1st couns/mental hlth ___ /___ /_____ (mm dd yyyy)

E. Hospice service/admission ☐

F. Date of 1st hospice/adm ___ /___ /_____ (mm dd yyyy)

A18. NextGen Sequencing (NGS) ☐

A19. Smoking /Tobacco Use

Packs per day ☐☐.☐

Non-cigarette tobacco use ☐

Num Years Smoked/non-cig use ☐☐

Pack years ☐☐

Smoking Status at DX ☐

A20. Secondhand Smoke Exposure ☐

A21. Family history of cancer of same site ☐

B1. Date of first positive bx/asp ___ /___ /_____ (mm dd yyyy)

B2. Date of path conf report ___ /___ /_____ (mm dd yyyy)

B3. Primary site surgery and date ☐☐

___ /___ /_____ (mm dd yyyy)

B4. Pathological margins ☐

B5. Size of primary tumor
Clinical ☐☐☐
Pathologic ☐☐☐

B6. Method of measurement ☐

Other _____

B7. Method of tumor detection ☐

Other _____

B8. Regional Node Dissection ☐

Other _____

B9. Lymph nodes positive ☐☐

B10. Lymph nodes examined ☐☐

B11. Prophylactic contralateral mastectomy ☐

Prophylactic oophorectomy/salpingo-ooph ☐

B12. Metastasis at diagnosis

- ☐ *Lung*
- ☐ *Distant LNs*
- ☐ *Bone*
- ☐ *Liver*
- ☐ *Brain/nervous system*
- ☐ *Peritoneal Cavity (pelvis and abdomen)*
- ☐ *Other (path)* _____
- ☐ *Other (clin)* _____
- ☐ *Other (clin AND path)* _____

B13. HER-2 (c-erbB-2, her2/neu): IHC ☐☐

B14. HER-2 (c-erbB-2, her2/neu): ISH ☐.☐

B15. Gene assays ☐ ☐☐☐
Test type *Score*

B16. PD-L1 Testing ☐ ☐☐☐
Test type *Score*

B17. BCI Score ☐☐☐.☐☐

B18. Other Mutations and testing
- ☐ *MSI/Microsatellite instability*
- ☐ *MMR deficiency*
- ☐ *Circulating tumor DNA (ctDNA)*

B19. EOD of primary tumor ☐☐☐

B20. Date radiation to primary site ___ /___ /_____ (mm dd yyyy)

Completion status ☐

B21. Radiation therapy received ☐

Other _____

B22. Metastasis or local recurrence ☐

___ /___ /_____ (mm dd yyyy)

Enter systemic therapy on next page

Notes

Systemic Therapy Agent	Date (mm/dd/yyyy)	Mode of Admin →
B23. Ado-trastuzumab emtansine (Kadcyla)	___/___/_____	☐
B24. Capecitabine (Xeloda)	___/___/_____	☐
B25. Carboplatin	___/___/_____	☐
B26. Cyclophosphamide	___/___/_____	☐
B27. Docetaxel (Taxotere, Docefrez)	___/___/_____	☐
B28. Doxorubicin (Adriamycin)	___/___/_____	☐
B29. Eribulin (Halaven)	___/___/_____	☐
B30. Fluorouracil (5-FU)	___/___/_____	☐
B31. Gemcitabine (Gemzar)	___/___/_____	☐
B32. Lapatinib (Tykerb)	___/___/_____	☐
B33. Nab-Paclitaxel (Abraxane)	___/___/_____	☐
B34. Paclitaxel (Taxol, Onxol)	___/___/_____	☐
B35. Pembrolizumab (Keytruda)	___/___/_____	☐
B36. Pertuzumab (Perjeta)	___/___/_____	☐
B37. Tamoxifen (Nolvadex)	___/___/_____	☐
B38. Trastuzumab (Herceptin)	___/___/_____	☐
B39. Vinorelbine (Navelbine)	___/___/_____	☐
B40. Aromatase Inhibitors	___/___/_____	☐
B41. GnRH analogs	___/___/_____	☐
B42. Other, specify	___/___/_____	☐

_____

O=Oral
P=Parenteral
B=Both Oral & Parenteral
U=Unknown
N=N/A

Coding Info

Abstractor ID
☐☐☐☐☐

Date Abstracted
___/___/_____
mm dd yyyy

List all co-morbids on next page

C. List all co-morbid conditions from the hospitalization for initial cancer treatment.

Registry ☐☐
Case # ☐☐☐☐☐☐☐☐

BREAST CANCER POC20

1.	
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Abstractor's questions, problems or comments. Attach pages and documentation as needed.

POC DATA ACQUISITION MANUAL

SECTION V

COLORECTAL CANCER DATA SET

SECTION V – COLORECTAL CANCER DATA SET

CONTENTS

DATE OF FIRST POSITIVE BIOPSY

ITEM B-1

1. **Code** MM-DD-YYYY
00-00-0000-No biopsy done.

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
.	.	
12 - December	31	
77	77	7777-Patient or guardian refused
95	95	9595-Recommended, not performed
96	96	9696-Recomm., unknown if performed
97	97	9797-Unknown if performed
99 - Month Unk	99 - Day Unk	9999-Year Unknown

2. Description

2.1. This item refers to the date of the first positive biopsy. This may be a biopsy of the primary site, lymph node or metastatic site that confirmed the diagnosis of colorectal cancer. Code the date the specimen was obtained (NOT the date of the pathology/cytology report).

2.2. If the biopsy/aspiration was performed on the same day as definitive surgery, the biopsy date and the Date of Cancer Directed Surgery to Primary Site (Item B-3) will be the same. The first positive biopsy may have been done as an outpatient procedure but must be no later than the Date of First Cancer-Directed Surgery to Primary Site.

2.3. If there was no biopsy done prior to the time of surgical resection, code "00- 00-0000".

2.4. Code “99-99-9999” if it is **KNOWN** that the patient had a biopsy but the day, month and/or year given cannot be determined. If the exact date of the first positive biopsy is unknown, code an estimate (e.g., if in history and physical, the physician states the patient had a biopsy two weeks ago, code date of biopsy as 14 days prior to date of admission). Coding closest approximation is preferable to coding unknown.

DATE OF FIRST POSITIVE BIOPSY/ASPIRATION PROCEDURE (cont)

2.5. Code “77-77-7777” if patient or the patient’s guardian refused biopsy.

2.6. Code “95-95-9595 – Recommended, not performed” when the records indicate that biopsy was recommended but was not performed for a reason other than refusal.

2.7. Code “96-96-9696 – Recommended, unknown if performed” if the records indicate that the biopsy was recommended but it is unclear whether the patient had the biopsy.

2.8. If it is unknown whether or not a biopsy was performed, code “97-97-9797”.

DATE OF PATHOLOGIC CONFIRMATION REPORT

ITEM B-2

1. **Code** MM-DD-YYYY
00-00-0000-No biopsy done.

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
12 - December	31	
77	77	7777-Patient or guardian refused
95	95	9595-Recommended, not performed
96	96	9696-Recomm., unknown if performed
97	97	9797-Unknown if performed
99 - Month Unk	99 - Day Unk	9999-Year Unknown

2. Description

2.1. This item refers to the date of the REPORT of the pathologic confirmation of colorectal cancer by the biopsy coded in Item B-1. This is NOT the date the specimen was obtained. This is NOT the date the colorectal cancer was suspected. If the pathology department has "real-time" reporting (the reports are sent electronically as they are completed to the physicians' offices), then the date of the report may be the same as the date of pathologic confirmation.

2.2. If the patient or guardian refused the biopsy, code "77-77-7777- Patient/guardian refused." This is unlikely for these patients because the diagnosis must be pathologically confirmed.

2.3. If the biopsy/aspiration was recommended but it is unknown if it was performed, code "96-96-9696 – Recommended, unknown if performed." This is unlikely for these patients because the diagnosis must be pathologically confirmed.

2.4. If it is unknown if biopsy/aspiration was offered or performed, code "97-97-9797 – Unknown if offered or performed." This is unlikely for these patients because the diagnosis must be pathologically confirmed.

