



By email to:

[REDACTED]

From

[REDACTED]

24 April 2012

Dear [REDACTED]

Re: Denosumab for the treatment of bone metastases from solid tumours (ID 81) - ACD

The Royal College of Physicians (RCP) plays a leading role in the delivery of high quality patient care by setting standards of medical practice and promoting clinical excellence. We provide physicians in the United Kingdom and overseas with education, training and support throughout their careers. As an independent body representing over 26,000 Fellows and Members worldwide, we advise and work with government, the public, patients and other professions to improve health and healthcare.

I write on behalf of the NCRI/RCP/RCR/ACP/JCCO who are pleased to be consulted on this Appraisal Consultation Document (ACD). Many of our experts consider this to be a well-balanced document, particularly from a breast cancer viewpoint. However, our experts in prostate cancer have raised the following specific issues with the ACD.

(1) There is an error on page 5 which states:

'Prostate cancer: diagnosis and treatment' (NICE clinical guideline 58) recommends bisphosphonates in men with hormone-refractory prostate cancer to prevent bone metastases only when other treatments such as analgesics and palliative radiotherapy have failed.'

The NICE guideline recommended bisphosphonates to relieve pain (not to prevent bone mets) only when other treatments had failed. It would be more pertinent to quote the recommendation in the same guideline that zoledronate should not be used to prevent SREs.

(2) The Prostate cancer guideline recommendation was based on the view that zoledronate did not impact on either overall survival or quality of life, and that SREs were of uncertain clinical significance. Precisely the same considerations apply to denosumab. It has not been shown to improve either survival or quality of life, and so the case rests on whether or not SREs are clinically significant, and if so, whether the drug is cost-effective. Our view is that some SREs are definitely clinically significant (eg spinal cord compression) and that other SREs are not clinically significant (eg asymptomatic fractures detected only on routine imaging). Other SREs are of some significance (eg palliative EBRT). Our experts that one needs to look at the individual SREs rather than merely the composite in order to evaluate whether the drug effect is clinically significant.

(3) We believe that prostate cancer should be considered as a separate entity. It should not be assumed that bone mets from prostate behave and respond in the same way as bone mets from other cancers

(4) In the case of prostate cancer, based on the NICE guideline from 2008, the appropriate comparator should be best standard of care and not zoledronate.

(5) Our experts were struck that the evidence concerning denosumab for SRE prevention in prostate cancer is very similar indeed to the evidence concerning zoledronate. Given that NICE Prostate Cancer Guideline in 2008 recommended that zoledronate should not be used, our experts in prostate cancer would anticipate the same recommendation with regard to denosumab.

(6) Our experts in prostate cancer are concerned that NICE is to approve an expensive drug that does not improve survival or quality of life at the same time that it is rejecting drugs that they feel do improve both survival and quality of life in Castration-Resistant Prostate Cancer.

Yours sincerely

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