Reviewer's report

Title: Eligibility criteria for breast intra-operative radiotherapy: a study about 12,025 patients treated in two distinct cohorts

Version: 6 Date: 15 August 2014

Reviewer: Jayant Vaidya

Reviewer's report:

This is an important paper that will inform the policy makers of the number and proportion of patients that would be suitable for intraoperative radiotherapy.

It is a well conceived, well performed and well written study. There are a few important changes that are relatively minor - but must be corrected before the paper is considered suitable for publication.

The statistics appear adequate.

Major / important revisions - the following changes are necessary to be made:

Essential revisions:
1. The term E-IORT can be easily confused with IOERT and therefore should be deleted from the manuscript. Simply saying exclusive intraoperative radiotherapy is adequate - alternatively, targeted intraoperative radiotherapy (TARGIT) would be preferred, because this is the technique used in the TARGIT-A trial, which is the basis of the extended eligibility suggested by the authors.

2. TARGIT-E study is a single arm and important study, but it is without a control arm and is similar to post-marketing audit. It is not expected to give any more comparative data than the TARGIT-A trial. So these sentences can be omitted.

3. In the conclusion the final line is confusing and should be omitted: a suggestion is to add: "Further data from subgroup analysis may further improve patient selection for receiving intraoperative radiotherapy as the only radiation treatment for early breast cancer."

4. The authors should comment in the discussion that absolute differences they have found between eligible and ineligible groups, although statistically significant, are really very small in absolute terms (e.g., 0.6% difference in 5-year survival between T1E and T1nE.

Optional: Discussion about other factors could be omitted but a suggested comment about patient selection can be added: However, these factors do not predict the actual effect of radiation. Only a subgroup analysis of randomised trials can inform us whether these known 'adverse' factors actually change the effectiveness of radiotherapy. The Oxford overview (2011) found that only grade and hormone receptor status changed the proportional benefit from radiotherapy.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I am the lead author of some of the papers cited in the manuscript.