

# MENOPAUSIA QUIRÚRGICA E INSUFICIENCIA OVÁRICA PREMATURA SECUNDARIA A PROCESOS GONADOTÓXICOS

What Does the Data Show for Premature Ovarian Insufficiency Prevention?

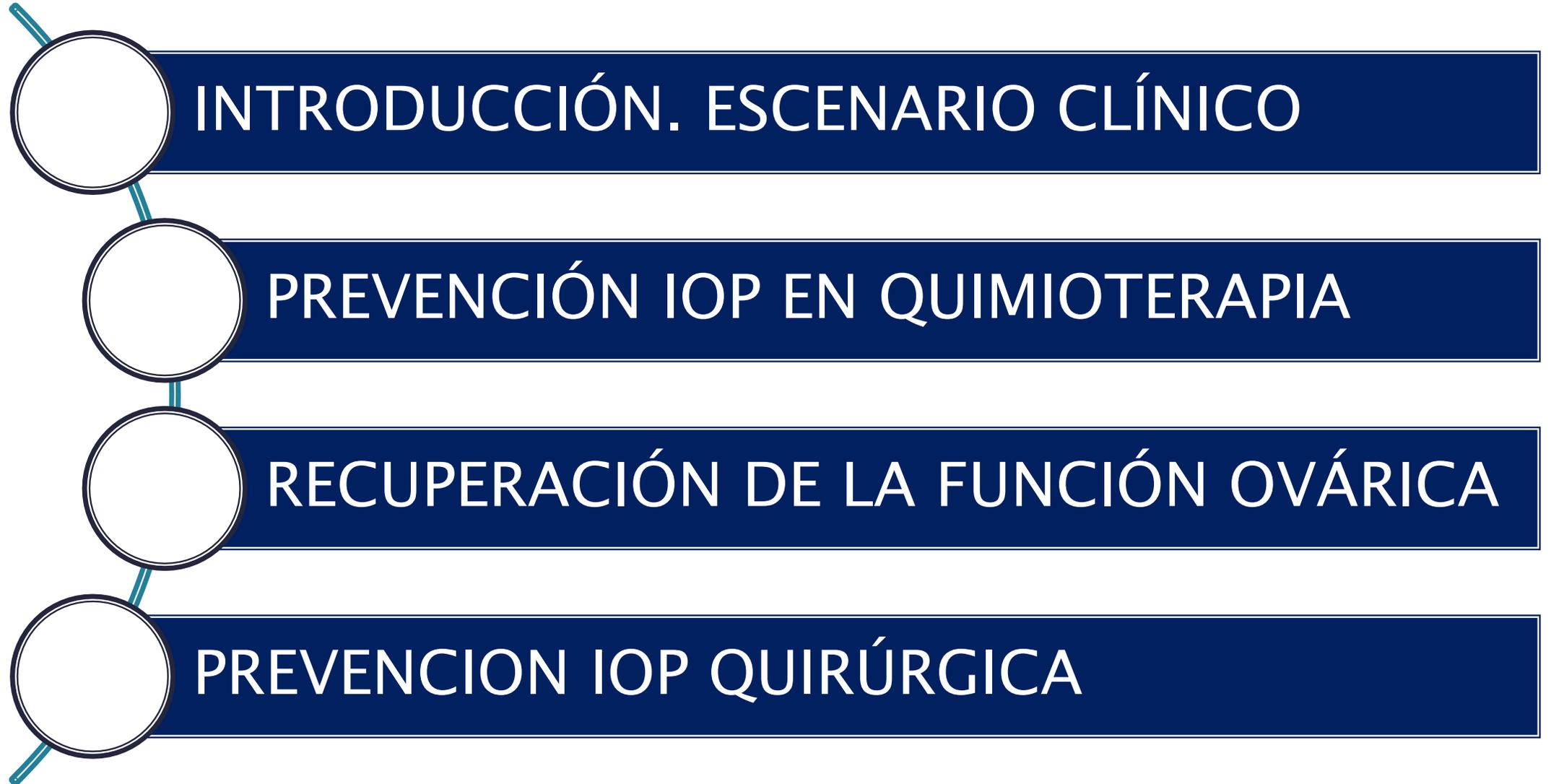


**CAMIL CASTELO-BRANCO**

Hospital Clínic de Barcelona  
Faculty of Medicine. University of Barcelona



# AGENDA



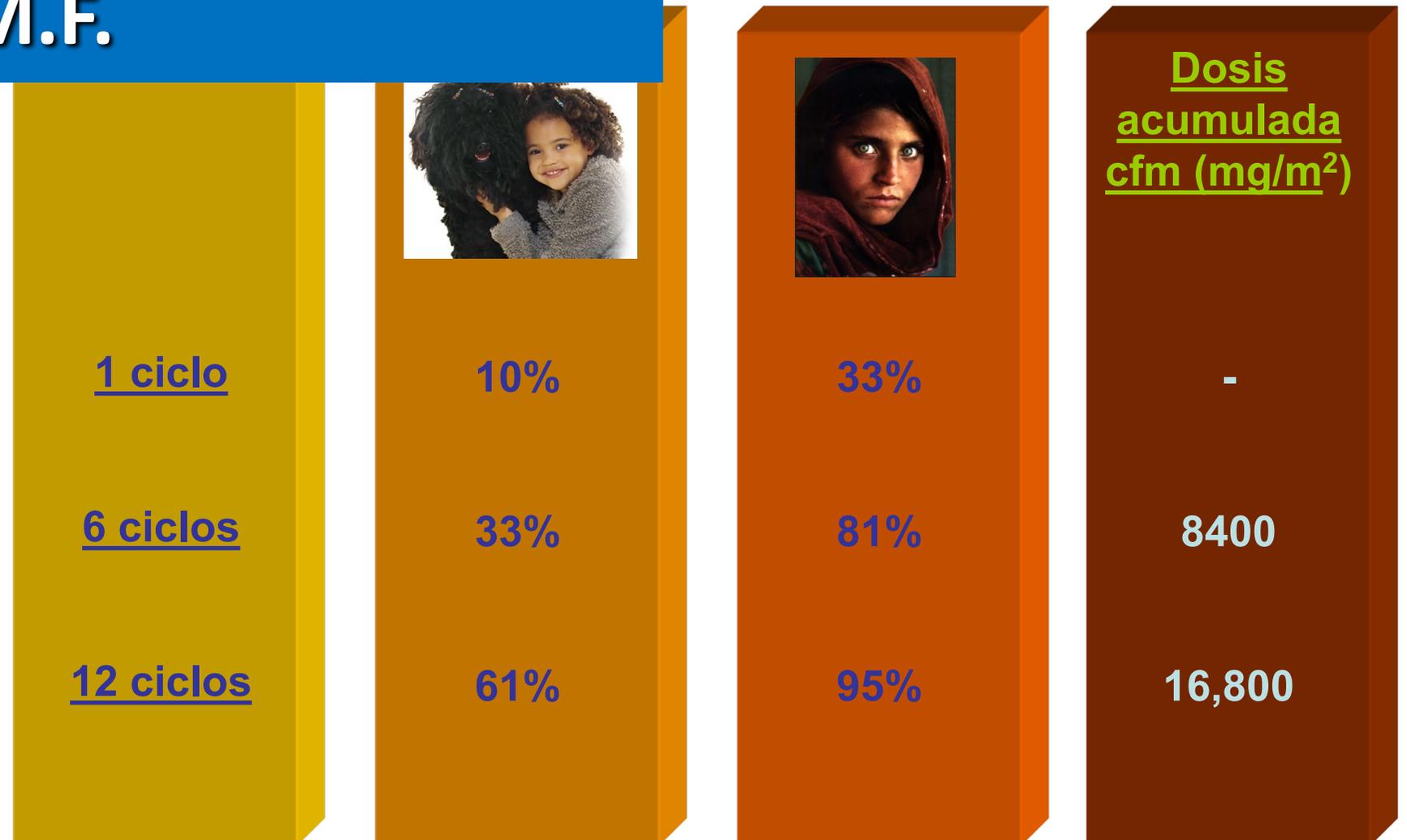
# INTRODUCCIÓN. ESCENARIO CLÍNICO

## OBVIIDADES

- QUIENES ANTES DE LOS 40 RECIBEN TRATAMIENTO QUIMIOTERÁPICO CON FÁRMACOS GONADOTÓXICOS POR PROCESOS NEOPLÁSICOS O AUTOINMUNES DESARROLLAN UNA IOP CON ELEVADA FRECUENCIA (SI TAMO, SCAT,... LA PRACTICA TOTALIDAD)
- QUIEN ES SOMETIDO A UNA OOFORECTOMIA BILATERAL PRESENTA DE MODO SUBSECUENTE UNA MENOPAUSIA QUIRÚRGICA

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## IOP TRAS C.M.F.



\*Ciclofosfamida, Metotrexate & Fluorouracilo

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## IOP TRAS 3 CICLOS PQT

	Quimioterapia	Amenorrea
Goldhirsch et al <sup>10</sup>	Classic CMF	61% (<40 yrs) 95% (≥40 yrs)
Bines et al <sup>3</sup>	AC	34%
Nabholtz et al <sup>13</sup>	FAC TAC	32.8% 51.4%
Hortobagyi et al <sup>17</sup>	Doxorubicin-based	59%
Levine et al <sup>12</sup>	CEF	51%

CMF = cyclophosphamide, methotrexate, 5FU

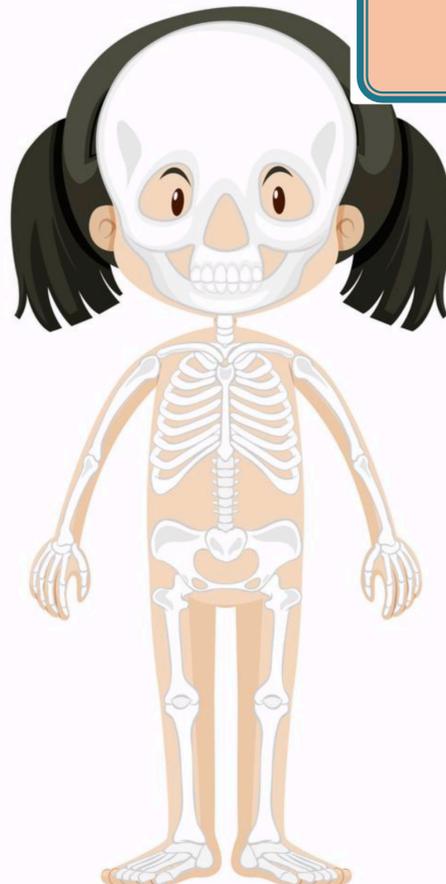
AC = doxorubicin, cyclophosphamide

FAC = 5FU, doxorubicin, cyclophosphamide

TAC = docetaxel, doxorubicin, cyclophosphamide

CEF = cyclophosphamide, epirubicin, 5FU

# ABORDAJE DE LA PACIENTE



**MORTALIDAD**

Aumento del riesgo de muerte prematura

**Urogenital**

AVV, DSF

Problemas de concentración, memoria. Aumento del riesgo de demencia

**Disfunción cognitiva**

Ansiedad, depresión, pérdida de la autoestima, disminución del bienestar y disfunción sexual

**Riesgo de enfermedades autoinmunes y tiroides**

**Riesgo de enfermedades cardiovasculares**

Alteración función endotelial, aumento de TG, Chol, LDL

**Salud ósea**

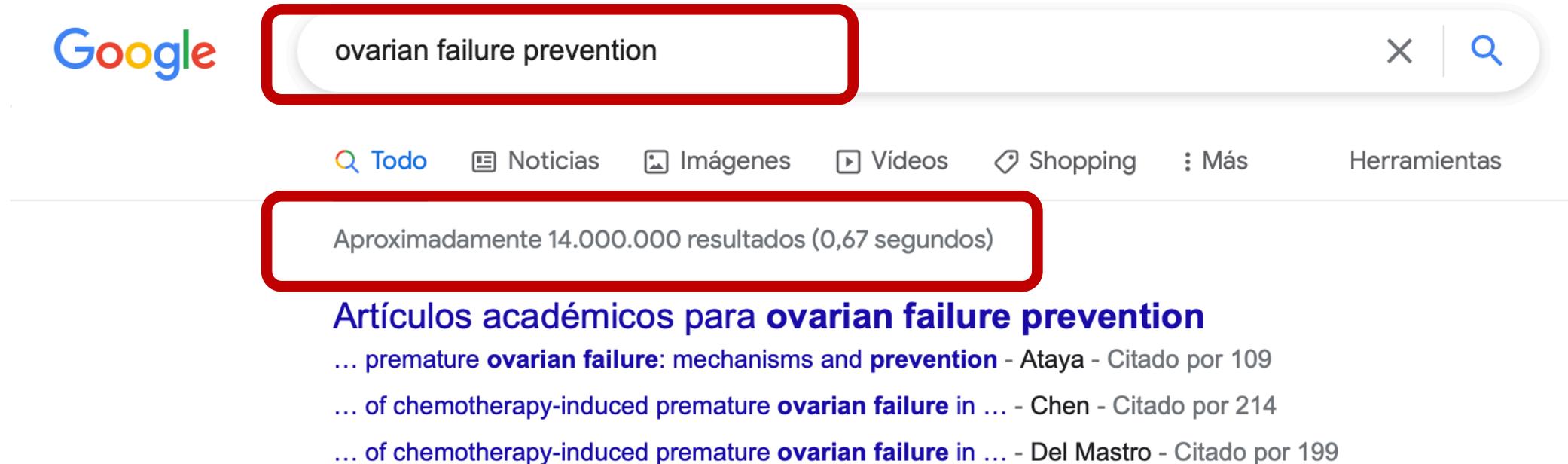
Osteopenia, osteoporosis, riesgo de fractura

**Endocrino**

Hipoestrogenismo. Esterilidad

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## PREVENCIÓN DE LA IOP



The image shows a Google search interface. The search bar contains the text "ovarian failure prevention". Below the search bar, there are navigation options: "Todo", "Noticias", "Imágenes", "Vídeos", "Shopping", "Más", and "Herramientas". The search results section shows "Aproximadamente 14.000.000 resultados (0,67 segundos)". Below this, there is a heading "Artículos académicos para ovarian failure prevention" followed by three search results:

- ... premature **ovarian failure**: mechanisms and **prevention** - Ataya - Citado por 109
- ... of chemotherapy-induced premature **ovarian failure** in ... - Chen - Citado por 214
- ... of chemotherapy-induced premature **ovarian failure** in ... - Del Mastro - Citado por 199

At this time, **there is no way to prevent primary ovarian** insufficiency. But you can take steps to protect your overall health. Women with this condition have a higher risk of bone thinning and fractures (osteoporosis), diabetes, and heart disease.

