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# Gestational breast cancer: safety of anti-cancer therapy during pregnancy

## KEY POINTS

- Good breast cancer treatment during pregnancy does not jeopardize maternal prognosis
- There are few differences between pregnant patients and non-pregnant in terms of recurrence and survival
- Fear about the risks of chemotherapy should not be a reason to terminate
- It is acceptable to delay chemotherapy until the second trimester
- The greatest risk to the foetus of a woman with breast cancer is induced premature delivery in order to enable treatment; this is unnecessary
- Oncologists, breast surgeons, obstetricians, midwives and General Practitioners all operate together to offer holistic family care

## Introduction

In recent years, the average age at childbirth in women in the western world has increased, and with this so has the likelihood of a breast cancer diagnosis occurring during pregnancy. These cases of breast cancer are referred to as gestational or pregnancy-associated breast cancer, and they include women who receive a diagnosis of breast cancer within one year of delivery.

Most cases of gestational pregnancy are diagnosed postpartum, but this article refers primarily to breast cancer diagnosed during pregnancy.

## Screening and Diagnosis

Due to the increased rates of gestational breast cancer in recent years, it has become advisable that every general review, prior to becoming pregnant or in early pregnancy, should include a clinician-led breast examination. This should be a particular component in general reviews for any woman with a family history of breast cancer, or in whom an inherited mutation such as BRCA1/BRCA2 might increase the risk of breast cancer at a young age. When examining women in the early stages of pregnancy, or who are trying to conceive, any unusual breast changes must warrant an immediate referral to a one-stop-diagnosis clinic. This should be done with the understanding that no pregnant woman will be subjected to mammography unless an ultrasound shows suspicious findings, and that foetal shielding will always be performed.



## Surgical Breast-cancer Treatment in Pregnancy

Although there are increased anaesthetic risks to pregnant women and practical complications regarding surgical approach and positioning, the difficulties related to surgical treatment for pregnant breast cancer patients are usually surmountable. For example, when staging the axilla, the use of low dose radiation involved in radioisotope sentinel node surgery is not associated with the production of birth defects (teratogenicity). There are of course adaptations to be made when operating on pregnant breast cancer patients. These include abandoning the use of blue-dye and delaying any reconstructive surgery, to avoid lengthening surgery, which is not recommended for pregnant women.

## Chemotherapy

For the majority of pregnant women presenting with breast cancer, the primary aim of treatment is to maximise the chances of maternal survival, while minimising the risk of foetal harm. Considerable amounts of research and investigation has gone into dispelling previous beliefs

about the use of chemotherapy as a treatment option for pregnant women with breast cancer; it is an effective treatment for breast cancer and so must never be denied to women who could respond positively, even if those women are pregnant. Large quantities of evidence has been gathered regarding the use of cytotoxics in pregnancy, particularly after the first trimester<sup>1,2</sup>.

It has also been established that anthracyclines and taxanes, the mainstays of adjuvant breast cancer treatment, are safe to be given to pregnant women, although platinum drugs are not yet recommended. As previously stated, the greatest risk to a foetus, carried by a woman with breast cancer, is induced pre-term labour.

By allowing the pregnancy to progress during chemotherapy, the infant reaches greater maturity before delivery, which drastically cuts the risks of foetal harm while maximising maternal survival.



### Biological Therapy

Unfortunately, although trastuzumab has revolutionised the treatment of HER2 positive breast cancer, in both the metastatic and adjuvant settings, it is not recommended for use during pregnancy. Though it has few directly teratogenic effects on the developing foetus, it is associated with oligohydramnios, a reduction of amniotic fluid, which can be associated with serious negative outcomes.

### Supportive Therapy

When considering symptom control for pregnant women with breast cancer, the issues are evidently two-fold. Many anti-emetics usually administered to manage nausea in cancer patients are considered safe for use during pregnancy, although some are best avoided due to lack of safety data. Steroids can also be safely used as chemotherapy anti-emetics and to prevent allergies, though of course their impact on gestational diabetes must be considered. It is unusual for a pregnant patient with breast cancer to require hospitalisation due to vomiting.