2.5. If the exact date of the first positive biopsy is unknown, then estimate. For example, if in history and physical, the physician states the patient had a biopsy two weeks ago, then code the date of biopsy as 14 days prior to date of admission. Coding closest approximation is preferable to coding unknown. If an estimate cannot be made, then code "99-99-9999". If the pathology department has real-time reporting, record the date the report was received.

PRIMARY SITE SURGERY AND DATE

ITEM B-3

1. Code **Surgery Code**: 00-99
   Refer to *SEER Program Coding and Staging Manual 2018, Appendix C.*

   Surgery Date: MM-DD-YYYY
   00-00-0000 -- No Surgery

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
12 - December	31	
77	77	7777-Patient or guardian refused
95	95	9595-Recommended, not performed
96	96	9696-Recomm., unknown if performed
97	97	9797-Unknown if performed
99 - Month Unk	99 - Day Unk	9999-Year Unknown

2. **Description**:

   2.1. Enter the site-specific surgery code as defined in the SEER Program Coding and Staging Manual 2018, Appendix C. This is only for the initial (first course) surgery to the primary site. See below for links to surgery codes by primary site.

   - Colon
   - Rectum
   - Rectosigmoid

   2.2. Enter the date on which the most definitive surgery of the primary site was performed. Code "00-00-0000" if no surgery to the primary site was performed.

   2.3. If the patient or patient's guardian refused surgery to the primary site, then code "77-77- 7777 – Patient/guardian refused".

   2.4. Code "95-95-9595 – Recommended, not performed" when the records indicate that surgery was recommended, but was not performed for a reason other than refusal.

   2.5. If surgery to the primary site was recommended, but it is unknown if it was performed, then code "96-96-9696 – Recommended, unknown if given".

   2.6. If it is unknown whether or not the patient had surgery to the primary site, then code "97-97-9797-Unknown if performed".

PRIMARY SITE SURGERY AND DATE (cont)

2.7. Code “99-99-9999” if it is **KNOWN** that the patient had surgery to the primary site, but the day, month and/or year given cannot be determined. If the exact date of the surgery is unknown, then code an estimate. For example, if in history and physical, the physician states the patient had surgery two weeks ago, then code the date of surgery as 14 days prior. Coding the closest approximation is preferable to coding unknown.

PATHOLOGICAL MARGINS

ITEM B-4

1. **Code** 0 – No resection/surgery performed or only biopsy performed
   1 – Margins of resection pathologically free of tumor
   2 – Tumor at margins of resection, or residual tumor in area of primary
   3 – Margins not stated in pathology report--surgeon indicates no residual tumor
   8 – Resection recommended unknown if performed
   9 – Unknown, not stated

2. **Description**:

   2.1. This item records the pathological margin status following the most definitive surgery performed after diagnosis (Item B-3). This refers to pathological margins only for the initial surgery at the primary site.

   2.2. Code "0 – No resection/surgery performed" when no cancer-directed surgery or only a biopsy was performed.

   2.3. Code "1 – Margins of resection pathologically free of tumor" when the pathologist reported no residual tumor in the area of the primary site.

   2.4. Code "2 – Tumor at margins of resection, or residual tumor in area of primary" when the pathologist reported involvement of the surgical resection margins.

   2.5. Code "3 – Margins not stated in pathology report--surgeon indicates no residual tumor" when the pathology report does not document the pathologic margin status, but the surgeon states in the operative report that no tumor was left in the area of the primary site.

   2.6. Code “8 – Resection recommended unknown if performed” if the physician recommended surgery, but it is unknown whether it was performed.

   2.7. Code "9 – Unknown, not stated" when there is no information in the pathology report regarding pathologic margins and the surgeon does not document margin status in the operative report.

SIZE OF PRIMARY TUMOR

ITEM B-5

1. Code
   - 000 – No mass/tumor found
   - 001 – 1 mm or described as less than 1 mm
   - 002-988 – Exact size in millimeters (2 mm to 988 mm)
   - 989 – 989 millimeters or larger
   - 990 – Microscopic focus or foci only and no size of focus is given
   - 998 – Familial/multiple polyposis
   - 999 – Unknown; size not stated/not documented in patient record; Size of tumor cannot be assessed; Not applicable

   Type of Staging (see notes below for further guidance)

   Clinical – size of primary tumor **before** any treatment

   Pathologic – size of primary tumor that has been resected

2. Description:

   2.1. Refer to the 2018 SEER Program Coding and Staging Manual for complete details. **Code information about both clinical and pathologic tumor size for each patient.** Code the tumor size recorded prior to initiation of therapy. This information should not be taken from autopsy records. When multiple masses are present, code the longest diameter. Code the exact value from 001 (00.1 cm) through 989 (98.9 cm) if available. Be certain that the units are correctly recorded. Do not confuse mm and cm; 5 mm and 5 cm are markedly different and have different therapies.

   2.2. For clinical tumor size, record the largest measurement of the primary tumor from the priority list below before any form of treatment. Use information available within four months of the date of diagnosis, in the absence of disease progression when no treatment is administered.

   Record largest size according to the following priority order:

   1. Operative report from surgical exploration without resection
   2. Diagnostic imaging
   3. Physical exam

   Note 1: Tumor size noted in a resection operative report is a clinical tumor size, and not a pathologic tumor size.

SIZE OF PRIMARY TUMOR (cont)

Note 2: Check the Clinical History/Clinical Impression/Clinical Information section of the pathology report for information on the clinical size of the tumor.

Note 3: A smaller size from a higher priority source should be coded.

2.3. For pathologic tumor size, code the size as recorded from the surgical resection specimen as noted in the pathology report or the synoptic/CAP protocol before adjuvant treatment. Code the largest size of the primary tumor (invasive portion) measured on the surgical resection specimen when **surgery is administered as part of the first course treatment.**

a. Code the size from the synoptic report (also known as CAP protocol or pathology report checklist) when there is a discrepancy among tumor size measurements in the various sections of the pathology report.

b. Use final diagnosis, microscopic, or gross examination, in that order, when only a pathology report is not available.

Example 1: CT shows 3.5 cm mass; the pathology report from the surgery states that the same mass is malignant and measures 2.8 cm. Record tumor size as 028 (28 mm).

Example 2: Pathology report states tumor is 2.1 cm x 3.2 cm x 1.4 cm. Record tumor size as 032 (32 mm).

Note: The pathologic tumor size is recorded from the surgical resection specimen when surgery (including after neoadjuvant therapy) is administered as part of the first course treatment.

2.4. If the tumor was palpable, but no size is documented, then code "999 - Not stated".

2.5. When there was a biopsy followed by a more extensive resection with residual tumor removed, code the largest tumor size recorded. Do not add the dimensions of the individually excised tumor tissue together.

2.6. When the tumor is multi-focal or when multiple tumors are reported as a single primary, code the size of the largest invasive tumor, or the largest in situ tumor if all tumors are in situ. Code the exact value in millimeters from 001 (00.1 cm) through 988 (98.8 cm).

SIZE OF PRIMARY TUMOR (cont)

2.7. Code only the size of the primary tumor. Do not code the size of other structures like cysts.

2.8. If there is no tumor or mass found after neoadjuvant therapy code pathologic tumor size "000 - No mass/tumor found."

2.9. Refer to the 2018 SEER Program Coding and Staging Manual for rules on rounding measurements, less than/greater than statements, priority order of reports and discrepancies between reports.

3. **Examples**:

A tumor of 0.9 cm (9 mm) in size is coded "009".

A tumor of 5.5 cm (55 mm) in size is coded "055".

A tumor of 8.3 cm (83 mm) in size is coded "083".

A tumor of 10.0 cm (100 mm) in size is coded "100".

PERFORATION

ITEM B-6

1. **Code** 0 – No bowel perforation, no mention
   1 – Bowel perforation present in operative or pathology report(s) only
   2 – Bowel perforation clinically evident only
   3 – Bowel perforation on clinical report and operative or pathology report(s)
   9 – Unknown

2. Description:

2.1. Bowel perforation, also known as ruptured bowel, is a hole in the wall of the colon or rectum. Information on the presence of a bowel perforation should come from the operative report, pathology report, colonoscopy report, and clinical records. Examine these records carefully for statements about the presence or absence of a bowel perforation.

