27 November 2009

Jeremy Powell
Technology Appraisal Project Manager
National Institute for Health and Clinical Excellence
MidCity Place
71 High Holborn
London
WC1V 6NA

Dear Mr Powell,

Azacitidine for the treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukaemia (CMML) and acute myeloid leukaemia (AML)

Thank you for forwarding the two individual requests for clarification relating to the single technology appraisal of azacitidine from the Decision Support Unit (DSU) and the Appraisal Committee.

Celgene would like to provide responses to both requests which are detailed in separate sections within this document.

Part A: Decision Support Unit clarification request
Celgene would like to thank the DSU for identifying these concerns with respect to the survival modelling and we are pleased to provide a response to each of the clarification points as requested.

We would like to highlight that these concerns within this clarification request have either no or minimal impact on the cost-effectiveness results previously presented for azacitidine. In order to provide reassurance to the Institute with respect to this, we have provided a revised electronic economic model and base-case analyses.

Part B: Appraisal Committee clarification request
Celgene are pleased to provide a response to each of the clarification points as requested by the Appraisal Committee.

Please do not hesitate to contact me if you require any further information.

Yours sincerely,

Part A: Decision Support Unit Clarification Points

1. The log-normal parameters (μ,σ) in the model are identical for both the BSC and LDC CCR sub-groups, despite the fact that observed survival between the two groups differs. The same is true for the Gompertz survival functions. In effect, the model calculates survival curves for the BSC and LDC CCR sub-groups using a common parameter set when the log-normal and Gompertz survival functions are chosen. Please correct this or provide justification for the use of common parameter sets.

- This is correct; the survival function parameters for low-dose chemotherapy (LDC) were identical to those for the best supportive care (BSC) subgroup. The parameters have been updated for the LDC survival analysis for both log-normal and Gompertz survival functions in the economic model. The corrected parameters are presented in Table A1.

Table A1. Log-normal and Gompertz survival parameters

Subgroup	Log-normal		Gompertz	
	μ	*σ*	*μ*	*σ*
Best-supportive care (CCR)	2.383	1.146	-2.759	-0.007
Low-dose chemotherapy (CCR)	2.447	1.189	-3.068	0.024

Key: CCR: conventional care regimen

2. Errors in the calculation of transitional probabilities affect both the deterministic and probabilistic analyses:

a. Calculations of the transitional probabilities contain errors for the exponential, lognormal and Gompertz functional forms (columns M-0 in each of the "Flow" sheets). These errors result in an illogical probability for the final cycle (Row 278). It is suspected that the relevant probability is being calculated by looking forward one cycle, rather than looking back. As a result, no legitimate estimates exist for the final cycle. Please correct this.

- This has been corrected. The survival functions have been amended so that the period survival is calculated by looking back one cycle rather than forwards. Legitimate values now exist in the final cycle of the transition probabilities.

b. Sampling errors occur within the probabilistic sensitivity analyses. As currently programmed, the model does not produce estimates of mean cost and effect for all simulations in the PSA. This can be seen in two ways.

i) In the model options, select Weibull for the survival curve for all treatments. Run a new PSA. You will note that in the PSA output sheets, there are numerous simulations that do not yield results. The relevant cells return error messages (#div/0!).

- This has been corrected. The #div/0! error messages occur in the tail of the distributions, where all the cohort has suffered mortality, and therefore the survival calculation was dividing by zero. The formulas in the patient flow sheets have been amended so that these situations are handled by the model and a probabilistic sensitivity analysis (PSA) can be run for each of the survival curves.

ii) Turn the PSA option on in the model controls (option 1c) and look at the transition probabilities in the flow sheets (e.g., AZA SDC flow sheet, columns K to 0, rows 278 upwards). Pressing f9 to sample values will show that some samples yield errors in the calculated probabilities once the probability reaches 1. This is apparent for several of the possible survival functions.

This has been corrected. These errors were due to the same reason described in the answer to question *b(i)*. The model programming has been amended to handle these situations.

3. Please provide an explanation for why the ICERs generated by the model do not match those in the written response to clarification (for all LDC pre-selected subgroups and the SDC pre-selected subgroup in Table 1.1; response dated 7 Oct 2009).

- The incremental cost-effectiveness ratios (ICERs) generated by the economic model and those in the written response to the clarification request (dated 7 October 2009) differ because the Celgene response to the clarification was provided as two partial responses at different time points. The first response provided answers to the entire clarification request except question 1, part v, which related to the incorporation of the Düsseldorf MDS Registry data and subsequent survival analyses.

- The response question 1, part v, was provided thereafter with a revised economic model, thus allowing the necessary time for the inclusion of the registry data into the economic model. Additionally, the revised model included two new functions: a function for the Patient Access Scheme and a function related to the clarification request regarding weekend administration costs of azacitidine. In the primary response, weekend administration costs were calculated and inserted as a figure in the model. Subsequently, this value was automated in the revised model (Cell BO17 in the 'Unit Costs' tab of the input sheet), which resulted in a non-rounded calculation of this figure. The differences in the ICERs are therefore due to the rounding of the weekend administration costs and a clarification response which was provided at two different time points.

4. Please demonstrate that the results of the deterministic and probabilistic analyses agree with one another, noting the number of Monte Carlo simulations required.

- The results of the deterministic and probabilistic analyses are shown in Table A2. These results were generated using 5,000 Monte Carlo simulations.

Table A2. Deterministic and probabilistic analyses

Comparator	Marginal costs incurred	Marginal QALYs gained	Incremental cost per QALY gained
Best supportive care			
Deterministic analyses	£79,623	1.68	£47,432
Probabilistic analyses	£75,739	1.68	£44,968
Low-dose chemotherapy			
Deterministic analyses	£74,485	1.83	£40,754
Probabilistic analyses	£69,480	1.70	£40,851
Standard-dose chemotherapy			
Deterministic analyses	£68,314	1.84	£37,105
Probabilistic analyses	£62,398	1.91	£32,600

Key: QALY: quality-adjusted life-year

Base-case cost-effectiveness results:

- Celgene would like to highlight that these concerns within this clarification request have either no or minimal impact on the cost-effectiveness results previously presented for azacitidine. In order to provide reassurance to the Institute with respect to this, we have provided a revised electronic economic model and base-case analyses. No revised sensitivity analyses have been provided due to the minimal impact of the amendments on these analyses.

- The cost-effectiveness results are shown for the base-case parameters in Table A3. Two scenarios are presented. The first assumes that, as at present, the 100 mg vial is available and there is no patient pooling on common treatment days to allow vial sharing. The second scenario assumes that 49% of treated patients are pooled to reduce the amount of unused medication. Results are presented in Table A4 examining the effect of implementing the Patient Access Scheme and applying a 7% discount to the acquisition cost of azacitidine.

Table A3. Summary of base-case cost-effectiveness results

Treatment option	Costs incurred	QALYs gained	Marginal costs [inc. vial sharing]	Marginal QALYs gained	Incremental cost per QALY gained	
					No vial sharing	Vial Sharing
Preselected for BSC						
Azacitidine	£114,289	2.97	£79,623 [£74,601]	1.68	£47,432	£44,400
BSC	£34,665	1.30				
Preselected for low-dose chemotherapy						
Azacitidine	£121,319	3.24	£74,485 [£69,323]	1.83	£40,754	£37,929
LDC	£46,834	1.41				
Preselected for standard-dose chemotherapy						
Azacitidine	£114,996	2.90	£68,314 [£63,271]	1.84	£37,105	£34,366
SDC	£46,682	1.06				

Key: BSC: best supportive care; LDC: low-dose chemotherapy; QALY: quality-adjusted life-year; SDC: standard-dose chemotherapy

Table A4. Summary of base-case cost-effectiveness results including the proposed Patient Access Scheme and applying a 7% discount to the acquisition cost of azacitidine

Treatment option	Costs incurred	QALYs gained	Marginal costs [inc. vial sharing]	Marginal QALYs gained	Incremental cost per QALY gained	
					No vial sharing	Vial Sharing
Preselected for BSC						
Azacitidine	£111,109	2.97	£76,443 [£71,772]	1.68	£45,538	£42,756
BSC	£34,665	1.30				
Preselected for low-dose chemotherapy						
Azacitidine	£118,051	3.24	£71,217 [£66,416]	1.83	£38,966	£36,339
LDC	£46,834	1.41				
Preselected for standard-dose chemotherapy						
Azacitidine	£111,803	2.90	£65,122 [£60,432]	1.84	£35,371	£32,823
SDC	£46,682	1.06				

Key: BSC: best supportive care; LDC: low-dose chemotherapy; QALY: quality-adjusted life-year; SDC: standard-dose chemotherapy

Part B: Appraisal Committee Clarification Points

1. Your response to the ACD states that the exponential function for the survival curve provides the best fit to the majority of the treatment arm data (azacitidine (pre-selected for BSC) and azacitidine (pre-selected for SDC)) and the lognormal function provides the best fit to the majority of the comparative care regimen data (BSC and SDC). Please provide the following analyses (all of which are to include the adjustment for age-dependent mortality) and the concomitant range of ICERs:

i. Estimating overall survival by using the Weibull function to model the survival of both patients receiving azacitidine and those receiving the comparative care regimens.

