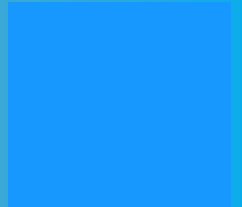


Clinical Experience With Corifollitropin alfa

L. Cem Demirel, M.D.

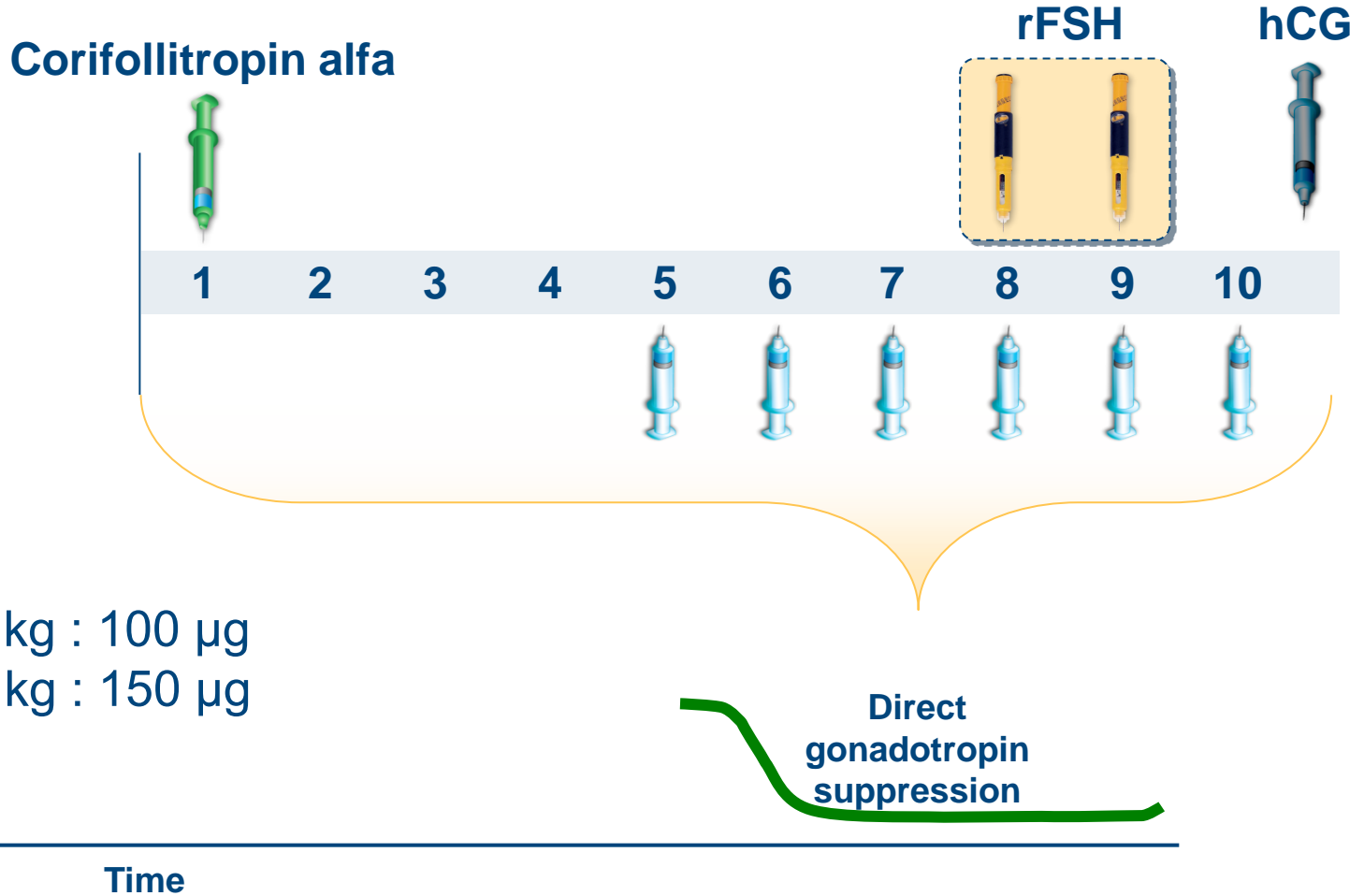
Memorial Ataşehir Hospital IVF Department, İstanbul



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 E₂ < 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 ≥ 14 mm

