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Abstract GS4-01: Pooled analysis of five randomized trials investigating temporary ovarian suppression with gonadotropin-releasing hormone analogs during chemotherapy as a strategy to preserve ovarian function and fertility in premenopausal early breast cancer patients

Daniela Dornelles Rosa, MD PhD

Hospital Moinhos de Vento
PPG Patologia UFCSPA
www.infomama.com.br
Porto Alegre, RS

HOSPITAL MOINHOS DE VENTO

UFCSPA

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Disclosures

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Lecture fees	Eisai, Roche, Novartis
Advisory board participation	Novartis, Roche
Academic research grant	L ‘Oreal
Stock owner	----

Pooled analysis of five randomized trials investigating temporary ovarian suppression with gonadotropin-releasing hormone analogs during chemotherapy as a strategy to preserve ovarian function and fertility in premenopausal early breast cancer patients

Matteo Lambertini[1], Halle C.F. Moore[2], Robert C.F. Leonard[3], Sibylle Loibl[4], Pamela Munster[5], Marco Bruzzone[6], Luca Boni[7], Joseph M. Unger[8], Richard A. Anderson[9], Keyur Mehta[4], Susan Minton[10], Francesca Poggio[6], Kathy S. Albain[11], Douglas J.A. Adamson[12], Bernd Gerber[13], Amy Cripps[14], Gianfilippo Bertelli[15], Sabine Seiler[4], Marcello Ceppi[6], Ann H. Partridge[16], and Lucia Del Mastro[6]

[1]Institut Jules Bordet and Université Libre de Bruxelles (U.L.B.), Brussels, Belgium. [2]Cleveland Clinic Foundation, Taussig Cancer Institute, Cleveland, OH. [3]Imperial College, London, UK. [4]GBG - German Breast Group, Neu-Isenburg, Germany. [5]UCSF - University of California, San Francisco, CA. [6]Ospedale Policlinico San Martino-IST, Genova, Italy. [7]AOU Careggi and Istituto Toscano Tumori, Firenze, Italy. [8]SWOG Statistical Center, Fred Hutchinson Cancer Research Center, Seattle, WA. [9]MRC Centre for Reproductive Health, University of Edinburgh, Edinburgh, UK. [10]Moffitt Cancer Center, Tampa, FL. [11]Loyola University Medical Center, Cardinal Bernardin Cancer Center, Maywood, IL. [12]Tayside Cancer Centre, Ninewells Hospital, Dundee, UK. [13]University Hospital Rostock, Rostock, Germany. [14]Nexgen Oncology, Dallas, TX. [15]Singleton Hospital, Swansea, UK. [16]Dana-Farber Cancer Institute, Boston, MA.

Background

- Fertility preservation and pregnancy-related issues are high priority areas of concern for young women with breast cancer
- Oocyte/embryo cryopreservation are standard strategies for fertility preservation but they do not prevent the risk of chemotherapy-induced premature ovarian insufficiency (POI)
- Temporary ovarian suppression with GnRHa during chemotherapy has been studied in several RCTs as a strategy to preserve ovarian function and potential fertility
- However, data are mixed and its role remains controversial

Study Methods

- Systematic review and meta-analysis of individual patient data from RCTs that investigated the role of temporary ovarian suppression with GnRHa during chemotherapy for early breast cancer patients

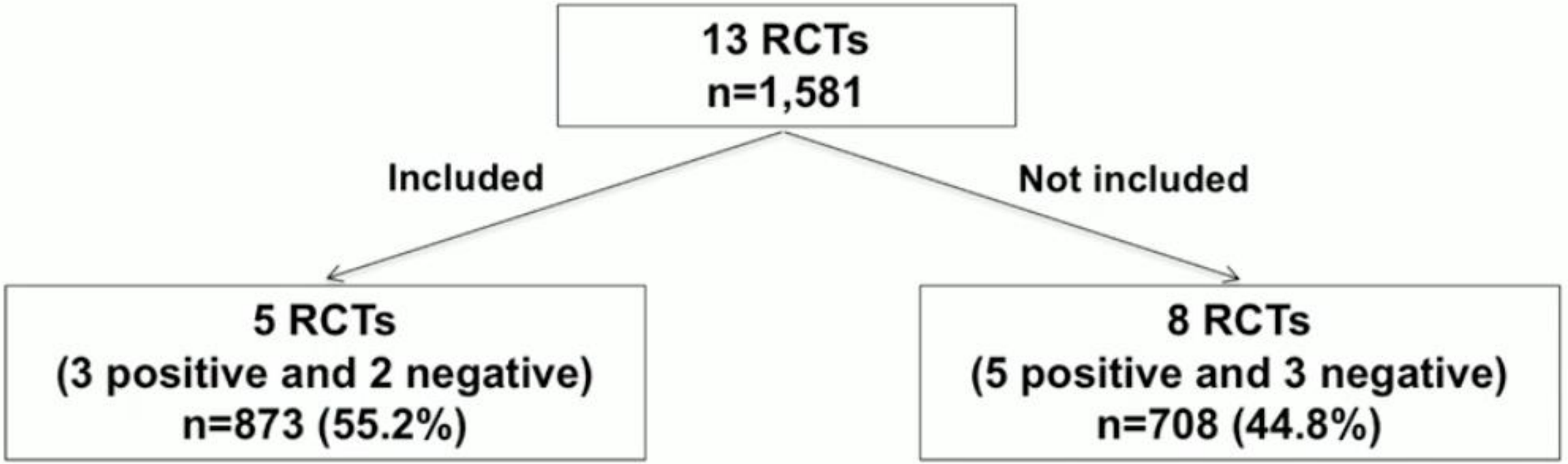
Study objectives

- To evaluate the efficacy (ovarian function and fertility preservation) and the safety (survival outcomes) of GnRHa use during chemotherapy

