

# **Clinical Experience With Corifollitropin alfa**

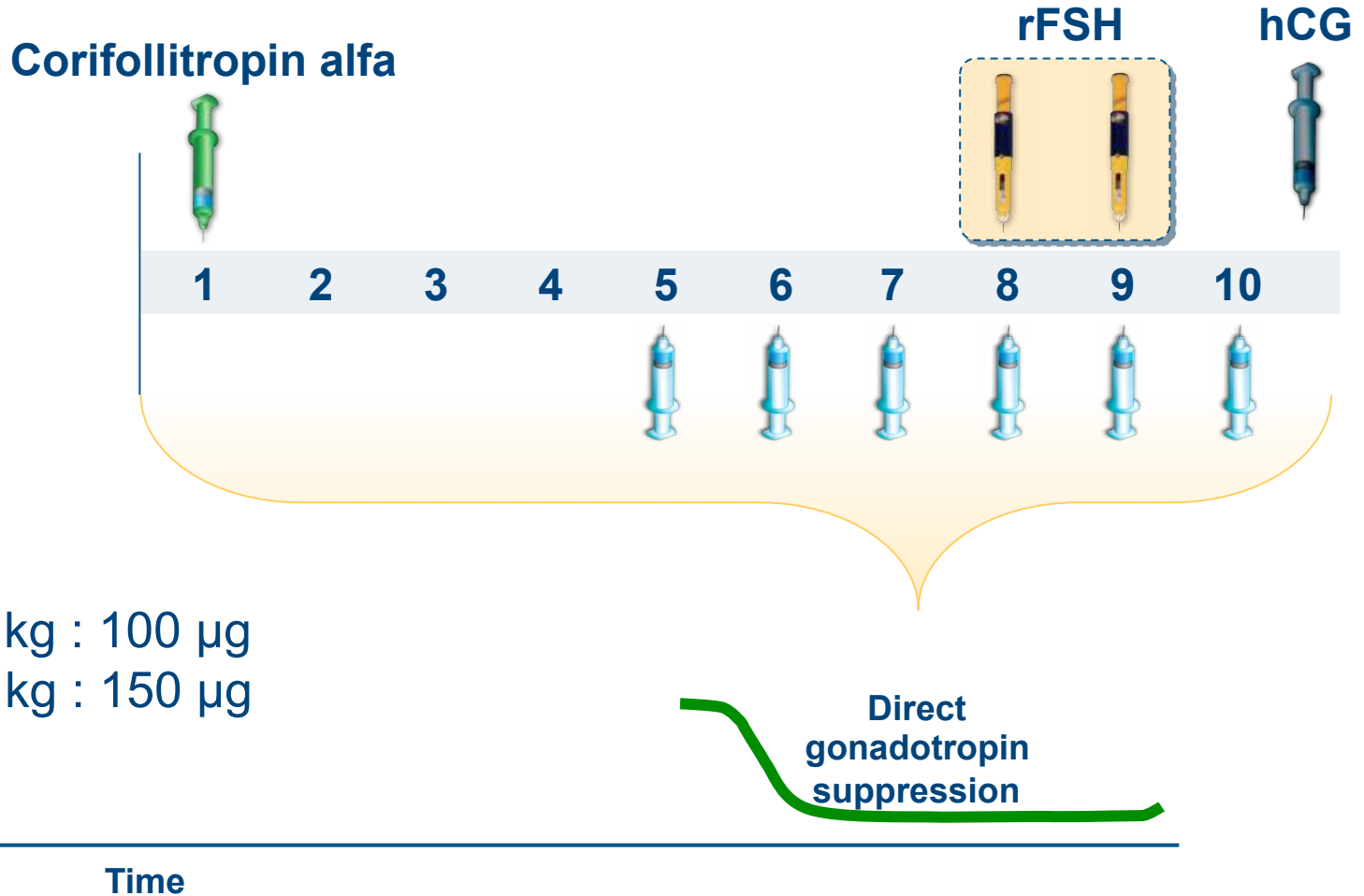
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# Conflict of interest

Our team has no financial interaction with MSD company, nor has received any support for the medications used by the patients

# Corifollitropin alfa



rFSH = recombinant follicle-stimulating hormone; hCG = human chorionic gonadotropin.

# Inclusion criteria

- First cycle
- All infertility etiologies excluding PCOS
- AFC > 5
- D3 FSH < 10 mIU / mL and E<sub>2</sub> < 80 pg / mL
- Ejaculate sperm
- Age < 42

## Patient and cycle characteristics

Age	33.7 ( range 25-42)
Mean number of oocytes and MII oocytes retrieved / OPU	11,2 and 7,2
Fertilization rate (%)	68
Mean number of embryos transferred / cycle	1.4 embryo / transfer
Pregnancy rate per transfer	% 66
Clinical pregnancy rate per transfer	% 57
Ongoing pregnancy rate per transfer	% 50

