

La preservazione della fertilità in oncologia: il carcinoma mammario come paradigma

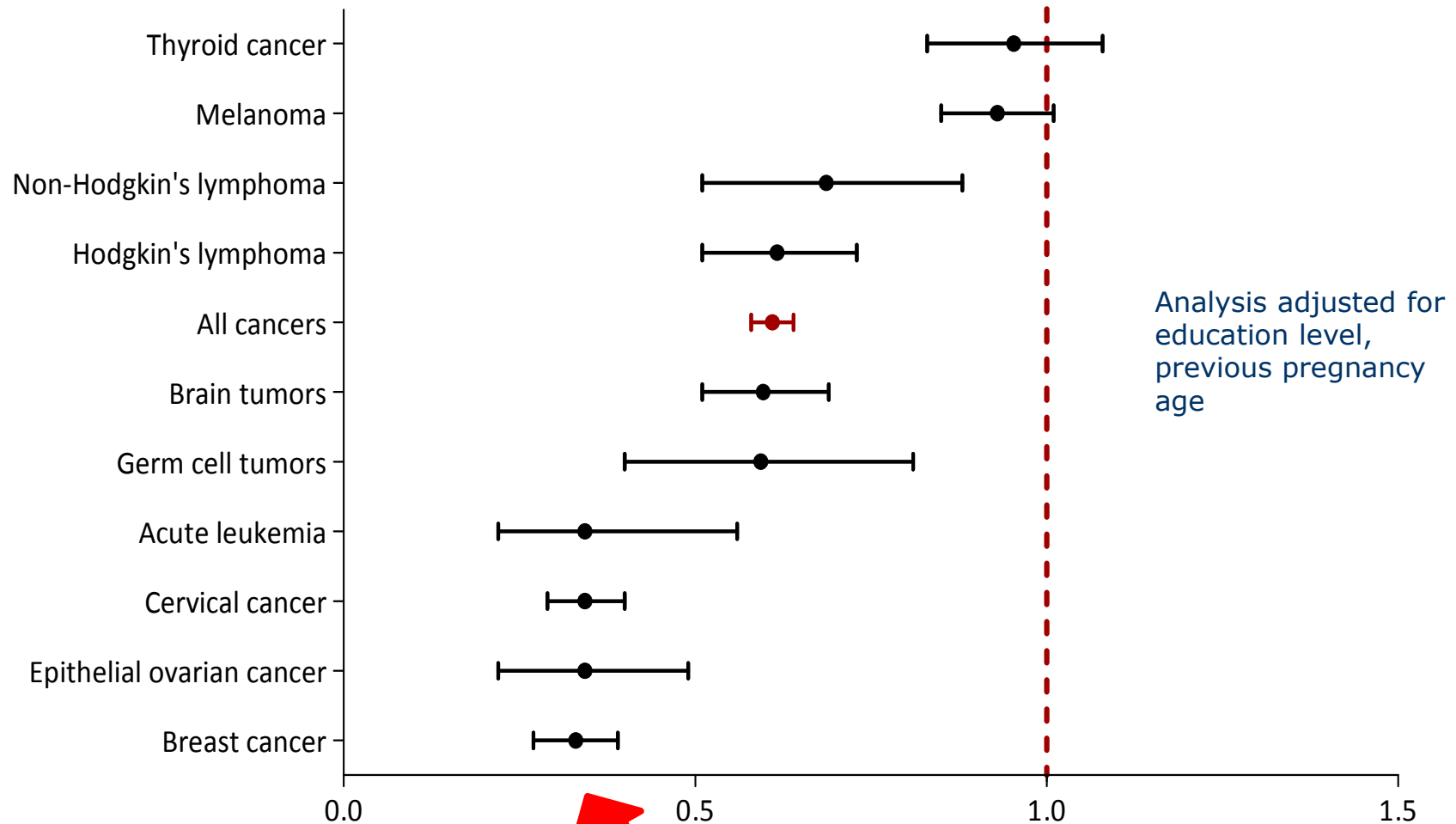


Olivia Pagani
Centro di
Senologia
della Svizzera
Italiana



Centro di
Senologia della
Svizzera Italiana

Pregnancy rate after cancer: not all alike



Stensheim et al; Int J Cancer 2011

Post-cancer pregnancy rates in 27,556 survivors and compared to controls from the general population from 1967 to 2004.

Premenopausal Early Breast Cancer Fertility Considerations

- **Chemotherapy may cause menopause or reduce ovarian reserve**
- **Delaying pregnancy for 5-10 years of endocrine therapy will reduce fertility**
- **Fertility after breast cancer treatment is age and regimen dependent**

Fertility concerns of breast cancer patients

Prospective Study of Fertility Concerns and Preservation Strategies in Young Women With Breast Cancer

Kathryn J. Ruddy, Shari I. Gelber, Rulla M. Tamimi, Elizabeth S. Ginsburg, Lidia Schapira, Steven E. Come, Virginia F. Borges, Meghan E. Meyer, and Ann H. Partridge

620 patients, median age 37 years

51% concerned about fertility

68% discussed fertility issues before starting therapy

10% used fertility preservation strategies



Ruddy C J Clin Oncol 32:1151, 2014

Fertility concerns of breast cancer patients

ARTICLE

Impact of Fertility Concerns on Tamoxifen Initiation and Persistence

Natalia C. Llarena, Samantha L. Estevez, Susan L. Tucker, Jacqueline S. Jeruss

515 ER+ patients <45 y/o in whom TAM was indicated

149 (28.9%) did not start or discontinued TAM

Fertility concerns associated with:

Non initiation (OR 5.04, 95%CI=2.29-11.07)