Study endpoints

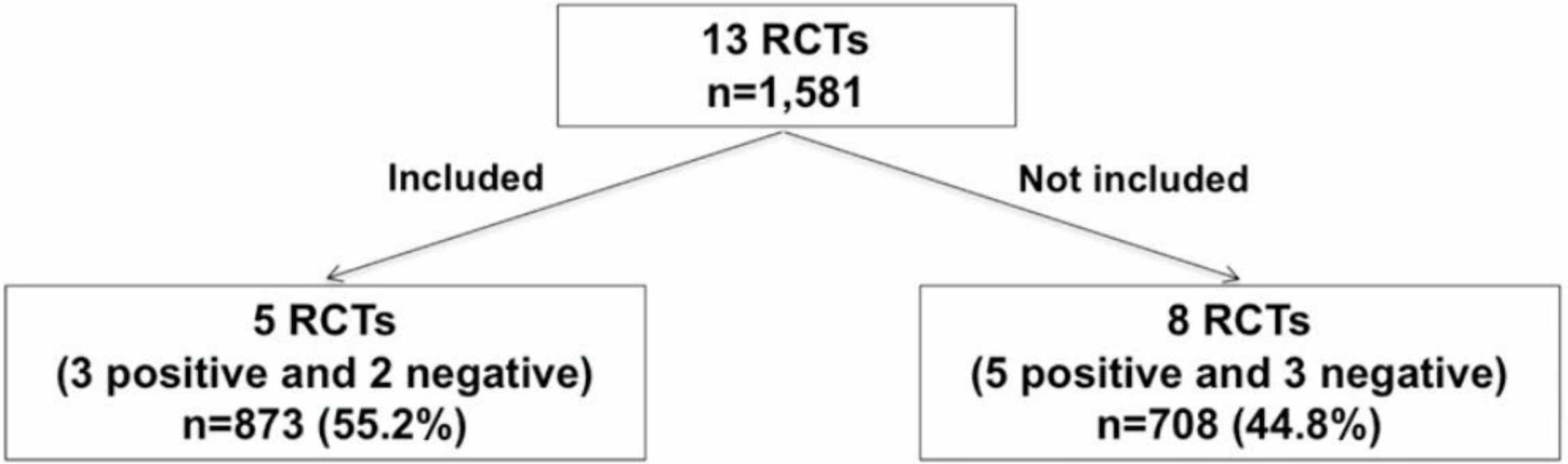
- **Primary endpoints**
  - POI rate (according to the definition used as primary endpoint in each trial)
  - Post-treatment pregnancy rate
- **Secondary endpoints**
  - Amenorrhea rates one year and two years after the end of chemotherapy
  - Disease-free survival (DFS) and overall survival (OS)

Results



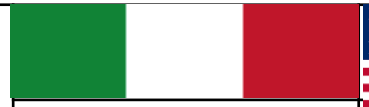
PROSPERO registration number: CRD42014015638

Results



PROMISE-GIM6[1,2]	POEMS/SWOG S0230[3]	Moffitt-led trial[4]	GBG-37 ZORO[5]	Anglo Celtic Group OPTION[6]

