

# #103 - MixMax Study: When Mixed Protocol Meets Maximum Dose – Are We There Yet?

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## INTRODUCTION

At our center, ovarian stimulation with follitropin delta (Rekovele, RKV) is performed according to the manufacturer's dosing algorithm, which determines the initial dose based on AMH and body weight. For patients in whom the algorithm indicates the maximum dose of 12 ug, we systematically add 300 IU of menotropin (Menopur, MNP) resulting in a 'mixed' protocol. This strategy has previously been shown to identify patients who require maximal stimulation, resulting in appropriate responses with minimal risk of hyperstimulation.

## AIM

- Evaluate if maximum-dose patients reached the target oocyte yield (8-14)
- Analyse outcomes in relation to AMH, age and body weight
- Identify subgroups potentially needing doses beyond the current maximum

## METHOD

- Design: Retrospective study
- Population: 1417 patients who underwent ovarian stimulation at Clinique Ovo between November 2018 and December 2024
- Protocol: Maximum dose mixed protocol of RKV (12 ug) + MNP (300 IU) using an AMH and weight-based algorithm
- Inclusion: Strict adherence to the AMH and weight-based dosing algorithm
- Exclusion: Patients with AMH  $\geq 2.1$  ng/mL and who had dose adjustments during the cycle
- Statistical analysis: Descriptive statistics of ovarian stimulation and embryo transfer outcomes. Spearman's correlation test was used to determine association between baseline characteristics and stimulation outcomes. Significance levels: \*p < 0.05; \*\*p < 0.01; \*\*\*p < 0.001

## RESULTS

Table 1. Baseline characteristics

| Variables                  | Study patients<br>n=1317             |
|----------------------------|--------------------------------------|
| Age (years)                | 37.7 $\pm$ 3.9<br>38.6 (35.1, 40.7)  |
| Weight (kg)                | 69.8 $\pm$ 16.6<br>66.0 (58.0, 78.8) |
| AMH (ng/mL)                | 1.1 $\pm$ 0.5<br>1.1 (0.7, 1.5)      |
| Number of attempted cycles | 1.5 $\pm$ 0.9<br>1.0 (1.0, 2.0)      |
| Proportion of first cycle  | 936 (71.1%)                          |

Table 2. Ovarian stimulation outcomes

| Variables                        | Study patients<br>n=1317         |
|----------------------------------|----------------------------------|
| Number of follicles $\geq 14$ mm | 7.3 $\pm$ 3.8<br>7.0 (5.0, 9.0)  |
| Retrieved oocytes                | 9.3 $\pm$ 5.7<br>8.0 (5.0, 12.0) |
| Mature oocytes (MII)             | 6.7 $\pm$ 4.3<br>6.0 (4.0, 9.0)  |
| Fertilized oocytes (2PN)         | 4.8 $\pm$ 3.5<br>4.0 (2.0, 6.0)  |
| Usable blastocysts               | 2.2 $\pm$ 2.0<br>2.0 (1.0, 3.0)  |
| Patients with no blastocysts     | 223 (16.9%)                      |

Figure 1. Relationship of stimulation outcomes with age, AMH and body weight (smoothed curves)