10/10/2021

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All Databases **PubMed** Nucleotide Protein Genome Structure

Search PubMed for ovarian failure   [Advanced Search \(beta\)](#)  
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Items 1 - 20 of 4314  1 of 216 [Next](#)

1 [Salazar FH, Loza EO, Lucas MT, Gutiérrez GR.](#) [Related Articles](#)

[Successful pregnancies after oocyte and embryo vitrification]  
Ginecol Obstet Mex. 2008 Feb;76(2):113-7. Spanish.  
PMID: 18798404 [PubMed - in process]

2 [Singh N, Dadhwal V, Sharma KA, Mittal S.](#) [Related Articles, Links](#)

04/03/2010

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Use OR premature ovarian insufficiency OR premature ovarian failure

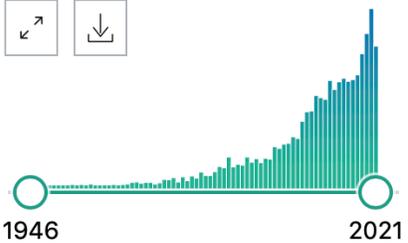
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RESULTS BY YEAR



1946 2021

**Hormone replacement therapy in young women with primary **ovarian insufficiency** and early **menopause**.**

1

Cite Sullivan SD, Sarrel PM, Nelson LM.  
Fertil Steril. 2016 Dec;106(7):1588-1599. doi: 10.1016/j.fertnstert.2016.09.046.

Share PMID: 27912889 **Free PMC article.** Review.

Primary **ovarian insufficiency** (POI) is a rare but important cause of **ovarian** hormone deficiency and infertility in women. ...To decrease morbidity associated with POI, we recommend using HRT formulations that most closely mimic normal **ovarian** hormone p ...

TEXT AVAILABILITY

10/10/2021

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Limits

Limits: published in the last 10 years, Child: 6-12 years, Adolescent: 13-18 years, Adult: 19-44 years

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All: 77 Review: 27

Items 1 - 20 of 77

Page 1 of 4 [Next](#)

[Mathelin C, Brettes JP, Diemunsch P.](#)

[Related Articles, Links](#)

[Premature ovarian failure after chemotherapy for breast cancer]

Bull Cancer. 2008 Apr 1;95(4):403-12. Review. French.  
PMID: 18495569 [PubMed - indexed for MEDLINE]

[Huser M, Crha I, Ventruba P, Hudecek R, Zakova J, Smardova L, Kral](#)

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04/03/2010

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menopause OR premature ovarian insufficiency OR premature ovarian failure

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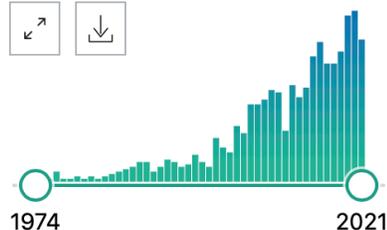
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RESULTS BY YEAR



TEXT AVAILABILITY

[Advances in human primordial follicle activation and premature ovarian insufficiency.](#)

1

Cite Ford EA, Beckett EL, Roman SD, McLaughlin EA, Sutherland JM.  
Reproduction. 2020 Jan;159(1):R15-R29. doi: 10.1530/REP-19-0201.  
Share PMID: 31376814 [Review.](#)

The excessive induction of primordial follicle activation may cause the development of **premature ovarian insufficiency** (POI), a condition characterised by **menopause** before age 40 years. ...Therefore, it is critical to further our understanding of primo ...

10/10/2021

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## PREVENCIÓN DE LA IOP

TEMA DE GRAN ACTUALIDAD

INTERÉS CRECIENTE

MOTIVO DE CONSULTA  
GINECOLÓGICA



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## TENDENCIA ACTUAL

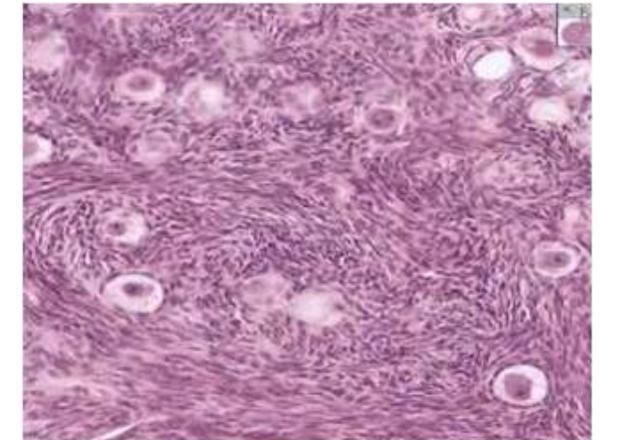
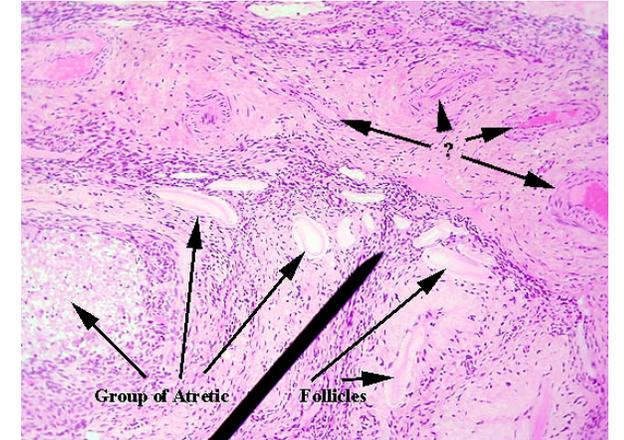
### **ESHRE Guideline: management of women with premature ovarian insufficiency<sup>†</sup>**

- ▶ HRT is indicated for the treatment of symptoms of low estrogen in women with POI
- ▶ Women should be advised that HRT may have a role in primary prevention of diseases of the cardiovascular system and for bone protection
- ▶ 17- $\beta$ estradiol is preferred to ethinyl estradiol or CEE for estrogen replacement
- ▶ Women should be informed that whilst there may be advantages to micronized natural progesterone, the strongest evidence of endometrial protection is for oral cyclical combined treatment

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## TENDENCIA ACTUAL

- ESTRADIOL:
  - a) ↓ Linfocitos T activados
  - b) Sensibiliza y diferencia las células de la granulosa, ↑ respuesta a la FSH & n de receptores LH inducidos por la FSH;
  - c) Down regulation de los receptores de FSH & LH
  - d) 46% ovulan mínimo una vez



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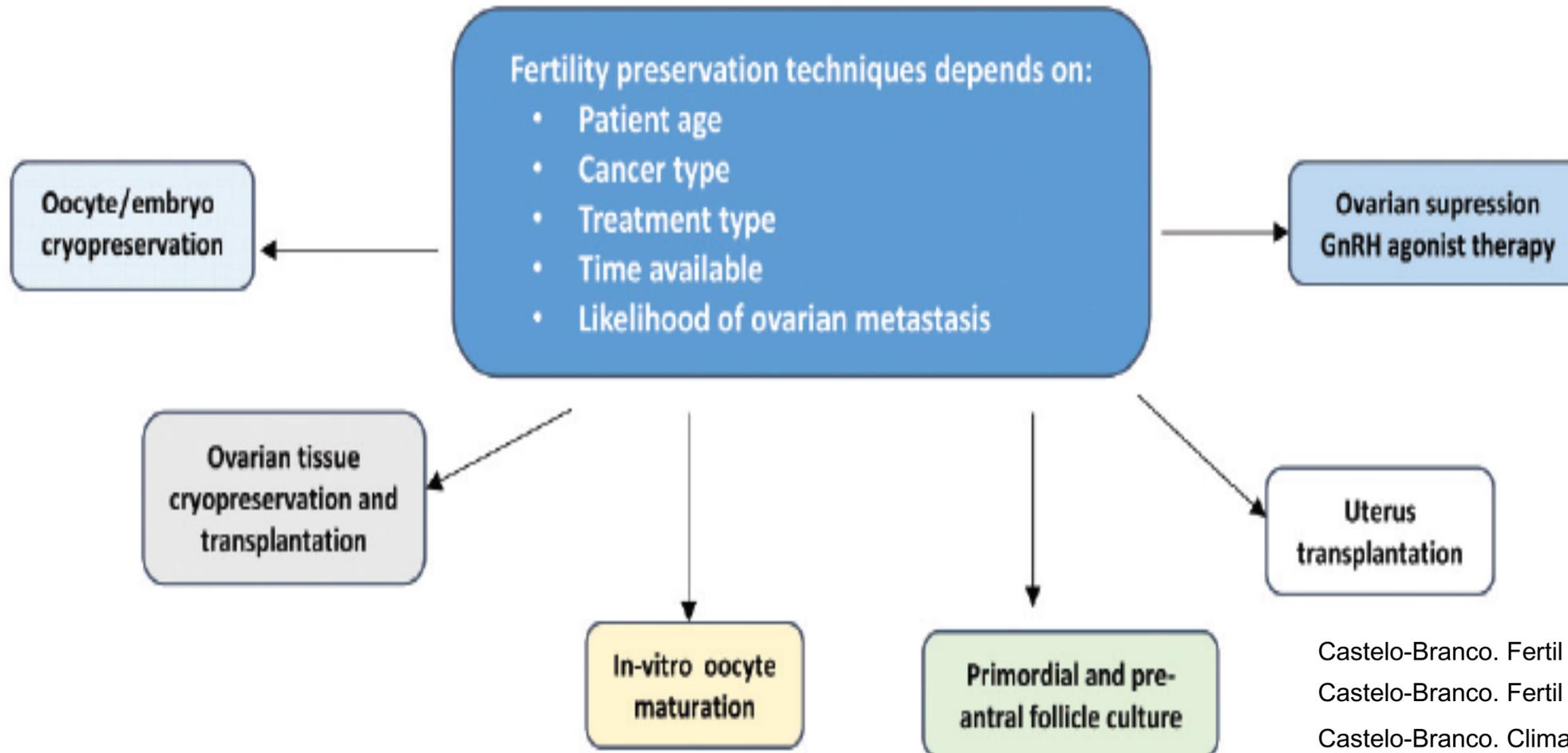
## PREVENCIÓN

- Prednisona (4x25 mg 4 semanas)
- Plasmaferesis (miastenia gravis)
- Pentoxifilina-tocoferol, Inhibidores de la apoptosis, esfingosina-1-fosfato
  
- Autotrasplante & xenotrasplante  
(problema:revascularización)

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## PREVENCIÓN

The playing field is changing...



Castelo-Branco. Fertil Steril. 2007;87(3):702-5  
Castelo-Branco. Fertil Steril. 2009;92(4):1260-3  
Castelo-Branco. Climacteric. 2016;19(6):522-5  
Zapardiel I, Hum Reprod Update 2016

Methods	¿Need ovarian stimulation?	¿Delay cancer treatment?	¿Need male partner or sperm donor?	Success rates	Special considerations
GnRHa	No	No	No		Controversial, just partially recommended in ER-negative breast cancer patient
Embryo freezing	Yes	Yes	Yes	Cumulative pregnancy rate of 66% among women with cancer	
Oocyte cryopreservation	Yes	Yes	No	Pregnancy rate per cycle of 50.2% or per embryo transfer 55.4%	
Immature oocyte cryopreservation	No	No	No		
Ovarian tissue cryopreservation	No	No	No	Pregnancy rate of 25% among women with cancer	No indication when high risk of ovarian metastases

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Portada > Salud > Cáncer

**URGENTE** Explota un coche bomba en Vitoria tras una llamada anónima a la Policía Municipal

**Un hospital de Barcelona realiza el primer trasplante de tejido ovárico en España**

- La técnica permite la recuperación de la función ovárica tras recibir quimioterapia
- El tratamiento contra el cáncer provoca en muchas pacientes una menopausia precoz

Actualizado jueves 21/12/2006 18:47 (CET)

EUROPA PRESS | ELMUNDO.ES

BARCELONA.- El Hospital de Sant Joan de Déu de Esplugues de Llobregat (Barcelona) ha conseguido con éxito recuperar la función ovárica de una paciente que había quedado estéril después de recibir tratamiento con quimioterapia y radioterapia a causa de una leucemia que sufrió hace tres años. A través de un trasplante de tejido ovárico -el primero que se realiza en España- la mujer ha recuperado su capacidad de producir hormonas ováricas y poder tener un hijo, bien por adopción



# PREVENCIÓN

*Hum Reprod* 1996 Aug;11(8):1668-73

## Fresh and cryopreserved ovarian tissue samples from donors with lymphoma transmit the cancer to graft recipients.

Shaw JM, Bowles J, Koopman P, Wood EC, Trounson AO

Laboratories for Human and Animal Reproductive Biology, Monash University, Clayton, Victoria, Australia.

Girls and young women who require ovariectomy or cancer therapy may consider having their own eggs, embryos or ovarian tissue stored (cryopreserved) for their own future use. Ovarian tissue is simple to collect and contains large numbers of germ cells. Transplantation of fresh and frozen-thawed ovarian tissue in healthy sheep and mice has resulted in normal live young. Similar techniques may be effective in the human but it is unclear whether ovarian tissue cryopreservation and grafting is suitable for ovaries from individuals with cancer or infections. If cancer cells were present in an ovary at the time of collection and survived cryopreservation and grafting they could establish cancer in the recipient. We therefore performed ovarian cryopreservation and transplantation trials using a mouse lymphoma model. This established that the lymphoma was transmitted by grafts of both fresh and frozen ovarian tissue. The normal healthy recipient mice died 9-43 days after receiving a small piece (1 mm<sup>3</sup>) of ovarian tissue from a donor with lymphoma. We conclude that ovarian tissue which is collected, cryopreserved and grafted while it contains cancer cells has the potential to spread the cancer to the graft recipient.

