



Meme Kanserinde Fertilite Koruyucu Yaklaşımlar

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Kadın Hastalıkları ve Doğum AD

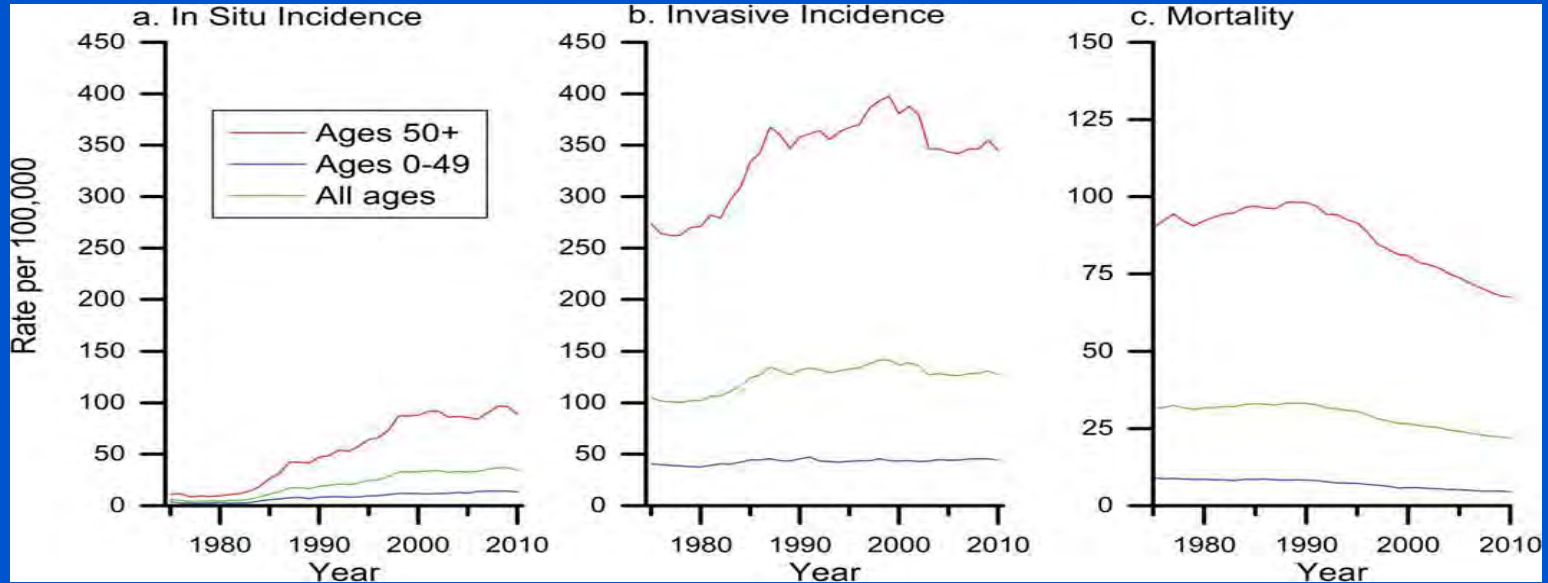
Meme Kanseri

- Kadınlarda en yaygın kanser (tüm kanserlerin 1/3'ü)
- Yaşam boyu meme kanseri riski 1/8
- Dünya çapında her yıl 1.4 milyon kadın kanser tanısı almaktadır
- 2011 yılında ABD'de 13,110 üreme çağındaki kadın yeni meme kanseri tanısı almaktadır

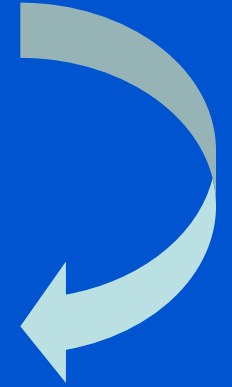
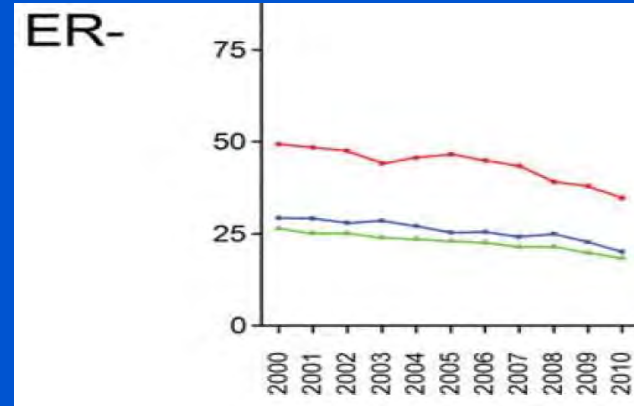
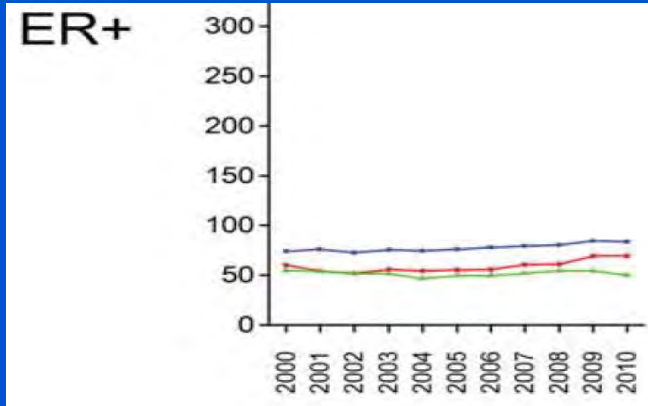
DeSantis, CA Cancer J Clin, 2014
GLOBOCAN, 2008

Meme Kanseri

Insidans - Mortalite



Meme Kanseri Östrojen Reseptör Durumu



ER (+) genç kadınlarda artmış insidans

Kemoterapi - Gonadal Hasar

Yüksek risk

- Siklofosfamid
- Klorambusil
- Melfalan
- Busufan
- Nitrojen mustard
- Prokarbazin

Orta risk

- Sisplatin
- Adriamisin
- Paklitaksel
- Imatinib

Düşük risk

- MTX
- 5-Fluorourasil
- Vinkristin
- Actinomisin D
- Bleomisin

Yeni ajanlar / risk ?

- Irinotekan
- Imatinib

Fertilite Prezervasyonu - Seçenekler

- Embriyo kriyoprezervasyonu
- Matür/immatür oosit kriyoprezervasyonu
- In vitro matürasyon
- Ovarian transpozisyon
- Donör oosit
- Overyan doku kriyoprezervasyonu
- Xenografting
- GnRHa tedavisi
- Antiapoptotik tedaviler \Rightarrow SP1P

Fertility prezervasyonu – Kritik Noktalar

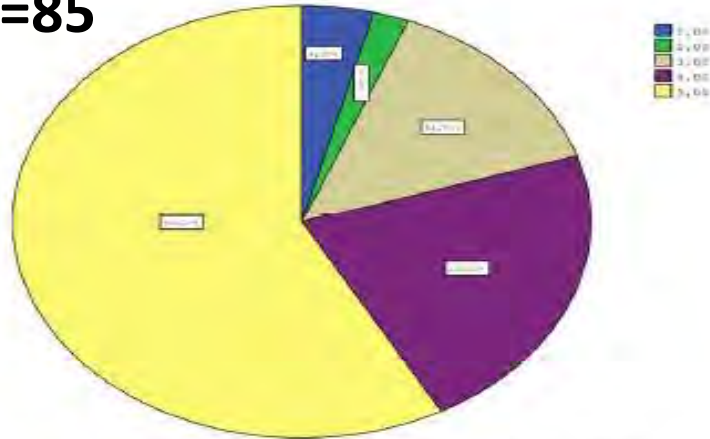
- Fertilite/overyan fonksiyonlar korunmalı
- Hastalıkla mücadele ve yaşam kalitesi üzerinde etki
- Overyan stimülasyonun ER bağımlı tümörlerde güvenilirliği - sağkalım etkisi
- Zaman kısıtlılığı

Overyan kriyo. vs. oosit/embriyo kriyo.

