Wolters Kluwer

Gestational breast cancer: Treatment

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INTRODUCTION

Gestational breast cancer (or pregnancy-associated breast cancer) is defined as breast cancer that is diagnosed during pregnancy, in the first postpartum year, or any time during lactation. Gestational breast cancer presents a challenging clinical situation, since the welfare of both the mother and the fetus must be taken into account. There are limited prospective data about diagnosis, treatment, and outcome of breast cancer during pregnancy; much of the clinical evidence is limited to retrospective case series and case reports.

The treatment and prognosis of gestational breast cancer will be reviewed here. The epidemiology and diagnosis of gestational breast cancer is discussed separately. (See "Gestational breast cancer: Epidemiology and diagnosis".)

TREATMENT

In general, pregnant women with breast cancer should be treated according to guidelines for nonpregnant patients, with some modifications to protect the fetus. However, the treatment should be approached with curative intent. Therefore, treatment of gestational breast cancer should not be unnecessarily delayed because of pregnancy. Informed consent is a critical component of choosing appropriate therapy. Although pregnancy termination may be considered during treatment planning, pregnancy termination has not been demonstrated to improve outcomes in gestational breast cancer. (See 'Elective termination of pregnancy' below.)

Importantly, all patients with gestational breast cancer should be evaluated for distant metastatic disease according to guidelines in nonpregnant patients with breast cancer. In order to protect the fetus, this can be attenuated to include: chest radiograph with fetal shielding, ultrasound of the liver or magnetic resonance imaging (MRI) of the liver, and MRI of the spine without contrast to evaluate for bone metastases [1,2]. (See "Gestational breast cancer: Epidemiology and diagnosis", section on 'Diagnosis and staging' and "Clinical features, diagnosis, and staging of newly diagnosed breast cancer", section on 'Postdiagnosis evaluation'.)

Locoregional treatment — The same local treatment options that are available for nonpregnant patients should be considered in pregnant women, with the exception of radiation therapy (RT). As in nonpregnant women, surgery is the definitive local treatment for gestational breast cancer. Breast and axillary lymph node surgery during any trimester of pregnancy appears to be associated with minimal fetal risk [3-8]. (See "Anesthesia for nonobstetric surgery during pregnancy".)

Mastectomy — Mastectomy may be chosen when the patient opts to continue the pregnancy, even for women with clinical anatomic stage I and II disease [3,9]. An advantage of mastectomy may be the elimination of the need for breast RT in some cases, as per treatment guidelines. If breast reconstruction is desired, delaying until after delivery may be preferred, depending upon the reconstruction chosen. (See "Mastectomy" and "Overview of breast reconstruction".)

Breast-conserving surgery — The therapeutic equivalence of mastectomy and breast-conserving therapy (breast-conserving surgery [BCS] followed by RT) has been demonstrated in nonpregnant women; this is also true for the pregnant patient. BCS can be used effectively as RT can be delayed after the administration of adjuvant or neoadjuvant chemotherapy. (See "Breast-conserving therapy".)

BCS is feasible and safe in the pregnant woman with breast cancer and is reported to have no adverse impact on locoregional recurrence rates or complication rates [10-13]. However, RT to the ipsilateral breast is important to achieve optimal local control, and therapeutic breast RT is contraindicated during pregnancy because of the risk associated with fetal radiation exposure [14]. Therefore, RT should be delayed until after delivery. Alternatively, mastectomy could be considered if the diagnosis is made early in a pregnancy, systemic therapy is not warranted, and there would be a significant delay to RT. (See "Adjuvant radiation therapy for women with newly diagnosed, non-metastatic breast cancer".)

Radiation therapy — RT is used in the routine management of breast cancer to optimize local control in women who undergo BCS and may improve survival in certain high-risk women treated with mastectomy. Radiation should be delayed until after delivery. If the clinician believes it is in the best interests of the patient, a discussion of potential risks and

harms for the patient and the developing fetus is warranted. (See "Adjuvant radiation therapy for women with newly diagnosed, non-metastatic breast cancer".)