+

the rest ≤ 10 mm

Asynchronous follicular growth



Specific problems of antagonist cycles

Definition

D5 of stimulation

Lead follicle ≥ 14 mm

+

the rest ≤ 10 mm

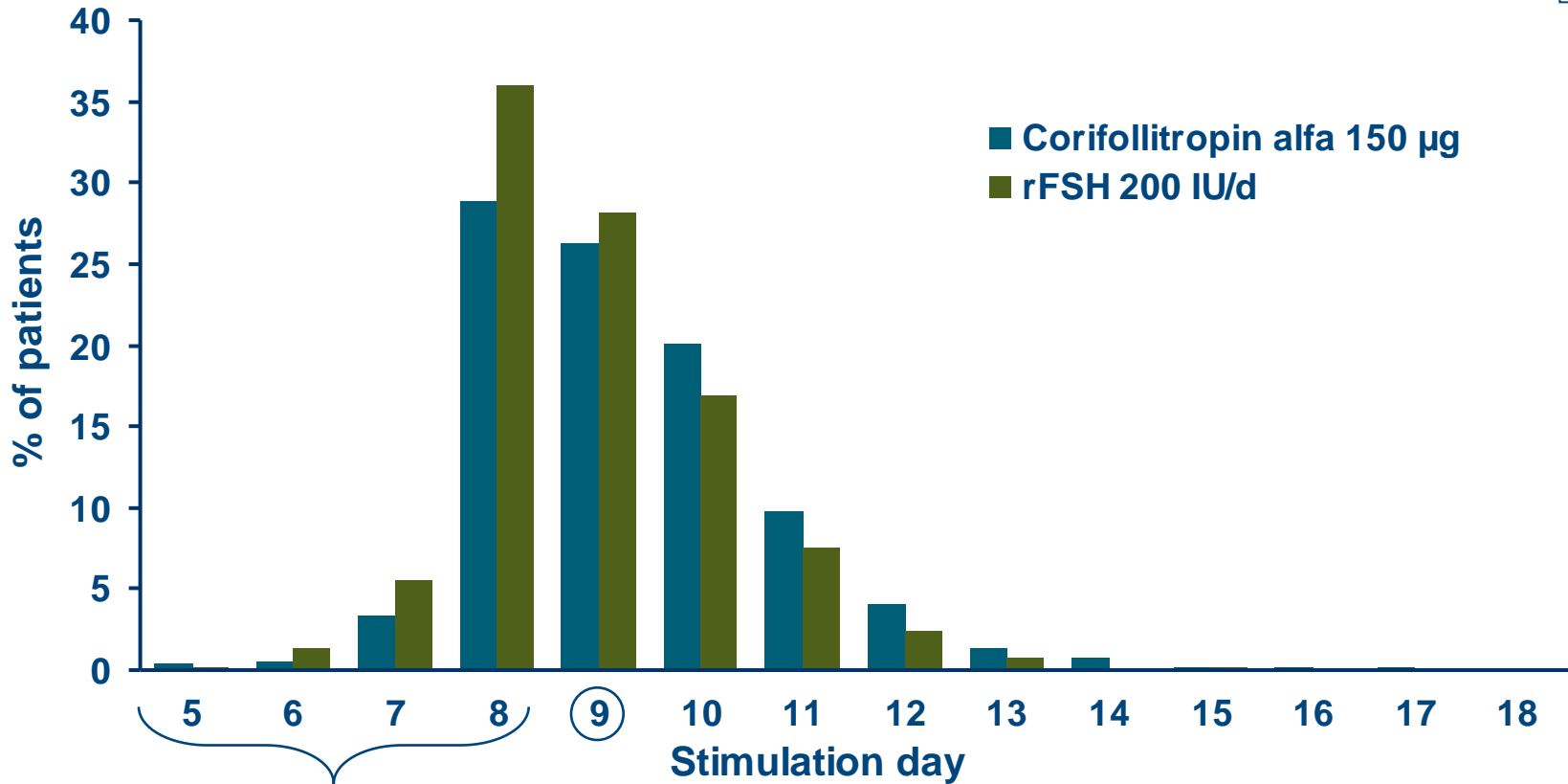
1 in 30 cycles

