# An exploratory study to evaluate a mixed protocol of MENOPUR (highly purified human menopausal gonadotrophin) and REKOVELLE (follitropin delta) for controlled ovarian stimulation in IVF (in-vitro fertilization)

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## OBJECTIVE

This is a multi-center, open label, exploratory study to evaluate the effect of adding HP-hMG (Menopur) to follitropin delta (REKOVELLE) in a 'mixed protocol' regimen, using individualized, fixed dose of follitropin delta based on the established algorithm, combined with a variable, adjustable dose of Menopur based on body weight and ovarian reserve. The primary objective is to evaluate the number of utilizable blastocysts on Day 5 and Day 6 of embryo culture.

## STUDY PROTOCOL

- AMH between D2 to D5 of cycle 1*
- Start Rekovelle and Menopur on D2 of cycle 2
- Ultrasound and blood test at D6 of stimulation
- Dose adjustments of Menopur according to Estradiol levels
- Start GnRH antagonist
- Ultrasound monitoring and dispense medication
- Ovulation triggering
- hCG 5000 IU if E2 < 10,000 pmol/L
- GnRH antagonist (0.2 mg of triptorelin acetate, Decapeptyl) if E2 ≥ 10,000 pmol/L
- Oocyte retrieval 36 ± 2 hours post triggering
- Blastocyst classification and embryo transfer

*** Blood samples sent to central laboratory at Dr. Librach's site.**

## STUDY DESIGN OVERVIEW

| | |
|---|---|
| **Study Design** | Multi center, open label, exploratory study |
| **Population** | Women undergoing their first IVF treatment |
| **Locations** | Quebec: Clinique ovo – Dr Bissonnette<br>Toronto: Hannam Fertility Centre – Dr Hannam<br>CReATe Fertility Centre – Dr Librach<br>Vancouver: Olive Fertility Centre – Dr Yuzpe |
| **Total patients** | 160 participants equally divided between sites |
| **Medication** | REKOVELLE (dose according to AMH and weight) and Menopur (dependant on REKOVELLE dose – next slide) |
| **Medication presentation** | REKOVELLE: 12µg cartridge for s/c injection<br>Menopur: vials of 75 IU to be dilutes for s/c injection |
| **Treatment Duration** | 1 IVF cycle until day 5 or 6 of embryo culture |

## REKOVELLE® DOSING ALGORITHM

**Step 1** Round measured AMH value to the nearest integer

**Step 2** Using the rounded AMH value, read off the appropriate factor from the table below

| Measure AMH concentration (pmol/L) | | Rounded AMH concentration (pmol/L) | | Dosing Factor |
|---|---|---|---|---|
| <14.5 | → | <15 | → | 12 mcg* |
| 14.5- 16.4 | → | 15-16 | → | 0.19 mcg/kg |
| 16.5- 17.4 | → | 17 | → | 0.18 mcg/kg |
| 17.5- 18.4 | → | 18 | → | 0.17 mcg/kg |
| 18.5- 20.4 | → | 19- 20 | → | 0.16 mcg/kg |
| 20.5- 22.4 | → | 21- 22 | → | 0.15 mcg/kg |
| 22.5- 24.4 | → | 23- 24 | → | 0.14 mcg/kg |
| 24.5- 27.4 | → | 25- 27 | → | 0.13 mcg/kg |
| 27.5- 32.4 | → | 28- 32 | → | 0.12 mcg/kg |
| 32.5- 39.4 | → | 33- 39 | → | 0.11 mcg/kg |
| ≥ 39.5 | → | ≥ 40 | → | 0.10 mcg/kg |

* For women with a rounded AMH concentration of <15 pmol/L, the daily dose of REKOVELLE® for the first treatment cycle is 12 mcg, irrespective of weight

**Step 3** Measure body weight of women and multiply by the factor

**Body Weight** (X) **Dosing Factor** (=) **Daily REKOVELLE® Dose**

**Step 4** Round dose to the nearest 0.33 mcg (.00 mcg, .33mcg, .66mcg)

## MENOPUR® DOSING

**Regimen A:** REKOVELLE dose < 12 µg: add one 75 IU vial of Menopur

**Regimen B:** REKOVELLE dose = 12 µg and body weight < 100 kg: add two 75 IU vials of Menopur

**Regimen C:** REKOVELLE dose = 12 µg and body weight ≥ 100 kg: add three 75 IU vials of Menopur

**Menopur dose may be adjusted (if necessary) at day 6. Details below:**

| **Dose Increase** | |
|---|---|
| **E2** | **Menopur dose** |
| <750 pmol/L | ⇧ MNP to 225 IU ⇨ from 1 or 2 to 3 vials |
| ≥ 750 to 999 pmol/L | ⇧ MNP by 75 IU ⇨ from 1 to 2 or from 2 to 3 vials |
| Further dose adjustment (from 2 to 3 vials) at physician's discretion | |
| ** Maximum dose of MNP should not exceed 225 IU/day (3 vials) ** | |
| **Dose decrease** | |
| >3,000 pmol/L | ⇩ MNP by 75 IU ⇨ from 3 to 2 or from 2 to 1 vial |
| If the patient is on 1 vial (75 IU), ⇩ MNP to ½ a vial (37.5 IU) or withdraw it completely to ensure a proper risk management | |
| Further dose adjustments (i.e. from 2 to one vial) will be at physician's discretion and can include an option of ⇩ MNP by ½ vial at a time (37.5 IU) or withdrawing it completely.<br>Dosage decrease may be done as frequently as necessary. | |
| **No dose change** | |
| 1,000 to 3,000 pmol/L | Continue with the initial dose of MNP (1, 2 or 3 vials) |

## OOCYTE TRIGGERING

**E2 < 10,000 pmol/L**

hCG 5,000 IU to 10,000 IU (site protocol)

**E2 ≥ 10,000 pmol/L**

GnRH agonist (0.2 mg of triptorelin acetate, Decapeptyl)

**E2 ≥ 15,000 pmol/L**

or ≥ 20 follicles of ≥ 12 mm, freeze-all