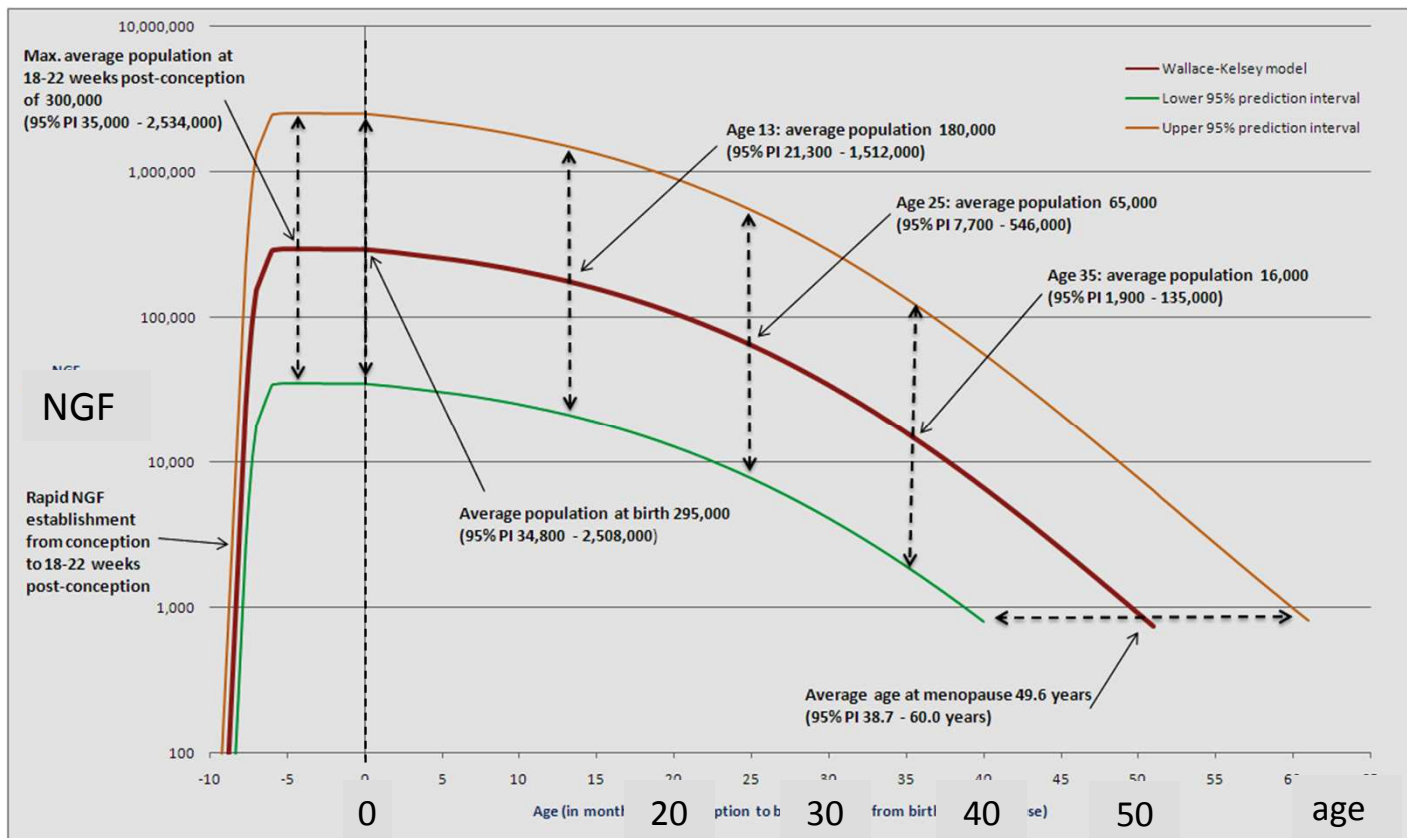
Early discontinuation (HR 1.78, 95%CI=1.09-3.38)



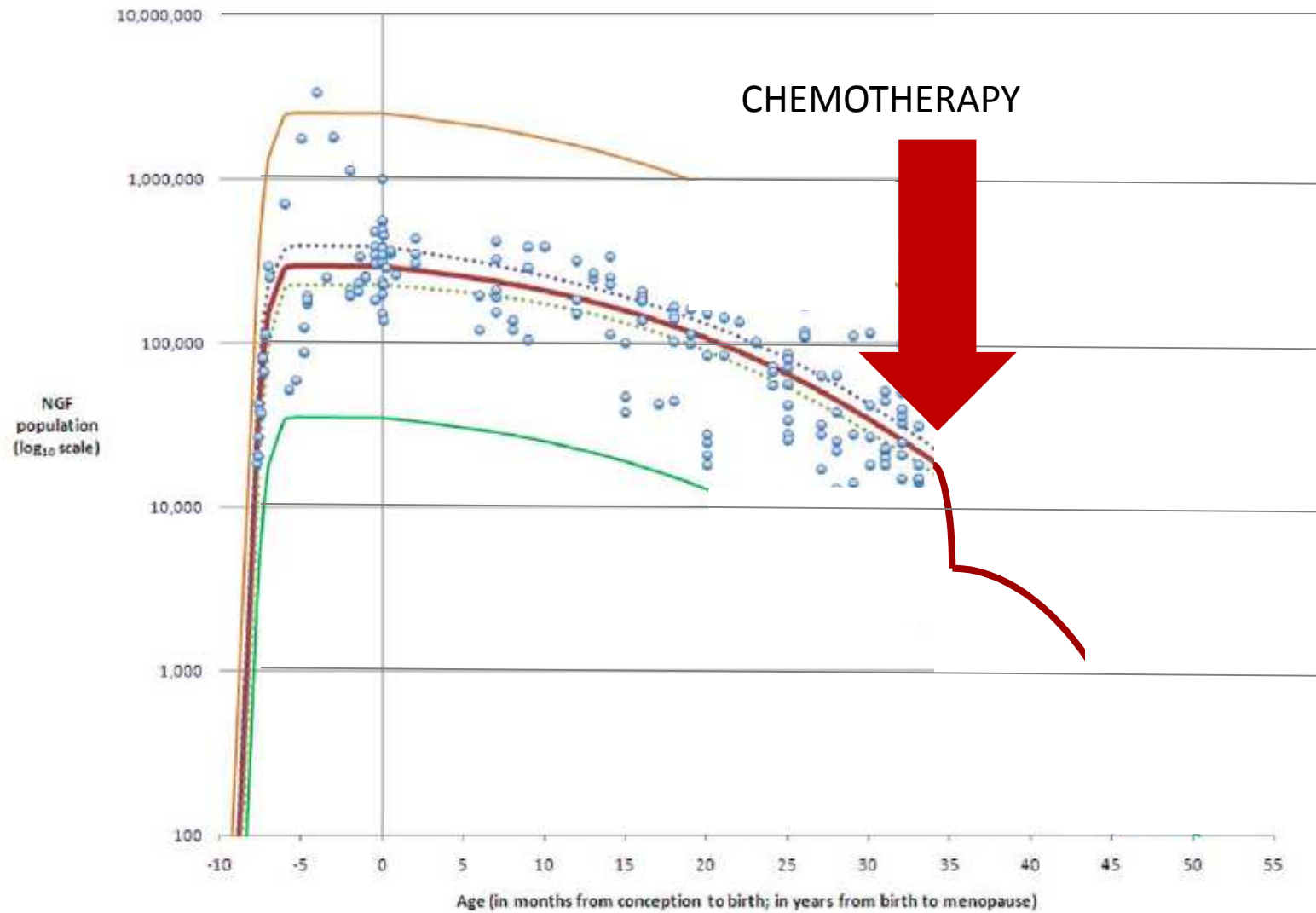
JNCI J Natl Cancer Inst (2015) 107(10): djv202

