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Chair's presentation – PART 1

Gemtuzumab ozogamicin for untreated acute myeloid leukaemia

2nd appraisal committee meeting

Committee C

Lead team: Derek Ward, Nigel Langford and David Chandler

ERG: CRD and CHE, University of York

NICE technical team: Julia Sus and Nicola Hay

Company: Pfizer

27th June 2018

Key issues

- Which utility value for the functionally cured patients is the most plausible?
  - 0.76 or 0.77 in the company's revised scenario analyses or the committee's preferred value of 0.74 in the ACD?
- What is the most appropriate number of hospital inpatient days for VOD to use in the cost effectiveness model?
  - 21 hospital inpatient days used by the company in its revised analyses or 26.8 days used by the ERG in its critique?
- Are the company's updated MCM parameters plausible?
- Should the intermediate cytogenetic subgroup be included in the recommendation?
  - What is the most plausible ICER for the intermediate cytogenetic subgroup?

Key issues

- Should the recommendation include the unknown cytogenetic subgroup who start treatment with gemtuzumab ozogamicin before cytogenetic tests are available?
  - Would a recommendation that excludes this subgroup be implementable in the NHS?
  - Is a stopping rule based on cytogenetic testing only appropriate (e.g. morphology and immunophenotyping)
  - How should the committee's preferred stopping rule be modelled - company's or ERG's approach?
  - What is the most plausible ICER?
- Should terms in the recommendation be clarified (e,g. favourable, intermediate)?
- Are there any potential equality issues?

Gemtuzumab ozogamicin (Pfizer)

Marketing authorisation (granted February 2018)	The treatment of adult patients with previously untreated, de novo acute myeloid leukaemia (AML)
Mechanism of action	Recombinant human nerve growth factor (rhNGF) that aims to improve nerve function and stimulate healing
Administration	Intravenous
Dosage	3 mg/m^2/day (maximum 5 mg/day) infused over 2 hours on days 1, 4 and 7 as part of induction therapy and day 1 of each course of consolidation therapy
List price	[redacted] for course of treatment

ACD: preliminary recommendation

- Gemtuzumab ozogamicin with daunorubicin and cytarabine, is recommended as an option for treating newly diagnosed de novo CD33-positive acute myeloid leukaemia (AML), except acute promyelocytic leukaemia, in people 15 years and over, only if the disease has:
  - favourable cytogenetics or
  - unknown cytogenetics because cytogenetic analysis was unsuccessful.

ACD summary (1)

ACD section	Committee conclusion
Urgent therapy (3.3 & 3.4)	Cytogenetic testing results will not always be available at the start of the treatment. • The clinical experts explained that around 15-20% of patients might require urgent treatment which would have to be initiated without cytogenetic results being available. • Patients with progressive acute myeloid leukaemia who require immediate treatment would be started on gemtuzumab ozogamicin before results are available and treatment would be stopped if test results confirmed unfavourable cytogenetics • associated costs with stopping rule should be included in the economic modelling.

ACD summary (2)

ACD section	Committee conclusion
Intermediate cytogenetic group (3.6 & 3.12)	• The intermediate 1 and 2 cytogenetic subgroup classification system is outdated as clinical experts explained that in the clinical practice the intermediate group is not split only by cytogenetics but it requires additional genetic testing. • Moreover, clinical evidence shown that there is a heterogeneity in the broader intermediate cytogenetic subgroup [redacted]
Clinical effectiveness (3.10- 3.12)	• Gemtuzumab ozogamicin increases event-free survival and relapse-free survival compared with chemotherapy alone in the overall ALFA-0701 population. • Gemtuzumab ozogamicin increases event-free survival and relapse free-survival in the combined favourable and intermediate cytogenetic group but not in the unfavourable group compared with chemotherapy alone. • There is heterogeneity in the clinical outcomes in the broader intermediate cytogenetic subgroup.