2.2. A tumor is sometimes said in a path report to have 'perforated the full thickness of the bowel wall' microscopically, that is, T3 -- **but this doesn't correspond to gross perforation and does not carry the same poor prognosis.** Be certain that you distinguish between these two meanings.

2.3. Code “0 – No bowel perforation” when the operative or pathological record states there was no bowel perforation present or when there is no mention of perforation in the operative or pathological records and there is no clinical evidence/symptoms of perforation reported.

2.4. Code “1 – Bowel perforation present in operative or pathology report(s) only” when there is evidence from either of these reports that there was perforation of the bowel but there were no pre-op reports of bowel perforation or symptoms thought to be due to bowel perforation prior to surgery.

2.5. Code “2 – Bowel perforation clinically evident only” when there are signs or symptoms that are reported in the medical record as potentially due to bowel perforation, such as peritoneal signs that a tumor might have perforated the bowel and thereby released bacteria and tumor cells into the peritoneal cavity, but there is no evidence of bowel perforation from surgery or pathology reports. That is, use Code 2 when bowel perforation is suspected pre-op and then no evidence of bowel perforation found during surgery. Also use this code when the history and physical record states there was bowel perforation, but this is not confirmed in either the operative report or the pathology report. If there are both clinical signs of a bowel perforation and evidence of a bowel perforation is found during surgery or in a pathology report, use Code 3.

PERFORATION (cont)

2.6. Code “3 – Bowel perforation on clinical report and operative or pathology report(s)” when there is clinical evidence of perforation and evidence of perforation on the operative or pathological records.

2.7. Code “9 – Unknown” when it is unclear from the operative or pathological record if there was a bowel perforation.

OBSTRUCTION

ITEM B-7

1. **Code** 0 – No bowel obstruction, no mention
   1 – Partial bowel obstruction
   2 – Complete bowel obstruction
   3 – Bowel obstruction; Partial or complete not specified
   9 – Unknown

2. **Description**:

   2.1. Bowel obstruction, also known as intestinal obstruction, is a mechanical or functional obstruction of the intestines which prevents the normal movement of the products of digestion. This can involve the colon or the rectum. **Information on the presence of a bowel obstruction should come from the operative report, pathology report, or colonoscopy report only**. Examine the record carefully for statements about the presence or absence of a bowel obstruction in the colon.

   2.2. Code "0 – No bowel obstruction" when the operative or pathology record states there is no bowel obstruction or if there is no statement in the operative or pathology records about the presence or absence of an obstruction.

   2.3. Code "1 – Partial bowel obstruction" when the operative or pathology record states there is a partial bowel obstruction. A "stricture" is a partial bowel obstruction.

   2.4. Code "2 – Complete bowel obstruction" when a separate operation for decompressing colostomy was performed prior to the procedure to remove the tumor, or when the operative report indicates there was a complete bowel obstruction.

   2.5. Code "3 – Bowel obstruction; Partial or complete not specified" when the operative or pathology record states the patient has a bowel obstruction, but it is not clear whether the obstruction was partial or complete.

   2.6. Code "9 – Unknown" when the presence or absence of bowel obstruction cannot be determined from the statements contained in the operative or pathology reports.

3. **Specifics**:

   3.1. If there is a statement about bowel obstruction in anything other than the operative report or the pathology report, and it is not confirmed in these reports, then it is unlikely to be an obstruction. Code "0 - No bowel obstruction" should be used.

METHOD OF TUMOR DETECTION

ITEM B-8

1. **Code**:
   - 01 – Screening fecal occult blood test (FOBT)
   - 02 – Screening fecal immumochemical test (FIT)
   - 03 – Cologuard/multi-targeted stool DNA test (MT-sDNA)
   - 04 – Other or unknown stool screening test
   - 05 – Screening colonoscopy
   - 06 – CT colonoscopy
   - 07 – Flexible sigmoidoscopy
   - 08 – Other or unknown type of endoscopy
   - 09 – Patient-reported blood in stool
   - 10 – Other patient-reported GI symptoms (abdominal pain, diarrhea, etc.)
   - 88 – Other, specify_____
   - 99 – Unknown/Not specified

2. **Description**:

   2.1. Code the method by which the tumor was initially detected. This refers to the first notice of a colorectal tumor, NOT the diagnostic procedures that followed.

   2.2. The first notice of a colorectal tumor may be symptoms, which are then evaluated by endoscopy. The initial reported symptoms should be coded for this item. For example, if the medical record indicates that the patient report blood in stool, and the presence of a tumor was then confirmed by colonoscopy, code as “09 – Patient-reported blood in stool”.

   2.3. Code “88 – Other, specify” when the tumor was discovered by some other means. Specify the method of discovery.

   2.4. Code “99 – Unknown/Not specified” when it cannot be determined from the records how the tumor was initially detected.

NUMBER OF REGIONAL LYMPH NODES POSITIVE and EXAMINED

ITEM B-9
ITEM B-10

1. **Code:** **B-9 – Number of positive regional lymph nodes**
   00 – All examined nodes negative
   01 – One positive node
   02 – Two positive nodes
   ...
   ...
   90 – 90 or more positive nodes
   95 – Positive aspiration or core biopsy of lymph node(s) performed
   97 – Positive nodes documented – number unspecified
   98 – No nodes examined
   99 – Unknown, not stated

   B-10 – Number of regional lymph nodes examined
   00 – No nodes examined (no nodal dissection performed)
   01 – One node examined
   02 – Two nodes examined
   ...
   ...
   90 – 90 or more examined
   95 – No regional nodes removed, but aspiration or core biopsy of regional nodes performed
   96 – Regional lymph node removal documented as sampling and number of nodes unknown/not stated
   97 – Regional lymph node removal documented as dissection and number of nodes unknown/not stated
   98 – Regional lymph nodes surgically removed but number of nodes unknown/not stated and not documented as sampling or dissection; nodes examined but number unknown
   99 – Unknown/not stated whether nodes examined

2. **Description**:

   2.1. For information on which nodes are considered regional, refer to the AJCC Staging Manual 8th Edition.

NUMBER OF REGIONAL LYMPH NODES POSITIVE & EXAMINED (cont)

2.2. Record the number of regional nodes examined by a pathologist and found to contain metastasis. These should be coded based only on data from lymph nodes that are pathologically examined, not from lymph nodes that are clinically examined or examined using imaging procedures.

2.3. Code the number of regional lymph nodes positive in Item B-9 and the number of regional lymph nodes examined in Item B-10. Include all node dissections done during the first course of therapy.

2.4. If more than one dissection was done during the first course of treatment, code the total number of lymph nodes positive and examined.

2.5. If the number of nodes positive was 90 or greater, code Item B-9 as "90". If the number of nodes examined was 90 or greater, code Item B-10 as "90".

2.6. If lymph nodes were known to be positive, but the exact number positive is unknown, code Item B-6 as "97".

2.7. If lymph nodes were known to be positive, but the exact number positive is unknown and the exact number examined is unknown, code Item B-9 as "97" and Item B-10 as "96", "97", or "98".

2.8. If no regional lymph nodes were positive, and the number examined is at least one, but the total is unknown, code Item B-9 "00" and B-10 "96", "97" or "98".

2.9. If no regional node dissection was done or no regional lymph nodes were removed/examined, code Item B-9 "98" and B-10 "00".

2.10. If it is unknown or not stated whether any nodes were either positive or examined, then code "99" in Items B-9 and B-10.

2.11. If regional lymph nodes were aspirated, code Item B-9 either "00" for negative or "95" if positive and code Item B-10 as "95".

2.12. When there is a difference in the number of nodes positive and/or examined between the body of the pathology report and the final medical report, code the information from the final medical report.

