

PKOS'lu HASTALARDA OVULASYON İNDÜKSİYONU

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CC Sonular

- PKOS'da ilk tedavi seeneėidir.
- 3- 6 siklus yeterli ovulasyon oranlarını saėlamaktadır.
- 50 – 150 mg yeterli ovulasyon ve gebelik oranlarını saėlamaktadır.
- zellikle ilk uygulamada monitorizasyon faydalı olabilir ancak gebelik oranlarını etkilememektedir.
- hCG ve luteal faz desteėi gebelik oranlarını etkilememektedir.

PKOS'da ilk seenek olarak neden

CC ?

Ara Sonu

- PKOS'da ek infertilite faktörünün olmadığı durumlarda ilk seenek CC'dır.
- CC'a metformin eklenmesi ovulasyon ve bazı alt gruplarda gebelik oranlarını artırabilse de canlı doğum oranlarını artıramamaktadır.

Alternatives as first line?

- **Insulin sensitizers (Metformin)**
- **Aromatase inhibitors (Letrozole)**
- **Laparoscopic ovarian drilling (LOD)**
- **Low-dose FSH**

CC Dışı Ajanlar

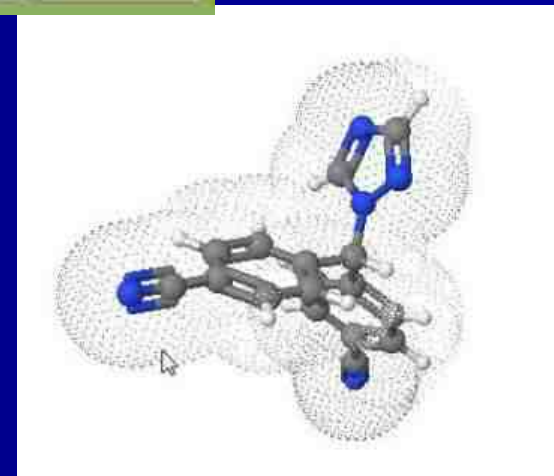
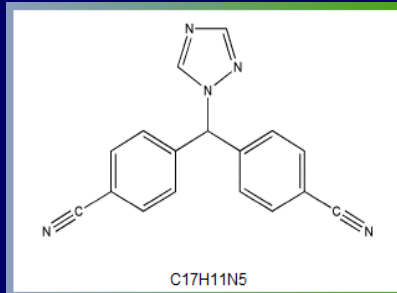
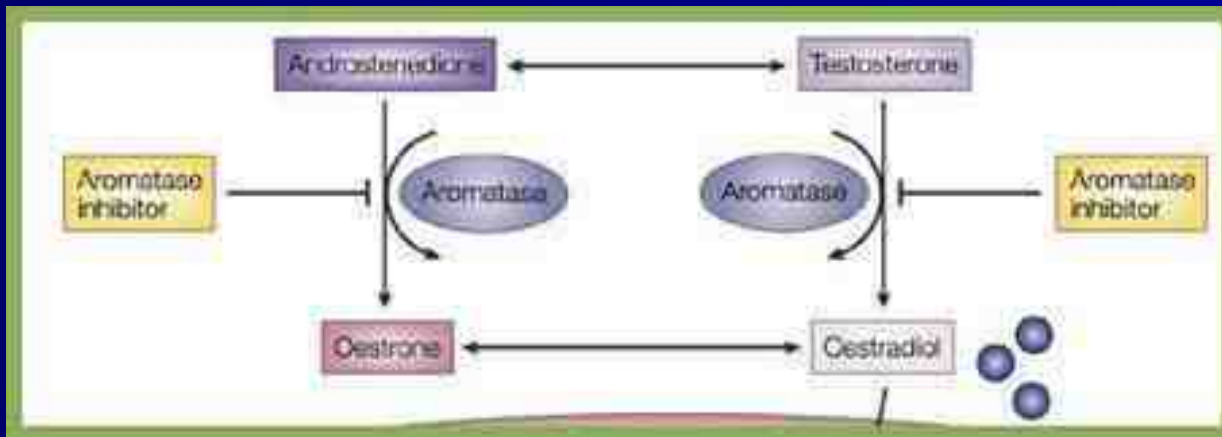
- Aromataz inhibitörleri (Tek başına veya CC ile)
- Anti-östrojenler (Tek başına veya CC ile)
- İnsülin hassaslaştırıcılar (Tek başına veya CC ile)
- Deksametazon (Sadece CC ile)
- CYP17a İnhibitörü (Sadece CC ile)
- Bromokriptin (Sadece CC ile)
- OC (Sadece CC ile)

Aromataz İnhibitörleri (AI)

- Etki
- Letrozole ve Anastrozole
 - Aromataz aktivitesi inhibe edilir
 - Estrojenik negatif feed back kalkar
 - FSH artar
 - Yarı ömrü 45 saat (CC-5 gün-3 hafta)
 - Geç folliküler dönemde negatif estrojenik etkisi daha az (Endometrium ve Cx)
 - Daha iyi gebelik? En az eşit?

Casper RF, Mitwally MF 2006 Review: aromatase inhibitors for ovulation induction. *Journal of Clinical Endocrinology and Metabolism* 91, 760–771.

Letrozole (4,4'-((1H-1,2,4-triazol-1-yl)methylene)dibenzonitrile)



PCOS'lu hastalarda ovulasyon: AI vs CC

Tablo-1 (İlk Seçenek)

	Author/year	Journal	Type of trial	Arms	Patients (cycles)	Age (years)	BMI	Pregnancy (n)	Miscarriage (n)	Multi gest	Ovulation cycle (%)	Endometrial thickness (mm)	Mature follicles (n)
<i>Letrozole trials</i>	Atay et al. (2006)	<i>J Int Med Res</i>	RCT	Letrozole 2.5 mg	51 (51)	27.1	26.1	11	NA	0	42 (82.4)	8.4	1.2
				Clomiphene 100 mg	55 (55)	26.2	25.8	5	NA	1	35 (63.6)	5.2	2.4
	Bayar et al. (2006a)	<i>Fertil Steril</i>	RCT	Letrozole 2.5 mg	38 (99)	32.2	<25	9	1	0	65 (65.7)	8 [*]	1 ^a
				Clomiphene 100 mg	36 (95)	30.6	<25	7	0	0	71 (74.4)	8 [*]	1 ^a
	Sohrabvand et al. (2006)	<i>Hum Reprod</i>	RCT	Letrozole 2.5 mg + metformin	29 (53)	28.2	30	10	0	0	48 (90.6)	8.2	1.9
				Clomiphene 100 mg + metformin	30 (67)	29.6	30.2	5	2	0	54 (80.6)	5.5	1.8
	Badawy et al. (2007a)	<i>Fertil Steril</i>	RCT	Letrozole 5 mg	218 (540)	27.1	28.1	82	4	0	365 (67.5)	8.1	2.3
				Clomiphene 100 mg	220 (523)	29.3	27.1	94	4	3	371 (70.9)	9.2	3.1
	Begum et al. (2008)	<i>Fertil Steril</i>	RCT	Letrozole 7.5 mg	32 (NA)	25.5	22.7	13	2	0	20 ^b	10.4	20 ^c
				Clomiphene 100 mg	32 (NA)	26.1	23.6	6	0	0	12 ^b	9	12 ^c