ACD summary (3)

ACD section	Committee conclusion
Cost effectiveness unknown cytogenetic status (3.22-3.25)	Patients with unknown cytogenetics consisted of patients where the test was not undertaken or that the test result analysis was unsuccessful in determining cytogenetic status. • It is uncertain why exclusion of the subgroup of people with unknown cytogenetics increased the ICER and lack of additional information made it impossible for ERG to explore this issue further. • Gemtuzumab ozogamicin is not recommended for people with unknown cytogenetics where there is an urgent need to start treatment before the cytogenetic test results are available.
Cost effectiveness by cytogenetic status (3.26-3.27)	• The ICERs for favourable and unknown cytogenetic subgroups were below 20,000 per QALY gained. • The ICER for the intermediate cytogenetic subgroup (excluding the unknowns) was £31,709 per QALY gained, on that basis gemtuzumab ozogamicin could not be recommended for people with intermediate cytogenetic status. • Above suggests that ICERs presented for the company's base case and the ERG's alternative base case were being driven by the effectiveness of gemtuzumab ozogamicin in patients with favourable and unknown cytogenetics, therefore additional analysis is required.

ACD consultation responses

- Consultee comments from:
  - Pfizer (company)
  - Leukaemia CARE (Patient Group)
  - National Clinical Research Institute, Association of Cancer Physicians and Royal College of Physicians (joint response) - endorsed by clinical experts Dr Steven Knapper and Dr Mike Den (Professional Group)
- Commentator comments from:
  - Novartis (company)
- Other comments from:
  - NHS England
- No comment response from:
  - Department of Health and Social Care
- No web comments submitted

Summary of consultation responses [1] Consultee

- **Current recommendation is not implementable in clinical practice**
  - Newly- diagnosed AML patients who are considered suitable for intensive chemotherapy treatment with gemtuzumab ozogamicin should start on days 1,4 and 7 of treatment cycle 1 whilst cytogenetic testing results are not known until day 7-14. (NCRI-ACP-RCP)
  - The majority of patients have to start treatment urgently without waiting for results of cytogenetic analysis. (NHSE)
  - Waiting for cytogenetic results when the patient is ready to start chemotherapy would be against current practice and potentially put patient safety at risk. (NCRI-ACP-RCP)
  - Survey of 373 AML patients found that 32% of AML patients started treatment on the same day that they were given their diagnosis and a further 47% started treatment within a week of receiving their diagnosis (Living with Leukaemia Report). (Leukaemia Care)

Summary of consultation responses [2] Consultee

- **Clinical evidence:**
  - Gemtuzumab ozogamicin is clinically effective in intermediate risk group based on ALFA-0701 study, AML15 and AML16 (UK) clinical trials and meta- analysis by Hill et al (2014). (NCRI-ACP-RCP)
  - The intermediate risk group could account for up to 60% of all AML cases (Veronika Rockova et al 2018), meaning that over 1,800 of the 3,100 patients diagnosed with AML each year (CRUK Incidence Data) will be ineligible gemtuzumab ozogamicin. The ALFA-0701 trial demonstrated that treatment is clearly beneficial in this group and therefore, it is a shame to see that the majority of AML patients could be excluded from accessing it. (Leukaemia Care)
  - Evidence suggests that 5-year survival for patients with intermediate risk cytogenetics is as low as 24% (John C. Byrd et al 2018). The restricted recommendation of gemtuzumab ozogamicin means that these patients with a high unmet need will be unable to access a treatment that could potentially enable them to live longer without relapse. (Leukaemia Care)

Summary of consultation responses [3] Consultee

- **Cost effectiveness**
  - Cost ineffective use of gemtuzumab ozogamicin in 80% of patients if only patients with favourable or unsuccessful cytogenetics will continue treatment past the 1st cycle. (NHSE)
  - Cost ineffective use of gemtuzumab ozogamicin in 20% of patients if gemtuzumab ozogamicin would be given to all patients who require urgent chemotherapy in the 1st cycle and continue in those patients with favourable, intermediate and unsuccessful cytogenetics. (NHSE)
  - Current recommendations are based on unplanned subgroup analysis whilst there is a wealth of clinical evidence supporting inclusion of intermediate and unknown subgroup. (NCRI-ACP-RCP)