Asynchronous follicular growth



Day when hCG criteria was met

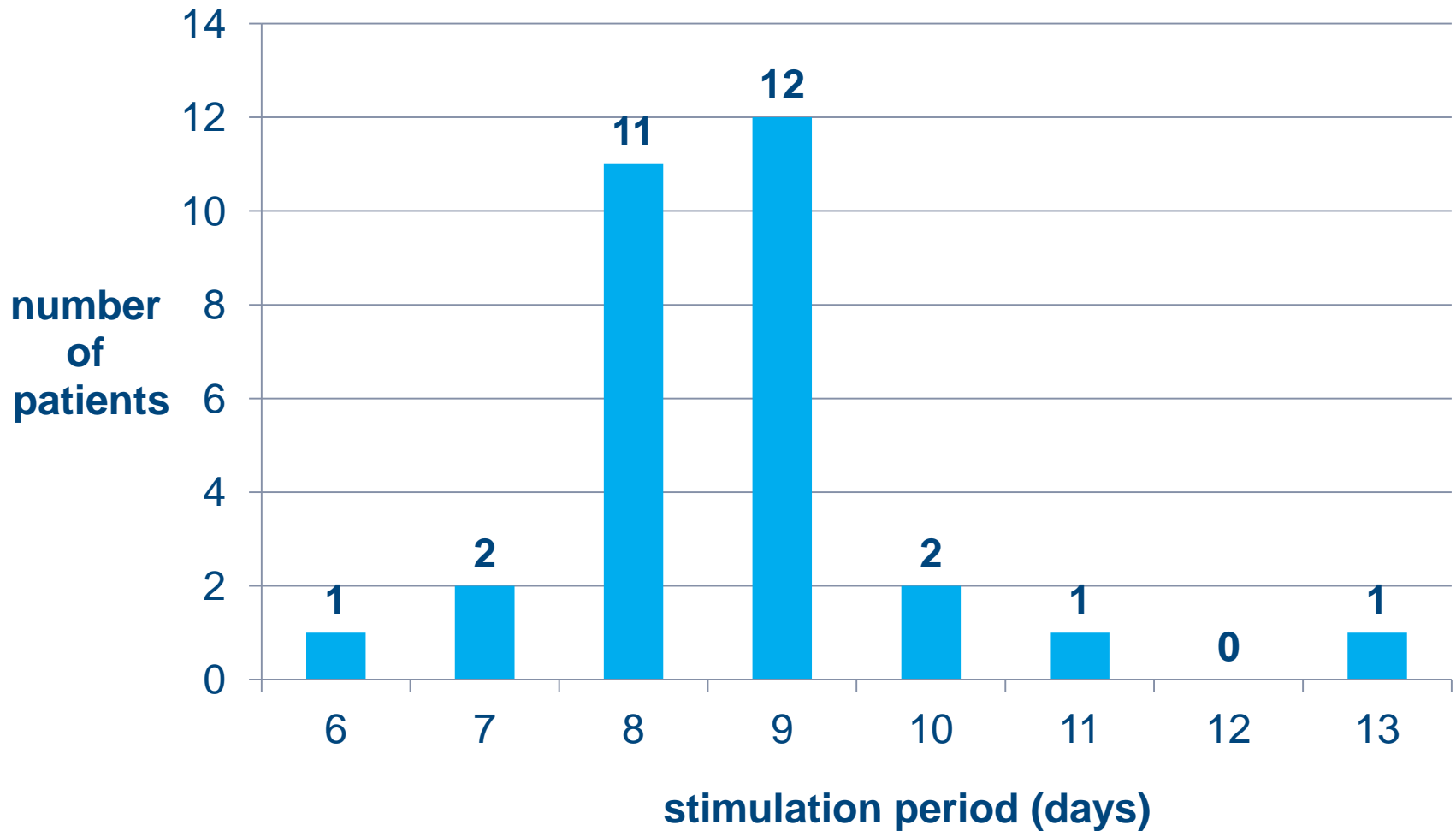
Engage



1/3 rd of patients had not required additional rFSH

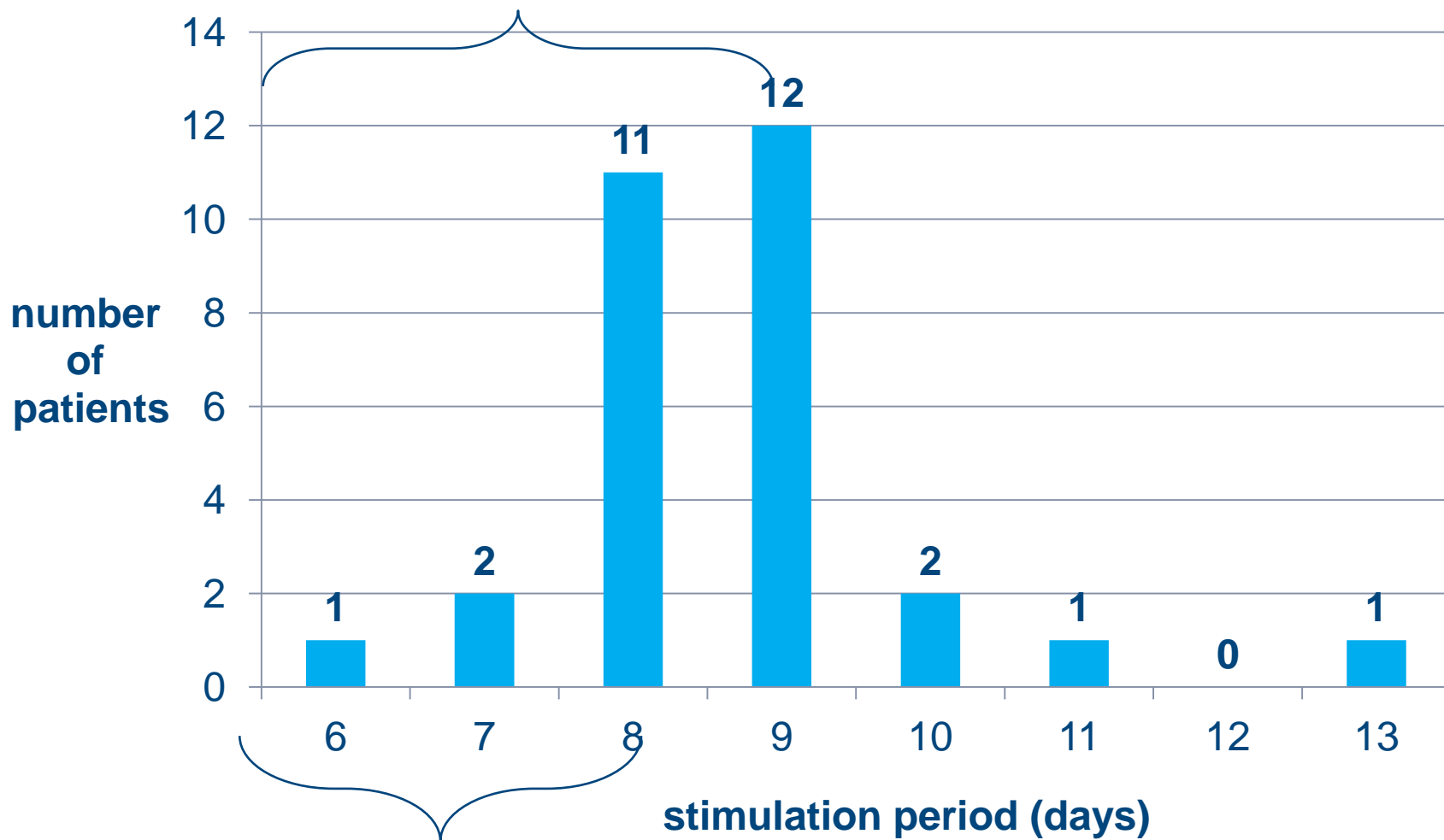
Data on file.