Ovarian reserve assessment

- Age
- Hormone profile (FSH, E2) AMH
- Previous IVF treatments



Ovarian reserve after chemotherapy



Human Ovarian Reserve from Conception to the Menopause

W. Hamish B. Wallace^{1*}, Thomas W. Kelsey²

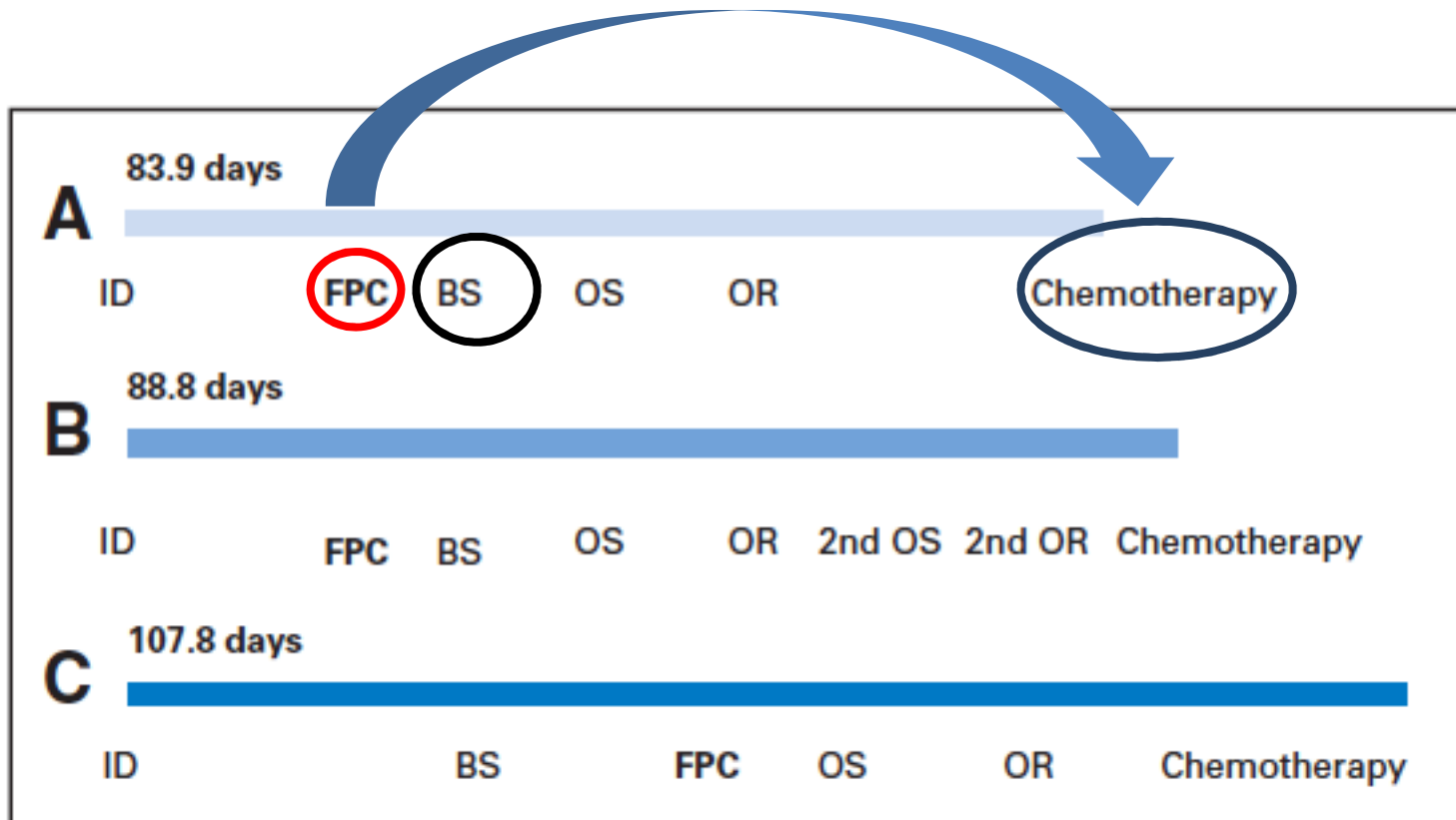
Reported Ovarian failure in breast cancer patients

Chemotherapy regimen	Age	Reported ovarian failure rate
AC	<30	0%
AC	30-39	13%
AC	≥40	57-63%
FAC	<30	0%
FAC	30-39	10-25%
CMF	<30	19%
CMF	30-39	51-77%
CMF	≥40	83-98%
+ Taxanes		79% (OR 4.05)

What are the available options for fertility preservation?

- Embryo cryopreservation:
delay treatment for 1 month to undergo 1 cycle of hormone stimulation, oocyte retrieval and in vitro fertilization
 - Cryopreservation of mature oocytes:
less effective, efficiency improving
 - In vitro follicle maturation,
ovarian tissue cryopreservation and transplantation
-
- ✓ Discuss at the early beginning the possibility of infertility as a risk of cancer treatment
 - ✓ Refer to appropriate specialists as early as possible

Early referral



ID: initial diagnosis, FPC: fertility preservation counseling
BS: breast surgery, OS/OR: ovarian stimulation/oocyte retrieval