MUTATIONS AND TESTING

ITEM B-11

1. **Code**: 0 – Test not performed
   1 – One or more of specified test performed, all positive
   2 – One or more of specified test performed, all negative
   3 – More than one of specified test performed, initially positive and subsequently negative
   4 – More than one of specified test performed, initially negative and subsequently positive
   8 – Test performed, result unknown
   9 – Unknown if test performed/no mention

   Code separately for each of the following tests
   MSI/Microsatellite instability
   MMR deficiency/Mismatch repair deficiency
   KRAS
   NRAS
   Extended RAS
   BRAF
   HER-2
   Circulating tumor DNA (ctDNA)

2. **Description**:

   2.1. Molecular marker or mutations status information can come from either the primary tumor or from metastases; if tests are performed using either, the specified marker/mutation should be coded using the values indicated.

   2.2. Microsatellites are short, repeated sequences of DNA. Microsatellite instability-high (MSI-H) cancer cells may have a defect in the ability to correct mistakes that occur when DNA is copied in the cell.

   2.3. Mismatch repair (MMR) deficiency describes cells that have mutations (changes) in certain genes that are involved in correcting mistakes made when DNA is copied in a cell. MMR deficient cells usually have many DNA mutations, which may lead to cancer. Knowing if a tumor is MMR deficient may help plan treatment or predict how well the tumor will respond to treatment.

   2.4. KRAS and NRAS are members of the RAS family of oncogenes, which are involved in helping control cell proliferation and apoptosis. RAS gene mutational status is useful in guiding therapy in patients with certain cancers.

MUTATIONS AND TESTING (cont)

2.5. Extended RAS includes any/all RAS mutations, not just codon 12 and 13 mutations.

2.6. BRAF is a gene that encodes a protein formally known as serine/threonine-protein kinase B-Raf. It is important in cell signaling and directing cell growth.

2.7. HER-2 (also called her2/neu, c-erbB-2, human EGF receptor 2, and human epidermal growth factor receptor 2) is a protein involved in normal cell growth. HER-2 may be made in larger than normal amounts by some types of cancer cells; this may cause cancer cells to grow more quickly. Determining the amount of HER-2 may help plan treatment.

2.8. Circulating tumor DNA (ctDNA) are small pieces of DNA that are released into a person's blood by tumor cells as they die. A sample of blood can be used to look for and measure the amount of circulating tumor DNA and identify specific mutations. Circulating tumor DNA is being used as a biomarker to help diagnose some types of cancer, to help plan treatment, or to find out how well treatment is working or if cancer has come back.

2.9. If the test was not performed, then code "0 – Test not performed".

2.10. If a test was performed one or more times and all test results were positive, code that test as "1 – One or more of specified test performed, all positive".

2.11. If a test was performed one or more times and all test results were negative, code that test as "2 – One or more of specified test performed, all negative".

2.12. If a test was performed more than one time and the test results were positive the first time but were negative for any subsequent test, code that test as "3 – More than one of specified test performed, initially positive and subsequently negative".

2.13. If a test was performed more than one time and the test results were negative the first time but were positive for **any** subsequent test, code that test as "4 – More than one of specified test performed, initially negative and subsequently positive".

2.14. If there is mention of the test being performed in the record but no results, then code "8 – Test performed, results unknown".

MUTATIONS AND TESTING (cont)

2.15. If a patient received a panel of tests (also called a “gene panel”) and the specified mutation is listed as being part of the panel, assume that it was tested for. However, if the result is not listed, don’t assume the test result was negative. If the specified test result is not listed, coded this as “8 – One or more test performed, result unknown”.

2.16. If it is unknown whether the test was performed or there is no mention in the record, then code “9 – Unknown if test performed/no mention”.

METASTASIS AT DIAGNOSIS

ITEM B-12

1. **Code**: 0 – No evidence of metastasis at the site
   1 – Yes, only pathologic confirmation of metastasis at the site
   2 – Yes, only clinical confirmation of metastasis at the site
   3 – Yes, both clinical and pathologic confirmation of metastasis at the site
   9 – Unknown if metastasis at the site

   Sites
   Lung
   Distant lymph node(s)
   Bone
   Liver
   Brain/Nervous system
   Peritoneal cavity (pelvis and abdomen)
   Other (Specify pathologic) _____
   Other (Specify clinical) _____
   Other (Specify clinical and pathologic) _____

2. **Description**:

   2.1. Refer to the 2018 SEER Program Coding and Staging Manual for complete details. Code information about metastasis identified at the time of diagnosis. Information about metastatic involvement may be clinical or pathologic. These codes are NOT the codes from the SEER Manual—the POC codes are expanded to capture clinical and pathologic information. This information should not be taken from autopsy records.

   2.2. Code "0 – No" if there is no evidence of distant metastasis in the medical record or imaging reports.

   2.3. Code "1 – Yes, only pathologic confirmation of metastasis at the site" when there is pathologic but no clinical evidence of distant metastasis. Pathologic confirmation requires a biopsy positive for cancer at the metastatic site and may be reported in a pathology report or surgical records.

   2.4. Code "2 – Yes, only clinical confirmation of metastasis at the site" when there is clinical but no pathologic evidence of distant metastasis. Clinical confirmation can be derived from documentation in patient history or physical examination and imaging reports. However, imaging of distant organs is not required.

METASTASIS AT DIAGNOSIS (cont)

2.5. Code "3 – Yes, both clinical and pathologic confirmation of metastasis at the site" when there is clinical and pathologic confirmation of distant metastasis.

2.6. Code "9 - Unknown" if it is unknown whether there is metastasis at the site. If there is no information about whether the patient had any metastatic disease, all sites should be coded "9 – Unknown."

2.7. There are three "Other (Specify)" text fields. It is possible there may be multiple sites of metastasis to record. Enter all sites confirmed pathologically in "Other (Specify pathologic)". Enter all sites confirmed clinically in "Other (Specify clinical)". Enter all sites with both pathologic and clinical confirmation in "Other (Specify clinical and pathologic)".

2.8. If the record indicates that there is "metastatic disease" but does not provide any information on the site of metastasis, code all sites as "9 – unknown" and code Other (Specify) as "1 – Yes." Enter "other site" in the text field. Choose the appropriate Other Specify field for clinical only, pathologic only, or both clinical and pathologic.

2.9. If there is no evidence of metastases at any site, all sites should be coded as "0 – No."

2.10. Refer to the 2018 SEER Program Coding and Staging Manual for interpretation of ambiguous terminology.

3. Specifics

3.1. Metastasis to all sites may be a single metastatic lesion or multiple in the same site.

3.2. Bone involvement does **NOT** include bone marrow involvement.

3.3. Distant lymph node involvement does **NOT** include regional lymph nodes.

LAPAROSCOPIC COLECTOMY (COLON ONLY)

ITEM B-13

1. **Code**: 0 – No laparoscopic colectomy (or rectal cancer patient)
   1 – Laparoscopic colectomy performed
   9 – Unknown if laparoscopic colectomy performed/no mention

2. Description

2.1. Code "0 – No laparoscopic colectomy" if the patient did not have surgery or had surgical removal of tumor and resection of colon through an abdominal incision. Also code "0 – No laparoscopic colectomy (or rectal cancer patient)" for all rectal cancer patients.

2.2. Code "1 – Laparoscopic colectomy performed" if the patient had the tumor removed and the colon resected using laparoscopic surgery at any time after diagnosis.

