Bortezomib for induction therapy in multiple myeloma before high dose chemotherapy and autologous stem-cell transplantation

ERG overview of manufacturer's response to the ACD – exploratory analyses

Produced by Southampton Health Technology Assessments Centre (SHTAC)

Authors Keith Cooper, Debbie Hartwell, Jackie Bryant

Date completed 17th January 2014

VTD vs. TD analysis

The ERG noted that the manufacturer's analysis of VTD vs. TD provided a poor fit for overall survival compared to the observed data in the Pethema trial. Figure 1 shows the OS for the manufacturer's base case analysis compared to the observed OS from the Pethema trial. The manufacturer provided sensitivity analyses using alternative data sources and parametric curves to model OS (Table 8 of manufacturer's response to the ACD). Figures 2 and 3 show the OS from the Pethema trial compared to the economic model analyses for two of these sensitivity analyses (Long term OS data from Alvares and NMSG 5/94). The ERG considers that these sensitivity analyses show a better fit for OS than the base case analysis (using long term OS data from MRC Myeloma VII). The ICERs using long term OS data from Alvares and NMSG 5/94 are £22,696 and £39,618 per QALY respectively compared to the manufacturer's base case (using long term OS data from MRC Myeloma VII) of £17,841 per QALY.

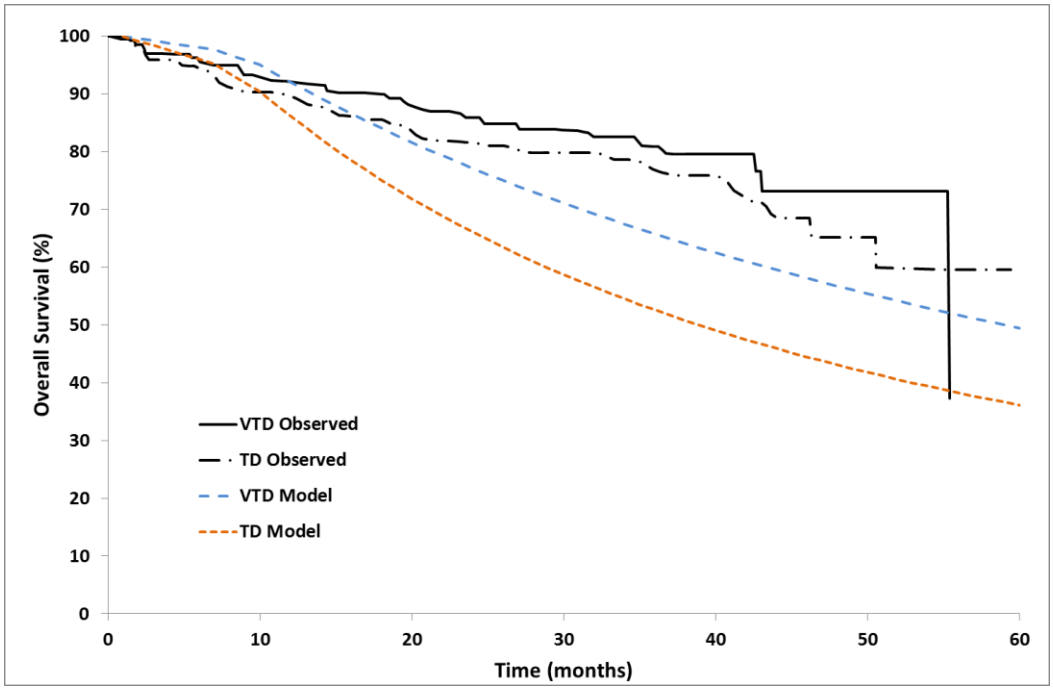

Figure 1: Comparison of OS observed in the Pethema trial and predicted by manufacturer's model for the base case analysis (using data for long term OS data from MRC Myeloma VII)

