Extended Aromatase Inhibitor treatment following 5 or more years of endocrine therapy: a meta-analysis of 22,192 women in 11 randomised trials

Early Breast Cancer Trialists' Collaborative Group

All authors declare no relevant conflict of interest

Extended AI treatment after 5+ years of prior endocrine therapy: methods

Meta-analysis of individual patient data on postmenopausal women with ER-positive (99%) or ER-unknown (1%) tumours in trials of:

Any third-generation AI (exemestane, anastrozole, letrozole) vs no further adjuvant therapy **following**:

a) ≈ 5 years of tamoxifen alone (n=7,500)

b) ≈ 5-10 years of tamoxifen then AI (n=12,600)

c) ≈ 5 years of AI alone (n=4,800)

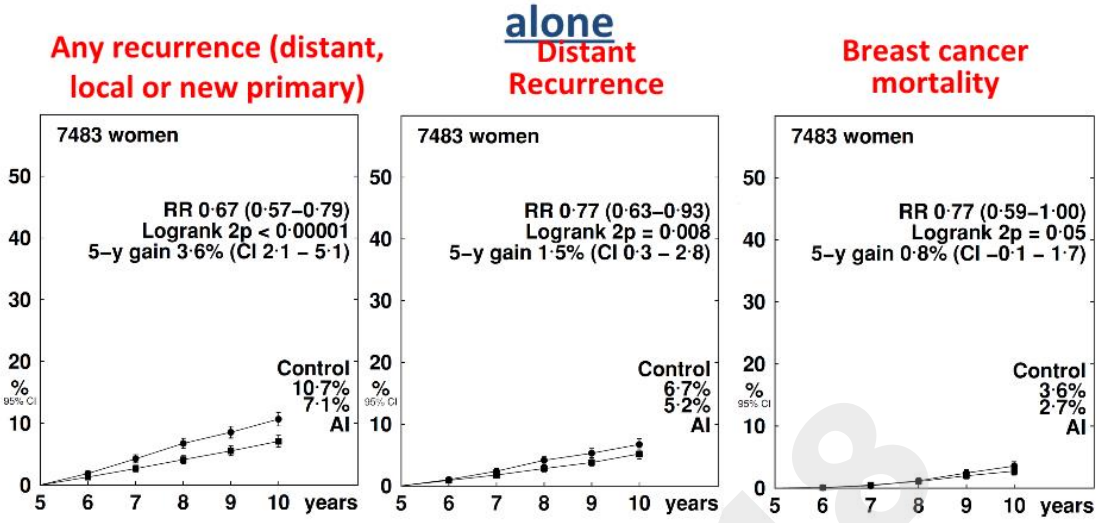
	Endocrine treatment prior to treatment divergence		
Trial (recruitment period)	**(a) Tamoxifen alone**	**(b) Tamoxifen then AI**	**(c) AI alone**
ABCSG VIa (1990–1995)	442	393	-
MA.17 (1998–2002)	4959	-	-
NSABP B-33 (2001–2003)	1550	-	-
ATENA (2001–2005)	358	-	-
SALSA (2004–2010)	-	3392	-
GIM 4 (2005–2015)	-	2031	-
NSABP B-42 (2006–2010)	-	1532	2387
DATA (2006–2009)	-	1827	-
LATER (2007–2012)	174	138	39
IDEAL (2007–2011)	-	1263	510
AERAS (2007–2012)	-	(≈255)	(≈1442)
MA.17R (2009–2015)	-	1473	386
All trials (% with data)	**7,483 (100%)**	**12,304 (98%)**	**4764 (70%)**
Median follow-up (yrs)	**4.9**	**6.1**	**6.5**

Methods: 'landmark' analysis for trials that randomised before treatment divergence