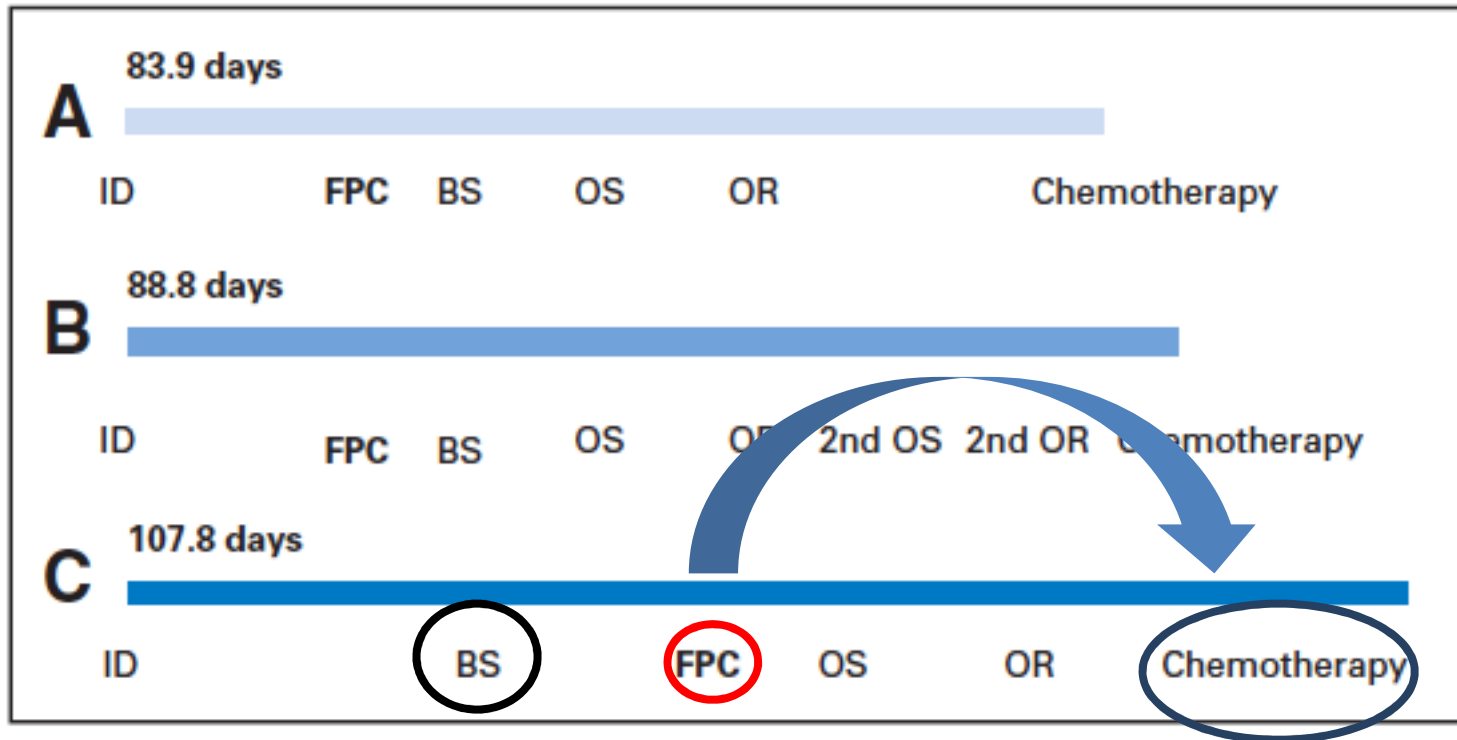


Value of Early Referral to Fertility Preservation in Young Women With Breast Cancer

Sanghoon Lee, Sinan Ozkavukcu, Elke Heytens, Fred Moy, and Kutluk Oktay

VOLUME 28 • NUMBER 31 • NOVEMBER 1 2010

Early referral



ID: initial diagnosis, FPC: fertility preservation counseling
BS: breast surgery, OS/OR: ovarian stimulation/oocyte retrieval



Value of Early Referral to Fertility Preservation in Young Women With Breast Cancer

Sanghoon Lee, Sinan Ozkavukcu, Elke Heytens, Fred Moy, and Kutluk Oktay

VOLUME 28 • NUMBER 31 • NOVEMBER 1 2010

Embryo freezing for fertility preservation

- **Currently the most widely used method.**
- **Cycle success rate— according with ovarian reserve.**
- **In cancer patients- thousands of patients worldwide.**

IVF in breast cancer patients - Dilemmas

- Time needed for IVF – flexible
- Early referral more cycles.
- Older patients- low ovarian reserve.
- No partner –Egg freezing or Donor sperm.
- Hormone sensitive tumors.
Aromatase inhibitor (Letrozole) reduce E2 levels.
Tamoxifen blocks Estrogen receptors.

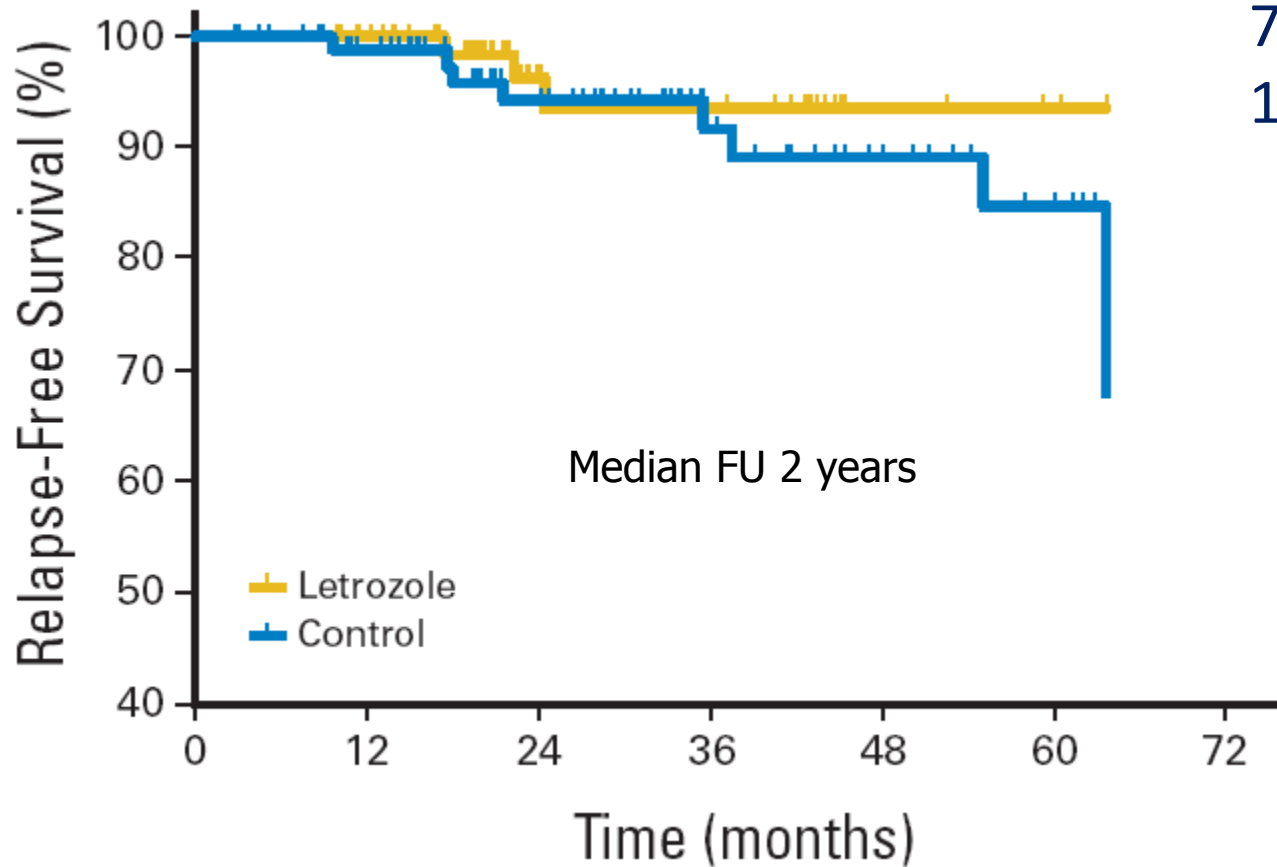
Egg Freezing for fertility preservation

Indications

- **No partner.**
- **Breast cancer patients before chemotherapy.**
- **BRCA mutation carriers before BSO.**
- **90% vitality and fertilization rate after thawing**
8-12 frozen oocytes - 30% probability of a baby

