Pregnancy After Breast Cancer: Is it Safe?

Authors:	Victoria Antoniou, EMJ, London, UK

Citation:	EMJ Oncol. 2023;11[1]:17-19. DOI/10.33590/emjoncol/10308535. https://doi.org/10.33590/emjoncol/10308535.

AN INSIGHTFUL session featuring a debate analysed the safety and feasibility of pregnancy amongst survivors of early breast cancer (EBC) at the European Society for Medical Oncology (EMSO) Annual Congress 2023, held in Madrid, Spain, from 20th–24th October. Chaired by Ann H. Partridge, Dana-Farber Cancer Institute, Boston, Massachusetts, USA, both sides of the argument were covered, before concluding with a vote from the audience, both in person and virtually.

FOR THE SAFETY OF PREGNANCY AFTER EARLY BREAST CANCER

Patrick Neven, Universitair Ziekenhuis (UZ) Leuven, Belgium, began by explaining that the age at which females are choosing to undergo their first full-term pregnancy is being delayed, leading to an increased need for assisted reproductive technologies. Such reproductive methods are also often used by females who have had EBC, and therefore these methods and their safety have been studied extensively, reported Neven. He discussed the ESMO 2020 guidelines, which state that part of the treatment-planning process for any type of cancer at any stage must involve oncofertility counselling. These guidelines further state that every patient is at risk of gonadotoxicity after taking anticancer drugs, and that special attention should be paid to hereditary cancer syndromes.

To demonstrate the safety of pregnancy after EBC, Neven presented a case of a female who had undergone surgery for pT2N1 Grade II ER+ PR+ HER2- breast cancer. Years later, at age 39, despite a uterine myoma and adenomysosis, she unintentionally fell pregnant again, gave birth at 38 weeks, and was able to breastfeed with the one breast that had not undergone radiation therapy. Neven went on to discuss a study which included 92 females who had been pregnant after EBC, aged 17–40 (median age: 32 years), only 39% of whom required the assistance of reproductive technologies (one-third of females required fertility treatment, and 29 out of 92 used *in vitro* fertilisation).

Guarantee-time bias (GTB) was highlighted as an important factor to correct for when considering pregnancy after breast cancer. GTB occurs when an analysis timed from enrolment is compared across two groups defined by a classifying event, such as pregnant after EBC or not pregnant after EBC. One must correct for changes during this time; for example, relapse, or females not wanting to become pregnant after breast cancer, as these factors may skew the data.

Neven presented a retrospective cohort study including 3,805 patients with ER+ EBC, of whom 2,285 had a subsequent pregnancy, and 2,520 did not, and where GTB was taken into account. The results showed that there was no harm in females becoming pregnant after EBC, and there was no difference in the breast cancer outcome between the two groups.

"This trial showed that there was no negative effect of interrupting the treatment for these individuals."

Neven concluded by presenting the results of the recent Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine responsive breast cancer (POSITIVE) trial,[1] which included an analysis of 516 females who had experienced treatment for either Stage I or Stage II EBC. This trial showed that there was no negative effect of interrupting the treatment for these individuals; nor was it dangerous to have a baby after therapy. The safety of the baby is dependent on the time after treatment; however, Neven explained that there is no risk for the baby if the mother falls pregnant more than 1 year after treatment. This part of the discussion concluded with a summary of Neven's points, highlighting the evidence in the literature that pregnancy after breast cancer is safe, so long as risk of recurrence and time after treatment is taken into account.

AGAINST THE SAFETY OF PREGNANCY AFTER EARLY BREAST CANCER

Sibylle Loibl, Goethe University of Frankfurt, Germany, agreed that more young females suffer from breast cancer today. She opened her presentation by pointing out, however, that younger females have higher risk of relapse, a higher likelihood of being treated with chemotherapy, and a lower chance of having had children already. Younger females have a worse breast cancer prognosis in HER2- forms of the disease; however, age differences are not significant in triple negative or HER2+ forms of breast cancer. Loibl also addressed chemotherapy-induced ovarian function suppression, a valid prognostic factor.

Research has previously shown that females who have had breast cancer are less likely to be able to become pregnant at all, for a variety of reasons, including limited ovarian reserve, which happens naturally to females above the age of 35 years. Those that do become pregnant after EBC, however, do not have a lower chance of disease-free survival than those who do not get pregnant, and in certain cases, pregnancy may even lead to a better outcome. Loibl highlighted that these studies, though they appear to support the safety of pregnancy after EBC, were all retrospective studies, and are therefore more biased than any prospective data. This type of research is also inherently non-randomised, which also makes it more biased, leading to potentially misinformed conclusions.

Furthermore, germline mutations (g*BRCA*) are vital to account for when analysing safety of pregnancy in patients with breast cancer, as

they may affect outcomes. Loibl discussed a prospective cohort study conducted in the UK, looking into germline mutations in breast cancer, which can lead to increased risk of contralateral breast cancer, ipsilateral breast cancer, and ovarian cancer. Patients need to be informed about this before attempting to become pregnant, in order to avoid relapse during pregnancy. Carriers of g*BRCA2* mutations also appear to have higher risk of chemotherapy-induced ovarian failure, which Loibl argued is an important factor often overlooked by studies supporting the safety of pregnancy after breast cancer.

Loibl concluded her side of the debate by also discussing the POSITIVE trial,[1] arguing that the results of the trial do not support the safety of pregnancy after EBC, but rather show that it is possible to interrupt endocrine therapy in patients, so long as this is resumed after a period of up to 2 years. She explained that this trial, in which patients were heavily selected, does not provide sufficient data to support safe pregnancy after EBC.

VOTING AND CHAIR'S PERSPECTIVE

Audience members were able to vote on five different questions addressing the wait time of patients with triple-negative EBC before pregnancy, which patients should become pregnant, the results of the POSITIVE trial,[1] and the treatments used on patients with EBC. The results, though in some cases leaning towards the safety of pregnancy after breast cancer, were mostly split amongst the audience. Partridge, Chair of this session, and lead author in the POSITIVE trial,[1] acknowledged the shortcomings of many of the studies in favour of becoming pregnant after breast cancer, and pointed out the higher rates of low birthweight and premature birth amongst females who have had EBC. Additionally, little data are available with regards to the safety of pregnancy after treatment with newer methods, such as CDK4/6 inhibitors or immune checkpoint inhibition.

Partridge concluded there is evidence to suggest that there is no worsening of disease-free survival or overall survival for pregnant groups versus non-pregnant groups, and that there is little risk in pregnancy after EBC, as long as females get through the early risk of recurrence period, and receive optimal endocrine therapy. Partridge went on to explain that pregnancy after EBC can be done safely, despite the drawbacks of the real-world study, including females not going back on their endocrine therapy. She argued that although the POSITIVE trial lacks long-term follow-up data, it adds significantly to the literature supporting the safety of pregnancy after EBC.

The second round of voting saw the results more often skew to the side of pregnancy being safe after breast cancer. Overall, it can be said that despite strong evidence to suggest that pregnancy after EBC is safe, these studies have several shortcomings that should be taken into account, and opinions on the topic are still divided.

References

1. Partridge AH et al. Interrupting endocrine therapy to attempt pregnancy after breast cancer. N Engl J Med. 2023;388(18):1645-56.