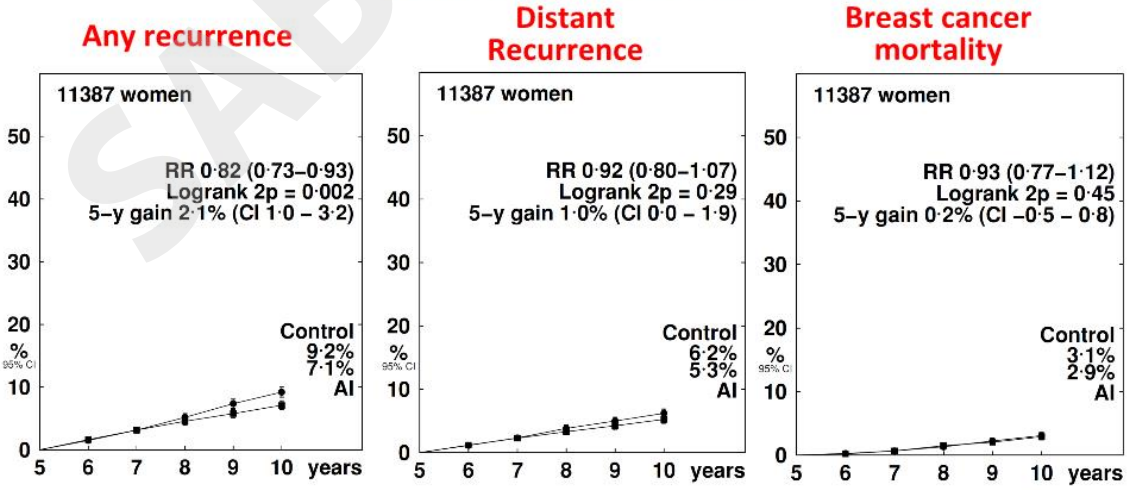
- **DATA** (Tam 2-3yrs then 6 vs 3 years Ana) , **GIM 4** (5 vs 2-3 years Let), **IDEAL** (5 vs 2.5 years Let), **SALSA** (5 vs 2 years Ana) randomised prior to treatment divergence
- Analyses exclude recurrences, second primary cancers, or deaths prior to point of treatment divergence:

Recurrences excluded	Deaths excluded
140 vs 143	**79 vs 79**

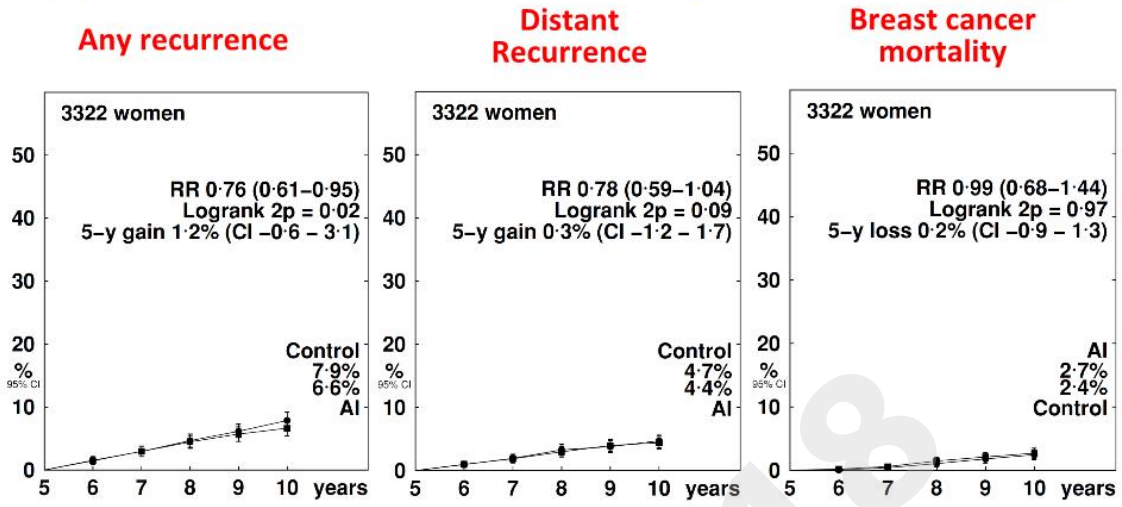
(a) Trials of AI after ≈5 years of Tamoxifen alone



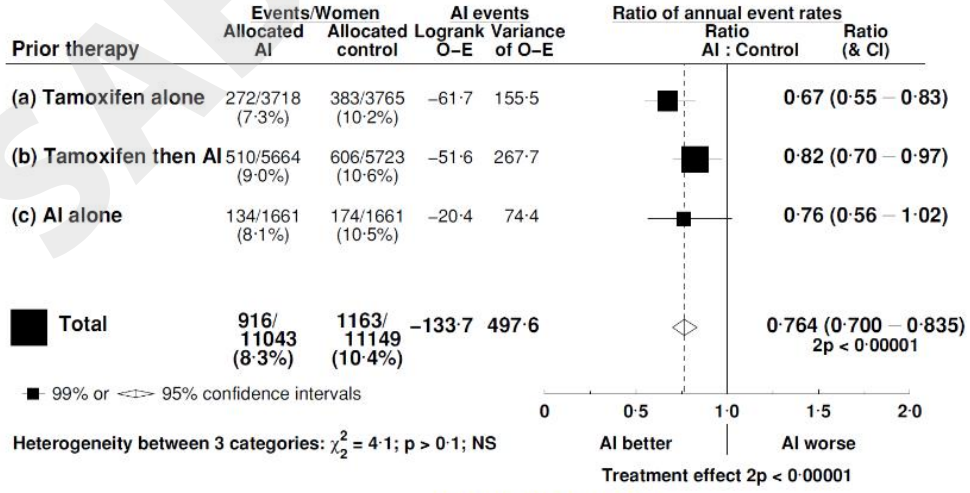
(b) Trials of Extended AI following 5-10 years of Tamoxifen then AI