PCOS'lu hastalarda ovulasyon: AI vs CC

Tablo-1 Devam (İlk Seçenek)

<i>Anastrozole trials</i>	Baruah <i>et al.</i> (2009)	<i>Arch Gynecol Obstet</i>	Quasi random	Letrozole 2.5–5 mg	25 (58)	29.7	23.6	11	NA	0	NA	6.9	1.63
				Clomiphene 100 mg	25 (56)	30.2	24.5	7	NA	0	NA	5.9	1.62
	Ganesh <i>et al.</i> (2009)	<i>J Assist Reprod Genet</i>	RCT	Letrozole 5 mg	372 (372)	30.3	24.5	87	12	NA	295 (79.3)	NA	NA
				Clomiphene 100 mg + rFSH 75 or 100 IU/day	669 (669)	30.4	24.8	96	16	NA	381 (57)	NA	NA
				rFSH 75 or 100 IU/day	346 (346)	30.8	24.1	62	9	NA	311 (90)	NA	NA
	Sipe <i>et al.</i> (2006)	<i>Fertil Steril</i>	RCT	Anastrozole 1 mg + FSH	12 (12)	30 ^d	30 ^d	3	0	0	NA	NA	NA
				Clomiphene 100 mg + FSH	8 (8)	32 ^d	28 ^d	2	0	1	NA	NA	NA
	Badawy <i>et al.</i> (2007b)	<i>Fertil Steril</i>	Prospective	Anastrozole 1 mg	115 (243)	23.8	31.1	25	4	0	165 (67.9)	10.1	1.9
				Clomiphene 100 mg	101 (226)	25.3	29.1	18	3	1	150 (68.6)	8.2	2.1

2008 Meta-Analiz

■ AI

- 4 RCT çalışmanın analizine göre AI lehine daha yüksek gebelik ve doğum oranı sağlanmakta
- Gebelik Oranı-OR=2.0 (95% CI 1.1–3.8)
- Doğum Oranı-OR= 2.4 (95% CI 1.2–4.6)
- Olgu sayısı az (265 hasta)

Polyzos NP, Tsappi M, Mauri D *et al.* 2008a Aromatase inhibitors for infertility in polycystic ovary syndrome. The beginning or the end of a new era? *Fertility and Sterility* **89**, 278–280.

Clomiphene citrate or letrozole for ovulation induction in women with polycystic ovarian syndrome: a prospective randomized trial

Ahmed Badawy, M.D.,^a Ibrahim Abdel Aal, M.D.,^b and Mohamed Abulatta, M.D.^c

First Line

Fertility and Sterility® Vol. 92, No. 3, September 2009

TABLE 2

Outcome in letrozole and clomiphene citrate (CC) groups.

	Letrozole group (n = 218)	CC group (n = 220)	t	P value
Total number of follicles	4.4 ± 0.4	6.8 ± 0.3	4.3	.042 ^a
Number of follicles >14 mm	2.1 ± 0.3	3.7 ± 0.5	6.13	.008 ^a
Number of follicles >18 mm	2.3 ± 0.1	3.1 ± 0.8	5.03	.03 ^a
Pretreatment endometrial thickness (mm)	4.5 ± 0.4	4.3 ± 0.5	1.41	.52
Endometrial thickness at hCG (mm)	8.1 ± 0.2	9.2 ± 0.7	5.44	.021 ^a
Serum E ₂ (pg/mL)	255.1 ± 64.2	384 ± 91.3	4.12	.022 ^a
Serum progesterone (ng/mL)	7.1 ± 0.9	11.1 ± 1.2	6.33	.024 ^a
Duration of stimulation (days)	12.1 ± 1.38	8 ± 2.9	4.91	.036 ^a
Pregnancy/cycle	82/540 (15.1%)	94/523 (17.9%)	1.33	.72
Miscarriage/patient	4 (12.1%)	4 (9.7%)	1.73	.43

^a Statistically significant difference: $P < .05$.

Badawy. Clomiphene citrate or letrozole. Fertil Steril 2009.

Letrozole 5 mg/gün 5 gün (3. gün) vs CC 100 mg/gün (3. gün) 5 gün+ Koitus

Comparison of efficacy of aromatase inhibitor and clomiphene citrate in induction of ovulation in polycystic ovarian syndrome

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Fertility and Sterility® Vol. 92, No. 3, September 2009

- Daha önceden CC 100 mg ile ovulasyon olmayan hastalar
- 32 hasta CC 150 mg/gün 5 gün
- 32 hasta 7.5 mg Letrozole 5 gün

TABLE 4**Outcome of ovulation induction.**

Parameters	Letrozole (n = 32)		CC (n = 32)		P value
	No.	%	No.	%	
Ovulation	20/32	62.50	12/32	37.50	< .05 ^a
Pregnancy	13/32	40.62	6/32	18.75	> .05 ^b
Pregnancy among ovulatory patients	13/20	65	6/12	50	> .05 ^c

^a $\chi^2 = 4$, df-1.

^b $\chi^2 = 3.66$, df-1.

^c $\chi^2 = 0.694$ df-1.

Begin. Comparison of efficacy of aromatase inhibitor. Fertil Steril 2009.

Extended letrozole therapy for ovulation induction in clomiphene-resistant women with polycystic ovary syndrome: a novel protocol

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Fertility and Sterility® Vol. 92, No. 1, July 2009

- Hepsi CC rezistans hasta
- Kısa letrozole 110 hasta-225 siklus
 - 5 mg/gün Day 1-5
- Uzun letrozole 108 hasta-219 siklus
 - 2.5 mg/gün Day 1-10

TABLE 2**Outcome in short letrozole and long letrozole groups.**

	Short letrozole group (n = 110)	Long letrozole group (n = 108)	t	P value
Number of ovulating patients	68 (61.8%)	71 (65.7%)	23.2	.11
Total number of follicles	3.9 ± 0.4	6.7 ± 0.3	8.0	.01*
Number of follicles >14 mm	2.1 ± 0.4	3.7 ± 0.3	9.2	.03*
Number of follicles >18 mm	1.8 ± 0.1	3.0 ± 0.4	6.3	.03*
Pretreatment endometrial thickness (mm)	4.8 ± 0.4	4.5 ± 0.6	0.64	.12
Endometrial thickness at hCG (mm)	10.4 ± 0.6	11.2 ± 0.6	0.90	.11
Serum E2 (pg/mL)	315.5 ± 60.2	338 ± 70.3	2.0	.08
Serum progesterone (ng/mL)	9.0 ± 0.8	10.3 ± 1.0	1.5	.08
Pregnancy/cycle	28/225 (12.4%)	38/219 (17.4%)	X ² = 4.37	.03*
Miscarriage/patient	5/28 (17.9%)	7/38 (18.4%)	X ² = 0.12	.64

* Significant difference as $P < .05$.