	Overyan kriyo.	Oosit /embriyo kriyo.
Avantajlar	<ul style="list-style-type: none">• KT gecikmez• Prepubertal tek seçenek• Endokrin fonksiyonlar korunur	<ul style="list-style-type: none">• Teknik standart• Yüksek başarı oranları• Yaygın kullanım
Dezavantajlar	<ul style="list-style-type: none">• L/S zorunlu• ~30 gebelik• Kanser yayılım riski	<ul style="list-style-type: none">• 2-3 hafta gerekli• Sınırlı oosit- embriyo• Çocuklarda zor uygulanım

Fertilite prezervasyonun hastalık ile mücadele ve «QoL» üzerine etkisi

n=85



Graph 4: Motivational morale contribution of ovarian cryopreservation to patients' struggle with a malignancy. (1-5, 1; no effect, 5; maximum boosting morale)

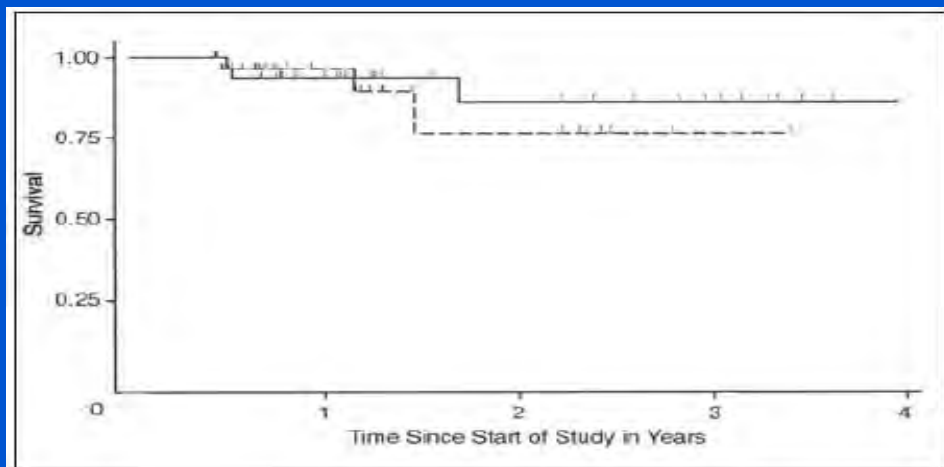
Letrozole / TMX - IVF

Fertility Preservation in Breast Cancer Patients: A Prospective Controlled Comparison of Ovarian Stimulation With Tamoxifen and Letrozole for Embryo Cryopreservation

Kutluk Oktay, Erkan Buyuk, Natalie Libertella, Munire Akar, and Zev Rosenwaks

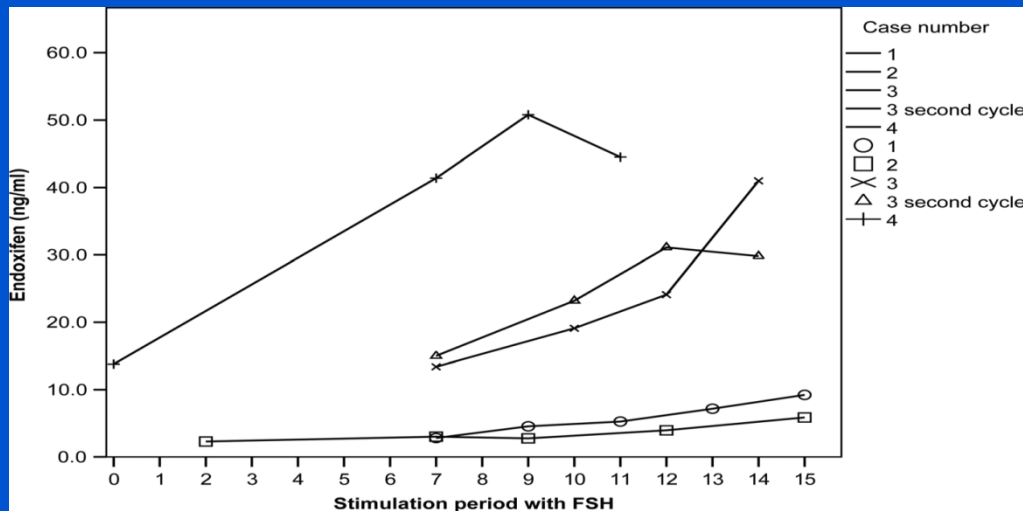
- 29 kadın 24-43 yaş, 33 KOH siklusu
 - TMX 60mg/g → 12 hasta, 13 siklus
 - TMX-FSH → 7 hasta, 9 siklus
 - Letrozole (5mg/d)-FSH → 11 hasta, 11 siklus

Variable	Mean ± Standard Deviation			P		
	Tam-IVF (a)	TamFSH-IVF (b)	Letrozole-IVF (c)	a v b	a v c	b v c
Age, years	36.6 ± 1.6	38.3 ± 1.9	38.5 ± 1	NS	NS	NS
Baseline FSH, mU/mL	9.4 ± 1.5	9.4 ± 1.5	6.2 ± 1.1	NS	NS	NS
PeakE ₂ , pg/mL†	419 ± 39	1,182 ± 271	380 ± 57	< .05	> .05	< .05
Total follicles, No.	2 ± 0.3	6 ± 1	7.8 ± 0.9	< .01	< .001	> .05
Follicle > 17 mm, No.	1.2 ± 0.1	2.6 ± 0.4	3.2 ± 0.4	< .05	< .001	> .05
Total oocytes, No.	1.7 ± 0.3	6.9 ± 1.1	12.3 ± 2.5	< .05	< .001	> .05
Mature oocytes, No.	1.5 ± 0.3	5.1 ± 1.1	8.5 ± 1.6	< .05	< .001	> .05
Total embryos, No.	1.3 ± 0.2	3.8 ± 0.8	5.3 ± 0.8	< .05	< .001	> .05



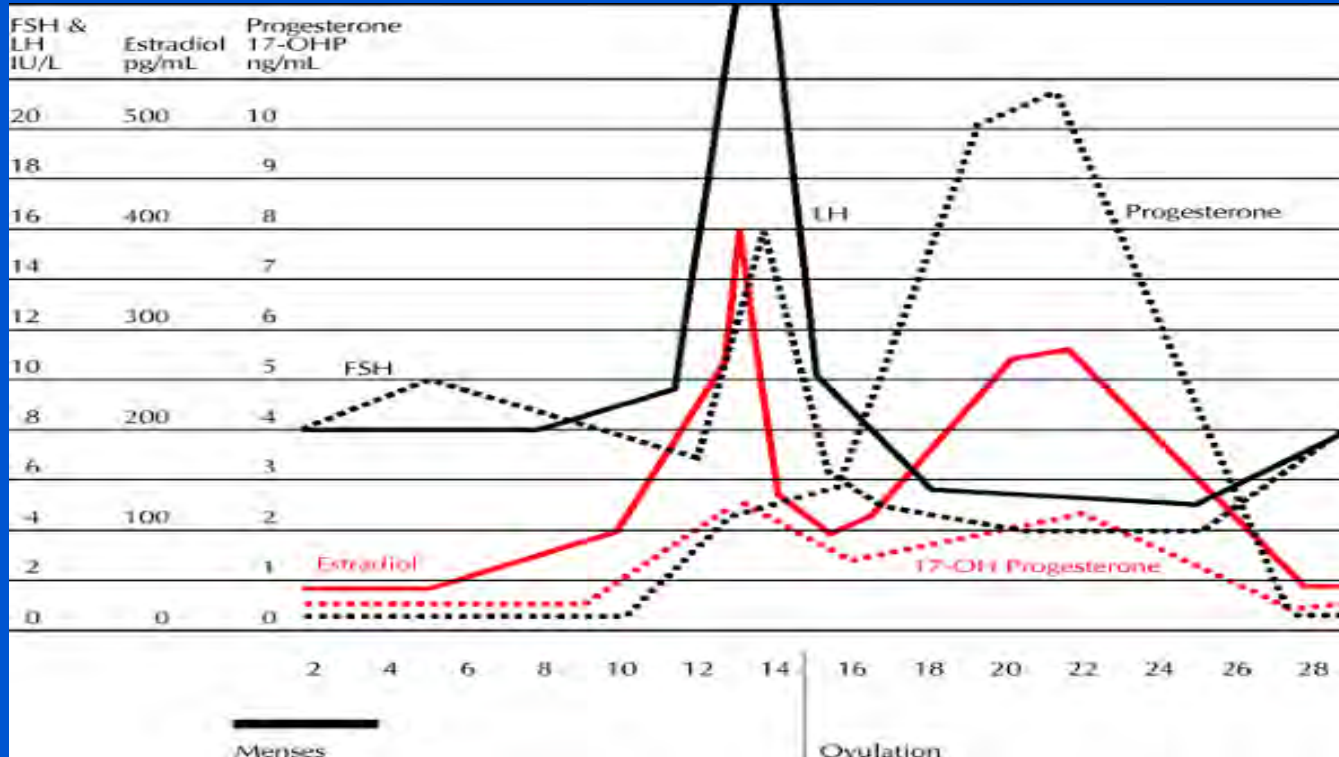
A prospective case series of women with estrogen receptor-positive breast cancer: levels of tamoxifen metabolites in controlled ovarian stimulation with high-dose tamoxifen

E.M.E. Balkenende¹, T. Dahhan^{1,*}, S.C. Linn², N.G.L. Jager³, J.H. Beijnen³, and M. Goddijn¹