2.3. Code "9 – Unknown" if it cannot be determined which surgical method was used or there is no mention.

2.4. **This information should be available in the operative report.**

EOD OF PRIMARY TUMOR

ITEM B-14

1. Code: Colon and Rectum

Code	Description	SS2018 T
000	In situ: Noninvasive; intraepithelial (Adeno)carcinoma in a polyp or adenoma, noninvasive	IS
050	Intramucosal, NOS Lamina propria Mucosa, NOS Confined to, but not through muscularis mucosa	L
100	Submucosa (superficial invasion) • Rectum: WITH or WITHOUT intraluminal extension to colon and/or anal canal/anus Through the muscularis mucosa but not into the muscularis propria Confined to polyp (head, stalk, NOS) Confined to colon, rectum, rectosigmoid, NOS Localized, NOS	L
200	Muscularis propria invaded • Rectum: WITH or WITHOUT intraluminal extension to colon and/or anal canal/anus	L
300	Extension through wall, NOS Invasion through muscularis propria or muscularis, NOS • Rectum: WITH or WITHOUT intraluminal extension to colon and/or anal canal/anus Non-peritonealized pericolic/perirectal tissues invaded (see Code 400 for peritonealized pericolic/perirectal tissues invaded. See Note 5) Pericolic/perirectal tissues invaded, NOS (unknown whether non-peritonealized or peritonealized. See Note 5) Perimuscular tissue invaded Subserosal tissue/(sub)serosal fat invaded	L

Code	Description	SS2018 T
	Transmural, NOS Wall, NOS	
400	Adjacent (connective) tissue(s), NOS Fat, NOS Gastrocolic ligament (transverse colon and flexures) Greater omentum (transverse colon and flexures) Mesentery (including mesenteric fat, mesocolon) Pericolic fat Perirectal fat Peritonealized pericolic/perirectal tissues invaded (see code 300 for non-peritonealized pericolic/perirectal tissues invaded. See Note 5) Rectovaginal septum (rectum) Retroperitoneal fat (ascending and descending colon only)	RE
500	Mesothelium Serosa Tunica serosa Invasion of/through the visceral peritoneum	RE
600	Adherent to other organs or structures clinically with no microscopic examination Tumor found in adhesion(s) if microscopic examination performed All Colon subsites • Abdominal wall • Retroperitoneum (excluding fat) • Small intestine Cecum (C180) • Greater omentum Ascending colon (C182) • Greater omentum • Kidney, right • Liver, right lobe • Ureter, right	RE

Code	Description	SS2018 T
	Transverse colon and flexures (C183, C184, C185) • Bile ducts • Gallbladder • Kidney • Liver • Pancreas • Spleen • Stomach Descending colon (C186) • Greater omentum • Kidney, left • Pelvic wall • Spleen • Ureter, left Sigmoid colon (C187) • Greater omentum • Pelvic wall Rectosigmoid (C199) • Cul de sac (rectouterine pouch) • Pelvic wall/pelvic plexuses • Small intestine Rectum (C209) • Anus/anal canal • Bladder (males only) • Cul de sac (rectouterine pouch) • Ductus deferens • Pelvic wall • Prostate • Rectovaginal septum • Rectovesical fascia (males only) • Seminal vesicle(s) • Skeletal muscles of pelvic floor	

Code	Description	SS2018 T
	• Vagina	
700	All Colon subsites • Adrenal (suprarenal) gland • Bladder • Diaphragm • Fallopian tube • Fistula to skin • Gallbladder • Other segment(s) of colon via serosa • Ovary(ies) • Uterus Cecum (C180) • Kidney • Liver • Ureter Transverse colon and flexures • Ureter Sigmoid colon • Cul de sac (rectouterine pouch) • Ureter Rectosigmoid • Bladder • Colon via serosa • Fallopian tube(s) • Ovary(ies) • Prostate • Skeletal muscles of pelvic floor • Ureter(s) • Vagina Rectum	D

Code	Description	SS2018 T
	• Bladder (females only) • Bone(s) of pelvis • Cervix • Perineum, perianal skin • Sacrum • Sacral plexus • Urethra Further contiguous extension	
800	No evidence of primary tumor	U
999	Unknown; extension not stated Primary tumor cannot be assessed Not documented in patient record Death Certificate Only	U

Note 1: Code 000 (behavior code 2) includes cancer cells confined within the glandular basement membrane (intraepithelial), or described as in situ.

Note 2: Code 050 (behavior code 3) includes the following:

- Intramucosal, NOS
- Lamina propria
- Mucosa, NOS
- Confined to, but not through the muscularis mucosa

Note 3: Ignore intraluminal extension to adjacent segment(s) of colon/rectum or to the ileum from the cecum; code depth of invasion or extracolonic spread as indicated.

Note 4: Tumor that is adherent to other organs or structures, macroscopically, is coded as 600 or 700. However, if no tumor is present in the adhesion, microscopically, the classification should be coded to 100-500.

Note 5: Invasion into "pericolonic/pericolorectal tissue" can be either codes 300 or 400, depending on the primary site. Some sites are entirely peritonealized; some sites are only partially peritonealized or have no peritoneum. Code 300 may not be used for sites that are entirely peritonealized (cecum, transverse colon, sigmoid colon, rectosigmoid colon, upper third of rectum).

EOD OF PRIMARY TUMOR (cont)

Code 300

Invasion through muscularis propria or muscularis, NOS

Non-peritonealized pericolic/perirectal tissues invaded [Ascending Colon/Descending Colon/Hepatic Flexure/Splenic Flexure/Upper two thirds of rectum: Posterior surface; Lower third of rectum]

Subserosal tissue/(sub)serosal fat invaded

Code 400

Mesentery

Peritonealized pericolic/perirectal tissues invaded [Ascending Colon/Descending Colon/Hepatic Flexure/Splenic Flexure/Upper third of rectum: anterior and lateral surfaces; Cecum; Sigmoid Colon; Transverse Colon; Rectosigmoid; Rectum: middle third anterior surface]

Pericolic/Perirectal fat

If the pathologist does not further describe the "pericolic/perirectal tissues" as either "non-peritonealized pericolic/perirectal tissues" vs "peritonealized pericolic/perirectal tissues" and the gross description does not describe the tumor relation to the serosa/peritoneal surface, and it cannot be determined whether the tumor arises in a peritonealized portion of the colon, code 300.

Note 6: Tumors characterized by involvement of the serosal surface (visceral peritoneum) by direct extension or perforation in which the tumor cells are continuous with the serosal surface through inflammation are coded to 500.

2. **Description**:

2.1. USE 2018 SEER CODING RULES – see EOD Colon and Rectum Data on SEER*RSA.

DATE RADIATION TO PRIMARY SITE BEGAN AND COMPLETION STATUS

ITEM B-15

1. **Code**: MM-DD-YYYY
   00-00-0000-No radiation

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
.	.	
12 - December	31	
77	77	7777-Patient or guardian refused
95	95	9595-Recommended, not given
96	96	9696-Recomm., unknown if given
97	97	9797-Unknown if given/no mention
99 - Month Unk	99 - Day Unk	9999-Year Unknown

Radiation course completion status

0 – No, not completed
1 – Yes, completed
2 – No radiation given to primary site
3 – Radiation given, unknown if completed
9 – Unknown/no mention whether radiation was given or completed

2. **Description**:

2.1. Enter the date the patient first received radiation **TO THE PRIMARY SITE** at any time after diagnosis.

2.2. Code "00-00-0000" if there was no radiation given or recommended.

2.3. Code “77-77-7777 – Patient/guardian refused radiation” if the patient or the guardian refused radiation.

2.4. Code “95-95-9595 – Recommended, not given” when the records indicate that radiation was recommended, but was not given for a reason other than refusal.

2.5. Code “96-96-9696 – Recommended, unknown if given" if it is unknown whether the recommended radiation was performed.

2.6. If it is unknown or it is not mentioned whether the patient had radiation therapy, code “97-97-9797 – Unknown if radiation given/no mention”.

DATE RADIATION TO PRIMARY SITE BEGAN AND COMPLETION STATUS (cont)

2.7. Code "99-99-9999" if it is KNOWN that the patient had radiation therapy, but the day, month and/or year given cannot be determined. If the exact date of the first therapy is unknown, code an estimate. For example, if in history and physical, the physician states the patient had radiation therapy beginning two weeks ago, code date of radiation as 14 days prior to that date. If the record states that radiation was given recently, code the month and year, but not the day. Code the day as "99." Coding the closest approximation is preferable to coding unknown.

2.8. Code whether the full course of radiation was completed (Code 1– Yes, completed) or if the patient received less than a full course of radiation (Code 0 – No, not completed).

2.9. If the patient did not receive radiation to the primary site, code date as "00-00-0000" and completion as "2 – No radiation given to primary site."

2.10. If the patient did receive radiation to the primary site, but it is unknown if the radiation therapy was completed, code date as specified above and completion as "3 – Radiation given, unknown if completed"

2.11. If it is unknown whether radiation to the primary site was given or completed, then code completion as "9 – unknown/no mention."

