SHTAC comments on NICE ACD: B&T for MM

| ACD section & text to which comment applies | SHTAC Comments | Other notes |
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| 4.1.4 IFM 01/01 study reported median progression-free survival of 24.1 months (95% confidence intervals [CI] 19.4 to 29.0) for the MPT group compared with 18.5 months (95% CI 0.39 to 0.66) for the MP group after a median follow up of 47.5 months. [….]. | The 95% CI values reported are those for the 99/06 PFS hazard ratio. The 95% CI that should have been reported is 95% CI 14.6 to 23.1 | |
| 4.1.5 […] The hazard ratio (HR) for overall survival from the meta-analysis was 0.62 (95% CI 0.50 to 0.77) and showed that there was little or no heterogeneity between the three trials for this outcome. | Only two trials included in this meta-analysis. | |
| 4.1.6 [….] Complete response outcomes from the three studies were combined by meta-analysis, and this confirmed that MPT was superior to MP in terms of the proportion of patients achieving a complete response (relative risk [RR] 5.49, 95% CI 2.55 to 11.38). | Value should be 11.83. | The incorrect value of 11.38 came from the text of the Assessment Group report, which has now been amended. Value in the accompanying Figure 3 is correct. |
| 4.1.7 [….] For thrombosis or embolism, somnolence, constipation and infections, the results were inconsistent between IFM 99/06 and IFM 01/01, with no significant difference in incidence in the IFM 01/01 study and statistically significantly more of these events in the MPT group in the IFM 99/06 study. This inconsistency may be a result of the different methods of reporting adverse events. | The statement on incidence is not true with regard to infections. There was no statistically significant difference in the number of patients with infections of grade 3 and 4 (p=0.32) in the IFM 99/06 study. There was no detailed reporting on infections for the IFM 01/01 study. | |
| 4.1.9 The Assessment Group identified one ongoing RCT, the UK Multiple Myeloma IX (MMIX) trial, which compared CTDa with MP. [….] | More than one ongoing RCT was identified by the Assessment Group – although the Assessment Group only had sufficient information on one, MMIX, enabling its inclusion in the report. Suggest text is changed to 'The Assessment Group identified an ongoing RCT, the UK Multiple Myeloma IX (MMIX) trial, which compared CTDa with MP.' | |
| 4.1.12 [….] Most, but not all analyses had followed the intention-to-treat but the methods used to account for any missing data were not described. | Suggest alter wording<br>Most, but not all analyses had followed intention-to-treat principles but the methods used to account for any missing data were not described. | |

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| 4.1.13 [….] More recently reported 3-year survival rates after a median follow-up of 36.7 months are 68.5% versus 54% respectively. A median overall survival of 43.1 months for participants receiving MP; it was not possible to estimate overall survival in the group receiving VMP.[….] | Rather confused sentence, needs amending. | |
| 4.1.13 [….] Median progression-free survival was 21.7 months for the VMP group compared with 15.2 months for the group receiving MP (HR 0.56, p < 0.001). [….] | For clarity, we suggest text is added to indicate this was after a median follow up of 16.3 months. | |
| 4.1.17 […] Three studies (IFM 99/06, IFM 01/01 and GIMEMA) provided evidence of a complete response in a statistically significantly greater proportion of participants receiving MPT (RR 5.49, 95% CI 2.155 to 11.38). [….] | Errors in the values provided:<br>(RR 5.49, 95% CI 2.55 to 11.83) | As noted before 11.38 was an error in the Assessment Group report. |
| 4.1.19 | Omits time to disease progression which was the primary outcome of the VISTA trial. | |
| 4.2.18 VMP compared with MPT associated with ICER of £28,907 per QALY gained. | This should read: VMP compared with CTDa associated with ICER of £28,907 per QALY gained. | |
| 4.2.22 The manufacturer of thalidomide conducted a mixed-treatment comparison for MPT versus MP with trials that included thalidomide maintenance. | This is incorrect and should be the manufacturer of bortezomib. | |
| 4.3.8 The Committee noted the differences in the ICERs presented by the Assessment Group and the manufacturer of bortezomib for VMP compared with MP. Apart from the fewer vials of bortezomib assumed by the manufacturer, which the Committee accepted, the manufacturer of bortezomib model also included costs for second-and third-line treatments. This included adding the cost of thalidomide to the bortezomib regimen, and of bortezomib to the thalidomide regimen, neutralising the approximately four-fold cost advantage of thalidomide, and greatly increasing the cost of MP. | As paragraph 4.3.8 currently reads it could be misinterpreted – the reader might believe that the Assessment Group omitted costs of second- and third-line treatment. In fact, the assessment group included costs for second-line therapy. Only the manufacturer of thalidomide did not include costs for second- and third-line treatments. | |