ACOG_2011_PGNVR 4/14/11 8:25 AM Page 1

Efficacy of a progesterone vaginal ring versus progesterone gel for luteal phase supplementation

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Abstract

Objective:

To determine the qualitative efficacy of a novel, weekly progesterone vaginal ring (VR) compared to a daily 8% progesterone vaginal gel (90 mg/day) for luteal phase supplementation after in vitro fertilization (IVF) by infertility duration and diagnosis.

Methods Used for Data Collection:

Prospective, randomized, multicenter non-inferiority study evaluating patients undergoing IVF. Patients were stimulated with a standard down-regulation protocol. hCG was administered when two follicles exceeded 17 mm. A transvaginal oocyte retrieval was performed 35-37 hours after hCG administration. 1:1 randomization to initiate the VR or gel was performed one day following retrieval. A serum pregnancy test was performed 14 days following retrieval. Pregnant subjects continued PGN dosing through 12 weeks gestation. Clinical pregnancy rates were determined after stratification based on duration and diagnosis of infertility.

Results Summarized:

A total of 1297 eligible women age 18-42 were randomized following retrieval. When stratified by duration of infertility, clinical pregnancy rates in subjects using the progesterone VR compared to the gel were: 53.1% vs. 47.6% (<1 year of infertility), 49.3% vs. 43.5% (1-2 years of infertility), 51.8% vs. 41.8% (2-3 years of infertility), and 41.5% vs. 47.9% (>3 years of infertility). When subgrouped by infertility diagnosis, clinical pregnancy rates ranged from 31.1% to 53.4% and were similar between treatment groups. Overall, clinical pregnancy rates were within nationally reported ranges for both treatment groups regardless of duration or diagnosis of infertility.

Conclusion Reached:

The PGN VR is effective for luteal phase supplementation in IVF regardless of duration or diagnosis of infertility.

Background

Normal luteal function is essential for maintaining pregnancy and data suggest that progesterone is necessary for normal luteal function.[1]

- For many women, in conjunction with Assisted Reproductive Technologies (ART), steps must be taken to prime the uterus for implantation, and to sustain the pregnancy after implantation.
- Oral, intramuscular (IM), and vaginal progesterone preparations are commercially available for use. Serum progesterone levels are highest with IM administration, but because of the uterine first pass effect, vaginal administration may result in higher endometrial progesterone levels.[1,2]
- Vaginal progesterone gel[3] is less painful and easier to use than IM, but also requires daily dosing, may be messy, and due to potential leakage may not provide a full dose with every application.
- The progesterone VR is a flexible silicone product containing the active ingredient micronized progesterone formulated to allow for weekly dosing.
- Regardless of type of progesterone used for luteal phase support after ART, pregnancy rates may vary by duration of infertility and infertility diagnosis (Table 1).

Table 1 National Pregnancy Rate (%) per Cycle after ART in Women up to Age 42 by Infertility Diagnosis[4]

Tubal Factor	31.6
Ovulatory Dysfunction	38.4
Endometriosis	36.0
Male Factor	36.9
Idiopathic Factor	33.4
Other Factors	27.0

Objective

- To determine the qualitative efficacy of a novel, weekly progesterone vaginal ring (VR) compared to a daily 8% progesterone vaginal gel (90 mg/day) for luteal phase supplementation after in vitro fertilization (IVF) by infertility duration and diagnosis.

Methods

- This was a prospective, randomized, multicenter non-inferiority study evaluating patients undergoing IVF.
- 1297 healthy women aged 18-42 with tubal, idiopathic, male factor, ovulatory dysfunction or endometriosis-linked infertility were included in the study.
- Patients were stimulated with a standard down-regulation protocol. hCG was administered when two follicles exceeded 17 mm. A transvaginal oocyte retrieval was performed 35-37 hours after hCG administration.
- 1:1 randomization to initiate the VR or gel was performed one day following retrieval. A serum pregnancy test was performed 14 days following retrieval. Pregnant subjects continued PGN dosing through 12 weeks gestation.
- Clinical pregnancy rates per retrieval were determined for each treatment group after stratification based on duration and diagnosis of infertility. Duration and diagnosis of infertility were self-reported by the patients.

Results

- Pregnancy rates were comparable between treatment groups and appeared to favor the PGN VR for women with less than three years of infertility; numerically, rates were higher for the PGN gel for those with three or more years of infertility (Table 2).

Table 2 Clinical Pregnancy Rate per Retrieval by Duration of Infertility

	Weeks of Pregnancy	PGN VR	N=646	PGN gel	N=651	DIFF (PGN VR - PGN gel)	95% C.I. for DIFF
		N	%	N	%		
< 1 Year	12	32	53.1%	42	47.6%	5.5%	(-17.5%, 28.5%)
1 Year-< 2 Years	12	138	49.3%	184	43.5%	5.8%	(-5.2%, 16.8%)
2 Years-< 3 Years	12	170	51.8%	158	41.8%	10.0%	(-0.8%, 20.7%)
> 3 Years	12	306	41.5%	267	47.9%	-6.4%	(-14.6%, 1.7%)

- In this study, subjects were allowed to select more than one infertility diagnosis, and many subjects (approximately 42.5%) did report more than one diagnosis. Overall, male factor was the most commonly selected infertility diagnosis (39.0%) followed by ovulatory dysfunction (29.1%) and tubal factor (25.7%) (Table 3).
- When grouped by infertility diagnosis, clinical pregnancy rates ranged from 31.1% to 53.4% and were similar between treatment groups (Table 4).

Results

Table 3 Distribution of Infertility Diagnosis

	PGN VR (N=646)	PGN gel (N=651)	Total (N=1297)
Multiple diagnoses	278 (43.0%)	273 (41.9%)	551 (42.5%)
Tubal factor	164 (25.4%)	169 (26.0%)	333 (25.7%)
Ovulatory dysfunction	193 (29.9%)	184 (28.3%)	377 (29.1%)
Endometriosis	146 (22.6%)	150 (23.0%)	296 (22.8%)
Male factor	247 (38.2%)	259 (39.8%)	506 (39.0%)
Idiopathic factor	160 (24.8%)	138 (21.2%)	298 (23.0%)
Other	69 (10.7%)	74 (11.4%)	143 (11.0%)

Table 4 Clinical Pregnancy Rate per Retrieval by Infertility Diagnosis

	Weeks of Pregnancy	PGN VR	N=646	PGN gel	N=651	DIFF (PGN VR - PGN gel)	95% C.I. for DIFF
		N	%	N	%		
Tubal Factor	12	164	42.1%	169	46.2%	-4.1%	(-14.7%, 6.6%)
Ovulatory Dysfunction	12	193	51.8%	184	50.5%	1.3%	(-8.8%, 11.4%)
Endometriosis	12	146	47.3%	150	47.3%	-0.1%	(-11.4%, 11.3%)
Male Factor	12	247	47.4%	259	47.5%	-0.1%	(-8.8%, 8.6%)
Idiopathic Factor	12	160	43.1%	138	39.9%	3.3%	(-7.9%, 14.5%)
Other Factors	12	69	42.0%	74	31.1%	10.9%	(-4.8%, 26.7%)

Conclusions

- Overall, clinical pregnancy rates were similar between patients assigned to weekly progesterone vaginal ring (VR) compared to a daily 8% progesterone vaginal gel (90 mg/day) for luteal phase supplementation after IVF for each infertility duration and diagnosis.
- Pregnancy rates in this study were similar to national rates across diagnoses.

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