# PREVENCIÓN

\*Xenotransplantation of human ovarian cortex transmitted malignant cells in Hodgkin's D, and Leukemia ( *Kim et al. 2001* )

\*The majority of ischaemic damage occurs after transplantation, confirming that grafting procedures are more deleterious to follicle survival than cryopreservation (*Aubard et al, 1999*)

Bajo riesgo (<0.2%)	Riesgo moderado (0,2-11%)	Riesgo alto (>11%)
Tumor de Wilm Rabdomiosarcoma no genital Sarcoma osteogénico C. escamoso cérvix Sarcoma de Ewing	Adenocarcinoma de cérvix	
Linfoma Hodgkin Linfoma no Hodgkin	Cáncer de mama	Leucemia Neuroblastoma

ovarian transplantation```|



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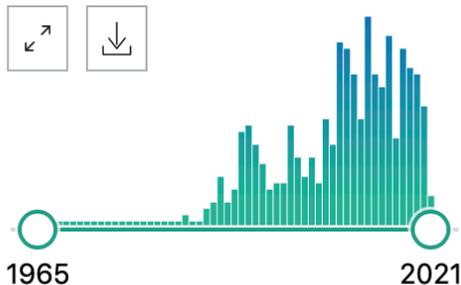
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RESULTS BY YEAR



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1

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**Transplantation of UC-MSCs on collagen scaffold activates follicles in dormant ovaries of POF patients with long history of infertility.**

Ding L, Yan G, Wang B, Xu L, Gu Y, Ru T, Cui X, Lei L, Liu J, Sheng X, Wang B, Zhang C, Yang Y, Jiang R, Zhou J, Kong N, Lu F, Zhou H, Zhao Y, Chen B, Hu Y, Dai J, Sun H.

Sci China Life Sci. 2018 Dec;61(12):1554-1565. doi: 10.1007/s11427-017-9272-2. Epub 2018 Mar 13. PMID: 29546669 Clinical Trial.

Premature **ovarian** failure (POF) is a refractory disease for clinical treatment with the goal of restoring fertility. ...Successful clinical pregnancy was achieved in women with POF after

## Análogos de la GnRH

### Use of gonadotropin-releasing hormone agonists in patients with Hodgkin's disease for preservation of ovarian function and reduction of gonadotoxicity related to chemotherapy

nancies included heterogeneous groups of women with

Received January 14, 2006; revised September 21, 2006; accepted October 6, 2006.

Reprint requests: Camil Castelo-Branco, M.D., Ph.D., Institut Clínic de Ginecologia, Obstetrícia i Neonatologia, Hospital Clínic, Villarroel 170, 08036, Barcelona, Spain (FAX: 34-932279325; E-mail: castelobranco@ub.edu).

Before they began the treatment and after each chemotherapy cycle, all patients underwent a medical history and physical examination that included clinical evaluation, gynecological examination, and laboratory tests (hematological and hormonal profile). In both groups, a pelvic ultrasound was performed and bone mineral density was assessed in the lumbar spine and hip before the start of treatment and after the end of chemotherapy.

## Análogos de la GnRH

**TABLE 2**

Bone mineral density (BMD) by hormonal profile in GnRH-a-treated and control groups.

Hormonal profile	GnRH-a group (n = 30)		Control group (n = 26)		P
	Baseline	Final	Baseline	Final	
FSH (mUI/mL)	6.34 ± 4.25	14.91 ± 18.65	5.97 ± 5.55	79.85 ± 45.83	.001
LH (mUI/mL)	9.80 ± 12.94	10.53 ± 15.19	7.55 ± 9.99	35.65 ± 40.25	.001
E <sub>2</sub> (pg/mL)	98.97 ± 126.15	59.74 ± 53.78	86.22 ± 99.78	25.71 ± 13.01	.05
T (ng/dL)	31.41 ± 9.88	41.39 ± 20.23	45.87 ± 15.9	21.54 ± 29.54	.05
SHBG (nmol/L)	73.26 ± 54.21	63.68 ± 24.56	66.29 ± 64.48	43.82 ± 31.5	NS
Androstenedione (ng/dL)	123.95 ± 51.58	127.4 ± 50.69	188.08 ± 78.52	122.7 ± 84.26	.05
DHEAS (μg/mL)	1.64 ± 0.87	1.75 ± 0.63	2.54 ± 1.25	2.01 ± 1.45	NS
Inhibin A (pg/mL)	11.78 ± 11.64	11.83 ± 6.52	10.54 ± 9.57	3.83 ± 5.87	.01
Inhibin B (pg/mL)	42.26 ± 25.59	30.45 ± 22.78	36.94 ± 21.5	15.45 ± 10.84	.05
BMD spine (g/cm <sup>2</sup> )	1,188 ± 0.104	1,171 ± 0.116	1,181 ± 0.145	1,169 ± 0.203	NS
BMD total hip (g/cm <sup>2</sup> )	1,028 ± 0.141	1,023 ± 0.165	1,031 ± 0.157	1,029 ± 0.133	NS

Note: SHBG = sex hormone-binding globulin; NS = not significant.

Castelo-Branco. Preservation of ovarian function. Fertil Steril 2007.

# PREVENCIÓN

Autores	País	Trastorno	análogo GnRH	Efecto FOP prevención	# Pacientes (%POF)	
					Treated	Control
Pacheco et al. (Gyn. Onc. 2001)	Argentina	Hematologic Polychemotx.	Leuprolide	Significant vs. Control	12 (0)	4 (100)
Mardesic et al. (2003)	Czech Rep.	Hematologic	Gonapeptyl	Rapid pit. Down-		
Kaplan et al. (2003)						
McCune et al (Arthr. Rheum. 2001)						8 (39%)
Recchia et al. (Anti-Cancer Drugs 2002)						-
Blumenfeld et al. 200						5 (>50%)
		SLE, Leukemia, Breast Ca.	GnRH-a	Control POF <7% vs > 50%		
Castelo-Branco et al (Fertil Steril 2007)	España	Hodgkin's disease	Gonapeptyl	Significant vs control POF 10% vs 77%	3/30 (10%)	20/26 (77%)

<u>IOP</u>	GnRHa	control
<u>Total</u>	181 (11%)	157 (65%)

GNRH a and premature ovarian insufficiency`````| × **Search**

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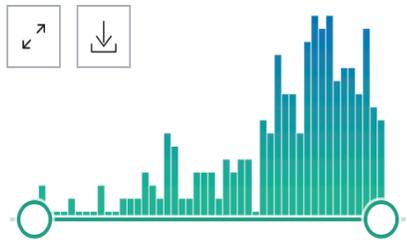
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RESULTS BY YEAR



1974

2021

TEXT AVAILABILITY

[How to Protect \*\*Ovarian\*\* Function before and during Chemotherapy?](#)

1 Arecco L, Ruelle T, Martelli V, Boutros A, Latocca MM, Spinaci S, Marrocco C, Massarotti C, Lambertini M.

Cite

J Clin Med. 2021 Sep 16;10(18):4192. doi: 10.3390/jcm10184192.

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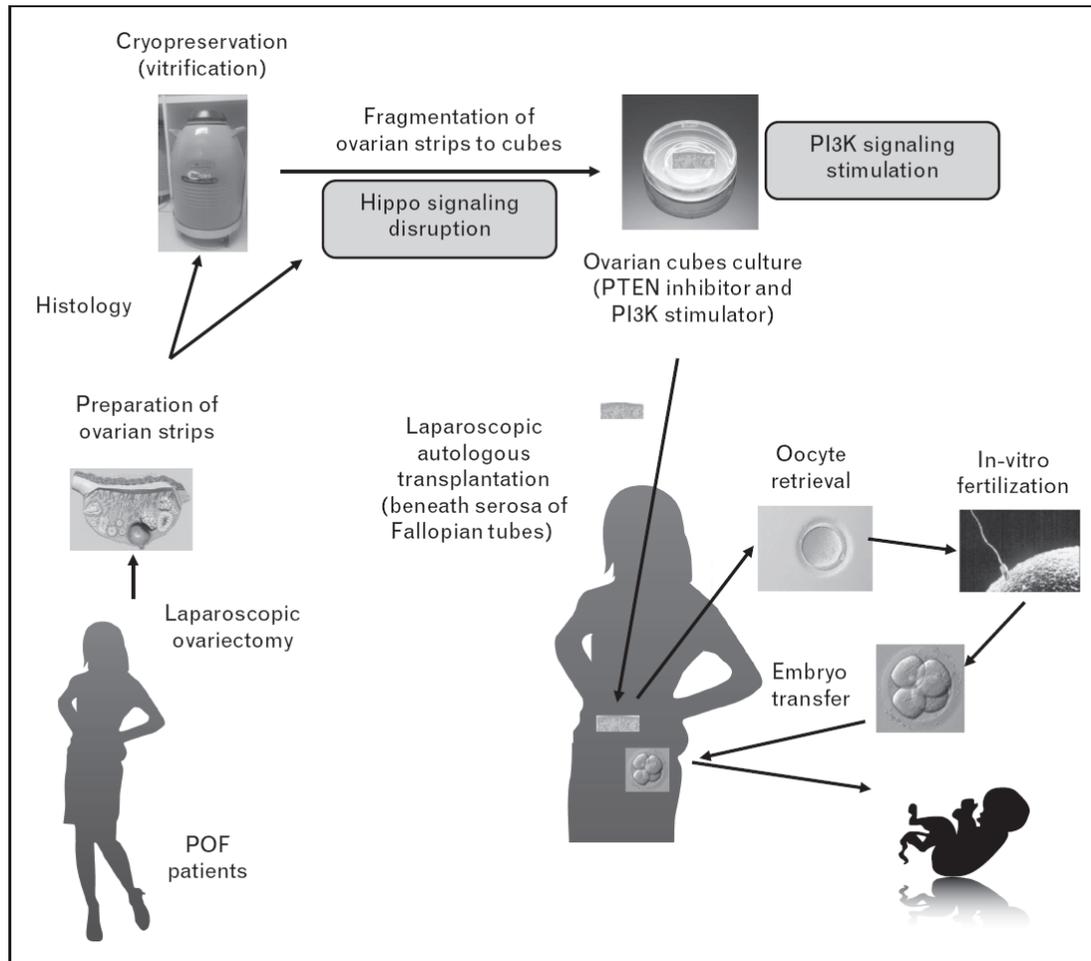
PMID: 34575299 [Free PMC article.](#) [Review.](#)

**Premature ovarian insufficiency** and infertility are among the most feared short- to long-term consequences of anticancer treatments in premenopausal patients. ...The cryopreservation of oocytes/embryos is a standard strategy for fertility preservations offere ...

[The PREgnancy and FERtility \(PREFER\) Study Investigating the Need for](#)

# RECUPERACIÓN FUNCIÓN OVÁRICA: IVA

## NOVEDADES



## Activation of dormant follicles: for premature ovarian failure?

### KEY POINTS

- The IVA approach leads to a new infertility treatment strategy for POF patients to conceive their own genetic children.
- The IVA is effective in POF patients who have residual follicles, but there is no established method to predict the presence of residual follicles before IVA treatment.
- In addition to POF patients, IVA is suitable for treating infertility in patients with diminishing ovarian reserve and in cancer survivors following germ cell-damaging therapies.

## ARTICLE

# Drug-free in-vitro activation of follicles and fresh tissue autotransplantation as a therapeutic option in patients with primary ovarian insufficiency



### BIOGRAPHY

Janisse Ferreri, MD, from Universidade do Brasil, completed her Human Reproduction Master's Degree at Universitat Autònoma de Barcelona, Spain. In 2017, Dr Ferreri received a grant for her research in ovarian in-vitro activation, and she continues her clinical practice at the Reproductive Unit, Hospital Clínic de Barcelona, Spain.

Janisse Ferreri<sup>1,\*</sup>, Francesc Fàbregues<sup>1</sup>, Josep Maria Calafell<sup>2</sup>, Roser Solernou<sup>2</sup>, Aina Borrás<sup>2</sup>, Adela Saco<sup>3</sup>, Dolors Manau<sup>1</sup>, Francisco Carmona<sup>1</sup>

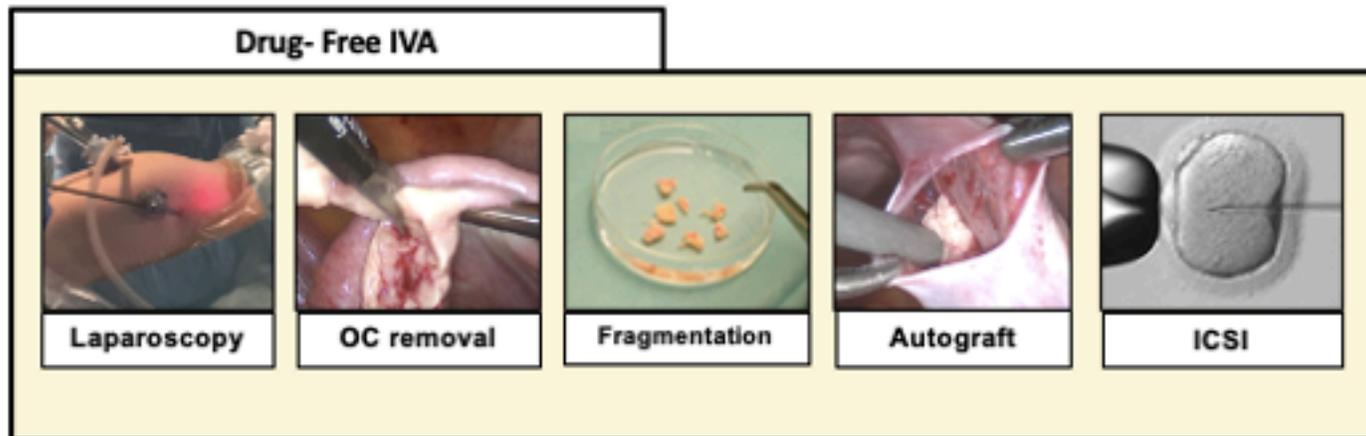
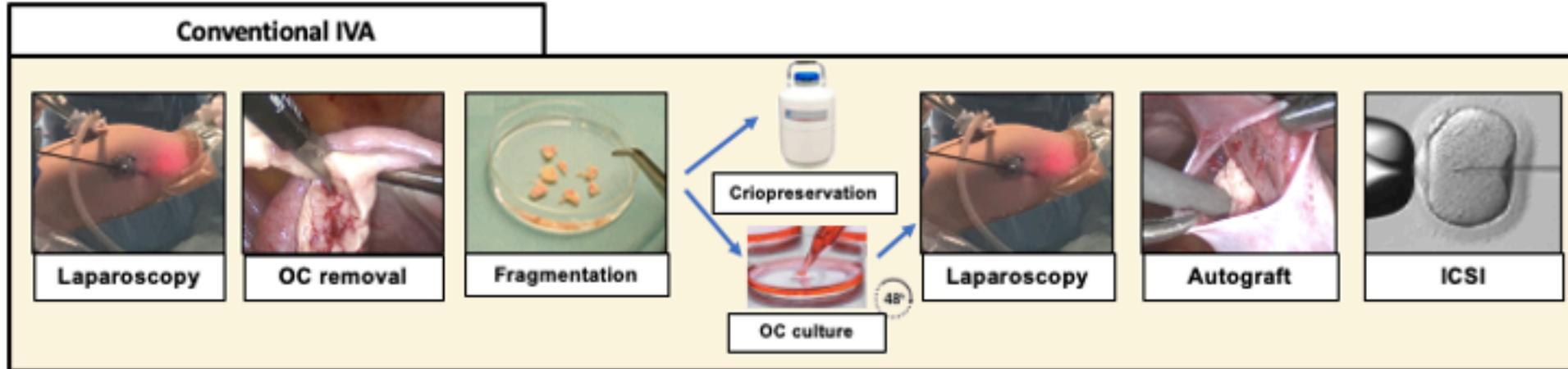
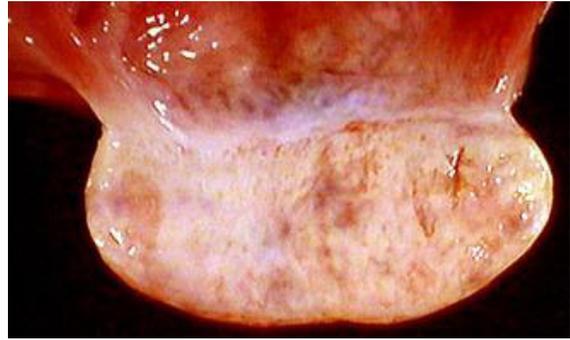