The use of therapeutic radiation is generally avoided during pregnancy because of the risk to the fetus. There are four categories of radiation sequelae to the fetus: pregnancy loss (miscarriage or stillbirth), malformation, disturbances of growth or development, and mutagenic and carcinogenic effects [14,15]. The amount of radiation to which the fetus is exposed depends upon the dose and the stage of pregnancy when therapeutic radiation is administered. Even with appropriate shielding, fetal exposure to therapeutic breast irradiation will increase as the fetus grows and moves closer to the diaphragm.

Typical radiation doses used in breast cancer are between 46 to 60 Gray (Gy). It has been estimated that the administration of 50 Gy external beam irradiation to the breast could result in a first trimester fetal dose of 0.04 to 0.15 Gy, or a third trimester dose as high as 2 Gy [16-18]. The threshold at which an increased risk of congenital malformations is observed in radiation-exposed embryos/fetuses has not been definitively determined. For the developing fetus under 14 weeks of gestation, the threshold for possible prenatal radiation effects is between 0.10 and 0.50 Gy (10 to 50 rads) [19]. After 14 weeks of gestation, the consensus of most researchers is that this threshold is at least 0.50 Gy (50 rads). (See "Diagnostic imaging in pregnant and lactating patients".)

Management of the axilla — Axillary staging and dissection are important components of breast cancer therapy. Assessment of nodal status provides prognostic information and is used in selecting adjuvant treatment, and axillary lymph node dissection improves local disease control. The use of sentinel lymph node biopsies during pregnancy is controversial, with case series demonstrating increasing evidence of safety and efficacy in pregnant patients [1,20-22].Should sentinel lymph node dissection be offered, the limited current data should be discussed with the patient. Those with clinically positive ipsilateral axillary lymph nodes or with inflammatory breast cancer are most likely to derive benefit from axillary lymph node dissection [23], as for nonpregnant patients. (See "Overview of management of the regional lymph nodes in breast cancer".)

The safety and efficacy of sentinel lymph node biopsy during pregnancy is discussed in detail elsewhere. (See "Overview of sentinel lymph node biopsy in breast cancer", section on 'Pregnancy'.)

The use of ultrasound and fine needle aspiration in the assessment of clinically suspicious lymph nodes is discussed separately. (See "Gestational breast cancer: Epidemiology and diagnosis", section on 'Lymph nodes'.)

Systemic therapy — The data suggest it is safe to administer many agents used in the treatment of breast cancer during pregnancy when initiated after the first trimester, and that

the majority of pregnancies result in live births with low related morbidity in the newborns [3,24-27]. The most data available are with anthracycline-based chemotherapy, often on an every-three-week schedule. In reported case series, chemotherapy given on a dose-dense schedule (ie, treatment every two weeks) does not appear to increase the risks of maternal or fetal complications compared with treatment administered every three weeks [28]. The subtype of breast cancer and the week of pregnancy may inform the schedule of chemotherapy to choose. (See 'Pregnancy and infant outcome' below.)

Decision making and use of adjuvant systemic therapy for breast cancer in premenopausal women is discussed in detail separately; specific considerations for gestational breast cancer are discussed below.

- (See "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer".)
- (See "Adjuvant systemic therapy for HER2-positive breast cancer".)
- (See "Overview of side effects of chemotherapy for early-stage breast cancer".)

Effect of pregnancy on drug pharmacokinetics — In general, pregnant women receive similar body surface-area based chemotherapy doses as nonpregnant women, which are adjusted with continued weight gains [29]. As in nonpregnant patients, potentially curative adjuvant chemotherapy is administered, if feasible, in pregnant women without dose modifications.

Little information is available regarding the pharmacokinetics of individual cytotoxic agents in the pregnant patient [29]. Alterations in drug distribution are expected due to the physiologic changes that occur with pregnancy.

- Increases in blood volume and renal and hepatic clearance might be expected to reduce active drug concentrations [29,30]. (See "Maternal adaptations to pregnancy: Renal and urinary tract physiology".)
- Diminished gastric motility may impact the absorption of orally administered drugs.
- Plasma albumin decreases in pregnancy, increasing the amount of unbound active drug; however, this effect is counterbalanced by high levels of estrogen, which increases other plasma proteins [29].
- The "third space" of the amniotic sac may impact drug concentration [31].
- The multidrug resistance p-glycoprotein has been detected in fetal tissues and in the gravid endometrium and may offer some degree of protection to the fetus [32,33].

