Preservazione della fertilità nelle donne con cancro della mammella in pre-menopausa

Alessia Levaggi
Oncologia Medica 2
Genova

V Zoom Journal Club 2015

Non un Congresso "classico" né un Corso, ma un'occasione per concreti aggiornamenti, confronto e dibattito su alcuni "Hot Topics 2015" dalla letteratura relativa alla radioterapia mammaria

Bologna
19 Febbraio 2016

IRCCS Azienda Ospedaliera Universitaria San Martino - IST
Istituto Nazionale per la Ricerca sul Cancro

Carcinoma mammario in Italia
Età: 0-49 anni

Età	STIMA NUOVI CASI anno 2015			DECESSI ISS – anno 2012	
	No.	%		No.	%
0-34	850	2%		50	0,4%
35-39	1.650	3%		146	1,2%
40-44	3.600	8%		322	2,7%
45-49	5.400	11%		583	4,9%
Tutte le età	47.900	100%		11.962	100%

5%

~ 24% sul totale di carcinomi mammari

The Oncologist®

Breast Cancer

Estimates of Young Breast Cancer Survivors at Risk for Infertility in the U.S.

KATRINA F. TRIVERS,[a] ALIZA K. FINK,[b] ANN H. PARTRIDGE,[c,d] KUTLUK OKTAY,[e,f] ELIZABETH S. GINSBURG,[d] CHUNYU LI,[a] LORI A. POLLACK[a]

Variable	NPCR and SEER, *n* (%)	PoC, *n* (%)	NSFG, *n* (%)
Age group (years)			
15–19	24 (0.0)	0	2,284 (17.0)
20–24	307 (0.5)	3 (0.4)	2,098 (16.8)
25–29	2,011 (3.4)	38 (2.9)	2,366 (17.1)
30–34	6,782 (11.3)	128 (10.2)	2,047 (14.9)
35–39	16,181 (26.9)	316 (26.3)	1,798 (17.1)
40–44	34,810 (57.9)	651 (60.3)	1,686 (17.2)
Chemotherapy	—		—
Received		879 (77.6)	
Not received		237 (20.2)	
Missing		20 (2.3)	

Outline

- **Premature ovarian failure (POF): impact of anticancer treatments on gonadal function**
- Strategies for fertility preservation in cancer patients (International guidelines)
- Preclinical evidence with the use of GnRh analogs
- Clinical evidence with the use of GnRh analogs
  - Non-randomized studies
  - Randomized studies
- Conclusions

Premature Ovarian Failure (POF)

- **Definition:** amenorrhea lasting more than 12 months before the age of 40 years

- **Health-related consequences:** **infertility**, osteoporosis, hot flashes, sleep disturbance, and sexual dysfunction

negative impact on short- and long-term QoL

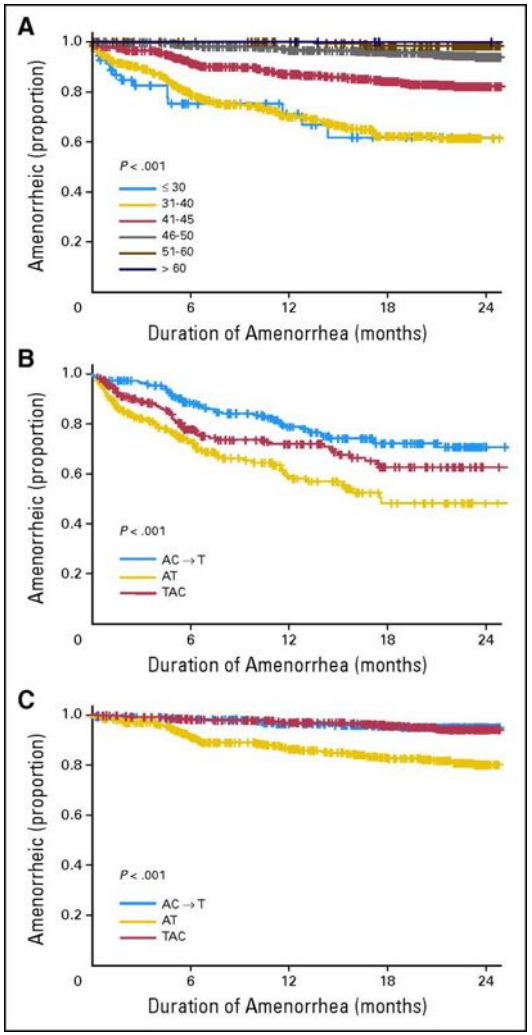
Schover LR et al, J Clin Oncol 2008; 26:753-758. Ruddy KJ & Partridge AH, J Clin Oncol 2012; 30:3705-3711

Key Factors for Treatment-Related POF

- **Patient's age**
- **Use and type of chemotherapy regimen**
- **Use of endocrine therapy**

Lee SJ et al, J Clin Oncol 2006; 24:2917-2931

(A) Duration of amenorrhea in months according to age group.



<= 40 years

> 40 years

Ganz P A et al. JCO 2011;29:1110-1116

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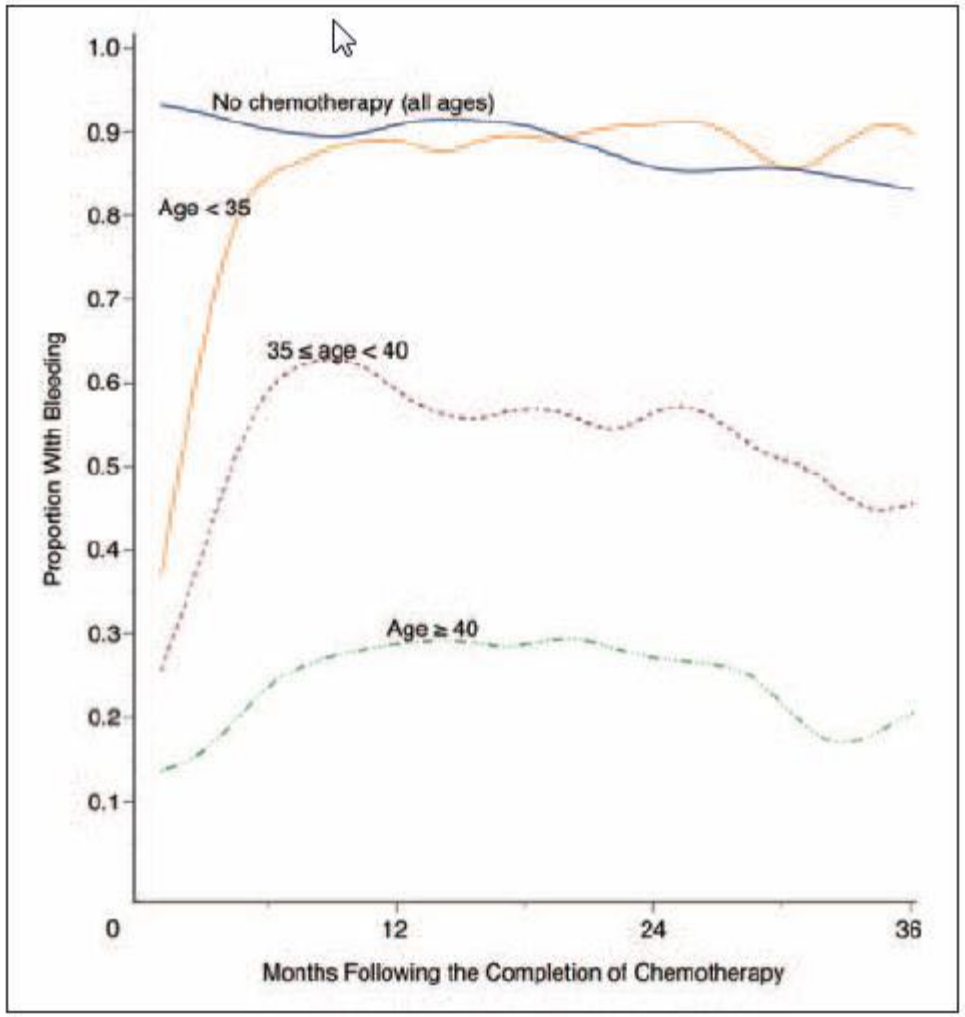
Early menopause by age
- < 35 y: 10%
- 35-40 y: 50%
- >40 y: 85%