METASTASIS OR LOCAL RECURRENCE AFTER DIAGNOSIS

ITEM B-16

1. **Code** *i) Metastasis or local recurrence after diagnosis*

0 – Patient had metastatic disease at diagnosis
1 – No evidence of metastasis or local recurrence after diagnosis/no mention
2 – Yes, metastasis at a distant site identified after diagnosis
3 – Yes, local recurrence at primary tumor site identified after diagnosis
4 – Yes, both metastasis and local recurrence identified after diagnosis
9 – Unknown if metastasis or local recurrence after diagnosis

ii) Date first metastasis or local recurrence identified after diagnosis

MM-DD-YYYY

00-00-0000-No evidence of metastasis or local recurrence; Patient had metastatic disease at diagnosis; or Unknown if metastasis or local recurrence after diagnosis

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
.	.	
12 - December	31	
99 - Month Unk	99 - Day Unk	9999-Year Unknown

2. **Description**:

2.1. This item collects information on whether a cancer metastasis or local recurrence is identified **after** the initial tumor diagnostic work-up. Metastasis refers to the presence of the same cancer at a site distant from the primary tumor. Local recurrence refers to the presence of the same cancer at the primary tumor site **after** the primary tumor has been removed. If the primary tumor is not removed, there cannot be a local recurrence.

2.2. For item (i), Code "0 - Patient had metastatic disease at diagnosis" if at initial diagnosis the patient was diagnosed with metastatic disease (M-stage M1 or coded as "Yes" in the data item "METASTASIS AT DIAGNOSIS").

METASTASIS OR LOCAL RECURRENCE AFTER DIAGNOSIS (cont)

2.3. Code "1 – No" if there is no evidence or no mention of metastasis or local recurrence in the medical record or imaging reports **after** the initial tumor diagnosis work-up. The initial tumor diagnostic work-up is not just the initial biopsy but also includes subsequent imaging studies to determine the initial stage of the patient's cancer. **This option should be selected only if the patient did not have metastatic disease at diagnosis.** If the patient had metastatic disease at diagnosis (M-stage M1 or coded as "Yes" in METASTASIS AT DIAGNOSIS), instead use code "0 - Patient had metastatic disease at diagnosis".

2.4. Code "2 – Yes, metastasis at a distant site identified after diagnosis" when there is clinical or pathologic evidence of distant metastasis **after** diagnosis for patients who did not have an initial diagnosis of metastatic cancer.

2.5. Code "3 – Yes, local recurrence at primary tumor site identified after diagnosis" when there was surgery to completely remove the primary tumor and after the surgery there is clinical or pathologic evidence of a new cancer of the same type at the site of the primary tumor. If local or regional lymph nodes were reported as positive at diagnosis or the status of these lymph nodes was not reported at diagnosis, later findings of positive local or regional lymph nodes should NOT be considered recurrence or metastasis.

2.6. Code "4 – Yes, both metastasis and local recurrence identified after diagnosis" when there is clinical and pathologic evidence of distant metastasis after diagnosis **AND** clinical or pathologic evidence of local recurrence at the primary tumor site (including the lymph node involvement described above).

2.7. Code "9 - Unknown" if it is unknown whether there is metastasis or local recurrence after diagnosis.

2.8. For item (ii), code the first date that the metastasis or local recurrence after initial diagnosis listed in the medical record. If the patient had metastatic disease at diagnosis (item (i) coded "0"), no evidence of metastasis or local recurrence (item (i) coded "1"), or unknown whether there is metastasis or local recurrence after diagnosis (item (i) coded "9"), code item (ii) "00-00-0000".

SYSTEMIC THERAPY AGENTS

ITEMS B17-B36

1. **Code** i). Date of start of therapy
MM-DD-YYYY
00-00-0000-No systemic therapy given

Month	Day	Year
01 - January	01	Use 4-digit Year
02 - February	02	
.	.	
12 - December	31	
77	77	7777-Patient or guardian refused
95	95	9595-Recommended, not given
96	96	9696-Recomm., unknown if given
97	97	9797-Unknown if given
99 - Month Unk	99 - Day Unk	9999-Year Unknown

ii) Mode of administration:
Oral (O)
Parenteral (P)
Both Oral and Parenteral (B)
Unknown (U)
N/A (N)

B-17 CAPOX

B-18 FOLFOX

B-19 FOLFOXIRI

B-20 FOLFIRI

B-21 Fluorouracil (5-FU)

B-22 Bevacizumab (Avastin)

B-23 Capecitabine (Xeloda)

B-24 Cetuximab (Erbitux)

B-25 Folinic acid (Leucovorin) (Ancillary drug)

B-26 Irinotecan (CPT-11, Camptosar)

B-27 Levamisole (Ergamisol)

SYSTEMIC THERAPY AGENTS (cont)

B-28 Nivolumab (Opdivo)

B-29 Oxaliplatin (Eloxatin)

B-30 Panitumumab (Vectibix)

B-31 Pembrolizumab (Keytruda)

B-32 Ramucirumab (Cyramza)

B-33 Regorafenib (Stivarga)

B-34 Trifluridine & Tipiracic (Lonsurf)

B-35 Ziv-Aflibercept (Zaltrap)

B-36 Other, specify:_____

Examples of other chemotherapeutic agents which might have been given are:

Mitomycin C (Mutamycin)

This list is by no means complete and if other systemic therapeutic agents are found, please list them as well. Please be sure to record only systemic therapeutic agents.

Please be sure to record all systemic therapy agents. SEER*Rx is useful for looking up chemotherapy, immunotherapy, and other agents used to treat cancer.

2. **Description**:

2.1. Enter information for each agent separately. If therapy agents are present in the medical record that are not included in this list, please include these in the "Other Specify" field. Please record information on all systemic therapy, from diagnosis to end of available medical records, not just the first course of systemic therapy

2.2. Code the date therapy started for each systemic therapy agent given at any time following diagnosis.

2.3. Code "00-00-0000-Not given" when the patient did not receive systemic therapy, even when it was recommended. Also, use this code when the agent was considered or recommended, and it is known that the patient did not receive it. (See also "77-77-7777-Refused".) If no systemic therapy agent was given, then all agents should be coded as "00-00-0000", unless the patient or the patient's guardian refused the systemic therapy. (See also code "7777-Patient/guardian refused").

SYSTEMIC THERAPY AGENTS (cont)

2.5. Code “77-77-7777” if an agent was recommended but was not administered because of patient or guardian refusal. If the patient refuses therapy, but it is not known which specific drug was refused, all agents known to have been recommended should be coded "77-77-7777”.

2.6. Code “95-95-9595 – Recommended, not given” when the records indicate that systemic therapy was recommended but was not given for a reason other than refusal.

2.7. Code “96-96-9696 - Recommended, unknown if given” when a patient was recommended to receive an agent, but it is unknown if it was actually received. When therapy was recommended, but the agents used were not documented, all agents must be coded “96-96-9696 – Recommended, unknown if given”.

2.8. Code “97-97-9797 - Unknown" when there is no documentation regarding therapy in the medical records reviewed and there is no information about the therapy from the treating physician.

2.9. Code “99-99-9999” if it is **KNOWN** that the patient had a particular agent, but the date given cannot be determined. If the exact date of the first administration is unknown, code an estimate. For example, if in history and physical, the physician states the patient had Bevacizumab beginning two weeks ago, code date of first Bevacizumab as 14 days prior to that date. If the record states that the Bevacizumab was given recently, code the month and year, but not the day. Code the day as “99”. Coding the closest approximation is preferable to coding unknown.

2.10. When a systemic therapy is administered as one or more arms of a clinical trial and it is not known whether the patient was in that arm, this therapy should be coded as “Unknown if given” (97-97-9797). For example, if a patient were in a trial of new investigational agent vs. bevacizumab, bevacizumab should be coded as “Unknown if given”. The new investigational agent should also be listed as “Unknown if given”. However, if a patient was in a trial of bevacizumab plus new investigational agent in one arm vs. bevacizumab plus placebo in the other arm, bevacizumab should be coded as given since it is part of both arms. Do not include “placebo” as part of systemic therapies.

