



Associazione Italiana di Oncologia Medica  
SEZIONE REGIONE LAZIO

## POST SAN ANTONIO BREAST CANCER SYMPOSIUM 2018



**28 Gennaio 2019**

**POLICLINICO UMBERTO I - ROMA**

Aula Bignami (Patologia Generale)  
Viale Regina Elena 324

# Extended hormonal therapy in Luminals: Have we arrived at the final step?

**Daniele Alesini**

**Ospedale Belcolle  
Viterbo**



“E pluribus...~~unum~~...duo”

Effects of prolonging adjuvant aromatase inhibitor therapy beyond five years on recurrence and cause-specific mortality: an EBCTCG meta-analysis of individual patient data from 12 randomised trials including 24.912 women.

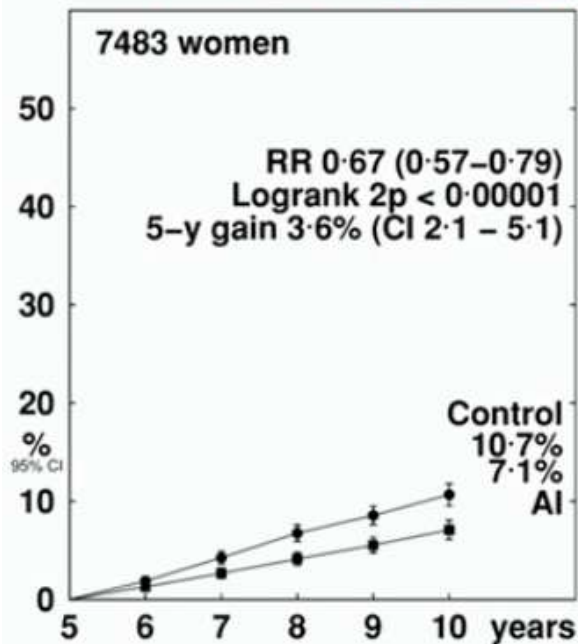
Gray R. et al.

- ✓ 3-5 years of third generation AI vs no further treatment
- ✓ 5 or more years of prior endocrine therapy (Tam alone, Tam→AI, AI alone)
- ✓ Recurrence and breast cancer mortality as primary outcomes
- ✓ Predefined subgroup comparisons: prior OT, site of recurrence, nodal status and period of follow up

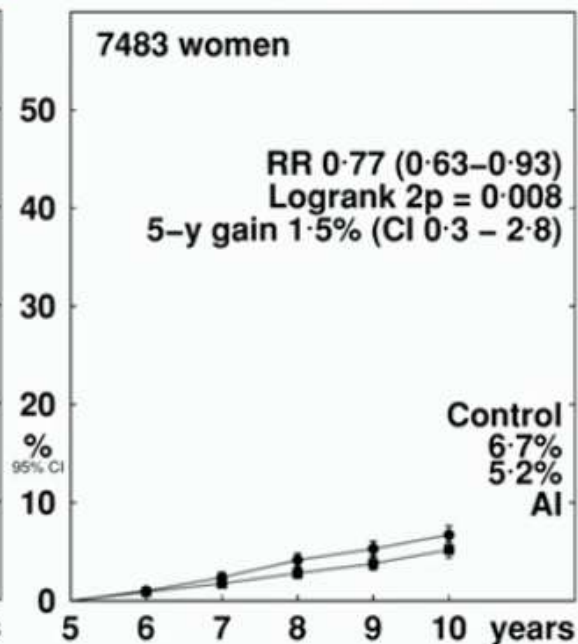
| OT prior to treatment divergence |             |             |            |
|----------------------------------|-------------|-------------|------------|
| Trial                            | TAM alone   | TAM→AI      | AI alone   |
| ABCSG V1a (1990-1995)            | 442         | 393         |            |
| MA.17 (1998-2002)                | 4959        |             |            |
| NSABP B-33 (2001-2003)           | 1550        |             |            |
| ATENA (2001-2005)                | 358         |             |            |
| SALSA (2004-2010)                |             | 3392        |            |
| GIM4 (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)         | 7483 (100%) | 12304 (98%) | 4764 (70%) |
| Median follow up (years)         | 4.9         | 6.1         | 6.5        |

## AI after ~5 years of TAM alone

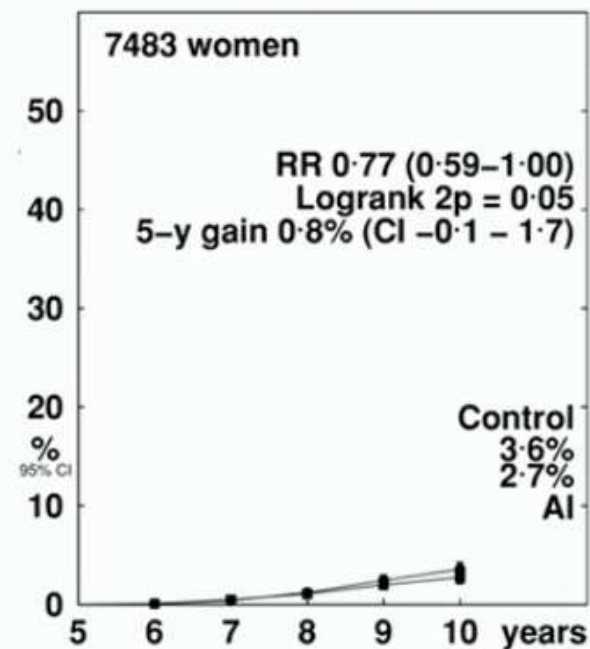
### Any recurrence (distant, local or new primary)