Fig 2. Bleeding after chemotherapy by patient age



Petrek, J. A. et al. J Clin Oncol; 24:1045-1051 2006

Incidence of CT induced amenorrhea by regimen

Regimen	% pts developing amenorrhea
CMF x 6 *(Bines JCO 96)*	20-75
AC x 4 *(Bines JCO 96)*	34
MF x 6 *(Bines JCO 96)*	9
CEF x 6 *(Venturini JNCI 05; Levine JCO 98)*	50-60
FAC x 6 *(Marty NEJM 05)*	51
TAC x 6 *(Marty NEJM 05)*	61
AC x 4 -> Tx4 *(Fornier Cancer 05)*	15*

* Only <= 40 yrs pts; amenorrhea >= 12 months

Ovarian reserve in women who remain premenopausal after chemotherapy for early stage breast cancer

Ann H. Partridge, M.D., M.P.H.,[a,b] *Kathryn J. Ruddy, M.D.,*[a,b] *Shari Gelber, M.S.,*[a] *Lidia Schapira, M.D.,*[c] *Mary Abusief, M.D.,*[b] *Meghan Meyer, B.S.,*[a] *and Elizabeth Ginsburg, M.D.*[a,b]

[a] Dana-Farber Cancer Institute; [b] Brigham and Women's Hospital; and [c] Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts

	Survivors (20)*	Controls (20)	P-value
Antral Follicle Count (AFC)	5.2	11.3	0.0042
Anti-Mullerian Hormone (AMH)	0.57	1.77	0.0004
FSH	11.56	8.04	0.02
Inhibin B (InB)	24.3	46.6	0.02
Estradiol (E2)	126.0	38.8	0.14

* 45% received AC
40% received AC-T (DD)

Partridge A et al; Fertil Steril 2010

EUROPEAN JOURNAL OF CANCER 47 (2011) 74–83

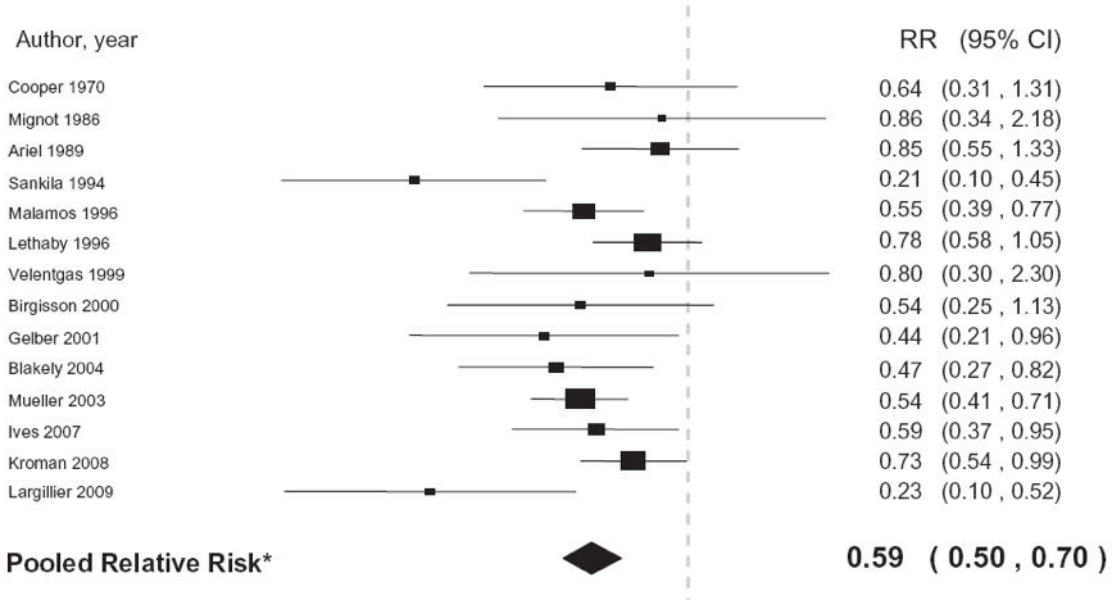
available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejconline.com

Safety of pregnancy following breast cancer diagnosis: A meta-analysis of 14 studies

Hatem A. Azim Jr. [a,b], *Luigi Santoro* [c], *Nicholas Pavlidis* [d], *Shari Gelber* [e], *Niels Kroman* [f], *Hamdy Azim* [g], *Fedro A. Peccatori* [h,*]



Outline

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VOLUME 31 · NUMBER 19 · JULY 1 2013

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Fertility Preservation for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update

Alison W. Loren, Pamela B. Mangu, Lindsay Nohr Beck, Lawrence Brennan, Anthony J. Magdalinski, Ann H. Partridge, Gwendolyn Quinn, W. Hamish Wallace, and Kutluk Oktay

clinical practice guidelines

Annals of Oncology 00: 1–11, 2013
doi:10.1093/annonc/mdt199

Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

F. A. Peccatori[1], H. A. Azim Jr[2], R. Orecchia[3], H. J. Hoekstra[4], N. Pavlidis[5], V. Kesic[6] & G. Pentheroudakis[5], on behalf of the ESMO Guidelines Working Group*

[1]Fertility and Procreation Unit, Division of Gynaecologic Oncology, European Institute of Oncology, Milan, Italy; [2]Department of Medicine, BrEAST Data Centre, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium; [3]Department of Radiotherapy, European Institute of Oncology, Milan, Italy; [4]Department of Surgical Oncology, University Medical Centre Groningen, Groningen, The Netherlands; [5]Department of Medical Oncology, University of Ioannina, Ioannina, Greece; [6]Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia;

Intervention	Definition	Comment	Considerations*
Embryo cryopreservation (S)	Harvesting eggs, in vitro fertilization, and freezing of embryos for later implantation	The most established technique for fertility preservation in women	• Requires 10-14 days of ovarian stimulation from the beginning of menstrual cycle • Outpatient surgical procedure • Requires partner or donor sperm • Approximately $8,000 per cycle, $350 per year storage fees
Oocyte cryopreservation (I)	Harvesting and freezing of unfertilized eggs	Small case series and case reports; as of 2005, 120 deliveries reported, approximately 2% live births per thawed oocyte (3-4 times lower than standard IVF)	• Requires 10-14 days of ovarian stimulation from the beginning of menstrual cycle • Outpatient surgical procedure • Approximately $8,000 per cycle, $350/yr storage fees
Ovarian cryopreservation and transplantation (I)	Freezing of ovarian tissue and reimplantation after cancer treatment	Case reports; as of 2005, two live births reported	• Not suitable when risk of ovarian involvement is high • Same day outpatient surgical procedure
Gonadal shielding during radiation therapy (S)	Use of shielding to reduce the dose of radiation delivered to the reproductive organs	Case series	• Only possible with selected radiation fields and anatomy • Expertise is required to ensure shielding does not increase dose delivered to the reproductive organs
Ovarian transposition (oophoropexy) (S)	Surgical repositioning of ovaries away from the radiation field	Large cohort studies and case series suggest approximately 50% chance of success due to altered ovarian blood flow and scattered radiation	• Same day outpatient surgical procedure • Transposition should be performed just before radiation therapy to prevent return of ovaries to former position • May need repositioning or in vitro fertilization (IVF) to conceive
Trachelectomy (S)	Surgical removal of the cervix while preserving the uterus	Large case series and case reports	• Inpatient surgical procedure • Limited to early stage cervical cancer; no evidence of higher cancer relapse rate in appropriate candidates • Expertise may not be widely available
Other conservative gynecologic surgery (S/I)	Minimization of normal tissue resection	Large case series and case reports	• Expertise may not be widely available
Ovarian suppression with gonadotropin releasing hormone (GnRH) analogs or antagonists (I)	Use of hormonal therapies to protect ovarian tissue during chemotherapy or radiation therapy	Small randomized studies and case series. Larger randomized trials in progress	• Medication given before and during treatment with chemotherapy • Approximately $500/mo

Lee SJ et al, J Clin Oncol 2006; 24:2917-2931

OOCYTE CRYOPRESERVATION

RISKS	SOLUTIONS
Delay in cancer treatment initiation (the 2-week duration of standard protocols)	In recent years, random stimulation protocols inducing luteolysis have been adopted to allow to start COS anytime during the menstrual cycle without having to wait until the follicular phase
Potential negative impact of ovarian stimulation on the prognosis of patients with hormone-responsive tumors in particular	Alternative protocols for ovarian stimulation with the use of tamoxifen or letrozole have been developed