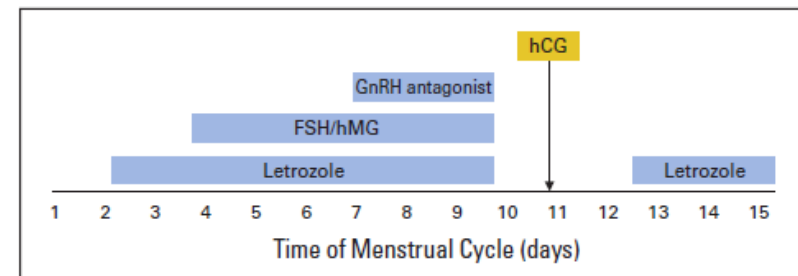
Controlled ovarian stimulation: Letrozole

79 letrozole
136 controls



No. of patients at risk

Letrozole	79	74	37	18	7	5
Control	136	81	56	38	26	19



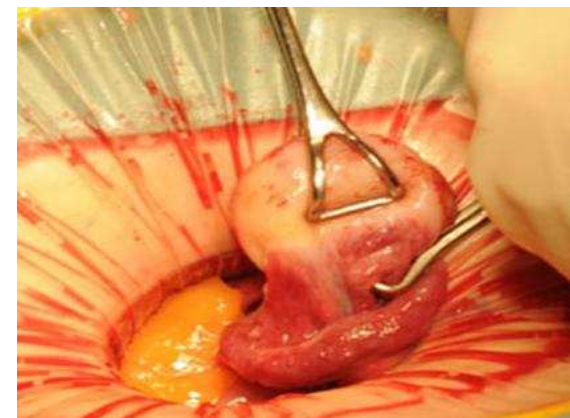
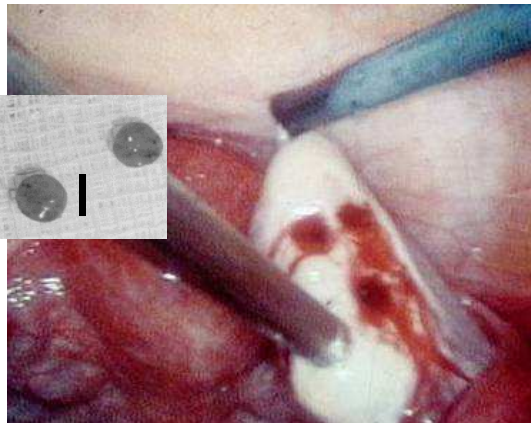
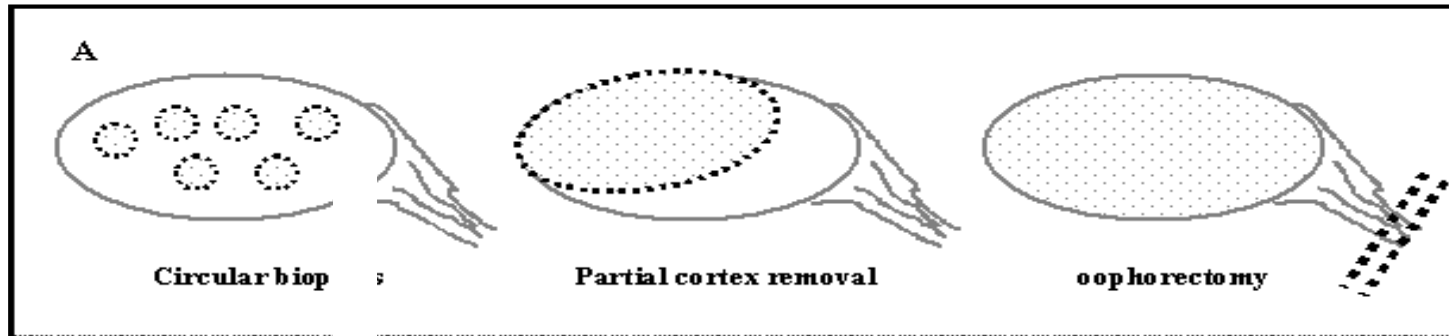
J Clin Oncol 26:2630-2635.

Ovarian tissue cryopreservation

Objectives

- **Fertility preservation using stored ovarian tissue WORKS!**
- **Ovarian tissue storage enables TREATMENT FLEXIBILITY.**
- **SAFETY ISSUES.**

Operation – laparoscopy



Children born after ovarian transplantation. A review of 13 live births.



- Age at tissue collection 19-36
- Previous chemotherapy 40%.
- IVF / Spontaneous pregnancy 50%.
- Pregnancy results- normal babies 100%.

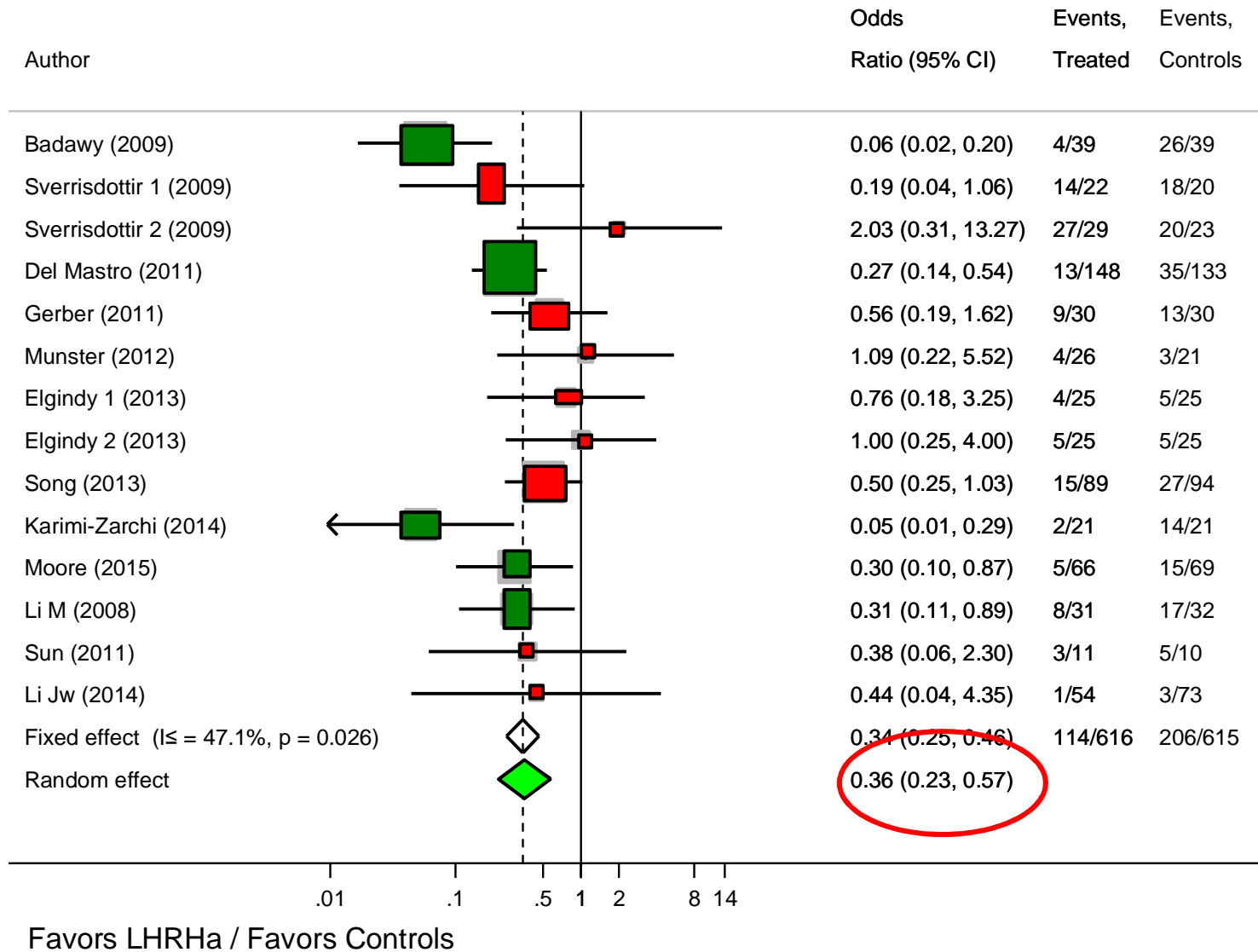
Donnez J, Silber S, Andersen CY, Demeestere I, Piver P, Meirow D, Pellicer A, Dolmans MM. **Ann Med 2011 .Jan 13**