### Breast radiotherapy

Currently, it remains preferable to avoid exposure to radiotherapy in utero. Data on the specific consequences of exposing an unborn child to medical radiation is scarce, as there have been few long-term follow-up studies of children prenatally exposed to radiotherapy. In those studied, neuropsychological, behavioural and general health outcomes appear to be within normal ranges, but due to the small sample size, most oncologists will generally recommend that breast or chest wall radiation is delayed until after delivery. New radiation techniques and more sophisticated simulations of the foetal dose may change future advice.

### HORMONE TREATMENT

Endocrine manipulation is not undertaken during pregnancy.

### Maternal Outcomes

Typically, the pregnant state is characterised by immunosuppression, increased hormonal exposure (higher concentrations of oestrogen, progesterone, and insulin-like growth-factor-1) and robust vascularisation. These have all been postulated as contributing factors to poor outcomes observed in pregnant women with breast cancer. However, there are studies suggesting that these factors do not contribute significantly to accelerated tumour growth in pregnancy. When matched in terms of stage (spread from the breast) and grade (inherent aggressive pattern of cancer), pregnant women do not in fact have a worse breast cancer prognosis than women who are not pregnant, as was previously thought. A 2013 International Collaborative Study compared pregnant patients with non-pregnant, and found no differences in disease free survival (DFS) or overall survival (OS).<sup>3</sup>

It has been established that providing chemotherapy treatment during pregnancy improves maternal outcome, which is then comparable to that of non-pregnant patients. In the past, obstetricians were encouraged by oncologists and surgeons to deliver infants as soon as viable, to allow aggressive systemic anti-cancer therapy. However, it has emerged that allowing

**It has been established that providing chemotherapy treatment during pregnancy improves maternal outcome**



chemotherapy in pregnancy will also improve foetal outcome by allowing greater maturity in utero.

Pregnancy is a known risk factor for cardiac failure, and pregnant women with established heart disease are at risk of significant cardiac and neonatal complications. But there is no direct evidence that a heart coping with the haemodynamic stresses of pregnancy and parturition, is more likely to suffer a chemotherapy-mediated cardiac insult. With this in mind, best practice is to arrange transthoracic echocardiogram prior to initiation of chemotherapy, as increased vigilance is always appropriate for higher risk patients. Potential harm to the mother must be weighed against the known risks of denying her the survival advantage of adjuvant treatment.

### Specific Foetal Concerns

Studies show that chemotherapy exposure during the second and third trimesters of pregnancy does not impair neonatal outcome, as the rate of congenital malformations is not increased, although the neonates are more commonly born before the 37th week of gestation to mothers receiving chemotherapy. Long-term cardiac and neurodevelopmental

assessments of children exposed to chemotherapy in utero are within normal. This indicates that allowing pregnancy progression, to as close to term as possible while chemotherapy is administered, is undoubtedly the best option for both mother and foetus. If we do not treat women with cytotoxic chemotherapy during pregnancy, we risk all the foetal complications of early pre-term delivery.





## Families: The Multidisciplinary Home Team

For many women, the idea of a diagnosis of breast cancer during pregnancy conjures images of being forced to choose between their life or the life of their child. This is a common misconception, but a very serious one. The fact that the foetus is at small risk of harm is not often realised, which is why it is vital that women with gestational breast cancer, and their families, must always be offered clear and accurate information. Women in this situation cannot be treated in isolation as a cancer patient or as a pregnant woman, but as a pregnant woman with cancer,

necessitating treatment by a multidisciplinary team of oncologists and obstetricians. The treatment of pregnant women with breast cancer must be a holistic practice, and needs to extend outside a hospital setting. Midwives and breast cancer clinical nurse specialists often develop strong relationships with their patients, and so are ideally positioned to support pregnant women with breast cancer, and their families. General Practitioners remain the central core of this coordinated care, as they are usually the first port of call in any pregnancy or cancer diagnosis.

### REFERENCES:

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