Valutazione delle evidenze: studio IBIS II

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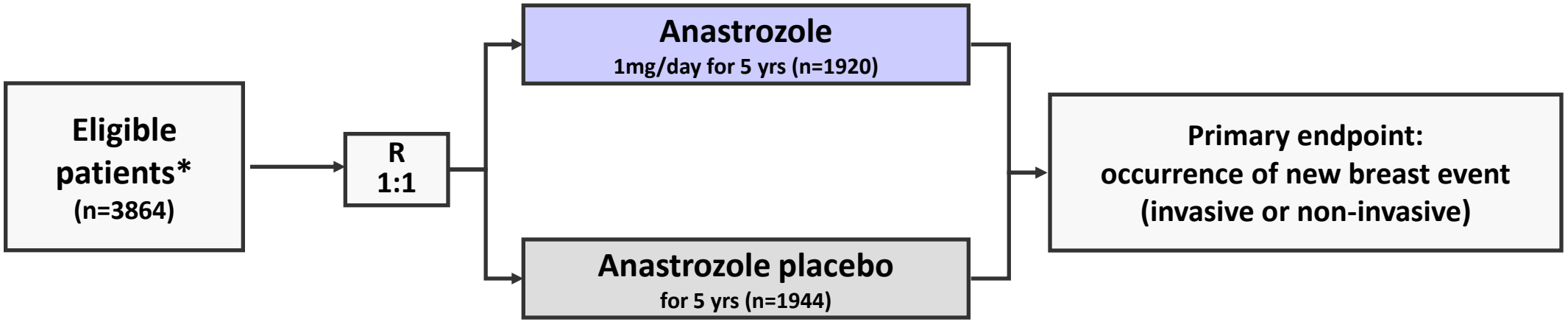
IBIS-II: Preventive Anastrozole in Postmenopausal Women at High Risk of BC

- Hormonal strategies for breast cancer shown to be efficacious in women with high risk of breast cancer
  - Including use of tamoxifen, raloxifene, and exemestane[1-4]
- IBIS-II, an international double-blind randomized placebo-controlled trial, explored use of anastrozole in postmenopausal women with high risk of breast cancer[5]
  - Criteria for women at high risk: family history, atypia/lobular carcinoma in situ, and/or breast density. Women who did not meet these criteria where included if the Tyrer-Cuzich model indicated a 10 –year risk of BC >5%
  - Primary endpoint: breast cancer incidence (invasive or DCIS)
  - Secondary endpoints: cancer incidence, mortality, safety

1. Fisher B, et al. J Natl Cancer Inst. 2005;97:1652-1662. 2. Vogel VG, et al. Cancer Prev Res (Phila). 2010;3:696-706. 3. Goss PE, et al. N Engl J Med. 2011;364:2381-2391. 4. NCCN. Clinical practice guidelines in oncology: breast cancer risk reduction. V.1.2013. 5. Cuzick J, et al. Lancet. 2013

IBIS-II: Study design

02/2003-01/2012



*Main inclusion criteria

- Postmenopausal women
  - ✓ 40-70 years of age
- No current HRT
- High risk of breast cancer
  - ✓ Family history
  - ✓ Atypia/LCIS
  - ✓ Breast density