Summary of consultation responses [4] Consultee and commentator

- **Definition**
  - Concern that there is no clear definition of favourable cytogenetic presented within the ACD especially that gemtuzumab ozogamicin is recommended for this group. (Novartis)
- **Diagnosis:**
  - Concern that standard of care for patients presenting with AML was not fully explored. The diagnosis can be made on bone marrow morphology and immunophenotyping within a few hours instead of waiting for cytogenetic testing. (NCRI-ACP-RCP)

Summary of consultation responses [5] Consultee

- **General**
  - Patient group would like to see the recommendation broadened to include patients with intermediate-risk AML and those with unknown cytogenetic results (not just those where the cytogenetic analysis was unsuccessful). (Leukaemia Care)
  - Patient group would like gemtuzumab ozogamicin to be utilised upfront (without a requirement to wait for cytogenetic test results) and discontinued in patients with adverse-risk cytogenetics (if deemed clinically appropriate to do so). (Leukaemia Care)
  - The company is concerned that current recommendation exclude patients with intermediate cytogenetic profile which accounts for approximately 60 % of patient population. (Company)
  - The company acknowledges that intermediate 1 and 2 classification is outdated but wants to highlight that intermediate-1 subgroup accounts for two thirds of the total patients expected to be treated in clinical practice and it has been deemed as cost-effective.(Company)

Company's new evidence

- Changes to the economic model:
  - Quality of life in functionally cured patients
  - Hospitality inpatient days for veno-occlusive disease
  - Update to mixture cured model (MCM) parameters
- Scenario analysis: stopping rule for patients with unknown cytogenetics

Company's new evidence: model changes
a. Quality of life in functionally cured patients [1]

- Adjustments to the utility values for functionally cured patients:

Version	Utility value in complete remission	Utility value in functionally cured
Company's base case	0.74	0.82
Committee's preferred utility value in ACD	0.74	0.74 (adjusted for age)
Company's revised base case	0.74	0.76 (adjusted for age)
		0.77 (adjusted for age)

- The company considered that it is not plausible to use the same utility value for both health states; complete remission and functionally cured patients.
- The company proposed 2 alternative scenarios:
  - Utility value of 0.76 taken from company's the time to trade-off (TTO) utility study.
  - Utility value of 0.77 taken from TA399 based on mapping algorithm (Proskorovsky 2014).

Company's new evidence: model changes
a. Quality of life in functionally cured patients [2]

- ICERs for favourable intermediate and unknown cytogenetic subgroups based on deterministic analysis (1)

	Total costs	Total QALYs	Incremental costs	Incremental QALYs	Single change ICER
ERG's analysis (0.74 with ageing)					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£16,910
DA	[redacted]	[redacted]	-	-	-
Company's base-case:					
Scenario 1: adjusted quality of life (0.76 with ageing)					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£16,279
DA	[redacted]	[redacted]	-	-	-
Scenario 2: adjusted quality of life (0.77 with ageing)					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£15,960
DA	[redacted]	[redacted]	-	-	-

Company's new evidence: model changes

a. Quality of life in functionally cured patients [3]

- ICERs for patients with intermediate cytogenetic profile, based on deterministic analysis (2)

	Total costs	Total QALYs	Incremental costs	Incremental QALYs	Single change ICER
ERG's analysis (0.74 with ageing)					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£31,709
DA	[redacted]	[redacted]	-	-	-
Company's scenario analyses:					
Scenario 1: adjusted quality of life (0.76 with ageing)					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£29,923
DA	[redacted]	[redacted]	-	-	-
Scenario 2: adjusted quality of life (0.77 with ageing)					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£29,048
DA	[redacted]	[redacted]	-	-	-

ERG's comments

a. Quality of life in functionally cured patients [1]

- Value from the time to trade-off (TTO) study conducted by the company suggested important difference between functionally cured and complete remission health states.
- Utility values proposed by the company for functionally cured state (0.76/0.77) and complete remission state (0.74) appear reasonable and the difference in the value between both health states is in line with the findings of the TTO study.
- ERG noted that company applied the same value to complete remission state as to functionally cured state and amended it to 0.74
- Correcting for the error in the utility value for the remission state, resulted in deterministic ICERs between £29,409-£30,091 per QALY gained.