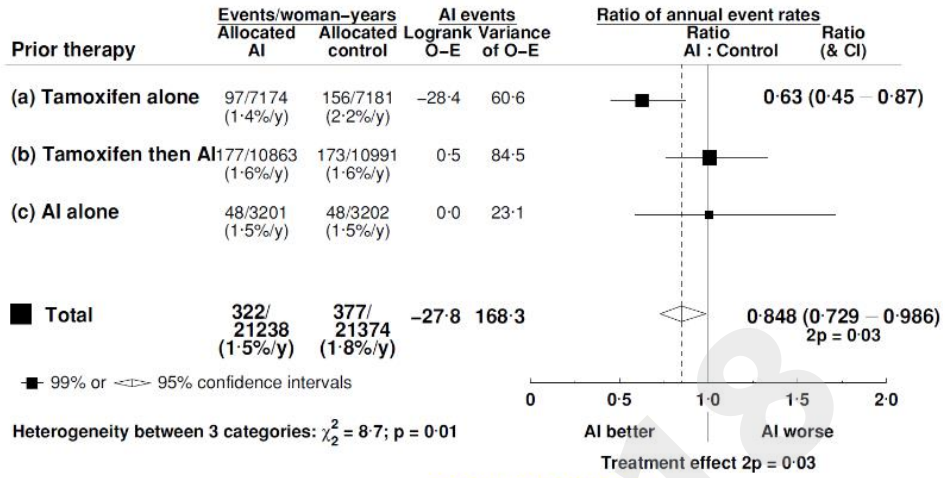
(c) Trials of Extended AI following 5 years of AI alone



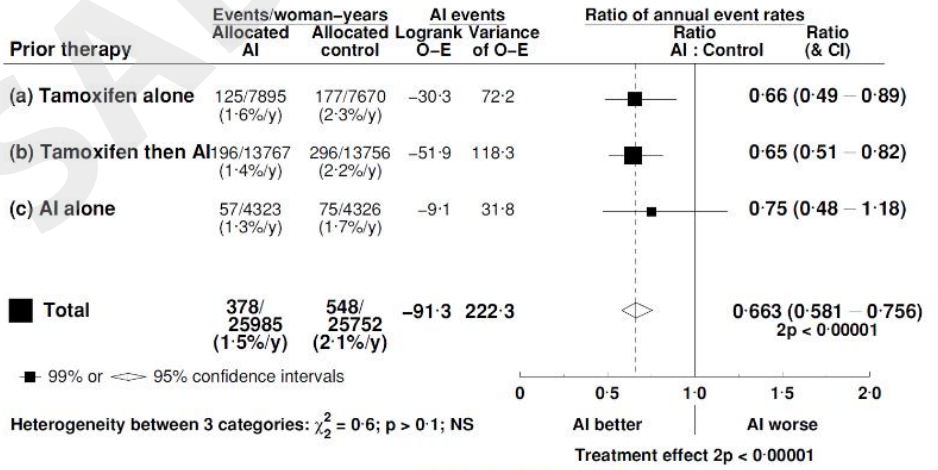
Effect on recurrence by prior endocrine therapy



