

# Case selection for TARGeted Intraoperative radioTherapy (TARGIT)

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## Background

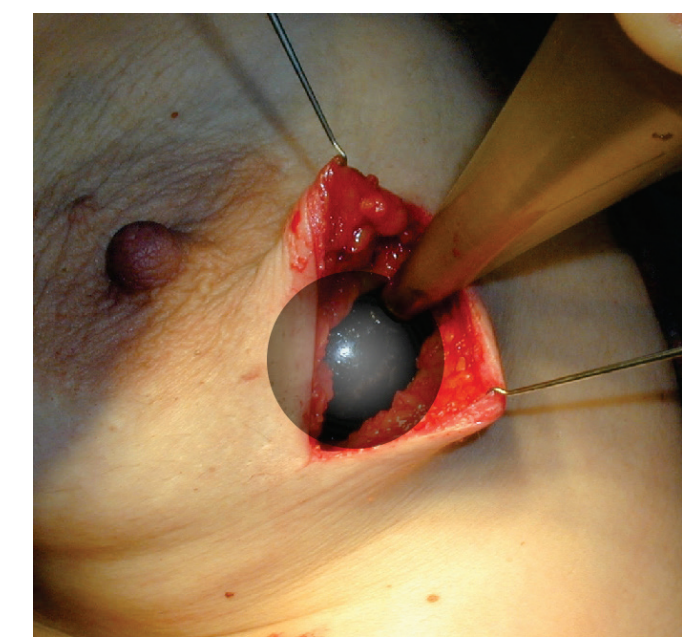
The TARGIT-A randomised trial compared a risk-adapted approach using targeted intraoperative radiotherapy (TARGIT) with whole breast external beam radiotherapy (EBRT) after lumpectomy for early breast cancer.



**Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial**  
*Lancet 2010; 376: 91-102*

Jayant S Vaidya, David J Joseph, Jeffrey S Tobias, Max Bulsara, Frederik Wenz, Christobel Saunders, Michael Alvarado, Henrik L Flyger, Samuele Massarut, Wolfgang Eiermann, Mohammed Keshitgar, John Dewar, Uta Kraus-Tiefenbacher, Marc Sütterlin, Laura Esserman, Helle M R Holtveg, Mario Roncadin, Steffi Pigorsch, Marinos Metaxas, Mary Falzon, April Matthews, Tammy Corica, Norman R Williams, Michael Baum

**Conclusion** For selected patients with early breast cancer, a single dose of radiotherapy delivered at the time of surgery by use of targeted intraoperative radiotherapy should be considered as an alternative to external beam radiotherapy delivered over several weeks.



**December 2012 San Antonio Breast Cancer Symposium<sup>2</sup>**  
**Updated results: : the preferred option is to give TARGIT concurrently with lumpectomy (prepathology).**

**How to select cases for TARGIT?:** In this analysis we describe patient and tumour factors that may help select patients for TARGIT based on the results of an *a priori* statistical analysis plan.

## Methods

- Large international randomised trial: 33 centres in 10 countries
- Randomisation to TARGIT vs. EBRT.
- If unexpected high risk factors are found postoperatively, after TARGIT, EBRT is added (in 15-20% of cases)
- 3451 patients
- Age >=45, unifocal invasive ductal carcinoma, size <=3.5cm
- Trial closed in June 2012

## Primary outcome

Local recurrence in the conserved breast

## Secondary outcome

Mortality – deaths from breast cancer and from other causes

## A priori hypothesis before unblinding for this analysis:

Before unblinding for this analysis, we hypothesised that **progesterone receptor (PgR) status, as an expression of a functionally active oestrogen receptor (ER), is a surrogate for radiation responsiveness and might be a predictive factor.**

We pre-specified a detailed analysis by PgR status.

This was based on the finding in the recent EBCTCG overview that radiotherapy is more effective in hormone responsive tumours. Furthermore, the suggestion that a positive PgR status is necessary for a tumour to be called luminal A and the ELIOT study had found that IORT works better in luminal A tumours.

We performed Kaplan Meier analysis for the primary and secondary end points as per PgR receptor status.

