It's POSITIVE: The News About Pregnancy After Breast Cancer

After the live webinar hosted on May 19, 2023, Ann Partridge, MD, MPH and Leticia Varella, MD answered additional questions about the POSITIVE (**P**regnancy **O**utcome and **S**afety of **I**nterrupting **T**herapy for Women With Endocrine-Respons**IVE** Breast Cancer) trial.

Breast Cancer Recurrence

1. Do we understand how and why pregnancy is not a risk for recurrence?

   It is interesting and we don't fully understand, but it may have to do with differences in hormone levels and their interactions. What many people are not aware of is that high dose estrogen is a breast cancer treatment, as well as progesterone, which are two of the common hormones of pregnancy.

2. When collecting the number of recurrences in the study, is that based on symptoms or are there exams/scans to check for recurrence?

   Routine scans were not required during the study, which is in accordance with the current surveillance guidelines.

3. Were the recurrence outcomes segmented at all? (based on cancer stage, # of positive nodes, ER, PR, HER2 status, genetic mutations, treatment with aromatase inhibitors vs. tamoxifen, type of surgery, use of bisphosphonates, etc.)

   The study did look into outcomes accordingly to tumor characteristics, germline genetic mutations, type of surgery, type of chemotherapy, and type of endocrine therapy. In general, things that are associated with increased risk, such as bigger and higher-grade tumors, as well as lymph node involvement, were also associated with greater recurrence risk in this study. However, due to the small number of recurrences, the analyses were descriptive only and there were no analyses looking at whether interruption of endocrine therapy or pregnancy itself impacted different groups differently.

4. Do you recommend additional screening/tests (other than what we are currently doing) during pregnancy?

   Currently there is no evidence that extra imaging or blood tests help with detecting recurrence during pregnancy.

5. Were there incidents where women who participated in the trial developed other types of cancer after the pregnancy?

   We have not looked at these data in detail yet.

6. Are you looking at Oncotype scores for people in the trial?

   There is not a plan for this at the present time.

7. Does breastfeeding for a longer time reduce the risk of a recurrence?

   We do not know the answer to this, but we can investigate more in the future.

8. Considering ER+ disease can come back 10/15 years later, what consideration does that have with POSITIVE's preliminary results?

   The median follow-up time for study participants was only 3.4 years, but the protocol-specified longer follow-up will be critical to inform the long-term safety of interrupting endocrine therapy.

Conception Outcomes

9. Is there more information on who could or couldn't get pregnant naturally - as in - what chemo (or not) did people have and how did that influence their ability to conceive?

   This is something we plan to look at in the future.

10. Will you separate the IVF data into efficacy based on type of IVF med protocol? (and then their subsequent recurrence) when you look deeper into that data?

    Yes, this analysis is underway.

Pausing and Restarting Endocrine Therapy

11. How long of a break is currently recommended before restarting endocrine therapy?

    The study required that women received at least 18 months and no more than 30 months of endocrine therapy prior to enrollment. And it was recommended that women come off endocrine therapy for no more than 2 years.

12. Is there any data about postpartum depression with resuming endocrine therapy?

    We have a robust psychosocial and quality of life survey that we administered to women participating in POSITIVE, so we will be sharing these data at some point in the future.

13. Are there guidelines that oncologists can refer to if they support a break in endocrine therapy? (E.g., monitoring, scans required, etc.)

    Currently there are not, but our group is working on putting together clinical guidelines to help guiding clinicians to make these decisions. We will post them on our website when they are available and send a link to members of the Young and Strong Program.

14. How quickly do you recommend women get back on endocrine therapy? Was there time for breastfeeding?

    In the study, patients were recommended to resume endocrine therapy as soon as pregnancy and breastfeeding were finished (the interruption should have a maximum duration of 2 years).

Treatment Considerations

15. Is there benefit to switch from AI + OFS to tamoxifen before pausing to see if ovaries wake up?

    We would recommend working with your doctor and a reproductive endocrinologist (IVF/Fertility doctor) if you are worried that your ovaries may not wake up.

16. Would you recommend doing more years of endocrine therapy if you pause for a pregnancy? (i.e. instead of 3 more years (for 5 total), add an additional year or two for added benefit)

    Total duration of endocrine therapy really depends on risk of disease as well as patient preference and tolerance of the treatment.

17. Do we know for certain if ovarian suppression during chemotherapy helps with fertility preservation?

    There have been a number of studies and a large, pooled analysis that showed that ovarian suppression during chemotherapy reduces the risk of premature menopause in the short term and is associated with increase in number of babies born in survivors

18. Will you release details on how many people were on ovarian suppression and an AI instead of tamoxifen?

    Yes, the data has been published as part of the study. Approximately 16% of women were taking AI with ovarian suppression.