Fig 3 : Comparación entre IVA convencional (arriba) y Drug-Free IVA evita una segunda laparoscopia y cultivo del tejido  
 OC: Cortex ovárico; ICSI: Microinyección espermática

**“ DRUG-FREE ” IVA IN POI PATIENTS**

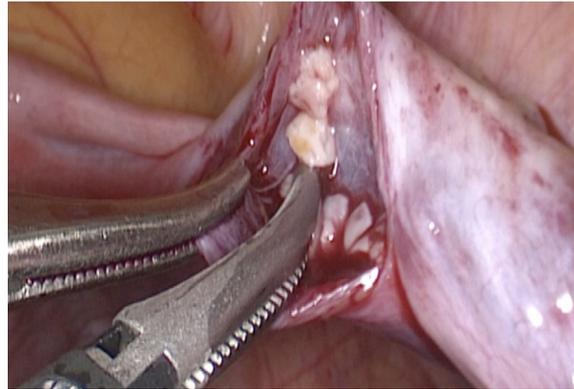
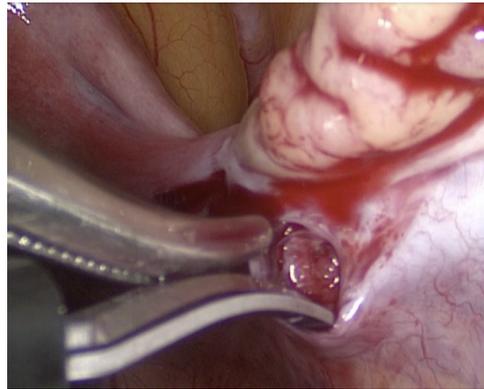


Remove ovary fragment



POI patients

Hippo Signaling Disruption  
Fragmentation of ovarian strips cubes



Return ovarian cubes in peritoneal pocket or contralateral ovary  
Gonadotropin stimulation



IVF/ICSI with sperm



**TABLE 1 CLINICAL CHARACTERISTICS OF PATIENTS WITH PRIMARY OVARIAN INSUFFICIENCY, OVARIAN ACTIVITY AND PREGNANCY OUTCOMES AFTER DRUG-FREE IN-VITRO ACTIVATION OF FOLLICLES**

<b>Number</b>	<b>Age (years)</b>	<b>FSH (mIU/ml)</b>	<b>Anti-Müllerian hormone (ng/ml)</b>	<b>Duration of amenorrhoea (years)</b>	<b>Residual follicles by biopsy</b>	<b>Follicle development</b>	<b>Pregnancy</b>
1	32	88.7	0.02	2	No	Yes	Yes (live birth)
2	30	40.3	0.10	3	No	Yes	
3	33	71.5	0.02	1	Yes	Yes	Yes (preterm birth/perinatal death)
4	33	69.0	0.03	3	Yes	No	
5	33	73.3	0.02	9	No	No	
6	33	69.4	0.01	4	No	No	
7	35	37.3	0.04	1	Yes	Yes	
8	34	96.7	0.02	1	No	No	
9	35	81.0	0.02	2	No	Yes	Yes (live birth)
10	35	36.1	0.11	1	No	Yes	Yes (pregnancy ongoing)
11	29	35.0	0.02	1	No	No	
12	35	43.6	0.02	1	No	No	
13	33	57.6	0.01	11	No	No	
14	29	78	0.04	10	No	Yes	

Yes/live birth

# DRUG-FREE IVA IN POR PATIENTS

Human Reproduction, pp. 1–13, 2019  
doi:10.1093/humrep/dez152

human  
reproduction

ORIGINAL ARTICLE *Infertility*

## Biopsying, fragmentation and autotransplantation of fresh ovarian cortical tissue in infertile women with diminished ovarian reserve

Stine Aagaard Lunding<sup>1,\*</sup>, Susanne Elisabeth Pors<sup>2</sup>,  
Stine Gry Kristensen<sup>2</sup>, Selma Kloeve Landersøe<sup>1</sup>,  
Janni Vikkelsø Jeppesen<sup>1</sup>, Esben Meulengracht Flachs<sup>3</sup>, Anja Pinborg<sup>4</sup>,  
Kirsten Tryde Macklon<sup>1</sup>, Anette Tønnes Pedersen<sup>1,5</sup>,  
Claus Yding Andersen<sup>2</sup>, and Anders Nyboe Andersen<sup>1</sup>

1 RBMO VOLUME 00 ISSUE 0 2019

RBMO



ARTICLE

Drug-free in-vitro activation of follicles for infertility treatment in poor ovarian response patients with decreased ovarian reserve

Kazuhiro Kawamura<sup>1,\*</sup>, Bunpei Ishizuka<sup>2</sup>, Aaron J.W. Hsueh<sup>3</sup>

Not increased AFC and AMH after 10 weeks. However in 12 of 20 patients pregnancies were achieved

In 9 of 11 patients increased AFC. 16 embryo transfers were performed in 5 patients leading one live birth, 2 ongoing pregnancies and one miscarriage. One pregnancy was achieved spontaneously

Human studies involving IVA and Drug-Free IVA in POI and POR patients							
Author	Ref.	Procedure type	No.of patients	Inclusion criteria	Follicle development/ Total	Pregnancies/ Total	Live birth:Total
Kawamura 2013; Suzuki 2015	10,11	IVA	37	POI	9/37	3/37	2:37
Zhai 2016	43	IVA	14	POI	6/14	1/14	1/14
Pellicer 2017 **		OFFA (Drug-Free IVA)	14	POI		3/14	3/14
Zhang 2018	46	Biopsy/Scratch	80	POI	11/80	1/80	1:80
Fabregues 2018, Ferreri 2020	13,14	Drug-Free IVA	14	POI	7/14	4/14	4/14
Mahajan 2019	45	Drug-Free IVA	1	POI	1/1	–	–
Kawamura 2020	15	Drug-Free IVA	11	POR	9/11*	5/11	2:11 2 ongoing 1 miscarriage

**19**

**15**

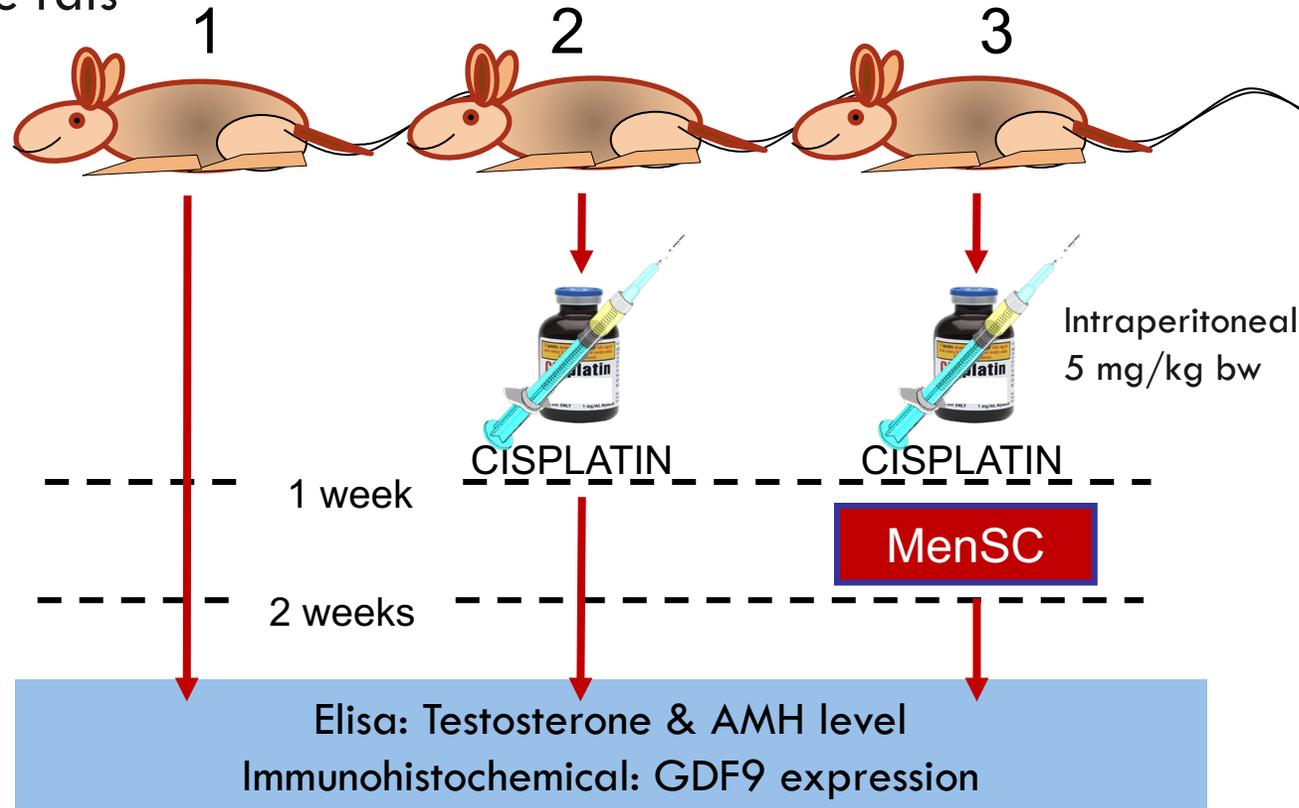
\*: Patients increased AFC; \*\* Unofficial data are from conference presentations of stated scientists

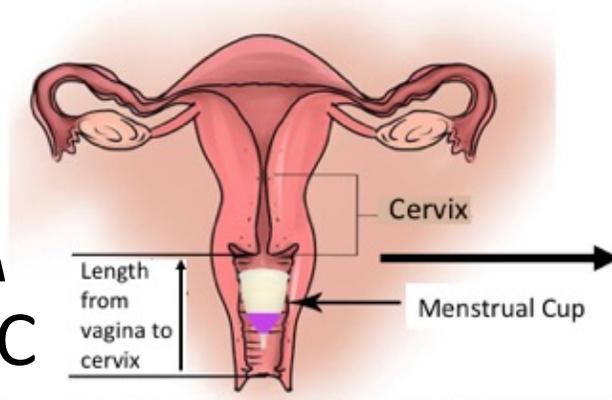
POI: Primary ovarian insufficiency; POR:Poor ovarian response; IVA: In vitro activation; OFFA: Ovarian fragmentation for follicular activation

# RECUPERACIÓN FUNCIÓN OVÁRICA: SC

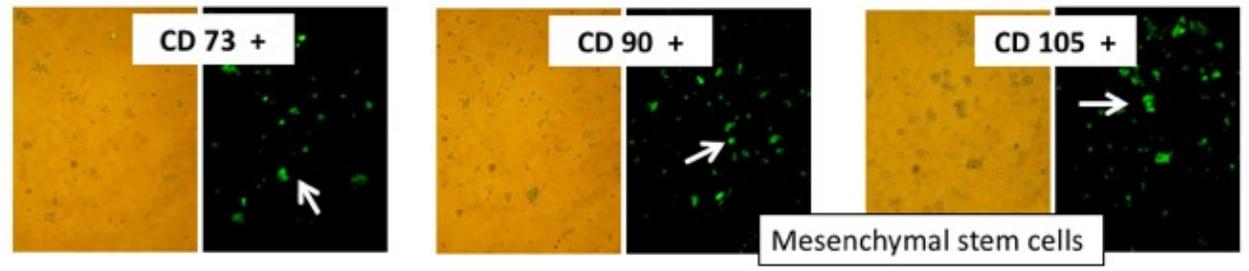
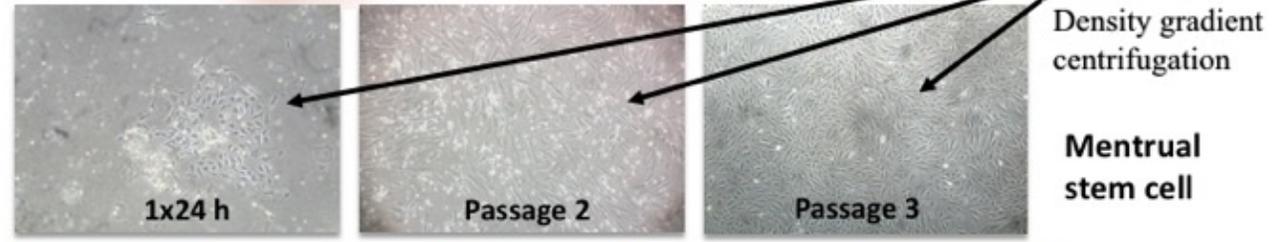
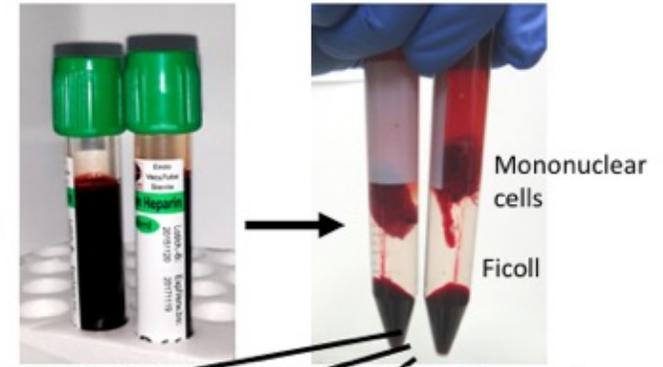
Methods:

36 female rats

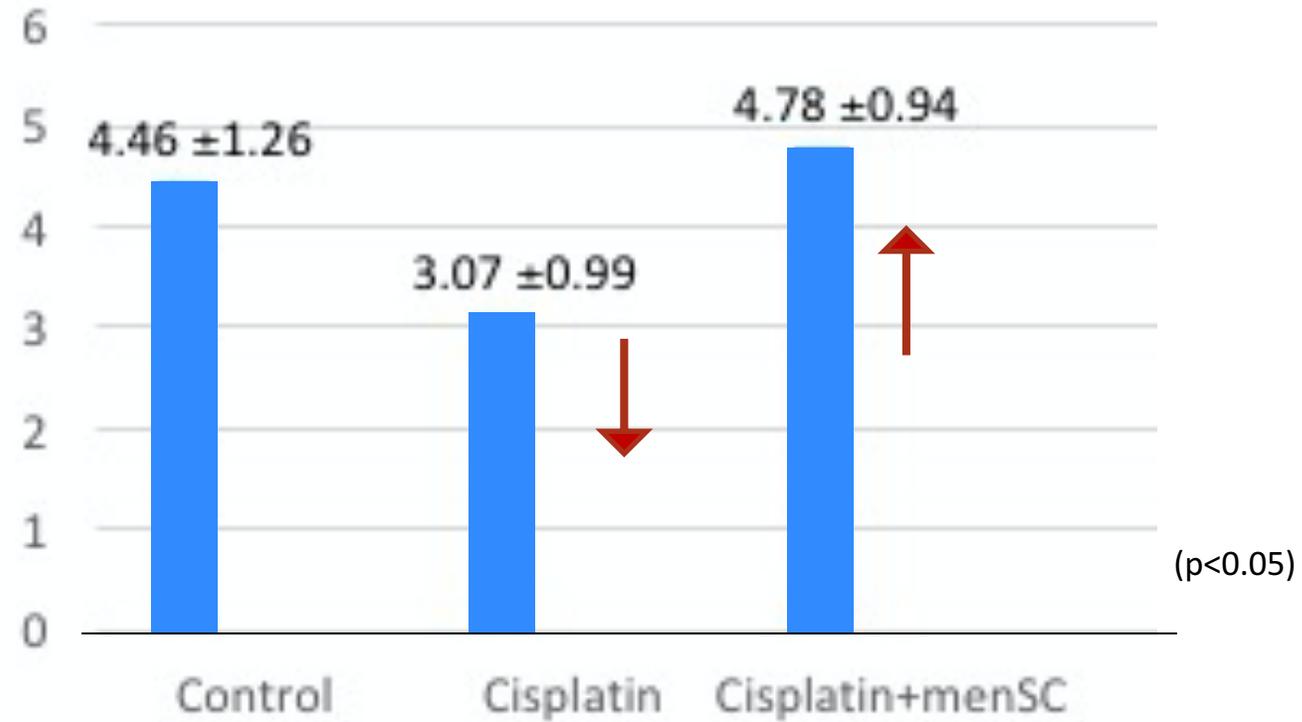




# Methods:

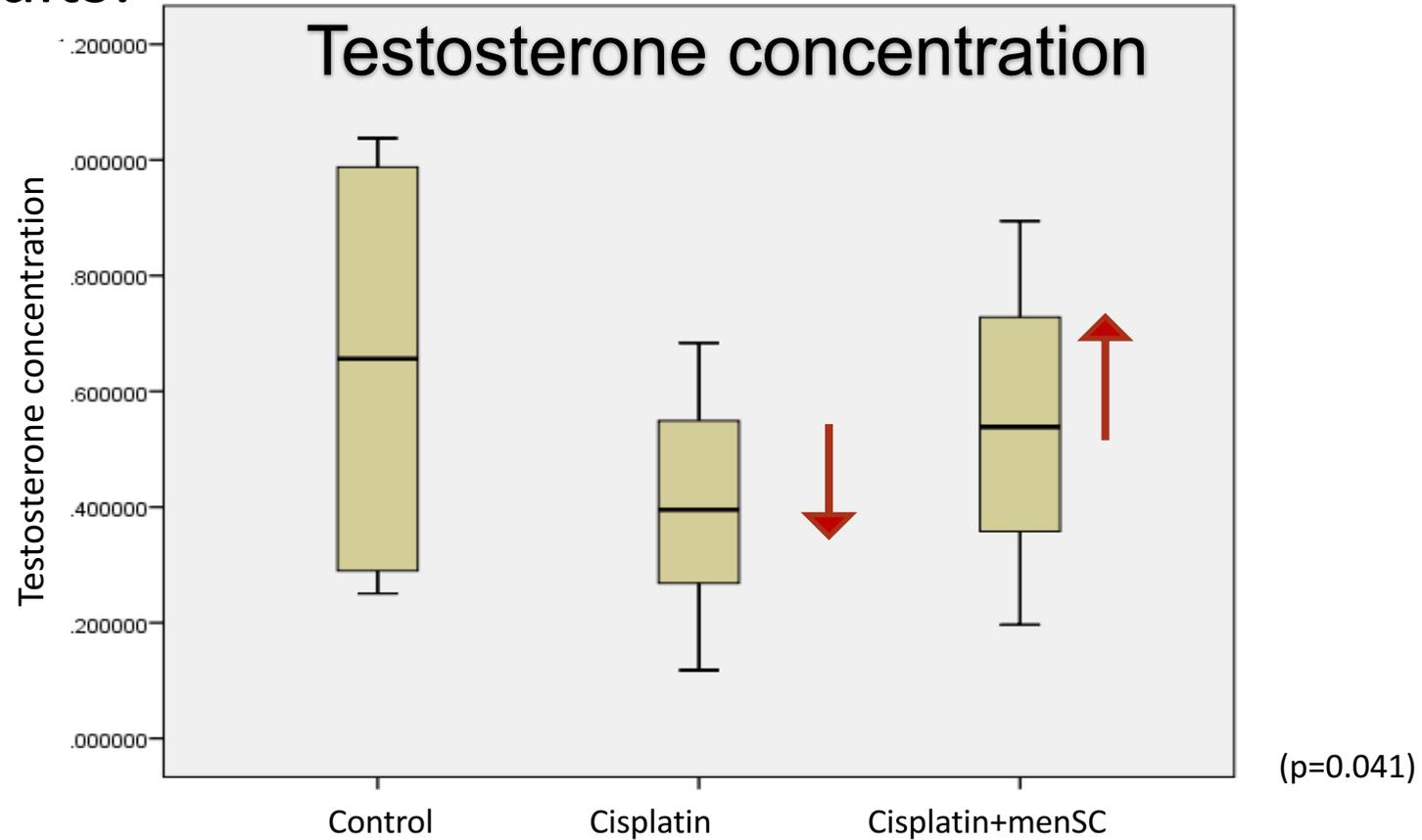


Results: AMH concentration (ng/ml)



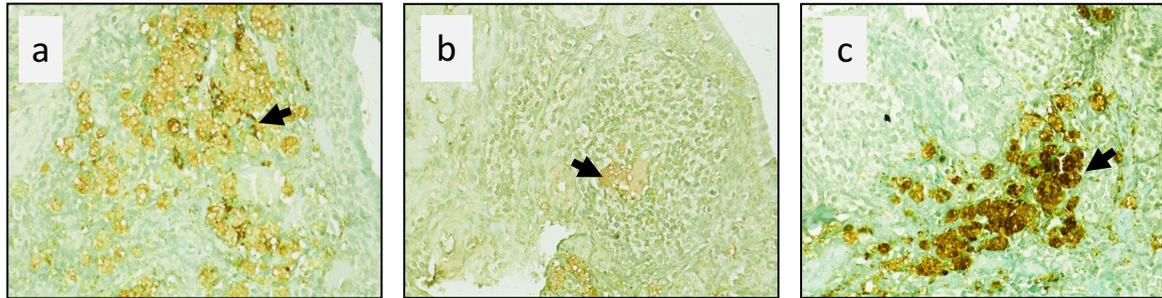
There was a significant difference of AMH concentration between 3 groups

# Results:



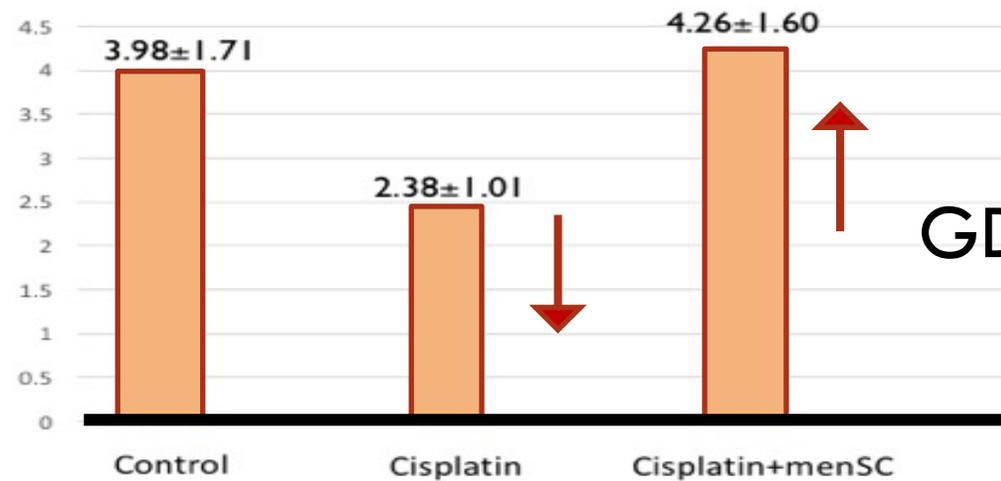
There was a significant difference of T concentration between 3 groups

# Results:



There was a significant difference of GDF9 expression between 3 groups

( $p < 0.05$ )



GDF9 expression

## Results:

### Ovarian Follicle number

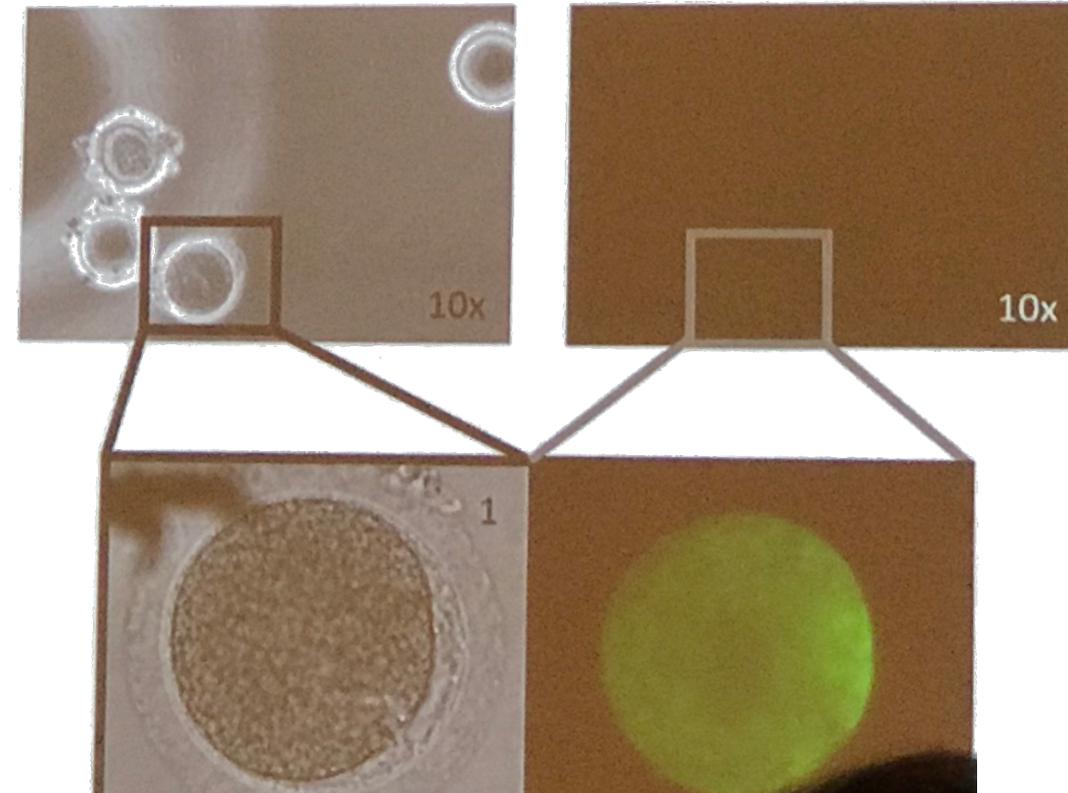
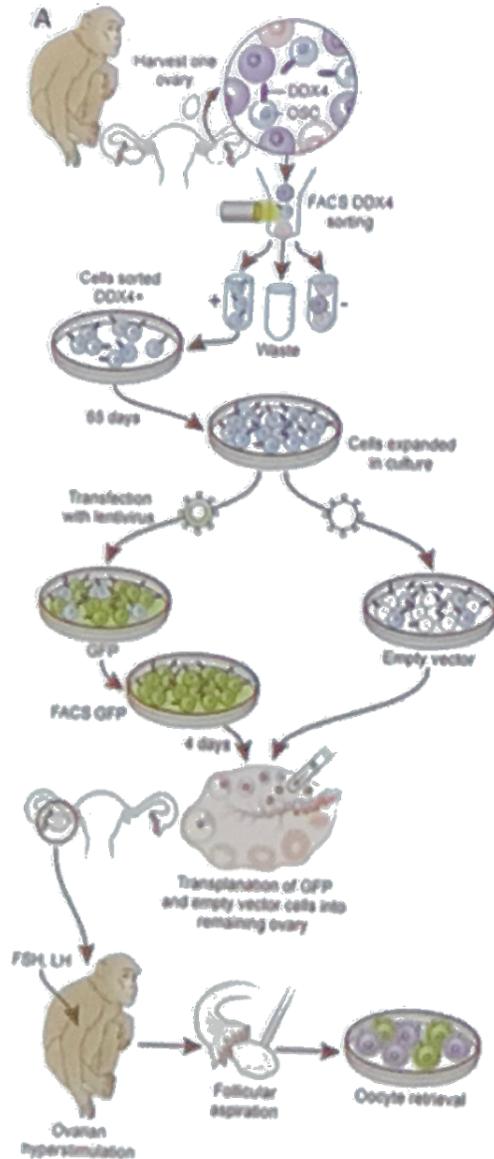
Group	Primordial Follicle	Primary Follicle	Secondary Follicle	Tertiary Follicle
Control	16,3 ± 5,3	15,6 ± 7,2	14,1 ± 7,2	4,0 ± 1,9
Cisplatin	8,5 ± 3,9	8,0 ± 5,0	8,7 ± 2,8	1,9 ± 1,5
Cisplatin+MenSCs	23,9 ± 8,2	15,4 ± 6,9	12,8 ± 4,4	4,5 ± 3,8