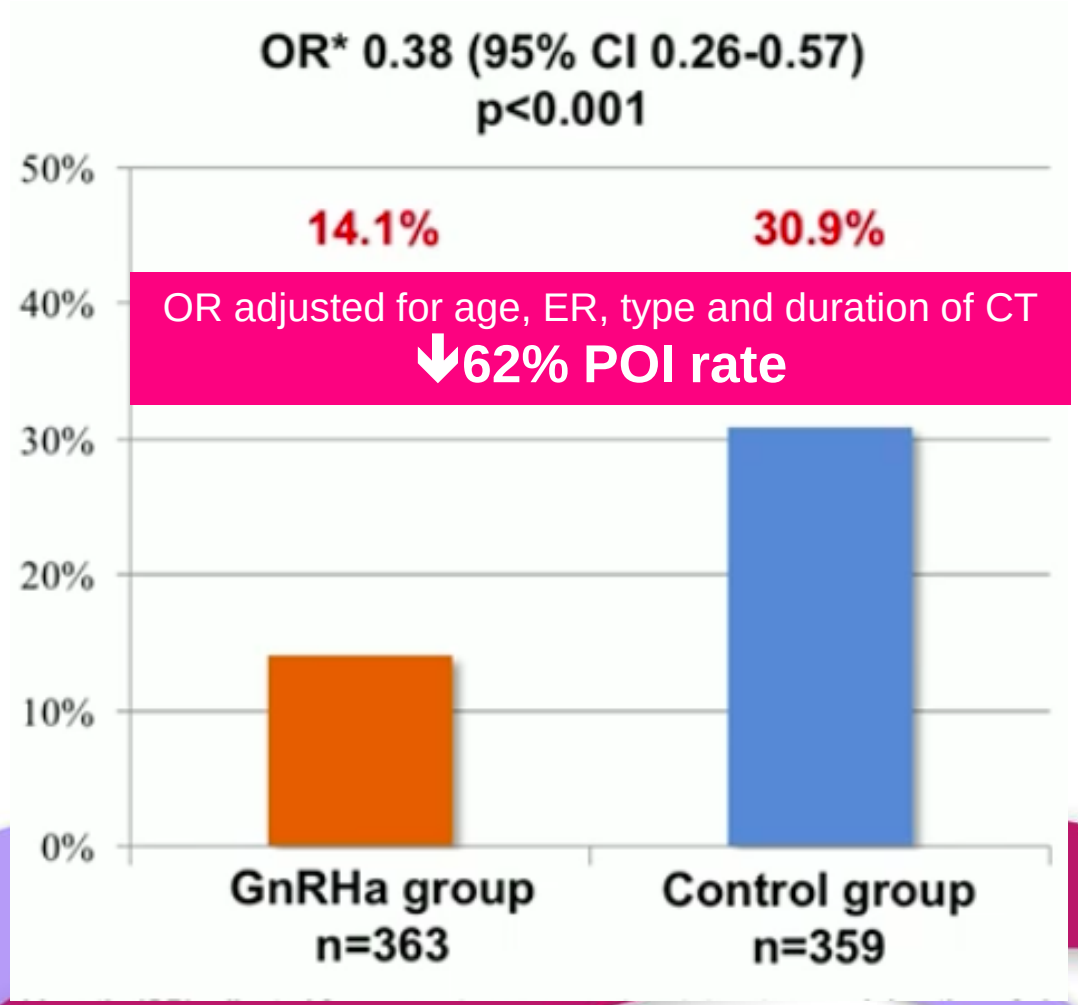
Study Characteristics

					
	PROMISE-GIM6[1,2]	**POEMS/SWOG S0230[3]**	**Moffitt-led trial[4]**	**GBG-37 ZORO[5]**	**Anglo Celtic Group OPTION[6]**
Definition of POI	No resumption of [illegible] Amenorrhea + FHS + E2	Amenorrhea for the [illegible] Amenorrhea + FHS	No maintenance of menses and no r[illegible]es Amenorrhea	No re-appearance of two consecutive [illegible] within 21 to 35 days Amenorrhea	Amenorrhea with [illegible] Amenorrhea + FHS
Timing of POI after chemotherapy	12 months	24 months	24 months	6 months	Between 12 and 24 months
Sample size	281	257	48	60	227
ER status for eligibility	ER-positive and ER-negative	ER-negative only	ER-positive and ER-negative	ER-negative only	ER-positive and ER-negative
Upper age limit for eligibility	≤ 45 years	≤ 49 years	≤ 44 years	≤ 45 years	None
Type of GnRHa	Triptorelin	Goserelin	Triptorelin	Goserelin	Goserelin

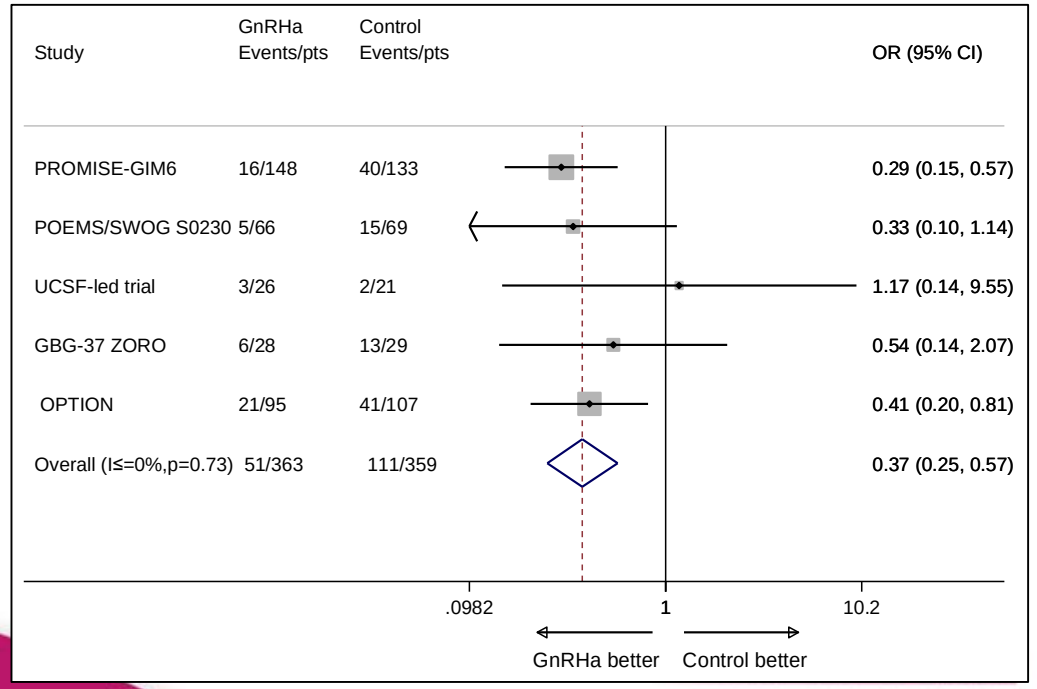
Results

	GnRHa group (n=436) No. (%)	Control group (n=437) No. (%)	p value*
Age, median (IQR), years	38 (34-42)	39 (35-42)	0.258
Age distribution, years			
≤ 40	297 (68.1)	283 (64.8)	0.316
≥ 41	139 (31.9)	154 (35.2)	
Estrogen receptor status			
Positive	177 (40.6)	173 (39.6)	0.782
Negative	257 (58.9)	262 (59.9)	
Missing	2 (0.5)	2 (0.5)	
Type of chemotherapy			
Anthracycline only-based	194 (44.5)	198 (45.3)	0.196
Anthracycline- and taxane-based	227 (52.1)	210 (48.0)	
Non anthracycline-based	6 (1.4)	13 (3.0)	
Missing	9 (2.1)	16 (3.7)	
Cumulative cyclophosphamide dose, median (IQR), mg/m^2	4000 (3420-5185)	3960 (3082-5400)	0.585