Badawy. Extended letrozole for ovulation induction. *Fertil Steril* 2009.

Letrozole versus combined metformin and clomiphene citrate for ovulation induction in clomiphene-resistant women with polycystic ovary syndrome: a randomized controlled trial

Hatem Abu Hashim, M.D., M.R.C.O.G., Tarek Shokeir, M.D., and Ahmed Badawy, M.D., Ph.D.

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Fertility and Sterility® Vol. ■, No. ■, ■ 2009

- CC resistant
- 123 hasta letrozole 2.5 mg/gün 5 gün
- 127 CC (150 mg/gün)+Metformin 500 mg/gün 6-8 hafta

TABLE 2

Outcome in letrozole and combined metformin-CC groups.

	Group A (letrozole group) (n = 123)	Group B (combined metformin-CC group) (n = 127)	t	χ^2	P value
Total no. of follicles	4.4 ± 0.4	6.8 ± 0.3	4.3		.042 ^a
No. of follicles >14 mm	2.1 ± 0.3	3.7 ± 0.5	6.13		.008 ^a
No. of follicles >18 mm	2.3 ± 0.1	3.1 ± 0.8	5.03		.003 ^a
Pretreatment endometrial thickness	5.5 ± 0.5	5.3 ± 0.6	1.31		.22
Endometrial thickness at hCG (mm)	9.5 ± 0.2	9.1 ± 0.1	1.44		.53
Serum E ₂ (pg/mL)	258 ± 62.2	386 ± 88.3	4.12		.022 ^a
Serum P (ng/mL)	7.3 ± 0.9	11.4 ± 1.2	6.33		.024 ^a
Duration of stimulation (d)	12.2 ± 1.3	8.1 ± 2.8	4.91		.036 ^a
Ovulation/cycle	185/285 (64.9%)	207/297 (69.6%)		1.63	.82
Pregnancy/cycle	42/285 (14.7%)	43/297 (14.4%)		1.32	.53
Miscarriage/patient	4 (10.2%)	4 (9.5%)		1.73	.43

^a Statistically significant difference: $P < .05$.Abu Hashim. Letrozole or CC-metformin for CC resistance. *Fertil Steril* 2009.

AI vs CC: Sonuç

- Anastrozolün kullanımı çok kısıtlı
- Letrozol (ilk seçenek veya CC resistant olgularda) kullanımı ile ilgili çalışmalar henüz yeterli değil
 - Doz net değil (2.5-7.5 mg/gün 5 gün)
 - Fazla oosit gelişmesi isteniyor ise CC?
 - Meme Ca (+) veya hikaye (+)
- www.clinicaltrials.com

Letrozole Versus Clomifene Citrate for Ovulation Induction

Official Title: Double Blind Cross-Over Randomized Controlled Trial Comparing Letrozole Versus Clomifene Citrate for Ovulation Induction in Women With Polycystic Ovarian Syndrome

İnsülin hassaslaştırıcı ajanlar

- Metformin
 - Biguanide
 - Laktik asidoz
 - Gebelikte B
- Pioglitazone ve rosiglitazone
 - Thiazolidinediones
 - Karaciğer toksisitesi
 - Gebelikte C

METFORMIN vs CC

First line

626 women with PCOS

	<u>Conception</u> <u>rate</u>	<u>Live-birth</u> <u>rate</u>
CC	39.5%	47/209 (22.5%)
CC + M	46.0%	56/209 (26.8%)
M	21.7%**	5/208 (7.2%)*

* $P < 0.001$

** $P = 0.002$

Legro et al., 2007
N. Engl. J. Med. 356, 551-66

Metformin use in infertile patients with polycystic ovary syndrome: an evidence-based overview

Vol 16. No 3. 2008 327-335 Reproductive BioMedicine Online

- Metaanalizlerin deęerlendirmesi, 2008

Metformin İlk Seçenek

Table 1. Metformin use as the first-step treatment in infertile anovulatory polycystic ovary syndrome patients: level of evidence 1a.

<i>Treatment</i>	<i>Ovulation rate</i>	<i>Pregnancy rate</i>	<i>Live birth rate</i>
Metformin versus placebo			
Lord <i>et al.</i> , 2003a	OR 3.88; 2.25, 6.69 ^a	OR 2.76; 0.85, 8.98	–
Kashyap <i>et al.</i> , 2004	RR 1.50; 1.13, 1.99 ^a	RR 1.07; 0.20, 5.74	–
Metformin versus CC			
Palomba <i>et al.</i> , unpublished data	RR 0.62; 0.04, 10.67	RR 0.87; 0.07, 10.95	RR 0.82; 0.04, 16.66
Metformin plus CC versus CC			
Palomba <i>et al.</i> , unpublished data	RR 0.92; 0.40, 2.16	RR 0.86; 0.62, 1.19	RR 1.01; 0.70, 1.44

Values are given as odds ratio (OR) or relative risk (RR); 95% confidence interval. CC = clomiphene citrate.

^a*P* < 0.05.

Metformin vs plasebo=Ovulasyon oranı yüksel fakat gebelik oranları benzer

Metformin vs CC= Fark yok

TABLE 2

Randomized trial from the National Institutes of Health Reproductive Medicine Network.

	CC	Metformin	Combination
N	209	208	209
Ovulation	49 ^a	29	60 ^b
Conception	20 ^a	12	38 ^a
Pregnancy	24 ^a	9	31 ^a
Live birth	23 ^a	7	27 ^a
Multiple	6	0	3

Source: Legro et al., N Engl J Med 2007;356:551–66.

Used with permission.

^a $P < .001$.

^b $P < .001$ (combination vs. clomiphene citrate [CC]).

Tarlatzis. Consensus on infertility treatment related to PCOS. Fertil Steril 2008.