How long did the stimulation last?



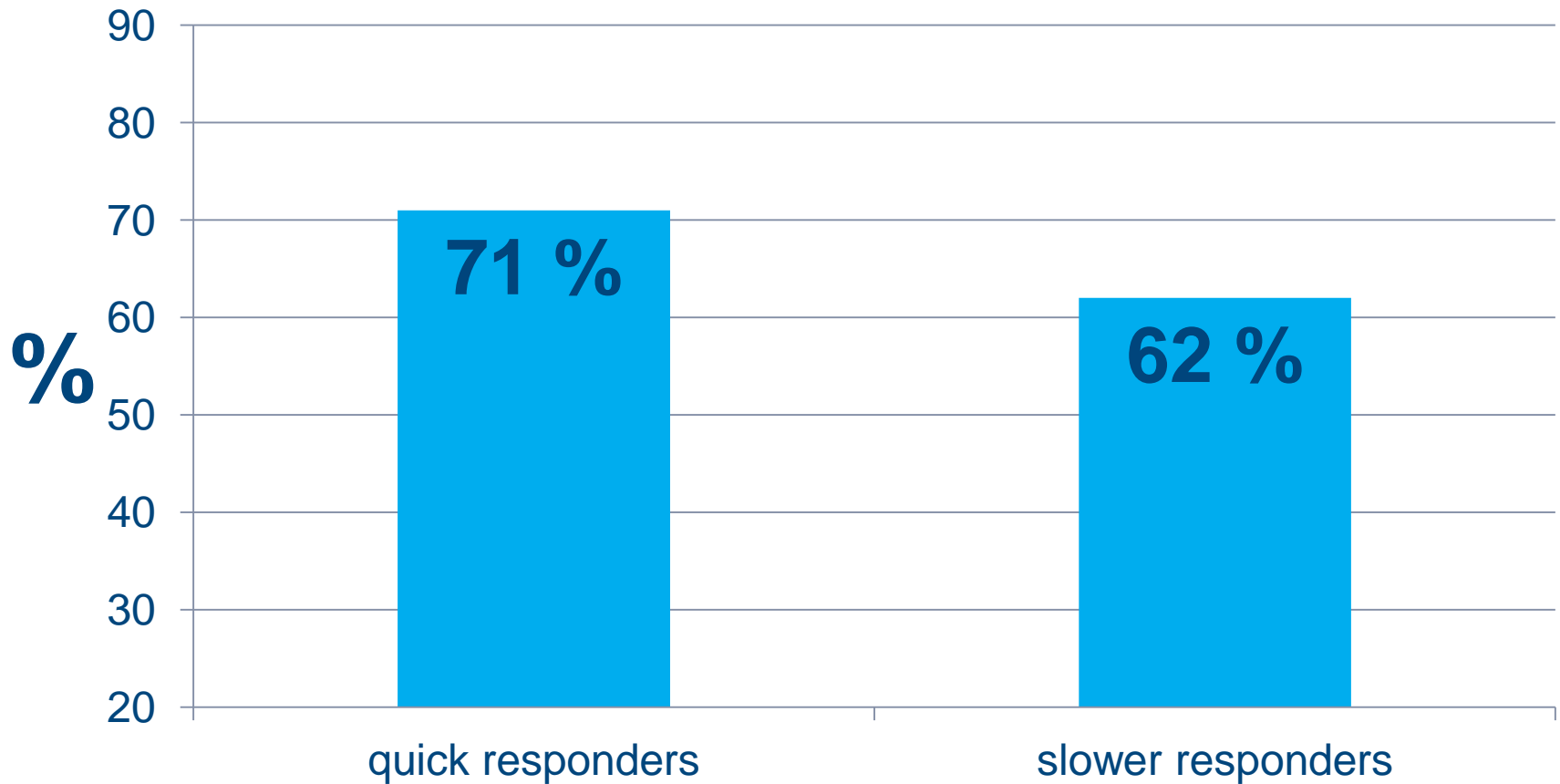
How long did the stimulation last?

% 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) ?