- This analysis has been performed as requested. The observed survival and fitted age-adjusted Weibull curves for each comparison between azacitidine and the comparative care regimes (best supportive care [BSC], low-dose chemotherapy [LDC] and standard-dose chemotherapy [SDC]) are presented in Figures B1.1 to B1.3. The cost-effectiveness results of the analyses are presented in Table B1.1 for scenarios assuming either no vial sharing or vial sharing, with or without the Patient Access Scheme.

Figure B1.1. Observed survival data from Study AZA-001 and a fitted age-adjusted Weibull curve for azacitidine patients preselected for BSC and patients treated with BSC alone

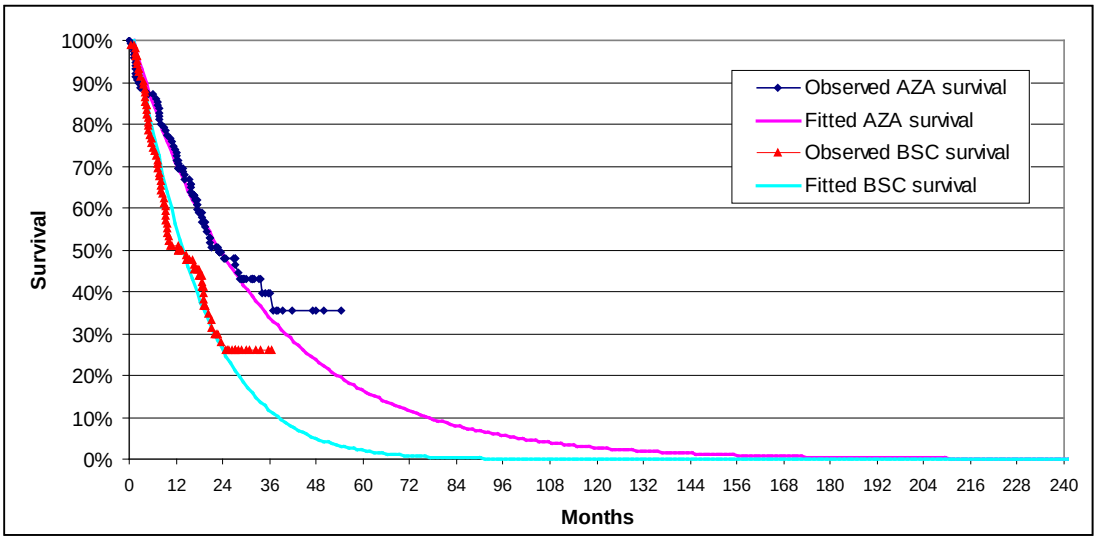

Figure B1.2. Observed survival data from Study AZA-001 and a fitted age-adjusted Weibull curve for azacitidine patients preselected for LDC and LDC-treated patients

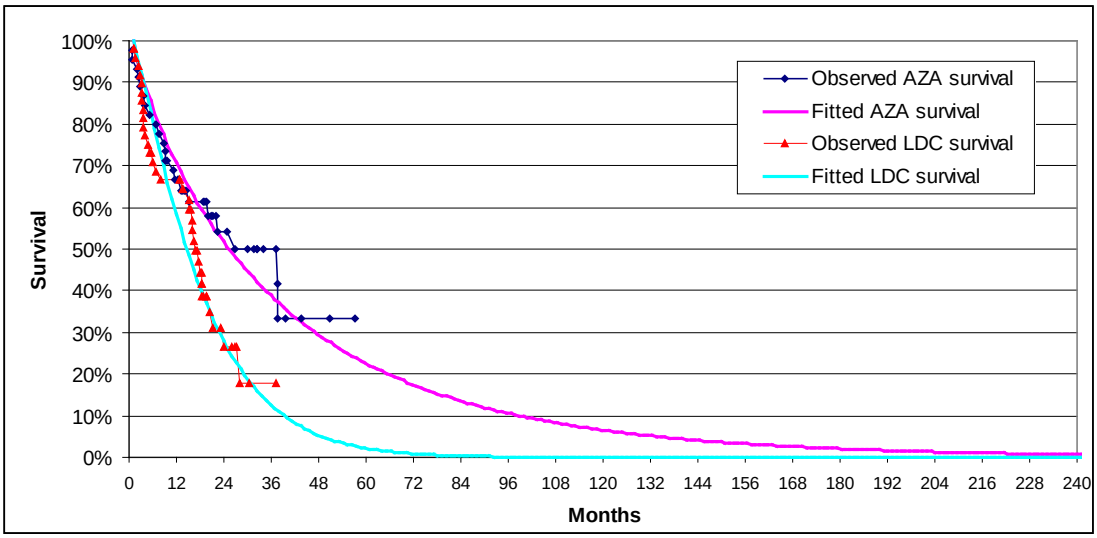

Figure B1.3. Observed survival data from Study AZA-001 and a fitted age-adjusted Weibull curve for azacitidine patients preselected for SDC and SDC-treated patients

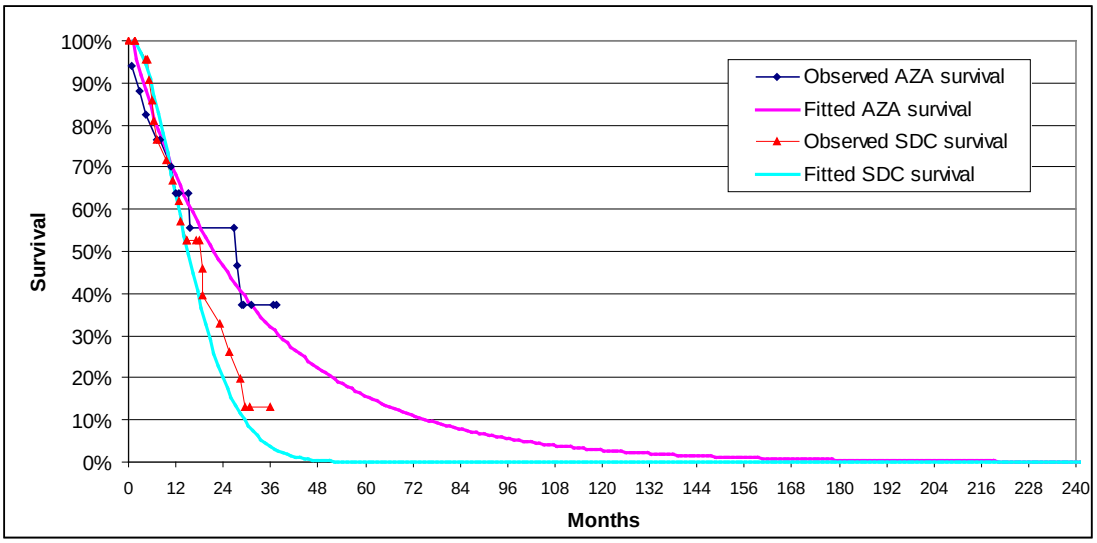

Table B1.1. Summary of cost-effectiveness results using an age-adjusted Weibull curve for the survival extrapolation of azacitidine

Treatment option	Life-years	Costs incurred	QALYs gained	Marginal costs (vs azacitidine)	Life-years gained on azacitidine	Marginal QALYs (vs azacitidine)	Incremental cost per QALY (vs azacitidine)
Preselected for BSC							
No vial sharing							
Azacitidine	2.69	£94,934	2.04	£66,937	1.19	1.01	**£66,329**
BSC	1.50	£27,998	1.03				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	2.69	£91,753	2.04	£63,756	1.19	1.01	**£63,177**
BSC	1.50	£27,998	1.03				
Vial sharing							
Azacitidine	2.69	£89,910	2.04	£61,912	1.19	1.01	**£61,350**
BSC	1.50	£27,998	1.03				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**2.69**	**£87,080**	**2.04**	**£59,083**	**1.19**	**1.01**	**£58,547**
BSC	**1.50**	**£27,998**	**1.03**				
Preselected for LDC							
No vial sharing							
Azacitidine	3.18	£104,625	2.44	£68,941	1.62	1.34	**£51,471**
LDC	1.56	£35,684	1.10				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	3.18	£101,355	2.44	£65,671	1.62	1.34	**£49,030**
LDC	1.56	£35,684	1.10				
Vial sharing							
Azacitidine	3.18	£99,460	2.44	£63,777	1.62	1.34	**£47,615**
LDC	1.56	£35,684	1.10				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**3.18**	**£96,552**	**2.44**	**£60,868**	**1.62**	**1.34**	**£45,444**
LDC	**1.56**	**£35,684**	**1.10**				
Preselected for SDC							
No vial sharing							
Azacitidine	2.60	£94,747	1.91	£50,687	1.21	0.93	**£54,719**
SDC	1.39	£44,060	0.98				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	2.60	£91,534	1.91	£47,475	1.21	0.93	**£51,252**
SDC	1.39	£44,060	0.98				
Vial sharing							
Azacitidine	2.60	£89,673	1.91	£45,613	1.21	0.93	**£49,242**
SDC	1.39	£44,060	0.98				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**2.60**	**£86,816**	**1.91**	**£42,756**	**1.21**	**0.93**	**£46,158**
SDC	**1.39**	**£44,060**	**0.98**				

Key: BSC: best supportive care; LDC: low-dose chemotherapy; QALY: quality-adjusted life-year; SDC: standard-dose chemotherapy

ii. Estimating overall survival by using the exponential function to model the survival of both patients receiving azacitidine and those receiving the comparative care regimens.