### Distant Recurrence

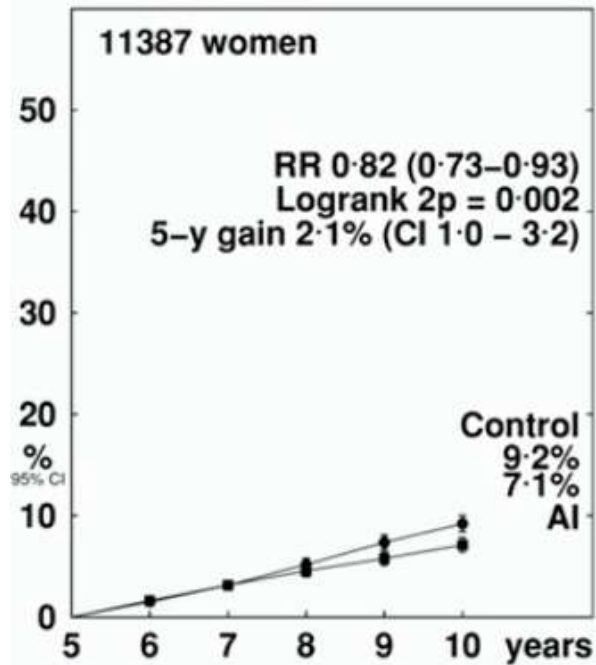


### Breast cancer mortality

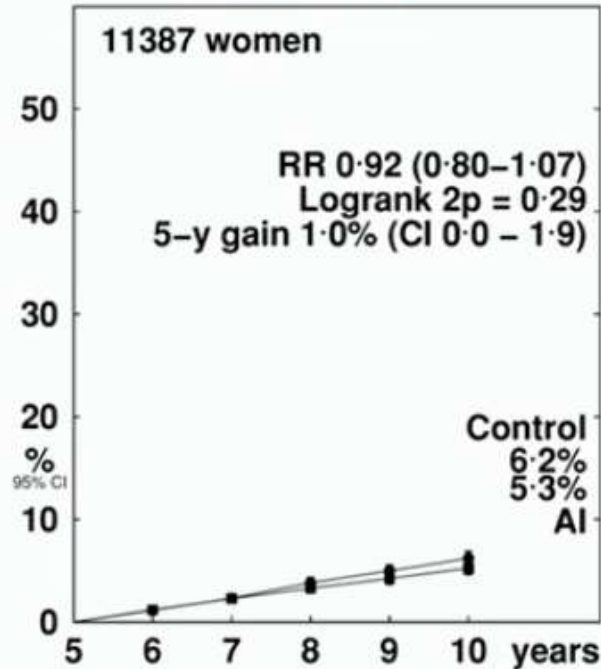


## AI after 5-10 years of TAM→AI

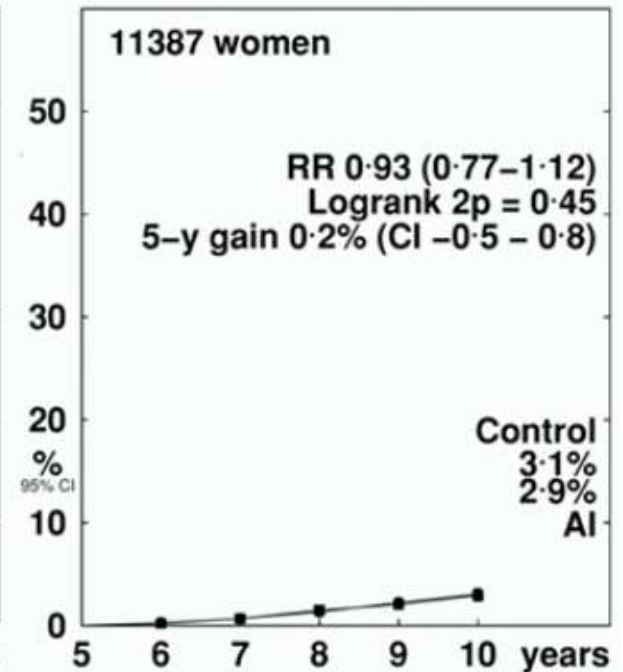
### Any recurrence



### Distant Recurrence



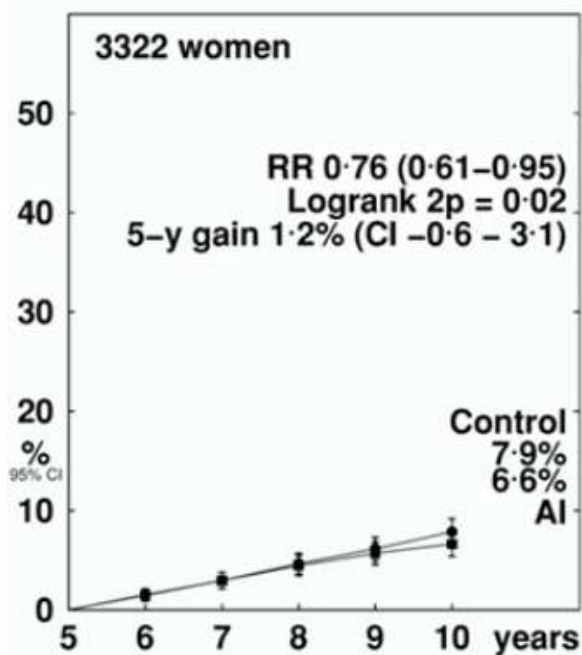