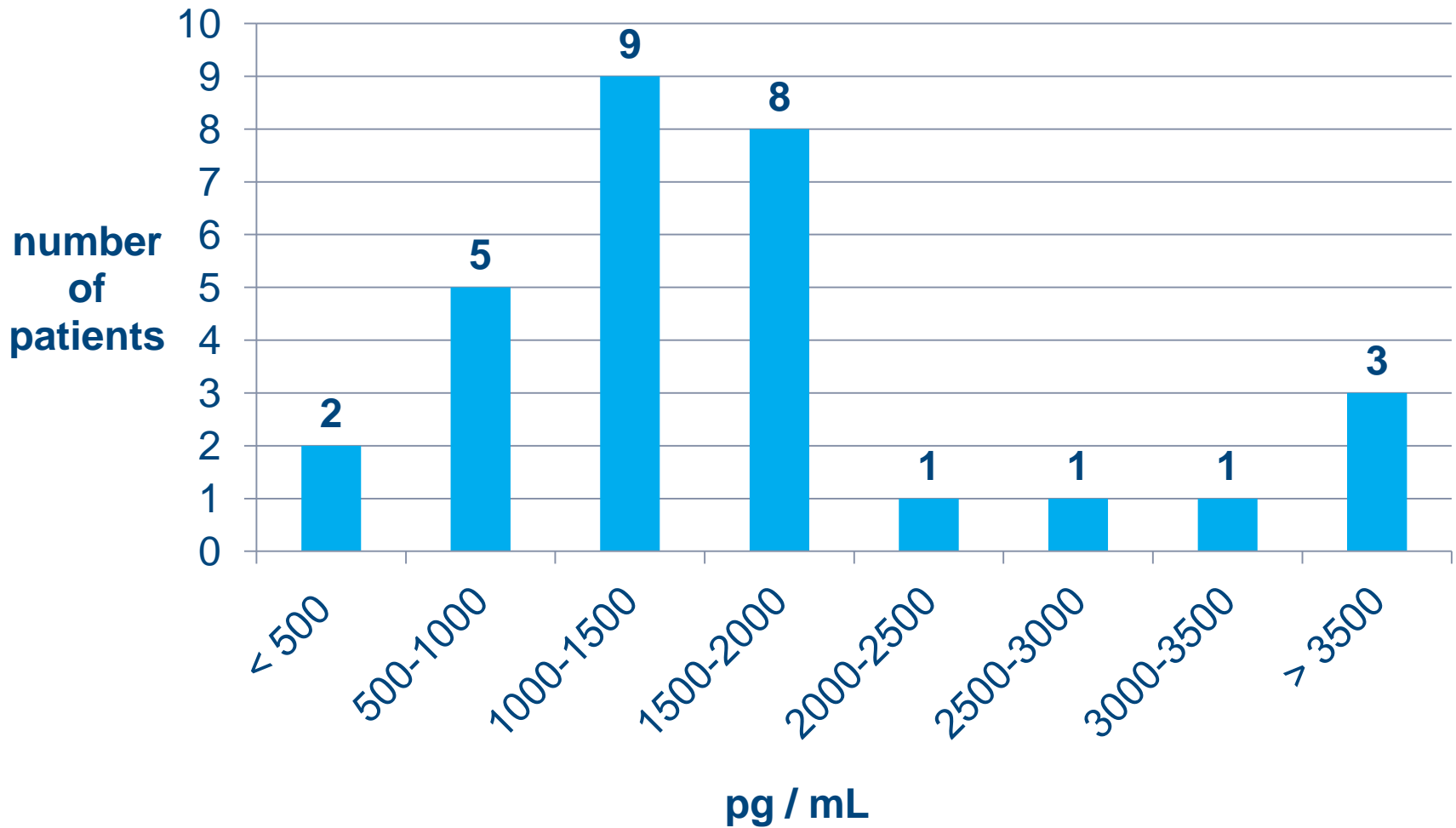
Pregnancy rate per embryo transfer

Additional dose requirement

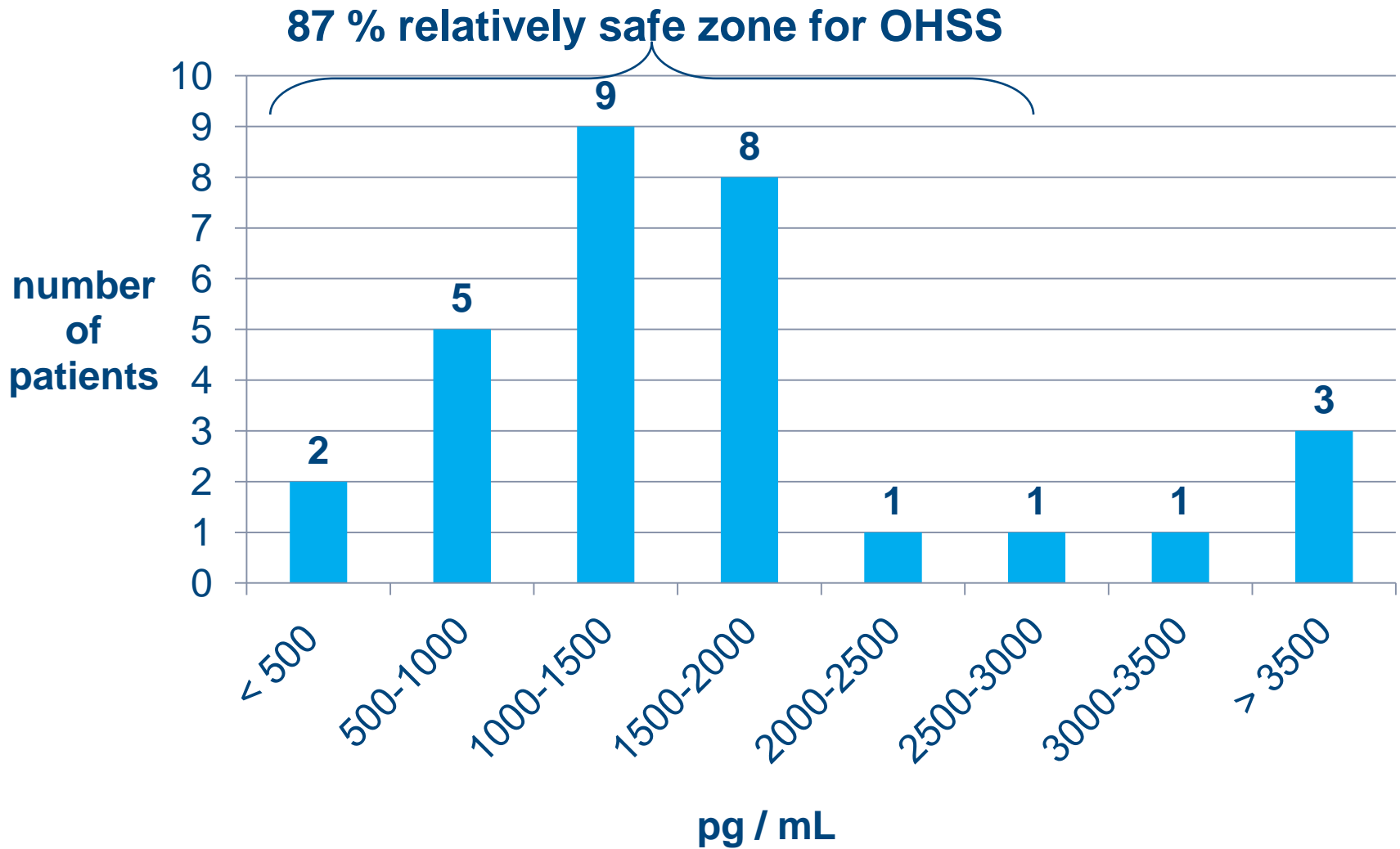
In 15 cycles that have not reached the criteria for hCG triggering within 7 days of corifollitropin alfa injection, the mean additional dose requirement per patient was;

