British Prostate Group

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Alana Miller
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Dear Alana

Thank you for the opportunity to comment on the HTA on Docetaxel for the treatment of hormone-refractory prostate cancer. We would compliment the team on the literature review and synthesis of the evidence, and recognise the enormous amount of work that has gone into this.

We would like to divide our comments into major comments and minor comments.

Major Comments

Our major criticisms relate to the assumptions underpinning the economic review. The statement that "docetaxel plus prednisolone is the most effective treatment for men with mHRPC" (page 105) is welcome and one that we endorse. However, the rider that it is cost effective only if "the NHS is willing to pay at least £32,706 per QALY" (page 168) is open to challenge. The economic assessment by Sanofi-Aventis is judged to be inadequate for the NHS setting, this being the primary reason why the CHE undertook another one. However:

1. This seems to ignore the fact that a number of patients in TAX 327 were recruited from the UK. As we are not given access to the Industry submission (understandably), we cannot say whether or not this industry analysis was restricted to Canadian patients.

2. The strategies in the CHE model, supposedly representative of the NHS, bear little relation to current practice (p126). Thus, D+E, D + E + P (70), D + E + P (35), and M + P + C are irrelevant. Estramustine is rarely used in the UK, and the bisphosphonate most commonly used in prostate cancer is Zoledronic Acid, not Clodronate, the latter having been shown to be of limited use in metastatic disease (Dearnaley et al, JNCI 2003).

3. Similarly, the strategic scenarios themselves seem unrealistic. In practice, a patient whose PSA rises after first-line hormone therapy might be offered docetaxel + prednisolone, but without this option might be offered bicalutamide, zoledronic acid (by monthly iv infusion), stilboestrol, palliative radiotherapy, surgery (e.g. for internal fixation), variously either seuqentially or in combination. Conceivably, this would impact on your economic modelling in one of 2 ways:

    a. A responding patient might make less use of these other alternative strategies, thus reducing the cost per QALY substantially compared to your assessment.

    b. Alternatively, a patient who lives longer might make more use of the above resources simply because he is around for long enough to be able to do so. However, this would be a pernicious argument were it used as a reason not to support the use of docetaxel – analogous, for example, to suggesting that patients should not be encouraged to quit smoking as they would consume more NHS resources if they did not die of a heart attack.

    We feel that there are sufficient uncertainties in the assumptions needed to model in this scenario, as to make estimates of cost per QALY extremely difficult to quantify. We welcome the cautionary comments in the conclusions to the economic evaluation, but our view is that the uncertainties are

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far greater than you acknowledge, for the reasons given above. £32,00 per QALY could be a gross over-estimate, or conceivably an under-estimate.1

5. The criticism of the Industry submission regarding their quoted body surface area needs more justification. What was the mean/median BSA in the TAX 237 (and SWOG 9916) reported? If it was 1.9 m^2, and not 1.7, then the statement might be justified, although North American men are generally larger than their UK counterparts. If there is good data that the mean BSA for the UK population of this age group is 1.9, this should be quoted, otherwise you are open to the suggestion of bias, inflating the economic costs of docetaxel.

6 The TAX 327 study did include a quality of life (QOL) assessment, using FACT-P. The study showed significant improvements in quality of life, but the study was not designed to measure this in QALYs. It seems harsh, therefore to assert that "an important omission from the current analysis is the lack of adjustment for the quality of life in this patient group…" It would have been more constructive to take the published QOL improvements, and if necessary refine the Industry economic analysis from that data, rather than starting again from a hypothetical standpoint.

Minor Comments

1. The WHO response criterion has been widely used for many years. The description of it as "an arbitrary percentage", while true, does not reflect the importance this has held over the years and is a bad choice of words (page 55)

2. While the indirect comparison of overall survival for D + P vs P has an upper 95% CI close to unity, the findings of the SWOG study do add weight qualitatively to the estimated improved HR, from a clinical point of view.

3. We are surprised that you are unable to make further recommendations for research. May we suggest:

    a. Further studies on the timing of docetaxel. The MRC-NCIC STAMPEDE study is now open, and will examine the benefits of docetaxel in patients starting long-term hormone therapy;
    b. Further studies on combination chemotherapy with docetaxel. Again, the ongoing MRC study will address this;
    c. Studies on patient selection – for example, it has been suggested that patients whose tumours express high levels of BCl-2 are more likely to repond to Docetaxel. This needs to be explored further (not least because it would further affect the economic evaluation).

Finally, may we ask whether patients groups are included among the list of consultees? Those, for example, linked to the NCRI study groups are well informed, and would have an important view on the conclusions of this HTA.

Malcolm Mason
Chairman
British Prostate Group *on behalf of the BPG*