### Breast cancer mortality



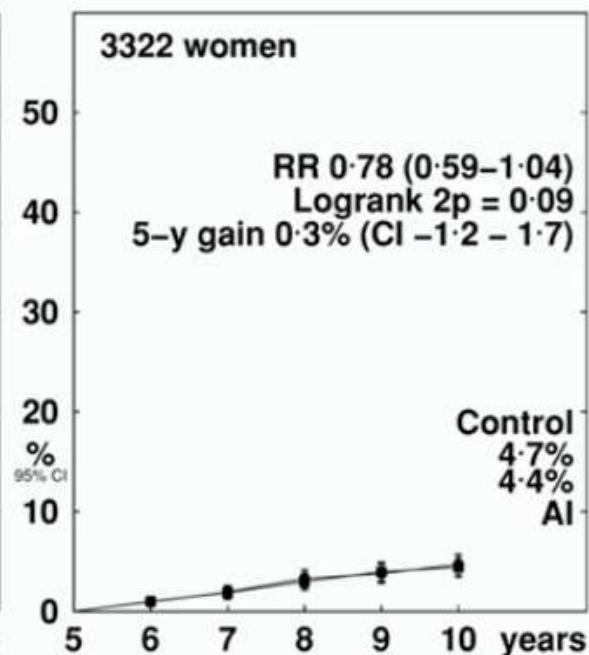


## AI after 5 years of AI alone

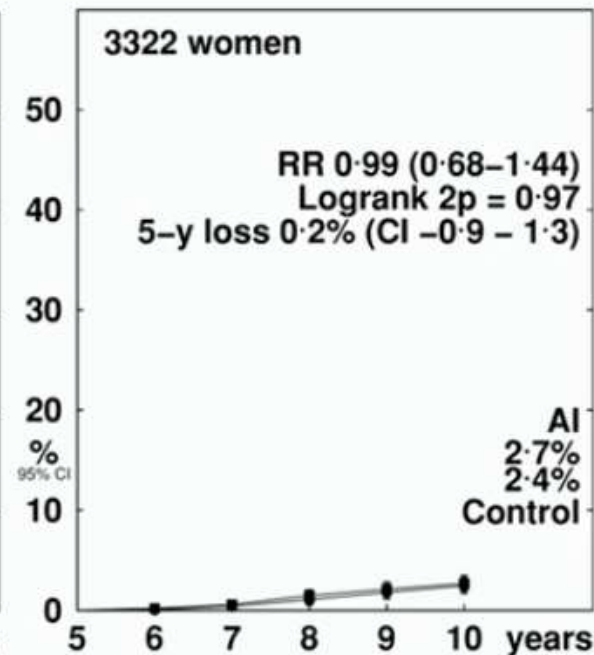
### Any recurrence



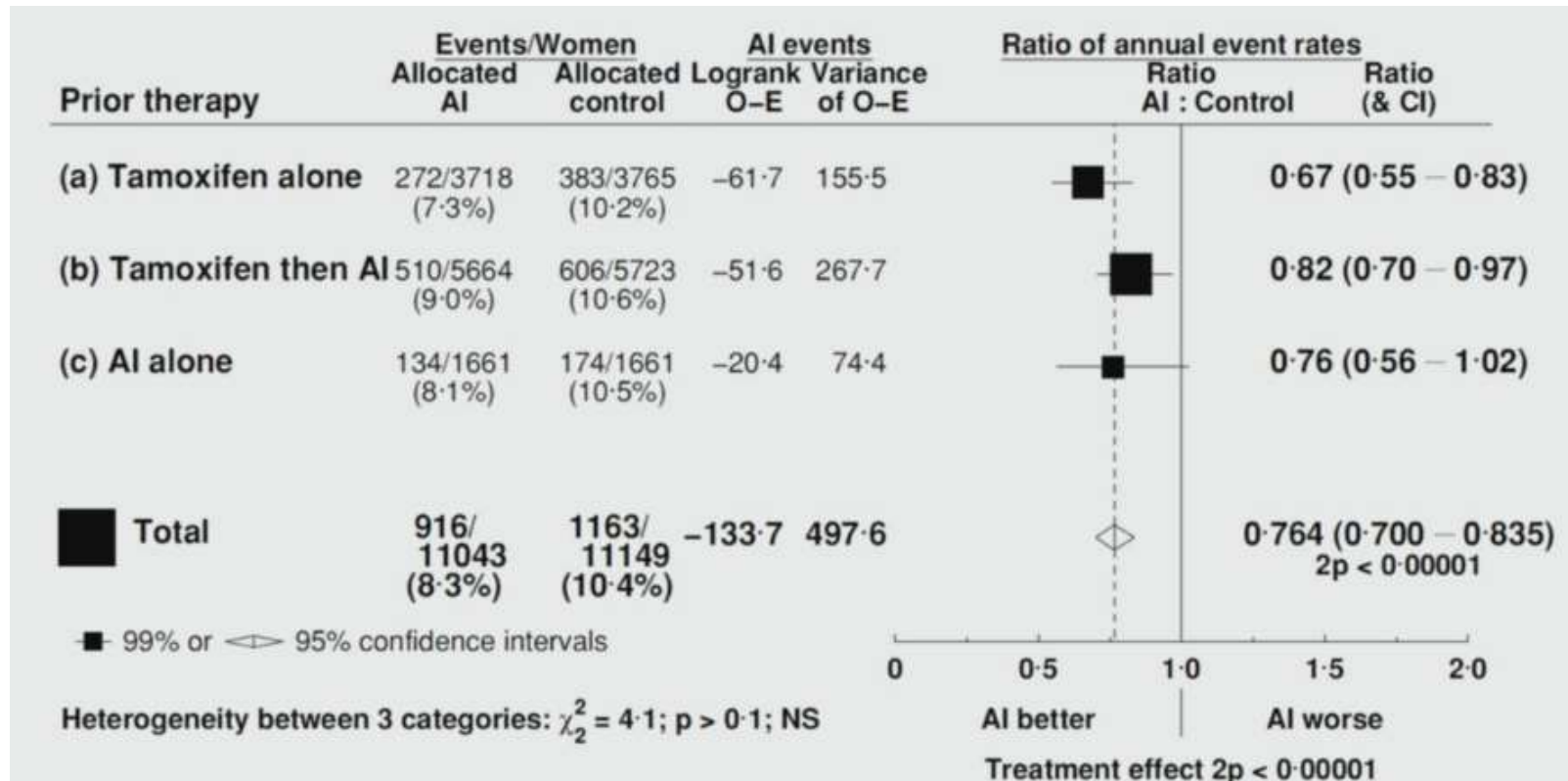