Erken gebelik kayıplarını azaltmıyor

Comparison of clomiphene citrate, metformin, or the combination of both for **first-line ovulation induction** and achievement of pregnancy in 154 women with polycystic ovary syndrome

Nathalie Neveu, M.D.,^{a,b} Louis Granger, M.D.,^{a,c} Pierre St-Michel, M.D.,^a and H el ene B. Lavoie, M.D.^{a,b}

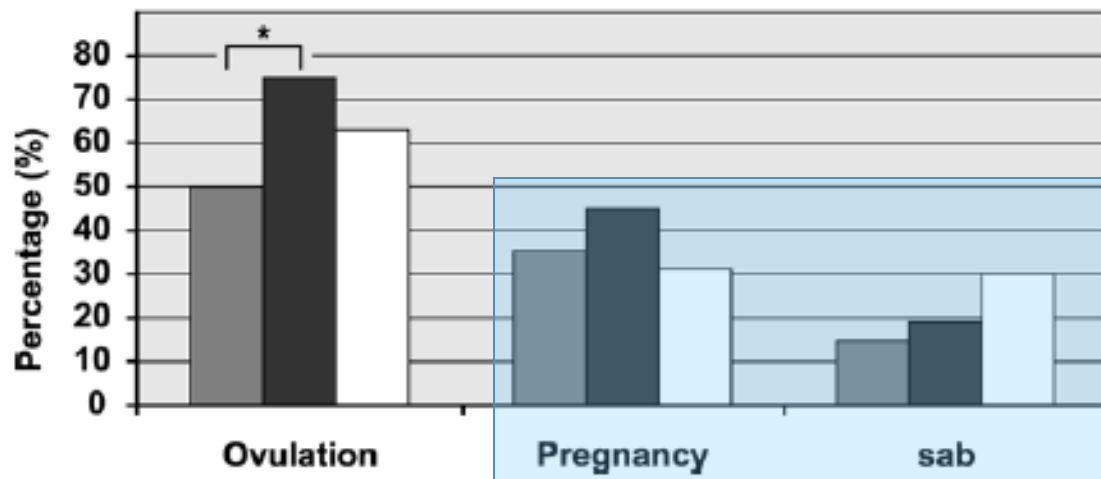
Fertility and Sterility[®] Vol. 87, No. 1, January 2007

- 56 hasta CC (50 mg) 5 g un
- 57 hasta Metformin 500 mg 3x1
- 41 hasta kombine olarak her ikisini de aliyor

FIGURE 1

Ovulation, pregnancy, and spontaneous abortion rates (*sab*) for patients taking CC (*gray*), metformin (*black*), or combination (*white*). Ovulation rate of patients taking metformin was significantly better than that of patients taking CC ($*P=.005$).

Pregnancy and spontaneous abortion rates were equivalent in the three groups.



Neveu. Metformin and clomiphene citrate in PCOS women. Fertil Steril 2007.

Comparison of clomiphene citrate, metformin, or the combination of both for **first-line ovulation induction**, achievement of pregnancy, and live birth in Asian women with polycystic ovary syndrome: a randomized controlled trial

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Fertility and Sterility® Vol. 91, No. 2, February 2009

- 39 hasta CC (50 mg)
- 38 hasta Metformin 3x500 mg
- 38 hasta kombine olarak her ikisini de alıyor

TABLE 3**Rates of ovulation, pregnancy, pregnancy loss, and live birth.**

	Metformin (n = 38)	CC (n = 39)	Combination (n = 38)	CC vs. Metformin <i>P</i> & OR (CI)	Combination vs. Metformin <i>P</i> & OR (CI)	CC vs. Combination <i>P</i> & OR (CI)
Ovulation	9/38 (23.7%)	23/39 (59%)*	26/38 (68.4%)*	.002* 4.63 (1.7-12.7)	.001* 6.98 (2.5-19.3)	.742
Pregnancy	3/38 (7.9%)	6/39 (15.4%)	8/38 (21.1%)	.306 2.12 (0.5-9.2)	.103 3.11 (2.5-19.3)	.416
First trimester loss	0	0	1/8 (12.5)			
Ectopic	0	0	0			
Second trimester loss	0	0	0			
Multiple gestation	0	0	0			
Live birth	3/38 (7.9%)	6/39 (15.4%)	7/38 (18.4%)	.306 2.12 (0.5-9.2)	.175	.126 2.64 (0.3-11)

Note: OR = odds ratio; CI = confidence interval.

* Ovulation rate significantly higher in CC vs. metformin and combination vs. metformin.

Zain. Clomiphene, metformin, or both for infertility. *Fertil Steril* 2009.

CC resistant olgularda: CC+ Metformin

Table 2. Metformin use as co-treatment with clomiphene citrate (CC) in CC-resistant patients: level of evidence 1a.

<i>Reference</i>	<i>Ovulation rate</i>	<i>Pregnancy rate</i>	<i>Live birth rate</i>
Lord <i>et al.</i> , 2003a	OR 9.34; 3.97, 21.97 ^a	OR 4.40; 1.96, 9.85 ^a	–
Kashyap <i>et al.</i> , 2004	RR 3.04; 1.77, 5.24 ^a	RR 3.65; 1.11, 11.99 ^a	–
Siebert <i>et al.</i> , 2006	OR 6.82; 3.59, 12.96 ^a	–	–

Values are given as odds ratio (OR) or relative risk (RR); 95% confidence interval.

^a $P < 0.05$.

CC+ Metformin sadece CC'ye göre oldukça etkili, Metformin genelde Kanama ile başlanıyor

METFORMIN vs CC

- **Metformin improves clinical pregnancy and ovulation rates.**
- **There is no evidence that metformin improves live birth rates whether it is used alone or in combination with CC, or when compared with CC.**

Tang et al., 2010

Cochrane Database Syst. Rev. Jan 20; (1): CD 003053

CC resistant olgularda: Önceden Metformin

Table 3. Metformin use as pre-treatment in clomiphene citrate (CC)-resistant patients before CC administration: level of evidence 1b.

<i>Treatment</i>	<i>Ovulation rate</i>	<i>Pregnancy rate</i>	<i>Live birth rate</i>
Metformin pre-treatment before CC versus placebo pre-treatment before CC			
Nestler <i>et al.</i> , 1998b	90.0% versus 8.0% ^a	–	–
Hwu <i>et al.</i> , 2005	42.5% versus 12.5% ^a	15.0% versus 0.0% ^a	–
Sturrock <i>et al.</i> , 2002	41.7% versus 28.6%	25.0% versus 14.3%	–
Sahin <i>et al.</i> , 2004	74.4% versus 61.8%	45.5% versus 30.0%	–
Metformin pre-treatment before CC versus HMG			
George <i>et al.</i> , 2003	40.0% versus 46.7% ^a	16.7% versus 23.3%	–
Metformin pre-treatment before CC versus LOD pre-treatment before CC			
Palomba <i>et al.</i> , 2005b	30.6% versus 31.1%	16.7% versus 16.2%	66.7% versus 58.3%

^a*P* < 0.05; CC = clomiphene citrate; HMG = human menopausal gonadotrophin; LOD = laparoscopic ovarian drilling.