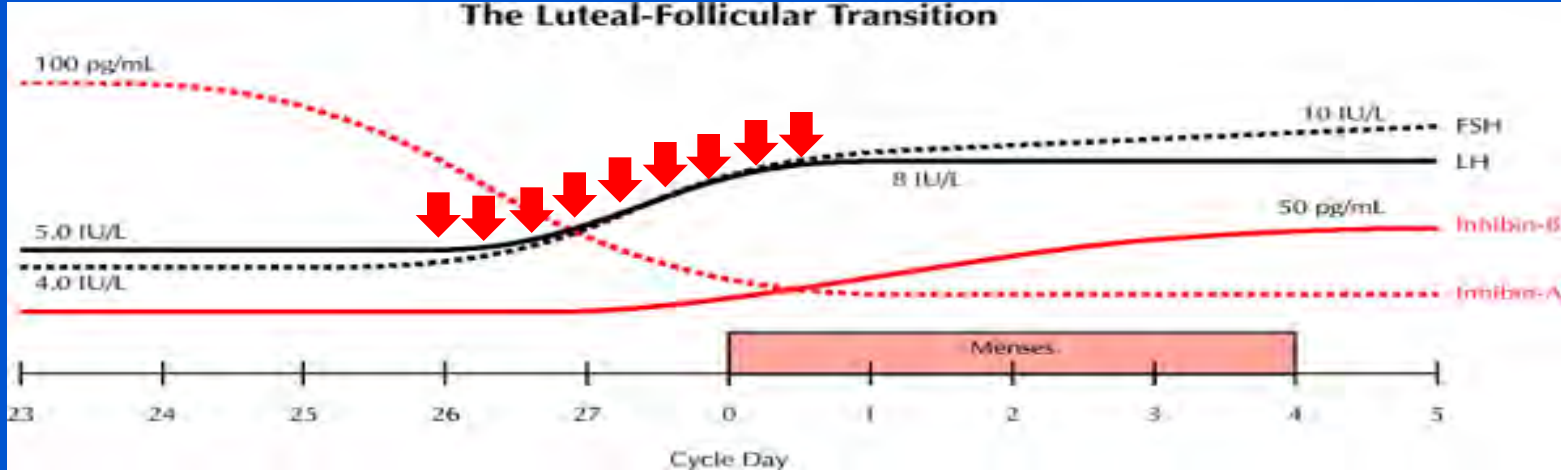


- TMX 60mg/day+FSH
- 4 hasta
- 5-11 oosit kriyo.
- Endoxifen >7ng/ml (ER inhibisyonu)

Overyan Foliküler Fizyoloji



Overyan Folikül Gelişim Fizyolojisi

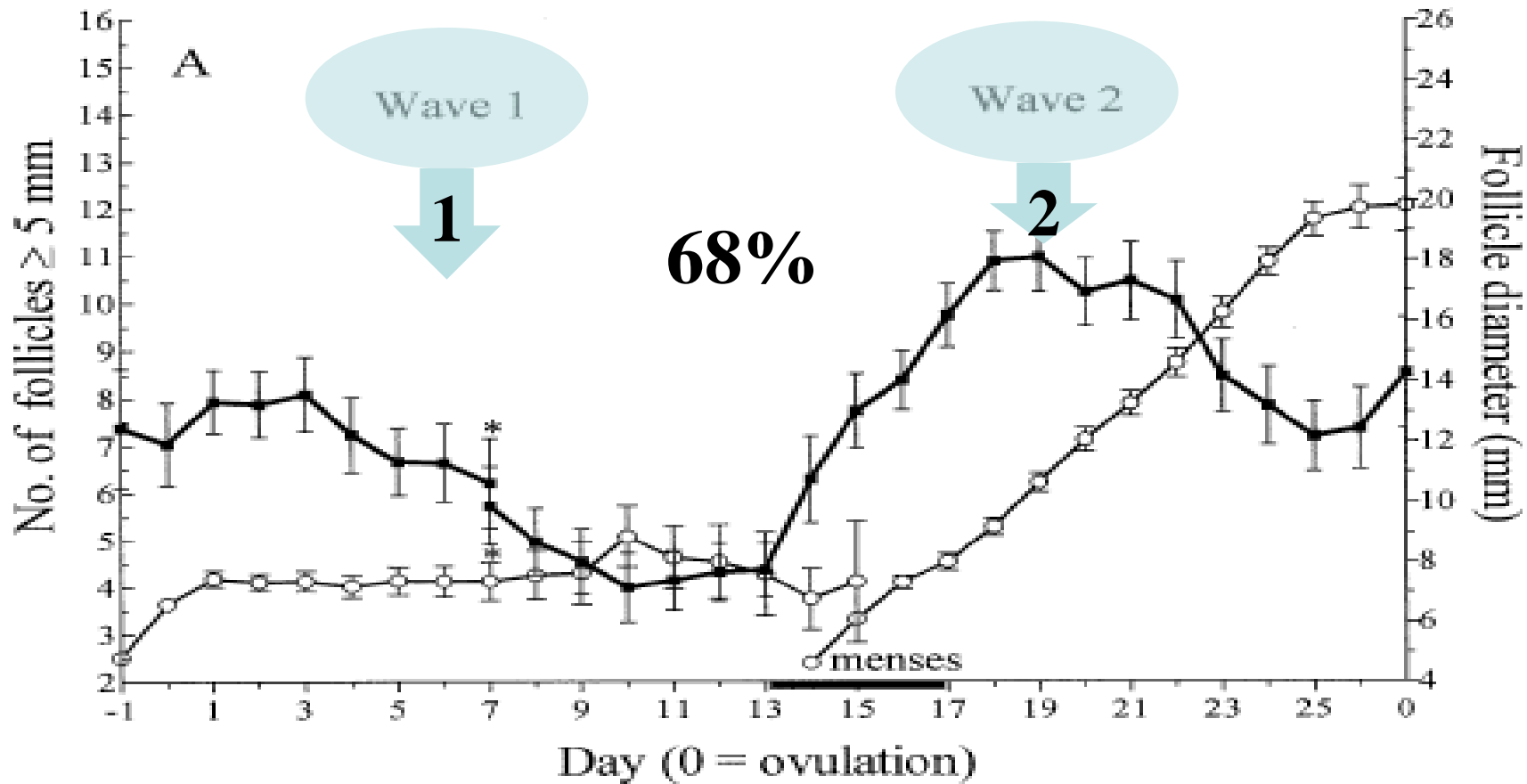


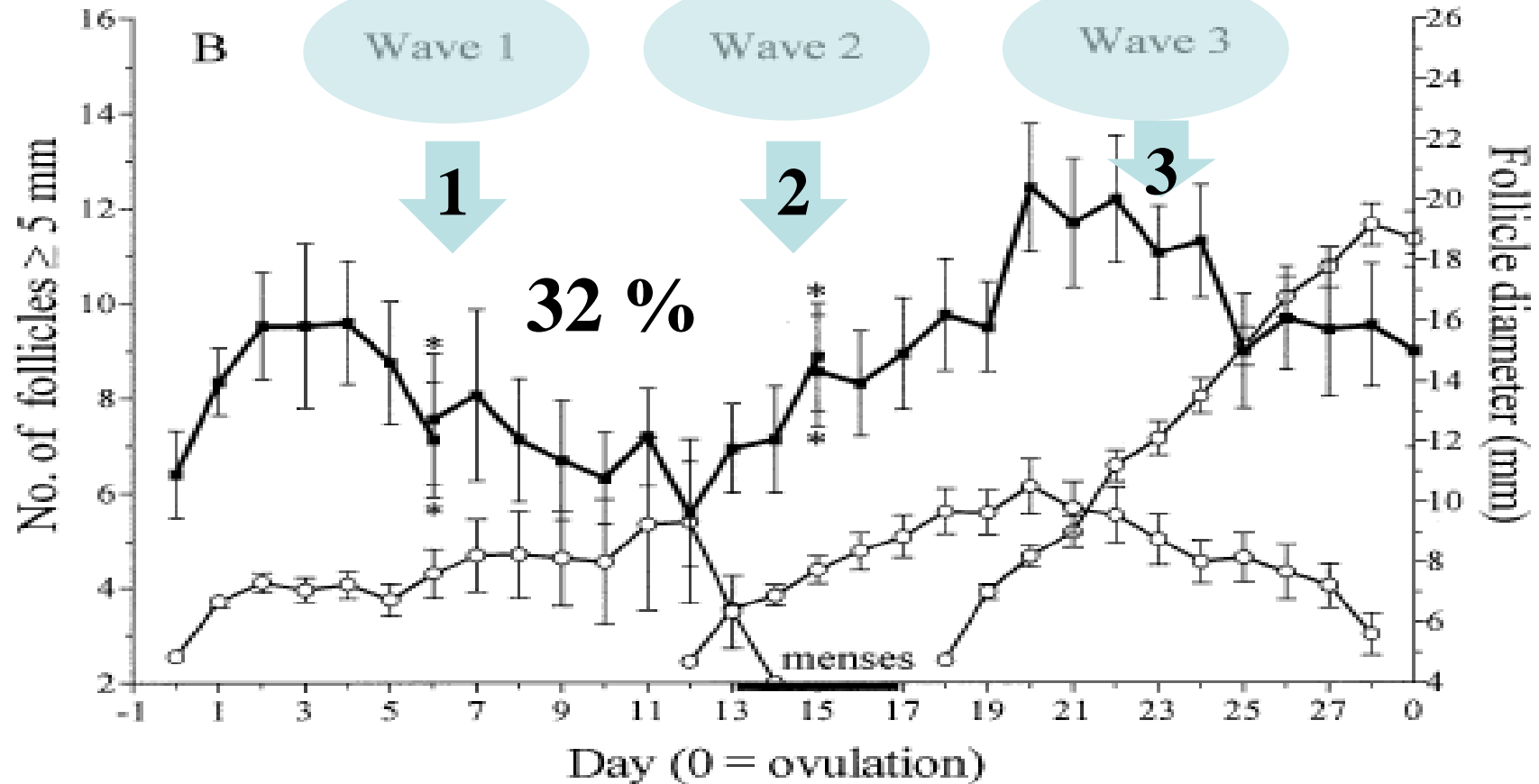
A new model for ovarian follicular development during the human menstrual cycle

Angela R. Baerwald, B.Sc. Hon.,^a Gregg P. Adams, D.V.M., M.S., Ph.D.,^b and Roger A. Pierson, M.S., Ph.D.^a

University of Saskatchewan, Saskatoon, Saskatchewan, Canada

- Bir menstrüel siklusta sadece 1 ana dalga mı vardır?
- n=50 sağlıklı ovulatuar kadın





Random-start controlled ovarian hyperstimulation for emergency fertility preservation in letrozole cycles

Murat Sönmezer, M.D.,^{a,b} Ilgın Türkçüoğlu, M.D.,^c Uğur Coşkun, M.D.,^d and Kutluk Oktay, M.D.^e

TABLE 1

Baseline characteristics and COH outcome of the patients with breast cancer undergoing emergency fertility preservation.

