Letter in reply to Fertility preservation before an ABVD protocol: no new evidence to support changing the recommendations

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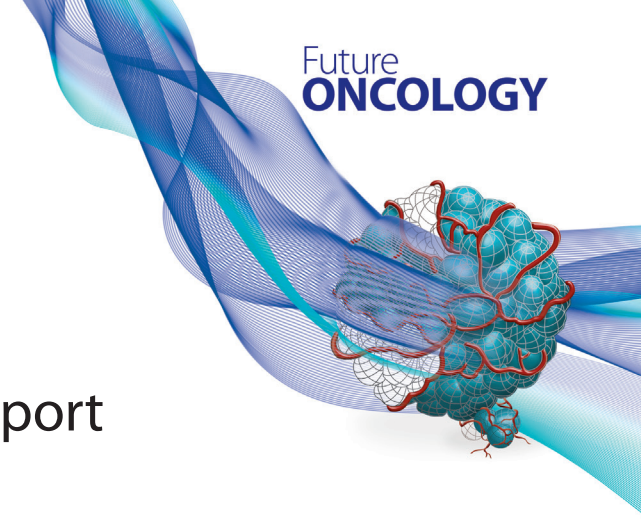

LETTER IN REPLY

Letter in reply to "Fertility preservation before an ABVD protocol: no new evidence to support changing the recommendations"

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• fertility preservation • Hodgkin lymphoma • *in vitro* maturation

We carefully read Poirot *et al.*'s reply [1] to our article entitled "History of ABVD alters the number of oocytes vitrified after *in vitro* maturation in fertility preservation candidates" [2]. Overall, we agree with the comments. Indeed, our study is retrospective including two groups of patients having either received ABVD (adriamycin/bleomycin/vinblastine/dacarbazine) chemotherapy for Hodgkin lymphoma (n = 22) and controls suffering from breast cancer, without previous history of chemotherapy (n = 44). All patients underwent transvaginal immature oocyte retrieval for urgent fertility preservation. Despite similar age, BMI, anti-Müllerian hormone level and antral follicle count, a lower number of cumulus oocyte complexes was recovered in patients with ovaries exposed to ABVD. However, oocyte maturation rates were comparable in both groups. These data lead us to question the relevance of oncofertility counseling and fertility preservation prior to ABVD treatment.

Regarding the comment on immature egg retrieval, and as mentioned by the authors, we have shown that both antral follicle count and serum anti-Müllerian hormone levels are tightly correlated with the number of cumulus oocyte complexes collected [3]. However, these data we obtained in *in vitro* maturation candidates without previous exposure to chemotherapy. It is conceivable that these correlations remain accurate even after history of chemotherapy but no strong data are currently available. In addition, we confirm that the practitioner experience represents a key element that might highly influence the output of the procedure. This point is easily explainable by the size of the small antral follicles punctured, which differs significantly from a conventional oocyte pick up following ovarian stimulation. In our study, all egg retrievals were performed by a single operator with great experience in *in vitro* maturation. Therefore, we hypothesized that postchemotherapy ovarian fibrosis, reported by Meirow *et al.* [4], might explain difficulties in oocyte collection. We are aware that these findings were not related to a specific type of drug and not systematically found, but it might constitute a viable reason for the lower output of egg retrieval in ABVD patients. However, due to the limited number of patients included in our study, a role of chance cannot be excluded. Moreover, as rightly emphasized by the authors, the cancer status might by itself impact the overall ovarian function [5,6]. From this point, we agree that Hodgkin lymphoma, in particular in advanced stages, might

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affect more profoundly the ovarian follicular status than the breast cancer. However, we do not believe that when antral follicles are visible into the ovaries, the disease by itself, would reduce the chance to obtained the immature oocyte, implying a increased risk of empty follicle, a strongly debated concept otherwise. When our study was designed, the expected consequence of malignancies was rather a modification of the maturation rate due to the history of chemotherapy.

Regarding the effect of ABVD on the ovarian function, we fully agree with the authors. Data available in the literature confirm the low ovarian toxicity of this chemotherapy protocol [7–9]. Indeed, as reported in Harel's review, fertility following ABVD is probably not or poorly impacted. However, the authors do not recommend not referring patients for oncofertility counseling in particular when they are over the age of 30 years. Due to the risk, even low, of recurrence of the Hodgkin lymphoma or the possibility of developing secondary breast cancer, we still consider that fertility preservation should be discussed, which does not mean recommended. Indeed, women should be informed that in these clinical situations the possibility of offering them optimal fertility preservation might be compromised, either in case of therapeutic intensification following recent chemotherapy [10], and/or in emergency. Our data, with the underlined limitations, might constitute an additional argument for patient information.

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