### Distant Recurrence



### Breast cancer mortality

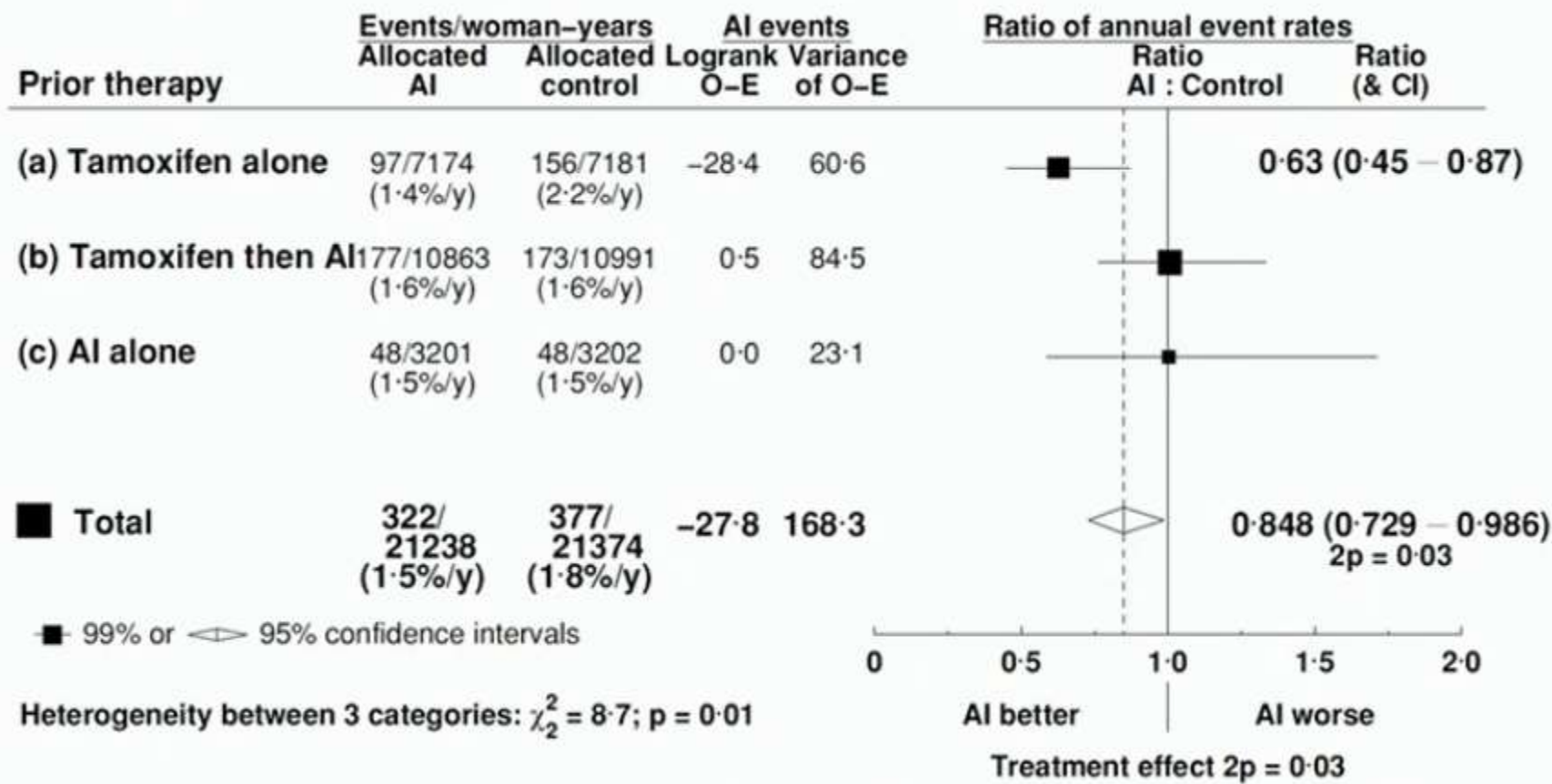


# Effect on recurrence by prior OT

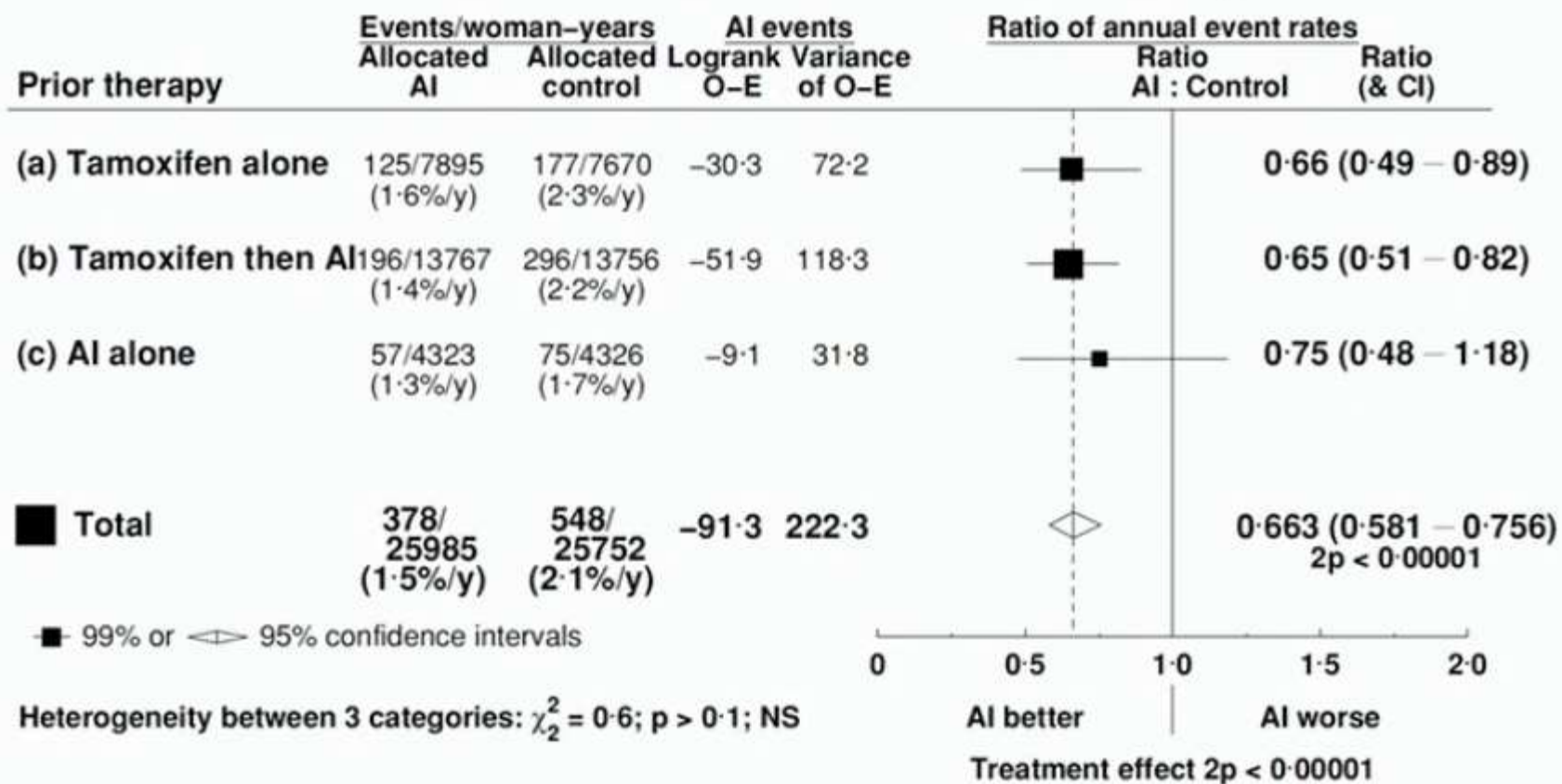




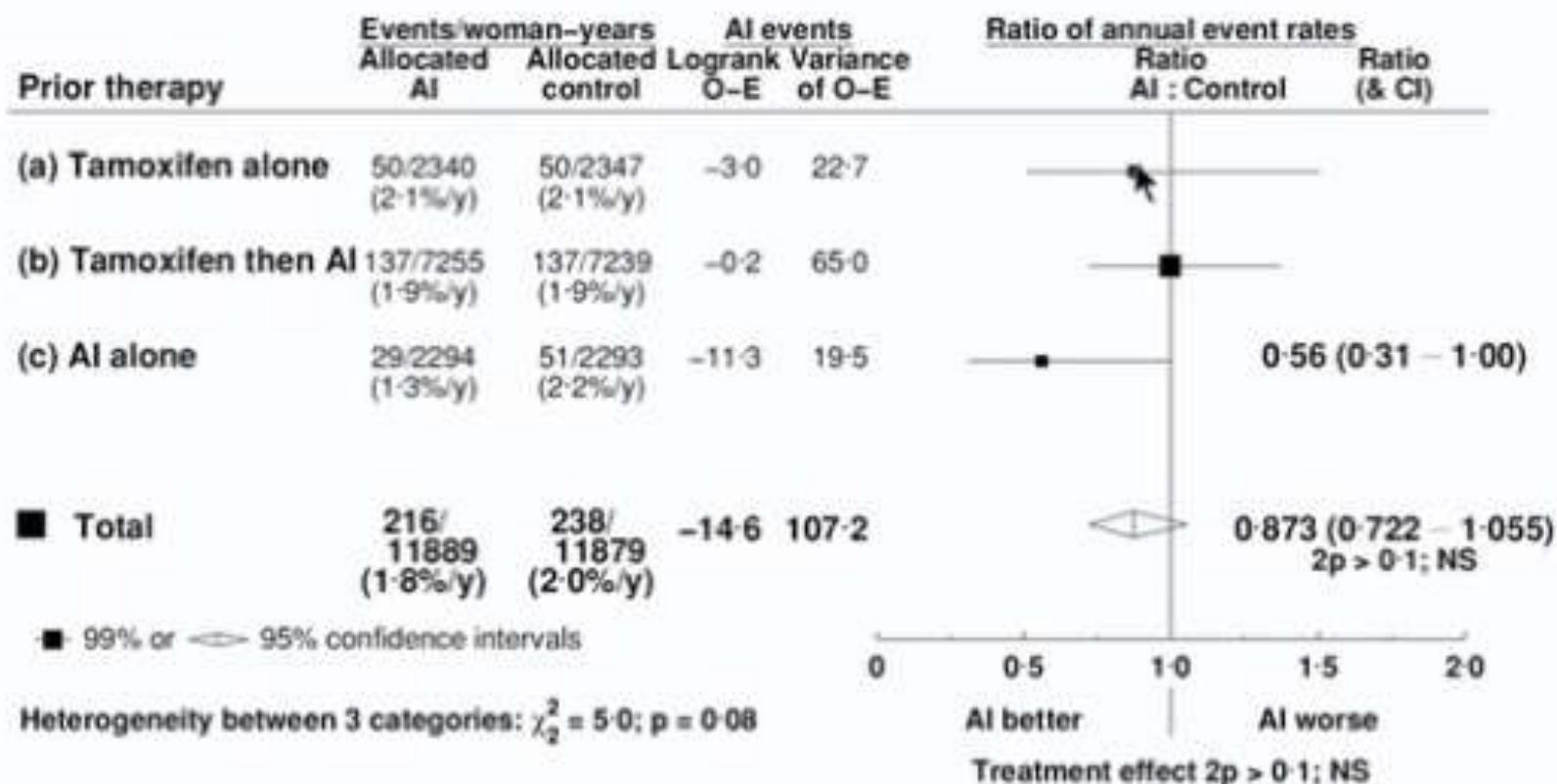
# Effect on recurrence in years 0-1 after treatment divergence by prior OT