**Many centers, sporadic cases, different conditions.
Success rate unknown.**

The risk of cancer cells in the ovaries of breast cancer patients

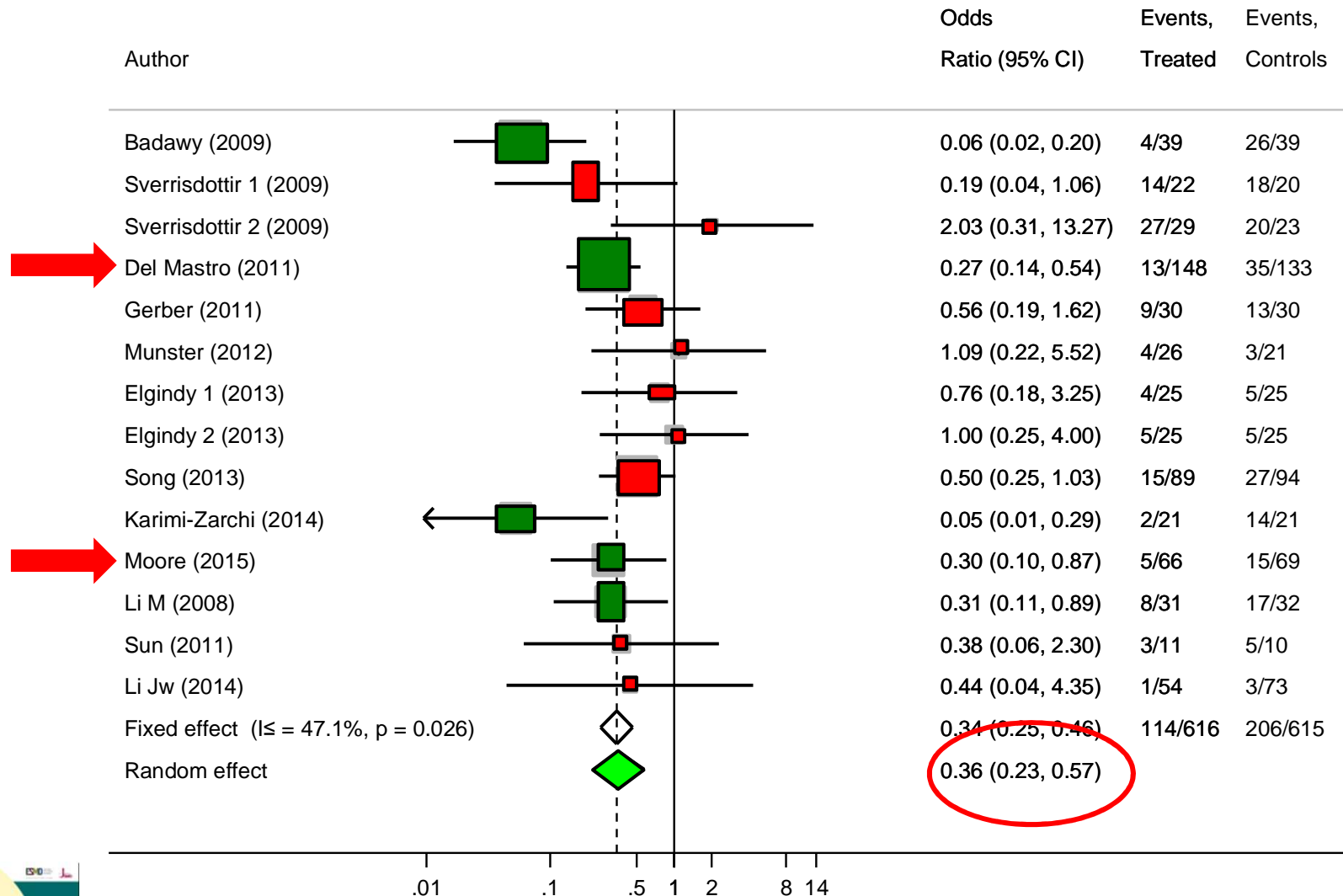
- **Risk of breast cancer cells metastasis.**
- **Risk of primary ovarian cancer in BRCA
mutation carriers.**

Consider offering LHRHa during chemo



Lambertini et 2015, Annals of Oncology

Consider offering LHRHa during chemo



Favors LHRHa / Favors Controls

Lambertini et 2015, Annals of Oncology



GRAVIDANZA DOPO UN TUMORE AL SENO



Study Design & Eligibility Criteria

Retrospective Matched-Controlled Trial

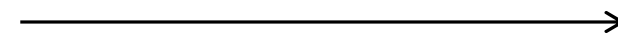
Pregnant cases

1. History of 1 BC
2. Became pregnant after BC diagnosis
3. No evidence of relapse before becoming pregnant
4. Known ER-status