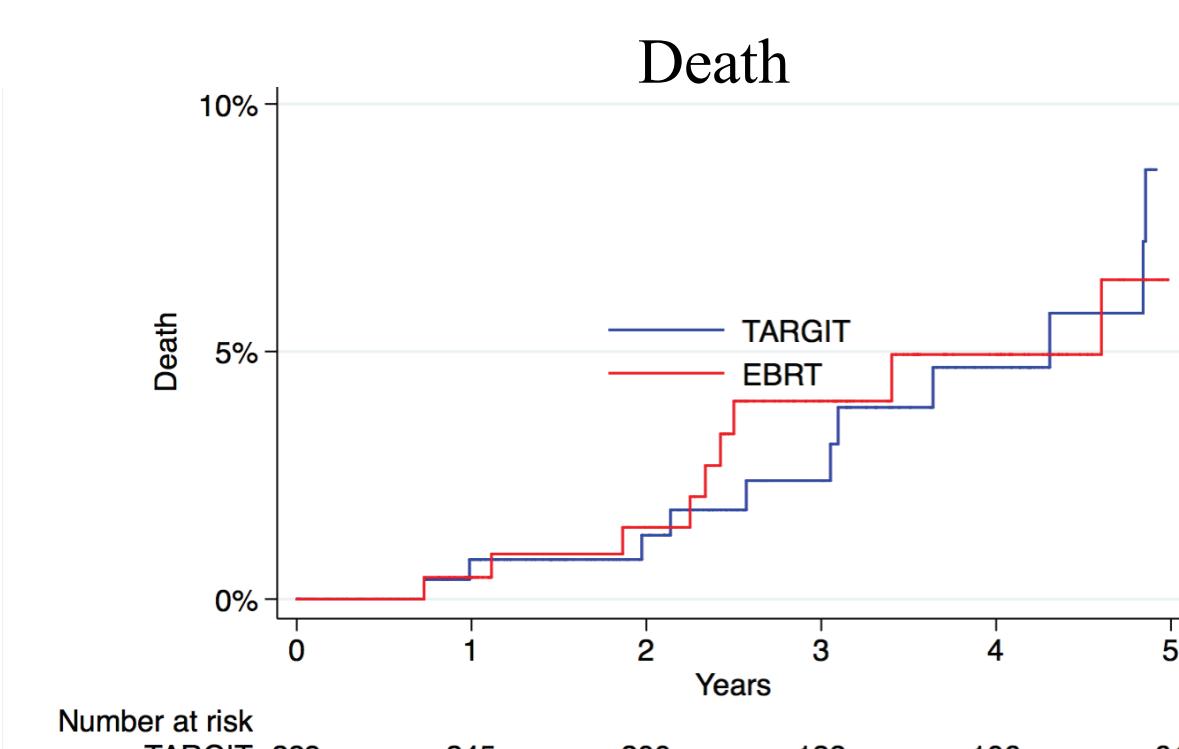
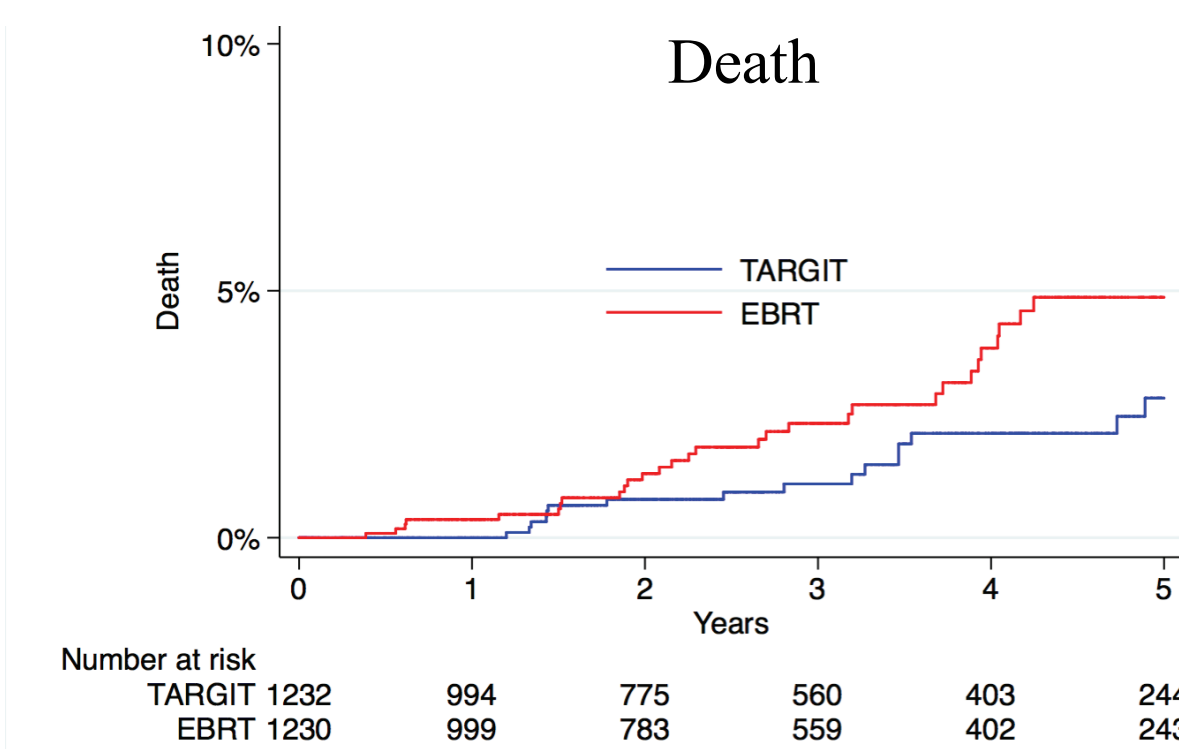
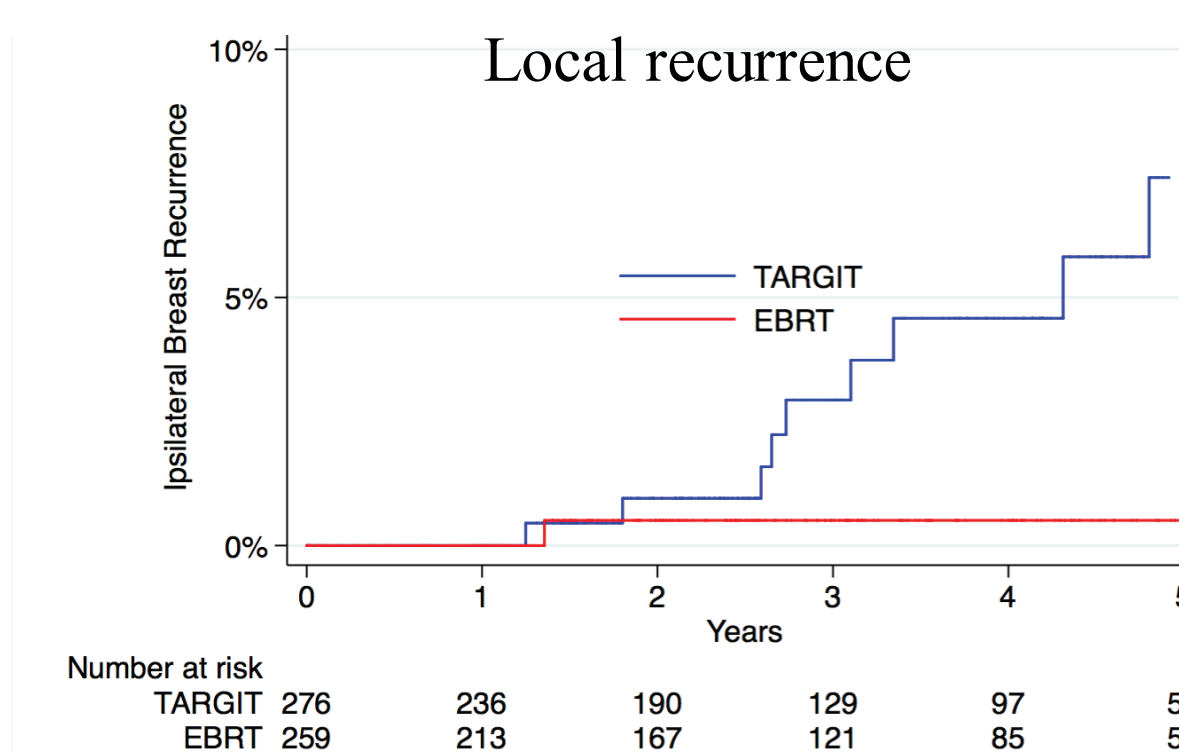