# Specific problems of antagonist cycles

## Definition

D5 of stimulation

Lead follicle  $\geq 14$  mm

+

the rest  $\leq 10$  mm

## Asynchronous follicular growth



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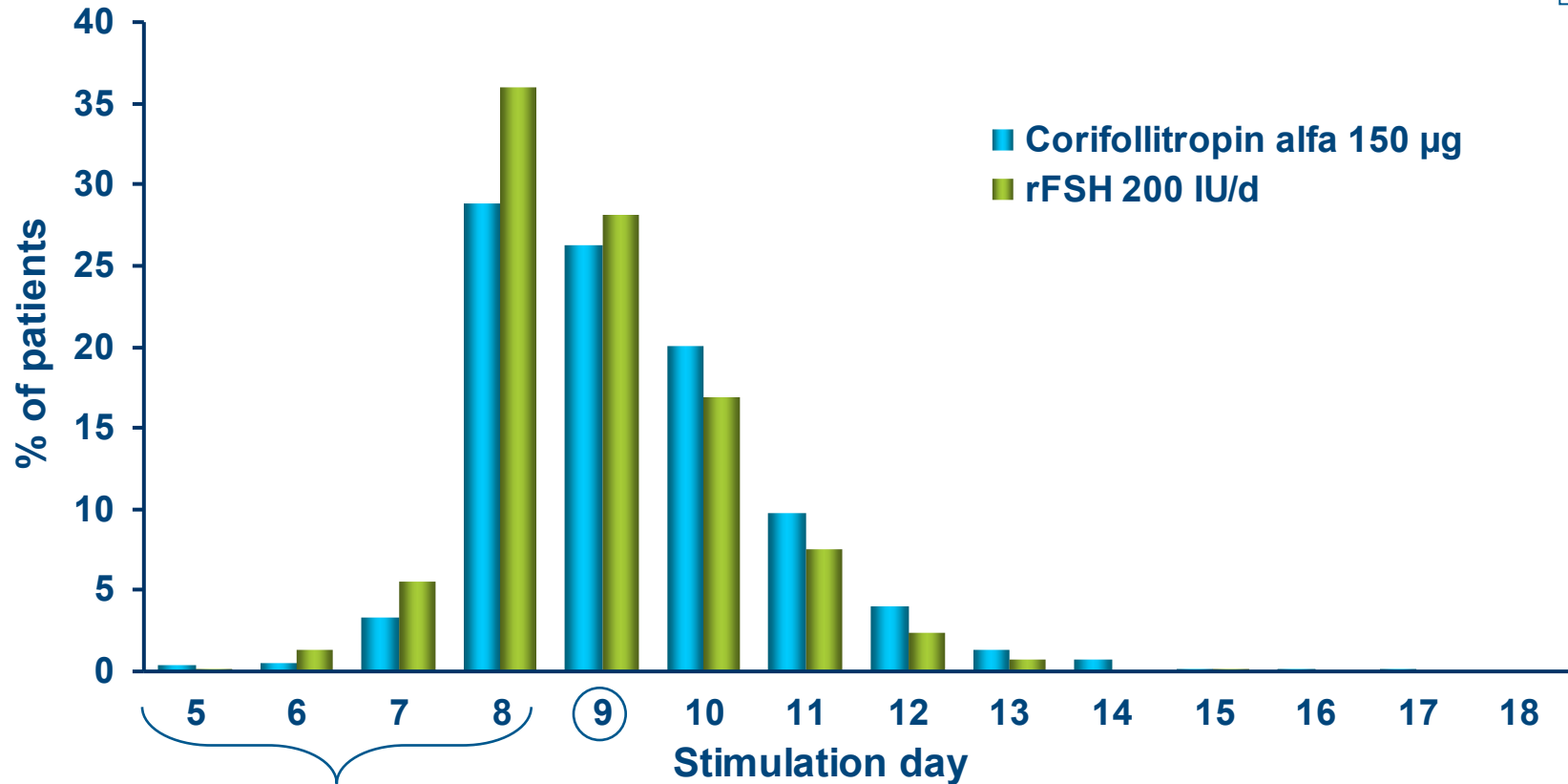
1 in 30 cycles