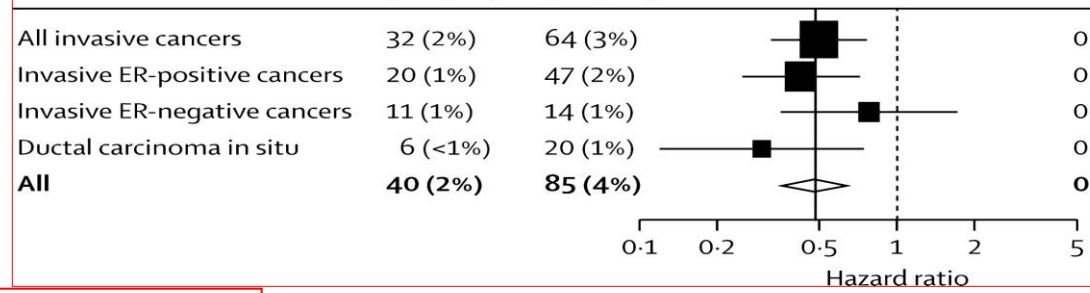
Follow-up after 5 years varied

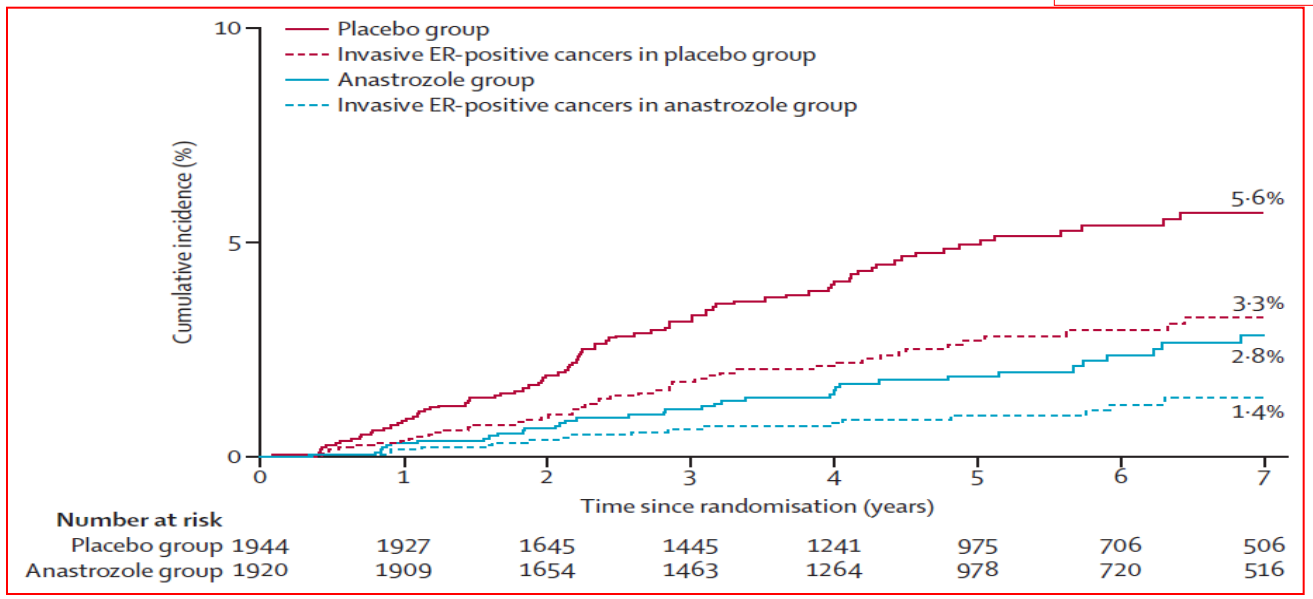
Cuzick et al, Lancet 2013

IBIS-II: Results (primary end point)

- Significant decrease in risk of invasive or non-invasive breast cancer with anastrozole
  - HR: 0.47, p<0.0001

	Number of women		Hazard ratio (95% CI)	p value
	Anastrozole group (n=1920)	Placebo group (n=1944)		
All invasive cancers	32 (2%)	64 (3%)	0·50 (0·32–0·76)	0·001
Invasive ER-positive cancers	20 (1%)	47 (2%)	0·42 (0·25–0·71)	0·001
Invasive ER-negative cancers	11 (1%)	14 (1%)	0·78 (0·35–1·72)	0·538
Ductal carcinoma in situ	6 (<1%)	20 (1%)	0·30 (0·12–0·74)	0·009
All	**40 (2%)**	**85 (4%)**	**0·47 (0·32–0·68)**	**<0·0001**