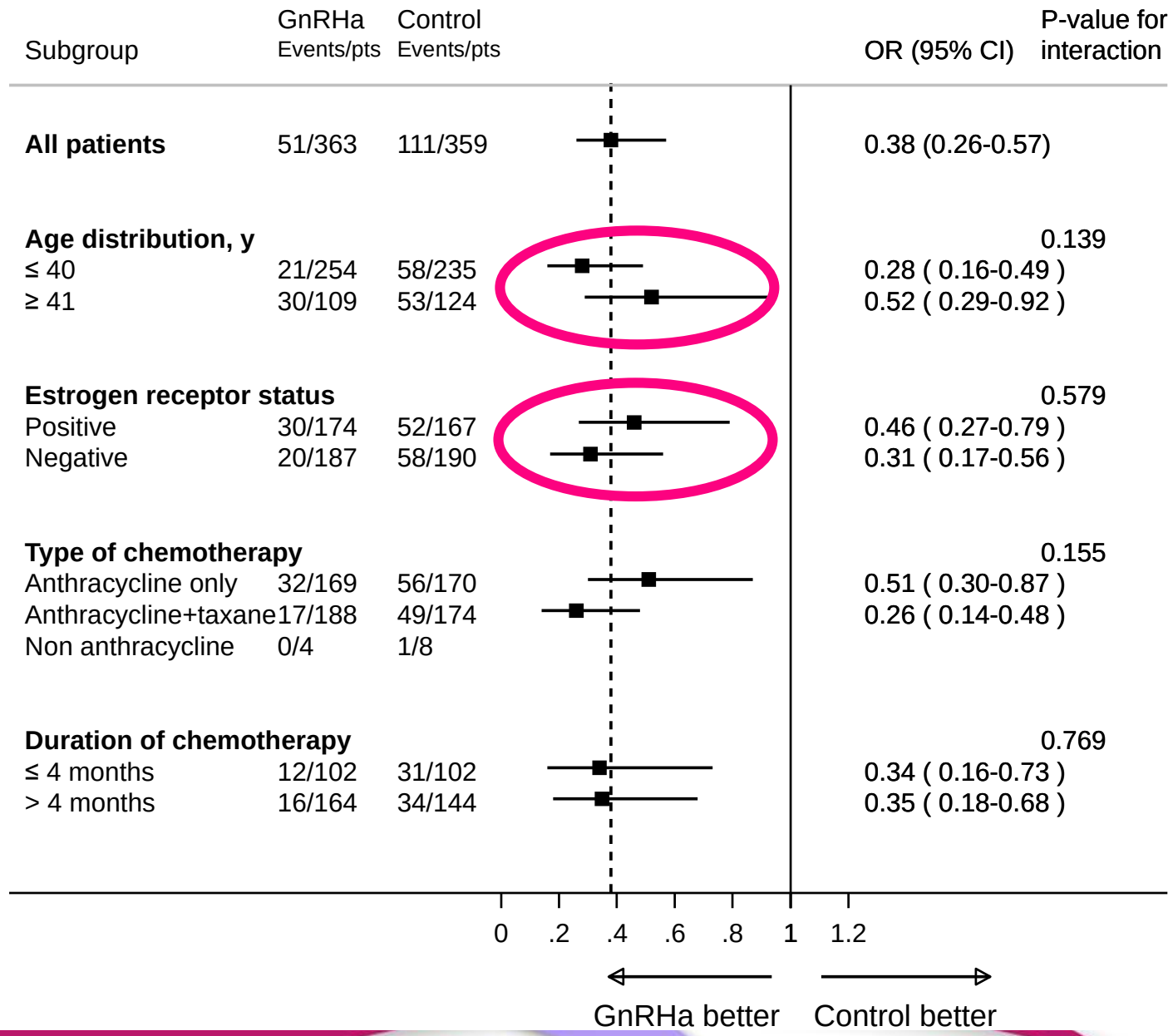
Premature ovarian insufficiency rate



No heterogeneity



Premature ovarian insufficiency rate



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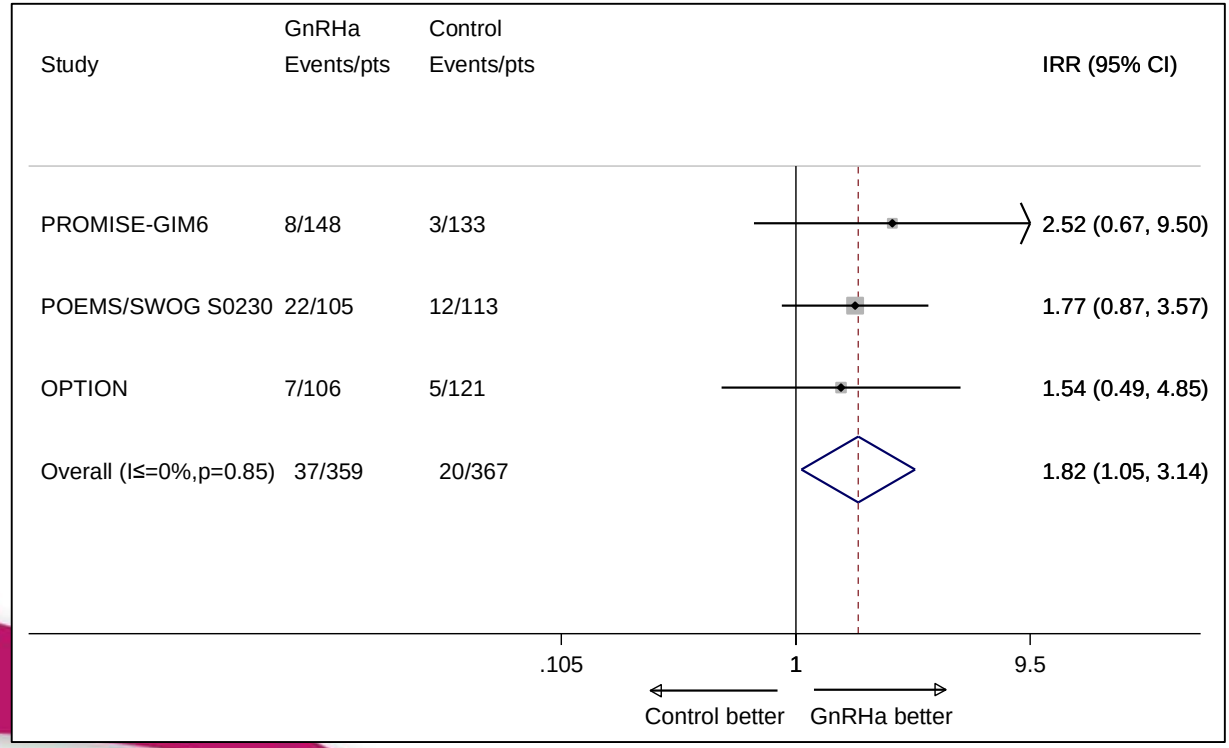
Post-treatment pregnancy rates

GnRHa Group: 37/359 (10.3%)
vs.
Control Group: 20/367 (5.5%)

IRR* 1.83 (95% CI 1.06-3.15)
p=0.030

	GnRHa group (n = 37) No. (%)	Control group (n = 20) No. (%)
Age distribution, years		
≤ 40	37 (100)	20 (100)
≥ 41	0 (0.0)	0 (0.0)
Estrogen receptor status		
Positive	6 (16.2)	2 (10.0)
Negative	31 (83.8)	18 (90.0)