(p=0.020)

# RECUPERACIÓN FUNCIÓN OVÁRICA

Mature Eggs from Ovarian Stem Cells

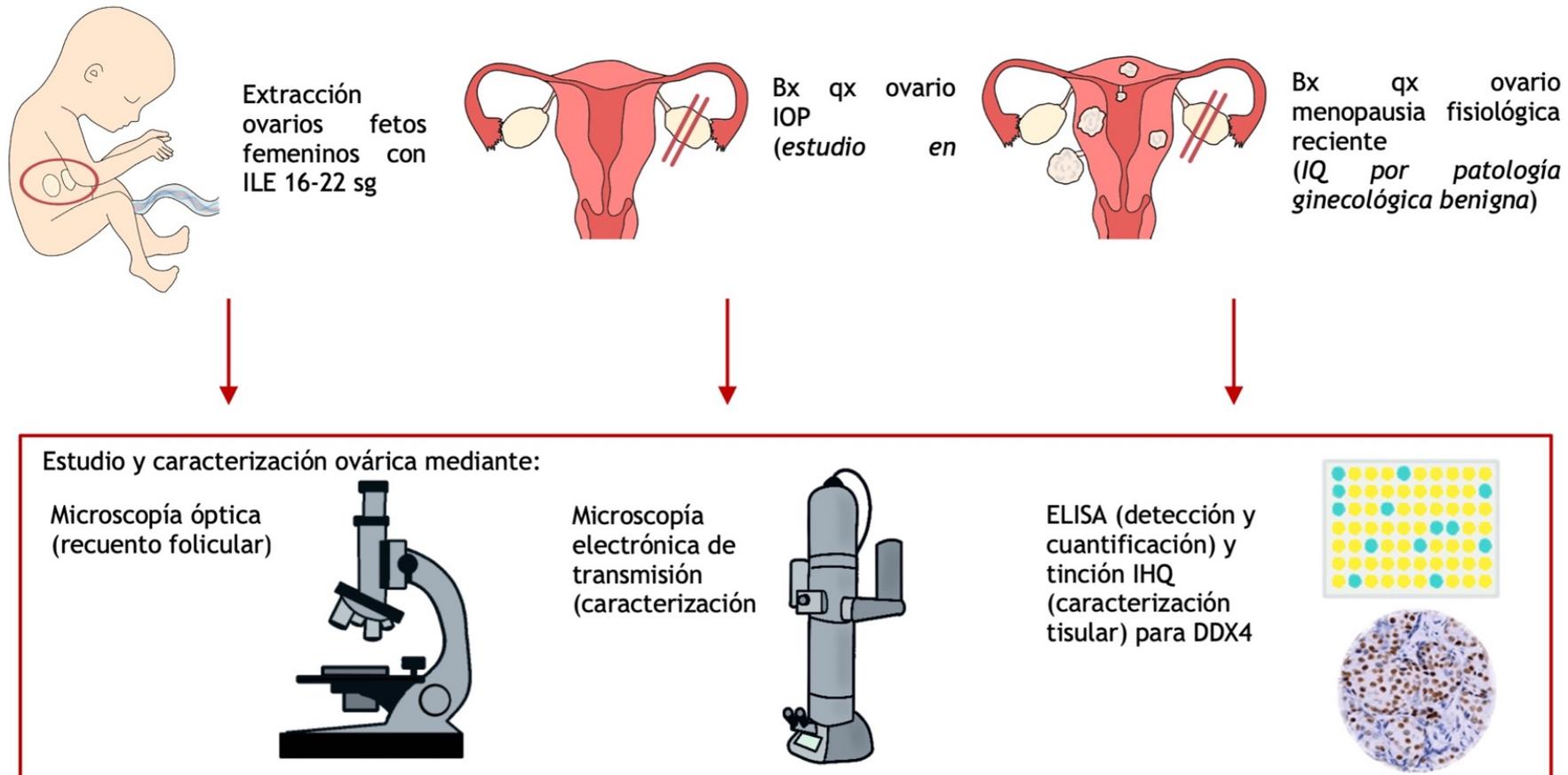
Non-human Primate: Dr E Wolff



# RECUPERACIÓN FUNCIÓN OVÁRICA

## Mature Eggs from Ovarian Stem Cells

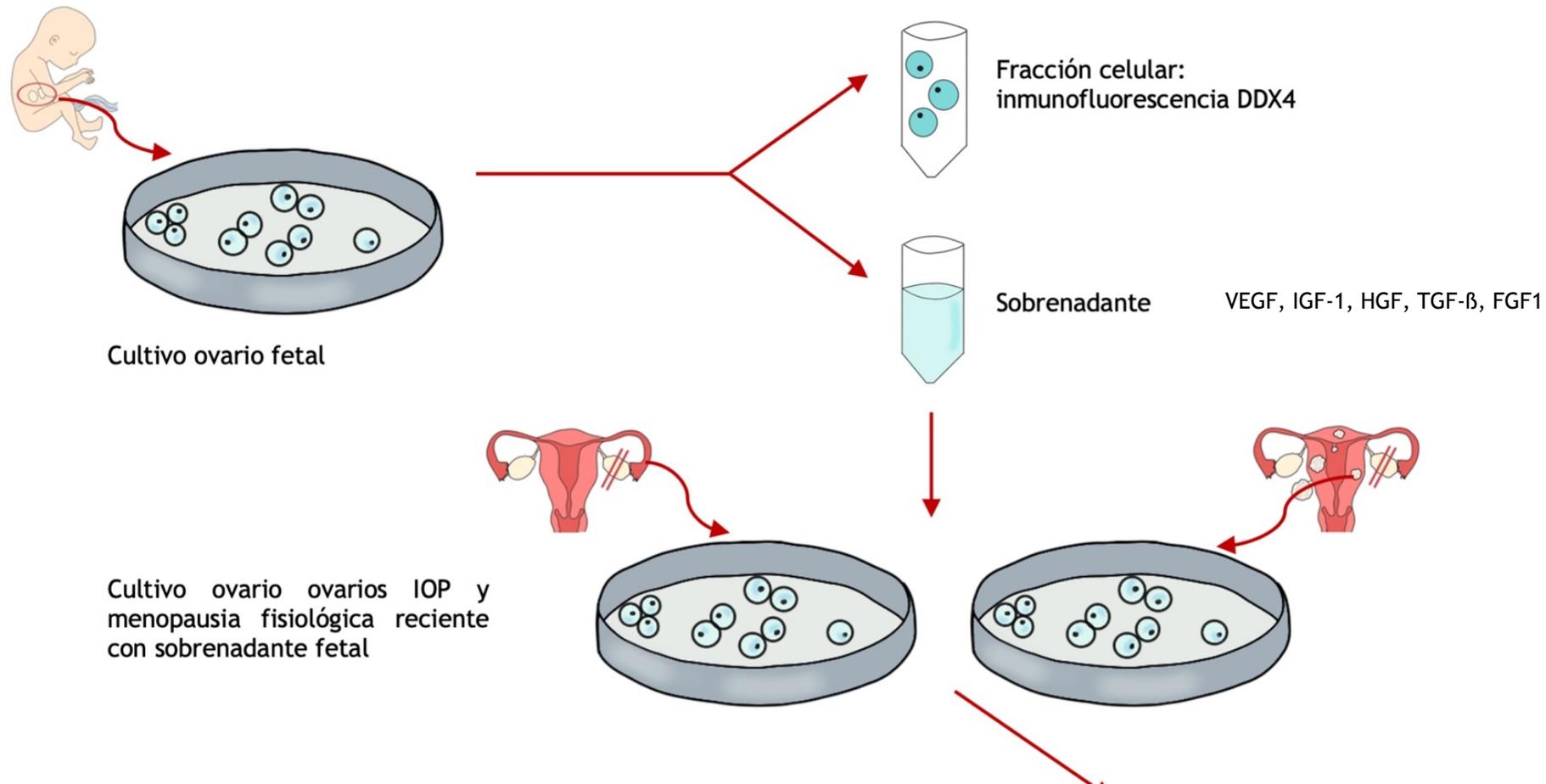
### Human embryo: Castelo-Branco & Ribera



# RECUPERACIÓN FUNCIÓN OVÁRICA

Mature Eggs from Ovarian Stem Cells

Human embryo: Castelo-Branco & Ribera

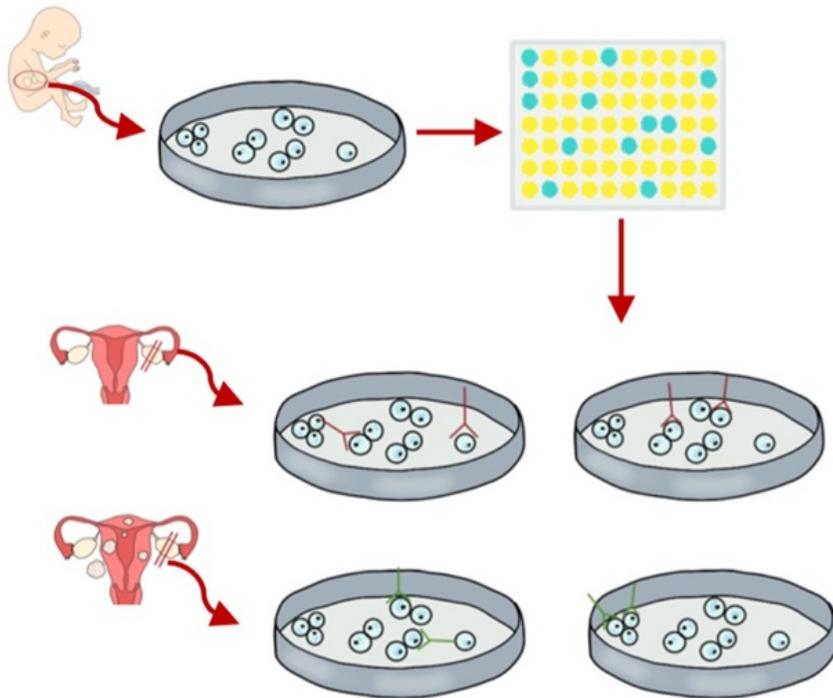


# RECUPERACIÓN FUNCIÓN OVÁRICA

Mature Eggs from Ovarian Stem Cells

Human embryo: Castelo-Branco & Ribera

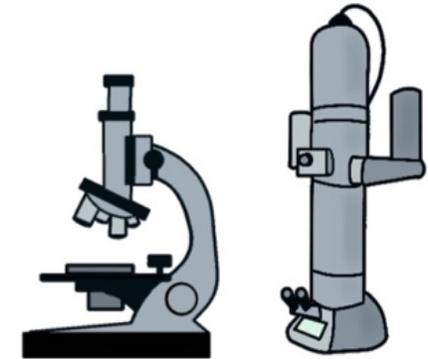
Estudio regeneración del nicho en ovarios no funcionantes:



Inhibición selectiva de factores solubles detectados para discriminar su relevancia en la activación folicular

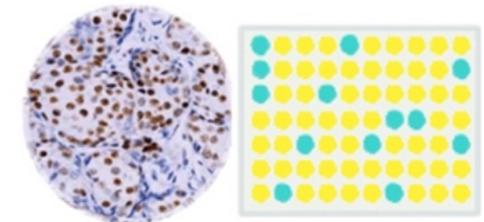
Estudio rescate folicular en ovarios no funcionantes mediante:

Microscopía óptica



Microscopía electrónica de transmisión

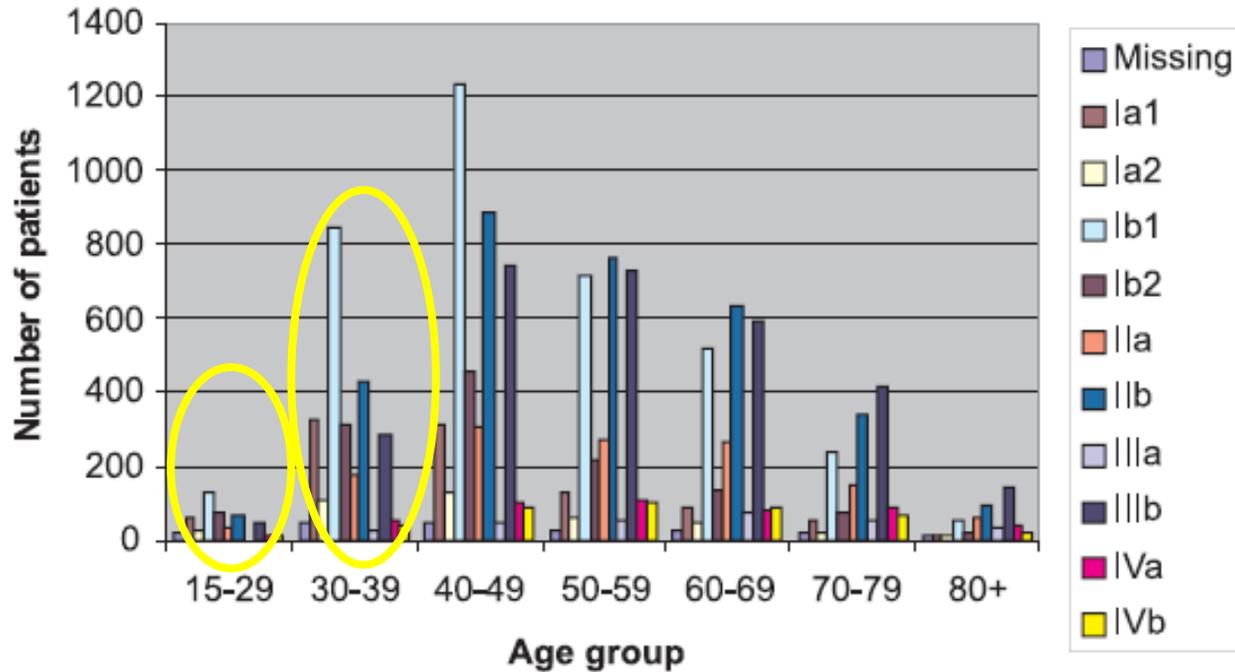
ELISA y tinción IHQ para DDX4



# PREVENCIÓN IOP QUIRÚRGICA



# I: C. CERVIX



## 36 Annual Report FIGO

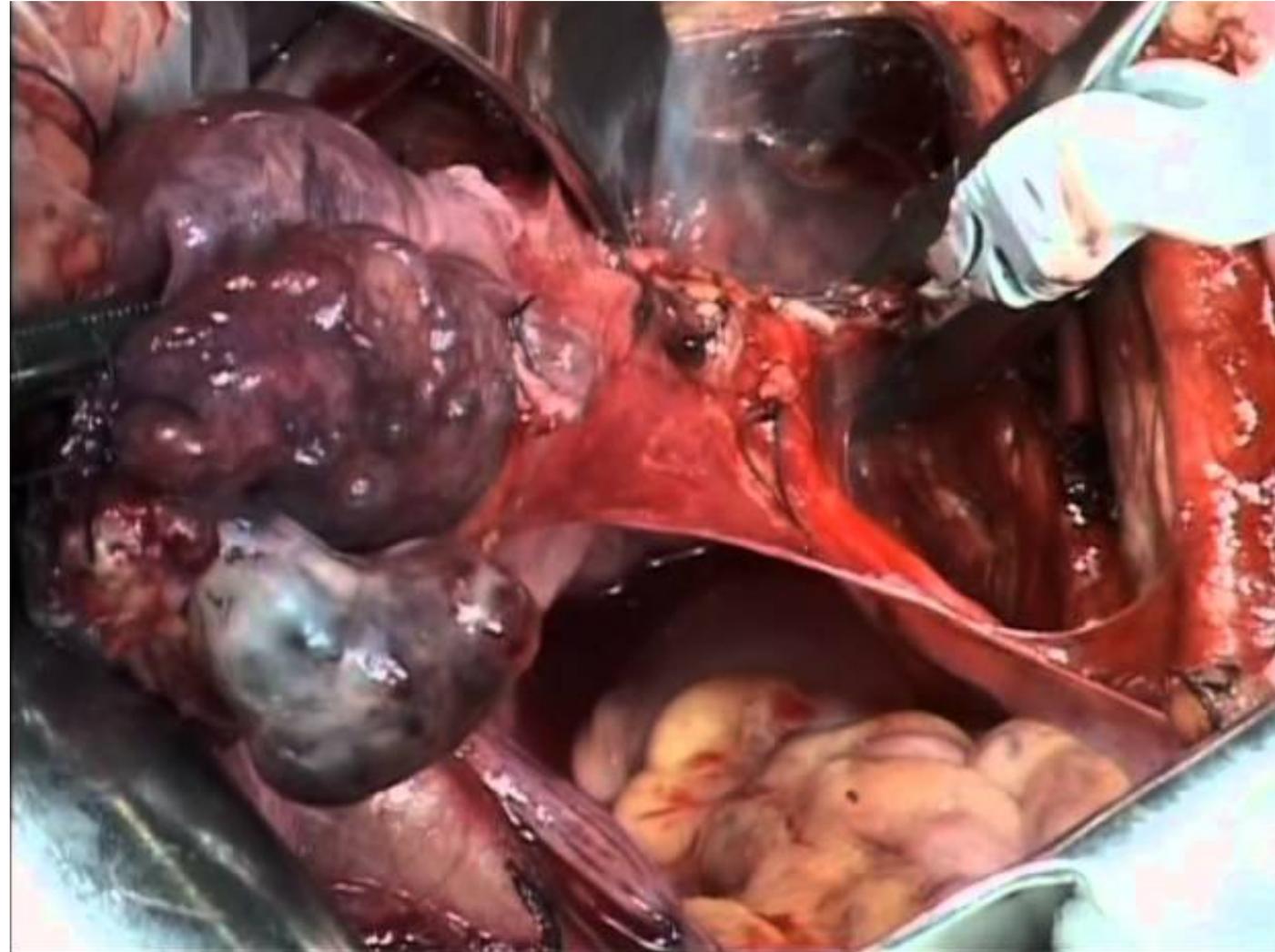
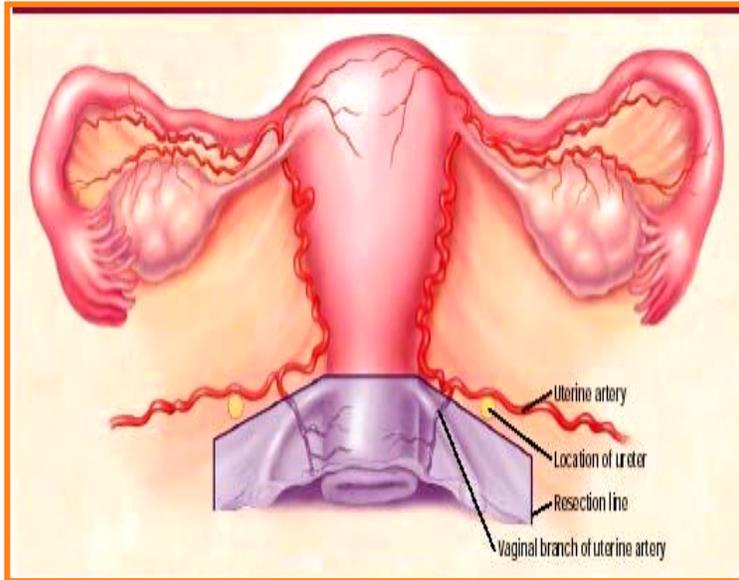
18 % cáncer de cérvix

45 % operables

Age group	Missing	Ia1	Ia2	Ib1	Ib2	IIa	IIb	IIIa	IIIb	IVa	IVb	Total
15-29	18	61	25	127	74	27	67	3	41	5	8	456
30-39	47	326	111	846	311	177	429	24	284	52	36	2643
40-49	46	310	126	1235	453	307	882	43	747	103	86	4338
50-59	25	126	58	717	218	267	763	50	729	112	101	3166
60-69	25	90	42	520	134	265	638	76	587	79	86	2542
70-79	14	51	18	230	72	149	334	51	417	85	64	1485
80+	5	4	4	51	13	57	96	27	141	36	17	451

# Tratamiento cáncer cérvix inicial

- ▶ Linfadenectomía pelviana
  - Si ganglios negativos:

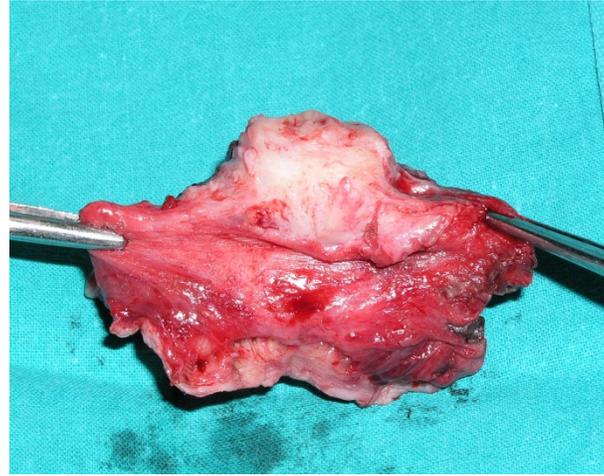


# Intervención de Dargent

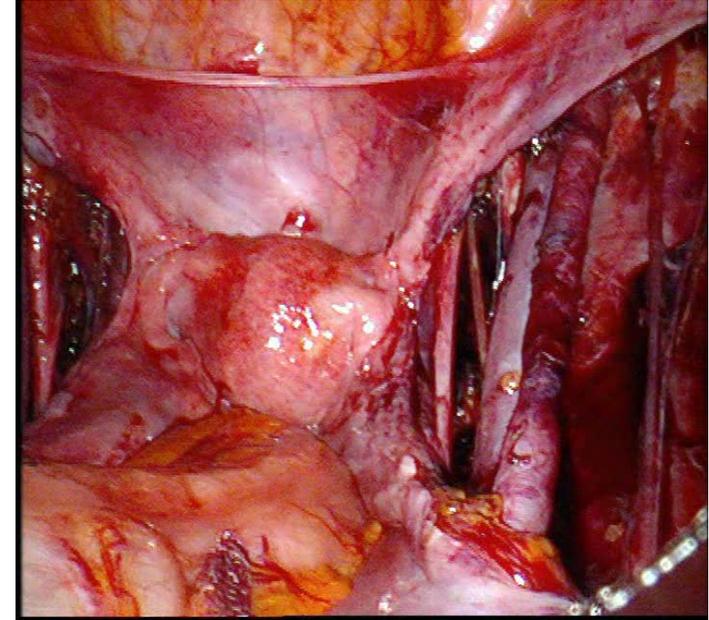
- **Criterios de selección:**
  - Deseo de preservar la fertilidad
  - Edad inferior a 40 años
  - Confirmación histológica de cáncer
  - Estadios Ia1 con invasión vículo-linfática, Ia2, Ib1
  - Tamaño  $\leq 2$  cm
  - Afectación endocervical limitada
  - No afectación ganglionar ni M1 a distancia
  - No histología desfavorable (neuroendocrino)
  - Experiencia quirúrgica en laparoscopia y cirugía vaginal



**Sección a < 1 cm del istmo**



**Visión laparoscópica finalizada la intervención**



**Cerclaje tipo McDonald y sutura a la vagina**



**Resultado final**



## Vaginal approaches to fertility-sparing surgery in invasive cervical cancer

Jaume Pahisa, Inmaculada Alonso\*, Aureli Tomé

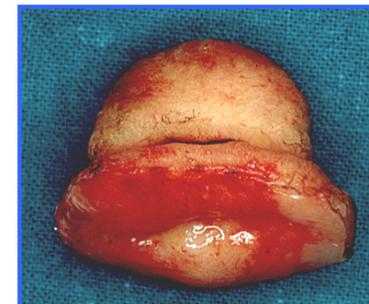
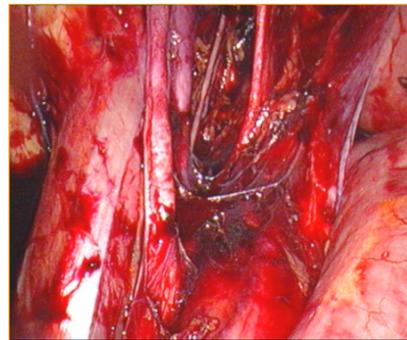
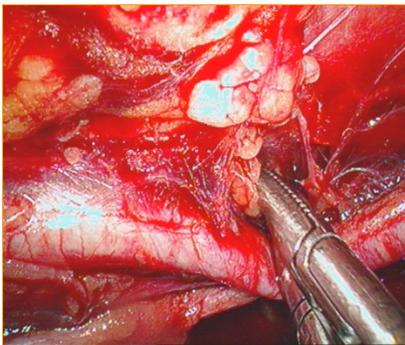
*Department of Obstetrics and Gynecology, Hospital Clínic, Barcelona, Spain*

Received 8 May 2008

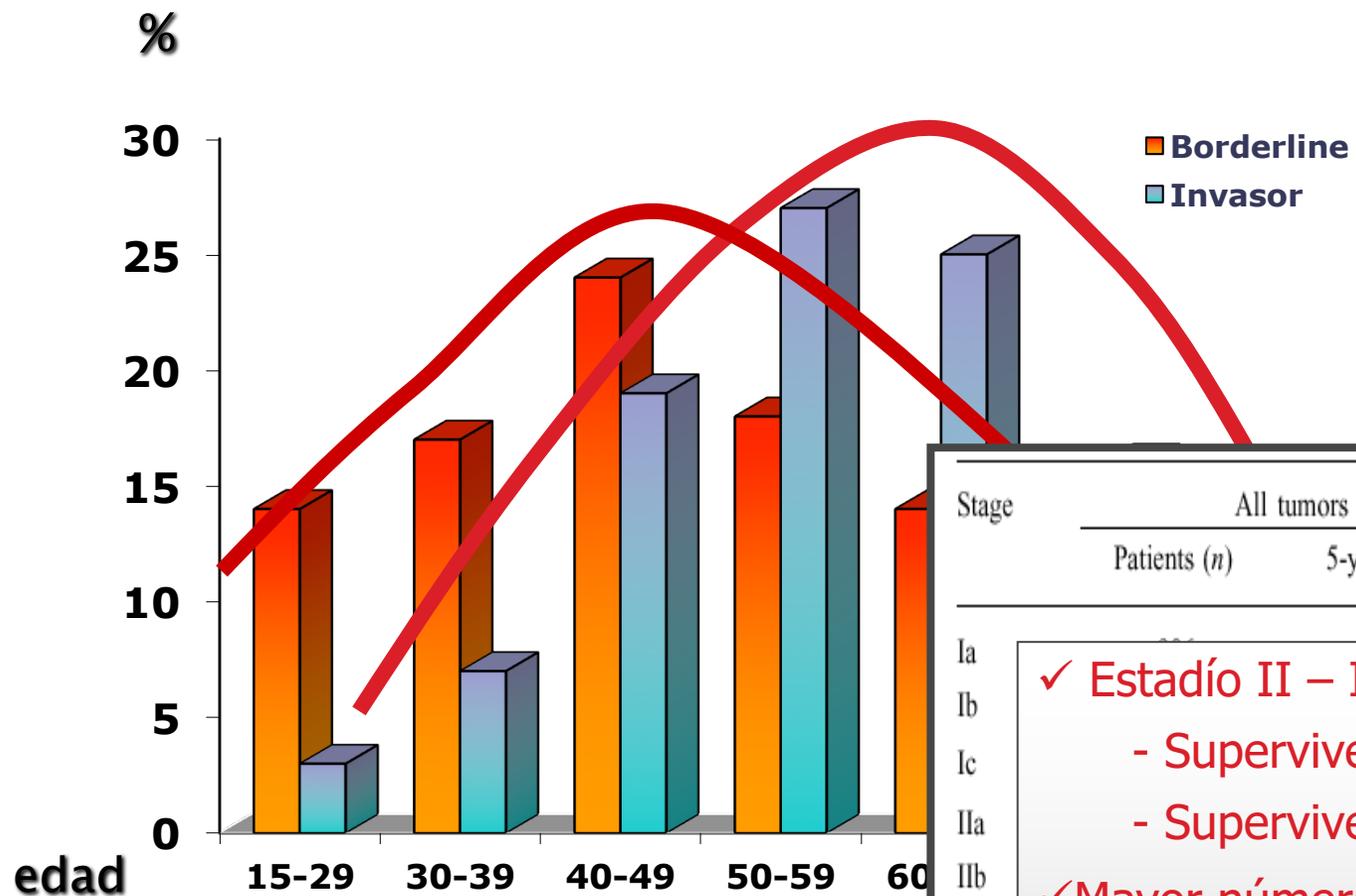
Nº caso	Estadio	Tamaño mm	Invasión estroma	IVL	AP	Rec	ILE meses	Gest.	Comp
1	Ib1	23	15	No	Esc	Si	67	No	No
2	Ib1	11	7	No	Ad	No	42	Si	No
3	Ib1	9	4	No	Ad	No	42	No	No
4	Ib1	9	3	No	Esc	No	38	No	No
5	Ib1	15	4	No	Esc	No	31	No	Anemia
6	Ib1	13	6	No	Esc	No	31	No	Her.Tro.
7	Ib1	16	6	No	Ad	No	29	Si	No
8	Ib1	8	5	No	Esc	No	27	No	No
9	Ib1	8	4	No	Esc	No	24	Si	No
10	Ib1	11	7	No	Ad	Si	7	No	No
11	Ib1	14	8	No	Esc	No	16	No	No
12	Ib1	35	7	Si	Esc	No	12	No	Vejiga Estenosis
13	Ib1	11	7	No	Esc	No	7	No	No
14	Ib1	17	5	No	Ad	No	7	No	No
15	Ib1	20	10	No	Ad	No	12	-	Histerc.
16	Ib1	35	6	No	Ad	No	4	-	Histerec.

