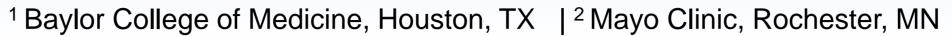
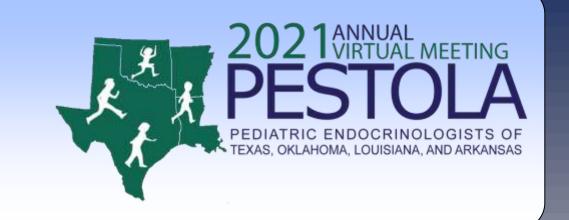


Leuprolide Therapy for the Preservation of Ovarian Reserve in Female Adolescents undergoing Gonadotoxic Treatment

Alfonso Hoyos-Martinez, MD,¹ Michael E. Scheurer, PhD, MPH,¹ Wendy Allen-Rhoades, MD, PhD,² M. Fatih Okcu, MD, MPH,¹ and Vincent E. Horne, MD.¹





Introduction

- Nearly 1 out of 10 female childhood cancer survivors will have primary ovarian insufficiency.
- Anti-müllerian hormone (AMH) is the best bio-marker of the ovarian reserve
- GnRH agonists have been studied in adults with inconclusive results. Pediatric literature is lacking.

Aim

To use AMH levels to ascertain if leuprolide use during gonadotoxic treatment preserves ovarian reserve in pubertal females.

Methods

Retrospective cohort study of pubertal females receiving gonadotoxic treatment from 1/2010 to 4/2020, with an AMH collected after completion of therapy.

- Wilcoxon rank sum test
- Linear regression models

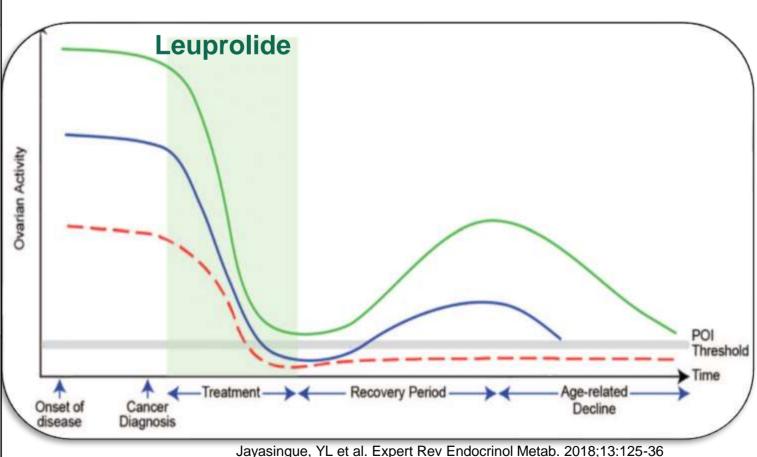
Results

Demographics, Disease and Treatment Characteristics

| by Leuprolide use | | | |
|------------------------------------|------------|------------|---------|
| | Leuprolide | No | p-value |
| | (n=35) | Leuprolide | |
| | | (n=17) | |
| Age at Diagnosis (mean [SD]) | 15.9 (1.9) | 13.8 (2.7) | 0.002 |
| Diagnosis | | | 0.61 |
| Leukemia | 7 | 3 | |
| Lymphoma | 13 | 6 | |
| Solid tumors | 6 | 2 | |
| Non-neoplastic | 3 | 0 | |
| HSCT | 6 | 6 | |
| Race | | | 0.84 |
| Hispanic | 18 | 7 | |
| Non-Hispanic White | 9 | 5 | |
| Non-Hispanic Black | 5 | 3 | |
| Non-Hispanic Asian | 3 | 2 | |
| Chemotherapy | | | |
| Cyclophosphamide | | | 0.37 |
| equivalent dose | 17 | 7 | |
| Low dose (0 - $<4 \text{ g/m}^2$) | 8 | 7 | |
| Moderate dose $(4 - < 8 g/m^2)$ | 10 | 3 | |
| High dose (≥ 8 g/m²) | | | |
| | | | |
| Receipt of platin therapy | 4 | 2 | 1.00 |
| Yes | 31 | 15 | |
| No | | | |
| Radiation therapy | | | 1.00 |
| No | 31 | 15 | |
| Proton | 3 | 1 | |
| Photon | 1 | 1 | |

No difference in median AMH levels between groups: 1.15 vs 0.081 ng/mL (P= 0.09).

After correcting for age, race, time after treatment, and treatment received the leuprolide group had higher AMH levels (OR=3.7, P= < 0.05; 95% CI:1.01-13.79)



Conclusions

Leuprolide use during gonadotoxic treatment helps preserve follicular reserve in adolescents after completion of treatment.

Future prospective studies are needed to determine the extent of the effect on ovarian reserve and function after completion of gonadotoxic treatment.

Limitations

- Different AMH assays
- Variable leuprolide doses and timing
- Low number of patients exposed to ovarian radiation

References

- 1. Ann Oncol. 2014;25(9):1719-1728.
- 2. J Clin Endocrinol Metab. 2006;91(5):1723-1728.
- 3. Hum Reprod. 2018;33(8):1474-1488.