2.11. Even if a systemic therapy agent is listed as being administered only for palliative therapy, record the name and date of first administration of that agent in this item.

SYSTEMIC THERAPY AGENTS (cont)

2.12. For item (ii), code the mode of administration for each therapy administered. This can be coded as O = Oral (by mouth), P = Parenteral, B = Both Oral and Parenteral, U = Unknown/not specified, or N = N/A. Parenteral administration is general intravenous (IV), but can also include intramuscular (IM), subcutaneous (SC or SQ), or administration via an angiocatheter; Broviac, Groshong, or Hickman catheter; PICC line; or port-a-cath. If a therapy was not administered (date of administration in item (i) coded as 00-00-0000, 77-77-7777, or 95-95-9595), code mode of administration as N = N/A. If it is unknown if a therapy was administered (date of administration in item (i) coded as 96-96-9696 or 97-97-9797) or a therapy was administered but date of administration is unknown (date of administration in item (i) coded as 99-99-9999), code mode of administration using any available information in the medical chart, including specified recommendations regarding mode of administration.

2.13. The code for both oral and parenteral administration (B) should be used for drug regimens (e.g., CAPOX) that include both orally administered and parenterally administered systemic therapy agents

Common Data Items

A1. SEER Participant

A2. Case Number

A3. Quality Control

A4. Tumor Record Number

A5. Sequence Number

A6. Primary Site

A7. Grade Clin Path Post-Th

A8. Hospital Code

A9. Insurance Status

	≤ 30 days	> 30 days
No ins/ Self Pay……		
Medicare FFS……		
Medicare HMO……..		
Medicare Part D/PDP…….		
Medicare + Private (supp)..		
Medicaid……..		
Medicaid pending……		
Private/IPA/HMO……		
Tricare/Other military……..		
Veterans Affairs……..		
Indian Health Service……		
Other (enter text below)….		

≤ 30 days _____

> 30 days _____

A10. Treatment Protocol Registration

A11. Protocol Sponsor and Number

A12. Case Information Verified

A13. Height/Weight

Ht Ht Units _____

Wt Wt Units _____

A14. Date of First Onco Consul ___ /___ /_____ mm dd yyyy

A15. Impact of COVID-19 on Cancer Care **AFTER cancer dx**

A. Patient Dx'd with C-19

B. Date of 1st Pos C-19 Dx ___ /___ /_____ mm dd yyyy

C. Date of 1st hosp adm for C-19 ___ /___ /_____ mm dd yyyy

A15. Impact of COVID-19 on:

		Other, specify
D. Cancer Diagnosis		
E. Surgery to primary site		
F. Radiation to primary site		
G. Systemic Therapy		
H. Palliative Care		

A16. Impact of COVID-19 on Finances/Insurance:

Only code info in A-15 through A-17 **for after cancer dx**

A. Patient's finances

B. Patient's Employment

C. Patient's Insurance

A17. Palliative Care **AFTER cancer dx**

A. Palliative Care Received

B. Date of 1st Pall Care ___ /___ /_____ mm dd yyyy

C. Counseling/mental health Received

D. Date of 1st couns/mental hlth ___ /___ /_____ mm dd yyyy

E. Hospice service/admission

F. Date of 1st hospice/adm ___ /___ /_____ mm dd yyyy

A18. NextGen Sequencing (NGS)

A19. Smoking / Tobacco Use

Packs per day

Non-cigarette tobacco use

Num Years Smoked/non-cig use

Pack years

Smoking Status at DX

A20. Secondhand Smoke Exposure

A21. Family history of cancer of same site

B1. Date of first positive biopsy ___ /___ /_____
mm dd yyyy

B2. Date of path conf report ___ /___ /_____
mm dd yyyy

B3. Primary site surgery and date ☐☐

___ /___ /_____
mm dd yyyy

B4. Pathological margins ☐

B5. Size of primary tumor
Clinical ☐☐☐
Pathologic ☐☐☐

B6. Perforation ☐

B7. Obstruction ☐

B8. Method of tumor detection ☐☐

Other _____

B9. Lymph nodes positive ☐☐

B10. Lymph nodes examined ☐☐

B11. Mutations and testing
- ☐ *MSI/Microsatellite instability*
- ☐ *MMR deficiency*
- ☐ *KRAS*
- ☐ *NRAS*
- ☐ *Extended RAS*
- ☐ *BRAF*
- ☐ *HER-2*
- ☐ *Circulating tumor DNA (ctDNA)*

B12. Metastasis at diagnosis
- ☐ *Lung*
- ☐ *Distant LNs*
- ☐ *Bone*
- ☐ *Liver*
- ☐ *Brain/nervous system*
- ☐ *Peritoneal Cavity (pelvis and abdomen)*
- ☐ *Other (path)* _____
- ☐ *Other (clin)* _____
- ☐ *Other (clin AND path)* _____

B13. Laparoscopic colectomy (colon only) ☐

B14. EOD of primary tumor ☐☐☐

B15. Date radiation to primary site ___ /___ /_____
mm dd yyyy

Completion status ☐

B16. Metastasis or local recurrence ☐

___ /___ /_____
mm dd yyyy

Enter systemic therapy on next page

Notes

Systemic Therapy Agent	Date (mm/dd/yyyy)	Mode of Administration →
B17. CAPOX	____/____/_____	☐
B18. FOLFOX	____/____/_____	☐
B19. FOLFOXIRI	____/____/_____	☐
B20. FOLFIRI	____/____/_____	☐
B21. Fluorouracil (5-FU)	____/____/_____	☐
B22. Bevacizumab (Avastin)	____/____/_____	☐
B23. Capecitabine (Xeloda)	____/____/_____	☐
B24. Cetuximab (Erbitux)	____/____/_____	☐
B25. Folinic acid (Leucovorin)	____/____/_____	☐
B26. Irinotecan (CPT-11, Camptosar)	____/____/_____	☐
B27. Levamisole (Ergamisol)	____/____/_____	☐
B28. Nivolumab (Opdivo)	____/____/_____	☐
B29. Oxaliplatin (Eloxatin)	____/____/_____	☐
B30. Panitumumab (Vectibix)	____/____/_____	☐
B31. Pembrolizumab (Keytruda)	____/____/_____	☐
B32. Ramucirumab (Cyramza)	____/____/_____	☐
B33. Regorafenib (Stivarga)	____/____/_____	☐
B34. Trifluridine & Tipiracic (Lonsurf)	____/____/_____	☐
B35. Ziv-Aflibercept (Zaltrap)	____/____/_____	☐
B36. Other, specify	____/____/_____	☐

_____

O=Oral
P=Parenteral
B=Both Oral & Parenteral
U=Unknown
N=N/A

Coding Info

Abstractor ID
☐☐☐☐☐

Date Abstracted
___/___/_____
mm dd yyyy

List all co-morbids on next page

C. List all co-morbid conditions from the hospitalization for initial cancer treatment.

Registry ☐☐
Case # ☐☐☐☐☐☐☐☐

COLORECTAL CANCER POC20

1.	
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Abstractor's questions, problems or comments. Attach pages and documentation as needed.

POC 2020 DATA ACQUISITION MANUAL

APPENDIX A

Overall Patterns of Care Study

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POC 2020 DATA ACQUISITION MANUAL

APPENDIX B

PHYSICIAN VERIFICATION FORMS

Patterns of Care Study 2020
Physician Verification Form

Patient Name _____

Patient Identification No. _____Physician_____

Date of Initial Diagnosis _____Type of Cancer Breast Cancer

PLEASE DESCRIBE ALL CANCER THERAPY GIVEN TO THE PATIENT, REGARDLESS OF WHERE, WHEN OR BY WHOM THE THERAPY WAS ADMINISTERED. If you did not see this patient, please go to question #12.

1. Did the patient receive **RADIATION** therapy to the **PRIMARY SITE** at any time after diagnosis? (circle one)

   ___ Yes (Date_____/_____/_____ No Patient/Guardian Refused Unknown

2. Did this patient receive any **SYSTEMIC THERAPY AGENTS?**
   _____Yes (Please mark all that apply in Q.3)
   _____Patient/Guardian refused ALL systemic therapy (Skip to Q.4)
   _____No (Skip to Q.4)
   _____Unknown (Skip to Q.4)

3. Please indicate whether each of the agents listed below was given, the date first administered if it was given, and whether the patient/guardian refused the agent if it was recommended. **If given**, please record the mode of administration in the last column.

