

Hormonal therapy may prevent ovarian failure and preserve fertility in breast cancer

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Young women undergoing chemotherapy for breast cancer may be more likely to remain fertile if they also receive hormonal treatment, according to new research presented to the 2015 European Cancer Congress on Monday and published simultaneously in *Annals of Oncology*.

Researchers will tell the Congress that the addition of treatment with a so-called luteinising hormone-releasing hormone analogue, or LHRHa, during [chemotherapy](#), could protect women's ovaries. The approach may increase the chances of pregnancy after [breast cancer](#) treatment.

Dr Matteo Lambertini, MD, a medical oncologist at the IRCCS AOU San Martino-IST, Genoa, Italy, will say: "Chemotherapy can damage the ovaries and push young women into the menopause. They may experience infertility, sleep disturbance, sexual dysfunction and osteoporosis. It is psychologically distressing, harmful to health, and affects the treatment decisions of many young women.

"We found that temporary suppression of ovarian function with LHRHa significantly reduces the risk of premature ovarian failure (POF) caused by chemotherapy. It also seems to be associated with a higher pregnancy rate in young breast cancer patients."

Dr Lambertini and his colleagues pooled the best available data. Their meta-analysis included 12 randomised trials and a total of 1,231 breast cancer patients receiving chemotherapy, with or without LHRHa. An

initial calculation found that rates of POF were reduced by 64%, approximately two-thirds, in patients who received LHRHa. However, the studies used different definitions of POF, and results ranged widely.

The analysis was then restricted to trials that included specific data on whether a woman's periods had re-started one year after chemotherapy. This is in line with the World Health Organization's definition of menopause. In the eight relevant trials, the overall reduction in POF with the addition of LHRHa was still striking. Rates were reduced by 45% with LHRHa, and this time there was close agreement in results from all studies.

The use of LHRHa was originally developed to preserve ovarian function rather than fertility, and only five of the studies reported on pregnancies after [breast cancer treatment](#). In these studies, overall there were 33 patients with pregnancies among those who received LHRHa alongside chemotherapy, and 19 among those who did not. This was an 83% increase in the chance of becoming pregnant. Rates were similar across the five studies.

Dr Lambertini will say: "Major international guidelines from ASCO and ESMO consider the administration of LHRHa during chemotherapy an experimental strategy to preserve ovarian function and fertility. This is mainly because of the lack of data on long-term ovarian function and pregnancies. However, these guidelines were published before two of the larger studies became available, the POEMS-SWOG S0230 trial [1] and the updated results of the PROMISE-GIM6 study [2].

"In breast cancer patients, we believe there is now sufficient evidence to suggest that the administration of LHRHa could be considered a potential standard strategy to preserve ovarian function and might also play a role in increasing the likelihood of pregnancy after chemotherapy."

Concerns about the safety of LHRHa treatment have been raised, particularly for breast cancers that are driven by hormones. These hormone receptor positive cancers have receptors on the cell surface that trigger the cancer's growth in response to circulating hormones. Standard treatment of these breast cancers includes anti-oestrogen therapy alongside chemotherapy. Previous work has implied that resumption of a woman's periods after treatment could have a detrimental impact on long-term health.

Dr Lambertini will say that results from the two recent, large studies are reassuring. Both looked at the length of time women remained free of cancer after treatment (disease-free survival). The POEMS-SWOG S0230 trial looked at women whose cancers lack hormone receptors (hormone receptor negative breast cancer). The women had improved disease-free survival if they received LHRHa. Furthermore, the PROMISE-GIM6 study found that adding LHRHa made no difference to disease-free survival, even within the sub-group of women with hormone receptor positive breast cancer who accounted for the majority of the patients enrolled in the study.

Dr Lambertini will say: "These data suggest that this strategy could be useful and safe not only in women with hormone receptor negative breast cancer, but also in those with hormone receptor positive tumours who account for two-thirds of new cases of breast cancer in young women."

The 2015 St Gallen International Expert Consensus panel and the National Comprehensive Cancer Network guidelines have been updated to acknowledge the role of LHRHa in preventing ovarian failure induced by chemotherapy, but only in [hormone receptor](#) negative cancer.

"Other guidelines are hesitating to recommend this technique," Dr Lambertini will say. "To date, the role of this approach in fertility

preservation remains controversial."

He will stress the need for new treatment options: "Pregnancy after breast cancer is safe, even in patients with endocrine sensitive disease. With the rising trend of delaying childbearing, more [breast cancer patients](#) are diagnosed without having completed their families and thus it is vital to provide reliable fertility preservation methods for these [young women](#)."

Dr Lambertini will add: "Pharmacological protection of the ovaries with LHRHa during chemotherapy is an attractive option to preserve ovarian function and fertility. Agents are widely available, do not require any invasive procedure and cause no delay in the initiation of anti-cancer therapies. Moreover, it is possible to use this technique in combination with other fertility preservation options, including cryopreservation strategies, thereby increasing the chance of fertility preservation as well as ovarian function after cancer therapies."

Professor Peter Naredi, the ECCO scientific co-chair of the Congress, who was not involved in the research, commented: "I find this study by Dr Lambertini and colleagues important for several reasons. At the 2015 European Cancer Congress we want to present and discuss new data with the patients in focus. Thanks to a global collaboration with data available from several studies, it is possible to reinforce a benefit of LHRHa treatment for all the women with breast cancer who still want to have the option to become pregnant. Survivorship of cancer patients is of major importance for the cancer community and, at the Congress, teams from different professions have a chance to evaluate and discuss new data."

More information: "Ovarian suppression using luteinizing hormone-releasing hormone agonists during chemotherapy to preserve ovarian function and fertility of breast cancer patients. A meta- analysis of randomized studies", by Matteo Lambertini et al. *Annals of Oncology*.

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[1] Moore HCF et al, 2015. Ovarian protection during adjuvant chemotherapy. *N Engl J Med*; 372(23):2269-70.

[2] Lambertini M et al, 2014. Long-term outcome results of the phase III PROMISE-GIM6 study evaluating the role of LHRH analog (LHRHa) during chemotherapy (CT) as a strategy to reduce ovarian failure in early breast cancer (BC) patients. *J Clin Oncol*; 32 (26): abstract 105.

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