

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) François Bissonnette¹, Albert Yuzpe², Tom Hannam³, Clifford Librach⁴

¹ Clinique Ovo (ovo fertilité), Montréal, QC, Canada. ² Olive Fertility, Vancouver, BC, Canada. ³ Hannam Fertility, Toronto, ON, Canada. ⁴ CReATe Fertility, Toronto., ON, Canada. Supported by Ferring Pharmaceuticals

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.

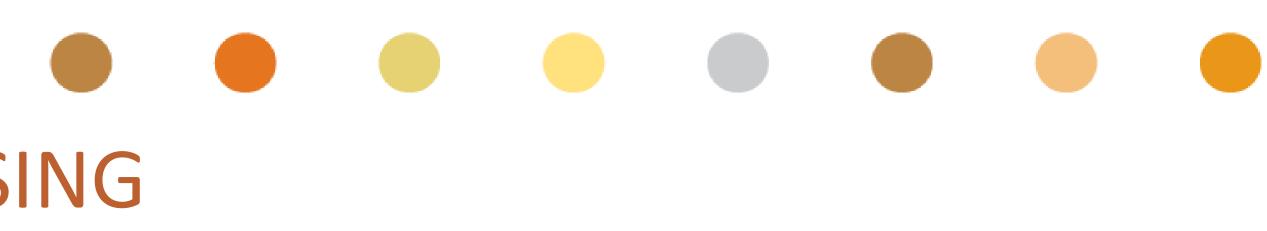
STUDY PROTOCOL

 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 Estradio 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	Multi center, open label, explora
Population	Women undergoing their first IV
Locations	Quebec: Clinique ovo – Dr Bisso Toronto: Hannam Fertility Centre CReATe Fertility Centre – Dr Vancouver: Olive Fertility Centre
Total patients	160 participants equally divided
Medication	REKOVELLE (dose according to A Menopur (dependant on REKOV
Medication presentation	REKOVELLE: 12µg cartridge for s Menopur: vials of 75 IU to be dil
Treatment Duration	1 IVF cycle until day 5 or 6 of em