It is unclear how these physiologic changes impact upon active drug concentrations and their resulting efficacy and toxicity. The deleterious effects of drug exposures on the fetus

are discussed separately. (See "Congenital anomalies: Approach to evaluation".)

Timing of chemotherapy — The period of exposure to chemotherapy is critical; chemotherapeutic exposure during the first trimester of pregnancy, the period of organogenesis (5 to 10 weeks after the first day of the last menstrual period), carries the greatest risk of congenital abnormalities, chromosomal abnormalities, stillbirth, and miscarriage, with one report estimating the risk of fetal malformation during first trimester exposure to be 15 to 20 percent (versus 2 to 3 percent among all liveborn infants) [26,31,34-39].

The incidence of congenital malformations is low if chemotherapy is administered to women in the second or third trimester, after the major period of organogenesis [3,9,25,26]. However, chemotherapy in the second or third trimester has been associated with intrauterine growth restriction, lower gestational age at birth (prematurity), and low birth weight in about one-half of exposed infants [26,29,40].

Among nonpregnant women, delaying the initiation of chemotherapy by three to six months diminishes the long-term value of the chemotherapy [41,42]. In pregnant patients who have breast cancer, the challenging decision is often whether it is better to start chemotherapy or wait until after delivery. Patients may desire waiting until after delivery to avoid risk to the pregnancy and to the baby, and this should be discussed on an individual basis depending upon the week of gestation and the biologic features of their cancer. For pregnant breast cancer patients who need chemotherapy treatment, clinicians should advise against a delay in the initiation of systemic chemotherapy once the pregnancy has safely reached the second or third trimester. As noted, care needs to be taken to avoid exposing the fetus to chemotherapy during the first trimester, and to stop chemotherapy prior to delivery so that the mother and infant are not experiencing treatment-related toxicities in the delivery or postpartum stages.

Indications for preoperative chemotherapy in gestational breast cancer are discussed above. (See 'Breast-conserving surgery' above.)

Timing of delivery — The timing of delivery in relation to chemotherapy administration should be carefully considered. Ideally, the delivery should occur following the mother's white blood cell count and platelet count nadir to reduce the potential risk of infectious complications and bleeding from thrombocytopenia.

Chemotherapy should be avoided for three to four weeks before delivery to avoid transient neonatal myelosuppression and potential complications of sepsis and death whenever possible. Also if possible, the fetus should be delivered after demonstration of fetal pulmonary maturity and at 34 or more weeks of gestation, at which time morbidity of

prematurity is relatively low. (See "Preterm birth: Definitions of prematurity, epidemiology, and risk factors for infant mortality".)

Excretion of drugs into breast milk — Many cytotoxic drugs, especially the alkylating agents, are excreted in breast milk [36]. Neonatal neutropenia has been reported in an infant breastfed during maternal treatment with cyclophosphamide [43]. In addition, little is known about excretion of endocrine agents in breast milk. As a general rule, breastfeeding should be avoided in women while receiving chemotherapy, trastuzumab and lapatinib, and endocrine therapy.

Chemotherapeutic and biologic agents — Most chemotherapy agents used in the treatment of breast cancer have been associated with teratogenic effects in humans. The risks for miscarriage, fetal death, and major malformations are highest when chemotherapy is administered in the first trimester. Outside of that window, most agents show a surprisingly low-risk profile. However, information on the effects of antineoplastic drugs administered during pregnancy is largely retrospective and likely reflects publication bias.

Anthracycline-based chemotherapy — The most commonly used regimens in pregnant women with breast cancer are doxorubicin plus cyclophosphamide (AC) or fluorouracil, doxorubicin, and cyclophosphamide (FAC) [2,4,9,29]. Although experience with anthracycline-based regimens in pregnancy suggests their safety and efficacy, there are limited prospective data, especially on the outcomes of children who were exposed in utero.

In a prospective single-arm study, 87 pregnant breast cancer patients were treated with FAC in the adjuvant or neoadjuvant setting [44]. No stillbirths, miscarriages, or perinatal deaths occurred in the cohort of patients who received FAC chemotherapy during their second and/or third trimester. The majority of the children did not have any significant neonatal complications. Three children were born with congenital abnormalities: one each with Down syndrome, ureteral reflux, or clubfoot. The rate of congenital abnormalities in the cohort was similar to the national average of 3 percent.