Lambertini et al., BMC Medicine 2016

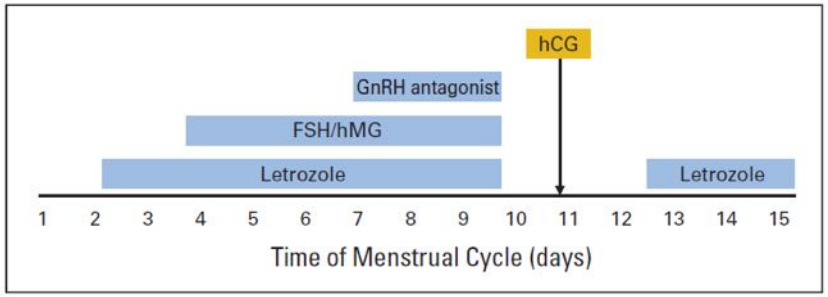
VOLUME 26 · NUMBER 16 · JUNE 1 2008

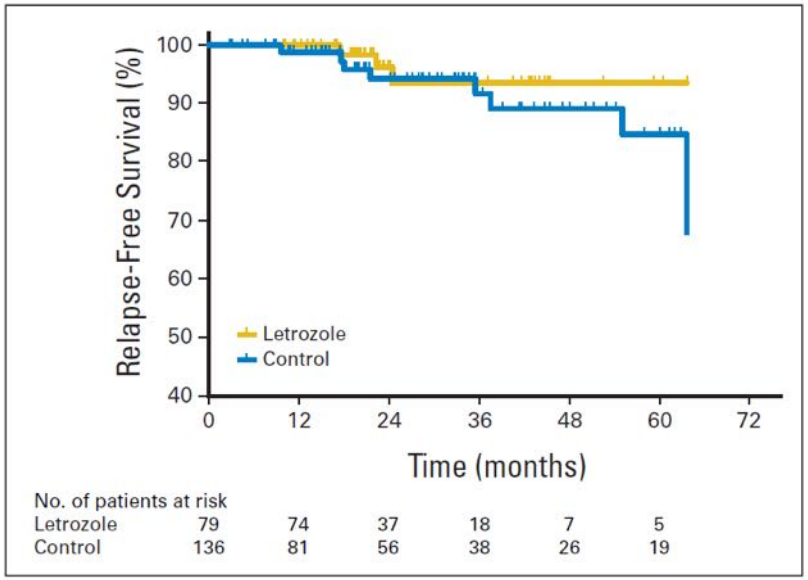
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Safety of Fertility Preservation by Ovarian Stimulation With Letrozole and Gonadotropins in Patients With Breast Cancer: A Prospective Controlled Study

Amr A. Azim, Maria Costantini-Ferrando, and Kutluk Oktay





OVARIAN TISSUE CRYOPRESERVATION

PRO	CONTRA
Does not require hormonal stimu-Lation	Still experimental technique
Only few days are required	Strongly dependent upon the patient’ s ovarian reserve
Can be performed at any time of the menstrual cycle	Potential risk of reintroducing malignant cells when the tissue is re-implanted

Lambertini et al., BMC Medicine 2016

Outline

- Premature ovarian failure (POF): impact of anticancer treatments on gonadal function
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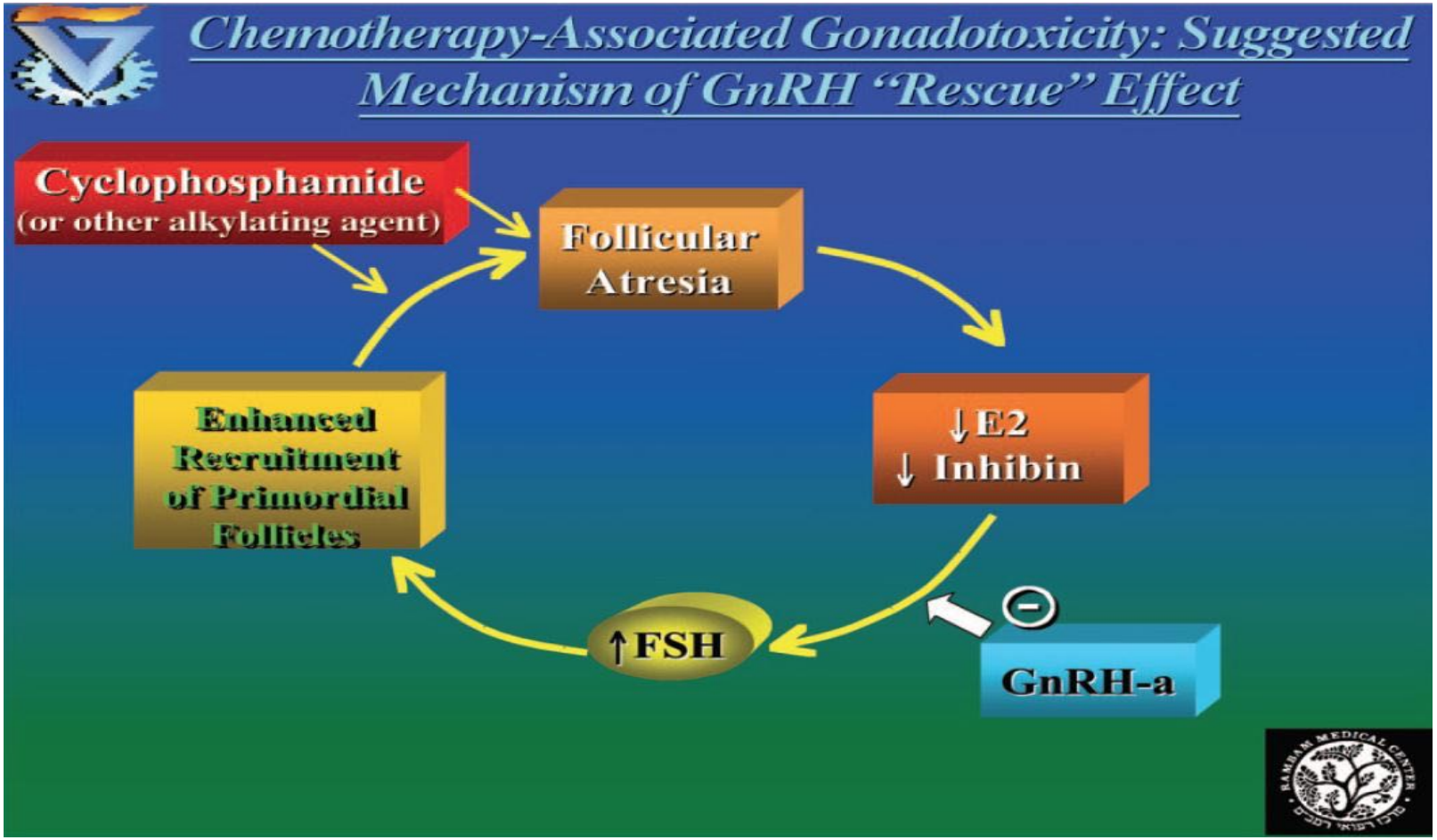
Possible Mechanisms of Action

1. **Interruption of FSH Secretion**
2. Decrease in utero-ovarian perfusion
3. Activation of GnRh receptors → decreased apoptosis
4. Upregulation of the anti-apoptotic molecule Sphingosine-1-Phosphate (S1P)
5. Protection of undifferentiated germ line stem cells