# Conización o traquelectomía simple + linfadenectomía

Autor	N	Cono	Traquelectomía	Recidiva (%)	Gestación (%)	Meses
Rob	26	7	15	3,8	73	18-84
Landoni	11	11	-	0	37,5	-
Bisseling	38	11	-	0	-	72



# II: C. OVARIO BORDERLINE



Stage	All tumors		Low malignancy		Obviously malignant	
	Patients (n)	5-year survival	Patients (n)	5-year survival	Patients (n)	5-year survival
Ia						
Ib						
Ic						
IIa						
IIb						
IIc						
IIIa						
IIIb	278	43.8	18	88.4	251	40.8
IIIc	1782	30.2	62	59.6	1653	28.9
IV	550	13.7	9	63.7	511	13.4

✓ Estadío II – III:

- Supervivencia 5 a.: 92 %
- Supervivencia 10 a.: 60 – 75 %

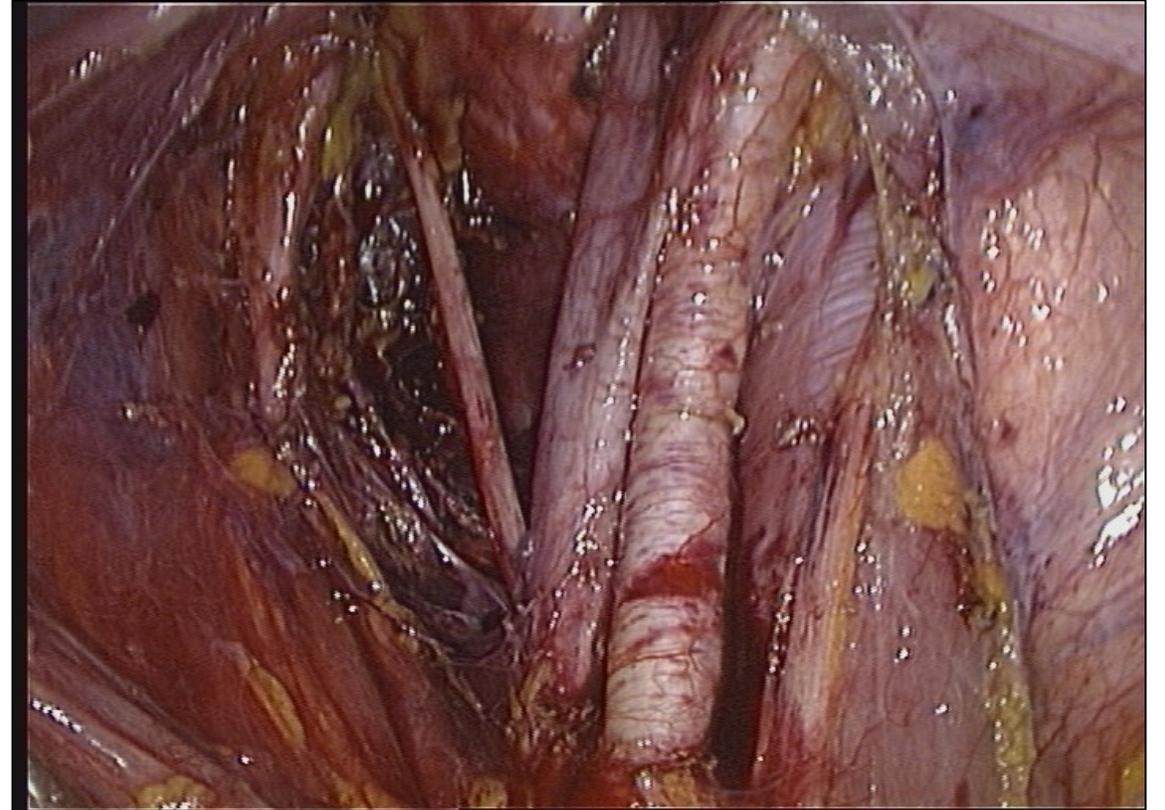
✓ Mayor número de pacientes mueren **con** la enfermedad que **de** la enfermedad.

# Escenarios clínicos

- ▶ > 1 / 3 de TBL en < 40 años.
- ▶ > 2 / 3 de TBL son estadios precoces.
- ▶ 2 / 3 aspecto ecográfico “benigno”.
  
- I. 2 / 3 Diagnóstico en biopsia peroperatoria.
- II. 1 / 3 de diagnósticos en bx. definitiva (diferida) tras tratamiento conservador de un quiste simple.

# Estadificación quirúrgica

- Lavados citológicos.
- Biopsias peritoneales.
- Omentectomía inframesocólica.
- Apendicectomía en tumores mucinosos.
- Exéresis de cualquier nódulo sospechoso.



**Exploración cuidadosa cavidad abdominal !**

**NO linfadenectomía**

# Cirugía conservadora C BORDERLINE OVARIO

## Procedimientos

Quistectomía unilateral

Quistectomía bilateral

Anexectomía unilateral

Anexectomía unilateral + Quistectomía contralateral

*¿Tratamiento de formas avanzadas con deseo genésico?.*

**En principio, no. Individualizar.**

# Cirugía conservadora C BORDERLINE OVARIO

## Resultados oncológicos. Recidivas.

- ▶ Aumento del riesgo
  - Mayoritariamente en serosos. La mayoría < 3 años.
  - Datos limitados.
- ▶ Recidivas: 10 – 35 % (a los 2–5 años).
  - Quistectomía unilateral: 15–30 %
  - Quistectomía bilateral: 30–50 %.
  - Anexectomía unilateral: 5–15 %.
  - No dif. en algunas series ente Q. / A.
  - Pélvicas en forma de B–L (muy raro forma agresiva)
- Tratables. Con nueva cir. conservadora si posible.
- No impacto en la supervivencia.

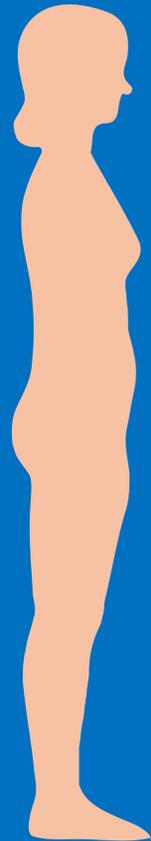
# Cirugía conservadora C BORDERLINE OVARIO

## Resultados reproductivos. Gestación.

		N.		N.			
Authors of study	Patients	Treatment	Recurrences	Pregnancy			
Bostwich et al.	24	Laparotomy	0	3 SVD			
Lim Tan et al. (3)	16	Laparotomy	0	7 SVD			
Barnhill et al. (18)	21	Laparotomy	0	3 SVD			
Gotlieb et al. (25)	15	Laparotomy	0	16 SVD; 3 CD			
Papadimitriou et al.	15	Laparotomy	5	10 Pregnancies			
Morris et al. (26)	12	Laparotomy	0	14 SVD; 2 CD			
Seracchioli et al. (19)	19	Laparoscopy	1	6 SVD			
Donnez et al.	3	Laparotomy	3	12 SVD			
	13	Laparoscopy					
Fauvet et al. (24)	40	Laparotomy	27	30 Pregnancies			
	25	Laparoscopy					
Boran et al. (21)	56	Laparotomy	4	13 Pregnancies			
	6	Laparoscopy					
Tinelli et al. (30)	43	Laparoscopy	3	12 SVD; CD			
Total	247			127			
SVD, spontaneous vaginal delivery; CD, caesarean delivery.							
<b>Ji et al.</b>	<b>1996</b>		<b>19</b>	<b>9</b>	<b>47,37</b>		<b>87 m (9-256)</b>
<b>Chan et al.</b>	<b>2003</b>	<b>29 (21-43)</b>	<b>6</b>	<b>6</b>	<b>100,00</b>	<b>0</b>	<b>80 m (4-157)</b>
<b>TOTAL</b>			<b>213</b>	<b>103</b>	<b>48,36</b>	<b>10</b>	<b>(4,7%– 6,5 %)</b>

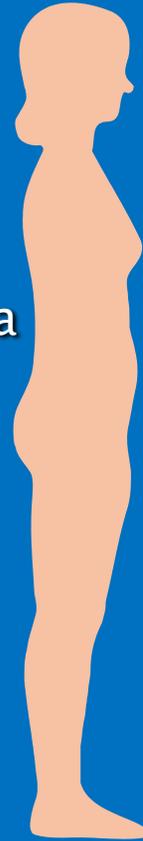
# III: C. ENDOMETRIO

Women (INCIDENCE)  
662,870



- 32% **Breast**
- 12% Lung and bronchus
- 11% Colon and rectum
- 6% **Uterine corpus**
- 4% Non-Hodgkin lymphoma
- 4% Melanoma of skin
- 3% **Ovary**
- 3% Thyroid
- 2% Urinary bladder
- 2% Pancreas
- 21% All Other Sites

Women (DEATHS)  
275,000



- 27% Lung and bronchus
- 15% **Breast**
- 10% Colon and rectum
- 6% **Ovary**
- 6% Pancreas
- 4% Leukemia
- 3% Non-Hodgkin lymphoma
- 3% **Uterine corpus**
- 2% Multiple myeloma
- 2% Brain/ONS
- 22% All other sites

\*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.

ONS=Other nervous system.  
Source: American Cancer Society, 2005.

# Diagnóstico por estadio

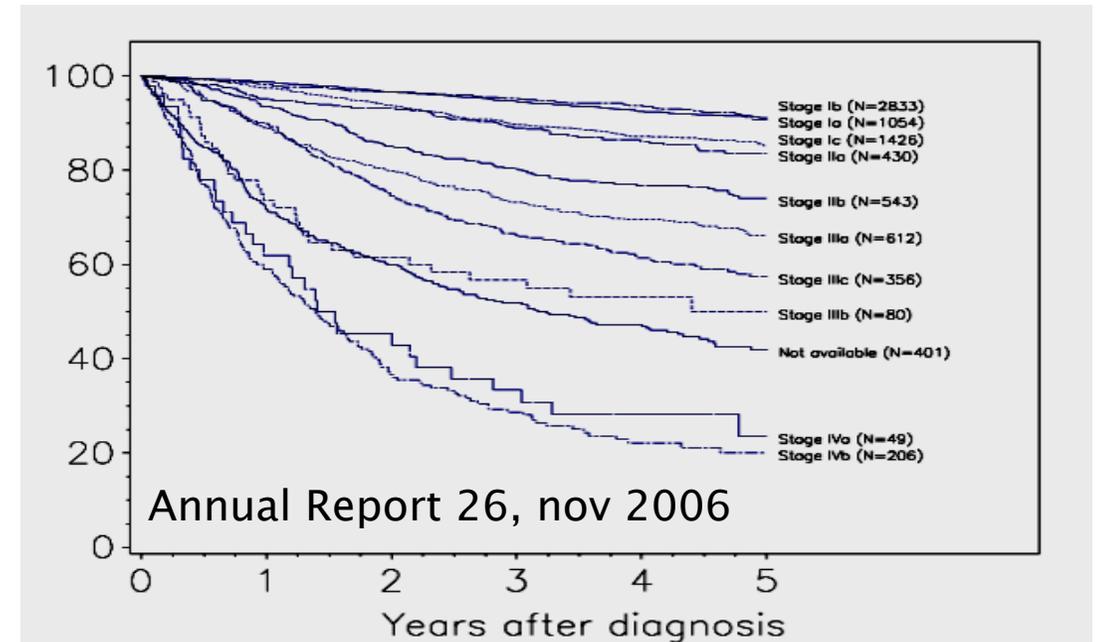
## supervivencia

Estadio	Superv. 5 a (%)
IA	91
IB	88
IC	81
IIA	77
IIB	67
IIIA	60
IIIB	41
IIIC	32
IVA	20
IVB	5

Grado histológico	
Grado	Superv. 5 años (%)
1	92
2	87
3	74

Global a los 5 años: 84%

Confinado al útero	estadio I	73 %
Afectación cervical	estadio II	11 %
Serosa uterina, anejos Citología (+), M1 vaginal Ganglios P/PA (+)	estadio III	13 %
Vejiga, intestino, M1 Ganglios inguinales	estadio IV	3 %



# C. ENDOMETRIO. CIRUGÍA CONSERVADORA

No respuesta: 25 %

Respuesta: 75 % (50-100)

- Tiempo hasta respuesta: 12 sem
- Recidivas: 25 % (0-60)
  - Eficacia retratamiento horm.: 75 %

*Eficacia: 60-70 %*



**KEEP  
CALM  
AND THANK YOU  
FOR YOUR  
ATTENTION**