- This analysis has been performed as requested. The observed survival and fitted age-adjusted exponential curves for each comparison between azacitidine and the comparative care regimes are presented in Figures B1.4 to B1.6. The cost-effectiveness results of the analyses are presented in

Table B1.2 for scenarios assuming either no vial sharing or vial sharing, with or without the Patient Access Scheme.

Figure B1.4. Observed survival data from Study AZA-001 and a fitted age-adjusted exponential curve for azacitidine patients preselected for BSC and patients treated with BSC alone

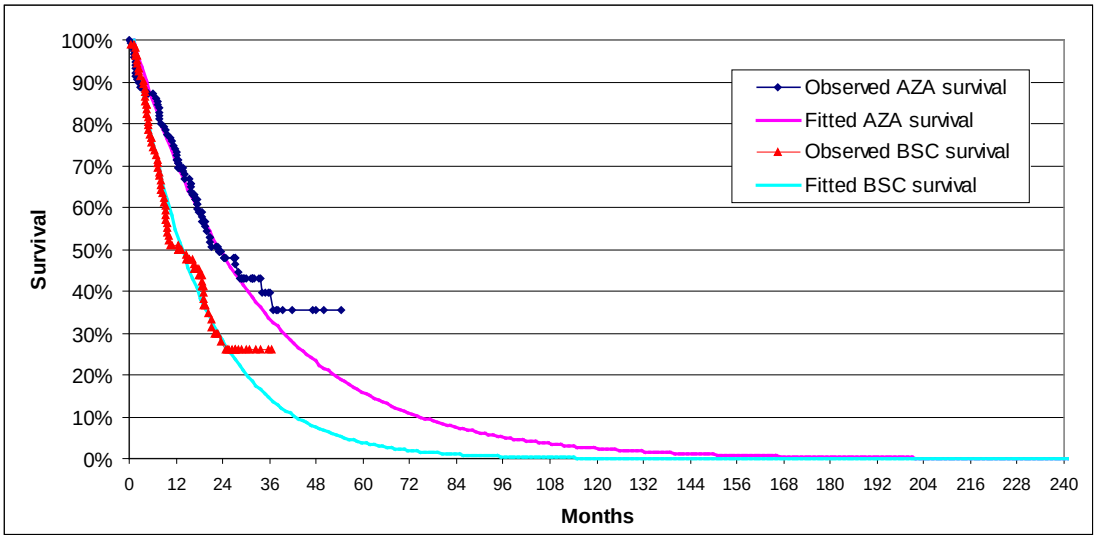

Figure B1.5. Observed survival data from Study AZA-001 and a fitted age-adjusted exponential curve for azacitidine patients preselected for LDC and LDC-treated patients

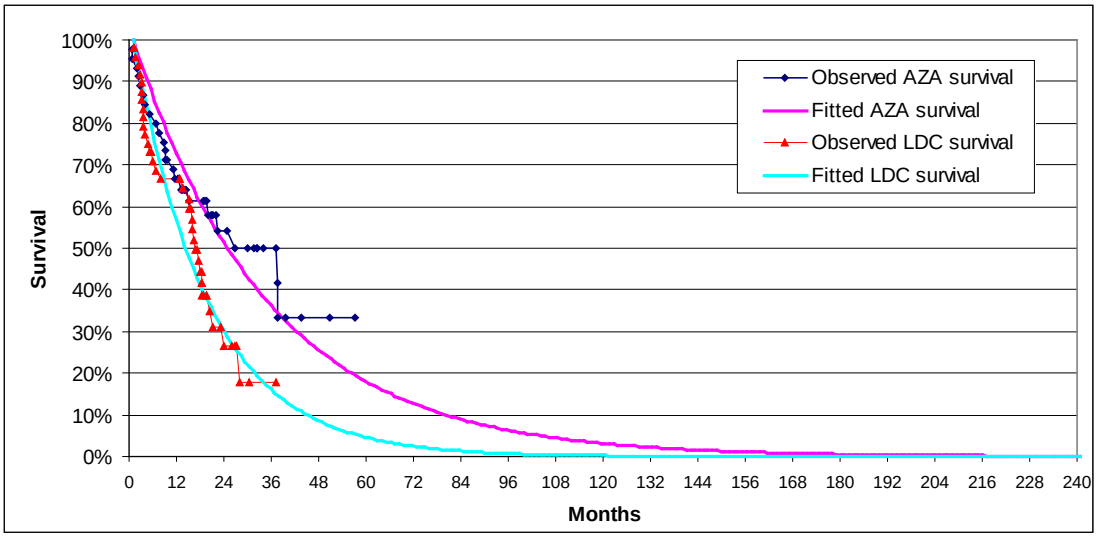

Figure B1.6. Observed survival data from Study AZA-001 and a fitted age-adjusted exponential curve for azacitidine patients preselected for SDC and SDC-treated patients

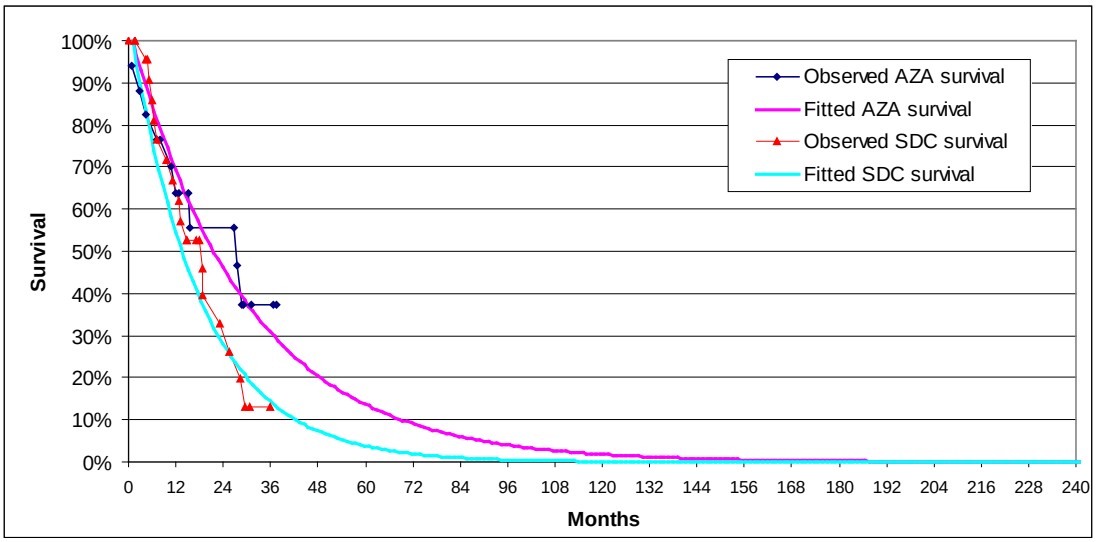

Table B1.2. Summary of cost-effectiveness results using an age-adjusted exponential curve for the survival extrapolation of azacitidine

Treatment option	Life-years	Costs incurred	QALYs gained	Marginal costs (vs azacitidine)	Life-years gained on azacitidine	Marginal QALYs (vs azacitidine)	Incremental cost per QALY (vs azacitidine)
Preselected for BSC							
No vial sharing							
Azacitidine	2.66	£94,379	2.01	£64,813	1.07	0.92	**£70,674**
BSC	1.58	£29,566	1.10				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	2.66	£91,195	2.01	£61,629	1.07	0.92	**£67,203**
BSC	1.58	£29,566	1.10				
Vial sharing							
Azacitidine	2.66	£89,350	2.01	£59,785	1.07	0.92	**£65,191**
BSC	1.58	£29,566	1.10				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**2.66**	**£86,519**	**2.01**	**£56,953**	**1.07**	**0.92**	**£62,103**
BSC	**1.58**	**£29,566**	**1.10**				
Preselected for LDC							
No vial sharing							
Azacitidine	2.83	£99,186	2.15	£60,846	1.16	0.99	**£61,759**
LDC	1.67	£38,341	1.17				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	2.83	£95,895	2.15	£57,554	1.16	0.99	**£58,418**
LDC	1.67	£38,341	1.17				
Vial sharing							
Azacitidine	2.83	£93,987	2.15	£55,646	1.16	0.99	**£56,481**
LDC	1.67	£38,341	1.17				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**2.83**	**£91,059**	**2.15**	**£52,718**	**1.16**	**0.99**	**£53,510**
LDC	**1.67**	**£38,341**	**1.17**				
Preselected for SDC							
No vial sharing							
Azacitidine	2.48	£92,912	1.81	£42,642	0.90	0.66	**£65,019**
SDC	1.57	£50,271	1.15				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	2.48	£89,685	1.81	£39,414	0.90	0.66	**£60,097**
SDC	1.57	£50,271	1.15				
Vial sharing							
Azacitidine	2.48	£87,815	1.81	£37,544	0.90	0.66	**£57,246**
SDC	1.57	£50,271	1.15				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**2.48**	**£84,944**	**1.81**	**£34,673**	**0.90**	**0.66**	**£52,869**
SDC	**1.57**	**£50,271**	**1.15**				

Key: BSC: best supportive care; LDC: low-dose chemotherapy; QALY: quality-adjusted life-year; SDC: standard-dose chemotherapy

iii. Estimating overall survival by using the lognormal function to model the survival of both patients receiving azacitidine and those receiving the comparative care regimens.