Blumenfeld Z, The Oncologist 2007; 12:1044-1054

Possible Mechanisms of Action

1. Interruption of FSH Secretion



Blumenfeld Z, The Oncologist 2007; 12:1044-1054

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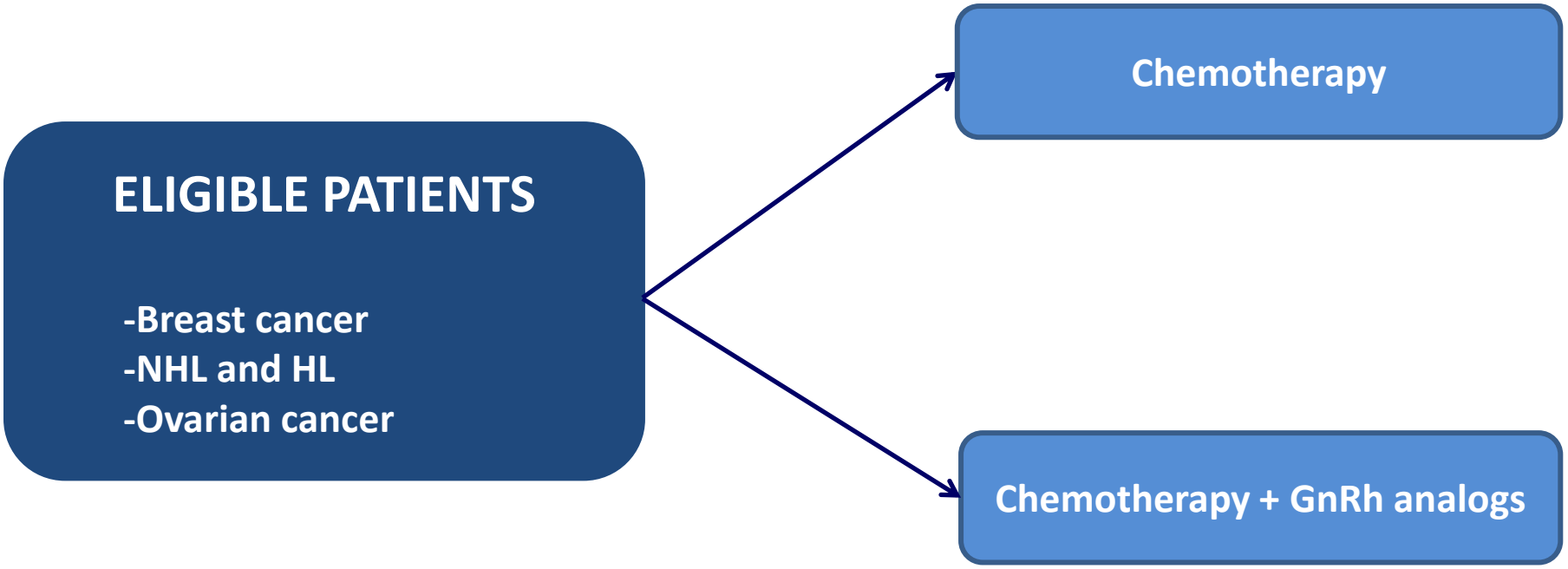
Non-Randomized Studies

Study	Study design	No. of patients	Pathology	GnRHa
Waxman *et al.* [56]	Phase III	18	HL	Buserelin
Pereyra Pacheco *et al.* [57]	Phase II	16	Hematology/Oncology	Leuprolide
Blumenfeld *et al.* [58]	Phase II	75	HL, NHL	Triptorelin
Franke *et al.* [59]	Observational Prospective	5	HL	Goserelin
Dann *et al.* [60]	Observational Prospective	7	NHL	Triptorelin
Somers *et al.* [61]	Observational Prospective	20	Systemic lupus erythematosus	Leuprolide
Del Mastro *et al.* [62]	Phase II	28	Breast cancer	Goserelin
Recchia *et al.* [63]	Observational Retrospective	100	Breast cancer	Goserelin
Giuseppe *et al.* [64]	Randomized	29	HL	Triptorelin
Castelo-Branco *et al.* [65]	Phase II	30	HL	Triptorelin
Blumenfeld *et al.* [66]	Phase II	65	HL	Triptorelin
Huser *et al.* [67]	Phase II	72	HL	Triptorelin

GnRHa: Gonadotropin-releasing hormone analogues; HL: Hodgkin lymphoma; NHL: Non-Hodgkin lymphoma.

Del Mastro L et al, Expert Opin Pharmacother 2011; 12:387-396

Randomized Studies



- **Primary endpoint:** Premature ovarian failure (POF)
- **Several limitations:** heterogeneous target population, different patients' age at the study entry, differences in chemotherapy regimens used, different duration of follow-up, and differences in the end points identified to assess treatment efficacy

ESMO GUIDELINES 2013

"Hence, the use of GnRh analogues concomitantly with chemotherapy should not be regarded as a reliable means of preserving fertility. Data on long-term ovarian function an pregnancy rates in these cohorts are warranted".

ASCO GUIDELINES 2013

"There are not definitive data[5,11,21,50] that show that GnRh-a preserves fertility, and it remains the subject of ongoing research. Given the current state of knowledge regarding these agents, it is the opinion of the Update Panel that GnRh-a is not an effective method of fertility preservation […] consider GnRh-a an unproven option (preferably as a part of a clinical trial), with special consideration of the patient's specific cancer and needs".

Loren AW et al, J Clin Oncol 2013; 31:2500-10. Peccatori F et al, Ann Oncol 2013; 24:vi160-70

ORIGINAL CONTRIBUTION

Effect of the Gonadotropin-Releasing Hormone Analogue Triptorelin on the Occurrence of Chemotherapy-Induced Early Menopause in Premenopausal Women With Breast Cancer

A Randomized Trial

Lucia Del Mastro, MD
Luca Boni, MD
Andrea Michelotti, MD
Teresa Gamucci, MD
Nina Olmeo, MD
Stefania Gori, MD
Monica Giordano, MD
Ornella Garrone, MD
Paolo Pronzato, MD
Claudia Bighin, MD
Alessia Levaggi, MD
Sara Giraudi, MD
Nicola Cresti, MD
Emanuela Magnolfi, MD
Tiziana Scotto, MD
Carlo Vecchio, MD
Marco Venturini, MD

Context Premenopausal patients with breast cancer are at high risk of premature ovarian failure induced by systemic treatments, but no standard strategies for preventing this adverse effect are yet available.

Objective To determine the effect of the temporary ovarian suppression obtained by administering the gonadotropin-releasing hormone analogue triptorelin during chemotherapy on the incidence of early menopause in young patients with breast cancer undergoing adjuvant or neoadjuvant chemotherapy.

Design, Setting, and Patients The PROMISE-GIM6 (Prevention of Menopause Induced by Chemotherapy: A Study in Early Breast Cancer Patients–Gruppo Italiano Mammella 6) study, a parallel, randomized, open-label, phase 3 superiority trial, was conducted at 16 sites in Italy and enrolled 281 patients between October 2003 and January 2008. The patients were premenopausal women with stage I through III breast cancer who were candidates for adjuvant or neoadjuvant chemotherapy. Assuming a 60% rate of early menopause in the group treated with chemotherapy alone, it was estimated that 280 patients had to be enrolled to detect a 20% absolute reduction in early menopause in the group treated with chemotherapy plus triptorelin. The intention-to-treat analysis was performed by including all randomized patients and using imputed values for missing data.

Interventions Before beginning chemotherapy, patients were randomly allocated to receive chemotherapy alone or combined with triptorelin. Triptorelin was administered intramuscularly at a dose of 3.75 mg at least 1 week before the start of chemotherapy and then every 4 weeks for the duration of chemotherapy.

Main Outcome Measure Incidence of early menopause (defined as no resump-

GRUPPO ITALIANO MAMMELLA

Long-term outcome results of the phase III PROMISE-GIM6 study evaluating the role of LHRH analog during chemotherapy as a strategy to reduce ovarian failure in early breast cancer patients

Matteo Lambertini, Luca Boni, Andrea Michelotti, Teresa Gamucci, Nina Olmeo, Stefania Gori, Monica Giordano, Ornella Garrone, Alessia Levaggi, Francesca Poggio, Sara Giraudi, Claudia Bighin, Paolo Pronzato, Lucia Del Mastro

