DSU Report for NICE – Azacitidine STA Economic Model

The DSU have been asked to undertake two tasks with respect to the economic model for the Azazcitidine STA. Specifically, the DSU were requested to:

1. Compare the incremental cost-effectiveness ratios (ICERs) as reported in the document from Celegene (dated October 7th 2009, tables 1.1-1.4 inclusive) with the latest economic model.

2. Assess the construction and implementation of the survival analysis in the economic model.

Task 1

All the (deterministic) ICERs in tables 1.1-1.4 were cross-referenced with the excel-based economic model. In all instances, the results relating to patients pre-selected for BSC were identical to those contained in the spreadsheet. The results for those pre-selected for SDC matched those in the spreadsheet in 3 of the 4 tables (not in table 1.1). The results in the tables for patients pre-selected with LDC did not match with those in the spreadsheet in any instance. However, in all instances where differences between ICERs were noted, they were arguably very minor (± £200 at the most).

Task 2

Patient survival is modelled in the economic evaluation in a number of different ways; specifically there is an option to choose between different methods of extrapolation in terms of fitting different forms of survival curve (e.g. exponential, weibull, log-logistic etc). The first step in terms of assessing whether this had been included appropriately was to replicate the survival curves, as reported in the 'Azacitidine Survival' worksheet using the reported MLE-derived parameters (eg. alpha and beta for the Weibull). In all instances, the survival curves could be replicated for the deterministic results. Focus then turned to the series of 'Flow' worksheets, which essentially contain / calculate appropriate transition probabilities from the MLE-derived parameters for each of the distributional forms. An error was noted for columns N-0 (representing the transition probabilities for the exponential, gompertz, lognormal functions respectively) which culminated in an erroneous

(strange) transition probability in the final cycle. The most likely explanation for this is that the relevant hazard function is being calculated by looking forward one cycle, rather than looking back one cycle (this is true for all cycles). Meaning that in the final cycle, no survival estimate exists. However, given the role of discounting and the fact that a very small proportion of patients are alive at this stage, this error is likely to have a negligible effect on the results.

As noted by the Leeds TAG, the lognormal and gompertz survival functions are identical for the BSC and LDC groups (in the non-Azacitidine treatment arms) meaning that some of the subgroup results will not be right when either lognormal- or gompertz-based results are reported. In effect, survival curves for the BSC and LDC subgroups are being calculated using a common parameter set whether a lognormal or gompertz function is chosen. However, it isn't immediately obvious from the spreadsheet which parameter set matches to which subgroup, so it is difficult to have confidence in any proposed fix, without conversations with the original authors.

The above commentary relates to the deterministic results. The model also contains the option to undertake probabilistic sensitivity analysis (PSA). However, as currently programmed, the option doesn't work – and literally produces error messages in relevant cells. Investigation suggests that this is not to do with the sampling methods employed in the model, but rather a structural problem with the way transition probabilities are calculated given these samples and the knock on effect in terms of calculating expected costs and benefits per sample. More specifically, while the model considers a total time horizon of 9,485 days, in some circumstances, patients will die before this point is reached (eg. say in day 10 the calculated probability of death is 1). In day 11, the model returns an error message rather than presumably calculating a probability of greater than 1 (which would also be incorrect) or 0 (which would be more sensible). The fix for this error is not complicated, but could be time consuming given the amount of syntax.

Alec Miners for the DSU; October 29th 2009