- This analysis has been performed as requested. The observed survival and fitted age-adjusted log-normal curves for each comparison between azacitidine and the comparative care regimes are presented in Figures B1.7 to B1.9. The cost-effectiveness results of the analyses are presented in Table B1.3 for scenarios assuming either no vial sharing or vial sharing, with or without the Patient Access Scheme.

Figure B1.7. Observed survival data from Study AZA-001 and a fitted age-adjusted log-normal curve for azacitidine patients preselected for BSC and patients treated with BSC alone

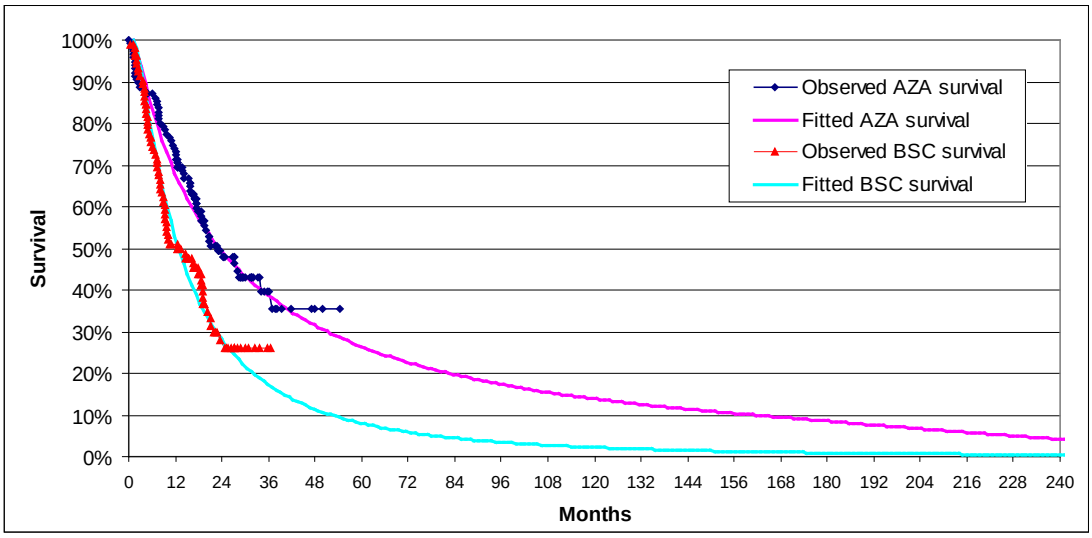

Figure B1.8. Observed survival data from Study AZA-001 and a fitted age-adjusted log-normal curve for azacitidine patients preselected for LDC and LDC-treated patients

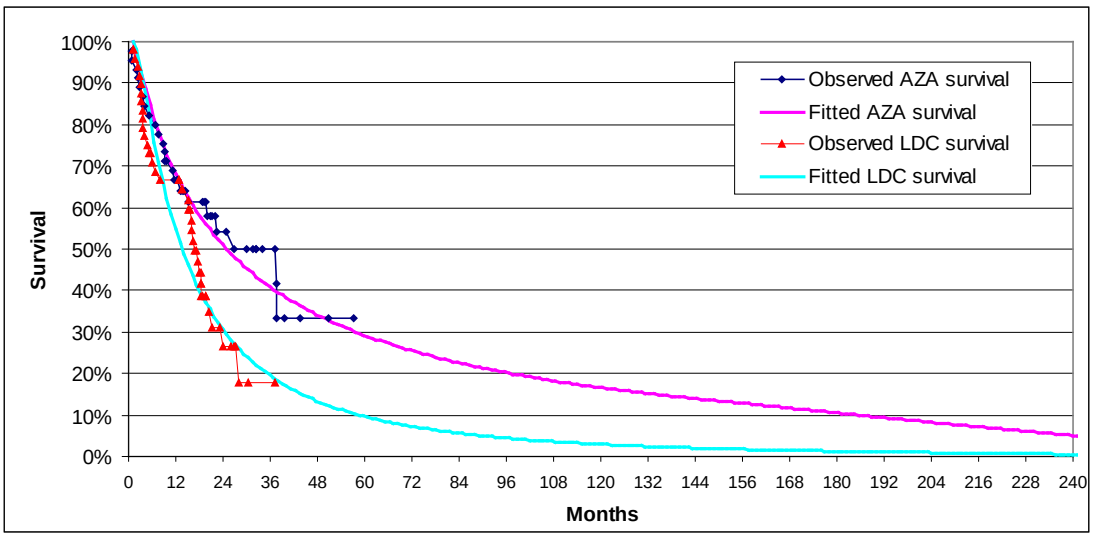

Figure B1.9. Observed survival data from Study AZA-001 and a fitted age-adjusted log-normal curve for azacitidine patients preselected for SDC and SDC-treated patients

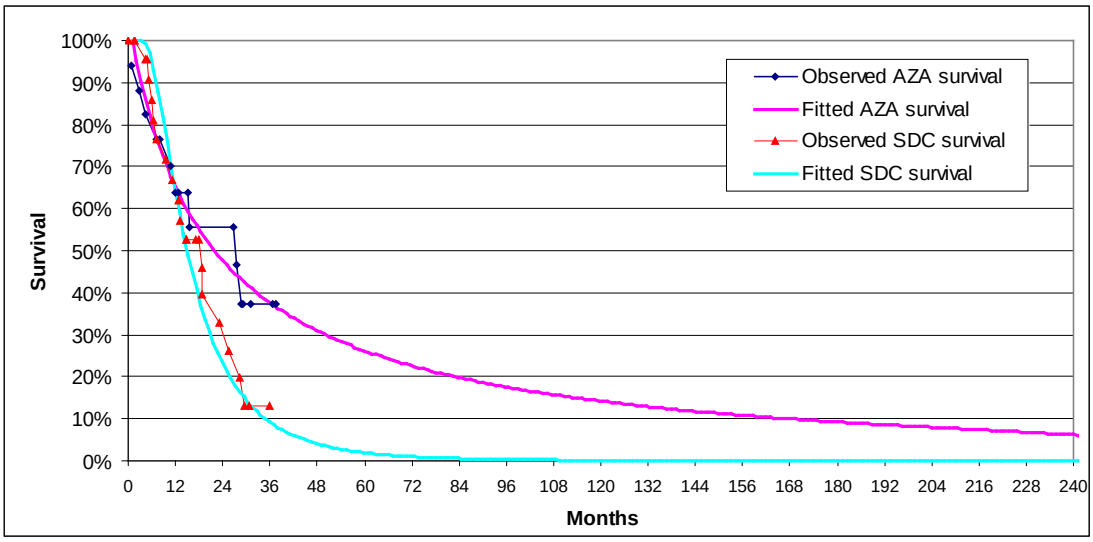

Table B1.3. Summary of cost-effectiveness results using an age-adjusted log-normal curve for the survival extrapolation of azacitidine and comparator regimes

Treatment option	Life-years	Costs incurred	QALYs gained	Marginal costs (vs azacitidine)	Life-years gained on azacitidine	Marginal QALYs (vs azacitidine)	Incremental cost per QALY (vs azacitidine)
Preselected for BSC							
No vial sharing							
Azacitidine	3.85	£114,289	2.97	£79,623	1.99	1.68	**£47,432**
BSC	1.86	£34,665	1.30				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	3.85	£111,109	2.97	£76,443	1.99	1.68	**£45,538**
BSC	1.86	£34,665	1.30				
Vial sharing							
Azacitidine	3.85	£109,266	2.97	£74,601	1.99	1.68	**£44,440**
BSC	1.86	£34,665	1.30				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**3.85**	**£106,438**	**2.97**	**£71,722**	**1.99**	**1.68**	**£42,756**
BSC	**1.86**	**£34,665**	**1.30**				
Preselected for LDC							
No vial sharing							
Azacitidine	4.18	£121,319	3.24	£74,485	2.15	1.83	**£40,754**
LDC	2.03	£46,834	1.41				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	4.18	£118,051	3.24	£71,217	2.15	1.83	**£38,996**
LDC	2.03	£46,834	1.41				
Vial sharing							
Azacitidine	4.18	£116,157	3.24	£69,323	2.15	1.83	**£37,929**
LDC	2.03	£46,834	1.41				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**4.18**	**£113,250**	**3.24**	**£66,416**	**2.15**	**1.83**	**£36,399**
LDC	**2.03**	**£46,834**	**1.41**				
Preselected for SDC							
No vial sharing							
Azacitidine	3.83	£114,996	2.90	£68,314	2.35	1.84	**£37,105**
SDC	1.48	£46,682	1.06				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	3.83	£111,803	2.90	£65,122	2.35	1.84	**£35,371**
SDC	1.48	£46,682	1.06				
Vial sharing							
Azacitidine	3.83	£109,953	2.90	£63,271	2.35	1.84	**£34,366**
SDC	1.48	£46,682	1.06				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**3.83**	**£107,113**	**2.90**	**£60,432**	**2.35**	**1.84**	**£32,823**
SDC	**1.48**	**£46,682**	**1.06**				

Key: BSC: best supportive care; LDC: low-dose chemotherapy; QALY: quality-adjusted life-year; SDC: standard-dose chemotherapy

iv. Estimating overall survival by using the exponential function to model the survival of patients receiving azacitidine and the lognormal function to model patients receiving the comparative care regimens.