Drug and Date	Circle if not given	Circle if refused	Circle Mode of Administration
Ado-trastuzumab emtansine (Kadcyla) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Capecitabine (Xeloda) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Carboplatin Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Cyclophosphamide Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Docetaxel (Taxotere, Docefrez) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Doxorubicin (Adriamycin) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Eribulin (Halaven) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Fluorouracil (5-FU) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Gemcitabine (Gemzar) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Lapatinib (Tykerb) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Nab-Paclitaxel (Abraxane) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Paclitaxel (Taxol, Onxol) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Pembrolizumab (Keytruda) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Pertuzumab (Perjeta) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Tamoxifen (Nolvadex) Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown

Trastuzumab (Herceptin)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Vinorelbine (Navelbine)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Aromatase Inhibitors	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
GnRH analogs	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Other, specify 1 _____	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Other, specify 2 _____	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Other, specify 3 _____	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown

4. Was this patient actively enrolled in an active/open clinical trial? ____Yes
   ____No (Skip to Q.6)

5. Please provide the name of the clinical trial sponsor and the clinical trial number.
   Sponsor (example: SWOG)_____
   Number (example: 8711)_____

6. Was the patient tested for and found to be positive for the following genetic mutations:

Mutation	**Tested (circle one)**	**Positive (Circle one)**
MSI/Microsatellite instability	Yes No	Yes No
MMR deficiency/Mismatch repair deficiency	Yes No	Yes No
Circulating tumor DNA (ctDNA)	Yes No	Yes No
NGS/Next-Generation Sequencing	Yes No	Yes No

7. Was the patient given the following molecular testing?

Other Tumor Molecular Testing	**Tested (circle one)**	**Test Result (circle one)**
IHC test for HER-2	Yes No	Neg 1+ 2+ 3+ Pos, value unk Equivocal
ISH/FISH test for HER-2	Yes No	Value ____ Neg Pos, value unk Equivocal
PD-L1 test	Yes No	Score (% PD-L1 positive) ____
Breast Cancer Index (BCI) test	Yes No	Score (xxx.xx%) ____
Multi-gene assay (e.g., Oncotype, Prosigna, MammaPrint)	Yes No	Recurrence Score™ _____ Low Risk Intermediate Risk High Risk
PreludeDx (DCIS recurrence risk)	Yes No	Value ____ (00.1 through 10.0)

Patterns of Care Study 2020
Physician Verification Form

8. Did this patient receive (check all that apply): ____ Palliative care → Type_____
____ Hospice care
____ Counseling/mental health svcs **after cancer dx**

9. Was the patient diagnosed with COVID-19 following cancer dx? ____ Yes → 1st pos test date _____
____ No

10. Did the COVID-19 pandemic impact the patient's care?

Type of Treatment	**Impact of COVID-19 (C-19) on Cancer Treatment (Check One per Row)**			
	Patient did not receive this tx OR no impact of C-19	Delayed, altered, or canceled treatment due to C-19	Patient refused this treatment due to C-19	Other impact of C-19 on this treatment
Primary site surgery	☐	☐	☐	☐
Primary site radiation	☐	☐	☐	☐
System therapy (any)	☐	☐	☐	☐
Palliative care	☐	☐	☐	☐

11. Did this patient experience a metastasis or recurrence AFTER diagnosis? ____Yes ____No

If Yes, site of metastasis or recurrence: _____

12. If you believe this information to be incomplete, are there other physicians we could contact who may have further information on this patient?

Dr._____ Address _____

_____

Dr._____ Address _____

_____

Comments: _____

_____

Signature_____ Date _____

Title/Role of person in the practice completing this form: _____

THANK YOU FOR YOUR HELP WITH THIS IMPORTANT STUDY.

Patient Name _____

Patient Identification No. _____Physician_____

Date of Initial Diagnosis _____Type of Cancer Colon/Rectum Cancer

PLEASE DESCRIBE ALL CANCER THERAPY GIVEN TO THE PATIENT, REGARDLESS OF WHERE, WHEN OR BY WHOM THE THERAPY WAS ADMINISTERED. If you did not see this patient, please go to question #10.

1. Did the patient receive **RADIATION** therapy to the **PRIMARY SITE** at any time after diagnosis? (circle one)

   ___ Yes (Date_____/_____/_____ No Patient/Guardian Refused Unknown

2. Did this patient receive any **SYSTEMIC THERAPY AGENTS?**
   _____Yes (Please mark all that apply in Q.3)
   _____Patient/Guardian refused ALL systemic therapy (Skip to Q.4)
   _____No (Skip to Q.4)
   _____Unknown (Skip to Q.4)

3. Please indicate whether each of the agents listed below was given, the date first administered if it was given, and whether the patient/guardian refused the agent if it was recommended. **If given**, please record the mode of administration in the last column.

Drug and Date		Circle if not given	Circle if refused	Circle Mode of Administration
CAPOX	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
FOLFOX	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
FOLFOXIRI	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
FOLFIRI	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Fluorouracil (5-FU)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Bevacizumab (Avastin)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Capecitabine (Xeloda)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Cetuximab (Erbitux)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Folinic acid (Leucovorin)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Irinotecan (CPT-11, Camptosar)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Levamisole (Ergamisol)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Nivolumab (Opdivo)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Oxaliplatin (Eloxatin)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Panitumumab (Vectibix)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Pembrolizumab (Keytruda)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Ramucirumab (Cyramza)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown

Regorafenib (Stivarga)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Trifluridine & Tipiracic (Lonsurf)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Ziv-Aflibercept (Zaltrap)	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Other, specify 1 _____	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Other, specify 2 _____	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown
Other, specify 3 _____	Yes (Date____/____/_____)	No	Patient/guardian refused	Oral Parenteral Both Unknown

4. Was this patient actively enrolled in an active/open clinical trial? ____Yes
   ____No (Skip to Q.6)

5. Please provide the name of the clinical trial sponsor and the clinical trial number.
   Sponsor (example: SWOG)_____
   Number (example: 8711)_____

6. Was the patient tested for and found to be positive for the following genetic mutations:

Mutation	**Tested (circle one)**	**Positive (Circle one)**
MSI/Microsatellite instability	Yes No	Yes No
MMR deficiency/Mismatch repair deficiency	Yes No	Yes No
KRAS	Yes No	Yes No
NRAS	Yes No	Yes No
Extended RAS	Yes No	Yes No
BRAF	Yes No	Yes No
HER-2	Yes No	Yes No
Circulating tumor DNA (ctDNA)	Yes No	Yes No

7. Did this patient receive (check all that apply): ____ Palliative care → Type_____
   ____ Hospice care
   ____ Counseling/mental health svcs **after cancer dx**

8. Was the patient diagnosed with COVID-19 following cancer dx? ____ Yes → 1st pos test date _____
   ____ No

9. Did the COVID-19 pandemic impact the patient's care?

Type of Treatment	**Impact of COVID-19 (C-19) on Cancer Treatment (Check One per Row)**			
	Patient did not receive this tx OR no impact of C-19	Delayed, altered, or canceled treatment due to C-19	Patient refused this treatment due to C-19	Other impact of C-19 on this treatment
Primary site surgery	☐	☐	☐	☐
Primary site radiation	☐	☐	☐	☐
System therapy (any)	☐	☐	☐	☐
Palliative care	☐	☐	☐	☐

10. Did this patient experience a metastasis or recurrence AFTER diagnosis? ____Yes ____No

If Yes, site of metastasis or recurrence: _____

11. If you believe this information to be incomplete, are there other physicians we could contact who may have further information on this patient?

Dr._____ Address _____

_____

Dr._____ Address _____

_____

Comments: _____

_____

Signature_____ Date _____

Title/Role of person in the practice completing this form: _____

THANK YOU FOR YOUR HELP WITH THIS IMPORTANT STUDY.