## Effect on recurrence in years 2-4 after treatment divergence by prior OT

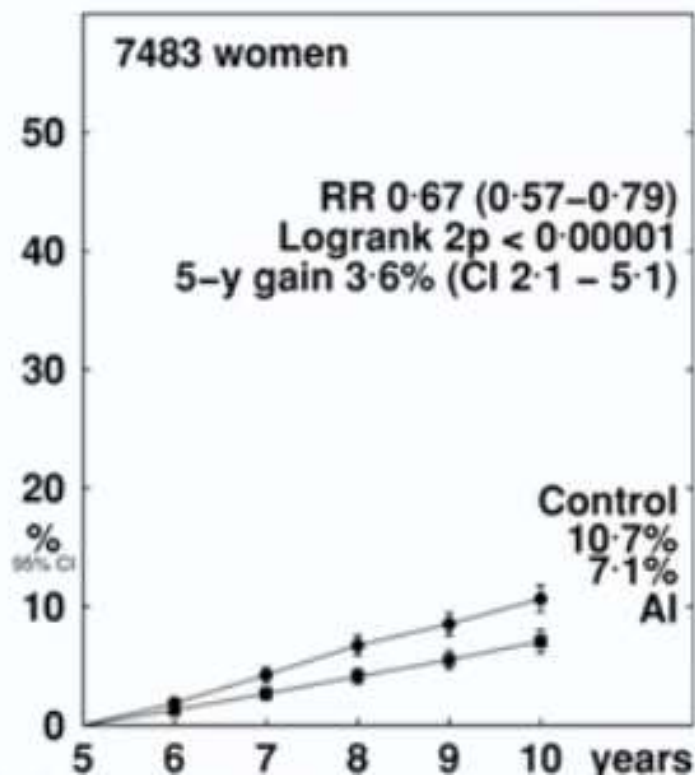


## Effect on recurrence in years 5+ after treatment divergence by prior OT

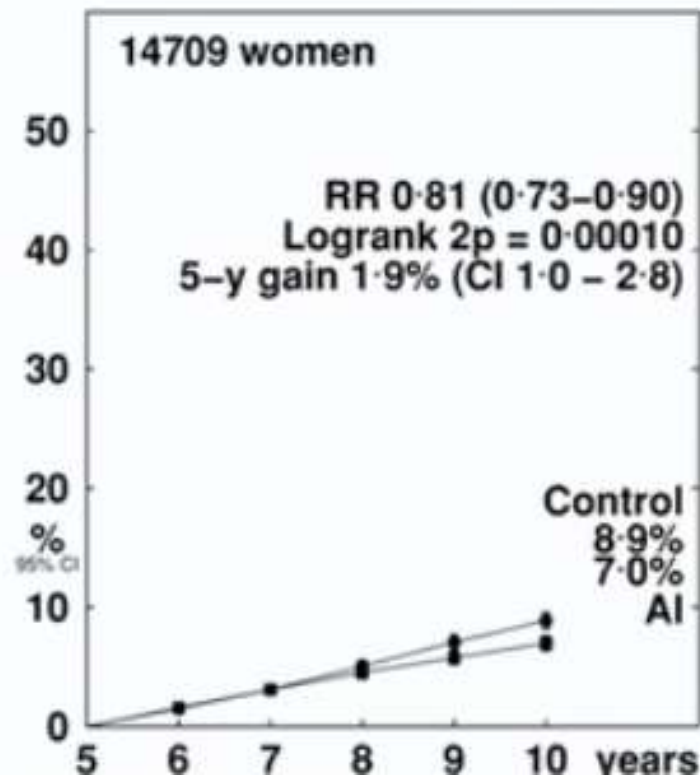


## Effect of extended AI therapy after 5-10 years on recurrence differs by type of prior OT

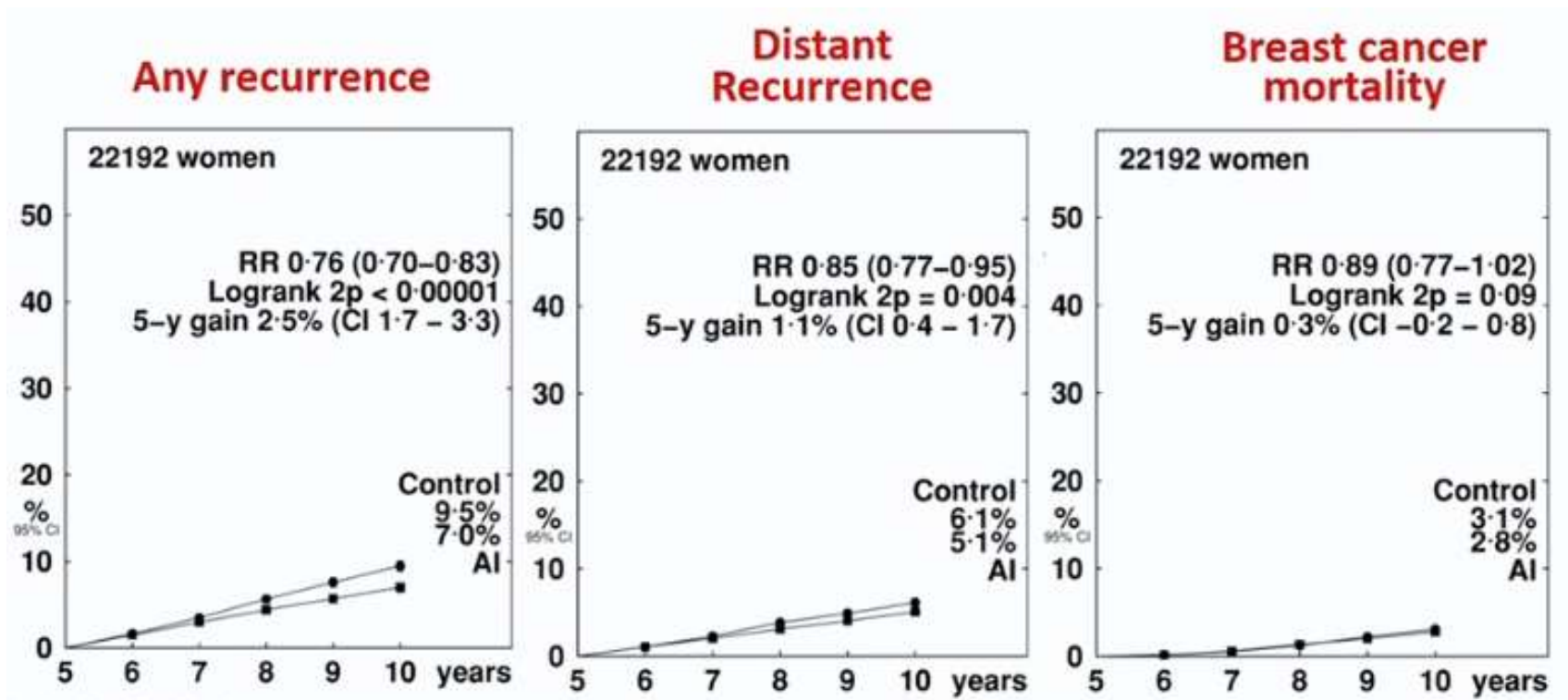
**Prior tamoxifen (a)**



**Prior AI (b + c)**

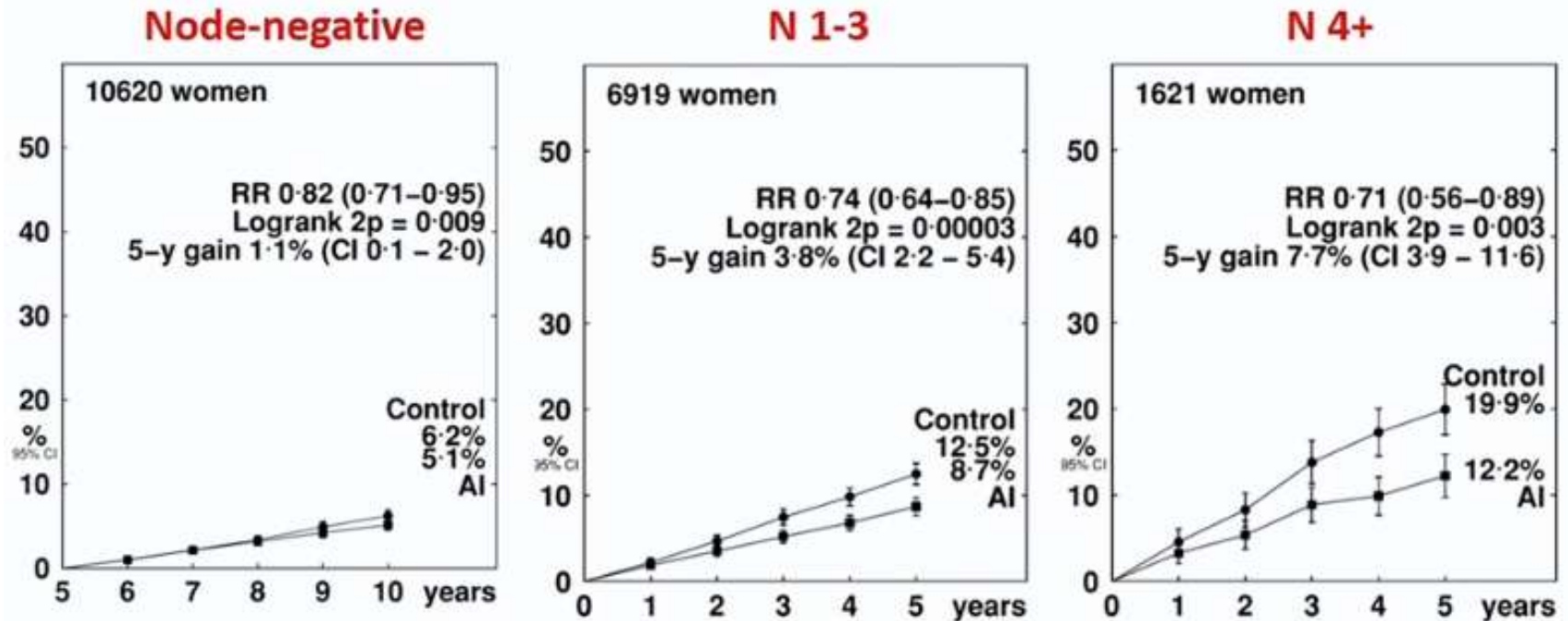


# Combined results of extended AI following 5-10 years of any prior OT





# Recurrence by nodal status



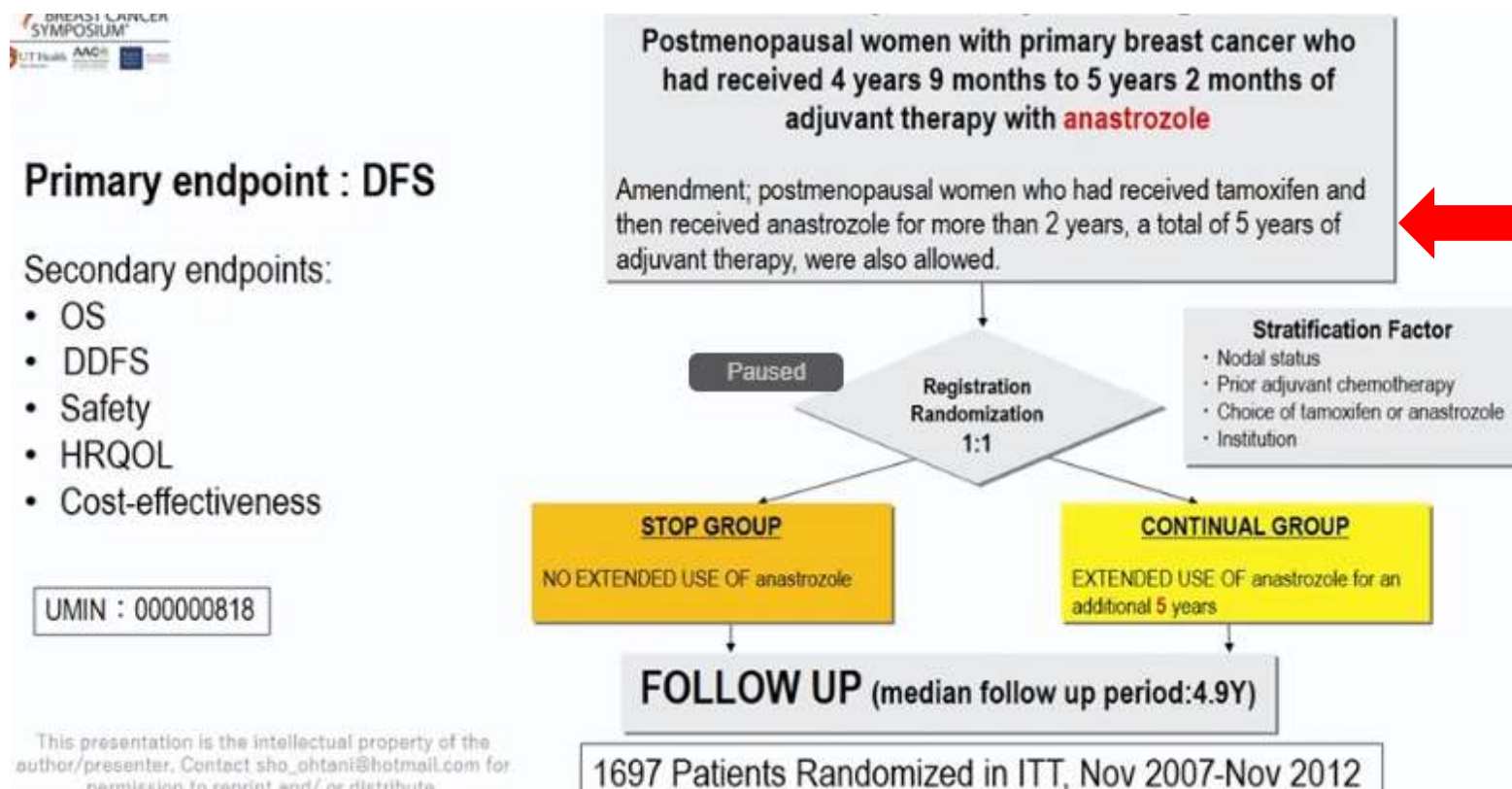


## Conclusions

- ✓ ~35% reduction in risk of recurrence after ~5 years of Tamoxifen
- ✓ ~20% reduction in risk of recurrence after AI (with or without Tamoxifen)
- ✓ Recurrence reductions apparent in the first two years after prior Tamoxifen but not until the third year after prior AI
- ✓ Benefits increase in node-positive patients
- ✓ Risk of bone fractures increased by 25% but no increase in death risk for other causes

# A prospective randomized multi-center open-label phase III trial of extending AI adjuvant therapy to 10 years: results from 1697 postmenopausal woman in the N-SAS BC 05 trial (AERAS study).