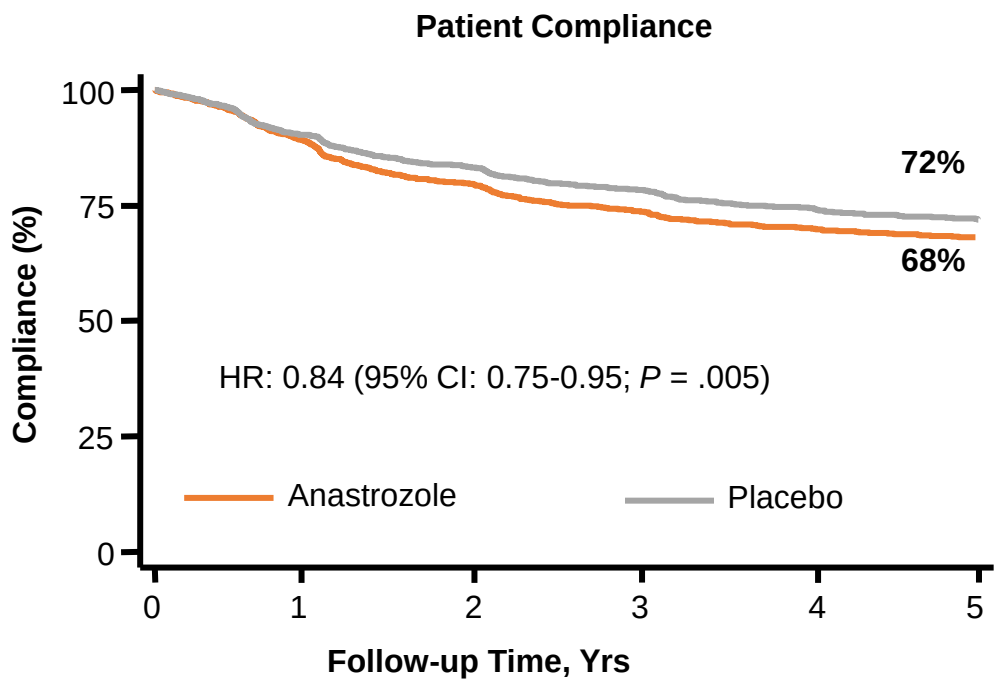


36 women (95% CI: 33-44) would need to be treated to prevent 1 cancer in 7 years of follow-up

Cuzick et al, Lancet 2013

IBIS-II: Toxicity and patient compliance

Select Adverse Events %	Anastrozole (n = 1920)	Placebo (n = 1944)	RR (95% CI)
Fractures	**8.5**	**7.7**	**1.11 (0.90-1.38)**
Musculoskeletal	**63.9**	**57.8**	**1.10 (1.05-1.16)**
• **Arthralgia (any)**	**50.6**	**46.0**	**1.10 (1.03-1.18)**
• Arthralgia (severe)	8	6	1.24 (0.99-1.56)
• **Joint stiffness**	**7.4**	**4.9**	**1.51 (1.17-1.94)**
• **Carpal tunnel/ nerve compression**	**3.5**	**2.2**	**1.58 (1.08-2.30)**
Vasomotor (any)	56.8	49.4	1.15 (1.08-1.22)
• **Hypertension**	**5**	**3**	**1.64 (1.18-2.28)**
Vasomotor (severe)	8	7	1.20 (0.95-1.50)
Gynecologic	23.9	21.8	1.10 (0.98-1.24)
• **Vaginal dryness**	**19**	**16**	**1.19 (1.03-1.37)**



Cuzick et al, Lancet 2013

IBIS-II: Trial conclusions

- 53% reduction in breast cancer incidence compared with placebo in high-risk postmenopausal women
  - Unexpected reduction in incidence of other cancer types
- Anastrozole well tolerated compared with placebo by most high-risk postmenopausal women
  - Small but significant decrease in compliance
  - Small, non significant increase in fractures
  - 10% increase in musculoskeletal adverse events
- Anastrozole effective risk-reduction option for high-risk postmenopausal women

Cuzick et al, Lancet 2013

PROCESSO DI PRODUZIONE RACCOMANDAZIONE CLINICA – METODO GRADE –

Gruppo di lavoro B

Coordinatori: C. Angiolini, M. Cinquini
C. Fontanella, M. Pestrin, B. Pistilli

Il QUESITO

P: donne in post-menopausa ad alto rischio di ca mammario invasivo
I: Antiaromatasici (ANASTROZOLE)
C: Placebo

Gli outcome

O1: Incidenza di ca mammario invasivo	9
O2: mortalità	8
O3: artralgia	7
O4: eventi cardiovascolari	9
O5: fratture	9
O6: osteoporosi	6
O7: disturbi cognitivi	8
O8: sindrome tunnel carpale	6
O9: vampate	5
O10: rigidità articolare	7
O11: dislipidemia	6
O12: Ipertransaminasemia	2