A case-control study and smaller retrospective series of anthracycline-based chemotherapy have yielded similar findings [35,45-48].

Although it appears that gestational breast cancer can be safely treated with AC or FAC chemotherapy during the second and third trimesters (without significant short-term complications for the children exposed to chemotherapy in utero), less is known about late sequelae, such as impaired cardiac function and fertility. Although children and adults receiving anthracyclines are at risk of developing a dose-related cardiomyopathy, in utero exposure to anthracyclines does not appear to carry a significant risk of clinical cardiotoxicity (although there may be changes in echocardiographic strain patterns) [49,50].

In one reported case of gestational breast cancer treated with four cycles of AC chemotherapy initiated early in the second trimester, fetal echocardiograms, performed every two weeks and repeated postnatally to age 2, showed no myocardial dysfunction [51]. However, at least four cases of neonatal cardiac effects have been reported after in utero exposure to anthracyclines, and there are several cases of in utero fetal death after exposure to idarubicin or epirubicin (among other agents) [26,52-55]. Largely because of these reports, doxorubicin is preferred over idarubicin or epirubicin for use in pregnancy [29]. (See "Clinical manifestations, diagnosis, and treatment of anthracycline-induced cardiotoxicity" and "Risk and prevention of anthracycline cardiotoxicity".)

Cyclophosphamide and doxorubicin can enter breast milk, and breastfeeding is contraindicated during chemotherapy. (See 'Excretion of drugs into breast milk' above.)

Taxanes — Safety data on the use of taxanes during pregnancy are expanding. A 2010 review of the literature identified 40 case reports of taxane administration during pregnancy (paclitaxel in 21, docetaxel in 16, and both drugs in three) [56]. Taxanes were administered in the second and third trimesters in 38 patients and for the treatment of breast cancer in 27 patients. Given the limitations and bias inherent in case reports, the use of taxanes appears feasible and safe during the second and third trimesters of pregnancy, with minimal maternal, fetal, or neonatal toxicity [1].

Anti-HER2 therapies — The use of trastuzumab during pregnancy is contraindicated. Exposure to trastuzumab during pregnancy can result in oligohydramnios, which in some cases may lead to pulmonary hypoplasia, skeletal abnormalities, and neonatal death [57,58]. A US Food and Drug Administration advisory regarding in utero exposure to trastuzumab recommends against use of trastuzumab due to fetal deaths, pulmonary hypoplasia, and fetal developmental abnormalities after exposure [57].

Women exposed to trastuzumab during pregnancy require ongoing monitoring of amniotic fluid volume, which is a marker of fetal renal status, throughout the pregnancy [57].

Nursing mothers are advised to discontinue nursing or discontinue trastuzumab. The manufacturer recommends that women should not breastfeed while receiving trastuzumab and for six months following the last dose.

Lapatinib is an orally active dual erbB-1/2 tyrosine kinase inhibitor that affects both human epidermal growth factor receptor 2 (HER2)/neu (erbB-2) and the epidermal growth factor receptor (EGFR, also called erbB-1). It has been approved for use in HER2-overexpressing advanced breast cancers that have progressed after exposure to trastuzumab, but it is not a standard treatment for early breast cancer.

In a case report of maternal exposure to lapatinib for 11 weeks during the first and second trimester of pregnancy, there was an uncomplicated delivery of a healthy female infant, who

was developmentally normal at 18 months of age [59]. However, until more information is available, we recommend against the use of lapatinib during pregnancy and lactation.

There are currently no significant data on the safety of other anti-HER2 agents such as pertuzumab, ado-trastuzumab emtansine (TDM-1), and other antibody drug conjugates to date and therefore we do not currently recommend these agents until after delivery.

Other — Methotrexate should be avoided at all stages of pregnancy because of delayed elimination from sequestered spaces (such as amniotic fluid) as well as its abortifacient effect and teratogenic potential [31,35].