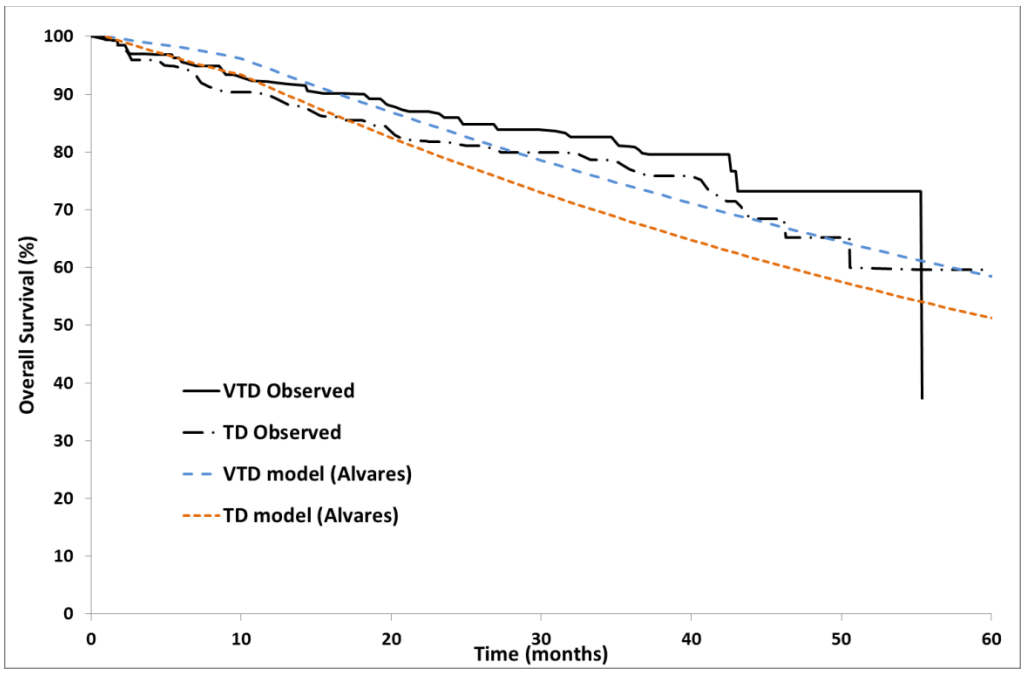

Figure 2: Comparison of OS observed in the Pethema trial and predicted by manufacturer's model using data from long term OS data from Alvares

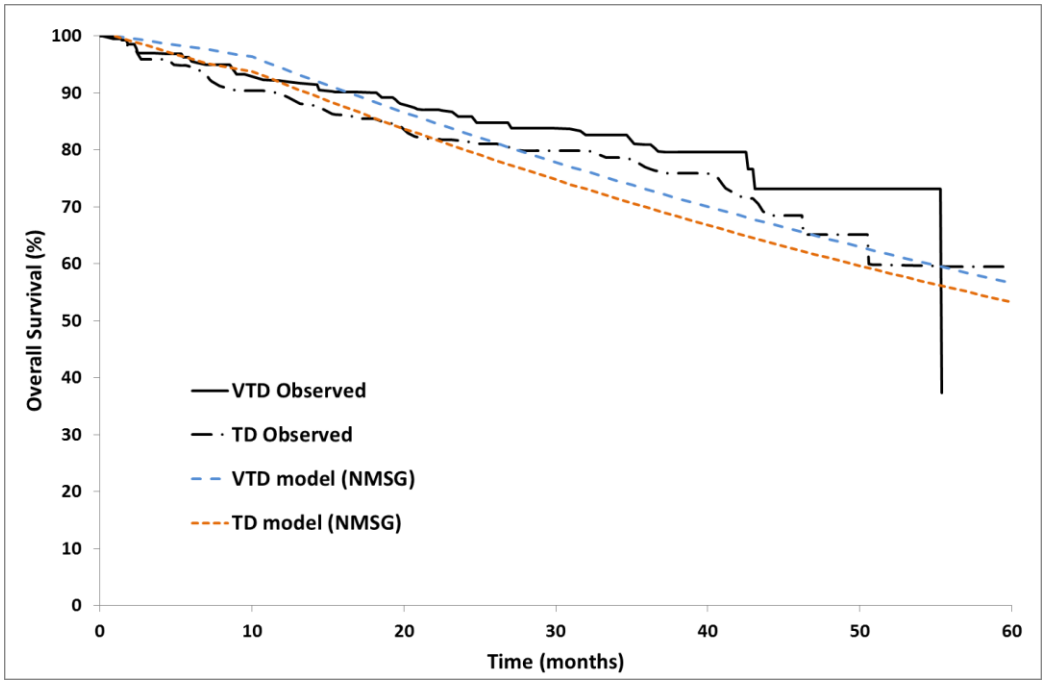

Figure 3: Comparison of OS observed in the Pethema trial and predicted by manufacturer's model using data from long term OS data from NMSG

VD vs. CTD analysis

The ERG noted that SCT rates for the analysis are taken from the respective trials for the treatment arms of VD vs. CTD. The SCT rate for CTD is 67% (MRC Myeloma IX) and 89% for VD (IFM 2005). Assuming a much lower SCT for CTD is inconsistent with the response data and provides a substantial bias to the VD cohort.

