Single Technology Appraisal

Radium-223 dichloride for treating metastatic hormone relapsed prostate cancer with bone metastases [ID576] ERRATUM

Produced by: Aberdeen HTA Group

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Although the ERG accepts that ALSYMPCA provides the main evidence in this submission, it suggests that studies should have been included based on the inclusion criteria of the scope issued by NICE and not based on similarity to one of the trials in the review. The ERG notes that full results for the COU-AA-301 and COU-AA-302 trials have not been presented in the manufacturer's submission or considered in the cost-effectiveness analyses, even though they have met the search criteria for the review.

The ERG asked at clarification for a baseline characteristics table for the abiraterone COU-AA-301 and COU-AA-302 trials so that the manufacturer argument for not combining based on populations could be assessed. The ERG reproduced a baseline characteristics table from data supplied by the manufacturer at clarification for the abiraterone COU-AA-301 and COU-AA-302 trials in Appendix 1. The ERG agrees that an important difference in the populations between ALSYMPCA and COU-AA-301 relates to the differing proportion of patients with visceral disease and agrees that clinically the groups are different.

4.2.6 Summary and critique of effectiveness results

This section summarises the main findings as reported in the MS and clarification responses to ERG queries. Where possible, emphasis is placed on the final updated results from ALSYMPCA trial (cut-off July 2011).

Overall survival

ALSYMPCA

Overall survival (OS) was the primary endpoint in ALSYMPCA. Radium-223 dichloride significantly improved OS in mCRPC patients with bone metastases when compared with placebo. Median OS for patients receiving radium-223 dichloride [n=614] was 14.9 months versus median OS of 11.3 months in patients receiving placebo [n=307] (two-sided P=0.00007; HR=0.695; 95% CI, 0.581-0.832)(19).

BC1-02

OS was a secondary endpoint for the BC1-02 study. At 24-months follow-up, patients who had received radium-223 had an improved median overall survival of 65.3 weeks when compared with placebo patients (46.4 weeks) (log-rank P=.056). The hazard ratio (HR) for OS, adjusted for baseline prognostic covariates, was 0.476 (95% confidence interval [CI], 0.258-0.877; Cox regression P=0.017)[ITT analysis] (6). At this time, 10 (30%) patients were alive in the radium-223 dichloride group and 4 (13%) patients were alive in the placebo group. OS for the ALSYMPCA and BC1-02 is presented in Table 3.

Table 30 First SREs and all SREs

	Model:1st SRE		All SREs	
	Radium	**Placebo**	**Radium**	**Placebo**
External Beam Radiation	[redacted]	[redacted]	[redacted]	[redacted]
Pathologic Bone Fracture	[redacted]	[redacted]	[redacted]	[redacted]
Surgical Intervention	[redacted]	[redacted]	[redacted]	[redacted]
Spinal Cord Compression	[redacted]	[redacted]	[redacted]	[redacted]
Total	[redacted]	[redacted]	[redacted]	[redacted]

It can be argued that for a given SRE duration, taking into account the subsequent SREs would tend to increase the proportion of time subsequent to the incidence of the first SRE spent that would be spent with an SRE. This might make it more reasonable to assume that the first SRE has a lifetime HRQoL impact.

The total number of SREs was [redacted] higher than the number of first SREs in the radium-223 arm and was [redacted] higher in the placebo arm. This might suggest that the impact of subsequent SREs might be larger in the placebo arm than in the radium-223 arm. But this is highly speculative given the incomplete KM survival curves and the manufacturer acknowledged difficulties in recording SREs beyond the 6 month point.

The model differentiates the SRE proportions being experienced between the arms. This is based upon the first SRE experienced. Despite using the time to 1st SRE curve within the model, it could be argued that for costing purposes the balance between all SREs might be a better reflection of the average cost per SRE. It could also be argued that this might also affect the quality of life impacts, though this is more tenuous given assumptions around costs being up front while quality of life impacts are for the period from first SRE to death. Possible impacts upon costs and quality of life for first and all SREs are presented in Table 31 below.