310 IU of gonadotropin per patient

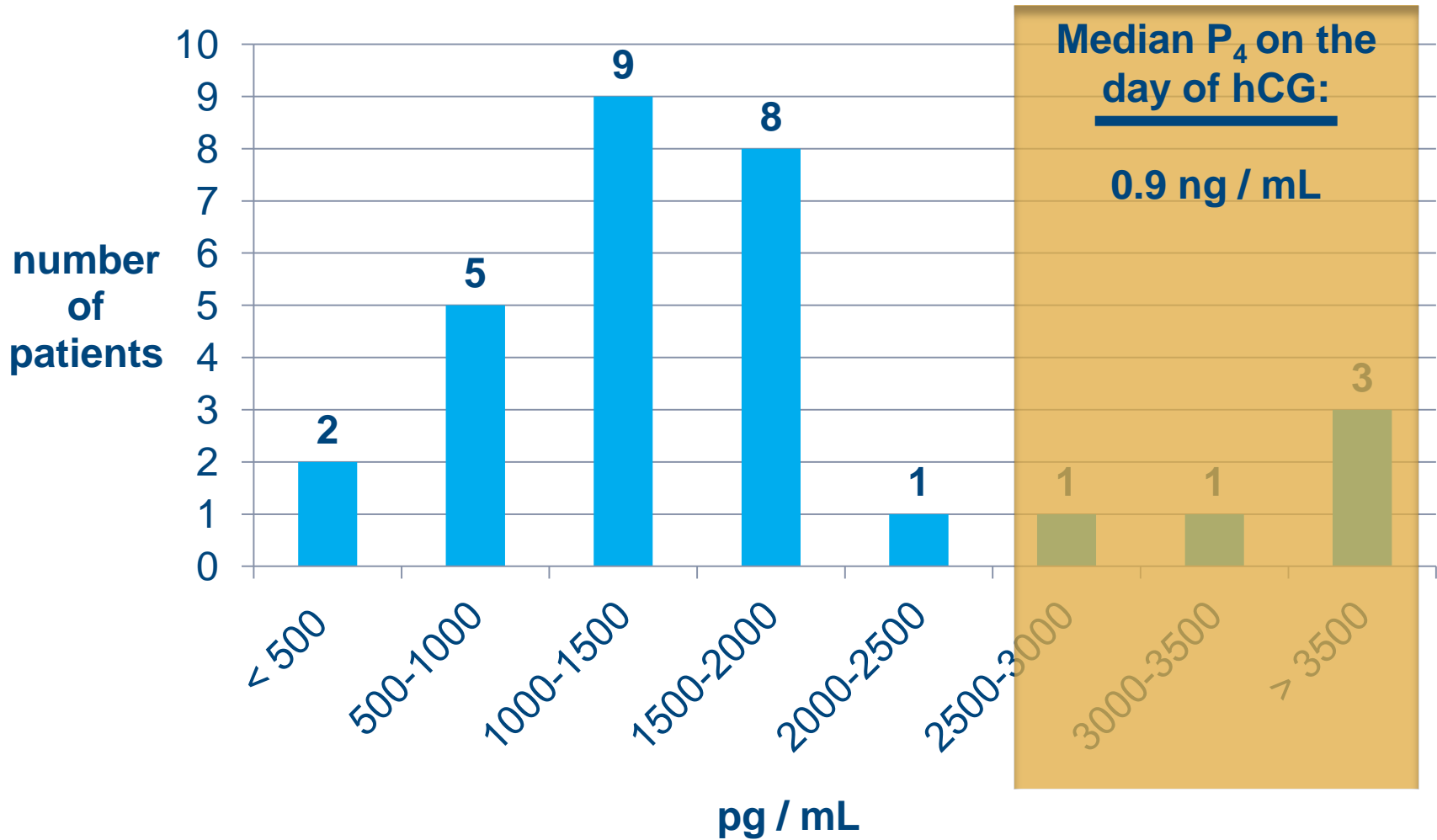
Peak serum E₂ levels on the day of hCG



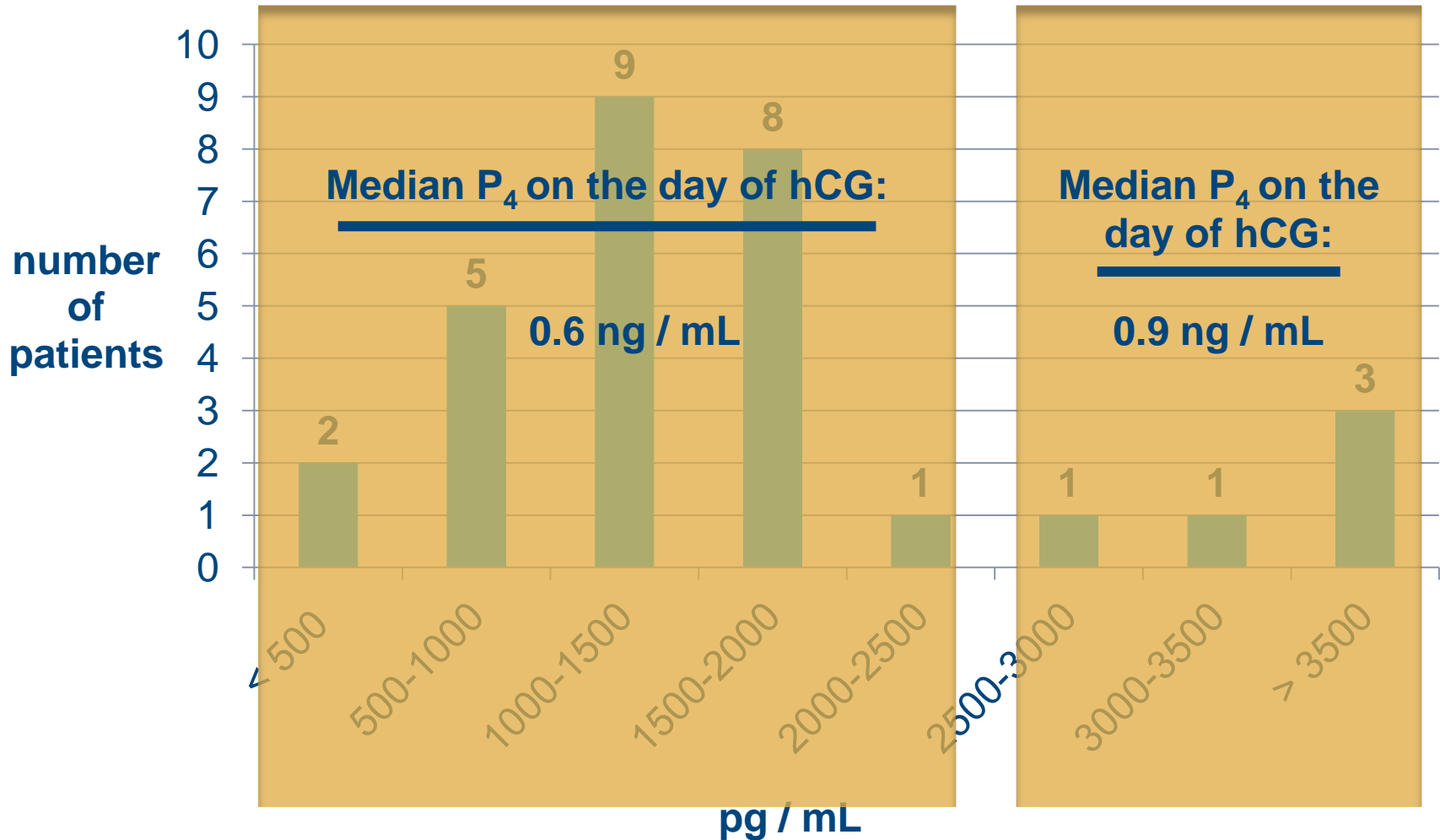
Peak serum E₂ levels on the day of hCG



Peak serum E₂ levels on the day of hCG



Peak serum E₂ levels on the day of hCG



What about P₄ elevation in follicular phase?

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

What about P₄ elevation in follicular phase?