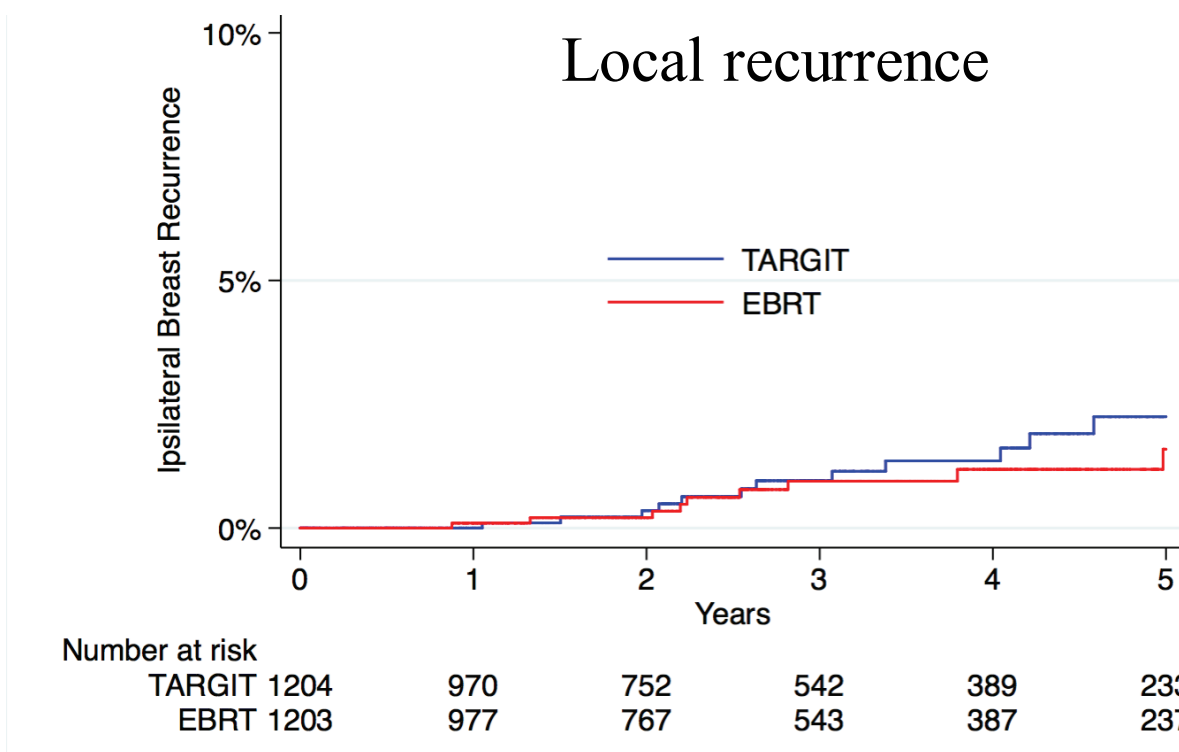
We also analysed using the Cox proportional hazard model (age, margin status, tumour grade, ER, PgR, HER2, vascular invasion and node positivity).