⊙ *Is a utility value of 0.76 or 0.77 for the functionally cured patients health state more plausible than the committee's preferred value of 0.74 in the ACD?*

Company's new evidence: model changes
b. Hospital inpatient days for VOD [1]

- Cost of hospital inpatient days for venous occlusive disease (VOD) were not included in the company's original submission.
- The ERG explored the impact of including costs of 26.8 inpatient hospital days based on NICE submission for inotuzumab ozogamicin.
- Company stated that the duration of VOD associated with HSCT, is not the same as the VOD associated with gemtuzumab ozogamicin treatment. VOD associated with gemtuzumab ozogamicin is of a milder form than that associated with HSCT.
- Company considered 21 inpatient hospital days is more appropriate (based on clinicians' opinion which suggested a range of 14 to 28 days to be more plausible).

Company's new evidence: model changes
b. Hospitality inpatient days for VOD [2]

- Adjusted number of hospital inpatient days for VOD based on deterministic analysis:

	Total costs	Total QALYs	Incremental costs	Incremental QALYs	Single change ICER
Base-case population:					
ERG's analysis (26.8 days)					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£16,910
DA	[redacted]	[redacted]	-	-	-
Scenario: adjusted inpatient days (21 days)					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£16,833
DA	[redacted]	[redacted]	-	-	-
Intermediate cytogenetics' profile:					
ERG's analysis (26.8 days)					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£31,709
DA	[redacted]	[redacted]	-	-	-
Scenario: adjusted inpatient days (21 days)					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£31,552
DA	[redacted]	[redacted]	-	-	-

ERG's comments
b. Hospital inpatient days for VOD [1]

- ERG's original duration of 26.8 days is within the range confirmed by the clinical experts and in line with the duration of disutility included by company in its submission.
- ERG agrees that number of hospital inpatient days is uncertain but still considers 26.8 as plausible

⊙ *What is the most appropriate number of hospital inpatient days for VOD to use in the cost effectiveness model?*

Company's new evidence: model changes
c. Update to mixture cured model (MCM) parameters [1]

- Company used annual mortality rates for the England and Wales general population published in life tables by the Office for National Statistics (2016) in its original submission
- ERG used a more up-to-date version of the lifetable (ONS 2017) in its analysis.
- Company re-estimated the base-case MCM curves with background mortality based on the new lifetables and updated the MCM parameters in the model. In this analysis, company adjusted individual patient level data with the new lifetables rates.

ERG's comments:

- The ERG considered update to MCM parameters based on more recent lifetables as reasonable.

⊙ *Are the company's updated MCM parameters plausible?*

Company's new evidence: model changes

c. Update to mixture cured model (MCM) parameters [2]

- Correction of MCM parameters based on deterministic analysis

	Total costs	Total QALYs	Incremental costs	Incremental QALYs	Single change ICER
Base-case population					
ERG's analysis					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£16,910
DA	[redacted]	[redacted]	-	-	-
Company's scenario: Correction to MCM parameters					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£17,006
DA	[redacted]	[redacted]	-	-	-
Intermediate cytogenetics' profile:					
ERG's analysis					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£31,709
DA	[redacted]	[redacted]	-	-	-
Company's scenario: Correction to MCM parameters					
GO + DA	[redacted]	[redacted]	[redacted]	[redacted]	£31,612
DA	[redacted]	[redacted]	-	-	-

