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Rooted in reality, living with hope: post-treatment fertility preservation

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RKC wrote the manuscript and created the table

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In this issue of Haematologica, Chalas and colleagues sought to determine the feasibility of post-treatment fertility preservation (FP) via oocyte cryopreservation in women with treated hematologic diseases.[1] FP has medically transformed our ability to build families after devastating diagnoses and treatment. Hematological diseases have high survival rates after treatment, but the resultant aftereffects can have profound impact on fertility outcomes. The degree of this impact depends on the type of therapy, the cumulative dose, and the age at treatment.[2] It is known that alkylating agents, total body irradiation, and hematopoietic stem cell transplantation (HSCT) possess the highest gonadotoxic risk. These treatments lead to severe reduction in ovarian reserve and premature ovarian insufficiency.[3] Others, such as ABVD (Adriamycin, bleomycin, vinblastine, and dacarbazine) for Hodgkin lymphoma are considered lower risk.[2] However, as the European Society of Medical Oncology (ESMO) emphasizes, there is no absolute safe threshold; every patient must be considered at risk.[4] Regardless, patients and their families may not choose to proceed with FP. Major determinants include the patient's medical condition, the safety of delaying treatment, prohibitive financial costs, and personal reasons. For those who cannot proceed, it is not uncommon for patients to inquire about the likelihood of future fertility. Age is the best predictor of fertility and is compounded by individual genetics and exposures. With limited research regarding post-treatment fertility, counseling often revolves around the unknowns. If no autologous gametes are available, alternative options for family building may include donor gametes or embryos, adoption, or living child-free. Even if future viable oocytes and embryos are available (either autologous or donor), the safety of carrying a pregnancy post-treatment needs to be assessed. We cannot assume that patients are aware or comfortable with these options. Therefore, it is imperative that patients are counseled appropriately.

American Society for Reproductive Medicine (ASRM) recently updated their practice committee opinion on FP in 2026.[5] They highlight the standard options for FP including oocyte and embryo cryopreservation, but this process takes time. When treatment is more urgent, ovarian tissue cryopreservation (OTC) is an established method and no longer labeled as experimental since 2021. It is the only option for prepubertal females. However, not all fertility centers have the capacity to do OTC, and not all centers have the capacity for ovarian tissue transplantation (OTT). The primary concern regarding OTT is seeding of malignant cells, especially in blood cancers. In vitro maturation is still an emerging therapy and testicular tissue cryopreservation remains experimental. American Society of Clinical Oncology (ASCO) also updated their FP guidelines most recently in 2025 (Table 1).[6, 7] A new, strong recommendation for post-treatment FP is discussed emphasizing that females after treatment may be at increased risk for accelerated depletion of the follicular pool and therefore may have shortened fertility window. Ideally, FP occurs prior to treatment; but, as noted, not all patients are able to proceed in this timeframe. With this ASCO recommendation, the work by Chalas et al is a timely and relevant study.[1]

Prior studies have highlighted low response to ovarian stimulation cycles; however, a recent 12-year retrospective study reported more promising results.[4, 8] Despite medium gonadotoxic risk chemotherapy, 65.3% of women achieved at least one live birth with 80% of pregnancies conceived without assistance post-treatment.[8] Additionally, a large study by Sockel et al using data from the German Transplant Registry revealed a favorable post-treatment pregnancy rate with and without the assistance of reproductive technology after non-myeloablative or reduced conditioning HSCT.[9] In this current 7.5-year retrospective study by Chalas et al, the authors specifically examined patients with hematologic disease categorizing them into three cohorts based on the intensity of treatment: (G1) HSCT, (G2) bifunctional alkylating agents (BFAA) without HSCT, and (G3) no BFAA.[1] Their primary outcomes included post-treatment ovarian reserve, pregnancy occurrence, and "feasibility" of ovarian cryopreservation. As expected, G1 had significantly lower anti-mullerian hormone levels as well as lower antral follicle counts than G2 and G3 with more participants with POI. G1 participants had very poor outcomes with FP post-treatment. Participants in G2 and G3 had better fertility outcomes with improved oocyte yield at the time of egg retrieval and more pregnancies conceived without assistance. G2 had more variability, and the ovarian risk profiles were mixed between diminished ovarian reserve and normal ovarian reserve. Meanwhile, patients in G3 had primarily normal ovarian reserve and the most favorable outlook. Although these findings are not unexpected, this is the largest known series on this topic, and we applaud the authors for providing tangible data that is relevant for counseling patients and furthering the field regarding post-treatment FP.

