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Letter to the Editor

DTC chemotherapy regimen is associated with higher occurrence of premature ovarian failure in women of reproductive age with breast cancer

Dear Editor,

In their paper Long et al[1] evaluated two different chemotherapy regimens, CAF (tegafur + pirarubicin + ifosfamide) versus DTC (docetaxel + pirarubicin + ifosfamide), with the aim of evaluating the differential effect on the development of Premature Ovarian Failure (POF). They concluded that" both tested chemotherapy regimens can cause POF; however, adverse effects of DCT chemotherapy regimen on ovarian function are more pronounced than those by CAF chemotherapy regimen".

We would like to underline some methodological problems that impair the quality of this study.

They enrolled 164 women of reproductive age with breast cancer (mean ± SD age of 34.56 ± 9.48 years) and divided them into two groups, which were respectively treated with CAF (n = 89) or DTC (n = 75) chemotherapy regimen.

Concerning chemotherapy, we were surprised by the choice of drugs used in this study. Apart from Docetaxel (which was given at an unusually low dose of 50 mg/m^2) other drugs are never used in the adjuvant treatment of breast cancer. Tegafur is a well known precursor of fluorouracil formulated for oral administration, in this sense it has some similarities with Capecitabine, which is widely used in metastatic breast cancer, much less rationale in the adjuvant treatment, but this does not represent by any means an endorsement of its use in this context. Pirarubicin is an anthracycline which has never gained adequate acceptance in the oncological community. Ifosfamide is, of course, similar to Cyclophosphamide and is widely employed in the treatment of sarcomas, but it is not used to treat breast cancer, either in early nor metastatic disease. It is very curious, and confusing, that the Authors indicate the combination of Tegafur, Pirarubicin and Ifosfamide as CAF since this acronym indicates Cyclophosphamide, Adriamycin and Fluorouracil, and none of these drugs in included in this scheme.

Concerning the results presented, it is well known that taxanes are toxic to the ovary while antimetabolites are associated with very limited side effects on the ovaries[2,3]. Therefore, it could be expected that using Docetaxel instead of a fluoropyrimidine would increase ovarian toxicity.

Concerning Ifosfamide, as already said its pharmacodynamic properties are largely superimposable on those of Cyclophosphamide, one of the most studied gonadotoxic agents[4] but the data presented in this paper should not be used to obtain any hint on the ovarian toxicity of Ifosfamide.

One of the most difficult tasks in papers dealing with chemotherapy-induced ovarian failure is the definition of POF. Here, Authors propose the use of amenorrhea and levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), and estradiol (E2). Unfortunately, these means have a value only if they are used prospectively and within a time frame that takes into account also patients' age. As the follow-up of most patients is rather short, the high percentage of what authors call POF may indeed be just only temporary amenorrhea.

The most important tools to evaluate ovarian reserves, like follicle antral count and AMH level were not assessed, and this is unfortunate, as those exams are necessary for a reliable evaluation of the gonadotoxic effects of chemotherapy[5,6].

In conclusion, this study has many methodological flaws and lacks the power to conclude which chemotherapy regimen has the best impact on premature ovarian failure. Fertility preservation counseling is a difficult task[7] and should be based on reliable data[8].

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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