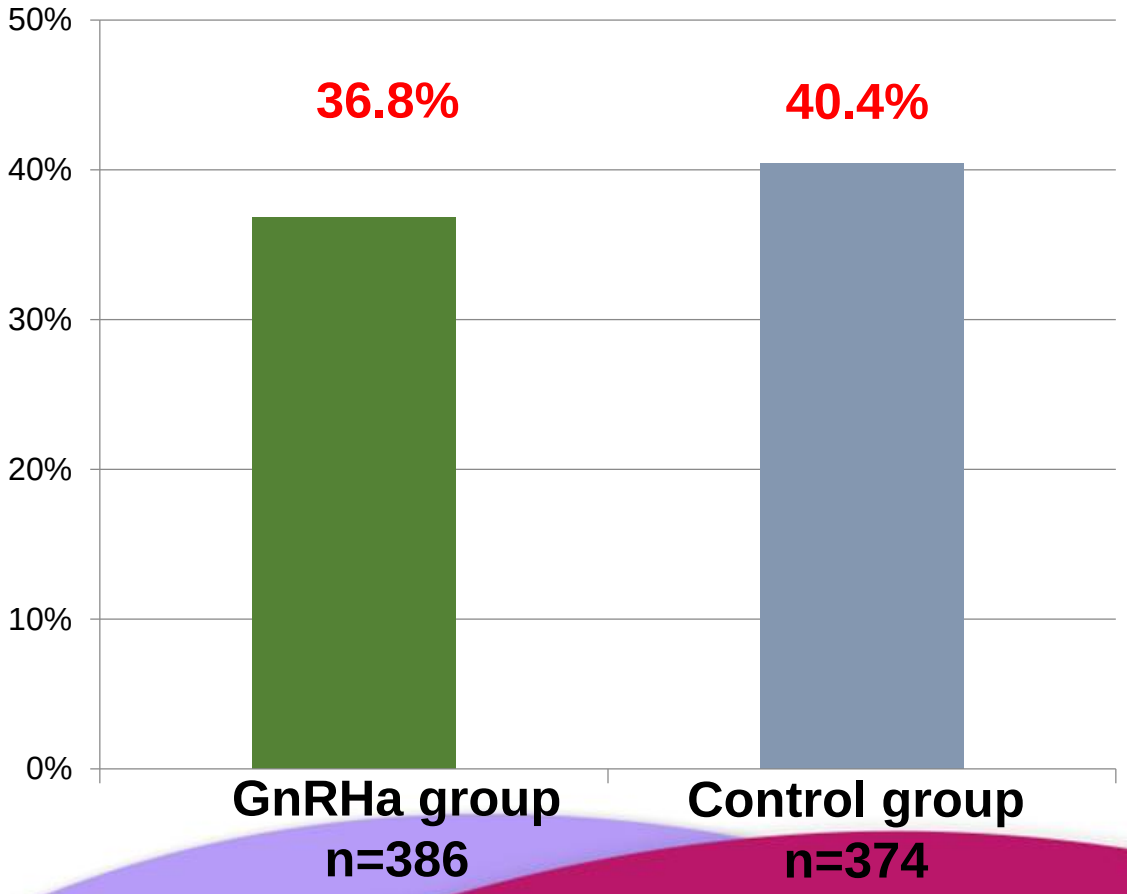
No heterogeneity



Amenorrhea rates

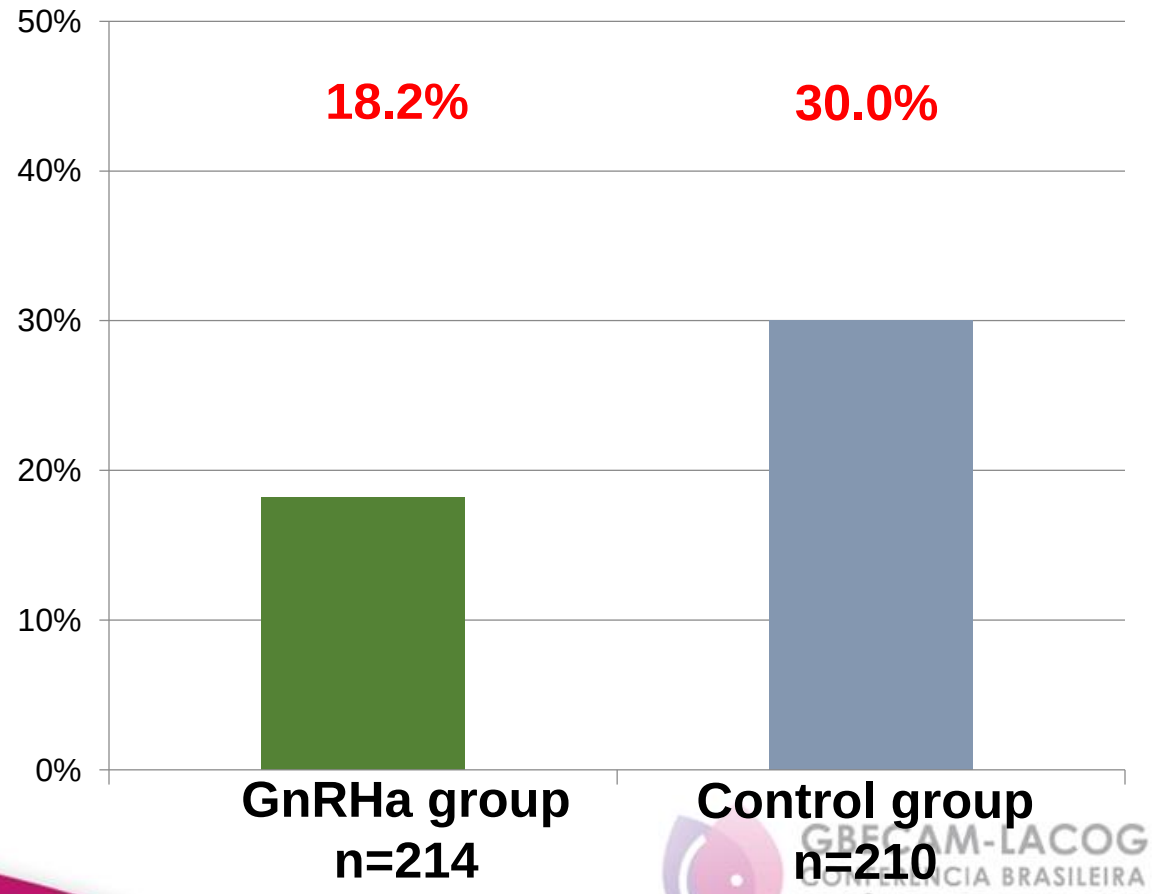
One-Year Amenorrhea

OR* 0.92 (95% CI 0.66-1.28); p=0.623



Two-Year Amenorrhea

OR* 0.51 (95% CI 0.31-0.85); p=0.009



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