Characteristic	Case 1	Case 2	Case 3
Age (y)	29	26	26
Stage	I	II	II
Histology	Invasive ductal	Mixed invasive ductal + lobular	Invasive ductal
COH start day	14	11	17
FSH (mIU/mL)	6.2	2.8	4.6
LH (mIU/mL)	5.8	2.8	1.2
E ₂ (ng/mL)	62	269	50
P (pg/mL)	1.2	0.4	2.5
Endometrial thickness (mm)	7	6.5	9
Antral follicle count (n)	11	20 ^a	20 ^b
GnRH antagonist start day	5	1	5
Peak E ₂ (pg/mL)	499	988	478
Duration of COH (d)	9	12	9
Oocytes retrieved (n)	9	17	16
Metaphase II, no. (%)	7 (77.7)	10 (58.8)	11 (68.75)
Metaphase I + germinal vesicle, no. (%)	2 (22.3)	7 (41.2)	5 (31.25)
Fertilization rate, no. (%)	7/8 (87.5)	10/12 (83.3)	9/13 (69.2)
Cleavage rate (%)	7/7 (100)	NA	NA
Embryos frozen (n)	7	10	9

«Random-Start» Overyan Stimulasyon

- Random başlangıç n=35
- Klasik başlangıç n= 93

Comparison of outcomes of conventional-and random-start controlled ovarian stimulation cycles.

	Conventional start (n = 88; 103 cycles)	Random start (n = 35; 35 cycles)	P value	Late follicular phase start (n = 13; 13 cycles)	Luteal phase start (n = 22; 22 cycles)	P value ^a
Antral follicle count (AFC)	13.0 (11.7–14.5)	11.5 (9.6–13.8)	NS	10.5 (7.8–14.2)	12.1 (9.6–15.2)	NS
Days of ovarian stimulation	9.3 (9.0–9.5)	10.9 (10.4–11.5)	< .001	10.5 (9.6–11.4) ^b	11.2 (10.5–12.0) ^c	< .001
Total dose of gonadotropins (IU) ^d	3,404 (3,180–3,628)	4,158 (3,774–4,542)	.001	3,842 (3,213–4,472)	4,344 (3,860–4,827) ^e	.005
Gonadotropin daily dose (IU/d) ^d	361 (345–378)	372 (343–400)	NS	371 (324–418)	373 (337–409)	NS
Follicles ≥ 13 mm	10.5 (9.3–11.9)	11.8 (9.6–14.5)	NS	10.9 (7.8–15.4)	12.3 (9.5–16.0)	NS
Oocytes retrieved	14.4 (12.8–16.2)	14.5 (11.8–17.8)	NS	13.0 (9.3–18.2)	15.5 (11.9–20.1)	NS
Mature oocytes (MII) retrieved	9.7 (8.4–11.2)	9.9 (7.7–12.7)	NS	9.1 (6.0–13.7)	10.3 (7.5–14.2)	NS
MI I oocytes/total oocytes ratio	0.66 (0.62–0.71)	0.67 (0.59–0.76)	NS	0.68 (0.56–0.82)	0.67 (0.58–0.78)	NS
Oocytes/AFC ratio	1.09 (0.99–1.19)	1.26 (1.07–1.49)	NS	1.24 (0.95–1.62)	1.28 (1.04–1.57)	NS
Mature oocytes/AFC	0.73 (0.65–0.82)	0.85 (0.70–1.04)	NS	0.84 (0.61–1.17)	0.86 (0.67–1.10)	NS
Fertilization rate after ICSI (2PN/MI I)	0.72 (0.65–0.80)	0.87 (0.72–1.00)	NS	0.85 (0.67–1.00)	0.88 (0.70–1.00)	NS

Ovulasyon tetiklemesi için hCG vs. GnRH-a «Letrozole + FSH»

	hCG (n = 47)	GnRH-a (n = 27)
Yaş (yıl)	35.0 ± 4.3	33.6 ± 4.4
BMI (kg/m ²)	23.3 ± 4.2 ^a	21.5 ± 2.5 ^a
Bazal FSH (mIU/ml)	6.8 ± 2.7	8.2 ± 2.9
FSH stimülasyon süresi (gün)	9.6 ± 1.6	9.9 ± 1.6
Total gonadotropin dozu (IU)	2012.8 ± 603.5	1994.4 ± 549.1

Parametre	hCG trigger (n =47)	GnRHa trigger (n= 27)	P-value
Peak estradiol (pg/ml)	472.6 ± 345.5	695.5 ± 539.0	0.044
Endometrial kalınlık (mm)	8.8 ± 1.8	8.4 ± 2.3	NS
Total oosit	12.8 ± 7.7	16.4 ± 10.3	NS
Matür oosit	7.4 ± 4.9	11.9 ± 6.6	<0.001
Oosit maturasyon oranı (%)	68.5 ± 23.3	77.3 ± 21.1	0.049
İki-pronukleus embriyo ^a	6.3 ± 4.6	9.3 ± 5.7	0.008
Fertilizasyon (%)	74.0 ± 24.9	84.1 ± 11.1	0.027
E2 düşüş oranı 0-4. günler (%)	79.0 ± 13.4	89.5 ± 6.3	0.013
Hafif ve orta şiddette OHSS (%)	10 (21.3)	1 (3.7)	0.047

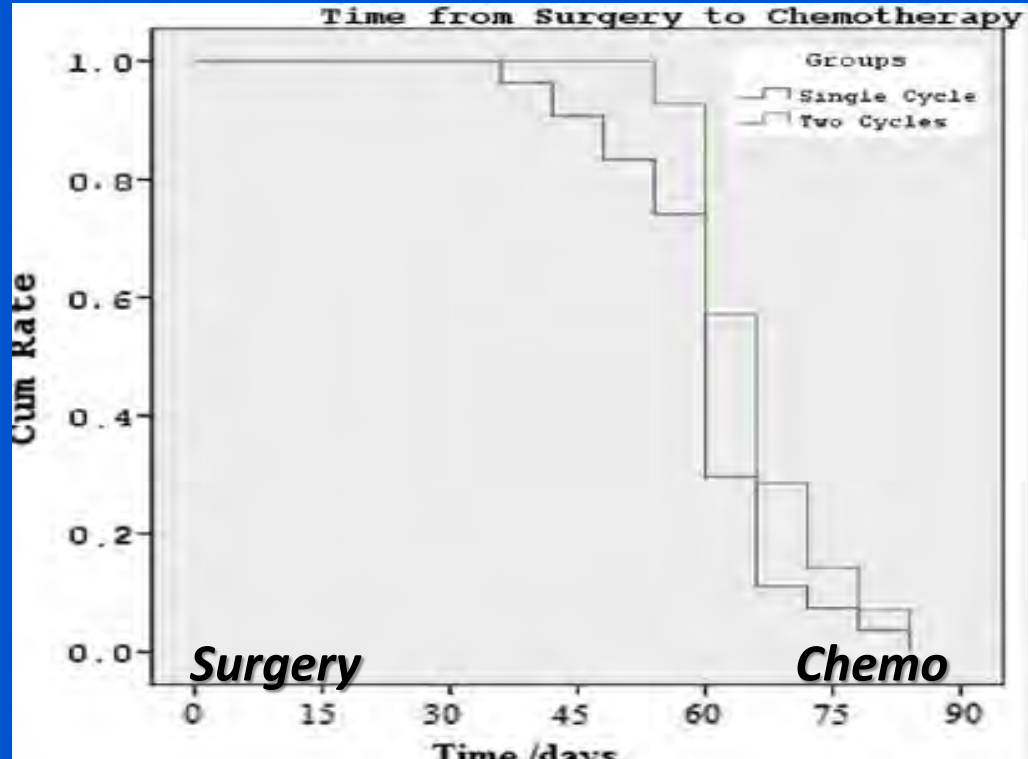
Letrozole ile Ardışık Stimulasyon

- Tek siklus stimulasyon n=61
- İki siklus stimulasyon n=17

Comparison of fertility preservation cycle outcomes of patients with breast cancer after performing two cycles.