Additional rigorous studies should address the fundamental outcome that is the gold standard for measuring fertility—live birth. Although natural pregnancy rates are an important measure, it is also important to understand the rate of miscarriage, clinical pregnancy, live birth and birth defects—questions that patients commonly have regarding their fertility. The median age at treatment in this study was 23.5 years while the median age at pregnancy was 30.8 years. The over 7-year gap may not be feasible due to age-related fertility decline, especially when the average age of diagnosis for Hodgkin lymphoma in females, for example, is 34-38 years of age.[10] Therefore, data regarding time to pregnancy after actively attempting to conceive can be a valuable and relevant metric. Ideally, future studies would address these knowledge gaps. As a limitation of this study, it is difficult to assess the true effect size in smaller studies, such as the current one. The differences between the study groups appear clinically significant; however, the use of multiple t-test comparisons can inflate Type 1 error leading to higher false positive rates. Ideally, a Kruskal-Wallis test to compare the three groups with post hoc analysis with a correction to adjust for multiple pair-wise comparisons could give readers more confidence in the data analysis provided.

Although pre-treatment fertility is the most effective strategy, the study highlights the importance of offering the option for post-treatment FP. Success may vary, but these findings provide hope for patients and future family building goals.

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Table 1. Summary of selected female and male fertility preservation guidelines

	2020 ESMO Guideline (4)	**2018 ASCO Guideline (6)**	**2025 ASCO Guideline (7)**
Infertility risk counseling	All reproductive-aged patients should receive counseling before starting treatments	Discuss as early as possible; refer interested/uncertain patients	New recommendation (1.4) adds that discussions/referrals should be offered yearly during follow-up, when treatment plans change, and throughout survivorship, and should be documented in the medical record
Oocyte and embryo cryopreservation	Established method	Established method	Established method
Sperm cryopreservation	Established method	Established method	Established method
Ovarian tissue cryopreservation (OTC)	Alternative option; considered experimental	Considered experimental	New recommendation (4.10) Established method; may be offered as an alternative or adjunct to embryo/oocyte cryopreservation (Evidence: Moderate; Recommendation: Strong)
In vitro maturation (IVM)	Not addressed	Not addressed	New recommendation (4.4): IVM of oocytes may be offered as an emerging FP method (Evidence: Low; Strength: Conditional)
Ovarian transposition	May be offered when pelvic irradiation is required	May be offered when pelvic irradiation is required	May be offered when pelvic irradiation is required
Uterine transposition	Not addressed	Not addressed	New recommendation (4.6): Uterine transposition remains experimental and should be offered only in clinical trials or approved experimental protocols (Evidence: Low; Strength: Conditional)
GnRH agonist (ovarian suppression)	May be offered when proven methods are not feasible; should	May be offered when proven methods are not feasible; should	May be offered when proven methods are not feasible; should not replace proven

	2020 ESMO Guideline (4)	2018 ASCO Guideline (6)	2025 ASCO Guideline (7)
	not replace proven methods	not replace proven methods	methods
GnRHa in oncologic emergencies	Not specifically addressed	Not specifically addressed	New recommendation (4.9): For patients with oncologic emergencies requiring urgent chemotherapy, GnRHa may be offered for menstrual suppression (Evidence: Low; Strength: Conditional)
Testicular sperm extraction (TESE)	Mentioned as an option	Mentioned as an option	New recommendation (3.2): TESE with sperm cryopreservation should be offered to pubertal/post-pubertal males who cannot produce a semen sample, before treatment (Evidence: High; Strength: Strong)
Post-treatment sperm collection	Advised higher risk of genetic damage post-treatment; recommended pre-treatment collection	Advised higher risk of genetic damage post-treatment; recommended pre-treatment collection	Advised higher risk of genetic damage post-treatment; recommended pre-treatment collection
Post-treatment FP (females)	Not addressed	Not addressed	New recommendation (4.3): Embryo and oocyte cryopreservation may be offered post-treatment to patients who did not undergo pretreatment FP, those who may not have banked enough gametes, or those facing age-related fertility decline (Evidence: Moderate; Strength: Strong)