İnsülin Hassaslaştırıcı Ajanlar-Metformin: Sonuç

- İlk seçenek olarak metformin tek başına etkili değil
- İlk seçenek olarak CC'ye Metformin eklemenin faydası yok
- CC resistans olgularda CC'ye Metformin eklemek faydalı olabilir fakat yeterli kanıt yok
- CC resistans olgularda CC öncesi Metformin vermek faydalı olabilir fakat yeterli kanıt yok

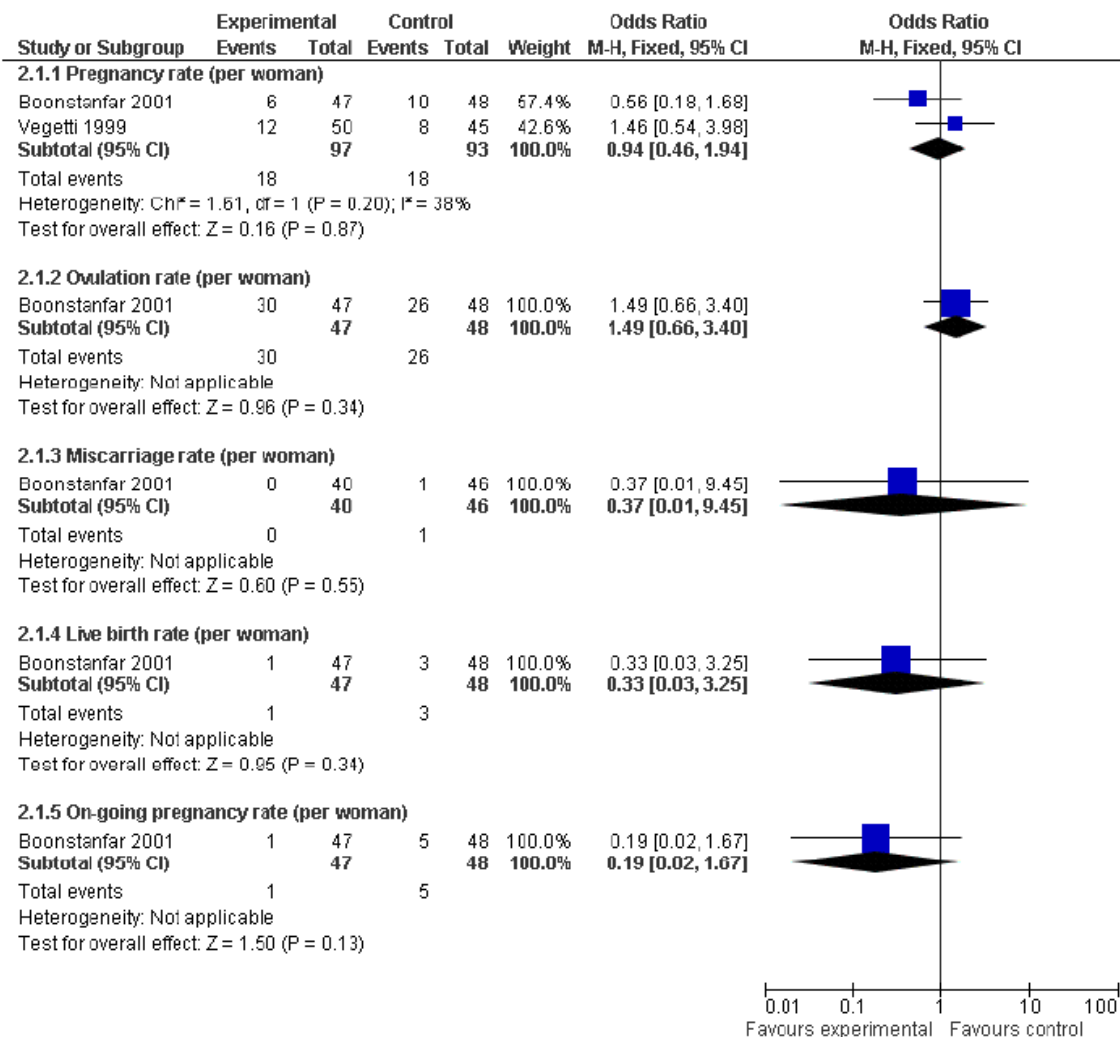
CC vs Tamoksifen

- 2 tane RCT (+)
- CC (50-200 mg) vs Tamoksifen (20-60 mg)

Clomiphene and anti-oestrogens for ovulation induction in PCOS (Review)

Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD002249.

Figure 4. Forest plot of comparison: 2 Anti-oestrogen versus anti-oestrogen, outcome: 2.1 Clomiphene versus tamoxifen.