## Asynchronous follicular growth



# Day when hCG criteria was met

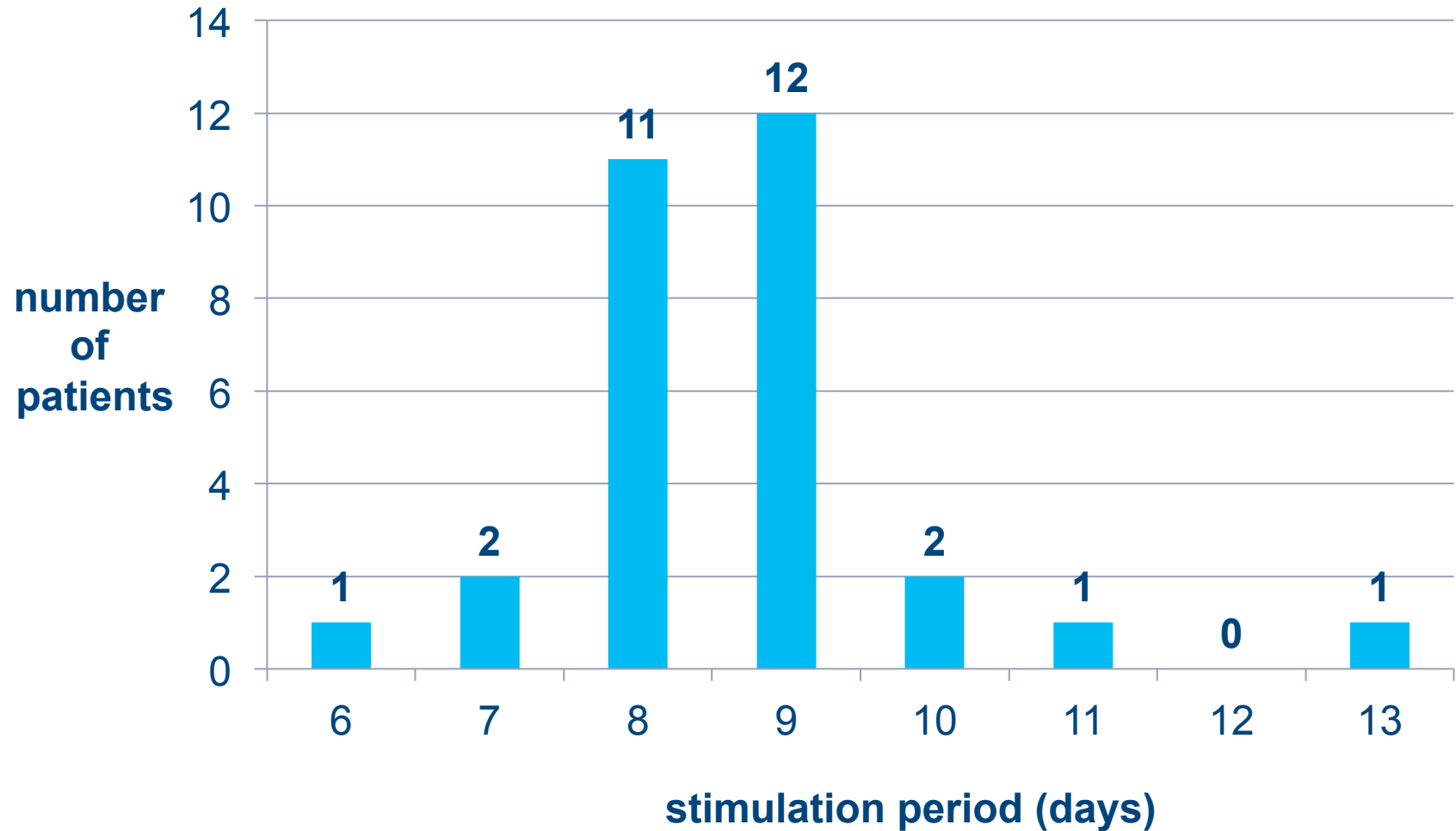
Engage



1/3 rd of patients had not required additional rFSH

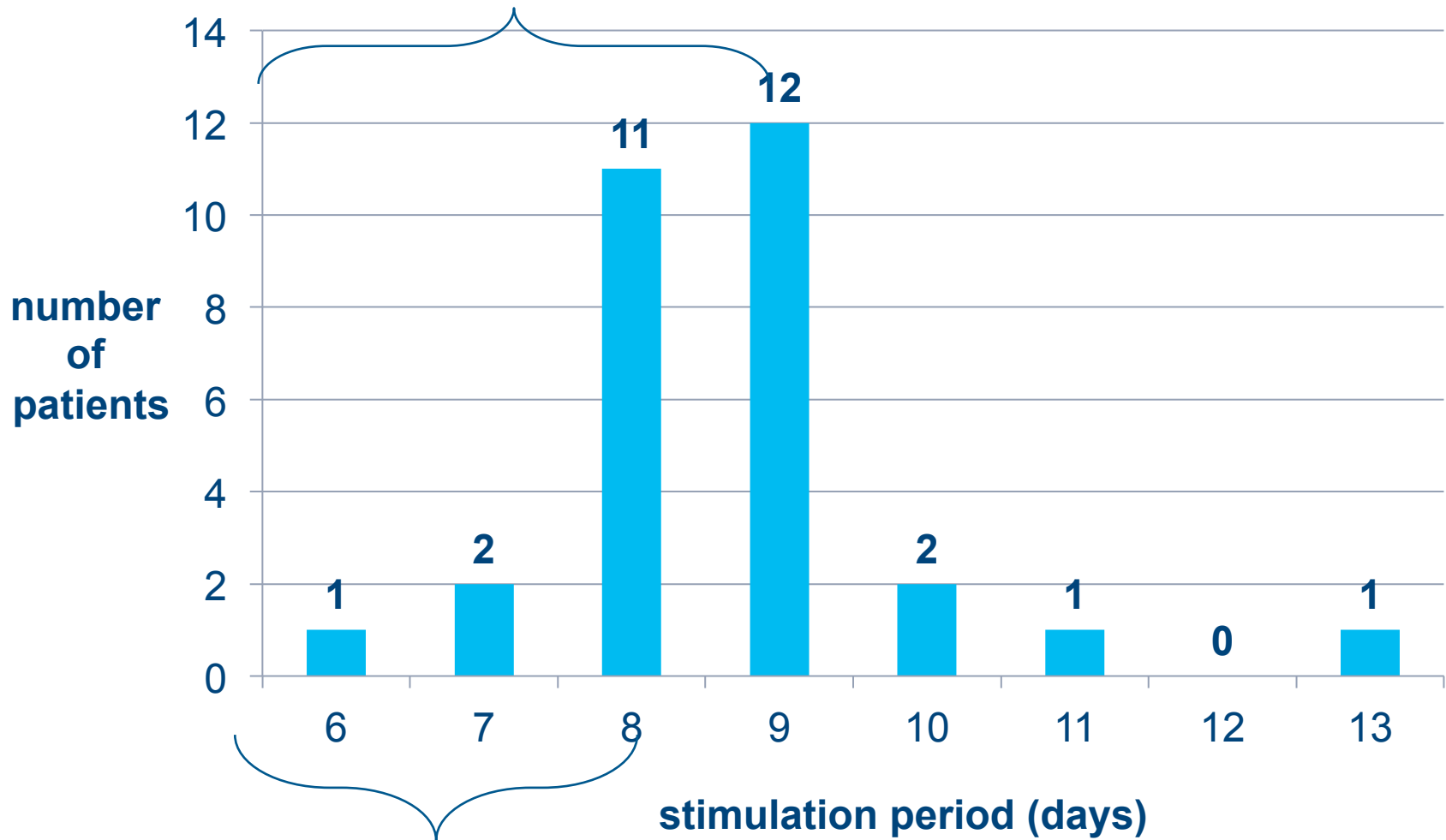
Data on file.