The ERG has re-run the manufacturer's model for the analysis of VD vs. CTD assuming the SCT rate for the treatment arm of CTD was similar to the IFM comparator arm (i.e. VAD). This analysis is shown in Table 1, together with results from the manufacturer's analysis and the sensitivity analysis conducted by the ERG previously. The ICER for VD vs. CTD increases to £36,712 per QALY gained when CTD treatment arms have an SCT rate of 82.6% (as seen for VAD in IFM trial).

Table 1: Sensitivity analysis for VD vs. CTD with alternative values for the SCT rates

Analysis	SCT rate VD, %	SCT rate CTD, %	ICER (£/QALY)
MS analysis	89.1%	66.7%	£20,588
Equal SCT rate for VD and CTD	89.1%	89.1%	£73,025
CTD SCT rate as for IFM arm (VAD)	89.1%	82.6%	£36,712

VD vs. VAD analysis

The ERG noted that the manufacturer's analysis of VD vs. VAD provided a poor fit for overall survival compared to the observed data in the IFM trial. Figure 4 shows the OS for the manufacturer's base case analysis compared to the observed OS from the IFM trial. The manufacturer provided sensitivity analyses using alternative data sources and parametric curves to model OS (Table 19 of manufacturer's response to the ACD). Figure 5 and 6 show the OS from the IFM trial compared to the economic model analyses for two of these sensitivity analyses (Long term OS data from Alvares and NMSG 5/94). The ERG considers that these sensitivity analyses show a better fit for OS than the base case analysis (using long term OS data from MRC Myeloma VII). The ICERs using long term OS data from Alvares and NMSG 5/94 are £25,575 and £42,811 per QALY respectively compared to the manufacturer's base case (using long term OS data from MRC Myeloma VII) of £18,914 per QALY.

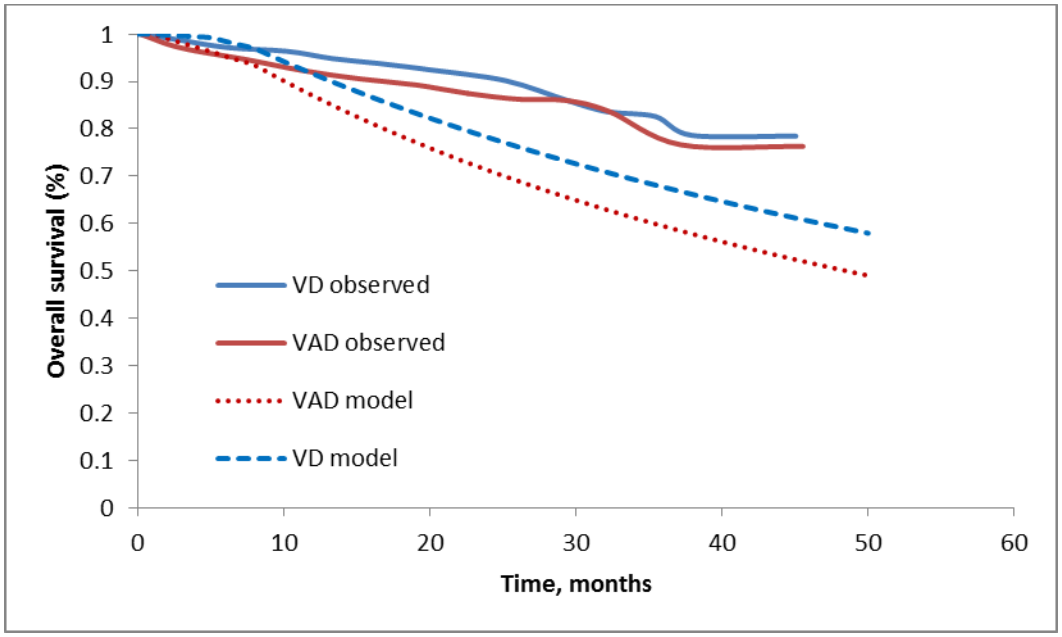

Figure 4: Comparison of OS observed in the IFM trial and predicted by manufacturer's model for base case analysis (using data from long term OS data from MRC Myeloma VII trial)