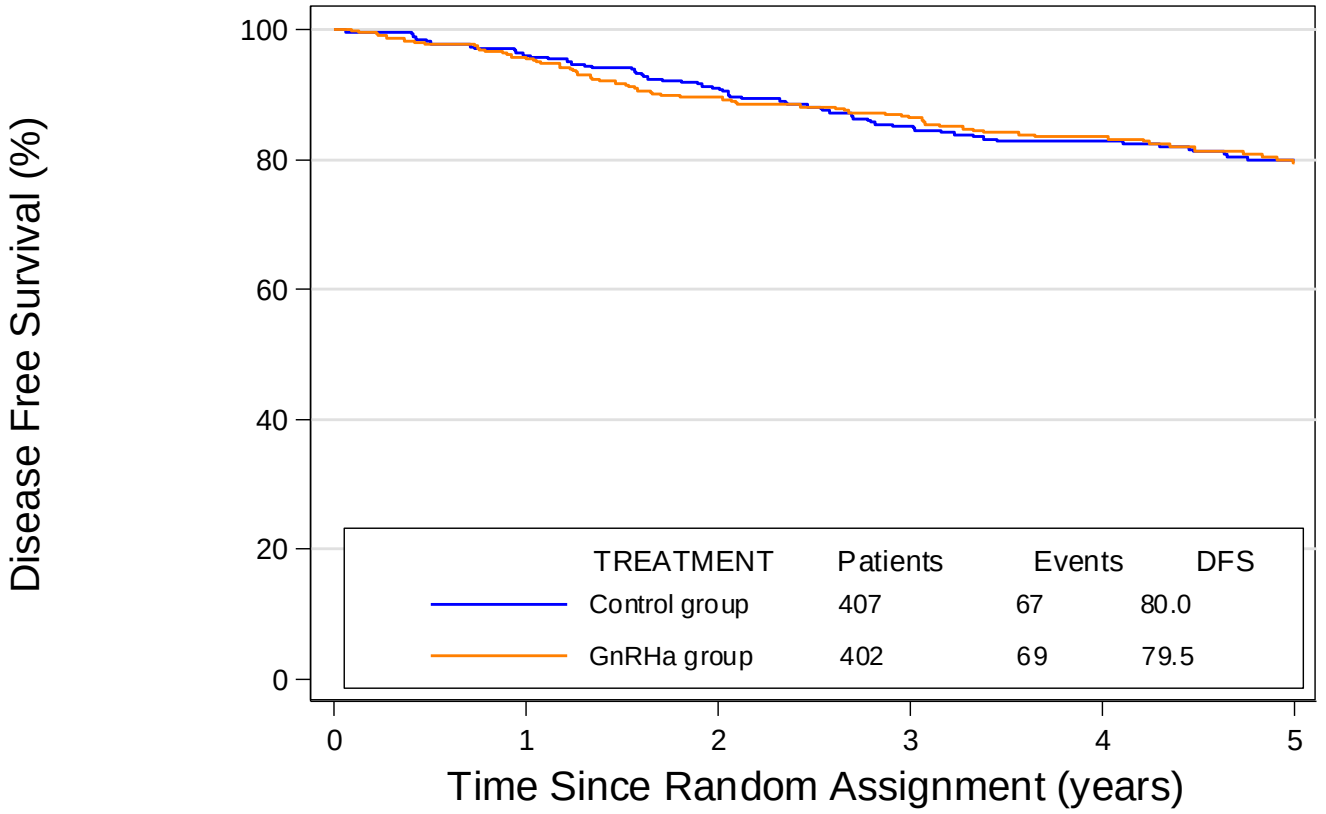
***Odds ratio (OR) adjusted for age, estrogen receptor status, type and duration of chemotherapy administered**

Disease-free progression

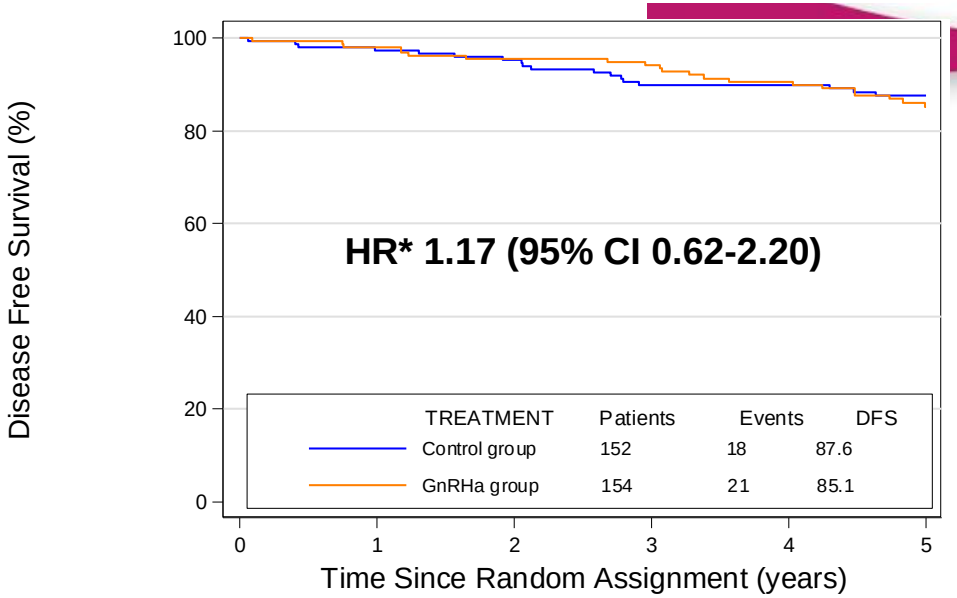
Median follow-up = 5.0 years (IQR, 3.0 - 6.3 years)