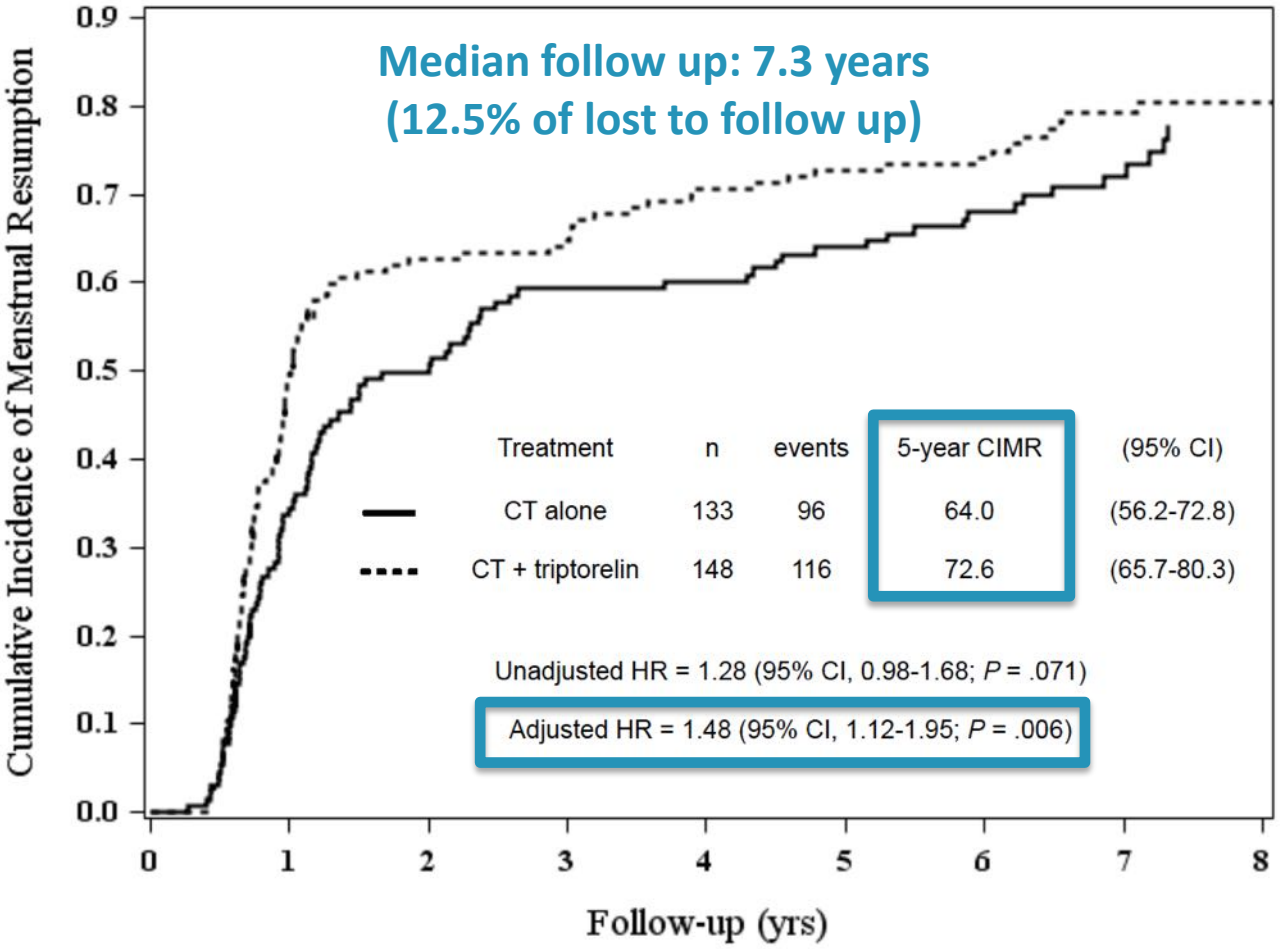
Presented at the BREAST CANCER SYMPOSIUM

- **Study characteristics:**

1. **Number of patients:** 281 evaluated (282 randomly assigned)
2. **Eligible patients:** Operable stage I-III, ER+ or ER- breast cancer
3. **Type of chemotherapy:** (Neo)adjuvant anthracycline plus taxane-based, anthracycline-based, or CMF-based chemotherapy
4. **Primary endpoint:** Ovarian failure rate at 1 year (defined no resumption of menses and levels of FSH and E2 in the post-menopausal range)

Study endpoints	Chemotherapy alone arm	Chemotherapy + triptorelin arm
Ovarian failure rate at 1 year	25.9%	8.9%
Adjusted odds ratio	0.28 (0.14 – 0.59); p < 0.001	
No. pregnancies	3	8
Adjusted hazard ratio	2.56 (0.68 – 9.60); p = 0.142	
5-year disease-free survival	83.7%	80.5%
Adjusted hazard ratio	1.17 (0.72 – 1.92); p = 0.519	

Del Mastro L et al, JAMA 2011; 306; 269-276. Lambertini M et al, ASCO Breast 2014 (submitted)



No. at risk

	0	1	2	3	4	5	6	7	8
CT alone	133	82	61	43	42	35	26	16	6
CT + triptorelin	148	73	49	46	38	32	28	14	8

Lambertini M et al, ASCO Breast 2014 (submitted)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Goserelin for Ovarian Protection during Breast-Cancer Adjuvant Chemotherapy

Halle C.F. Moore, M.D., Joseph M. Unger, Ph.D., Kelly-Anne Phillips, M.D., Frances Boyle, M.B., B.S., Ph.D., Erika Hitre, M.D., David Porter, M.D., Prudence A. Francis, M.D., Lori J. Goldstein, M.D., Henry L. Gomez, M.D., Carlos S. Vallejos, M.D., Ann H. Partridge, M.D., M.P.H., Shaker R. Dakhil, M.D., Agustin A. Garcia, M.D., Julie Gralow, M.D., Janine M. Lombard, M.D., John F. Forbes, M.B., B.S., Silvana Martino, D.O., William E. Barlow, Ph.D., Carol J. Fabian, M.D., Lori Minasian, M.D., Frank L. Meyskens, Jr., M.D., Richard D. Gelber, Ph.D., Gabriel N. Hortobagyi, M.D., and Kathy S. Albain, M.D., for the POEMS/S0230 Investigators

N Engl J Med 2015;372:923-32.

- **Study characteristics:**

1. **Number of patients:** 218 evaluated (256 randomly assigned)
2. **Eligible patients:** Operable stage I-III, ER- and PR- breast cancer
3. **Type of chemotherapy:** (Neo)adjuvant cyclophospamide-containing chemotherapy
4. **Primary endpoint:** Ovarian failure rate at 2 years (defined as absence of menses in the preceding 6 months and levels of FSH in the post-menopausal range). **Only 61.9% of patients were included in the primary endpoint analysis.**

Study endpoints	Chemotherapy alone arm	Chemotherapy + goserelin arm
Ovarian failure rate at 2 years	22%	8%
Stratified odds ratio	0.30 (0.09 – 0.97); p = 0.04	
No. pregnancies	12	22
Adjusted odds ratio	2.45; p = 0.03	
4-year disease-free survival	78%	89%
Adjusted hazard ratio	0.49 (0.24 – 0.97); p = 0.04	

Moore HCF et al, N Engl J Med 2015; 372:923-932

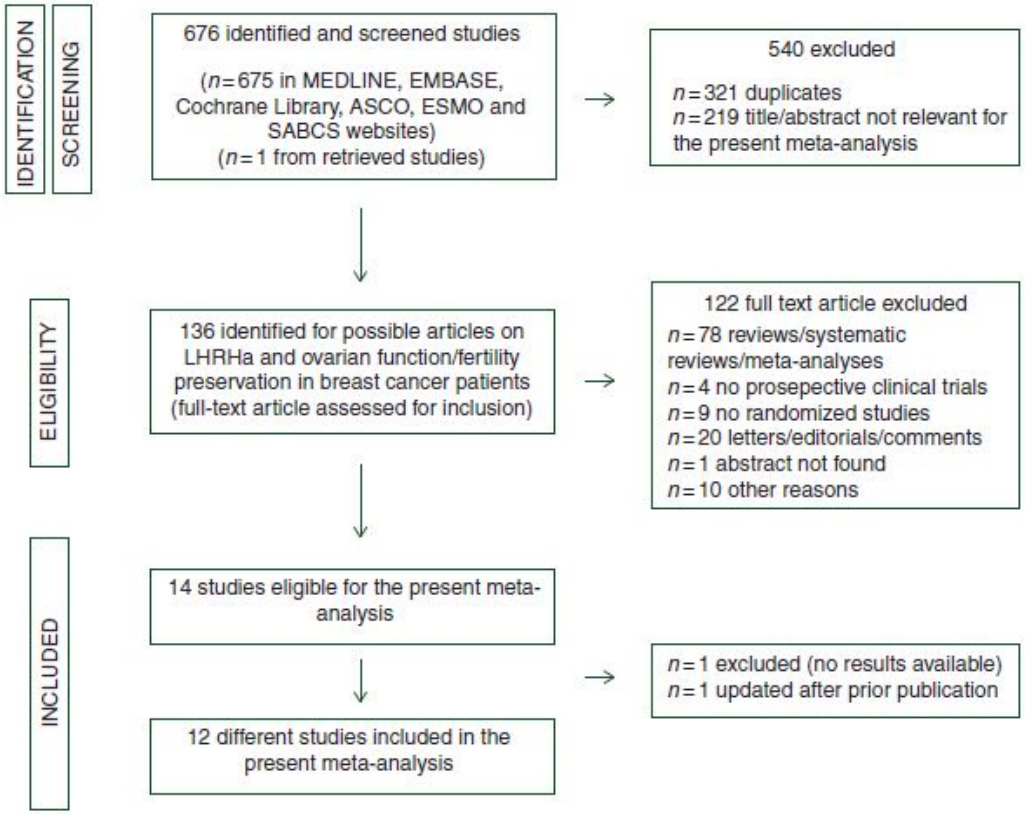
Toxic effects

Adverse Event	Chemotherapy Alone (N=111)			Chemotherapy plus Goserelin (N=103)		
	Grade 2	Grade 3	Grade 4	Grade 2	Grade 3	Grade 4
Diarrhea	2	0	0	0	0	0
Fatigue	1	0	0	2	0	0
Hot flashes	14	3	0	29	4	0
Irregular menses	2	0	0	5	2	0
Decrease in libido	6	0	0	9	0	0
Agitation	4	1	0	6	0	0
Anxiety	4	0	0	9	0	0
Depression	3	0	0	8	1	0
Joint pain	1	1	0	0	0	0
Muscle pain	2	0	0	1	0	0
Headache	1	1	0	12	0	0
Sweating	7	0	0	10	0	0
Thromboembolism	0	0	0	0	0	1
Vaginal dryness	9	0	0	12	0	0