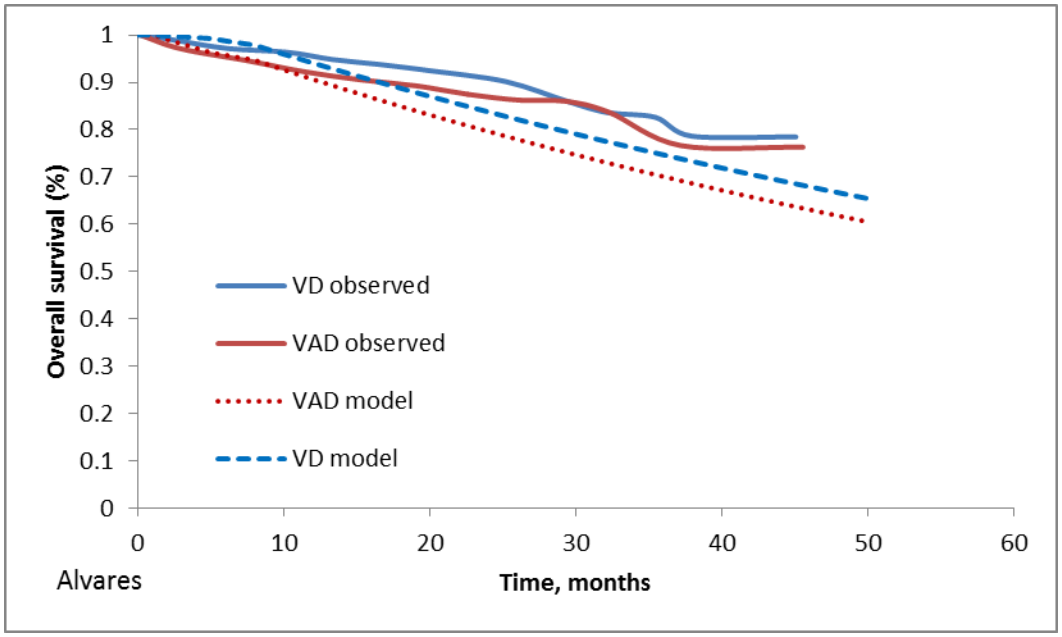

Figure 5: Comparison of OS observed in the IFM trial and predicted by manufacturer's model using data from long term OS data from Alvares

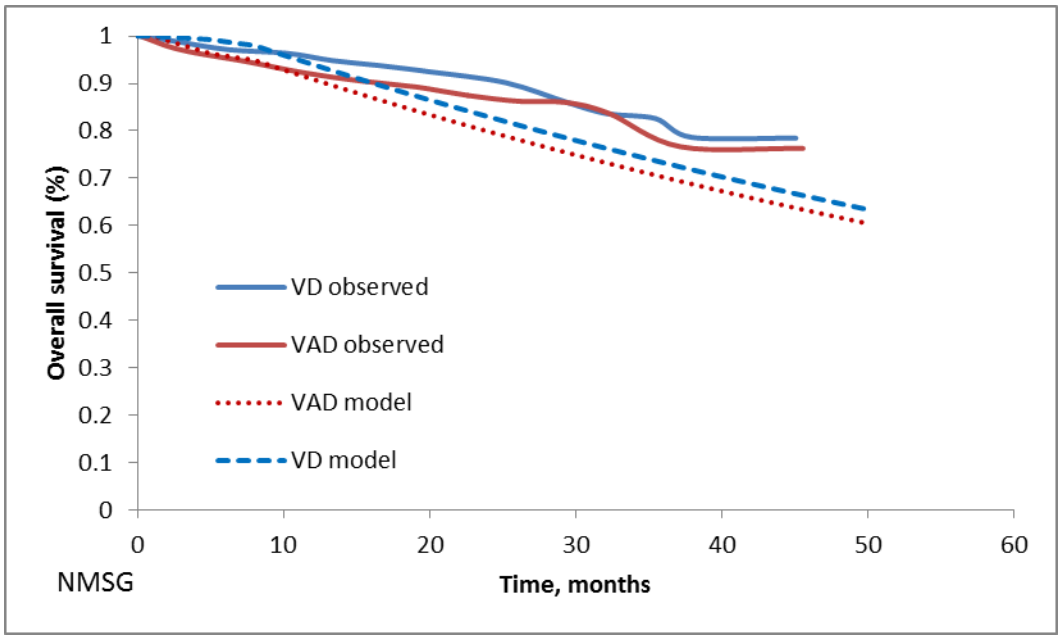

Figure 6: Comparison of OS observed in the IFM trial and predicted by manufacturer's model using data from long term OS data from NMSG