- This analysis has been performed as requested. The observed survival, the fitted age-adjusted exponential curves for each of the azacitidine arms and the fitted log-normal curves for the comparative care regimes are presented in Figures B1.10 to B1.12. The cost-effectiveness results of the analyses are presented in Table B1.4 for scenarios assuming either no vial sharing or vial sharing, with or without the Patient Access Scheme.

- Although in this scenario the curve fits are chosen based on the best fit according to the Akaike Information Criterion (AIC) score, the extrapolation does not have face validity in the tail. For example, after 120 months, the survival curves cross, resulting in patients treated with BSC having better long-term survival than azacitidine-treated patients. A similar effect is also seen for the LDC subgroup. This effect is caused by the use of different parameterisations for the extrapolations beyond the trial data and results in diminishing overall survival gains beyond the observed trial data for active treatment. Celgene recommends that the results of this scenario should therefore be treated with caution for all the subgroups.

Figure B1.10. Observed survival data from Study AZA-001, a fitted age-adjusted exponential curve for azacitidine patients preselected for BSC and a fitted log-normal curve for patients treated with BSC alone

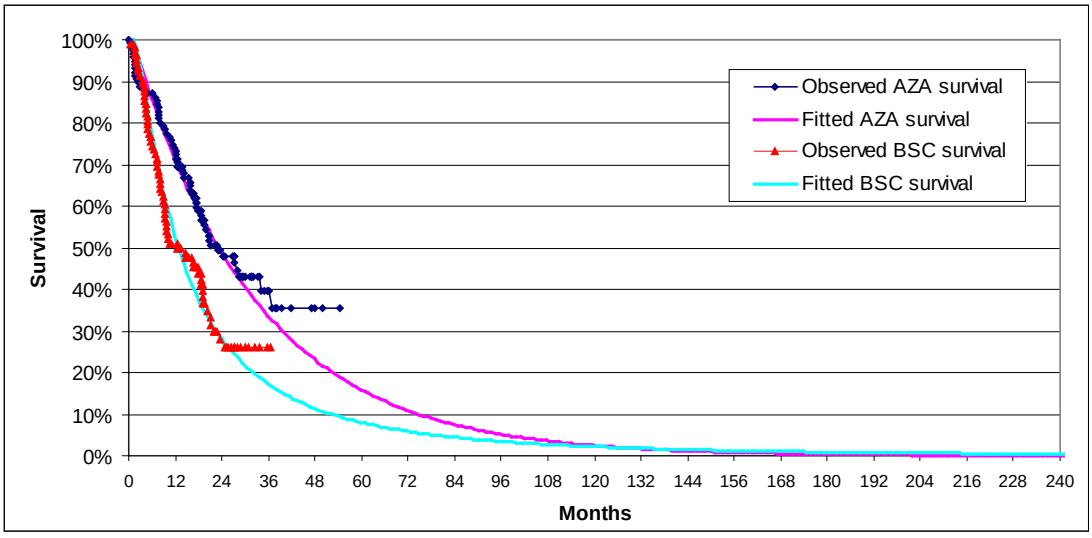

Figure B1.11. Observed survival data from Study AZA-001, a fitted age-adjusted exponential curve for azacitidine patients preselected for LDC and a fitted log-normal curve for LDC-treated patients

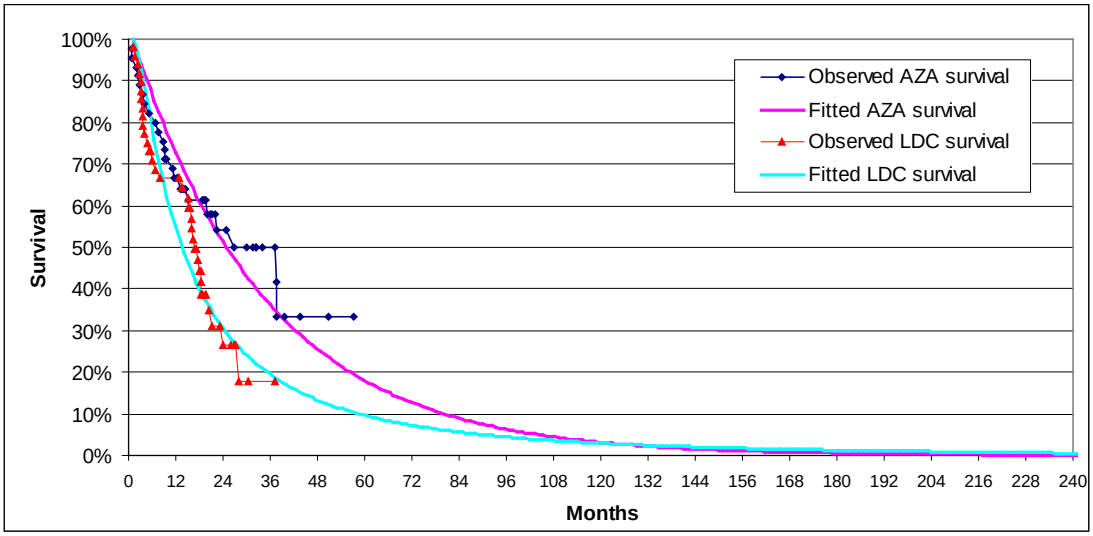

Figure B1.12. Observed survival data from Study AZA-001, a fitted age-adjusted exponential curve for azacitidine patients preselected for SDC and a fitted log-normal curve for SDC-treated patients

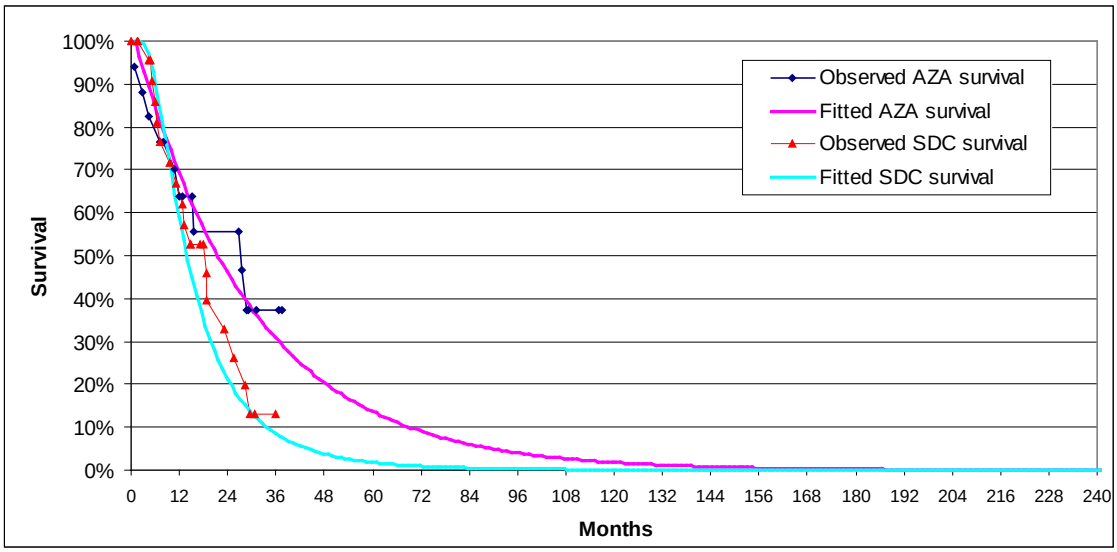

Table B1.4. Summary of cost-effectiveness results using an age-adjusted exponential curve for the survival extrapolation of azacitidine and a log-normal curve for the comparator regimes

Treatment option	Life-years	Costs incurred	QALYs gained	Marginal costs (vs azacitidine)	Life-years gained on azacitidine	Marginal QALYs (vs azacitidine)	Incremental cost per QALY (vs azacitidine)
Preselected for BSC							
No vial sharing							
Azacitidine	2.66	£94,379	2.01	£59,714	0.80	0.72	**£83,024**
BSC	1.86	£34,665	1.30				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	2.66	£91,195	2.01	£56,530	0.80	0.72	**£78,598**
BSC	1.86	£34,665	1.30				
Vial sharing							
Azacitidine	2.66	£89,350	2.01	£54,685	0.80	0.72	**£76,032**
BSC	1.86	£34,665	1.30				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**2.66**	**£86,519**	**2.01**	**£51,853**	**0.80**	**0.72**	**£72,095**
BSC	**1.86**	**£34,665**	**1.30**				
Preselected for LDC							
No vial sharing							
Azacitidine	2.86	£99,186	2.15	£52,353	0.80	0.74	**£70,406**
LDC	2.03	£46,834	1.41				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	2.86	£95,895	2.15	£49,061	0.80	0.74	**£65,979**
LDC	2.03	£46,834	1.41				
Vial sharing							
Azacitidine	2.86	£93,987	2.15	£47,153	0.80	0.74	**£63,414**
LDC	2.03	£46,834	1.41				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**2.86**	**£91,059**	**2.15**	**£44,226**	**0.80**	**0.74**	**£59,476**
LDC	**2.03**	**£46,834**	**1.41**				
Preselected for SDC							
No vial sharing							
Azacitidine	2.48	£91,912	1.81	£46,231	0.99	0.75	**£61,697**
SDC	1.48	£46,682	1.06				
No vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	2.48	£89,685	1.81	£43,003	0.99	0.75	**£57,389**
SDC	1.48	£46,682	1.06				
Vial sharing							
Azacitidine	2.48	£87,814	1.81	£41,113	0.99	0.75	**£54,893**
SDC	1.48	£46,682	1.06				
Vial sharing – 7% discount (Patient Access Scheme)							
Azacitidine	**2.48**	**£84,944**	**1.81**	**£38,262**	**0.99**	**0.75**	**£51,062**
SDC	**1.48**	**£46,682**	**1.06**				

Key: BSC: best supportive care; LDC: low-dose chemotherapy; QALY: quality-adjusted life-year; SDC: standard-dose chemotherapy

v. Estimating overall survival by modelling baseline survival from the registry data, and then applying the respective hazard ratios associated with azacitidine or active chemotherapy (LDC and SDC) treatment. Please explore through sensitivity analysis the impact of changing the assumption that the hazard ratios will remain constant over time.