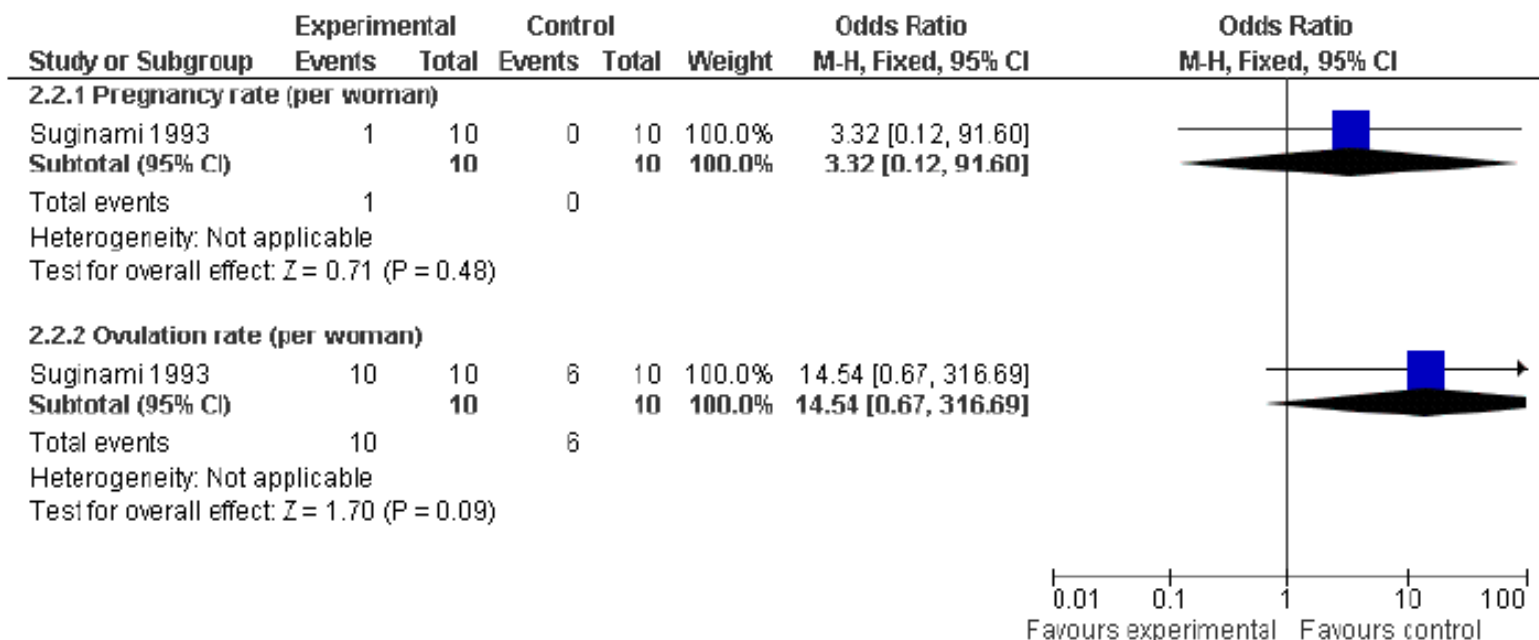
CC vs CC+ Tamoksifen

- 1 tane RCT (+), 20 olgu (+)
- CC (50 mg) + Tamoksifen (20 mg) vs CC (100 mg)

Clomiphene and anti-oestrogens for ovulation induction in PCOS (Review)

Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD002249.

Figure 5. Forest plot of comparison: 2 Anti-oestrogen versus anti-oestrogen, outcome: 2.2 Clomiphene plus tamoxifen versus clomiphene.



CYP17a İnhibitörü

- Ketokanozol
 - Sitokrom P enzim sistemini inhibe eder.

CC vs CC+ Ketokanozol

- 1 tane RCT (+)
- CC (150 mg) + Ketoconazole (400 mg) vs CC (150 mg)
- Gebelik Oranı=OR=2.37, 95% CI 0.88 to 6.40; P = NS)
- Çoğul Gebelik Oranı=OR=1.18, 95% CI 0.37 to 3.78; P = NS)

Bromokriptin (Sadece CC ile)

- Dopamine PCOS'deki yükselmiş LH seviyesini azaltabilir

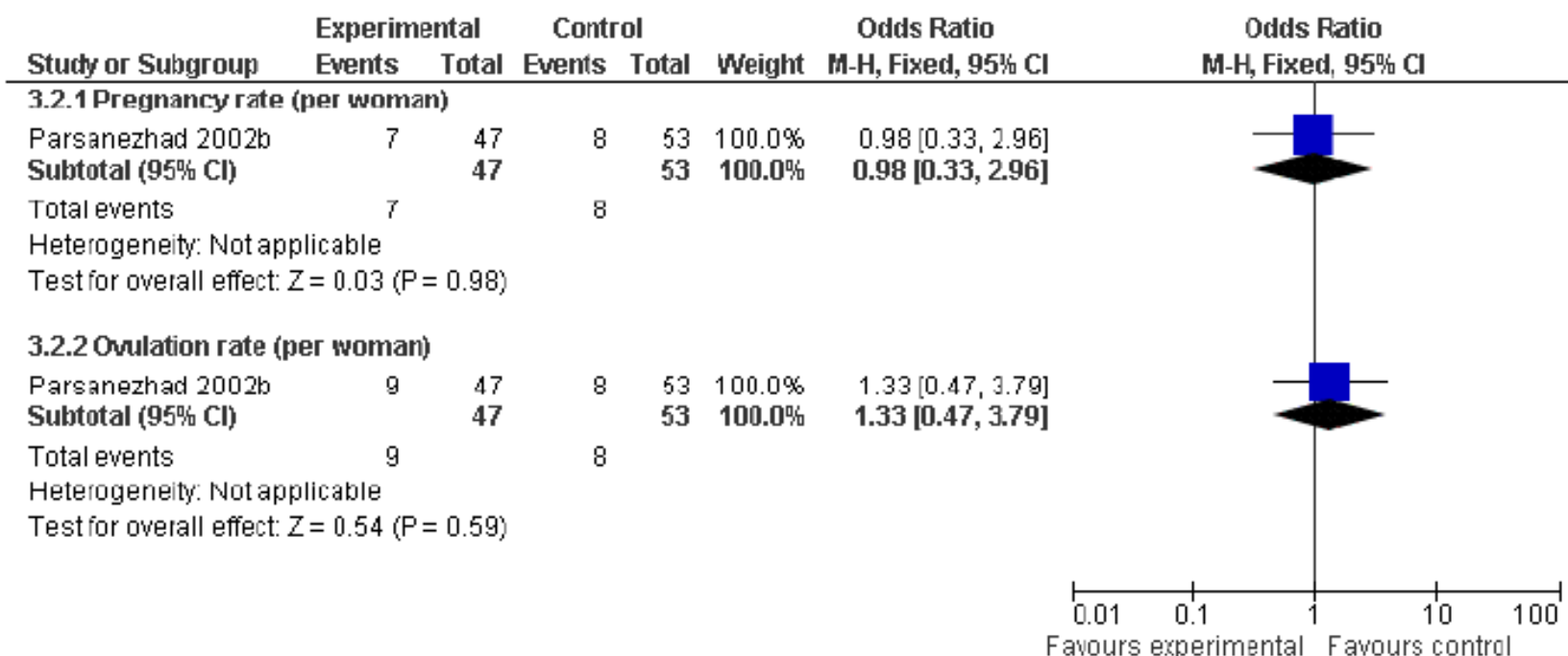
CC vs CC+ Bromokriptin

- 1 tane RCT (+)
- CC (200 mg) + Bromokriptin (7.5 mg) vs CC (200 mg)
- Gebelik oranı=OR=0.98, 95% CI 0.33-2.96; P =NS)
- Ovülasyon oranı=OR=1.33, 95% CI 0.47-3.79; P =NS)

Clomiphene and anti-oestrogens for ovulation induction in PCOS (Review)

Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD002249.

Figure 6. Forest plot of comparison: 3 Anti-oestrogen plus medical adjunct versus anti-oestrogen alone, outcome: 3.2 Clomiphene plus bromocriptine versus clomiphene.



