Author’s response to reviews

Title: Single blind randomized Phase III trial to investigate the benefit of a focal lesion ablative microboost in prostate cancer (FLAME-trial)

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Author’s response to reviews: see over
21 November, 2011

Dear Editor-in-Chief,

Please find attached our revised manuscript entitled: “Single blind randomized Phase III trial to investigate the benefit of a focal lesion ablative microboost in prostate cancer (FLAME-trial)”.

Thank you for the review procedure and the helpful comments on our manuscript.

We are pleased to be able to respond to the reviewer’s comments. We have corrected the manuscript following the reviewer’s comments. All changes in the text are indicated below.

Yours sincerely,

Irene Lips, M.D., Ph.D.
Corresponding author
We thank the reviewer for all valuable suggestions for improvement of the manuscript.

Response to the comments from the reviewer:
More of their responses need to be incorporated in the text. Instead of just saying “we thought a one-sided p value is fine” in the rebuttal letter, they need to add something to the paper itself.

We incorporated the responses in the text by adding to the methods/design section:

- Page 9/10: ‘The disease- and treatment-related side effects are only a component of health-related quality of life (Litwin et al, 1999). To address the components of overall well-being, a general instrument is used in addition to the disease-specific questionnaires (Inoue et al, BJU Int, 2009; Nout et al, JCO, 2011; Kornblith et al, JCO, 2011).’
- Page 10: ‘It is important to measure QoL every 6 months after treatment, to be able to determine the point in time at which the QoL changes, for example due to side-effects after treatment.’
- Page 11: ‘The reason to choose a one sided p-value is that, although extremely improbable, an increase in biochemical failure in the experimental arm would lead to the same action as no difference at all between the two treatment arms. This is because the experimental treatment will only be implemented if it is significantly better than the usual treatment, due to the increased toxicity risk in the experimental arm.’

I urge the authors to reconsider their main analysis, which involves waiting for five years after treatment of the final patient.

We changed the main analysis into a time to event analysis (Methods/design, page 12). We further changed the sample size consideration on page 11 into: ‘A one-sided log rank survival power analysis shows that the length of follow-up after accrual of the last patient should be 3.5 years to detect a difference of 10% (64% and 74% free from biochemical failure after 5 years, in the control arm and experimental arm, respectively) with a power of 80% at a one-sided 5% significance level. This is under the assumption that the patients enter the study during an accrual period of 5 years, 50% of the enrollment is complete when 70% of the accrual time has past and that 20% of the patients in both arms are lost to follow-up during the follow-up period of 5 years.’ and removed from the data analysis section: ‘To test the difference between the two treatment arms in the proportions of patients who are still free from biochemical failure after five years the Chi square test will be used.’