- This analysis has been performed as requested. The Düsseldorf MDS Registry data have been used to model the survival of BSC patients. The first analysis uses the annual risk of mortality from the registry data to estimate a cycle mortality rate for the BSC arm (see Table B1.5), while the survival for the other treatment arms is estimated based on the hazard ratios compared with BSC given in Table B1.6. A further analysis is presented in which the hazard ratios between BSC and the other treatment arms are varied over time. The results of these analyses are presented in Table B1.7.

- Use of the Düsseldorf MDS Registry data as the base-line mortality for BSC patients and using hazard ratios from the trial to model the survival of the active treatments (azacitidine and chemotherapy) results in an implicit assumption that the shape of disease progression is the same for active treatments as it is for BSC-treated patients. There is an absence of evidence to suggest that this is the case. Therefore Celgene recommends that the results of these analyses are treated with caution.

Table B1.5. Five-week mortality rate based on Düsseldorf MDS Registry data

Year	Patients starting year	Number of patients died	Number of patients censored	Overall survival(s)	Annual mortality rate	Five-week cycle mortality
1	655	346	95	0.430	0.570	0.078
2	214	90	10	0.245	0.431	0.053
3	114	38	2	0.163	0.336	0.039
4	74	23	13	0.107	0.341	0.039
5	38	7	7	0.085	0.203	0.022
6	24	6	3	0.063	0.267	0.029
7	15	4	0	0.046	0.267	0.029
8	11	1	3	0.041	0.105	0.011
9	7	4	1	0.016	0.615	0.088
10	2	2	0	0.000	1.000	1.000

Table B1.6. Hazard ratios for survival in each treatment arm compared with survival of BSC patients

Treatment arm	Hazard ratio (compared with BSC)
Azacitidine (BSC)	0.58
Azacitidine (LDC)	0.52
Azacitidine (SDC)	0.65
LDC	1.04
SDC	0.85

Key: BSC: best supportive care; LDC: low-dose chemotherapy; SDC: standard-dose chemotherapy

Table B1.7. Cost-effectiveness results for analysis using Düsseldorf MDS Registry data as basis for survival

Comparator	Incremental cost-effectiveness ratio (cost/QALY gained)			
	Base case	Base case including PAS	Base case including vial sharing	Base case including PAS and vial sharing
Düsseldorf data used to estimate BSC annual mortality rate				
BSC	£75,332	£71,522	£69,314	£65,926
LDC	£61,440	£58,167	£56,271	£53,360
SDC	£96,246	£85,789	£79,730	£70,429

Key: BSC: best supportive care; LDC: low-dose chemotherapy; PAS: Patient Access Scheme; QALY: quality-adjusted life-year; SDC: standard-dose chemotherapy

- The effect of varying the hazard ratio over time is also examined as a sensitivity analysis. We assume that the hazard ratio remains constant over the trial period (14.5 months) but after that time examine two alternative scenarios:
  1) The hazard ratio returns linearly to 1 over a five-year period after the end of the trial period. The hazard ratio then remains at 1 for the remainder of the model.
  2) The hazard ratio is squared for the azacitidine-treated patients. This increases the benefit beyond the trial period and also incorporates the hypothesised disease-modifying effect based on the epigenetic mechanism of action of azacitidine.

- These scenarios are applied to the Düsseldorf data analysis and the results presented in Table B1.8.

Table B1.8. Sensitivity analysis assuming different survival hazard ratio scenarios in the post-trial period of the model

Analysis	Incremental cost-effectiveness ratio (cost/QALY gained)			
	Base case	Base case including PAS	Base case including vial sharing	Base case including PAS and vial sharing
Patients preselected for BSC				
Declining benefit beyond trial period	£86,992	£82,357	£79,671	£75,548
Constant benefit	£75,332	£71,522	£69,314	£65,926
Increasing benefit beyond trial period	£63,271	£60,312	£58,597	£55,965
Patients preselected for LDC				
Declining benefit beyond trial period	£71,310	£67,197	£64,813	£61,154
Constant benefit	£61,440	£58,167	£56,271	£53,360
Increasing benefit beyond trial period	£53,388	£50,774	£49,259	£46,934
Patients preselected for SDC				
Declining benefit beyond trial period	£127,859	£113,258	£104,798	£91,811
Constant benefit	£96,246	£85,789	£79,730	£70,429
Increasing benefit beyond trial period	£65,475	£59,373	£55,836	£50,408

Key: BSC: best supportive care; LDC: low-dose chemotherapy; PAS: Patient Access Scheme; QALY: quality-adjusted life-year; SDC: standard-dose chemotherapy

- A summary of the incremental cost-effectiveness ratios (ICERs) from the analyses in this question is presented in Table B1.9. This illustrates that across all examined parameterisations of the survival data fit, the ICER ranges from £42,756 to £72,095 for BSC, from £36,399 to £59,476 for LDC and from £32,823 to £52,869 for SDC when the Patient Access Scheme is considered with the inclusion of vial sharing in the NHS (excluding the cost-effectiveness results for the Düsseldorf MDS Registry analyses).

Table B1.9. Summary of cost-effectiveness results based on curve selection

Curve fit selection		**Incremental cost per QALY gained (vs azacitidine) for each comparator [including vial sharing]**		
Azacitidine	**CCR**	**BSC**	**LDC**	**SDC**
No Patient Access Scheme				
Weibull	Weibull	£66,239 [61,350]	£51,471 [47,615]	£54,719 [49,242]
Exponential	Exponential	£70,674 [65,191]	£61,759 [56,481]	£65,019 [57,246]
Log-normal	Log-normal	£47,432 [44,440]	£40,754 [37,929]	£37,105 [34,366]
Exponential	Log-normal	£83,024 [76,032]	£70,406 [63,414]	£61,697 [54,893]
Düsseldorf MDS Registry		£75,332 [69,314]	£61,440 [56,272]	£96,246 [79,730]
Patient Access Scheme (7% discount)				
Weibull	Weibull	£63,177 [58,547]	£49,030 [45,444]	£51,252 [46,158]
Exponential	Exponential	£67,203 [62,103]	£58,418 [53,510]	£60,097 [52,869]
Log-normal	Log-normal	£45,538 [42,756]	£38,996 [36,399]	£35,371 [32,823]
Exponential	Log-normal	£78,598 [72,095]	£65,979 [59,476]	£57,389 [51,062]
Düsseldorf MDS Registry		£71,522 [65,926]	£58,282 [53,360]	£85,790 [70,429]

Key: BSC: best supportive care; CCR: conventional care regimen; LDC: low-dose chemotherapy; QALY: quality-adjusted life-year; SDC: standard-dose chemotherapy

2. In your response to the ACD, you present data obtained from the Düsseldorf MDS registry for patients treated with best supportive care alone. Please describe the search strategy (including inclusion and exclusion criteria) used to identify these data, and the rationale for choosing these data if other sources were also identified through your searching.

- Celgene is aware of three European registries which could have been used as potential data sources. These are: German (Düsseldorf), French (GFM) and Spanish registries. The use of the Düsseldorf MDS Registry was recommended by international MDS clinical experts (for example, Professor Ghulam Mufti), since it is the most established, with high data quality and extent of patient follow-up. For example, the analysis of the BSC cohort of patients provided by Professor Ulrich Germing demonstrated that of the 665 patients analysed, only 31 (5%) were lost to follow-up within the registry. Therefore, Celgene used this data source for overall survival in patients treated with BSC alone.

- Professor Ulrich Germing and his team at the University of Düsseldorf conducted an analysis to include patients that would be higher-risk MDS (International Prognostic Scoring System intermediate-2 or high risk), in accordance with the licensed patient population for azacitidine.

- The inclusion criteria for patients from the Düsseldorf MDS registry as included in the response to the ACD were as follows:
  - Adults aged over 18 years
  - French-American-British classification of refractory anaemia with excess blasts (RAEB), RAEB in transformation (RAEB-T) or CMML
  - World Health Organization classification of RAEB-I, RAEB-II, CMML-I or CMML-II.