Annals of Oncology 00: 1–12, 2015
doi:10.1093/annonc/mdv374

Ovarian suppression using luteinizing hormone-releasing hormone agonists during chemotherapy to preserve ovarian function and fertility of breast cancer patients: a meta-analysis of randomized studies

M. Lambertini[1], M. Ceppi[2], F. Poggio[1], F. A. Peccatori[3], H. A. Azim Jr[4], D. Ugolini[5], P. Pronzato[1], S. Loibl[6,7], H. C. F. Moore[8], A. H. Partridge[9], P. Bruzzi[2] & L. Del Mastro[10*]



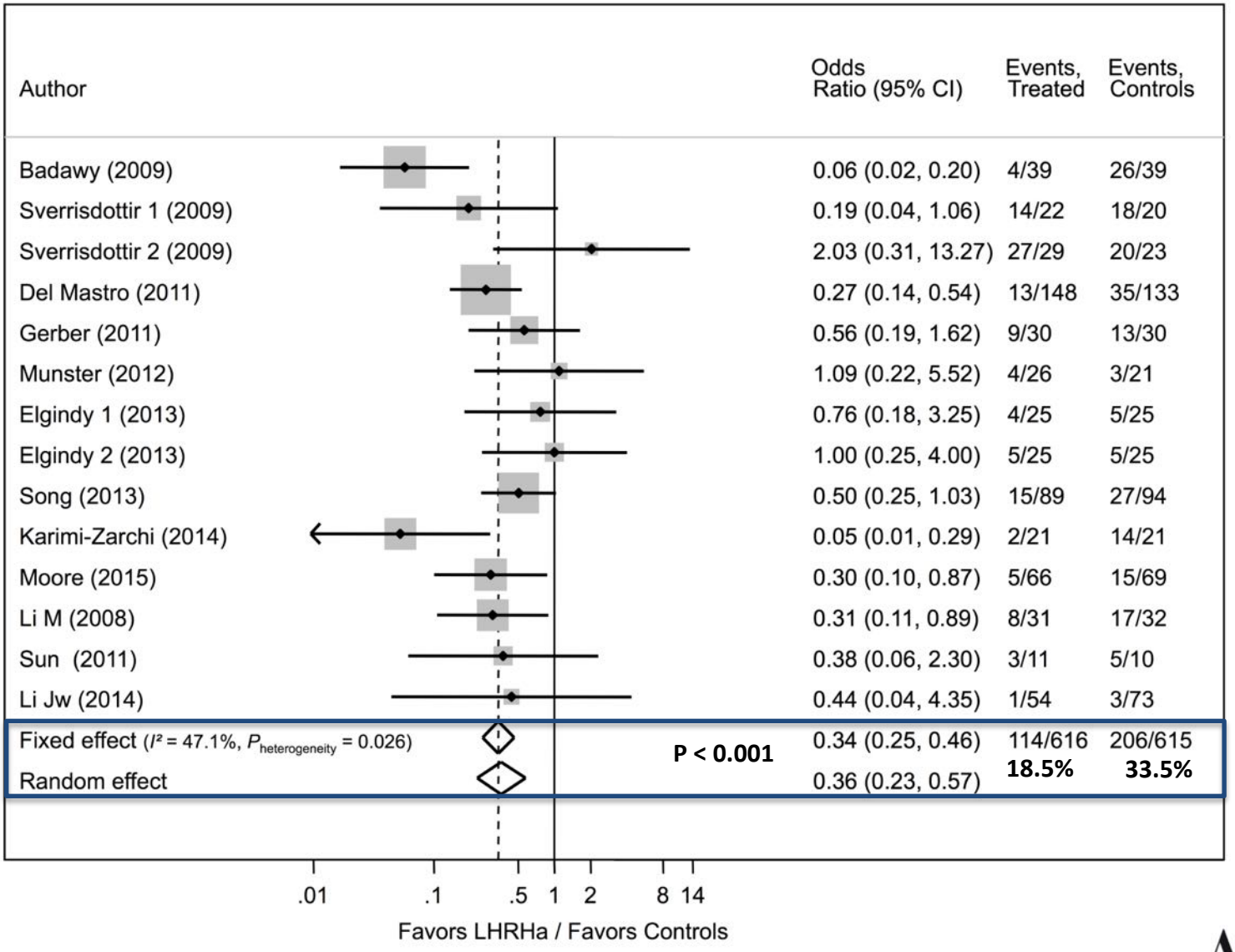
Study Objectives and Endpoints

- **Primary objective:** to compare the incidence of treatment-related POF between patients treated with concurrent temporary ovarian suppression with LHRHa during chemotherapy and those who received chemotherapy alone.

- **Secondary objectives:**
  a) to compare the incidence of treatment-related amenorrhea 1 year after the end of chemotherapy;
  b) to compare pregnancy rates;
  c) to evaluate the impact of concurrent administration of LHRHa and chemotherapy on disease-free survival (DFS).

Results:

Premature Ovarian Failure

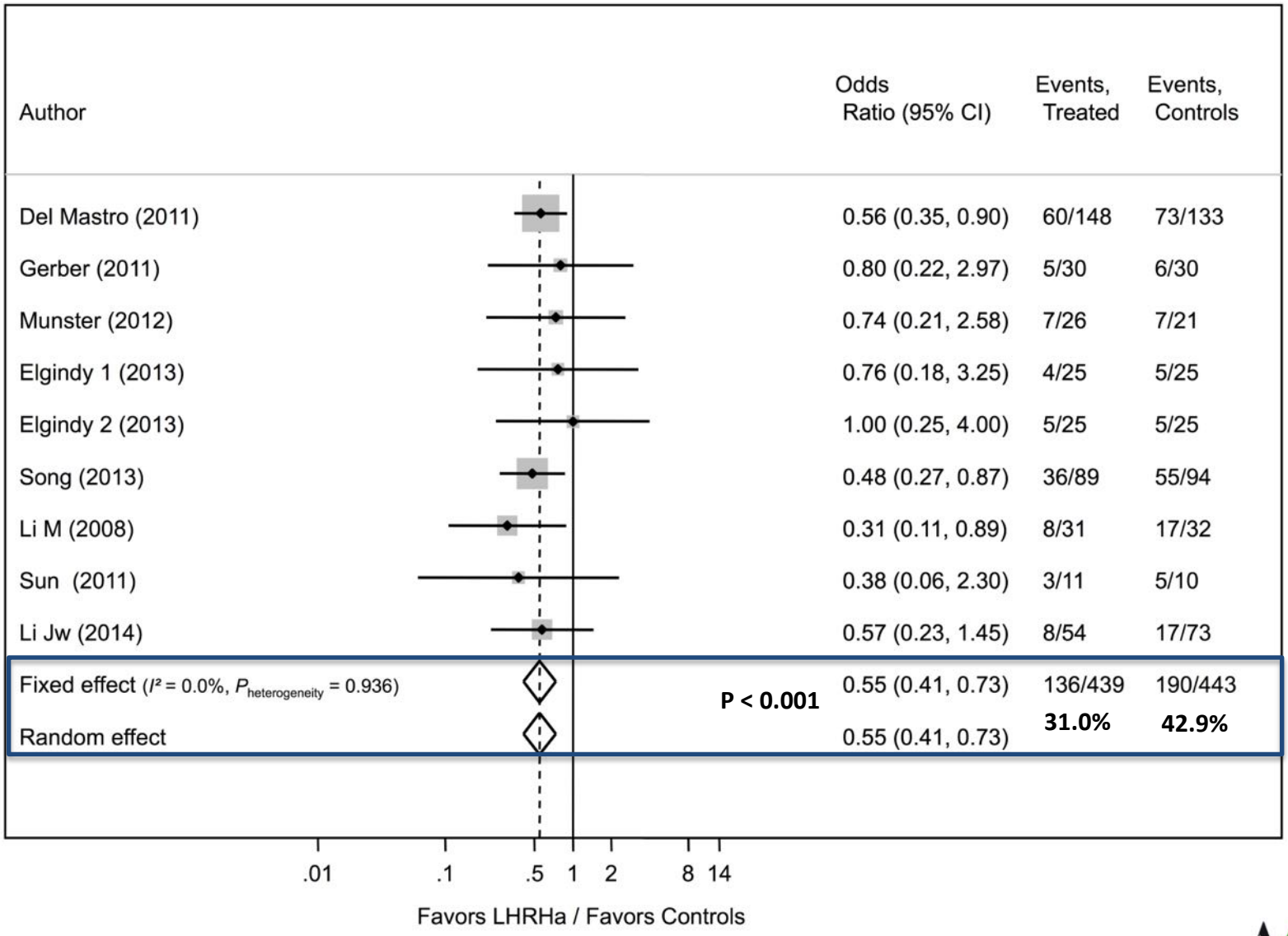


Presented at the **XVII Congresso Nazionale AIOM**

Presented by: Francesca Poggio, MD

Results:

One-Year Amenorrhea

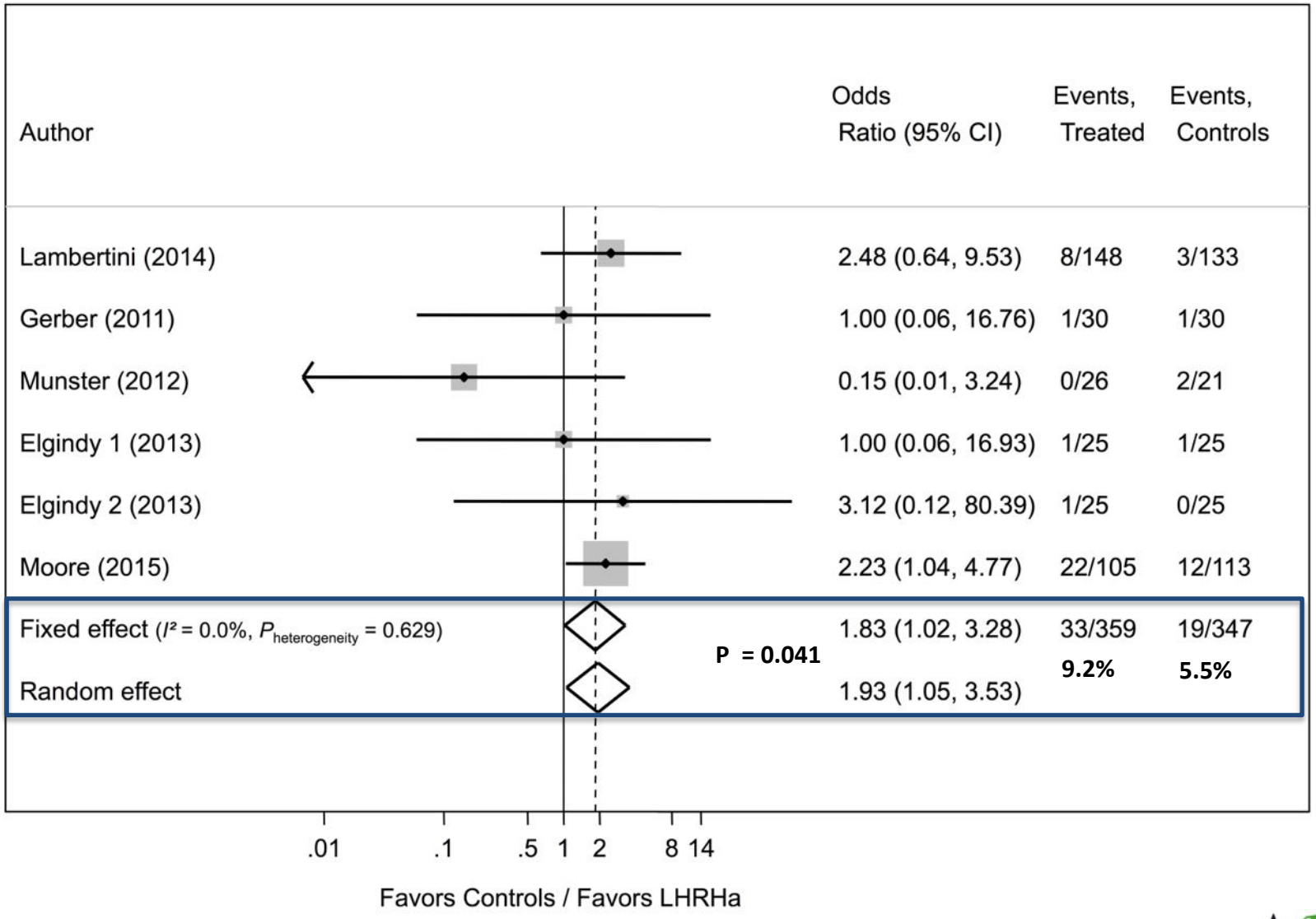


Presented at the **XVII Congresso Nazionale AIOM**

Presented by: Francesca Poggio, MD

Results:

Patients with Pregnancy

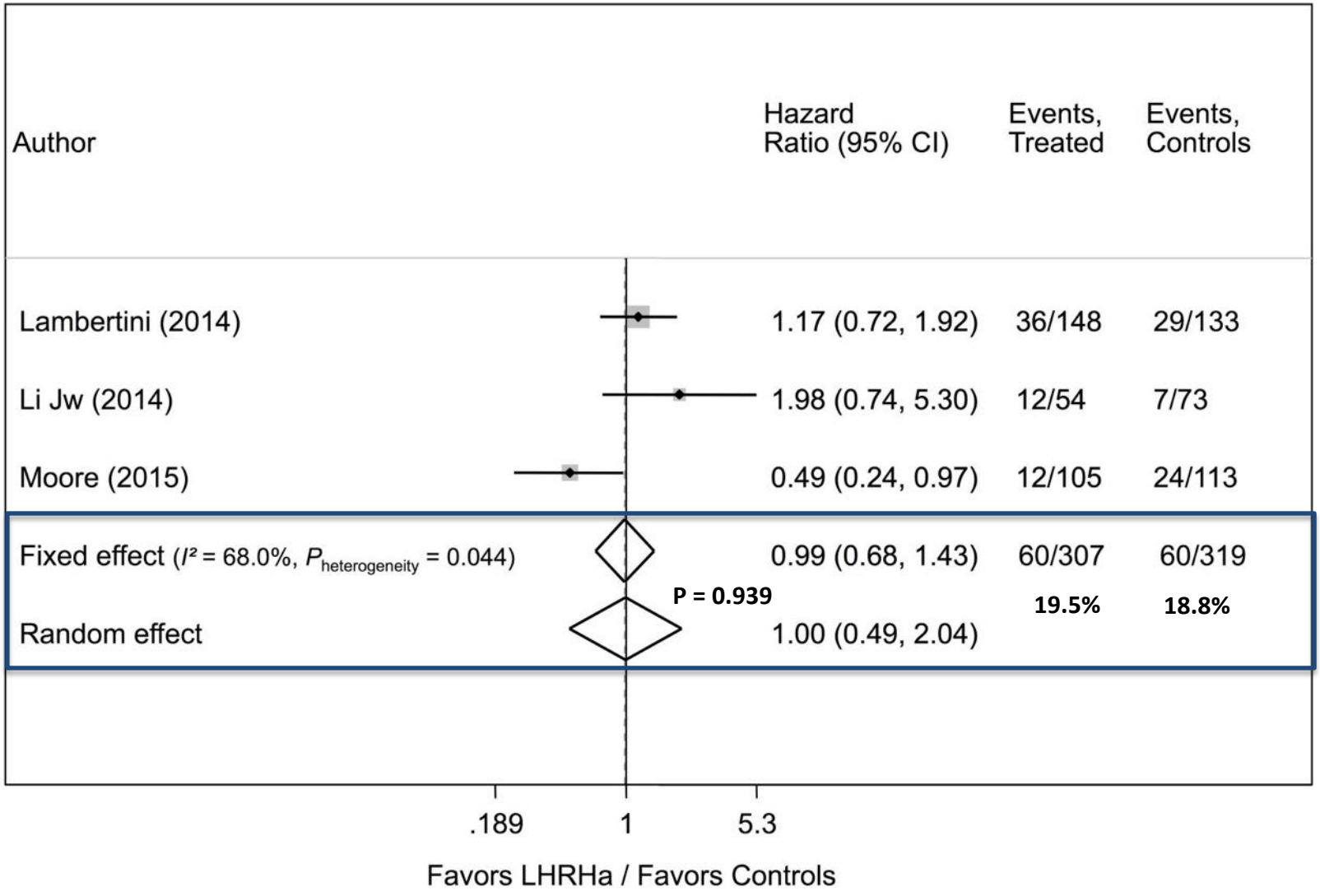


Presented at the **XVII Congresso Nazionale AIOM**

Presented by: Francesca Poggio, MD

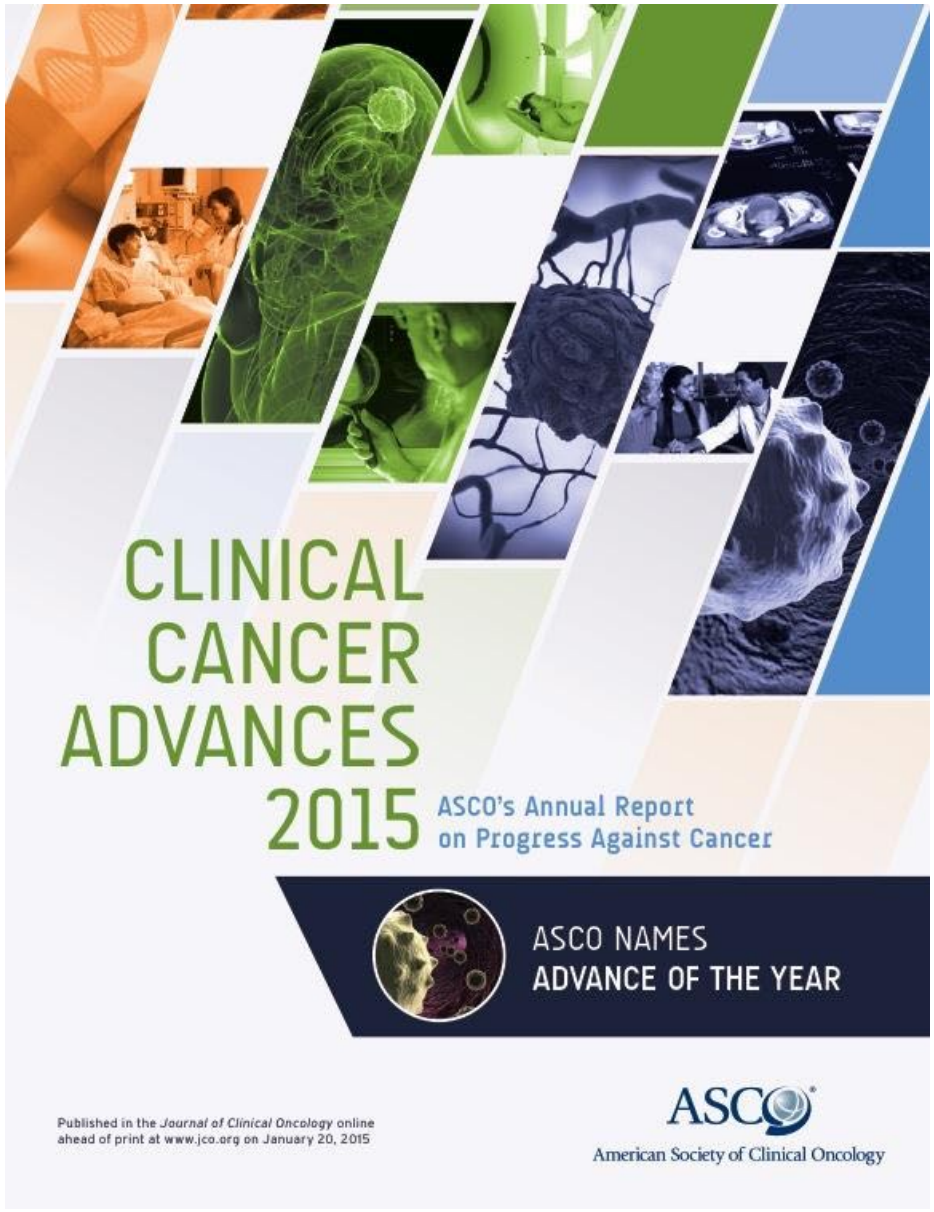
Results:

Disease-Free Survival



Presented at the **XVII Congresso Nazionale AIOM**

Presented by: Francesca Poggio, MD



GOOD NEWS FOR WOMEN HOPING TO HAVE A BABY AFTER BREAST CANCER TREATMENT

Premature ovarian failure (early menopause) is a common adverse effect in young women undergoing chemotherapy for breast cancer, often making it impossible for women to become pregnant after treatment. Two studies reported a promising new way to preserve fertility, by simply adding a hormone drug to chemotherapy.

Luteinizing hormone-releasing hormones (LHRHs) temporarily shut down ovarian function, essentially putting the patient into a postmenopausal state. It is speculated that this protects follicles (developing eggs) from chemotherapy damage. These medications are widely used to control ovulation timing for infertility treatments, such as in vitro fertilization. LHRH drugs are also widely used as hormonal therapies for advanced prostate and breast cancers.

LHRH analogo concomitante a chemioterapia

	Indicazioni
NCCN[1]	"Randomized trials have shown that ovarian suppression with GnRH agonist therapy administered during adjuvant chemotherapy in premenopausal women with ER-negative tumors may preserve ovarian function and diminish the likelihood of chemotherapy-induced amenorrhea"
SAN GALLEN[2]	"LHRH agonist therapy during chemotherapy proved effective to protect against premature ovarian failure and preserve fertility in young women with ER negative breast cancer undergoing chemotherapy"
ESMO[3]	"The role of GnRH agonists in preventing chemotherapy-related ovarian failure has been recently supported by the efficacy data (less premature ovarian failures and more pregnancies) from the POEMS trial (ER-negative patients) and safety data from TEXT trial (ER-positive patients). However, due to contradictory results from previous trials, the decision must be taken in a case-by-case manner and after careful discussion with the patient regarding benefits and risks of such an approach."

1 NCCN National Comprehensive Cancer Network®

V. 3. 2015

2 BCC 2015

3 ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

European Society for Medical Oncology

Conclusions

Linee Guida AIOM Fertilità 2015

Qualità globale delle evidenze GRADE	Raccomandazione clinica	Forza della raccomandazione clinica
Moderata	Nelle pazienti in premenopausa candidate a trattamento chemioterapico per neoplasia mammaria e desiderose di preservare la funzionalità ovarica, gli analoghi LHRH **dovrebbero essere proposti**. ** La valutazione complessiva della qualità delle evidenze ad oggi disponibili circa "l'utilizzo degli analoghi LHRH per la preservazione della funzionalità ovarica nelle pazienti in premenopausa candidate a trattamento chemioterapico per neoplasia mammaria e desiderose di preservare la funzionalità ovarica", la valutazione del rapporto tra i benefici ed i rischi correlati e la formulazione della raccomandazione relativa al quesito posto, sono state analizzate secondo metodologia GRADE (vedere capitolo 7).*	**Positiva forte**

What Women Want? The PREFER Study

Main results of oncofertility counseling by oncologist	No. pts = 87 (%)
Not interested in ovarian function/fertiliy preservation	9 (10.3)
Interested in ovarian function/fertiliy preservation	78 (89.7)
Took special steps to lessen chance of risk of POF/infertility: -LHRH analogs during chemotherapy -Counseling by fertility specialist	 75 (86.2) 20 (23.0)
Among patients who underwent fertility counseling: -Accepted oocyte cryopreservation -Accepted ovarian tissue cryopreservation	 4 (4.6) 1 (1.1)

Presented by Matteo Lambertini at the **BCY2 – Breast Cancer in Young Women Conference**

Outline

- Premature ovarian failure (POF): impact of anticancer treatments on gonadal function
- Strategies for fertility preservation in cancer patients (International guidelines)
- Preclinical evidence with the use of GnRh analogs
- Clinical evidence with the use of GnRh analogs
  - Non-randomized studies
  - Randomized studies
- **Conclusions**

Conclusions

- Pharmacological protection of the ovaries with the use of GnRh analogs during chemotherapy is an attractive option, yet still experimental, to preserve gonadal function and fertility.

- Recent data suggests both safety and efficacy for the use of GnRh analogs in women receiving (neo)adjuvant chemotherapy for breast cancer.

- Embryo/oocyte cryopreservation might be used together with ovarian suppression with GnRh analogs during chemotherapy to maximize the probability of preserving fertility, since the two techniques are not mutually exclusive.