## Results

- **In PgR positive cases**, there was no significant difference in the primary outcome of Ipsilateral breast recurrence between TARGIT and EBRT 2.3%(1.3-4.3) vs. 1.5%(0.75-3.0) p=0.51, and there were fewer deaths 2.7% (1.6-4.5) vs 4.9% (3.3-7.1) p=0.0487
- **In PgR negative cases** there were more local recurrences after partial breast irradiation using TARGIT: 7.0%(3.5-13.6) vs. 0.5%(0.1-3.7) p=0.017, but number of deaths was similar 8.1%(4.4-14.7) vs. 6.3 (3.2-12.3).
- Age, margin status, tumour grade, tumour size, vascular invasion, node positivity, ER and Her2 status were not found to be significant predictors. Even age younger than 50 or grade 3 cancers had similar outcome with TARGIT or EBRT.

Progesterone receptor positive

Progesterone receptor negative



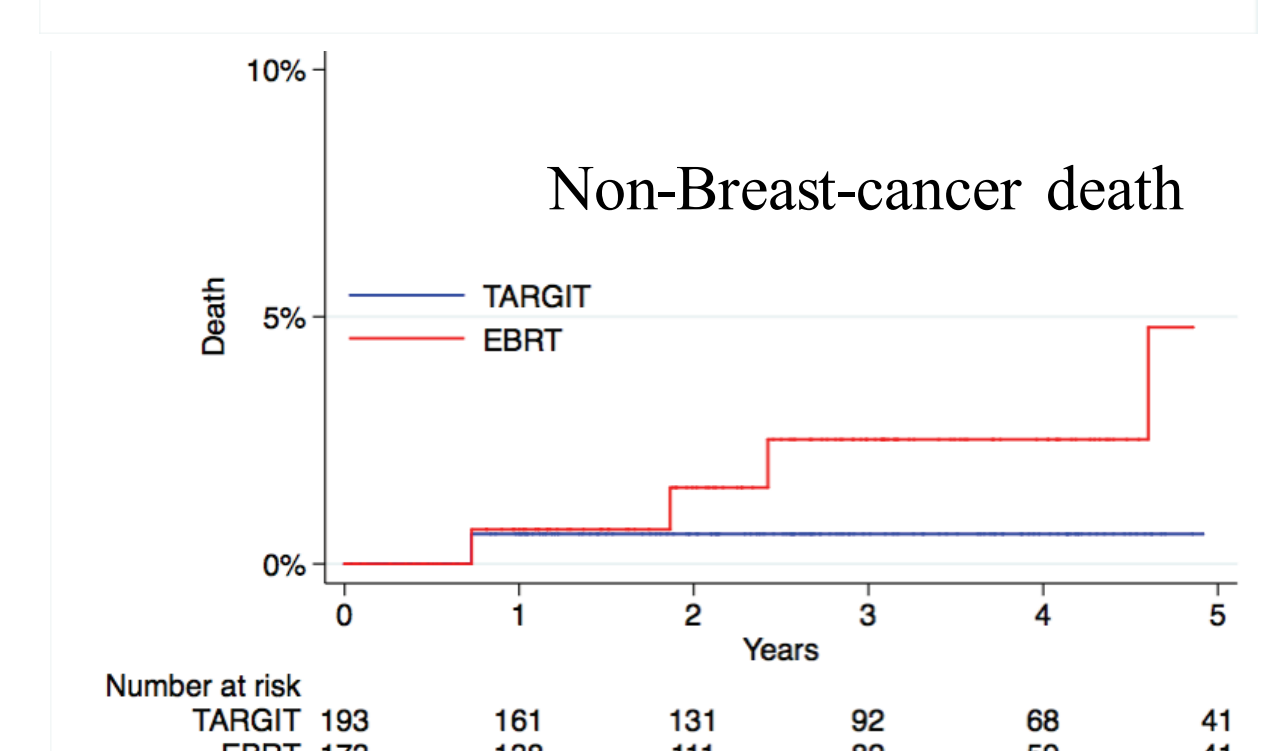
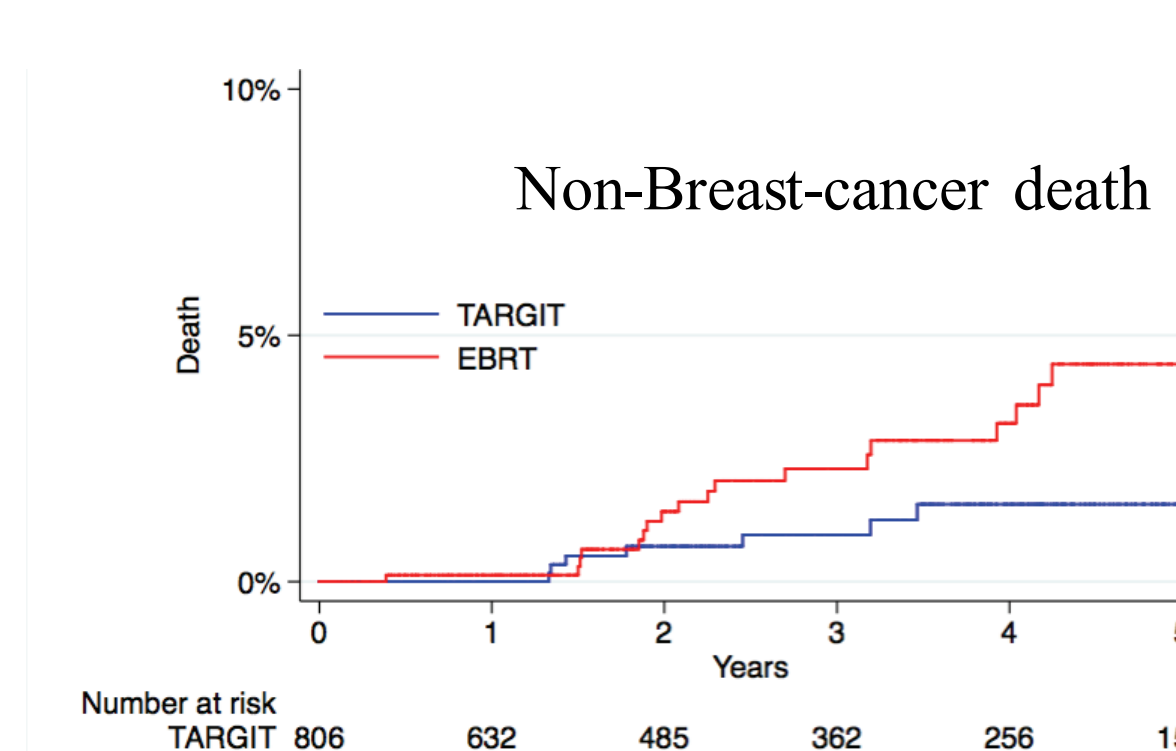
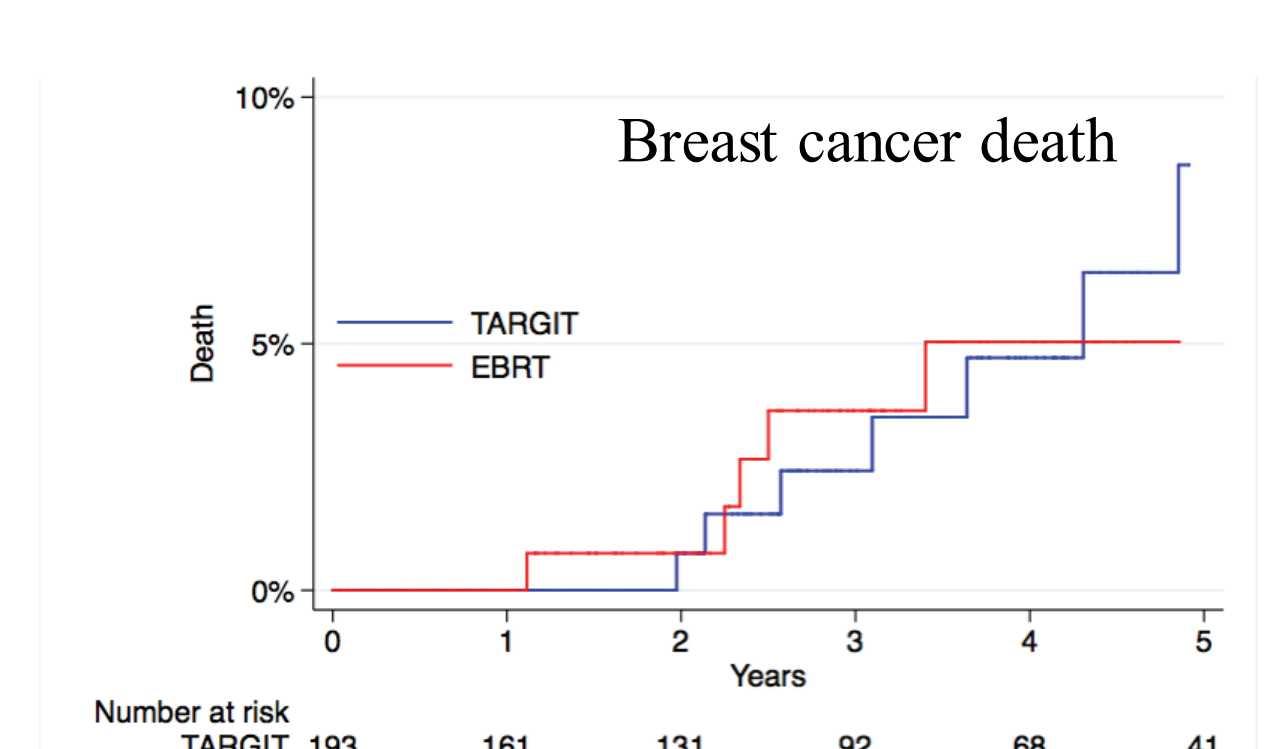
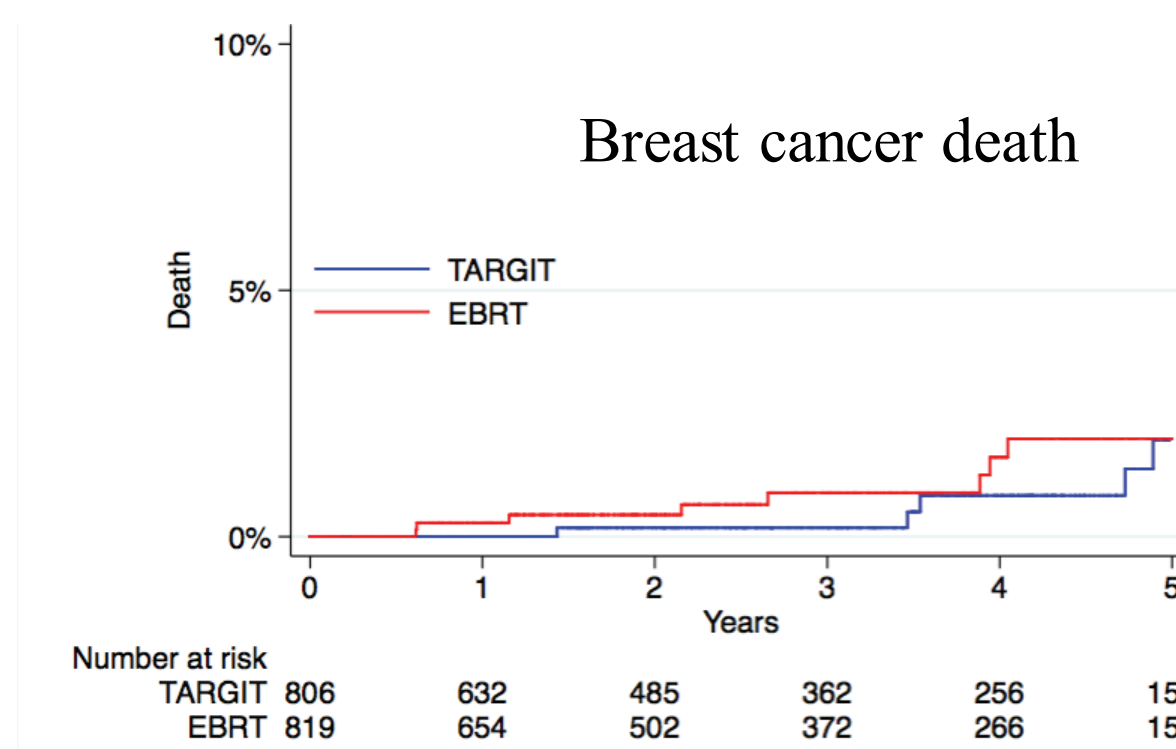
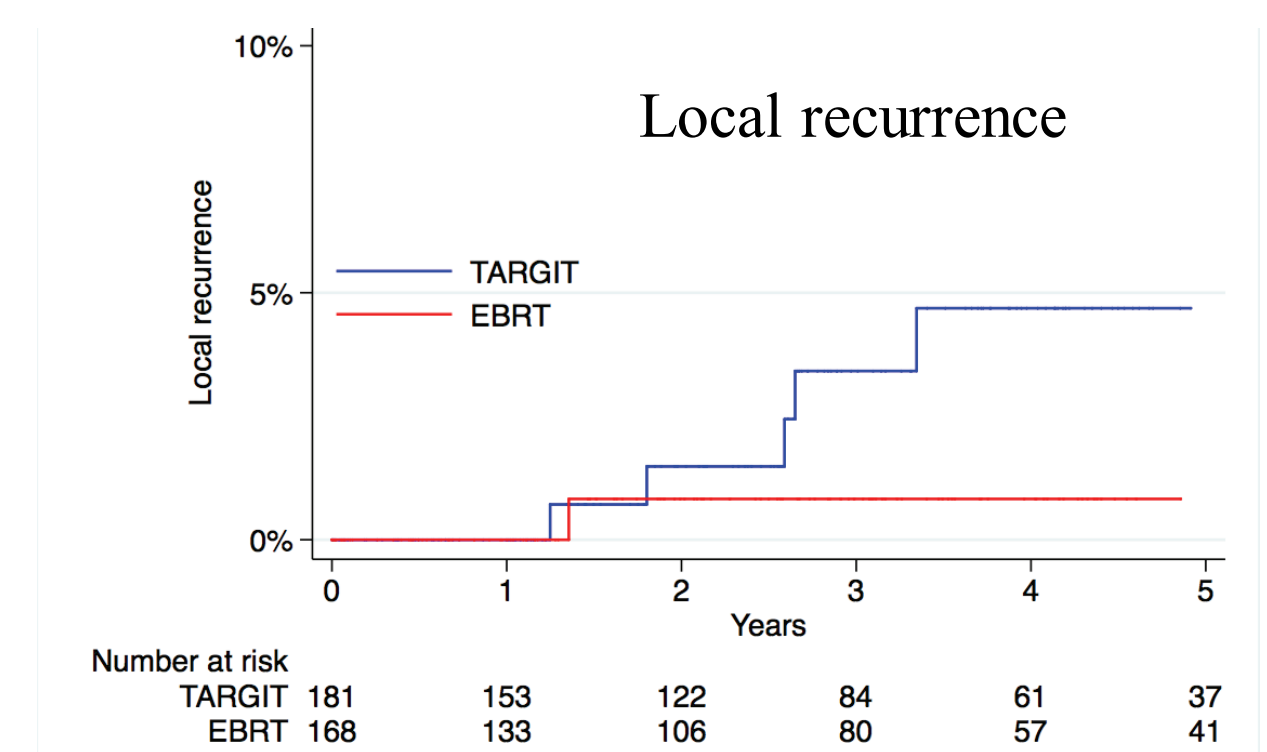