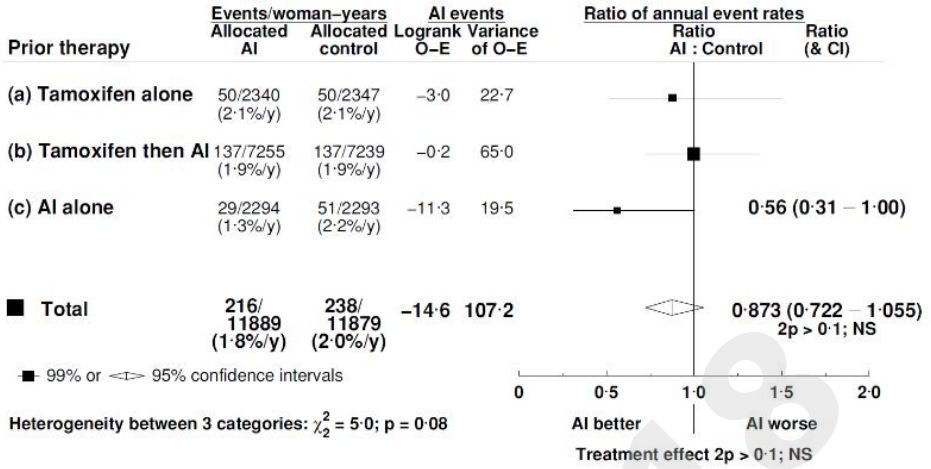
Effect on recurrence in years 0-1 after treatment divergence by prior endocrine therapy



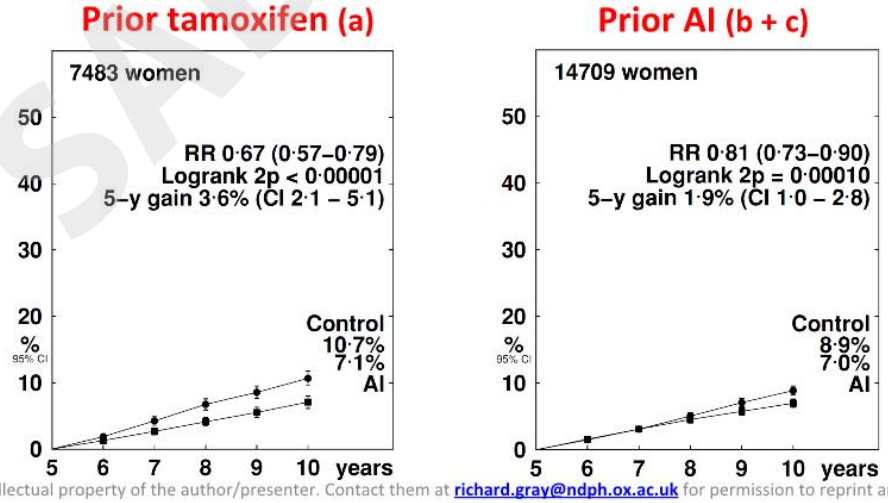
Effect on recurrence in in years 2-4 after treatment divergence by prior endocrine therapy



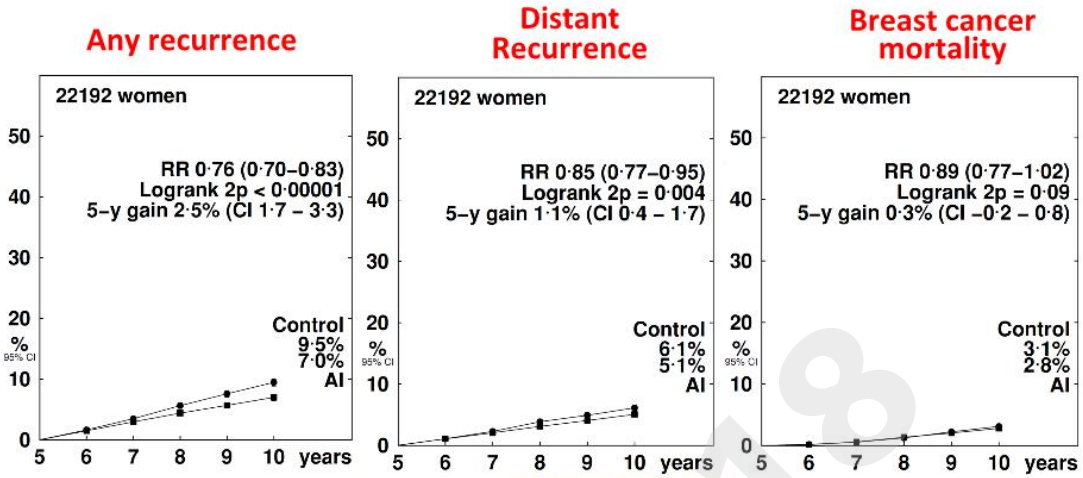
Effect on recurrence in years 5+ after treatment divergence by prior endocrine therapy