STUDY DESIGN OVERVIEW Study Design Multi center, open label, exploratory study							NOPUR® D		
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Population Women undergoing their first IVF treatment Quebec: Clinique ovo – Dr Bissonnette						1.05	Regimen B: REKOVELLE do vials of Menor		
Locatio	DNS	Toronto: Hanı CReATe F	que ovo – Dr B nam Fertility Ce ertility Centre ive Fertility Ce	Reg	Regimen C: REKOVELLE do vials of Menop				
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			ose according			Dose	Increase		
Medica	ation	•	•		• ·		E2		
Medication presentation		Menopur (dependant on REKOVELLE dose – next slide) REKOVELLE: 12µg cartridge for s/c injection				<750	pmol/L	仓	
						≥ 750) to 999 pmol/L	仓	
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Duratio		1 IVF cycle until day 5 or 6 of embryo culture					** Maximum dose o		
						Dose	decrease		
RFK		E [®] DOSI							
				RITHIV			10 nmol/l		
							00 pmol/L	↓ ~↓ / 7 ⊑	
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STU	DY DE	SIGN OV	ERVIEW				MENOPUR® D)OSI	
Study	Study Design Multi center, open label, exploratory study						Regimen A: REKOVE	LLE do	
Popula	ation	Women unde	rgoing their firs	st IVF treat	ment		Regimen B: REKOVELLE de		
							vials of I		
Locatio	ons	Quebec: Clinique ovo – Dr Bissonnette Toronto: Hannam Fertility Centre – Dr Hannam CReATe Fertility Centre – Dr Librach Vancouver: Olive Fertility Centre – Dr Yuzpe					Regimen C: REKOVELLE do vials of Menop		
Total n	atients		, nts equally divi				Menopur dose may be adj		
			lose according				Dose Increase		
Medica	ation	•	•		• •		E2		
Modic	otion		Menopur (dependant on REKOVELLE dose – next slide)				<750 pmol/L	仓	
Medication presentation		REKOVELLE: 12µg cartridge for s/c injection Menopur: vials of 75 IU to be dilutes for s/c injection					≥ 750 to 999 pmol/L	仓	
Treatm		menopuli na			i sy e myeeren		Further dose adjustme	ent (fro	
Duratio		1 IVF cycle un	til day 5 or 6 of	f embryo c	ulture		** Maximum	•	
							Dose decrease		
RFK			NG ALGO	RITHN/				Û	
							>3,000 pmol/L		
Step 1	Round	measured AIVIF	I value to the n	learest inte	eger		If the patient is on 1 vial (75 completely to ensure a prop		
Step 2			/H value, read	off the app	oropriate factor				
	from th	e table below					Further dose adjustme	•	
Measur	e AMH conce (pmol/L)	entration Rou	unded AMH concentra (pmol/L)	ation	Dosing Factor		can include an option	Ot ↔ N	
	<14.5	\rightarrow	<15	\rightarrow	12 mcg*		completely. Dosage decrease may be do		
14.5-16.4		\rightarrow	15-16	\rightarrow	0.19 mcg/kg		Dusage decrease may		
16.5- 17.4 17.5- 18.4		\rightarrow \rightarrow	17 18	\rightarrow \rightarrow	0.18 mcg/kg 0.17 mcg/kg		No dose change		
17.5-18.4		\rightarrow	19-20	\rightarrow	0.16 mcg/kg				
20.5-22.4		\rightarrow	21-22	\rightarrow	0.15 mcg/kg		1,000 to 3,000 pmo	′L C	
	22.5-24.4	\rightarrow	23-24	\rightarrow	0.14 mcg/kg				
	24.5-27.4	\rightarrow	25-27	\rightarrow	0.13 mcg/kg				
	27.5-32.4 32.5-39.4	\rightarrow \rightarrow	28- 32 33- 39	\rightarrow \rightarrow	0.12 mcg/kg 0.11 mcg/kg		OOCYTE TRIG	GFR	
32.5- 39.4 ≥ 39.5		\rightarrow	≥ 40	\rightarrow	0.10 mcg/kg				
* For women					t cycle is 12 mcg, irrespective of weigh	nt	E2 < 10,000 pmol/L		
Step 3	Measur	e body weight	of women and	multiply b	y the factor		hCG 5,000 IU to 10,00 E2 ≥ 10,000 pmol/L	0 IU (s	
Body	Weight	X Dosir	ng Factor (=	Daily F	REKOVELLE [®] Dos	e	GnRH agonist (0.2 mg E2 ≥ 15,000 pmol/L	of trip	
Step 4	Round	dose to the nea	arest 0.33 mcg	(.00 mcg, .	33mcg, .66mcg)		or ≥ 20 follicles of ≥ 12	2 mm,	



dose < 12 μ g: add one 75 IU vial of Menopur

dose = 12 μ g and body weight < 100 kg: add two 75 IU opur

lose = 12 μ g and body weight \geq 100 kg: add three 75 IU opur

justed (if necessary) at day 6. Details below:

Menopur dose

 \widehat{U} MNP to 225 IU \Rightarrow from 1 or 2 to 3 vials

 \widehat{U} MNP by 75 IU ⇒ from 1 to 2 or from 2 to 3 vials

from 2 to 3 vials) at physician's discretion

of MNP should not exceed 225 IU/day (3 vials) **

 \bigcirc MNP by 75 IU \Rightarrow from 3 to 2 or from 2 to 1 vial '5 IU), $\sqrt[3]{}$ MNP to $\frac{1}{2}$ a vial (37.5 IU) or withdraw it oper risk management

(i.e. from 2 to one vial) will be at physician's discretion and MNP by ½ vial at a time (37.5 IU) or withdrawing it

one as frequently as necessary.

Continue with the initial dose of MNP (1, 2 or 3 vials)

RING

(site protocol)

riptorelin acetate, Decapeptyl)

, freeze-all