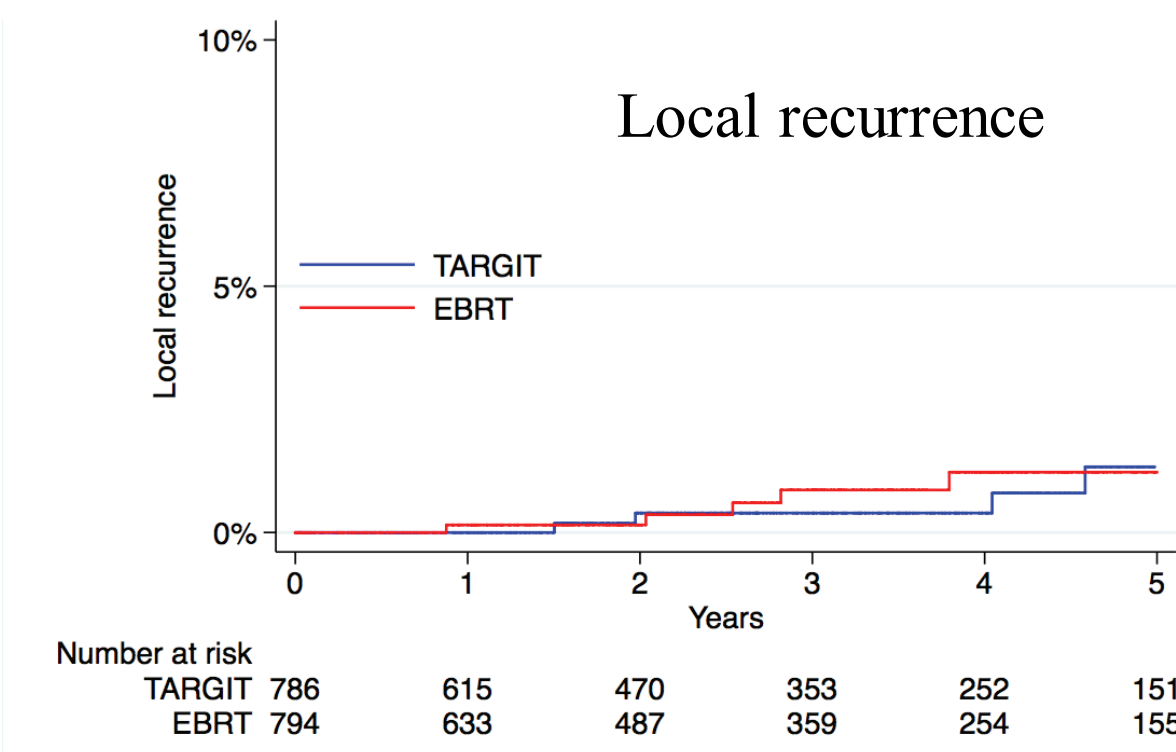
## When TARGIT was given concurrently in PgR positive cases (n=1625)

- 5-year risk of local recurrence in the conserved breast  
TARGIT 4 events, 1.4%(0.46-3.9)  
vs.  
EBRT 5 events 1.2%(0.48-2.9)  
HR 0.82(0.22-3.06)
- 5-year risk of overall mortality  
TARGIT 18 deaths 3.3%(1.83-6.04)  
vs.  
EBRT 31 deaths 6.4%(4.3-9.6)  
HR 0.60(0.34-1.08)

## TARGIT given at the time of lumpectomy

Progesterone receptor positive

Progesterone receptor negative



## Conclusions

- Progesterone receptor status could be useful in selecting cases for using PBI with targeted intraoperative radiotherapy (TARGIT)
- When TARGIT is given concurrently with lumpectomy in PgR positive cases, local recurrence and breast cancer deaths are similar to EBRT and there are significantly fewer deaths from other causes (p=0.04), with a trend for improvement (3.1% higher) in overall survival.



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