# How long did the stimulation last?



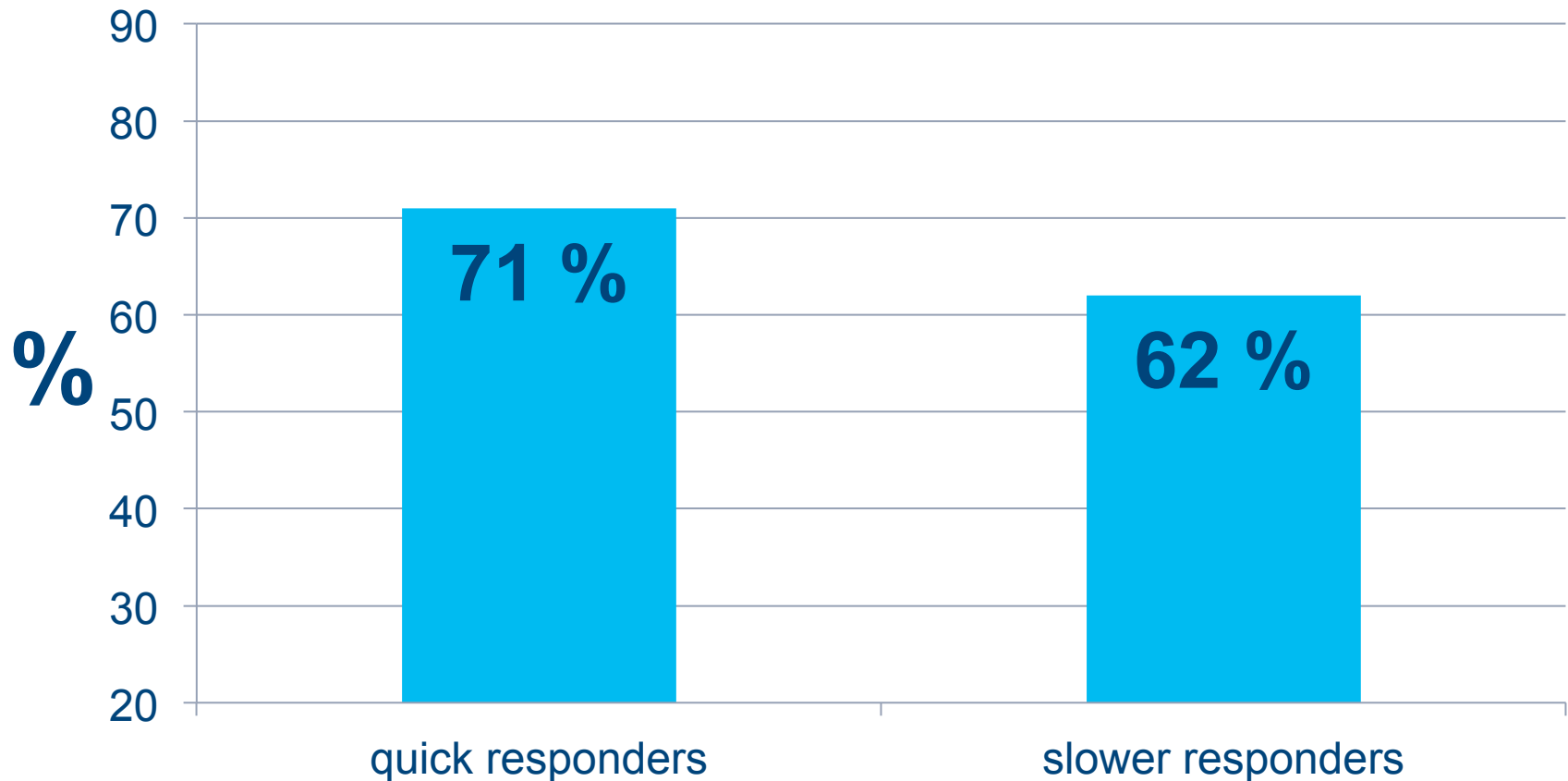
# How long did the stimulation last?