Deksametazon (Sadece CC ile)

- Adrenal androjen üretimini azaltırlar
- FSH miktarını artırır
- Yüksek pulsatif LH miktarını azaltır

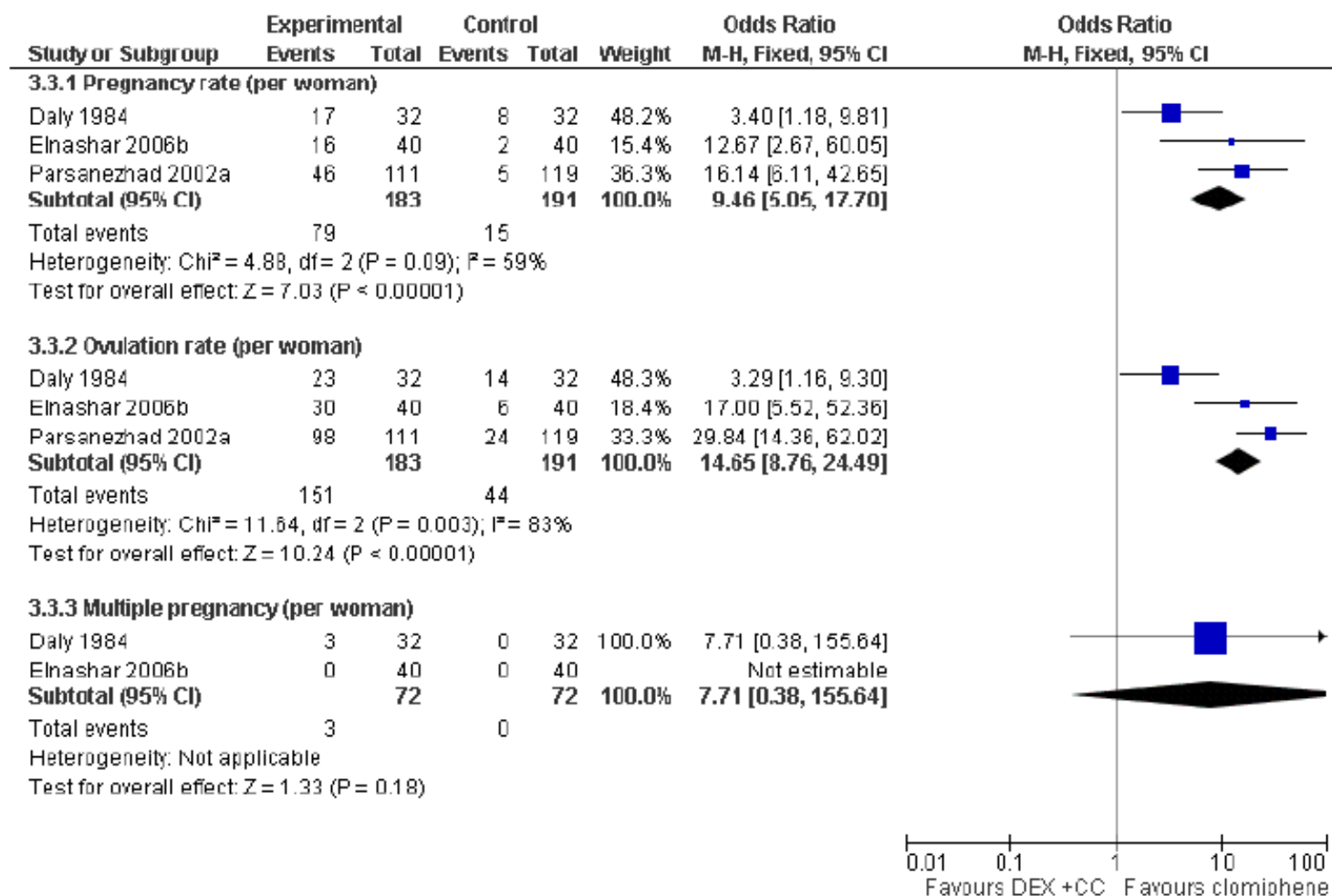
CC vs CC+Deksametazon

- 3 tane RCT (+)
- CC (50-200 mg) vs + Deksametazon (0.5-2.0 mg)+ CC (50 to 200 mg)
- CC (3-7 gün), Deksametazon (3-12 gün)

Clomiphene and anti-oestrogens for ovulation induction in PCOS (Review)

Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD002249.

Figure 7. Forest plot of comparison: 3 Anti-oestrogen plus medical adjunct versus anti-oestrogen alone, outcome: 3.3 Clomiphene plus dexamethasone versus clomiphene.