Outcome	Single cycle (n = 61)	Two cycles (n = 17)	P value
Oocytes (n)	9.1 ± 5.2	16.1 ± 13.2	.008
Mature oocytes (n)	6.2 ± 3.0	10.3 ± 7.7	.004
Inseminated oocytes (n)	6.0 ± 3.9	9.8 ± 5.5	.002
Fertilized oocytes (n)	5.4 ± 2.3	7.4 ± 3.9	.040
Embryos (n)	3.7 ± 3.1	6.4 ± 2.9	.019

Letrozole ile Ardışık Stimulasyon

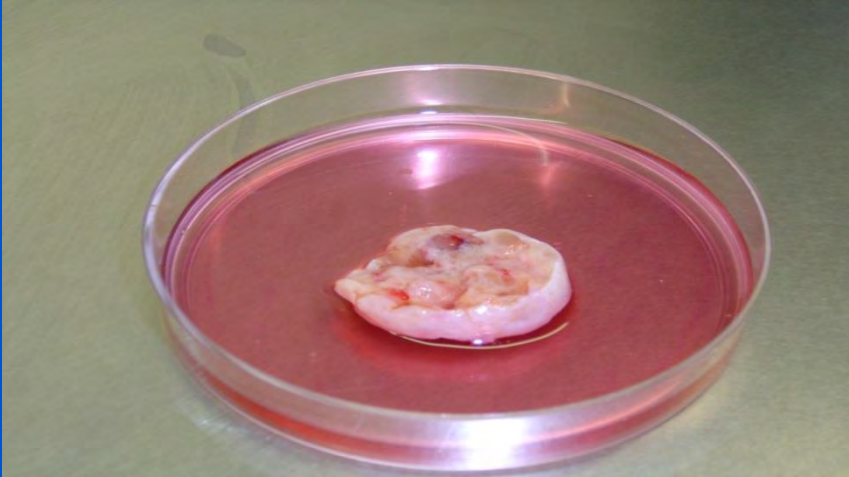


- KT, ardışık stimulyasyonda 5.7 gün ge başlanmıř ($p > 0.05$)
- Meme kanser rekürensisi iki grupta da yok (mean 58 ay)

Luteal faz immatür oosit toplanması ve in vitro maturasyon

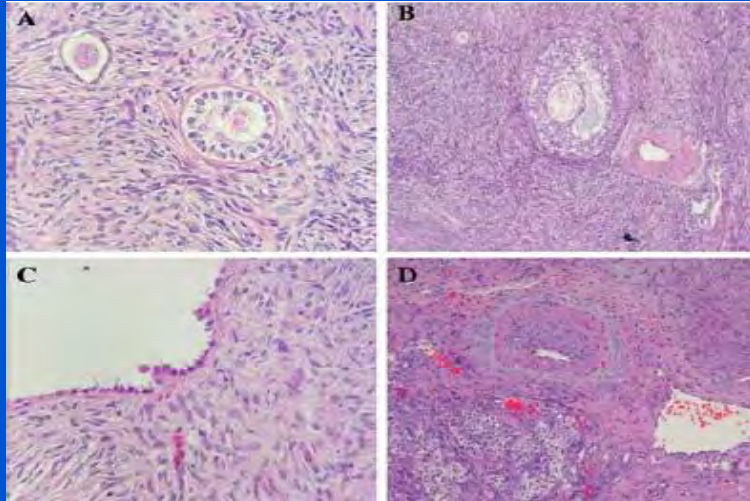
- 21,30, ve 40 yaşlarında evli olmayan hastalar
- KT öncesi fertilitite prezervasyonu
- 7,5, ve 7 immatür oosit toplandı
- İn vitro maturasyon sonrası 5,3, ve 5 MII oosit donduruldu

Ovaryan Doku Kriyoprezervasyonu

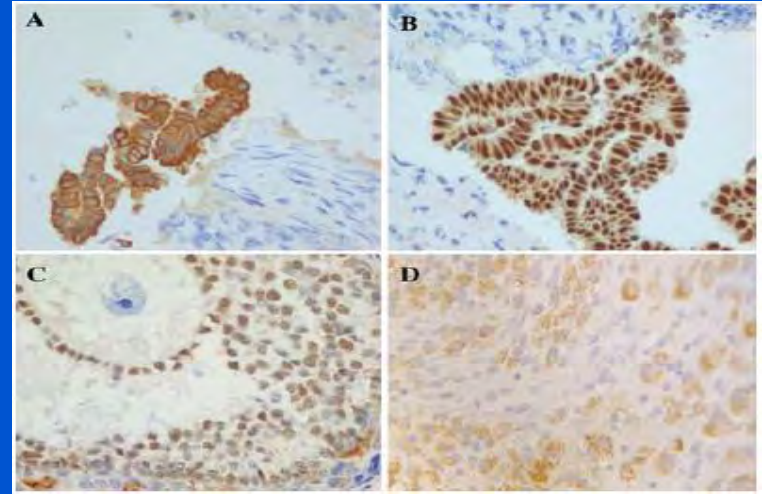


Erken Evre Meme Kanseri Ovaryan Metastaz (histoloji and IHC)

IHC



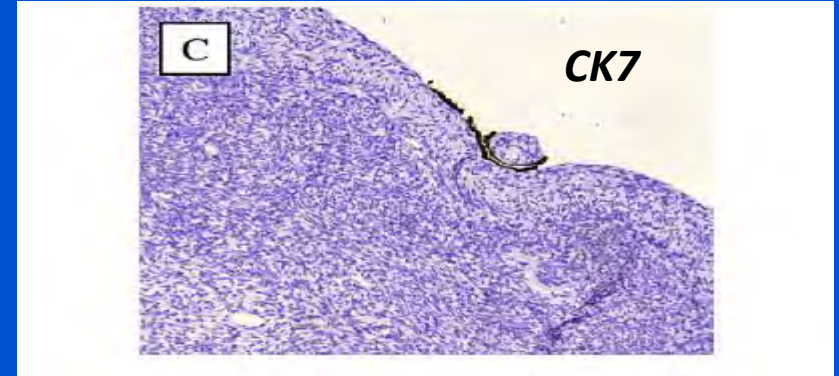
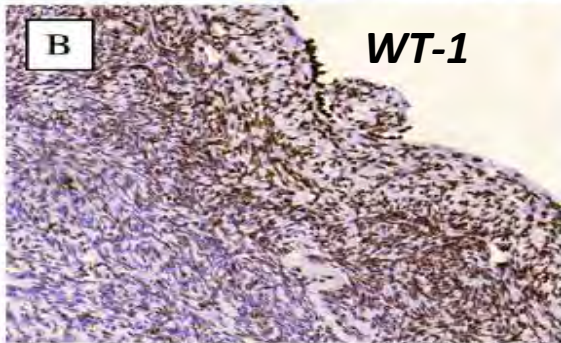
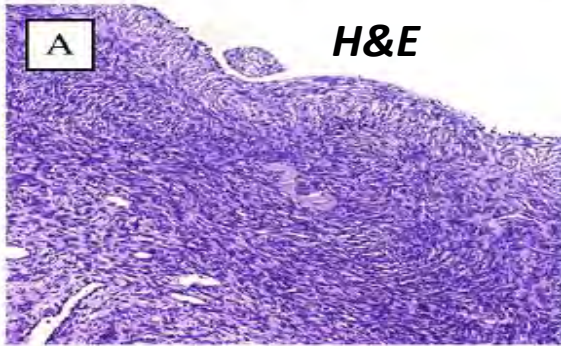
Standard histology



Ovarian tutulum: 0/63 hasta (100 kortikal parça) ovaryan kriyoprezervasyon

Erken Evre Meme Kanseri Ovaryan Metastaz (histoloji and IHC)

Ovarian cortex from one of the 51 women with breast cancer. Histologic and immunohistochemical analysis shows no signs of metastatic infiltration. (A) H&E. (B) WT-1. (C) CK-7. Magnification, $\times 10$.



Ovarian tutulum: 0/51

Non jinekolojik ovaryan metastaz 150 hastanın analizi

- Kolon 30%
- Mide 16%
- Appendiks 13%
- Meme 13%
- Pankreas 12%
- Biliar sistem 15%
- Karaciğer 4%

Overyan Doku Kriyoprezervasyonu ve In vitro Maturasyon



Combining ovarian tissue cryobanking with retrieval of immature oocytes followed by in vitro maturation and vitrification: an additional strategy of fertility preservation

Jack Y. J. Huang, M.D., Togas Tulandi, M.D., M.H.C.M., Hananel Holzer, M.D., Seang Lin Tan, M.D., M.B.A., and Ri-Cheng Chian, Ph.D.