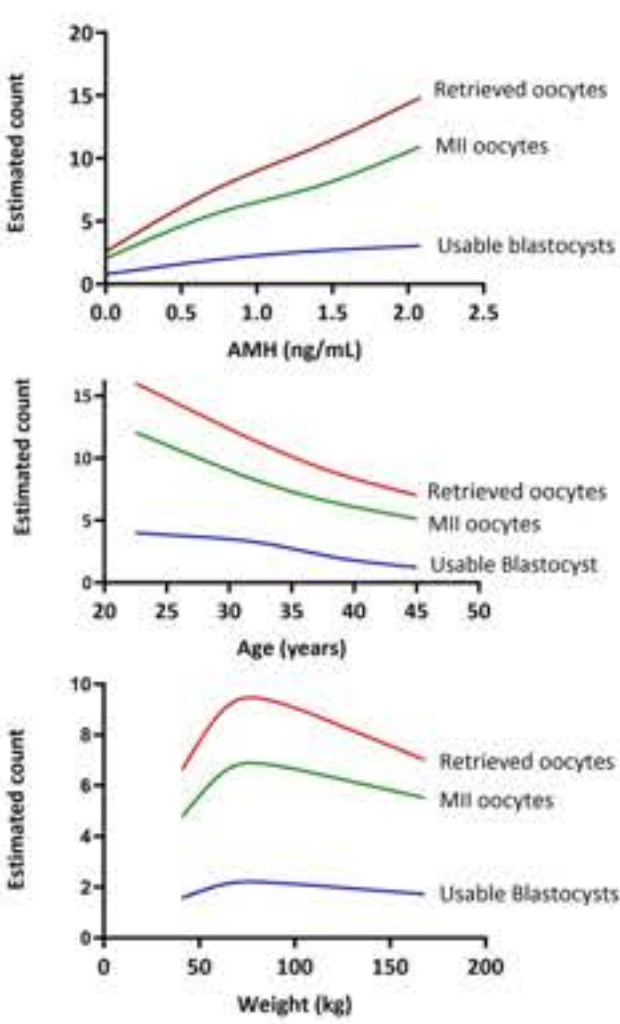


Table 3. Spearman correlations between stimulation outcomes and demographic variables (age, AMH, body weight)

| Correlations (Spearman)      | AMH (ng/mL) | Age (years) | Weight (kg) |
|------------------------------|-------------|-------------|-------------|
| Number of retrieved oocytes  | 0.517 ***   | -0.237 ***  | 0.087 **    |
| Number of MII oocytes        | 0.464 ***   | -0.232 ***  | 0.095 **    |
| Number of usable blastocysts | 0.257 ***   | -0.294 ***  | 0.052 NS    |

Table 4. Ovarian stimulation outcomes of patients with AMH  $\leq 1.1$  ng/mL

| Variables                        | Study patients<br>n=700         |
|----------------------------------|---------------------------------|
| Number of follicles $\geq 14$ mm | 5.9 $\pm$ 3.0<br>5.0 (4.0, 7.0) |
| Retrieved oocytes                | 7.1 $\pm$ 4.2<br>6.0 (4.0, 9.0) |
| Mature oocytes (MII)             | 5.3 $\pm$ 3.2<br>5.0 (3.0, 7.0) |
| Fertilized oocytes (2PN)         | 3.8 $\pm$ 2.7<br>3.0 (2.0, 5.0) |
| Usable blastocysts               | 1.8 $\pm$ 1.7<br>1.0 (1.0, 3.0) |
| Patients with no blastocysts     | 140 (20.0%)                     |

Notes: Data are expressed as mean  $\pm$  SD and median (25<sup>th</sup> - 75<sup>th</sup> percentile) or n (%)

Usable blastocysts: blastocysts considered suitable for transfer and/or cryopreservation

- The cohort had a median age of 38.6 years, median body weight of 66.0 kg, and median AMH of 1.1 ng/mL; 71.1% were undergoing their first stimulation cycle.
- A median of 8 oocytes was retrieved, corresponding to the target yield (8-14), with median of 6.0 MII, 4.0 2PN and 2.0 usable blastocysts.
- AMH correlated positively with all outcomes (r = 0.26-0.52, \*\*\*), while age correlated negatively (r = -0.23 to -0.29, \*\*\*). No correlation was found with body weight.
- Patients with AMH  $\leq 1.1$  ng/mL showed consistently lower responses, with a median of 6.0 retrieved oocytes, 5.0 MII, 3.0 2PN and 1.0 usable blastocyst, even under maximal dosing.

## CONCLUSIONS

In our clinical practice, the AMH- and weight-based algorithm, combined with systematic addition of MNP for patients prescribed 12  $\mu$ g of RKV, has proven safe and effective in limiting ovarian over-response. Nonetheless, this analysis indicates that a subset of patients with low AMH, particularly those with AMH around or below 1.1 ng/mL, may fail to reach the target oocyte yield despite maximal stimulation.

These findings highlight the need to investigate whether specific subgroups could benefit from stimulation beyond current algorithm-defined limits and underscore the importance of more individualized strategies for low responders.

## ACKNOWLEDGEMENTS

We thank Ferring Pharmaceuticals for the financial support. We also thank Marion Vivien, Marya Far and Michelle Roberge for their valuable contribution to this study.

## CONTACT INFORMATION

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