Matched controls 3 controls/pregnant case

History of 1 BC matched according to

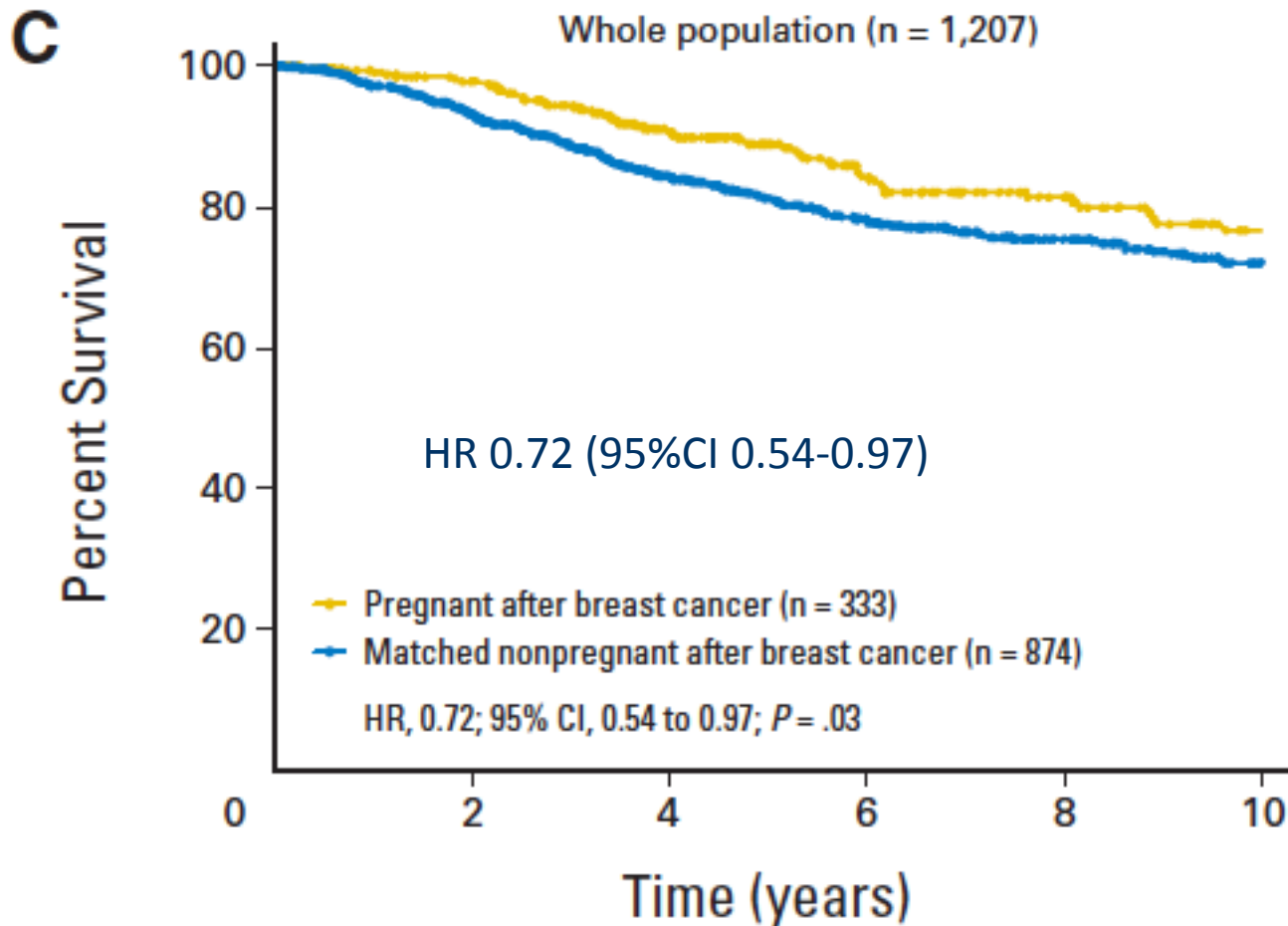
1. ER status (+ vs. -)
2. Nodal status (N0 vs. N+)
3. Adjuvant chemo, hormonal (Yes vs. No)
4. Age at diagnosis (< vs. > 35)
5. Year of diagnosis (\pm 5 years)