Number at risk

Control group	407	352	322	268	232	172
GnRHa group	402	356	323	286	240	174

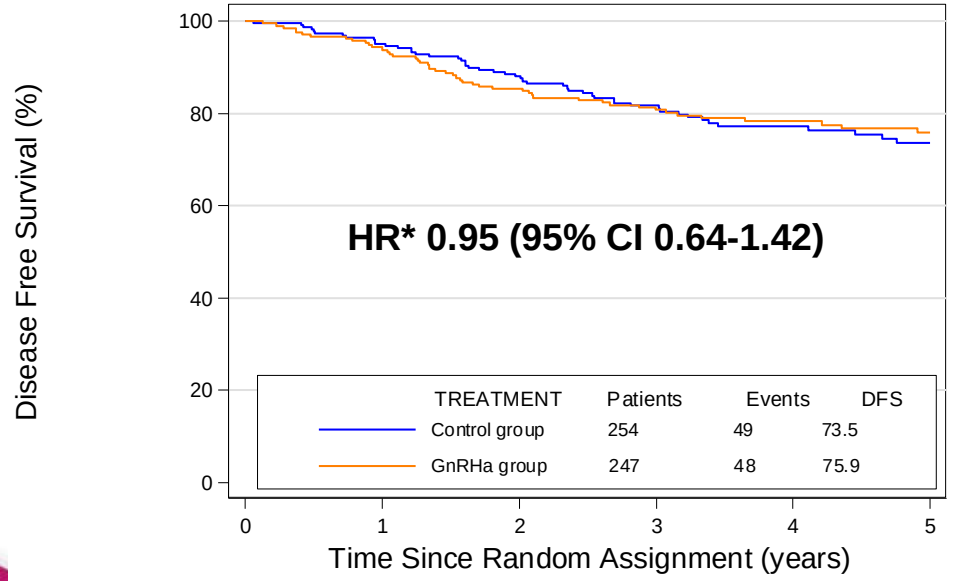
Estrogen receptor-positive disease



Number at risk

Control group	1					
GnRHa group	1					

Estrogen receptor-negative disease

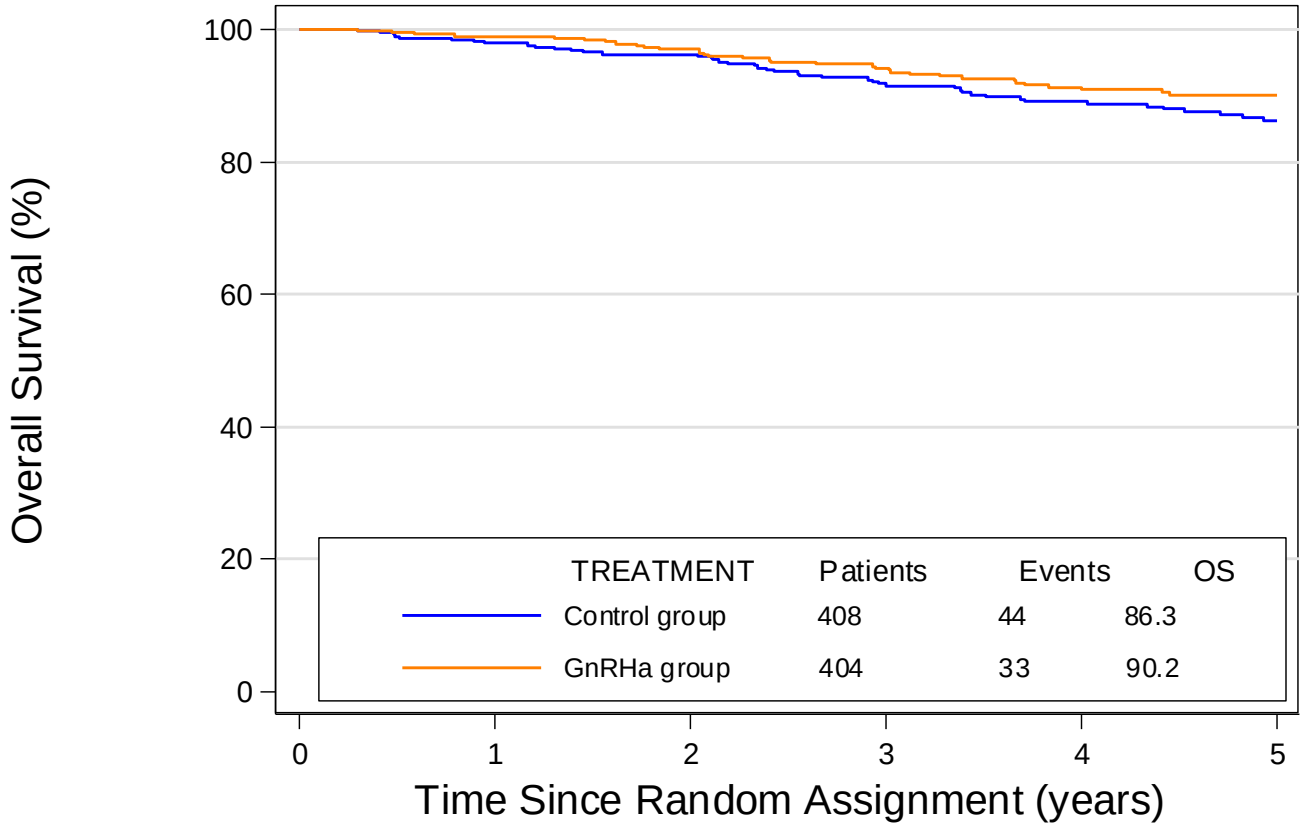


Number at risk

Control group	254	206	181	138	108	62
GnRHa group	247	204	178	148	116	71

Overall survival

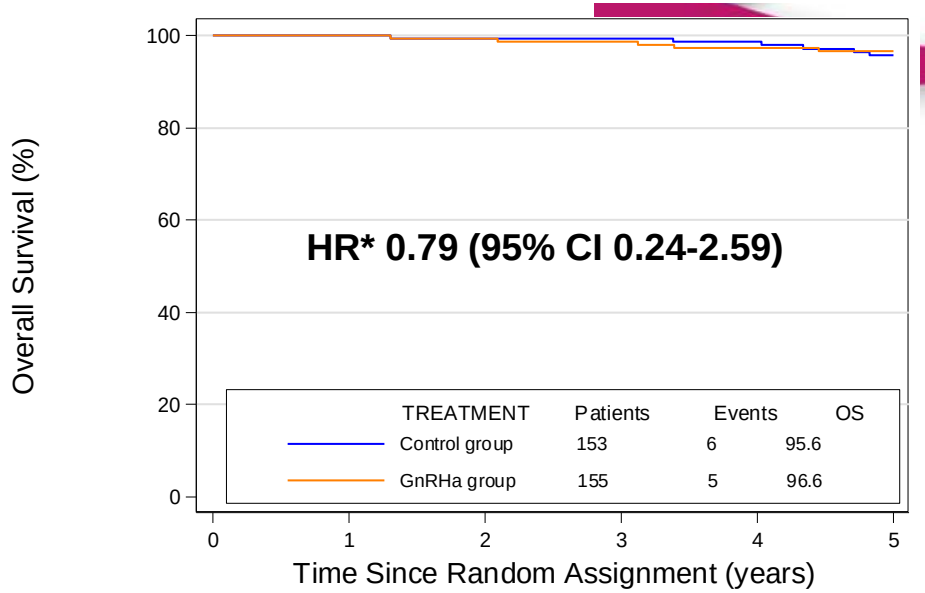
Median follow-up = 5.0 years (IQR, 3.0 - 6.3 years)