Although there is no evidence that cisplatin (and carboplatin) is harmful during pregnancy, higher levels of free drug in the mother and fetus (due to changes in cisplatin protein binding caused by lower albumin levels) may increase the risk of toxicity in both [60]. (See "Chemotherapy of ovarian cancer in pregnancy".)

Endocrine therapy — The use of selective estrogen receptor modulators (SERMs) such as tamoxifen during pregnancy is generally avoided. They have been associated with vaginal bleeding, miscarriage, congenital malformations, and fetal death [61-63]. In addition, the long-term effects of tamoxifen and whether it may increase gynecological cancers in daughters (as diethylstilbestrol does) are unknown. In pregnant rats, tamoxifen has been associated with breast cancer in female offspring [63].

Aromatase inhibitors (AIs) are not used in premenopausal women, but the use of AIs combined with ovarian suppression, particularly luteinizing hormone-releasing hormone (LHRH) agonists, may be used following term delivery. AIs and LHRH agonists are both contraindicated in pregnancy.

Since tamoxifen can suppress postpartum lactation and its excretion into breast milk is not known, its use should be avoided in nursing mothers [64]. Taking into account potential benefits from tamoxifen therapy and the availability of alternative treatment options, a decision should be made whether to avoid or discontinue nursing or to avoid or discontinue tamoxifen. AIs and LHRH agonists should also be avoided during lactation.

Immunotherapy — There remains very limited data of the use of immune checkpoint inhibitors (anti-programmed cell death protein 1, anti-programmed cell death ligand 1, and anti-cytotoxic T-lymphocyte antigen) during pregnancy. In one series of seven published reports of immune checkpoint inhibitors given during pregnancy, including two twin pregnancies, five patients conceived while on checkpoint inhibitors and two initiated during (week 9 and week 18). Six of these patients had melanoma and one patient with a placental trophoblastic tumor. Four of these patients had intrauterine growth restriction and/or placental insufficiency. Two of nine neonates had hypothyroidism that recovered at six

months, one twin was missing a left hand and this was felt to not be due to the therapy but due to cord strangulation of the limb [65].

Antiemetics — Antiemetics, including promethazine, selective serotonin (5-HT) antagonists, neurokinin 1 (NK1) antagonists, and droperidol combined with diphenhydramine or dexamethasone are used to treat severe nausea and vomiting in pregnant women and are generally considered safe. However, long-term dexamethasone therapy should be avoided, if possible, because of potential maternal and fetal risks. (See "Nausea and vomiting of pregnancy: Treatment and outcome".)

Granulocyte colony stimulating factor — Safe use of G-CSF (and recombinant erythropoietin) in human pregnancy has been reported [36]. Although there are no prospective trials evaluating the use of G-CSF or granulocyte macrophage colony stimulating factor (GM-CSF) in pregnant women, these agents are safe in the treatment of neonatal neutropenia and/or sepsis [66,67].

Elective termination of pregnancy — The decision to continue or terminate the pregnancy should be individualized and made by a fully informed woman in conjunction with her clinician. Early termination of pregnancy does not improve the outcome of gestational breast cancer [68]. In fact, some series suggest decreased survival in pregnant women who electively terminate their pregnancies compared with those who continue the pregnancy [69]. However, these studies are retrospective case reviews and do not account for possible bias; women with more advanced disease or poorer prognostic features possibly were more likely to be counseled to have an abortion [18].

In addition to the usual reasons for pregnancy termination, some factors that should be considered in women with gestational breast cancer include:

- Whether she is willing to assume a possible risk of fetal toxicity or complications from breast cancer treatment during pregnancy.
- Her prognosis and ability to care for her offspring.
- The effect of breast cancer treatment on future fertility. (See "Overview of infertility and pregnancy outcome in cancer survivors".)

PROGNOSIS

The impact of the diagnosis of gestational breast cancer on maternal health, fetal outcome, and risks to the fetus should be considered individually.

Maternal health — Traditionally, pregnancy-associated breast cancer has included a diagnosis during and within one to three years after pregnancy. Observational data have

demonstrated survival differences for those patients diagnosed during pregnancy compared with those diagnosed after a pregnancy. For pregnant patients diagnosed and treated with standard local and systemic therapies, multiple series describe no significant survival differences compared with nonpregnant patients. However, data are conflicting. There are also large retrospective reviews suggesting worse survival in those diagnosed both during and after a pregnancy compared with cancers not associated with pregnancy [27,48,70,71].