- Exclusion criteria were as follows:
  - Treatment with chemotherapy or stem cell transplantation.

3. Table A1 in your response to the ACD presents a limited set of patient characteristics from the Düsseldorf MDS registry. Please provide a more complete description of patient characteristics as they relate to the types of BSC received (such as the percentage receiving GSF, etc.), with full details of the treatments and how these compare with current practice in the UK.

- Celgene has been kindly provided with additional data from the Düsseldorf MDS Registry by Professor Ulrich Germing. Less than 5% of patients in the BSC cohort received either granulocyte colony-stimulating factor (G-CSF) and/or erythropoietin. Furthermore, the use of G-CSF was limited to the treatment of episodes of febrile neutropenia alone and not maintenance support. This support mirrors the treatment patterns and indications for use specified by UK haematologists (see Appendix 8 of primary evidence submission). Furthermore, none of the 13 UK physicians interviewed indicated that erythropoietin is used in higher-risk MDS. No further detailed data on the characteristics in relation to the specific types of BSC received were available.

4. As stated in your response to the ACD, the costs of preparation and administration are assumed to be two-fold greater for the two days of weekend administration per cycle. Please provide justification as to why a two-fold increase appropriately represents the expected increase in costs associated with weekend administration.

- The twofold increase in the total costs of preparation and administration of azacitidine during weekends was an assumption made due to the absence of any such cost data. The additional cost of weekend administration would be associated with pharmacy services which may operate an 'out-of-hours' weekend service to allow preparation of weekend doses.

- In the ACD response (and revised model submitted), a twofold increase in cost was assumed (and applied in the model) for all healthcare professionals associated with the preparation and administration of each cycle of chemotherapy. Hence, the total cost was inflated by a factor of 1.29

(equivalent to five days at the designated cost and two days at the 100% increased designated cost). This factor is applied to all the cost components (physician, nursing and pharmacy time). However, based on the current absence of provision of pharmacy services in some NHS organisations during weekends, this assumption more accurately represents an assumed 4.75-fold increase in the cost of pharmacy preparation. This is because there would be no additional resources associated with physician or nursing time during weekends, as these are currently provided within the NHS. This is illustrated below in Table 4.1.

Table B4.1. Preparation and administration of treatment costs of azacitidine

Staff type	Mean time (mins)	Mean cost per cycle [initial assumption] (£)	Mean cost per cycle including increased weekend cost [revised base case] (£)
Consultant	12.3	21.74	21.74
Foundation house officer	5.0	2.63	2.63
Nurse	253.1	113.88	113.88
Pharmacy	107.7	50.26	104.12
Total	N/A	188.51	242.37*

* Total cost equivalent to 188.51 multiplied by weekend factor of 1.29

- Since each dose of azacitidine would cost £7.18 (or 15.4 minutes) of pharmacy preparation time, the weekend doses would be assumed to cost £34.11 (equivalent to 73.1 minutes) of pharmacy preparation time per dose.

- Further sensitivity analyses of increased costs associated with weekend administration of azacitidine are provided in Table B4.2.

Table B4.2. Sensitivity analysis of increased pharmacy preparation costs of azacitidine during weekends

Total weekend cost inflator	Pharmacy weekend cost inflator	Total cost per cycle (£)	Cost per QALY for each comparator (vs azacitidine)* [with vial sharing]		
			BSC	LDC	SDC
2.00 [base case]	4.75	242.37	47,432 [44,440]	40,754 [37,929]	37,105 [34,366]
2.33	6.00	260.30	47,543 [44,551]	40,858 [38,034]	37,206 [34,467]
2.87	8.00	289.02	47,721 [44,729]	41,026 [38,201]	37,369 [34,630]
3.40	10.00	317.74	47,898 [44,906]	41,193 [38,369]	37,531 [34,792]
6.07	20.00	461.33	48,785 [45,793]	42,031 [39,206]	38,343 [35,604]

* These cost per QALY estimates represent the base case of using the log-normal curve fit for all subgroups
Key: BSC: best supportive care; LDC: low-dose chemotherapy; QALY: quality-adjusted life-year; SDC: standard-dose chemotherapy

- Furthermore, although this is an unlicensed regimen and not recommended by Celgene, some NHS organisations have given an indication that they would likely administer azacitidine in a weekday-only schedule in the absence of weekend pharmacy services.

- In summary, a twofold increase in total costs for weekend administration was assumed based on the absence of specific cost data. This more accurately represents a 4.75-fold increase in pharmacy preparation costs and we feel is a reasonable assumption for the increased costs of weekend administration. Finally, the results of the scenario analysis presented in Table B4.2 demonstrate that the cost-effectiveness results are not sensitive to this factor.

5. Please clarify component costs and the assumptions which underpin the calculation of the costs of blood transfusion.

- The cost components for blood transfusions used in the economic analysis are taken from the 2007 health technology assessment by Wilson *et al*, which examines the cost-effectiveness of treatment for anaemia associated with cancer.[1] In this analysis the cost of transfusing one unit of blood is calculated. The components of this analysis are presented in Table B5.1. These figures are 2005–06 prices and are therefore inflated to 2008 prices using the inflation index from the Personal Social Services Research Unit (PSSRU).[2]

Table B5.1. Cost components of the cost of a unit of blood

Component	2005–06 cost	2008 inflated cost
Blood unit cost	£120	£127
Blood transfusion administration per unit of blood	£158	£168
Total cost per unit of blood	**£278**	**£295**

- The cost of platelet transfusions was elicited from the NHS *Audit of the Use of Platelets* in the UK.[3] This gave a total cost to the health service for platelet transfusions and an estimate of the number of units transfused, resulting in an estimate of £220 per unit of platelets (2006–07 cost), which was then inflated to £230 (2008 cost). There were no details or breakdown of the component of this cost.

- The amount of blood and platelets transfused in each treatment arm is based on the average number of units transfused in each arm in Study AZA-001. These values were converted to a five-week cycle rate adjusted for exposure and applied to all surviving patients in each treatment arm of the model. The rates used are shown in Table B5.2. It is assumed that these rates apply to patients in each treatment arm whether they are on or off active treatment (the observed rates are based on all patients in each treatment arm). Azacitidine-treated patients therefore have a reduced blood transfusion burden throughout their survival in MDS compared with patients receiving comparator treatments.

[1] Wilson J, Yao GL, Raftery J *et al*. A systematic review and economic evaluation of epoetin alpha, epoetin beta and darbepoetin alpha in anaemia associated with cancer, especially that attributable to cancer treatment. *Health Technol Assess* 2007; **11:** 1–202.

[2] Personal Social Services Research Unit. *Unit Costs of Health and Social Care 2008.* www.pssru.ac.uk/pdf/uc/uc2008/uc2008.pdf (last accessed 17 September 2009)

[3] National Health Service. *National Comparative Audit of Blood Transfusion: Audit of the Use of Platelets.* http://hospital.blood.co.uk/library/pdf/Platelet_%20Audit_St_Elsewhere's_NHS_Foundation_Trust.pdf (last accessed 19 March 2009)

Table B5.2. Five-week transfusion requirements for azacitidine and comparators in the model

Treatment arm	Units of blood transfused per cycle	Units of platelets transfused per cycle
Azacitidine	1.48	1.15
Best supportive care	2.42	0.61
Low-dose chemotherapy	2.75	2.22
Standard-dose chemotherapy	2.82	4.42

6. The Committee has noted that the use of the NHS 2009/10 tariff was expected to increase to the ICER, while in your response to the ACD, even with the use of the tariff in the base case, and a survival analysis that lead to shorter overall survival in the model, the ICERs are significantly lower than originally estimated. Please describe what changes in the model have driven these change in the ICERs.

- The main effect of using the 2009–10 tariff rather than the 2006–07 reference costs is a reduction in the cost of hospitalisation for patients treated with SDC. In the other treatment arms, the tariff prices are only used to cost the treatment of adverse events (AEs) and have little effect on the ICER. The differences in costs are shown in Table B6.1.

Table B6.1. Differences in cost between 2006–07 reference costs and 2009–10 tariff

Healthcare resource item	2006–07 reference costs (inflated to 2008)	2009–10 HRG 4.0 costs	Difference
Inpatient standard-dose chemotherapy treatment (SA25F)	£9,610.00[†]	£4,473.00	-£5,137.00
Outpatient consultant visit (Clinical Haematology Total Contacts)	£107.67	£83.00	-£24.67
Neutropenia/leucopenia (Other Haematological or Splenic Disorders without CC	£1,233.54	£1,270.00	£36.46
Febrile neutropenia/pyrexia/pneumonia/sepsis (PA45Z – Febrile Neutropenia with Malignancy)	£4,894.44	£5,530.00	£635.56

[†] Full cost calculated based on SA25F and additional inpatient attendance days beyond trim point

- The age adjustment of the survival curve also has little effect on the cost-effectiveness, as the model for the original ICER calculation was capped at 25 years. When the age adjustment is included, however, it gives survival in the model better face validity. The Evidence Review Group (ERG) criticised the survival analysis in the original model because when the time horizon was extended beyond 25 years, a proportion of patients survived well beyond their centenary year. However, the 25-year cap in the original model means that this has no impact on the ICER. The updated model includes an age adjustment which means that there are no patients who have unrealistic survival when the model is extended. The ICER is not impacted by this change.