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

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

Unexpected poor response rate

	n (%)
number of cycles with ≤ 3 eggs retrieved	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	1.9%	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]
Subtotal (95% CI)		1341		905	100.0%	1.49 [1.09, 2.04]

Total events 148
 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

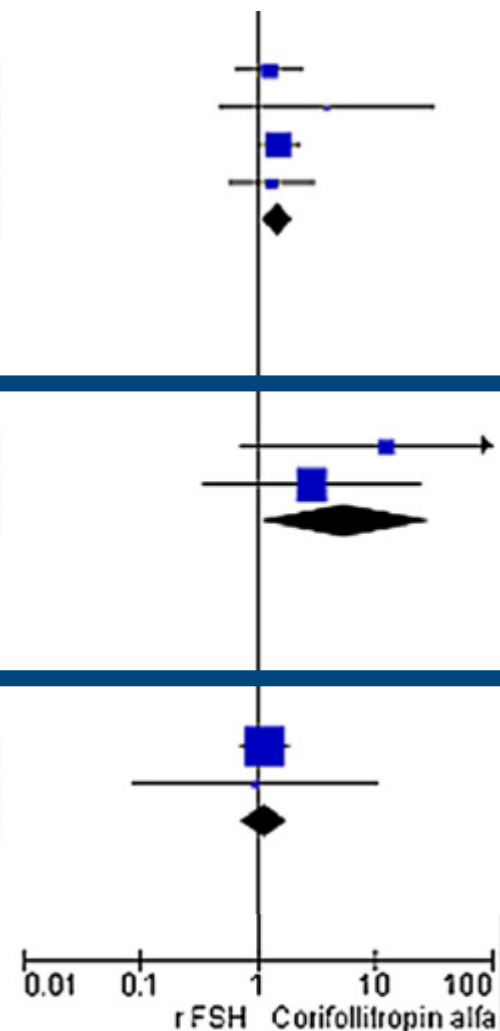
Engage study 2009	6	756	0	750	27.3%	13.00 [0.73, 231.17]
Ensure study group 2010	6	268	1	128	72.7%	2.91 [0.35, 24.41]
Subtotal (95% CI)		1024		878	100.0%	5.67 [1.07, 30.13]

Total events 12
 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]
Subtotal (95% CI)		1024		878	100.0%	1.14 [0.72, 1.81]

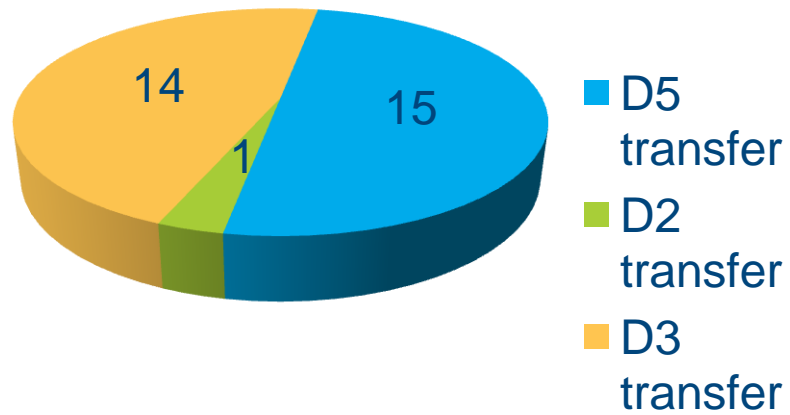
Total events 41
 Heterogeneity: $\text{Chi}^2 = 0.02$, $\text{df} = 1$ ($P = 0.88$); $I^2 = 0\%$
 Test for overall effect: $Z = 0.55$ ($P = 0.58$)



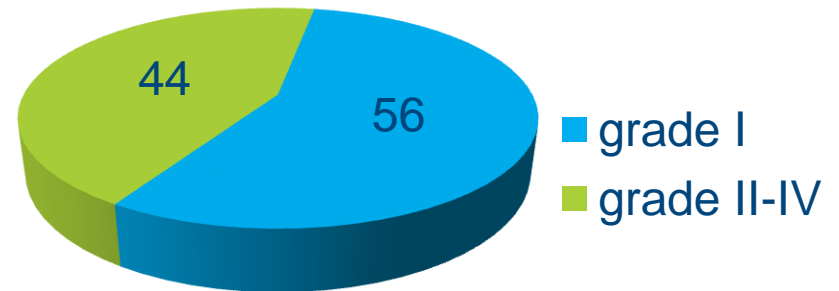
no cancellation in this first series of patients

	% of patients		
	Corifollitropin alfa (n=30)	Engage trial	Ensure trial
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^a

	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 ^b , 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.

^aRestricted to patients treated with hCG.

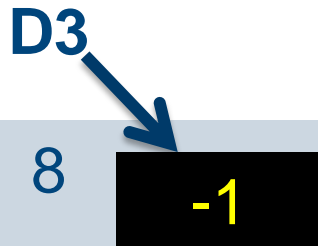
^bData are median (P5, P95).

D2 vs D3 start of corifollitropin alfa

	D2	D3
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 %

D2 vs D3 start of corifollitropin alfa

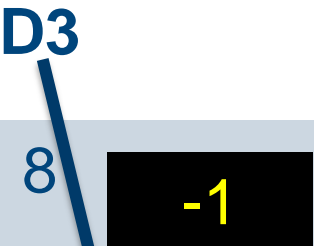

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D2 vs D3 start of corifollitropin alfa

	D2	D3
Stimulation phase in days (median)	9	8 -1
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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Pregnancy rate / ET (%)	63 %	+ 12	75 %	



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