Department of Obstetrics and Gynecology, McGill University Health Center, McGill University, Montreal, Quebec, Canada

Patient no.	Age	Cancer type	Day of menstrual cycle	Surgical procedure	No. of GV oocytes retrieved from ovarian tissue	No. of MII oocytes following IVM	Maturation rate (%)	No. of MII oocytes vitrified
1	21	Hodgkin lymphoma	2	Ovarian wedge resection	3	3	100	3
2	35	Breast	19	Oophorectomy	1	1	100	1
3	18	Hodgkin lymphoma	5	Ovarian wedge resection	4	2	50	2
4	38	Rectal cancer	14	Ovarian wedge resection and oophoropexy	3	2	67	2

Çıkarılan Over Dokusundan Oosit Eldesi

Characteristic of the patient's menstrual cycle	Patients n	Mean age \pm SEM	Mean fragments of ovarian tissue (range)	Oocytes retrieved n (range)	Mean oocytes retrieved /fragment	Mean oocytes retrieved /patients	Stage at collection (%)			IVM rate
							GV	MI	MII	
OC	11	23.1 \pm 1.3	20.1 (10-29)	38 (0-9)	0.17 \pm 0.07 ^a	3.4 \pm 1.06 ^a	71%	29%	0%	42.1%
Natural cycle FP	19	26.3 \pm 1.5	21.6 (7-32)	69 (0-15)	0.17 \pm 0.06 ^a	3.6 \pm 1.09 ^a	80%	19%	1%	27.9%
Natural cycle LP	16	27.9 \pm 1.1	18.1 (12-26)	44 (0-13)	0.15 \pm 0.05 ^a	2.8 \pm 0.83 ^a	84%	14%	2%	39.5%
Post-partum	5	31 \pm 2.2	26.3 (16-36)	33 (1-12)	0.23 \pm 0.12 ^a	6.6 \pm 1.86	91%	6%	3%	28.1%
Unknown	2	29.5 \pm 0.5	20-32	8 (0-8)	0.15 \pm 0.26	4 \pm 4	100%	0%	0%	12.5%
Prepubertal	4	9.2 \pm 1.4	31.7 (17-40)	46 (2-22)	0.36 \pm 0.28 ^b	11.5 \pm 4.27 ^b	93%	7%	0%	23.9%
Total	57	26 \pm 0.9	21.8 (7-40)	238 (0-22)	0.19	4	84%	14.7%	1.3%	31%

- Menstrüel siklustan veya OK kullanımdan bağımsız olarak etkin bir şekilde yapılabilir

**Improving fertility preservation in cancer:
ovarian tissue cryobanking followed by
ovarian stimulation can be efficiently
combined**

- Çalışma grubu : n=12 hasta
- Kontrol grubu : n=28 hasta
- Çalışma grubunda overyan dokunun yarısı çıkarılıyor

Main characteristics and stimulation outcome of patients with (study group) and without (control group) ovarian biopsy.

Parameter	Study group (n = 12) ^a	Control group (n = 28)
Age of patients (y), mean ± SD	31.1 ± 6.2	27.6 ± 5.0
Days of stimulation, mean ± SD	10.2 ± 2.6	10.6 ± 2.5
Dosage of stimulation (IU), mean ± SD	2527 ± 942	2255 ± 945
Total no. of aspirated oocytes	145	367
Aspirated oocytes per patient, n	12.1	13.1
MII-oocytes/aspirated oocytes, % ^b	65.5	83.8
No. of MII oocytes (processed for ICSI) ^c	44	66
Fertilization rate/MII oocytes, %	75.0	60.6

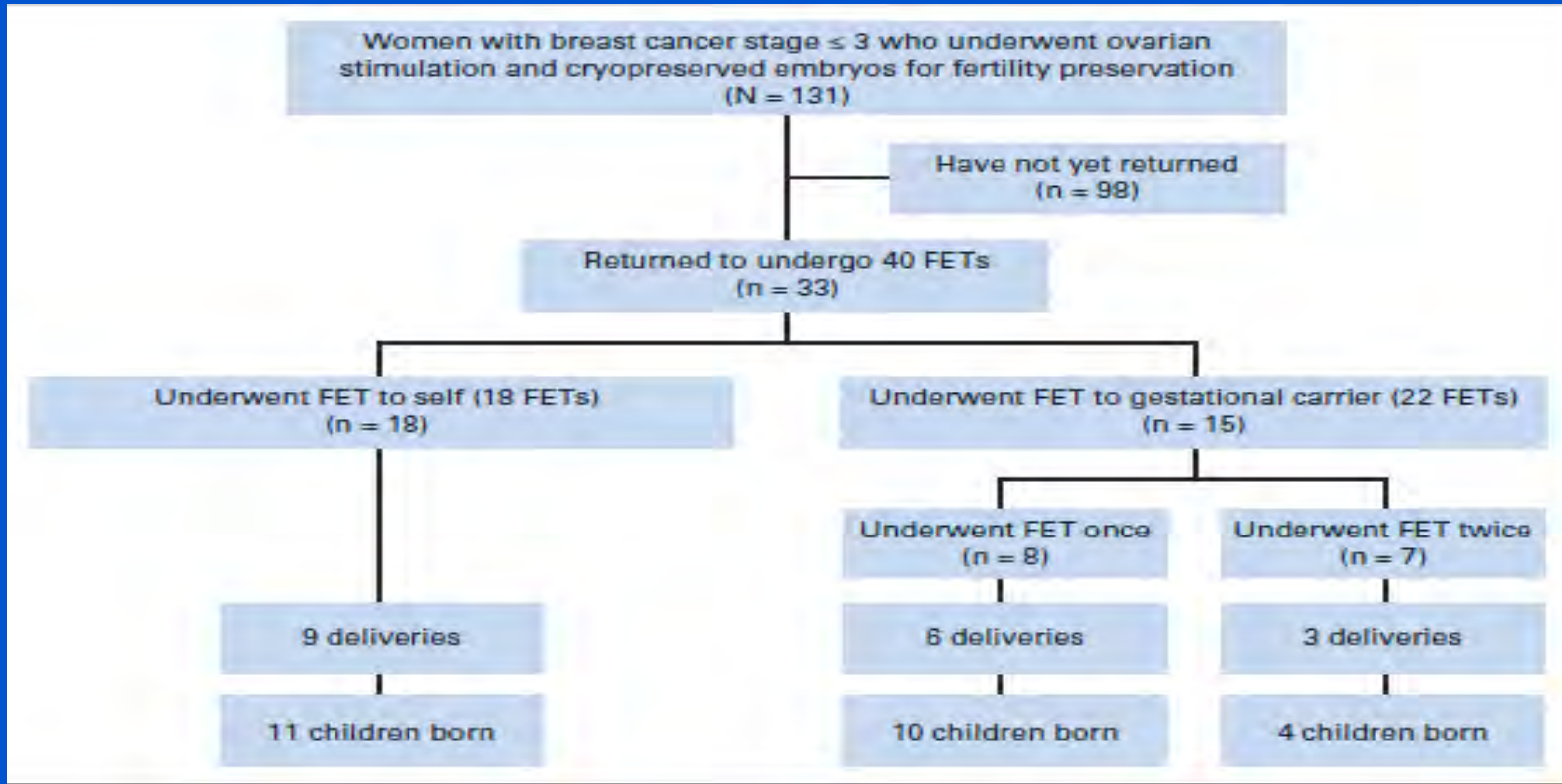
Subgroup analysis of biopsied and nonbiopsied ovaries in the study group.

Parameter	Oocyte source	
	Biopsied ovaries	Nonbiopsied ovaries
Total no. of aspirated oocytes	70	75
Aspirated oocytes per patient, n ^a	5.8	7.5
MII oocytes/aspirated oocytes, %	70.0	61.3
No. of MII oocytes (processed for ICSI) ^b	25	19
Fertilization rate/MII oocytes, %	80.0	68.4

BRCA 1 pozitif meme kanserli hastalarda fertilite prezervasyonu

- Meme kanseri tanısı almış hastalarda ilerdeki bir gebeliğin teorik olumsuz etkisi ?
- Over kanseri birlikteliği
- **BRCA mutasyonlarının aktarılmasını önlemek için PGD**
- BRCA mutasyonları taşıyan hastalarda azalmış overyan rezerv – hatalık DNA tamir mekanizması

Fertilite Prezervasyonu Sonrası Gebelik



Fertilite Prezervasyonu Sonrası Gebelik

Table 2. Comparison of Pregnancy Outcomes of \

Cycle Outcomes	FP Group		FET and Infe		Infertile Group		Transfer
	No. (%)	Mean \pm SD	No. (%)	Mean		P	
No. of cycles	40		20,545				
Embryos transferred		1.97 \pm 0.7		2.3		.014	
Implantation rate†	33 of 81 (40.7)		(26.1)			.010	
Live births per embryo transfer	18 of 40 (45.0)		(38.2)			.225	
Twinning rate	7 of 18 (38.8)		(27.4)			.189	



FARK YOK

Meme Kanseri Sonrası Spontan Gebelik ve IVF Gebelikleri

Pregnancy outcomes.			
	Spontaneous pregnancy group, <i>N</i> = 247 (%)	ART pregnancy group, <i>N</i> = 34 (%)	<i>P</i> value
Mean age at conception (years)	35.3	38.5	<0.001
Interquartile range	33–38	34–43	
Median time from diagnosis to conception (mo)	42	48	0.01
Interquartile range	24–63	36–84	
Outcomes			0.08
Miscarriage	31 (12.6)	8 (23.5)	
Induced abortion	24 (9.7)	0	
Term pregnancy	190 (76.9)	26 (76.5)	
Other*	2 (0.8)	0	
Live birth	<i>N</i> = 190	<i>N</i> = 26	0.24
Single	184 (99.8)	24 (92.3)	
Twins	6 (3.2)	2 (7.7)	