Number at risk

Control group	408	362	342	291	254	188
GnRHa group	404	370	350	313	265	199

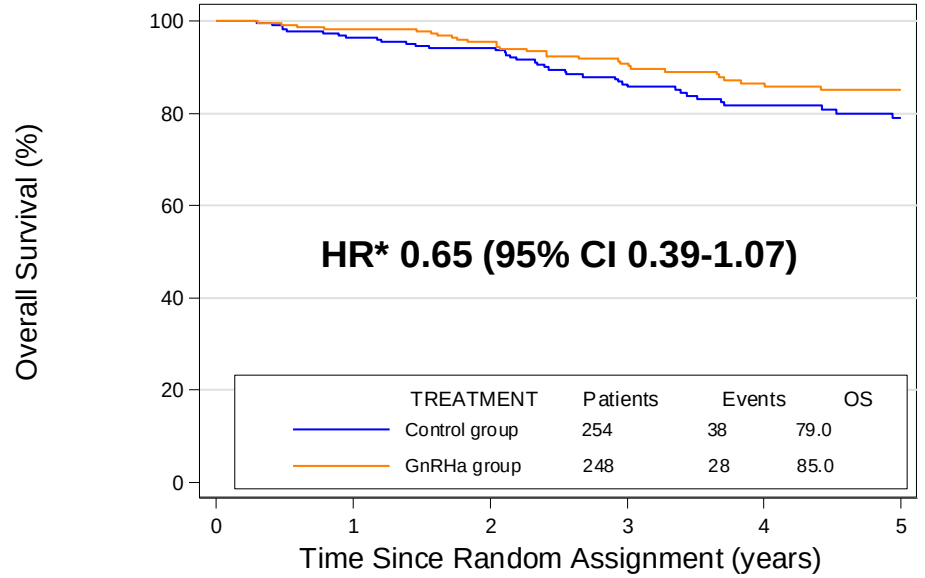
Estrogen receptor-positive disease



Number at risk

Control group						
GnRHa group						

Estrogen receptor-negative disease



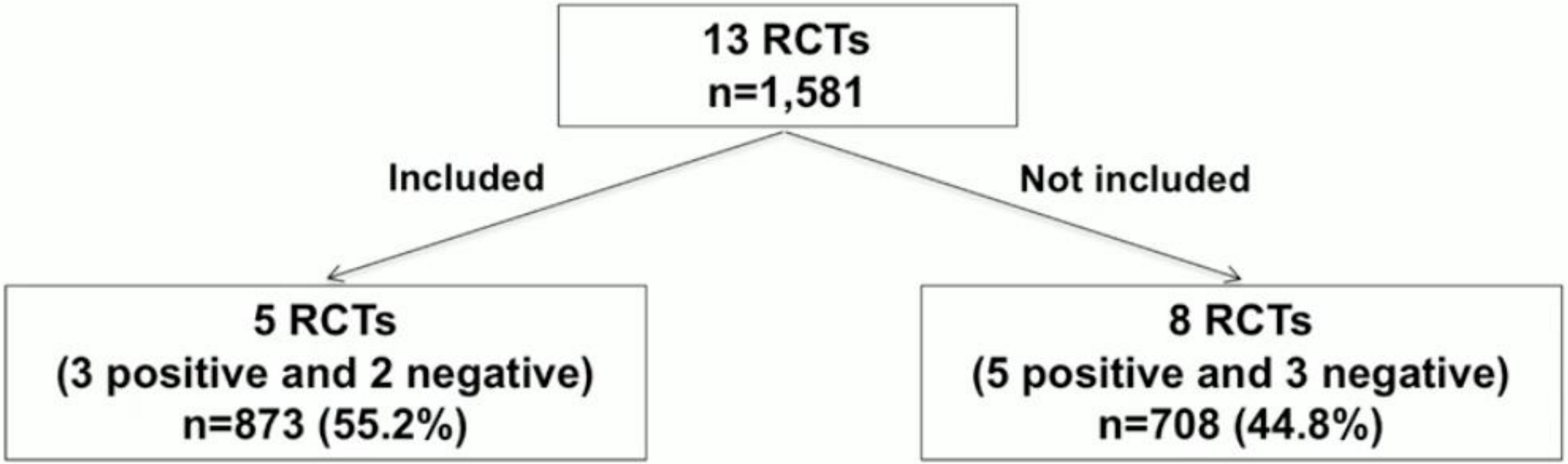
Number at risk

Control group	254	211	195	149	118	69
GnRHa group	248	214	198	166	129	80

Conclusions

- Administration of GnRHa during chemotherapy was associated with a significant reduction in the risk of chemotherapy-induced POI
- A greater number of women in the GnRHa group had a post-treatment pregnancy
- Similar DFS and OS were observed between groups irrespective of the estrogen receptor status of the disease
- This strategy should be considered as an option to reduce the likelihood of chemotherapy-induced POI and potentially improve future fertility in premenopausal early breast cancer patients undergoing (neo)adjuvant chemotherapy

Potential issues



PROSPERO registration number: CRD42014015638

- No individual data
- Similar results to other 5 included

Potential issues

- **Studies limited to breast cancer – 3 negative studies in hematologic diseases**
  - **Heterogeneity of patients and chemo doses**
  - **Younger age in hematologic studies**
  - **Low number of patients**

Thank you!

dornellesrosa@gmail.com

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