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Temporary Ovarian Suppression With Hormone Analog May Preserve Fertility During Breast Cancer Chemotherapy

SAN ANTONIO — Meta-analysis of individual patient data from five randomized clinical trials provided a high level of evidence that treatment with a gonadotropin-releasing hormone analog (GnRHa) could safely and effectively protect ovarian function and potentially preserve fertility in premenopausal women receiving chemotherapy for early-stage breast cancer, according to a study presented at the 2017 San Antonio Breast Cancer Symposium, held Dec. 5–9.

"Temporary ovarian suppression obtained by administering GnRHa during chemotherapy is a medical intervention with the potential to preserve ovarian function and fertility in premenopausal breast cancer patients; however, to date, the role of this option remains controversial and it is still considered an experimental technique by the American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology (ESMO)," said Matteo Lambertini, MD, medical oncologist and ESMO fellow at the Institut Jules Bordet in Brussels, Belgium.

The possibility that anticancer treatments will cause premature ovarian insufficiency (POI) and subsequent infertility are prevalent concerns affecting young women diagnosed with breast cancer, which adds significant anxiety and emotional strain as they make treatment decisions, explained Lambertini.

Temporary ovarian suppression with GnRHa during chemotherapy was primarily developed as a strategy to reduce the risk of developing treatment-induced POI than as a fertility-preserving procedure; therefore, the majority of the trials that investigated this strategy had a very short follow-up and did not report on post-treatment pregnancies, Lambertini said. Further, different randomized clinical trials that investigated the efficacy of this approach showed conflicting results, and some of these trials included very few patients, making it difficult to draw solid conclusions based on the results of individual studies, he added.

Lambertini and team aimed to provide more conclusive clinical evidence on this topic by conducting an individual patient data meta-analysis of five randomized clinical trials in which premenopausal women with early-stage breast cancer were randomly assigned to receive chemotherapy alone (437 women) or with concurrent GnRHa (436 women).

The study found that the POI rate in the GnRHa group was 14.1 percent, versus 30.9 percent in the control group; patients in the GnRHa group had 62 percent less risk to develop POI as compared to those treated with chemotherapy alone. Treatment effect was homogeneous among the different patient subgroups.

Patients in the GnRHa group had one- and two-year amenorrhea (absence of menstrual periods) rates of 36.8 percent and 18.2 percent, respectively. One- and two-year amenorrhea rates in the control group were 40.4 percent and 30 percent, respectively.

"Although the absolute numbers remain low, we observed a doubling in the number of post-treatment pregnancies in patients in the GnRHa group compared with those treated with chemotherapy alone. This suggests that GnRHa during chemotherapy is not only a strategy to preserve ovarian function but may also potentially improve future fertility," Lambertini said.

Thirty-seven patients in the GnRHa group had at least one post-treatment pregnancy during the follow-up period, versus 20 patients in the control group.

There were no significant differences in disease-free survival and overall survival between the two groups; this suggests that administering GnRHa during chemotherapy can be considered safe in breast cancer patients, he said.

"Our study adds important evidence on both the efficacy and the safety of temporary ovarian suppression with GnRHa during chemotherapy, not only in patients with estrogen receptor [ER]-negative disease but also in women with ER-positive tumors, who account for the majority of new cases of breast cancer in young women," Lambertini commented.

"This study provides solid evidence on this specific topic," Lambertini said. "We believe that the results of our study would serve as the reference evidence for updating the international ASCO and ESMO guidelines on the use of this strategy."

The five clinical trials studied were PROMISE-GIM6, POEMS/SWOG S0230, Angelo Celtic Group OPTION, GBG-37 ZORO, and a Moffitt Cancer Center-led trial.

Limitations of the study include the impossibility of including all the randomized clinical trials on this topic, the lack of data on the extent of ovarian function preservation using more sensitive biomarkers, and limited information on patients' wish to have a pregnancy, according to Lambertini.

This study was partly funded by the Italian Association for Cancer Research. Lambertini does not have any relevant conflicts of interest to disclose.

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The mission of the 2017 San Antonio Breast Cancer Symposium is to produce a unique and comprehensive scientific meeting that encompasses the full spectrum of breast cancer research, facilitating the rapid translation of new knowledge into better care for patients with breast cancer. The UT Health San Antonio Cancer Center, the American Association for Cancer Research (AACR), and Baylor College of Medicine are joint sponsors of the San Antonio Breast Cancer Symposium. This collaboration

utilizes the clinical strengths of the UT Health San Antonio Cancer Center and Baylor and the AACR's scientific prestige in basic, translational, and clinical cancer research to expedite the delivery of the latest scientific advances to the clinic. For more information about the symposium, please visit www.sabcs.org.