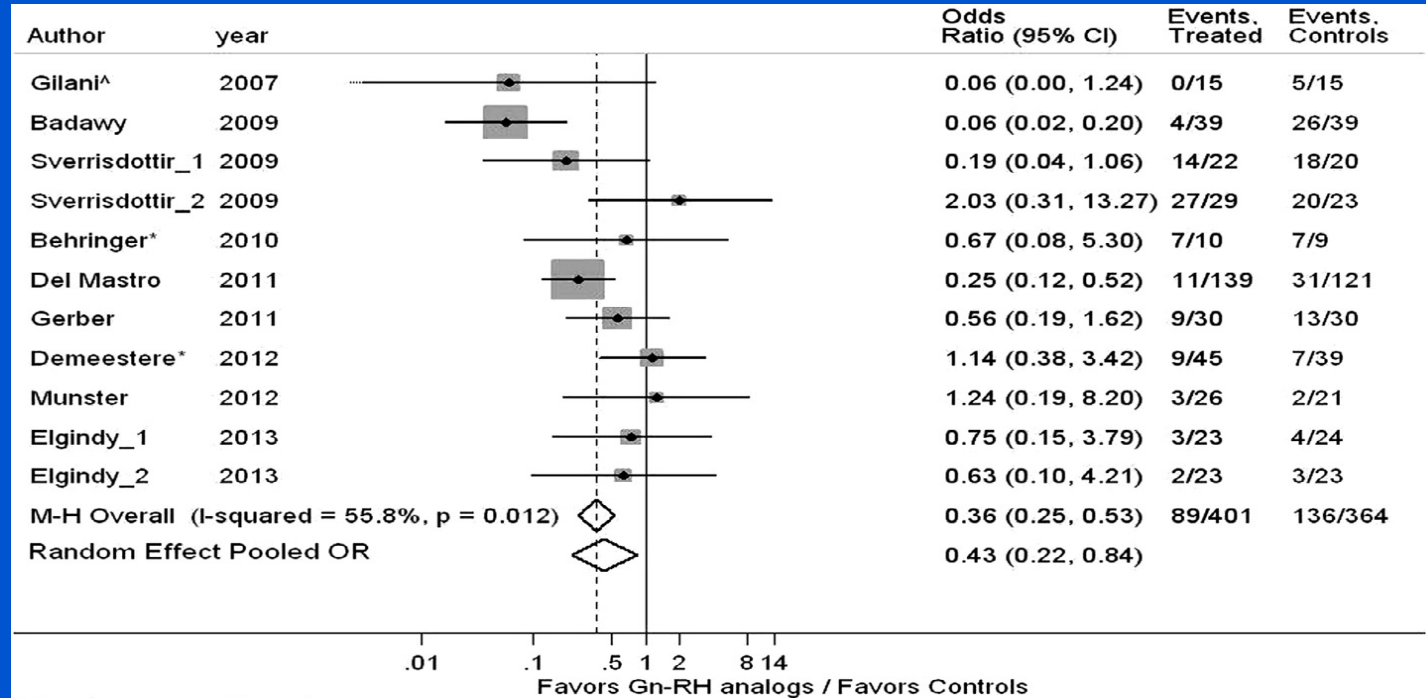
Meme Kanseri Sonrası Spontan Gebelik ve IVF Gebelikleri

Long-term survival outcome.

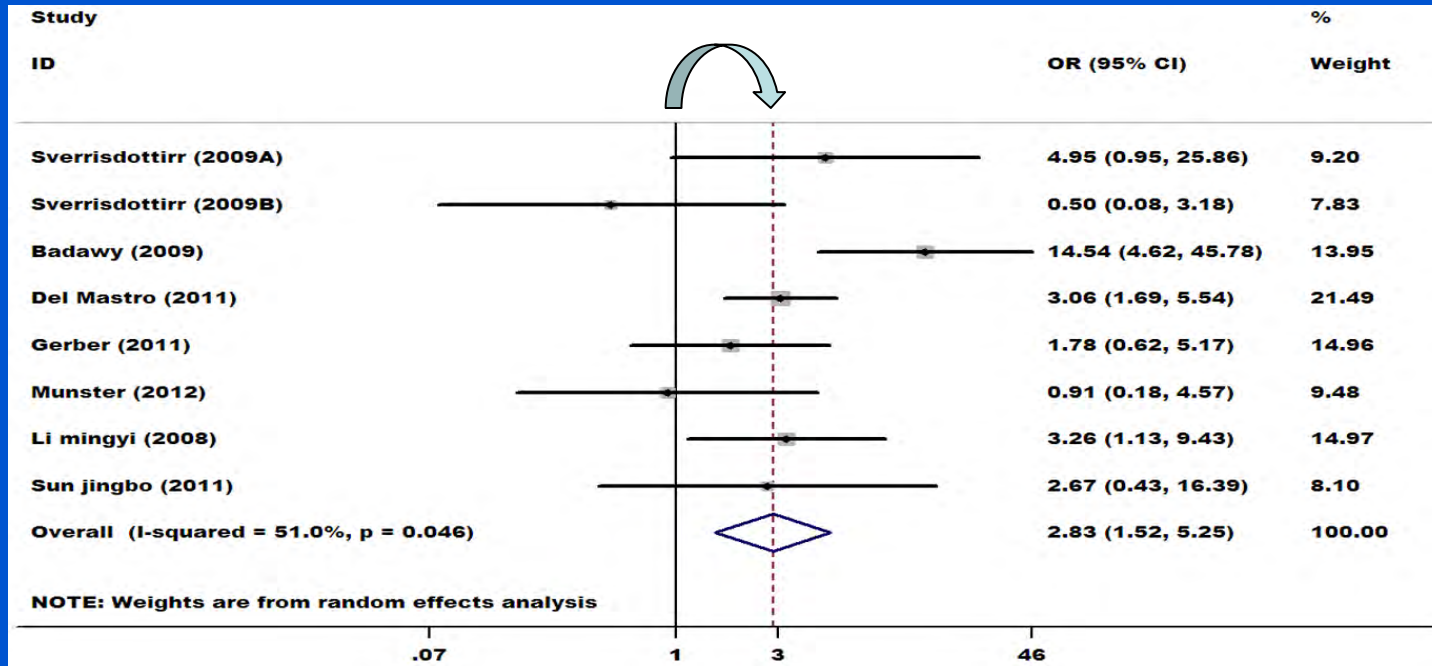
	Spontaneous pregnancy group, <i>N</i> = 173 (%)	ART pregnancy group, <i>N</i> = 25 (%)	<i>P</i> value
Interval diagnosis-last clinical FU (mo)	107	102	0.50
Interquartile range	81–131	85–123	
Interval conception-last clinical FU (mo)	63	50	0.06
Interquartile range	37–89	27–72	
Cancer related events (%)	28 (16)	2 (8)	0.54
Local recurrence	8 (4.6)	0	
Distant recurrence	10 (5.7)	2 (8)	
Contralateral breast cancer	7 (4)	0	
2nd primary cancer (non-breast)	3 (1.7)	0	
Death (<i>n</i>)	11 (6.3)	1 (4)	

ART, assisted reproductive technology; FU, follow-up; mo, months.

Kemoterapi ile birlikte GnRHa Kullanımı Spontan menstruasyon



Kemoterapi ile birlikte GnRHa Kullanımı Spontan menstruasyon

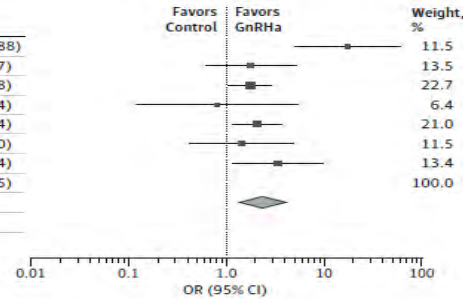


Kemoterapi ile birlikte GnRHa Kullanımı Spontan menstruasyon

Figure 2. GnRHa Use and the Resumption of Menses and Pregnancies

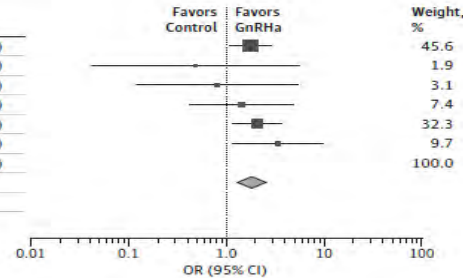
A Menses resumption after 6 mo

Source	GnRHa		Control		OR, 95% (CI)
	Events	Total	Events	Total	
Badawy et al, ³² 2009	35	39	13	39	17.50 (5.11-59.88)
Gerber et al, ²⁹ 2011	21	30	17	30	1.78 (0.62-5.17)
Del Mastro et al, ^{30,51} 2011	88	139	60	121	1.75 (1.07-2.88)
Munster et al, ²⁸ 2012	23	26	19	21	0.81 (0.12-5.34)
Song et al, ³⁷ 2013	53	89	39	94	2.08 (1.15-3.74)
Elgindy et al, ³⁵ 2013	41	46	40	47	1.44 (0.42-4.90)
Moore et al, ³⁶ 2015	61	66	54	69	3.39 (1.16-9.94)
Total		435		421	2.41 (1.40-4.15)
Total events	322		242		
Heterogeneity: $\tau^2 = 0.28$, $X^2 = 14.13$, $df = 6$ ($P = .03$); $I^2 = 58\%$					
Test for overall effect: $Z = 3.16$ ($P = .002$)					