As examples, comparing pregnancy versus nonpregnancy associated cancers:

- In an analysis of two registry studies including 662 pregnant and 2081 nonpregnant patients treated with chemotherapy for breast cancer, at a median follow-up of 66 months, both disease free and overall survival were similar for pregnant and nonpregnant patients [27].

- By contrast, in a retrospective analysis from 2003 to 2017 of 24,307 patients with any type of cancer, including approximately 7000 patients with breast cancer, there was an increased risk of mortality with breast cancers diagnosed during pregnancy (adjusted hazard ratio [HR] 2.0) and during the first year postpartum (adjusted HR 1.6) compared with other breast cancers [72]. While this study did evaluate for time to treatment start, the local and systemic interventions (versus standard of care treatments) were not described and may limit interpretation of the findings.

  Similarly, in a nationwide cohort study conducted in Sweden between 1970 and 2018, there were approximately 42,000 nonpregnancy-associated breast cancers and 975 pregnancy-associated breast cancers [71]. While the authors of the study reported breast cancer deaths were more frequent among those with pregnancy-associated cancers compared with other breast cancers (HR 1.72, 95% CI 1.54-1.93), irrespective of whether the cancer was diagnosed during pregnancy or during the postpartum period, other factors including age, stage, tumor subtype, and treatment history were not taken into account for this analysis.

Earlier data suggest a higher risk of poor outcomes with postpartum cancers compared with cancers diagnosed in pregnancy. A 2012 meta-analysis comprising over 3000 cases of gestational breast cancer and 37,100 controls found that although gestational breast cancer was associated with a higher risk of death (HR 1.44, 95% CI 1.27-1.63), the association appeared to be limited primarily to women diagnosed in the postpartum period (HR 1.84, 95% CI 1.28-2.65) rather than during pregnancy (HR 1.29, 95% CI 0.72-2.24) [73].

Further studies with standardized systemic and local therapies are needed before definitive conclusions can be drawn regarding relative mortality risk of pregnancy-associated breast cancers; nevertheless, we continue to consider the use of standard systemic and local therapies for pregnant breast cancer patients.

Pregnancy and infant outcome — Data suggest early development among children born to women with cancer appears similar to that of children of the same gestational age, irrespective of in utero exposure to radiation or chemotherapy.

In a study of 129 children born to mothers diagnosed with cancer during pregnancy (over half of whom had breast cancer), cardiac, cognitive, and general development after a median of 22 months were equivalent with controls matched for gestational age [24]. In a subgroup analysis of children exposed to anticancer therapy in utero, similar outcomes were reported for the 96 children exposed to chemotherapy after the first trimester and the 11 children exposed to radiation compared with gestational age-matched controls. There was a nonsignificant trend towards higher rates of small for gestational age birth among infants born to women with cancer (22 versus 15 percent), particularly if exposed to chemotherapy or radiation. While the median gestational age of the children born to women with cancer was 36 weeks and thus late preterm, it is unclear if these children were born early because of early induction given their mothers' diagnosis of cancer.

In a cohort study of 1170 pregnant women with all types of cancer treated at multiple institutions, 39 percent of whom had breast cancer, 88 percent of pregnancies resulted in live births [74]. Half of these deliveries were preterm, almost 90 percent of which were iatrogenic. However, it was not possible to determine whether these findings were related to in-utero drug exposure or to other factors, such as effects of other medications, maternal stress, lack of adequate gestational weight gain, and other prenatal factors. The International Network of Cancer Infertility and Pregnancy reported on 201 pregnant cancer patients with fetal growth abnormalities in 75 of the pregnancies that may correlate with the length of chemotherapy used during pregnancy [75]. This series did not include long-term outcomes in the children, but other reports demonstrate that these children do catch-up [24].

These findings support results of smaller studies that suggested low neonatal complication rates associated with in-utero exposure to chemotherapy, but long-term data are limited [26,44]. Moreover, studies may be limited by the fact that treating providers may sometimes opt for early pregnancy induction, even when pregnancy does not affect treatment.

The topic of pregnancy outcomes in breast cancer survivors is discussed elsewhere. (See "Overview of infertility and pregnancy outcome in cancer survivors".)