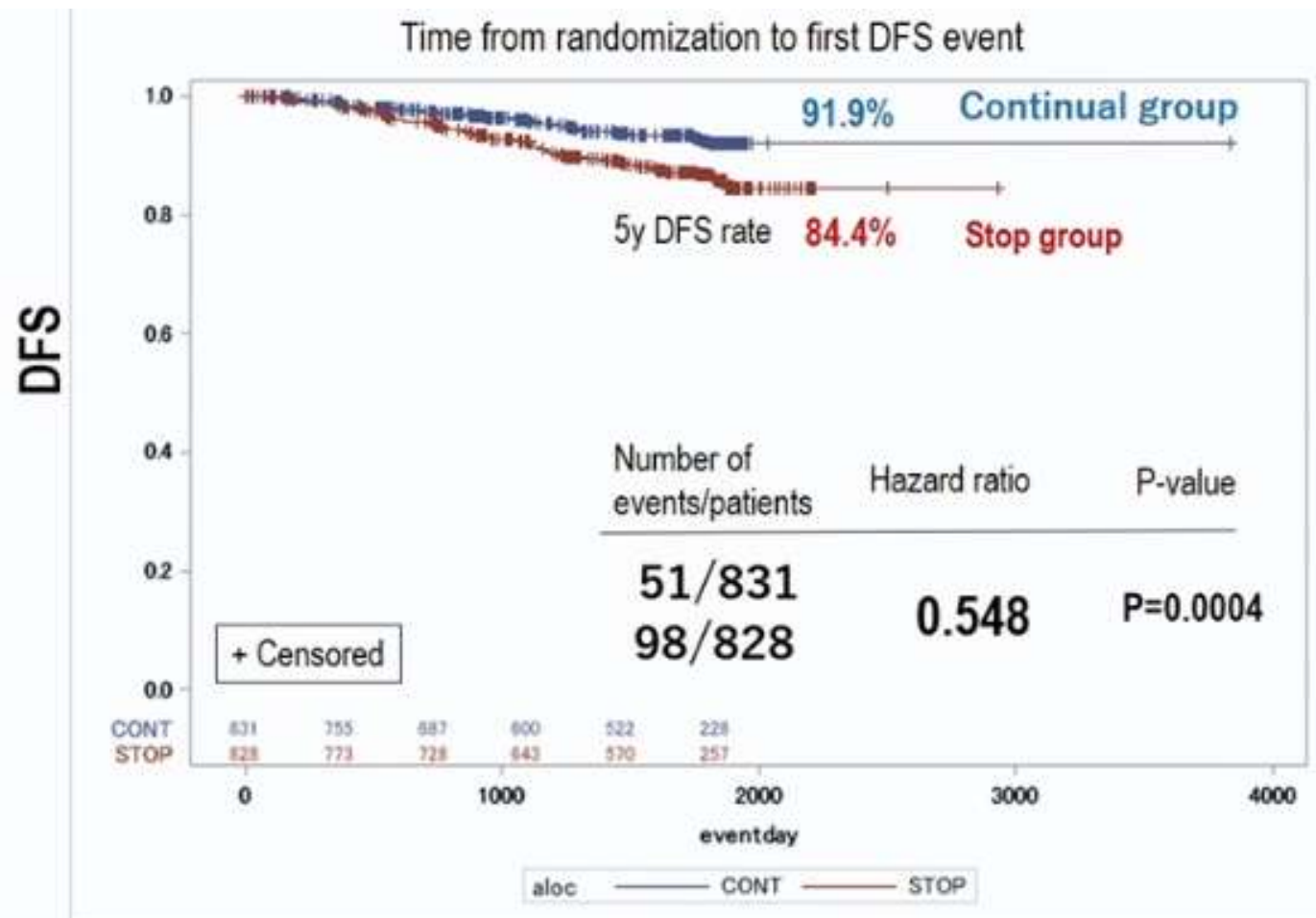
Ohtani S. et al.