**% 87 completed the stimulation with a maximum of single dose**



**% 47 completed the stimulation without any extra dose**

# Did the outcome differ in cycles reaching hCG criteria with a single corifollitropin alfa shot (quick responders) ?



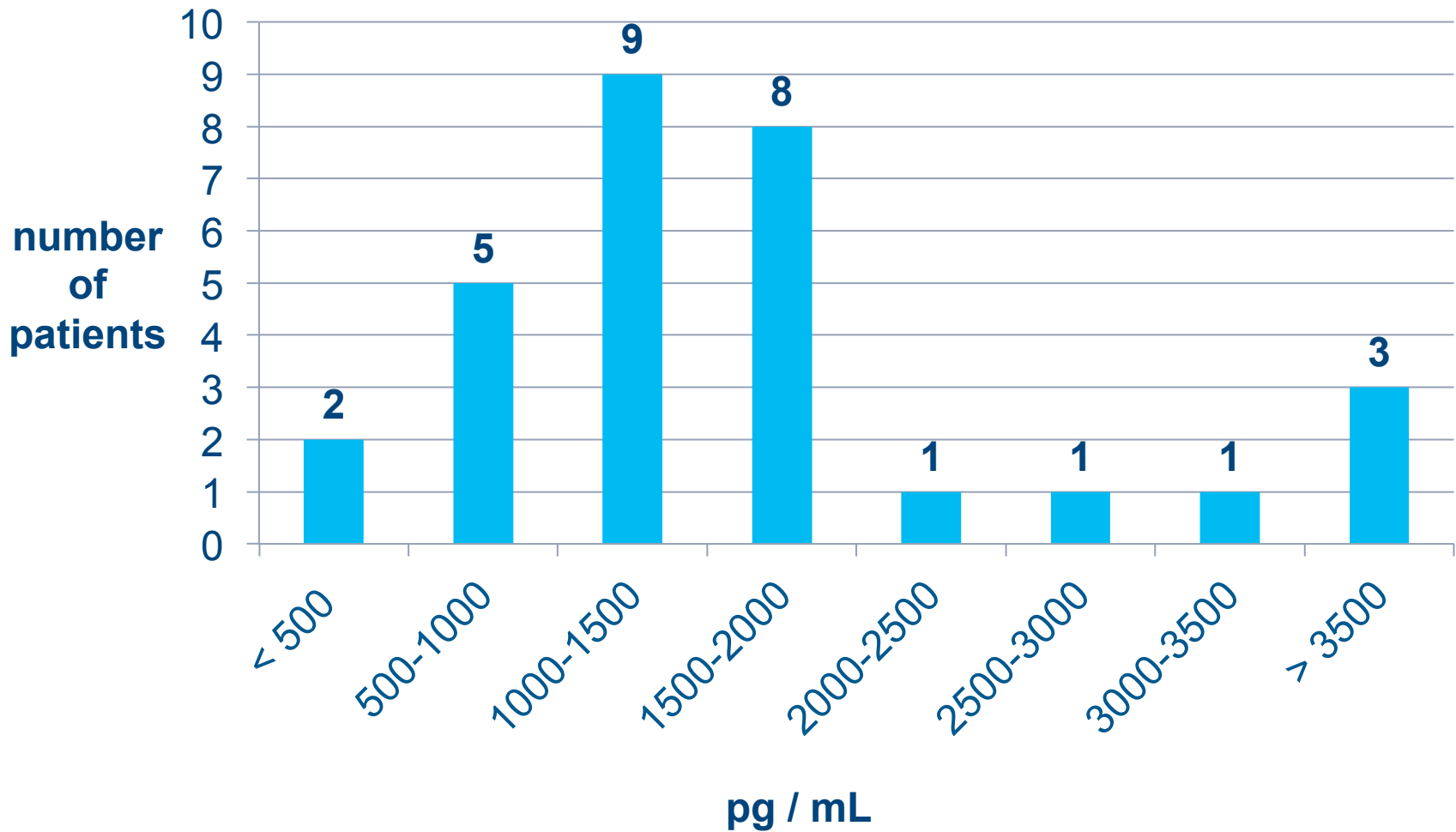
**Pregnancy rate per embryo transfer**

# Additional dose requirement

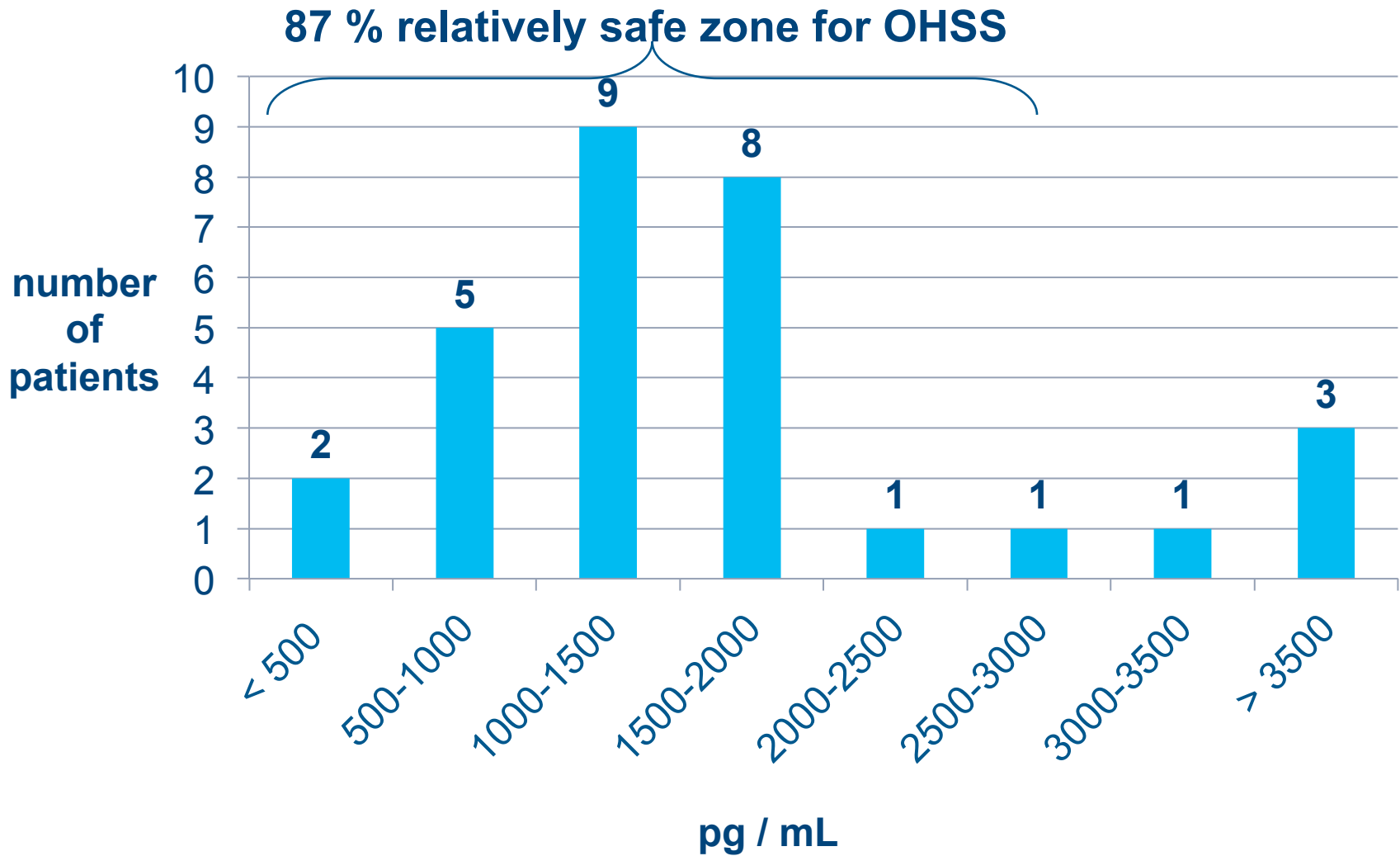
In 15 cycles that have not reached the criteria for hCG triggering within 7 days of corifollitropin alfa injection, the mean additional dose requirement per patient was;