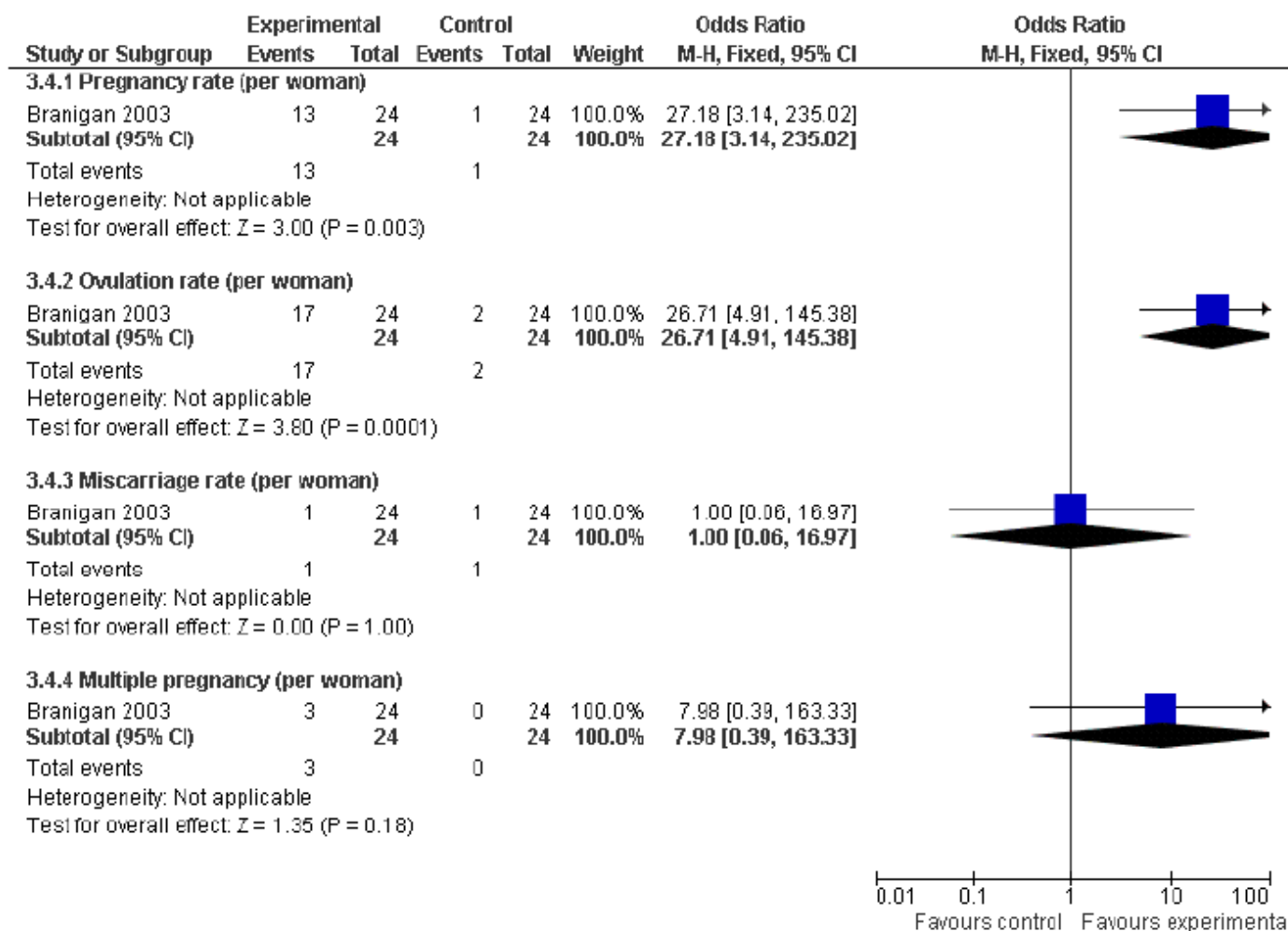
CC vs CC+OC

- 1 tane RCT (+), 51 olgu (+)
- CC (100 mg) vs OC + CC (100 mg)

Clomiphene and anti-oestrogens for ovulation induction in PCOS (Review)

Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD002249.

Figure 8. Forest plot of comparison: 3 Anti-oestrogen plus medical adjunct versus anti-oestrogen alone, outcome: 3.4 Clomiphene plus combined oral contraceptive vs clomiphene.



Eve Götürme Mesajları-1

- İlk tedavi seçeneği CC
- Tamoksifen
 - CC'ye üstünlüğü yok, FDA onayı yok, CC'ye yan etkilerin olduğu (sıcak basması vb.) durumlarda kullanılabilir.
- Aromataz inhibitörleri
 - Anastrozolün kullanımı çok kısıtlı
 - Letrozol ile ilgili çalışmalar henüz yeterli değil (ilk veya CC resistant olgularda)
 - Doz net değil (2.5-7.5 mg/gün 5 gün)
 - Fazla oosit gelişmesi isteniyor ise CC?, Meme Ca
 - FDA onayı yok, yaygın kullanım için yeterli çalışma yok

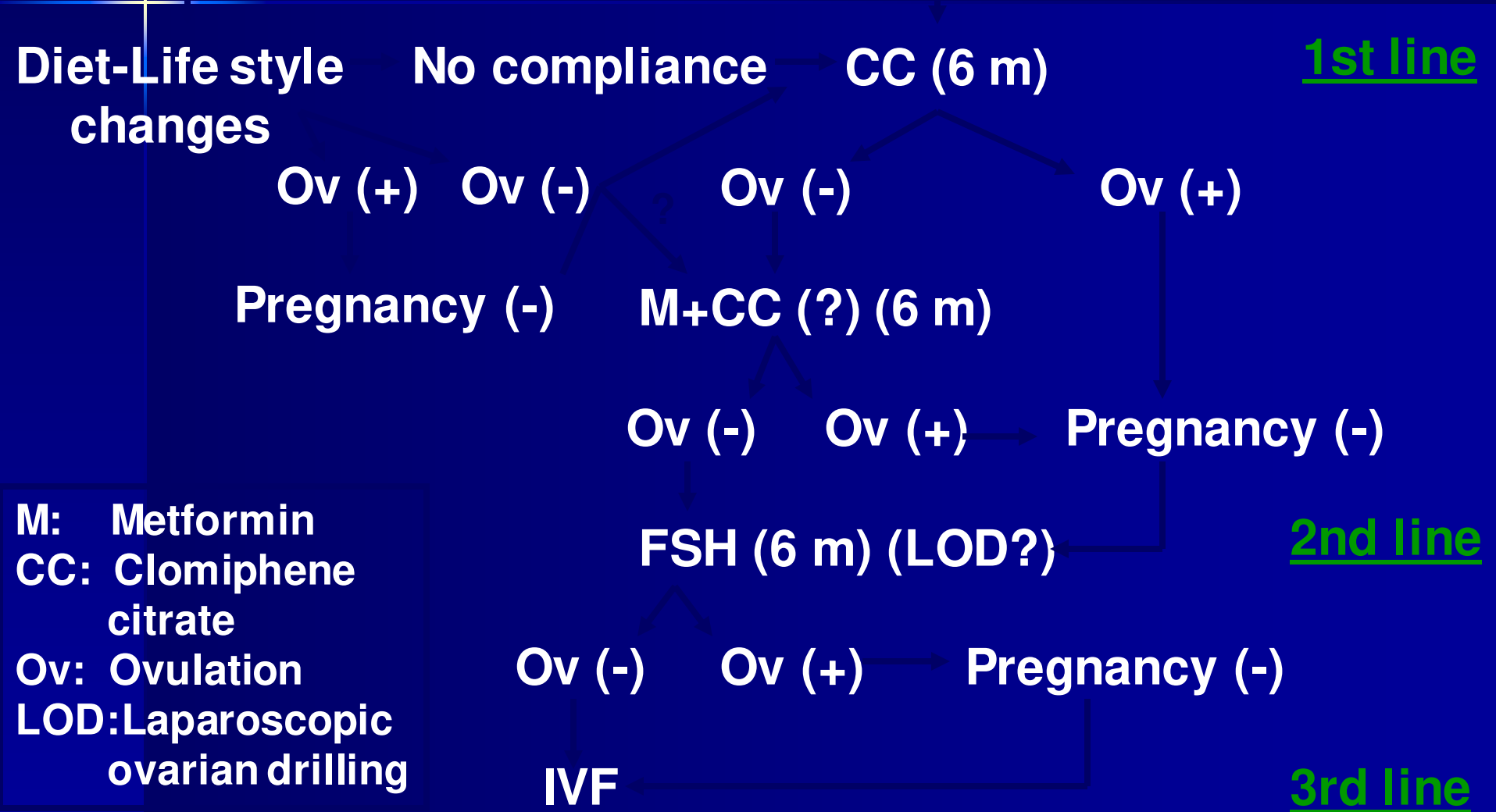
Eve Götürme Mesajları-2

- İlk seçenek olarak metformin tek başına etkili değil
- İlk seçenek olarak CC'ye Metformin eklemenin faydası yok
- CC resistans olgularda CC'ye Metformin eklemek faydalı olabilir fakat yeterli kanıt yok
- CC resistans olgularda CC öncesi Metformin vermek faydalı olabilir fakat yeterli kanıt yok
- CC'ye Deksamethason eklemek?

OVULATION INDUCTION ALGORITHM IN WHO GROUP II (PCOS)

Obese

Lean



Sabrınız İin Teřekkürler