- The main impact on the ICER is that the use of the log-normal rather that the log-logistic curve results in a gain in marginal overall survival. In the ACD response, Celgene compared the survival

gain reported by the ERG for the log-logistic curve against the survival gain estimated from the updated analysis using the log-normal curve. However, the life-years gained reported by the ERG were not discounted, while the values reported by Celgene were discounted. Using an age-adjusted log-normal curve which has a better AIC value compared with the log-logistic fit increases the overall survival gain. A summary of the life-years gained and discounted life-years gained is presented in Table B6.2. The increased survival benefit has the effect of reducing the ICER.

Table B6.2. Estimated survival gain from using different curve fits

Treatment arm	Life-years gained			
	Unadjusted log-logistic fit		Age-adjusted log-normal fit	
	Not discounted	Discounted	Not discounted	Discounted
Azacitidine	4.56	3.73	4.65	3.85
Best supportive care	2.13	1.92	2.02	1.86
Azacitidine survival gain	*2.42*	*1.82*	*2.63*	*1.99*
Azacitidine	5.28	4.21	5.12	4.18
Low-dose chemotherapy	2.49	2.19	2.23	2.03
Azacitidine survival gain	*2.79*	*2.01*	*2.90*	*2.15*
Azacitidine	4.53	3.69	4.71	3.83
Standard-dose chemotherapy	1.64	1.57	1.53	1.48
Azacitidine survival gain	*2.89*	*2.11*	*3.19*	*2.35*

- The ICER was also reduced by the correction of an error that was discovered in the model following the ACD (but not identified in the ERG evaluation) and reported in the ACD response (page 32 of ACD response). This error resulted in the double-counting of AEs for patients that were in MDS but were not receiving active treatment. Amending this error reduced the overall costs incurred and had the resultant effect of also reducing the ICERs for each comparator (see Table B6.3).

Table B6.3. Effect of double-counting of adverse events

Comparator (vs azacitidine)	Primary model (with AE double-counting)		Revised primary model* (without AE double-counting)	
	Weibull	Log-logistic	Weibull	Log-logistic
BSC	£66,209	£51,139	£61,125	£45,478
LDC	£63,429	£47,178	£60,492	£43,065
SDC	£45,179	£34,207	£44,198	£31,185

* These values only include the correction of AE double-counting. No other changes included in this ICER
Key: AE: adverse event; BSC: best supportive care; ICER: incremental cost-effectiveness ratio; LDC: low-dose chemotherapy; SDC: standard-dose chemotherapy

7. A number of arithmetic errors are noted in your response to the ACD (including, but not limited to, Table C3). Please correct these.

- The arithmetic errors identified in the response to the ACD occurred in the breakdown summary tables C3a, b and c. These errors were caused by the double-counting of AEs described above.

They only affected the breakdown summary of the results and did not have any influence on the presented ICERs. Updated summary tables of the results are presented below in Tables B7.1, B7.2 and B7.3.

Table B7.1. A detailed breakdown of the cost-effectiveness results. Comparison with BSC. No vial sharing assumed to occur

Item	Azacitidine (preselected for BSC)				BSC		
	MDS state (on active treatment)	MDS state (off active treatment)	AML state	Total	In MDS (BSC alone)	AML state	Total
Premedication	£482			£482			£0
Treatment administration	£2,513	£1,379		£3,892	£800		£800
Pharmacology (active treatment)	£45,426			£45,426			£0
Follow-up appointments	£2,501	£6,008	£1,508	£10,017	£3,486	£1,547	£5,033
Blood/platelet transfusion	£7,254	£17,424	£4,076	£28,754	£12,356	£4,180	£16,536
Concurrent medication on treatment	£1,342			£1,342	£1,367		£1,367
Concurrent medication off treatment		£2,356	£687	£3,043		£704	£704
Routine tests on treatment	£629			£629	£613		£613
Routine tests off treatment		£1,057	£202	£1,260		£208	£208
Adverse event management	£5,015	£12,111	£2,318	£19,444	£7,026	£2,377	£9,404
Total cost	**£65,161**	**£40,336**	**£8,792**	**£114,289**	**£25,649**	**£9,017**	**£34,665**

Key: AML: acute myeloid leukaemia; BSC: best supportive care; MDS: myelodysplastic syndrome

Table B7.2. A detailed breakdown of the cost-effectiveness results. Comparison with LDC. No vial sharing assumed to occur

Item	Azacitidine (preselected for LDC)				LDC			
	MDS state (on active treatment)	MDS state (off active treatment)	AML state	Total	MDS state (on active treatment)	MDS state (off active treatment)	AML state	Total
Premedication	£496			£496	£42	£562		£604
Treatment administration	£2,583	£1,559		£4,141	£1,102			£1,102
Pharmacology (active treatment)	£46,691			£46,691	£113			£113
Follow-up appointments	£2,571	£6,791	£1,465	£10,827	£1,462	£2,446	£1,549	£5,457
Blood/platelet transfusion	£7,456	£19,694	£3,960	£31,110	£8,017	£13,411	£4,185	£25,613
Concurrent medication on treatment	£1,379			£1,379	£825			£825
Concurrent medication off treatment		£2,663	£667	£3,331		£959	£705	£1,665
Routine tests on treatment	£646			£646	£337			£337
Routine tests off treatment		£1,195	£197	£1,392		£431	£208	£638
Adverse event management	£5,366	£13,689	£2,252	£21,307	£3,168	£4,931	£2,380	£10,479
Total cost	**£67,187**	**£45,591**	**£8,541**	**£121,319**	**£15,066**	**£22,740**	**£9,027**	**£46,834**

Key: AML: acute myeloid leukaemia; LDC: low-dose chemotherapy; MDS: myelodysplastic syndrome

Table B7.3. A detailed breakdown of the cost-effectiveness results. Comparison with SDC. No vial sharing assumed to occur

Item	Azacitidine (preselected for SDC)				SDC			
	MDS state (on active treatment)	MDS state (off active treatment)	AML state	Total	MDS state (on active treatment)	MDS state (off active treatment)	AML state	Total
Premedication	£484			£484				
Treatment administration	£2,523	£1,380		£3,903	£9,933	£404		£10,336
Pharmacology (active treatment)	£45,611			£45,611	£1,220			£1,220
Follow-up appointments	£2,511	£6,012	£1,423	£9,946		£1,760	£1,867	£3,626
Blood/platelet transfusion	£7,283	£17,434	£3,845	£28,563	£4,110	£13,498	£5,045	£22,653
Concurrent medication on treatment	£1,348			£1,348	£330			£330
Concurrent medication off treatment		£2,358	£648	£3,006		£690	£850	£1,540
Routine tests on treatment	£631			£631				
Routine tests off treatment		£1,058	£191	£1,249		£310	£251	£560
Adverse event management	£5,951	£12,118	£2,187	£20,255		£3,547	£2,869	£6,416
Total cost	**£66,343**	**£40,360**	**£8,294**	**£114,996**	**£15,592**	**£20,208**	**£10,882**	**£46,682**

Key: AML: acute myeloid leukaemia; MDS: myelodysplastic syndrome; SDC: standard-dose chemotherapy

- An indirect arithmetic error was also included in Table B1 of the ACD response due to the omission of a haematologist response regarding treatment patterns of higher-risk MDS. While the reported mean treatment patterns in the table provided in the response were correct, one response was omitted. A corrected table is provided below.

Table B1. Haematologist treatment patterns of higher-risk MDS (February 2009)

Physician name	Location	Treatment strategy (%)		
		BSC alone	LDC (and BSC)	SDC (and BSC)
Professor David Bowen	Professor of Haematology and Consultant Haematologist, St James's Institute of Oncology, Leeds	80	0	20
Professor Richard Clark	Professor of Haematology and Consultant Haematologist, Royal Liverpool University Hospital, Liverpool	20	30	50
Dr Christopher Dalley	Consultant Haematologist, The Royal Hallamshire Hospital, Sheffield	20	30	50
Dr Ranjit Dasgupta	Consultant Haematologist, Arrowe Park Hospital, Merseyside	70	20	10
Dr Mike Dennis	Consultant Haematologist, The Christie Hospital, Manchester	25	25	50
Dr Aloysius Ho	Consultant Haematologist, King's College Hospital, London	5	65	30
Dr Jonathan Kell	Consultant Haematologist, University Hospital of Wales, Cardiff	50	25	25
Dr Alan MacWhannell	Consultant Haematologist, New Cross Hospital, Wolverhampton	15	40	45
Dr Kavita Raj	Consultant Haematologist, Guy's and St Thomas' Hospital, London	40	50	10
Dr Paresh Vyas	Consultant Haematologist, John Radcliffe Hospital and the Weatherall Institute of Molecular Medicine, Oxford	95	0	5
Anonymous*	Anonymous	80	0	20
Anonymous*	Anonymous	0	50	50
Average [range]		**43.3% [0–95%]**	**27.1% [0–65%]**	**29.6% [5–50%]**

* Anonymised treatment pattern responses at the request of the haematologist interviewed. One (of the 13) haematologists was unable to estimate their MDS treatment practice patterns