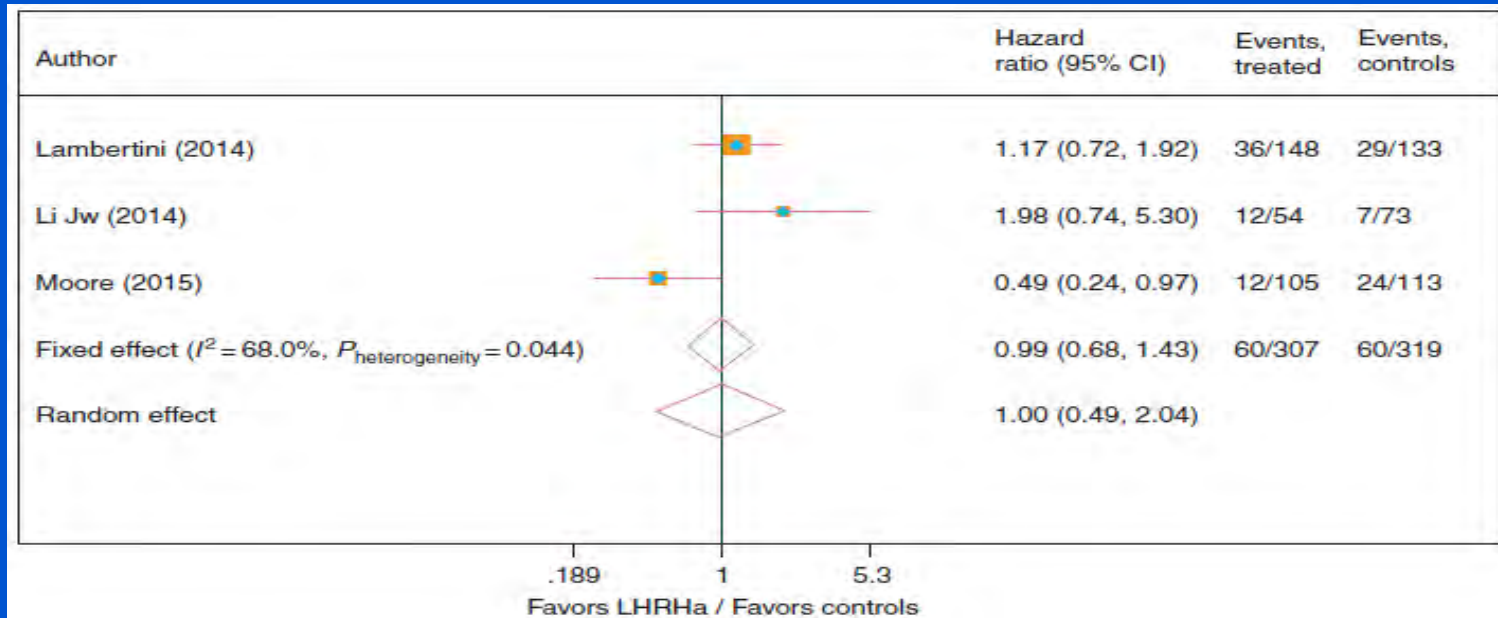


B Menses resumption after 12 to 24 mo

Source	GnRHa		Control		OR, 95% (CI)
	Events	Total	Events	Total	
Del Mastro et al, ^{30,51} 2011	88	139	60	121	1.75 (1.07-2.88)
Gerber et al, ²⁹ 2011	28	30	29	30	0.48 (0.04-5.63)
Munster et al, ²⁸ 2012	23	26	19	21	0.81 (0.12-5.34)
Elgindy et al, ³⁵ 2013	41	46	40	47	1.44 (0.42-4.90)
Song et al, ³⁷ 2013	53	89	39	94	2.08 (1.15-3.74)
Moore et al, ³⁶ 2015	61	66	54	69	3.39 (1.16-9.94)
Total (95% CI)		396		382	1.85 (1.33-2.59)
Total events	294		241		
Heterogeneity: $\tau^2 = 0.00$, $X^2 = 3.46$, $df = 5$ ($P = .63$); $I^2 = 0\%$					
Test for overall effect: $Z = 3.61$ ($P < .001$)					



Kemoterapi ile birlikte GnRHa Kullanımı Sağkalım analizi



Kemoterapi ile birlikte GnRHa Kullanımı

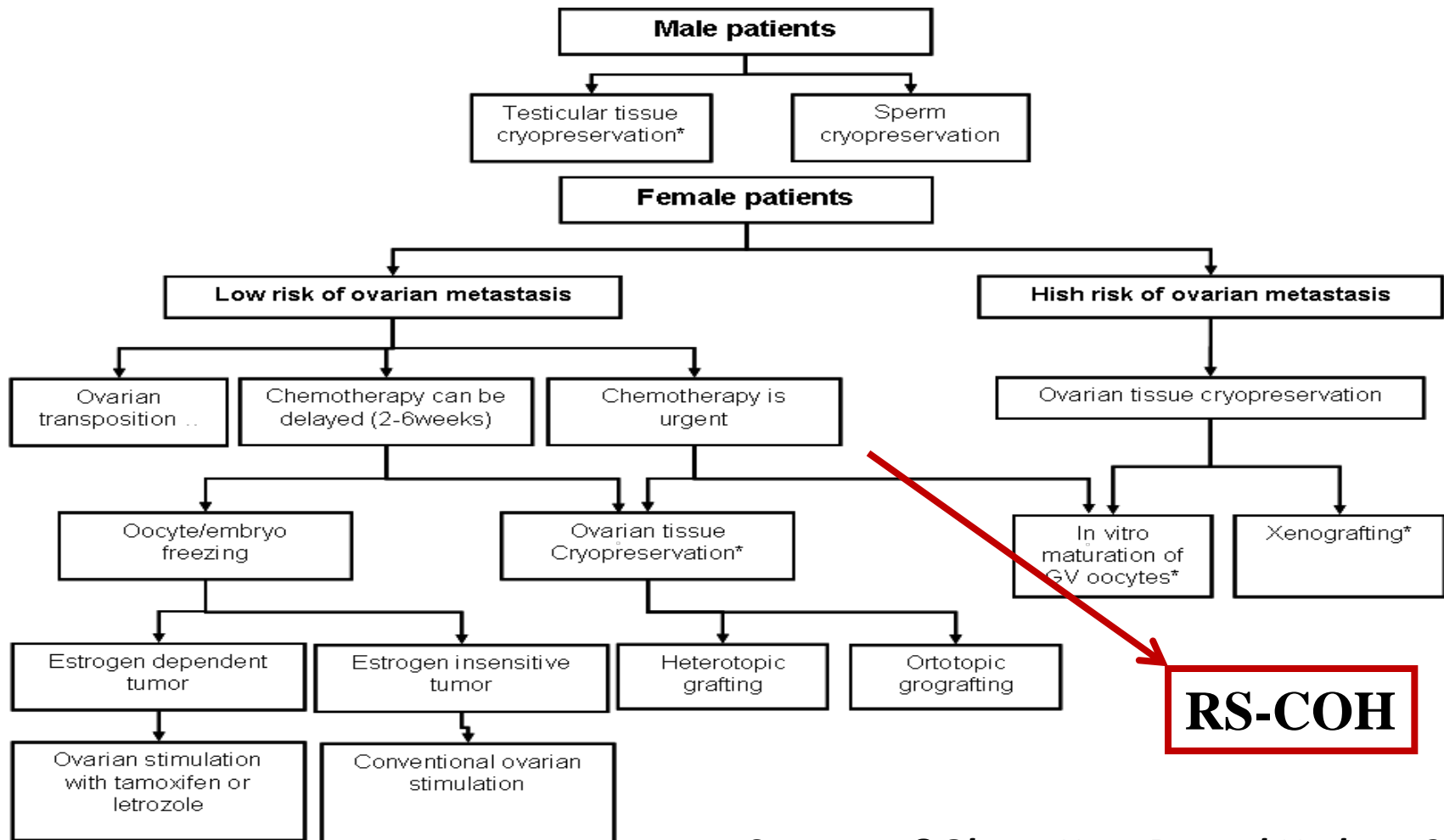
Overyan rezerv

- Bir çalışmada GnRHa kullanımı sonrasında kontrol grubuna oranlar artmış AMH düzeyleri (iyileşmiş overyan rezerv) (1.4 ± 0.35 vs. 0.5 ± 0.15 ng/mL)
- Bir yıllık takip sonrasında her iki grupta da %20 hasta POF gelişti; overyan koruma yok

Kemoterapi ile birlikte GnRHa Kullanımı

Kritik noktalar

- Elde edilen çocuğun kromozomal olarak normal olması – DNA kırıkları (Down Syndrome)
- Artmış gonadotoksisite, detoksifiye edici enzim etkisinde azalma – GST
- Extrapitüiter GnRH reseptörleri
 - Antigonadotropik, antiproliferatif, antiapoptotic etkiler
 - Kemoterapi etkisinde olası azalma !
- Overyan yetmezlik tanımında heterojenite
- Çalışmalarda artmış fertilité gösterilmemiştir



SONUÇ- I

- Hastalar fertilitate prezervasyon başarı şansını arttırmak için mümkün olan en erken zamanda referedilmelidir
- Acil durumlarda, «random start COH» etkin ve güvenilir bir şekilde kullanılabilir
- Letrozole-IVF protokolünde meme kanseri riski artmamış gözükmemektedir

SONUÇ- II

- Erken evre-lokal yayılmış meme kanserinde overyan doku dondurma güvenilir bir teknolojidir
- Yöntem başarısını arttırmak için overyan doku dondurma işlemi, embriyo-oosit dondurma ile birlikte yapılabilir
- Overyan baskılamamanın doğurganlık üzerindeki kesin etkisini belirlemek için daha geniş çaplı ve uzun takipli çalışmalara gereksinim vardır