

CORRESPONDENCE

Safety and efficacy concerns of long-acting GnRHa trigger for ovulation induction in oncological patients undergoing oocyte cryopreservation: a call for caution and further investigation



We are writing in response to the recent manuscript entitled 'Long-Acting GnRHa Trigger for Ovulation Induction in Oncological Patients Undergoing Oocyte Cryopreservation.'¹

We would like to express our appreciation to the authors for their efforts to explore new strategies for fertility preservation in patients with cancer. However, we have some concerns about the safety and efficacy of using long-acting gonadotropin-releasing hormone (GnRH) agonists (GnRHAs) for ovulation induction in this patient population.

This study presents data from a retrospective analysis of ovarian stimulation for oocyte cryopreservation in patients with cancer and compares the use of long-acting GnRHa triggers with other standard methods. The reported results show favourable oocyte maturation rates and a lower risk of ovarian hyperstimulation syndrome (OHSS). Although these results are intriguing, several important considerations must be made before advocating the routine use of long-acting GnRHa for ovulation induction in patients with cancer.

OHSS is a significant problem in controlled ovarian hyperstimulation (COH) of patients with cancer because it can delay or complicate the initiation of oncologic treatment.² The absence of OHSS cases after the use of long-acting GnRHa for ovulation induction is promising, but the study sample size is relatively small. Robust, well-controlled studies are needed to confirm these findings and adequately assess OHSS risk associated with long-acting GnRHa in this context. In addition, the lack of OHSS cases could be influenced by specific patient characteristics, particularly the low ovarian reserve in the included population. Patients with lower ovarian reserve might be at a lower risk of OHSS because fewer corpora lutea form after oocyte retrieval. However, this is not necessarily true for patients with higher ovarian reserve.

The proposed mechanism for the development of OHSS after administration of long-acting GnRHa involves a sustained increase in gonadotropin levels leading to the production of angiogenic factors. While this is consistent with existing knowledge of the pathophysiology of OHSS, it raises concerns about the potential risk of OHSS in patients undergoing this triggering method.³ A comprehensive understanding of the underlying biology is critical for patient safety.

It is important to acknowledge that cases of OHSS have been reported following the use of long-acting GnRHa after COH for fertility preservation.⁴⁻⁷ These reports highlight the need for further investigation of the potential adverse effects of this treatment in oncology patients.

Ultimately, the decision to offer long-acting GnRHa triggering should be made with extreme caution, taking into account

individual patient characteristics, cancer type, stage, and overall treatment plan. Fertility preservation should not compromise oncologic outcomes, and the potential benefits and risks of any intervention must be carefully weighed.

In summary, although the study presents preliminary data, the results should be interpreted with caution, and further research is needed to validate the safety and efficacy of long-acting GnRHa triggers for ovulation induction in oncology patients undergoing oocyte cryopreservation. In the absence of more robust evidence, adherence to established ovarian stimulation protocols for fertility preservation in this vulnerable population remains advisable.

C. Ingold¹ & G. Bedoschi^{2*}

¹*Faculdade de Medicina do ABC, Santo André, São Paulo;*

²*University of Sao Paulo, Ribeirao Preto Medical School, Department of Gynecology and Obstetrics, Reproductive Medicine Division, Ribeirao Preto, São Paulo, Brazil*

(*E-mail: giulianobedoschi@gmail.com).

Available online xxx

© 2023 The Author(s). Published by Elsevier Ltd on behalf of European Society for Medical Oncology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.esmoop.2023.101825>

DOI of original article: <https://doi.org/10.1016/j.esmoop.2023.101597>

FUNDING

None declared.

DISCLOSURE

The authors have declared no conflicts of interest.

REFERENCES

1. Massarotti C, Stigliani S, Gazzo I, Lambertini M, Anserini P. Long-acting gonadotropin-releasing hormone agonist trigger in fertility preservation cycles before chemotherapy. *ESMO Open*. 2023;8(4):101597.
2. Practice Committee of the American Society for Reproductive Medicine. Prevention and treatment of moderate and severe ovarian hyperstimulation syndrome: a guideline. *Fertil Steril*. 2016;106:1634-1647.
3. Oktay K, Bedoschi G. Appraising the biological evidence for and against the utility of GnRHa for preservation of fertility in patients with cancer. *J Clin Oncol*. 2016;34:2563-2565.
4. Christ J, Herndon CN, Yu B. Severe ovarian hyperstimulation syndrome associated with long-acting GnRH agonist in oncofertility patients. *J Assist Reprod Genet*. 2021;38:751-756.
5. Iorio GG, Rovetto MY, Conforti A, et al. Severe ovarian hyperstimulation syndrome in a woman with breast cancer under letrozole triggered with GnRH agonist: a case report and review of the literature. *Front Reprod Health*. 2021;3:704153.
6. Marin L, Vitagliano A, Capobianco G, et al. Which is the optimal timing for starting chemoprotection with gonadotropin-releasing hormone agonists

- after oocyte cryopreservation? Reflections on a critical case of ovarian hyperstimulation syndrome. *J Gynecol Obstet Hum Reprod*. 2021;50:101815.
7. Ingold C, Navarro PA, de Oliveira R, Barbosa CP, Bedoschi G. Risk of ovarian hyperstimulation syndrome in women with malignancies undergoing treatment with long-acting gonadotropin-releasing hormone agonist after controlled ovarian hyperstimulation for fertility preservation: a systematic review. *Ther Adv Reprod Health*. 2023;17:26334941231196545.