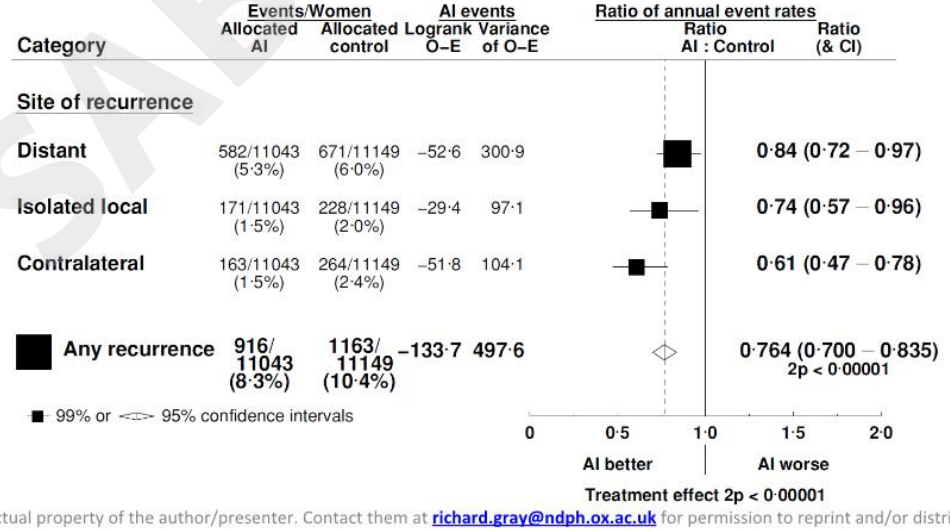
Summary: effect of extended AI therapy after 5-10 yrs on recurrence differs by type of prior endocrine therapy



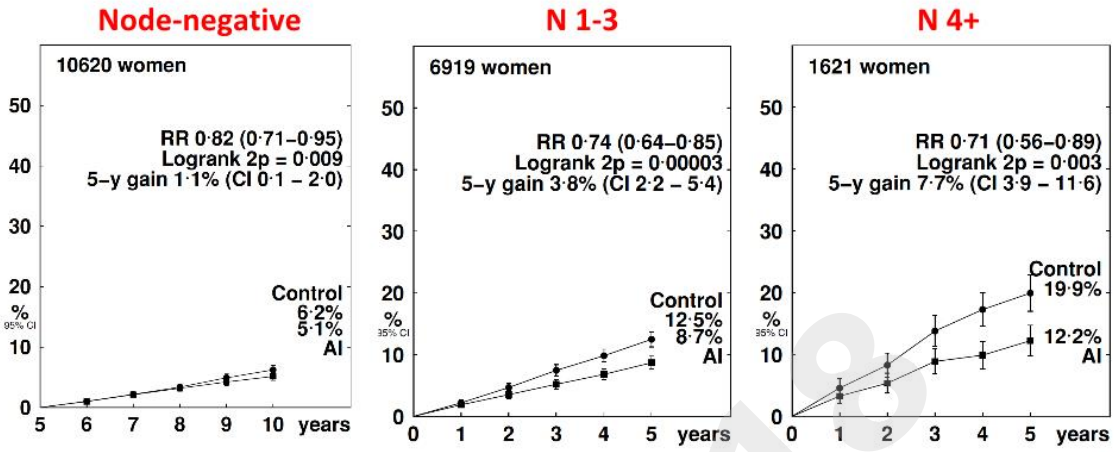
Combined results from all trials of Extended AI following 5-10 years of any prior endocrine therapy



Recurrence by site – combined results from all trials



Recurrence by nodal status – all trials



Bone fracture and death without recurrence

Conclusions: Benefits and risks of AI after 5+ years of prior endocrine therapy

- ≈35% proportional reduction in recurrence for women who have received ≈5 years of tamoxifen
- ≈ 20% proportional reduction in risk of recurrence for women receiving AI (with or without prior tamoxifen)
- Recurrence reductions apparent in first two years following prior tamoxifen, but not until the third year following prior AI
- Absolute benefits increase the more nodes were involved
- Risk of bone fracture increased by ≈25%

Limitations

- Short follow-up: 10 or more years of follow-up is needed to assess the effects of extending AI on breast cancer mortality
- Need to obtain more information on side-effects, for example bone fractures
- Impact of AIs on Quality of Life was not assessed
- One trial (AERAS) still to be included

SAN ANTONIO BREAST CANCER SYMPOSIUM

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