310 IU of gonadotropin per patient

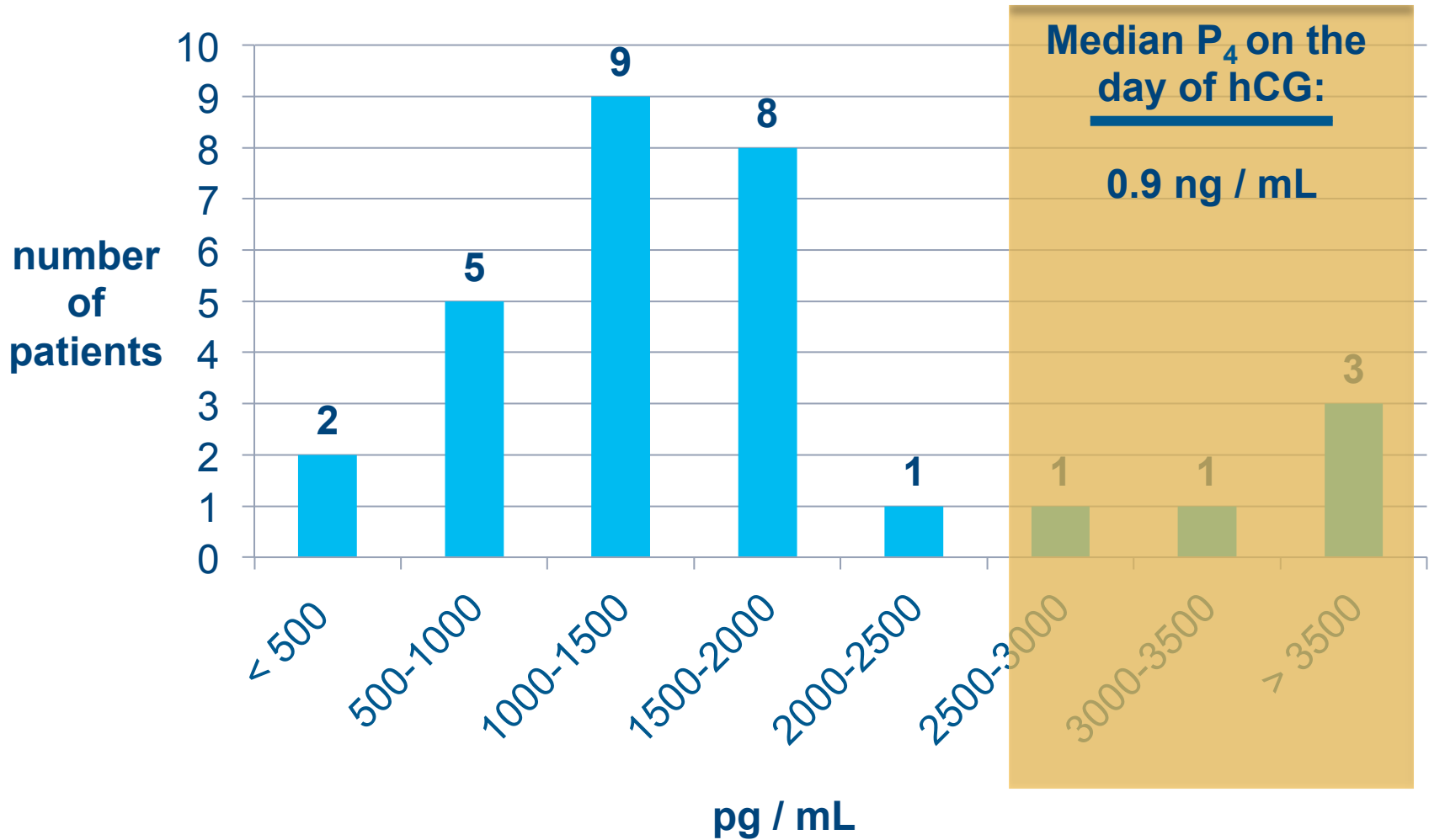
# Peak serum E<sub>2</sub> levels on the day of hCG