1,207 eligible patients



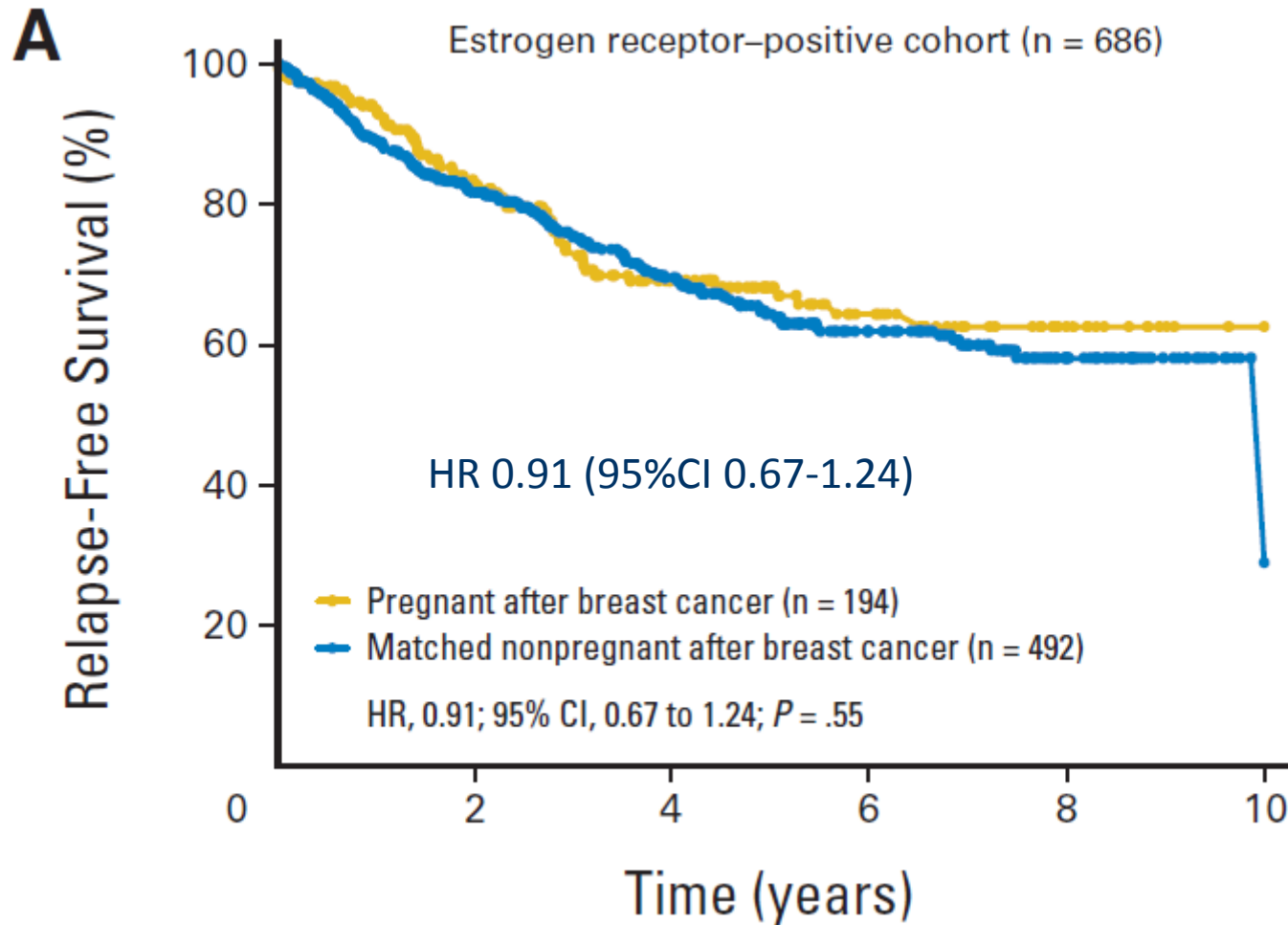
Safety: OS all patients



Prognostic Impact of Pregnancy After Breast Cancer According to Estrogen Receptor Status: A Multicenter Retrospective Study

Hatem A. Azim Jr, Niels Kroman, Marianne Paesmans, Shari Gelber, Nicole Rotmensz, Lieveke Ameye, Leticia De Mattos-Arruda, Barbara Pistilli, Alvaro Pinto, Maj-Britt Jensen, Octavi Cordoba, Evandro de Azambuja, Aron Goldhirsch, Martine J. Piccart, and Fedro A. Peccatori

Safety: DFS in ER+



Prognostic Impact of Pregnancy After Breast Cancer According to Estrogen Receptor Status: A Multicenter Retrospective Study

Hatem A. Azim Jr, Niels Kroman, Marianne Paesmans, Shari Gelber, Nicole Rotmensz, Lieveke Amey, Leticia De Mattos-Arruda, Barbara Pistilli, Alvaro Pinto, Maj-Britt Jensen, Octavi Cordoba, Evandro de Azambuja, Aron Goldhirsch, Martine J. Piccart, and Fedro A. Peccatori

Screening/eligibility:

Patients with **ER+**
early breast cancer

≥ 18 and ≤42 years at
enrollment

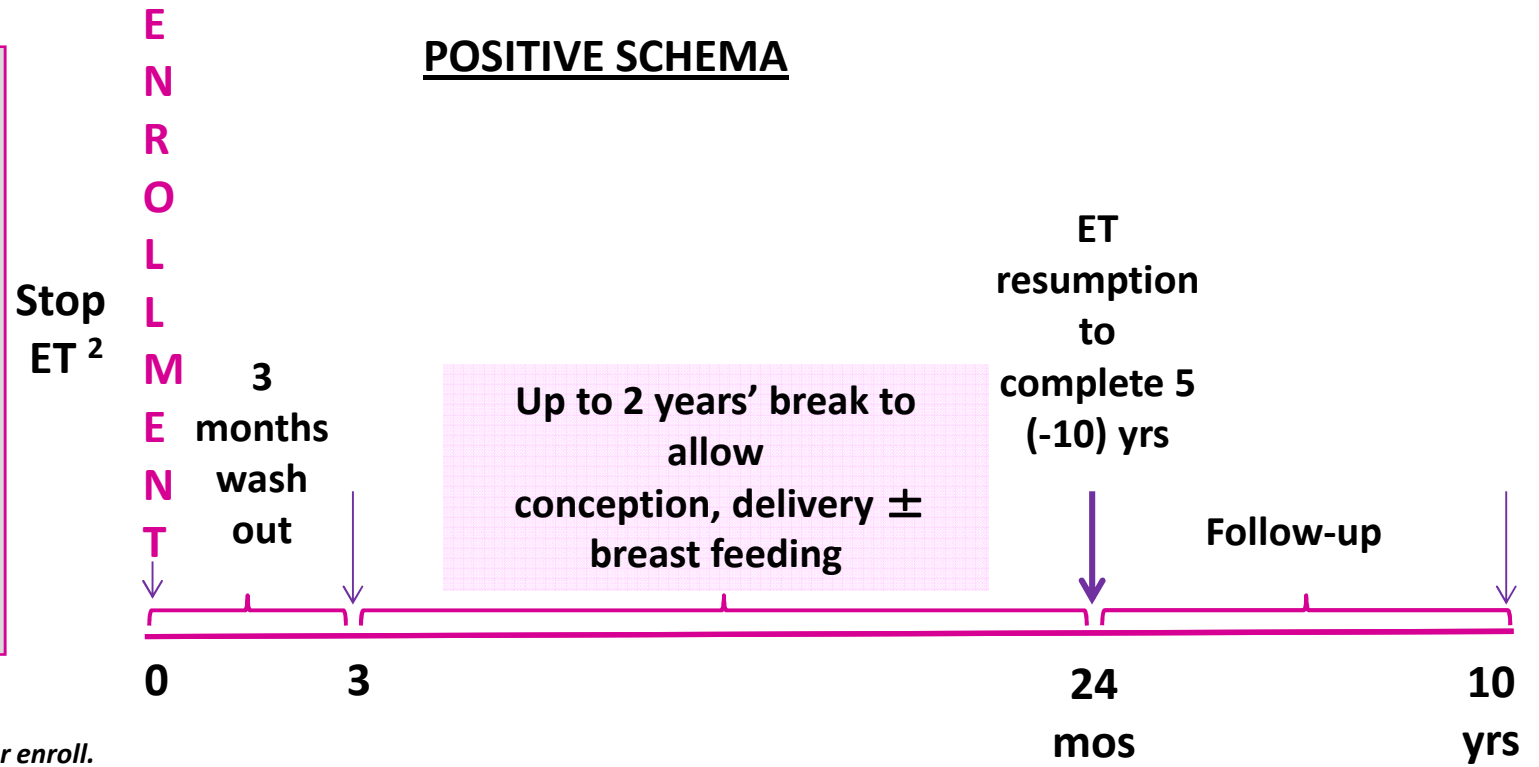
**Completing 18-30
months of ET** (SERMs
alone, GnRH
analogue + SERM or
Als) ¹

Pregnancy desire

¹ ± CT

² No more than 1 month prior enroll.

POSITIVE SCHEMA



Translational research

Ovarian function evaluation

Uterine evaluation

Circulating tumor DNA (ctDNA)

Genomic evaluation of primary breast tumor

Conclusioni

- Evaluate sterilization risks.
- Choose fertility preservation approach.
- Egg, embryo freezing; results similar to non-cancer patients.

Not post exposure to chemotherapy.

- Ovarian tissue freezing- established clinical method.

Grazie

