'Dose-dense' chemo for premenopausal breast cancer patients improves survival

March 10 2016

Amsterdam, The Netherlands: Premenopausal women with breast cancer have a better chance of survival if they are given cycles of adjuvant chemotherapy closer together, every two weeks rather than every three weeks. Furthermore, this regimen, known as "dose-dense" adjuvant chemotherapy, does not seem to be associated with an increased risk of treatment-induced early menopause.

The findings will be presented today (Thursday) at the 10th European Breast Cancer Conference (EBCC-10) and the researchers say they are important for helping younger breast cancer patients and their doctors to make better-informed decisions about the choice of chemotherapy regimens that are given in addition to other treatments such as surgery, hormone therapy and radiotherapy.

Dr Matteo Lambertini, MD, a medical oncologist at IRCCS AOU San Martino-IST, National Institute for Cancer Research, Genoa, Italy, and at the Institut Jules Bordet, Brussels, Belgium, will tell the conference: "Our results confirm the superiority of dose-dense chemotherapy as compared to standard interval regimens in premenopausal patients at higher risk of relapse, and its use should be implemented in Europe, as it is in the United States."

Currently, treatment guidelines vary between Europe (where there are no clear recommendations) and the USA (where dose-dense chemotherapy is now given more often than in Europe). Until now, there have been no good data on any increased risk of dose-dense chemotherapy triggering

early menopause with its associated complications, including infertility.

Dr Lambertini and colleagues, led by Dr Lucia Del Mastro (also from IRCCS AOU San Martino-IST), carried out a meta-analysis of two large randomised phase III clinical trials that compared adjuvant chemotherapy given every two weeks (dose dense) or every three weeks (the standard interval); the MIG1 study looked at this in breast cancer patients whose disease had spread to their lymph nodes (node positive) or who were at high risk of relapse (high-risk, node-negative), while the GIM2 study investigated it in women with early stage, node positive disease. Treatment-induced amenorrhea (when the chemotherapy damages the ovaries, causing menstrual periods to stop and other menopausal symptoms) was defined as the absence of periods after the end of chemotherapy after three months in the MIG1 study and after 12 months in the GIM2 study.

A total of 3,305 patients were included in both studies, of which 1,549 were pre-menopausal and were included in Dr Lambertini's analysis. These women had an average age of 44 years. The researchers also looked at the effect of the treatments according to whether the women had hormone receptor positive or negative breast cancer (i.e. whether or not their cancer grew in response to the hormones oestrogen or progesterone).

The researchers found that dose-dense adjuvant chemotherapy significantly improved overall survival after ten years by nearly a third (29%) compared to chemotherapy given at the standard interval of three weeks. Dose-dense chemotherapy was not associated with an increased risk of treatment-induced amenorrhea.

Dose-dense chemotherapy seemed to be effective irrespective of hormone receptor status: it improved ten-year overall survival in patients with hormone receptor positive tumours by 22%, and by 35% in those

with hormone receptor negative tumours.

The researchers also found that treatment-induced amenorrhea did not affect survival. "We found no significant differences in overall survival between patients who developed treatment-induced amenorrhea and those who did not," said Dr Lambertini. "However, there was a non-statistically significant trend towards improved survival for women with hormone receptor positive tumours who developed treatment-induced amenorrhea."

He concluded: "The take-home message of our study is that dose-dense adjuvant chemotherapy is associated with a significant improvement in overall survival as compared to standard-interval chemotherapy in high-risk, premenopausal breast cancer patients; the benefit of dose-dense chemotherapy is larger in women with hormone receptor negative tumours than in those with hormone receptor positive tumours. Moreover, the use of dose-dense chemotherapy seemed not to be associated with an increased risk of developing treatment-induced amenorrhea.

"This is very important information for counselling young patients regarding the choice among the available adjuvant chemotherapy regimens. Chemotherapy remains a mainstay adjuvant treatment for the majority of young breast cancer patients, but its psychosocial impact can be substantial. The development of treatment-induced amenorrhea and the consequent loss of ovarian function has a negative impact on the overall health of young breast cancer survivors, as it is associated with several side effects, such as hot flushes, sweats, breast pain or sensitivity, vaginal dryness, vaginal discharge, lack of sexual desire, and weight gain.

"Moreover, strongly associated with the loss of ovarian function is the risk of infertility: fertility issues represent a major concern for young breast cancer patients and can also influence their treatment decisions.

Taking into account the current trend of postponing pregnancy to later in life, especially in western countries, it is expected that an increasing proportion of young women will be diagnosed with cancer before completing their family plans. These findings highlight the importance of trying to maintain ovarian function and fertility of young breast cancer patients who are candidates to receive chemotherapy during their reproductive age."

Chair of EBCC-10, Professor Fatima Cardoso, who is Director of the Breast Unit at the Champalimaud Clinical Centre, Lisbon, Portugal, said: "This meta-analysis provides important information that has the potential to change and improve the treatment of breast cancer in premenopausal patients. It gives us evidence-based answers as to whether or not dose-dense chemotherapy can be used in these patients without increasing their risks of treatment-induced amenorrhea, as well as showing a survival benefit."

More information: Abstract no: 5. "Dose-dense adjuvant chemotherapy, treatment-induced amenorrhea and overall survival in premenopausal breast cancer patients: a pooled analysis of the MIG1 and GIM2 phase III studies", Thursday, Best Oral Abstract session, 11.30-12.30 hrs, Elicium.

Provided by ECCO-the European CanCer Organisation