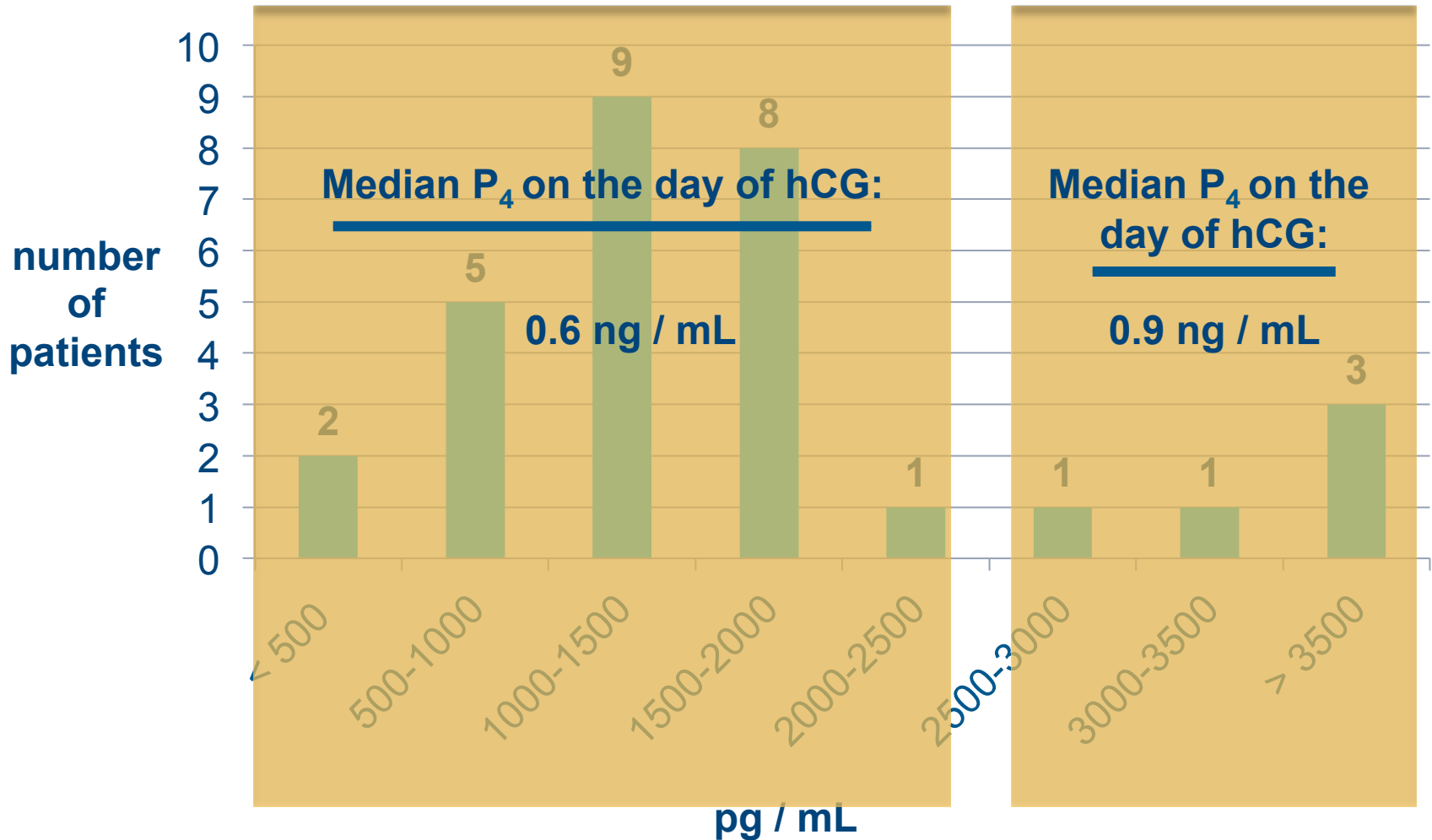
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# What about P<sub>4</sub> elevation in follicular phase?

Serum P <sub>4</sub> on the day of hCG	Number of cycles
≥ 1.5 ng / mL	0

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cases	Peak estradiol (pg / mL)	Corresponding P <sub>4</sub> (ng / mL)
13	5412	1,01
18	3802	0,4
26	4926	0,7

# Unexpected poor response rate

	n (%)
<b>number of cycles with <math>\leq 3</math> eggs retrieved</b>	3 / 30 ( %10)

# A systematic review and meta-analysis

Mahmoud Youssef, et al. Fertil Steril 2012

## 3.2.2 Cancellation rate per woman randomized

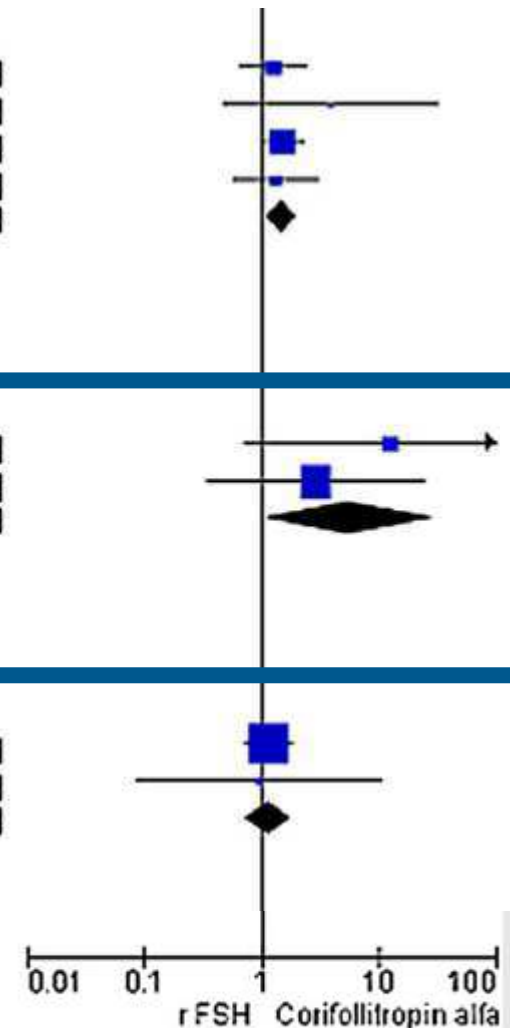
Corifollitropin alfa study	53	242	15	83	26.2%	1.27 [0.67, 2.40]
Devroey 2004	11	75	1	24	1.8%	3.95 [0.48, 32.34]
Engage study 2009	62	756	41	750	56.9%	1.54 [1.03, 2.32]
Ensure study group 2010	22	268	8	128	15.0%	1.34 [0.58, 3.10]
<b>Subtotal (95% CI)</b>		<b>1341</b>		<b>905</b>	<b>100.0%</b>	<b>1.49 [1.09, 2.04]</b>
Total events	148		65			
Heterogeneity: $\text{Chi}^2 = 1.16$ , $\text{df} = 3$ ( $P = 0.76$ ); $I^2 = 0\%$						
Test for overall effect: $Z = 2.49$ ( $P = 0.01$ )						