Bibliographic search

Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial

*Jack Cuzick, Ivana Sestak, John F Forbes, Mitch Dowsett, Jill Knox, Simon Cawthorn, Christobel Saunders, Nicola Roche, Robert E Mansel, Gunter von Minckwitz, Bernardo Bonanni, Tiina Palva, Anthony Howell, on behalf of the IBIS-II investigators**

Summary

Background Aromatase inhibitors effectively prevent breast cancer recurrence and development of new contralateral tumours in postmenopausal women. We assessed the efficacy and safety of the aromatase inhibitor anastrozole for prevention of breast cancer in postmenopausal women who are at high risk of the disease.

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S0140-6736(13)62292-8

METODO GRADE

METODO TRASPARENTE CHE ANALIZZA DETTAGLIATAMENTE UNO STUDIO CLINICO METTENDO IN RISALTO SIA I RISULTATI SIA LA QUALITA’ DELL’EVIDENZA OUTCOME-CENTRED

Summary of Findings Table (SoF)
Outcome di beneficio

Author(s): Group B
Date: 2014-03-21
Question: Should Anastrozole be used in invasive breast cancer high-risk postmenopausal women?
Settings:
Bibliography: Cuzick, Lancet 2013

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Anastrozole	Control	Relative (95% CI)	Absolute		
Invasive breast cancer incidence (follow-up median 5 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness[3]	no serious imprecision	none	32/1920 (1.7%)	64/1944 (3.3%)	RR 0.51 (0.33 to 0.77)	2 fewer per 100 (from 1 fewer to 2 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Mortality (follow-up median 5 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness[3]	no serious imprecision[4]	none	18/1920 (0.94%)	17/1944 (0.87%)	RR 1.07 (0.55 to 2.07)	0 more per 100 (from 0 fewer to 1 more)	⊕⊕⊕⊕ HIGH	CRITICAL

Arthralgia (follow-up median 5 years; assessed with: CTC-NCI)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness[3]	no serious imprecision	none	872/1920 (45.4%)	894/1944 (46%)	RR 1.10 (1.03 to 1.18)	5 more per 100 (from 1 more to 8 more)	⊕⊕⊕⊕ HIGH	CRITI
Carpal tunnel syndrome (follow-up median 5 years; assessed with: CTC-NCI)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness[3]	no serious imprecision	none	67/1920 (3.5%)[4]	43/1944 (2.2%)[4]	RR 1.58 (1.08 to 2.3)	1 more per 100 (from 0 more to 3 more)	⊕⊕⊕⊕ HIGH	IMPOR
Fractures (follow-up median 5 years; assessed with: CTC-NCI)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness[3]	no serious imprecision	none	164/1920 (8.5%)	149/1944 (7.7%)	RR 1.11 (0.9 to 1.38)	1 more per 100 (from 1 fewer to 3 more)	⊕⊕⊕⊕ HIGH	CRITI
Hot flushes (follow-up median 5 years; assessed with: CTC-NCI)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness[3]	no serious imprecision	none	1090/1920 (56.8%)[4]	961/1944 (49.4%)[4]	RR 1.15 (1.08 to 1.22)	7 more per 100 (from 4 more to 11 more)	⊕⊕⊕⊕ HIGH	IMPOR
Cardiovascular events (follow-up median 5 years; assessed with: CTC-NCI)												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness[3]	no serious imprecision[5]	none	8/1920 (0.42%)[4,6]	9/1944 (0.46%)[4]	RR 0.90 (0.35 to 2.32)	0 fewer per 100 (from 0 fewer to 1 more)	⊕⊕⊕⊕ HIGH	CRITI
articolar rigidity - not reported												

Gli outcome

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O12: Ipertransaminasemia	2

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Votazione Bilancio
Beneficio/Danno

FAVOREVOLE

Votazione Forza della Raccomandazione

POSITIVA DEBOLE

Raccomandazione Clinica

Nelle donne in post-menopausa ad alto rischio di recidiva il trattamento con anastrozole può essere considerato