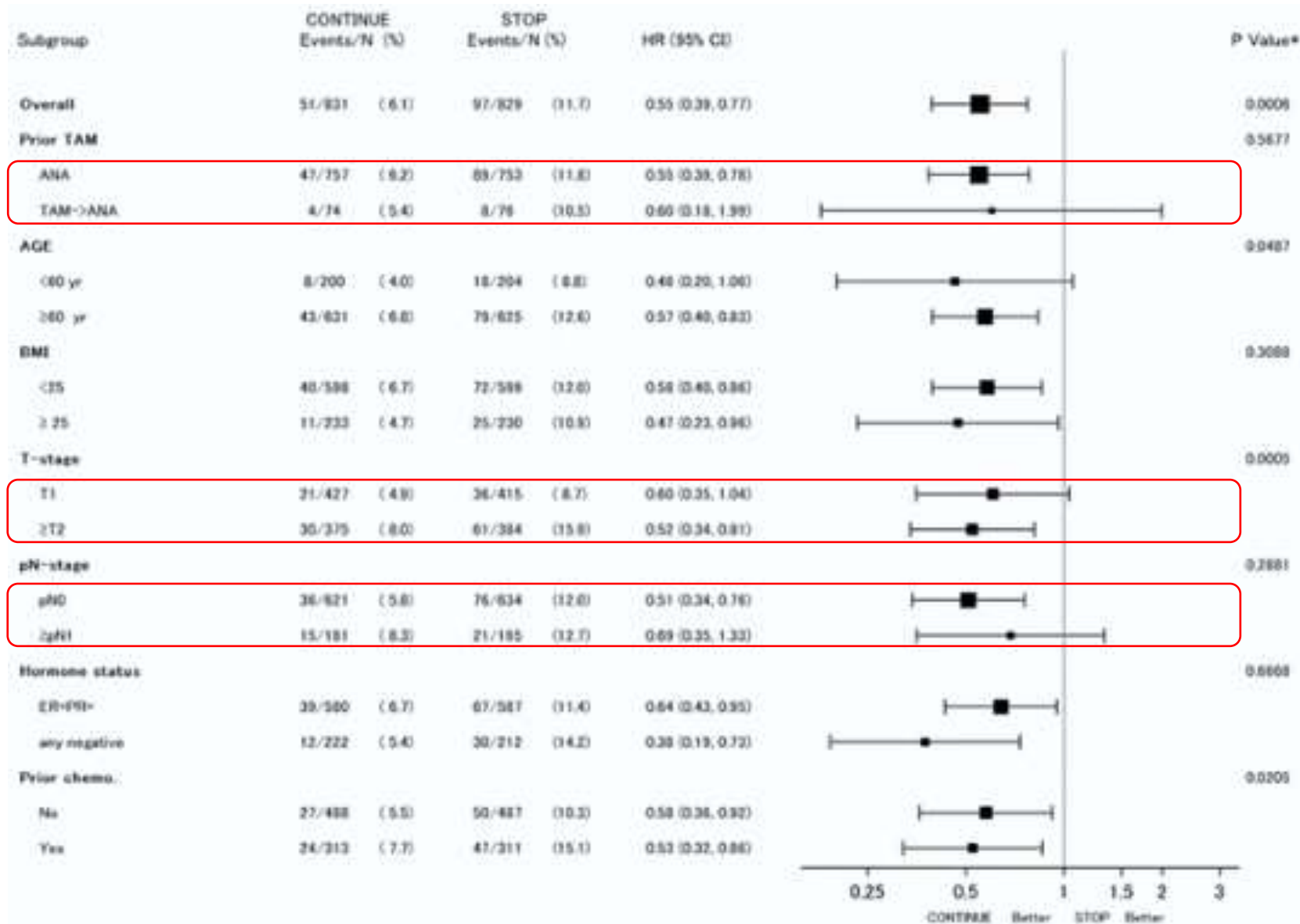


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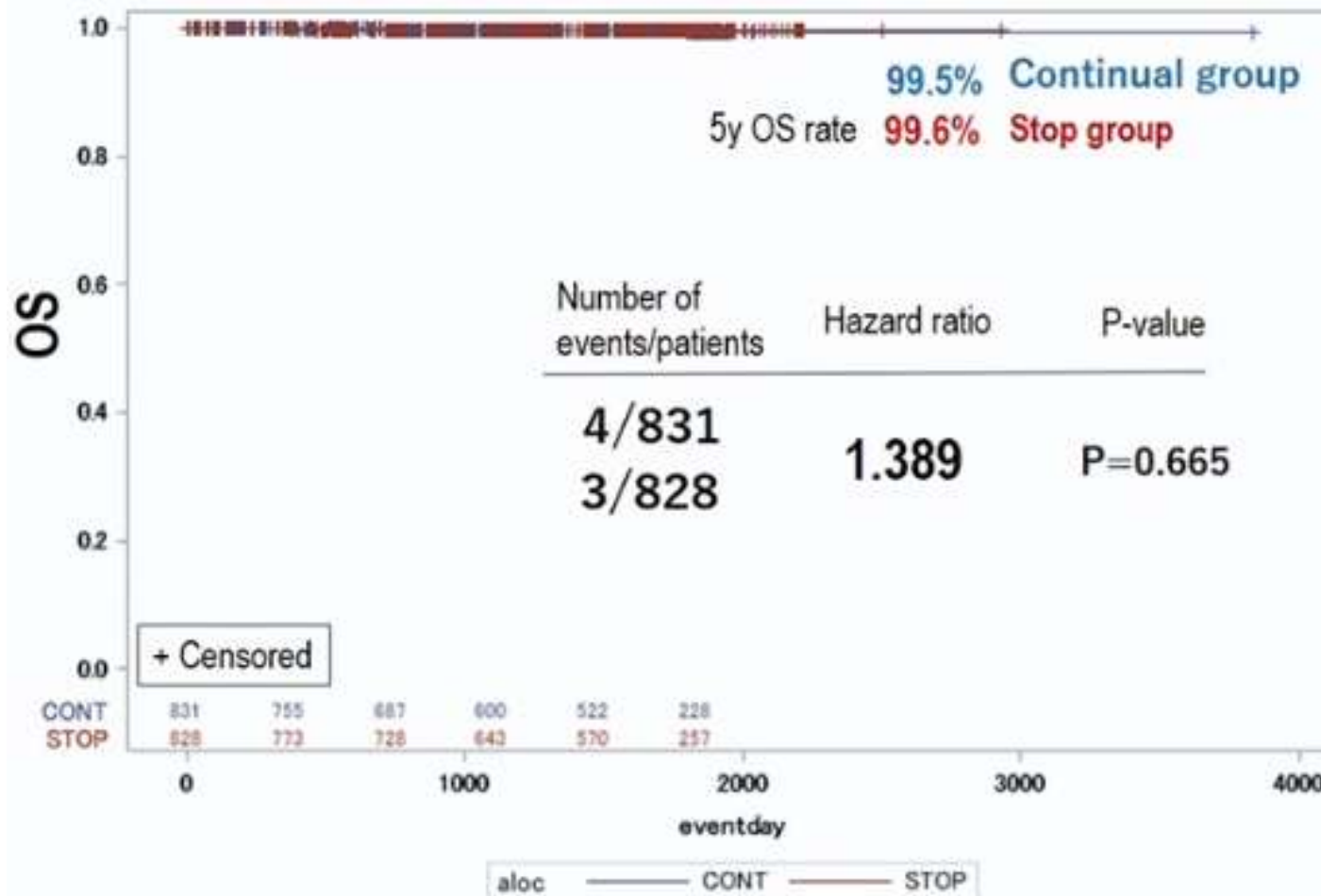
| Demographics and Characteristics |                 |                     |                          |
|----------------------------------|-----------------|---------------------|--------------------------|
|                                  |                 | STOP GROUP<br>(843) | CONTINUAL GROUP<br>(840) |
| Median Age                       |                 | 64,5                | 64,3                     |
| T-stage                          | T1              | 51,8%               | 53,4%                    |
|                                  | T2              | 44,8%               | 42,6%                    |
|                                  | T3-T4           | 3,3%                | 3,9%                     |
| N-stage                          | N0              | 79,1%               | 77,3%                    |
|                                  | N1              | 19,3%               | 20,3%                    |
|                                  | N2              | 1,5%                | 2,2%                     |
| Aduvant Chemotherapy             | Yes             | 39,3%               | 39.1%                    |
|                                  | No              | 60,3%               | 60,9%                    |
| Prior adjuvant OT                | TAM→Anastrozole | 9%                  | 8,9%                     |
|                                  | Anastrozole     | 91%                 | 91,1%                    |

# Disease-Free Survival





# Overall Survival





## Adverse Events

|                | STOP GROUP<br>(843) |                | CONTINUAL GROUP<br>(840) |                |
|----------------|---------------------|----------------|--------------------------|----------------|
|                | Any                 | Grade $\geq 3$ | Any                      | Grade $\geq 3$ |
| Bone fractures | 1,1%                | 0,1%           | 2,8%                     | 0,5%           |
| Osteoporosis   | 28%                 | 0,1%           | 33%                      | 0,3%           |
| Arthralgia     | 11,7%               | 0,1%           | 19,2%                    | 0,8%           |
| Stiff joints   | 4,9%                | 0%             | 11,7%                    | 0,3%           |
| Hot flashes    | 3,2%                | 0%             | 6,7%                     | 0,5%           |
| Headache       | 1,8%                | 0%             | 2,1%                     | 0,1%           |

# Conclusions

- ✓ Higher rates of Disease-Free Survival
- ✓ No significant nor life-threatening increase of adverse events

## Conclusions (definitive?)

- ✓ In postmenopausal women, prolonging adjuvant OT with AI does seem to increase DFS
- ✓ Longer follow up is needed to observe increasing in OS
- ✓ This gain is independent from prior OT (TAM alone, TAM→AI or AI alone) but is higher in the former group
- ✓ Benefit continues throughout the years (although with different timing according to prior OT)
- ✓ Patients at higher risk (i.d. with node-positive disease) have better outcomes
- ✓ Adverse events don't seem to be an issue but the real impact on QoL because of prolonged side effects should be carefully evaluated

Grazie!