## 3.2.3 Cancellation due to overstimulation

Engage study 2009	6	756	0	750	27.3%	13.00 [0.73, 231.17]
Ensure study group 2010	6	268	1	128	72.7%	2.91 [0.35, 24.41]
<b>Subtotal (95% CI)</b>		<b>1024</b>		<b>878</b>	<b>100.0%</b>	<b>5.67 [1.07, 30.13]</b>
Total events	12		1			
Heterogeneity: $\text{Chi}^2 = 0.70$ , $\text{df} = 1$ ( $P = 0.40$ ); $I^2 = 0\%$						
Test for overall effect: $Z = 2.03$ ( $P = 0.04$ )						

## 3.2.4 Cancellation due to understimulation

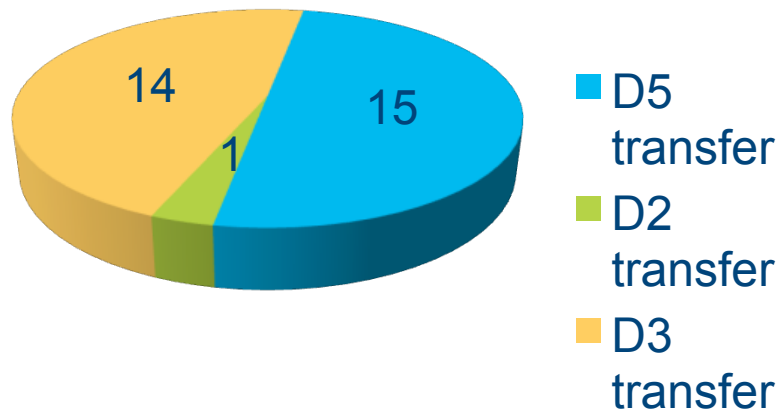
Engage study 2009	39	756	34	750	96.0%	1.15 [0.71, 1.84]
Ensure study group 2010	2	268	1	128	4.0%	0.95 [0.09, 10.63]
<b>Subtotal (95% CI)</b>		<b>1024</b>		<b>878</b>	<b>100.0%</b>	<b>1.14 [0.72, 1.81]</b>
Total events	41		35			
Heterogeneity: $\text{Chi}^2 = 0.02$ , $\text{df} = 1$ ( $P = 0.88$ ); $I^2 = 0\%$						
Test for overall effect: $Z = 0.55$ ( $P = 0.58$ )						



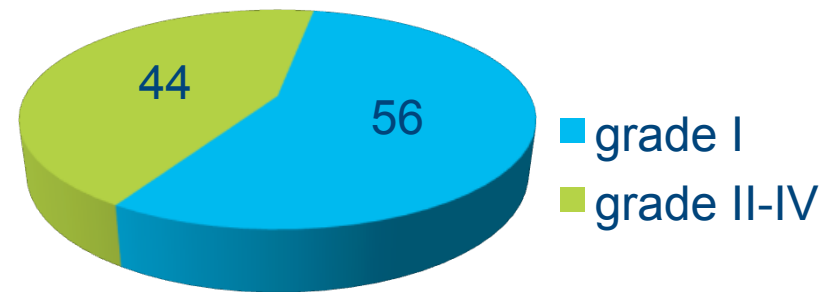
*no cancellation in this first series of patients*

% of patients			
	<b>Corifollitropin alfa (n=30)</b>	<b>Engage trial</b>	<b>Ensure trial</b>
Hafif	3.3	2.9	3.0
Orta	0	2.3	2.2
Şiddetli	0	1.9	1.8

## Day of ET



## Embryo quality



## Day 2 vs Day 3 Initiation of Stimulation<sup>a</sup>

	Corifollitropin alfa	
	Cycle Day 2 n=343	Cycle Day 3 n=368
Duration of stimulation, days	9.8 (1.4)	9.4 (1.5)
Estradiol on day of hCG <sup>b</sup> , pmol/L	4239 (1512, 11,891)	4899 (1762, 11,671)
Number of oocytes retrieved	14.1 (8.1)	14.0 (7.9)
Ongoing pregnancy rate, % (n)	37.9 (130)	43.5 (160)

Data are mean (SD) unless otherwise stated.

<sup>a</sup>Restricted to patients treated with hCG.

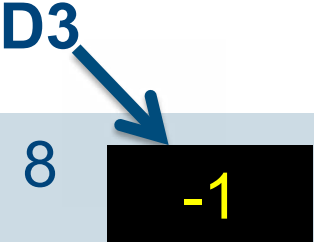
<sup>b</sup>Data are median (P5, P95).

# D2 vs D3 start of corifollitropin alfa

	<b>D2</b>	<b>D3</b>
Stimulation phase in days (median)	9	8
Duration of antagonist use in days (median)	5	4
Number of oocytes retrieved per OPU (mean)	10	14,4
Number of MII oocytes per OPU (mean)	6,4	9,6
Pregnancy rate / ET (%)	63 %	75 %

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D3



-1


-1

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# Conclusions

- Corifollitropin alfa can be adopted easily to clinical practice without any compromise in cycle outcomes
- It has additional benefits of simplicity and patient friendliness
- Just like the introduction of antagonists into COH, this mode of ovarian stimulation will have a prominent role in the management of IVF cycles