Dissemination of disease to the fetus — For women with breast cancer during pregnancy, the risk of cancer to the unborn is unknown, although vertical transmission of cancer to the placenta has been rarely reported [76,77]. However, there are no reported cases of childhood cancer arising in children exposed to chemotherapy for breast cancer in utero.

BREASTFEEDING

Breastfeeding completion after treatment for breast cancer appears to be safe and feasible. Breastfeeding is most successful from the contralateral breast, even among women who have undergone breast-conserving surgery, and when women receive lactation counseling. Although the evidence is limited to small case series, there is no evidence to suggest that breast-feeding affects prognosis [78].

Milk production from the contralateral (nontreated) breast is not affected after breast-conserving surgery and radiation therapy (RT) [79,80]. Although many women are able to produce milk from the treated breast, the amount of milk is typically reduced, particularly if the excision site was close to the areolar complex or transected by many ducts [81,82]. In addition, breastfeeding from the irradiated breast is not advised because women are at risk for mastitis, which can prove difficult to treat if it occurs [83].

Breastfeeding during treatment is discussed above. (See 'Excretion of drugs into breast milk' above.)

FOLLOW-UP FOR BREAST CANCER

Women with a history of gestational breast cancer should undergo the same clinical monitoring as other patients with breast cancer. (See "Approach to the patient following treatment for breast cancer".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Breast cancer".)

SUMMARY AND RECOMMENDATIONS

- **Introduction** – Gestational or pregnancy-associated breast cancer is commonly defined as breast cancer that is diagnosed during pregnancy, in the first postpartum year, or any time during lactation. (See 'Introduction' above.)
- **Treatment** – In general, pregnant women with breast cancer should be treated according to guidelines for nonpregnant patients, with some modifications to protect the fetus. (See 'Treatment' above.)
- **Locoregional treatment**

- Either breast-conserving surgery or mastectomy is a reasonable option in the pregnant woman with breast cancer. A choice between them is guided by tumor characteristics and patient preferences. (See 'Locoregional treatment' above.)

- Women with breast cancer during pregnancy should undergo an axillary node evaluation. While axillary lymph node dissection may be preferred, there are increasing data on the safety and efficacy of sentinel lymph node dissection. (See 'Management of the axilla' above.)

- For women who require adjuvant radiation therapy (RT), we recommend adjuvant RT be administered **after** delivery rather than during pregnancy (**Grade 1C**). (See 'Locoregional treatment' above.)

- **Systemic therapy**

  - For women in whom chemotherapy is recommended, we initiate treatment after the first trimester. (See 'Systemic therapy' above.)

  - Chemotherapy should be avoided for three to four weeks before delivery whenever possible to avoid transient neonatal myelosuppression and potential complications of sepsis and death. (See 'Timing of chemotherapy' above.)

  - We avoid trastuzumab during pregnancy due to fetal risks for oligo-and anhydramnios, pulmonary hypoplasia, fetal developmental abnormalities after exposure, and fetal death. Until more information becomes available, we also avoid pertuzumab, ado-trastuzumab emtansine (TDM-1), lapatinib, and other HER2-directed antibody drug-conjugates during pregnancy. (See 'Anti-HER2 therapies' above.)

  - Breastfeeding should be avoided in women while receiving chemotherapy, trastuzumab, lapatinib, and endocrine therapy. However, breastfeeding after treatment completion for breast cancer appears to be safe and feasible, especially from the contralateral breast and with lactation counseling. (See 'Excretion of drugs into breast milk' above and 'Breastfeeding' above.)

- **Elective termination of pregnancy** – Although pregnancy termination may be discussed during treatment planning, it does not appear to improve survival. (See 'Elective termination of pregnancy' above.)

- **Prognosis** – The data show that outcomes for women with breast cancer diagnosed **during** pregnancy are equivalent to breast cancer in nonpregnant women, provided that the patient receives standard and timely therapy. Some data suggest that a diagnosis of cancer diagnosed in the **postpartum** period results in worse outcomes,

but causation remains unclear. To date, there is no evidence that subsequent pregnancy **after** the treatment of breast cancer worsens prognosis. (See 'Prognosis' above.)

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