Reviewer's report

Title: Finasteride in the treatment of clinical benign prostatic hyperplasia: A systematic review of randomised trials

Authors:

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Reviewer: Mark Emberton

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Other (see below)

MY BRIEF

I have been asked to review the above manuscript and also read the referees report on the manuscript and the authors' response to that report. My task is to act as 'tie breaker' in view of the 'impass' that has resulted between the reviewer and the authors

SUMMARY OF THE MANUSCRIPT

The authors have presented the results of a systematic review based on 8820 patients who received finasteride and 5909 who received placebo over periods that varied from 3 to 48 months. The conduct of the review and the analysis of the data conform to the highest methodological standards. Of the 19 trials reviewed all had quality scores of 3/5 or higher.

The authors conclude that, compared to placebo, patients treated with finasteride experienced a reduction in urinary symptoms, an improvement in flow rate and a reduction in prostate volume. Moreover, the rate of serious adverse events was similar in both groups (12% with finasteride, 13% with placebo)

The authors have presented a detailed account of potential competing interests and have explicitly described the involvement of the sponsors (MSD) both in the contractual details of the funding and also the process of manuscript review. It is not stated whether review of the manuscript by representatives from MSD resulted in any changes prior to submission.

As is now expected in systematic review, the authors alert the reader to methodological problems encountered. They cite the reporting of the various outcomes in the trials as sub-optimal and call for dichotomous outcomes. The European regulatory agencies now require this kind of reporting so it will become standard in the future BPH studies.

The manuscript is well written. The authors have attempted to put the results into a clinical context in
order to help both patient and clinician in making the decision to treat or not to treat. This can only be achieved by weighing up the likely benefits of treatment against the likely harms. This manuscript will assist in this decision making process.

SUMMARY OF COMMENTS MADE BY DR WILT

Dr Wilt acknowledges that the methodological approach adopted by the authors was ‘high quality’.

Dr Wilt expresses concerns about ‘unbalanced conclusions’. I re-read the conclusions presented within the discussion section with these comments in mind. My opinion is that the conclusions are appropriate. I particularly liked the authors’ device of placing their findings within a clinical context. In other words, what is it that a man can expect to experience were he to chose to start finasteride?

Dr Wilt is concerned that the magnitude of effect is too small to make a difference to the patient. This is a reasonable concern but is one that is not directly pertinent to the review of this manuscript. The authors can only report what they find. They have done just this and quite properly. To have strayed into the very difficult and ill understood area of patients own perception on and satisfaction with their transition in health state would have been inappropriate and beyond their brief and expertise.

Dr Wilt has reservations about the degree to which the study population can be generalised to the normal population. Again I have to disagree with this comment. So well were the men characterised in PLESS that we that it is possible to apply the results of PLESS to men with similar characteristics. It is because of PLESS (and a few other similar studies) that clinicians can use the determination of prostate size as a predictor of response to treatment with finasteride.

Dr Wilt requests the authors to broaden the discussion by including comparative data from studies comparing alpha blockers to placebo. I see no benefit in doing this. To do properly would require another systematic review that included all these studies.

Dr Wilt's request for cost information is understandable but again requires the authors to venture beyond the scope of their review.

RECOMMENDATION

For the reasons given above I feel that this manuscript should be published. None of the comments made by Dr Wilt threaten the validity of the findings.

Competing interests:

I have acted as a clinical adviser to a large number of pharmaceutical companies including MSD. I have received honoraria for speaking at MSD sponsored symposia. I have received financial support to develop a CD ROM to assist patients in making decisions about all aspects of urological care including LUTS/BPH. I receive no regular payment from MSD nor do I have any direct shareholdings with the company.

I will not gain financially or otherwise by the publication of this manuscript.