Company's revised cost effectiveness analyses

#	Company adjustment	Company's base-case population	Patients with intermediate cytogenetics' profile
Single change ICERs:			
1	0.76 (with aging) utility for functionally cured patients	£16,279	£29,923
2	0.77 (with aging) utility for functionally cured patients	£15,960	£29,048
3	21 excess inpatient days for VOD	£16,833	£31,552
4	Updated MCM parameters	£17,006	£31,612
All change ICERs:			
ERG's original base case analysis		£16,910	£31,709
Company's revised base-case (2+3+4)		£15,977	£28,813
Company's revised base-case (1+3+4)		£16,296	£29,682
Company's revised base-case (2+4)		£16,050	£28,956

- Company's revised base-case ICERs for all above scenarios, below £30,000 per QALY gained.

ERG‘s results: intermediate cytogenetics group

- Presented below are deterministic estimates reported by the company as well as the corrected deterministic and probabilistic ICERs estimated by the ERG.

	Deterministic ICER (company)	Deterministic ICER (ERG-corrected)	Probabilistic ICER (95% CI)	P(CE) at £20,000	P(CE) at £30,000
ERG’s base-case	£31,709	£31,709	£34,681 (£30,070 - £40,768)	34%	47%
Company’s revised base-case (2+3+4)	£28,813	£29,409	£32,403 (£28,108 - £38,066)	33%	47%
Company’s revised base-case (1+3+4)	£29,682	£30,091	£34,962 (£30,231 - £41,275)	33%	45%
Company’s revised base-case (2+4)	£28,956	£29,556	£33,355 (£28,957-£39,149)	33%	47%

⊙ *Which is the most plausible ICER for the intermediate cytogenetic group?*

Company's new evidence: Stopping Rule

Output	Company base-case population (favourable, intermediate and unknown cytogenetics)		Restricted population (favourable and unknown cytogenetics)	
	Scenario 1	Scenario 2	Scenario 1	Scenario 2
Induction 1 cost offset	£113	£157	£2,955	£4,116
Consolidation 1 total cost offset	£24	£34	£918	£1,279
Consolidation 2 total cost offset	£24	£34	£918	£1,279
New ICER (ERG's base-case)	£16,739	£16,672	N/A	N/A
New ICER (company's adjusted)	£15,815	£15,752	N/A	N/A

- Company suggests that the analyses imply that implementing a stopping rule will decrease costs in the gemtuzumab ozogamicin arm because less gemtuzumab ozogamicin will be used.
- Company suggests that the relative efficacy of gemtuzumab ozogamicin would not change significantly with inclusion of the stopping rule.
- Company suggest that there is little effect on the ICER because of small number of patients in the trial.

ERG's critique of the stopping rule

- ERG recreated the company's analysis of the stopping rule - reduced the ICER in the company base-case population from £16,910 to £16,739, under the ERG's base-case assumptions.
- ERG used alternative assumptions to the company; all of the patients at presentation are unknown, and scenarios of various proportions of all patients who would receive urgent treatment with GO was examined.

Proportion of unfavourable patients receiving one induction course of GO	ICER
0%	£16,910
10%	£19,033
20%	£21,156
30%	£23,279
40%	£25,403

Note: ERG's analysis based on a framework included by the company in their model: no further adjustments made to these calculations.

Proportion of unfavourable patients receiving one induction course of GO	ICER
50%	£27,526
60%	£29,649
70%	£31,772
80%	£33,895
90%	£36,018
100%	£38,142

Key issues

- Which utility value for the functionally cured patients is the most plausible?
  - 0.76 or 0.77 in the company's revised scenario analyses or the committee's preferred value of 0.74 in the ACD?
- What is the most appropriate number of hospital inpatient days for VOD to use in the cost effectiveness model?
  - 21 hospital inpatient days used by the company in its revised analyses or 26.8 days used by the ERG in its critique?
- Are the company's updated MCM parameters plausible?
- Should the intermediate cytogenetic subgroup be included in the recommendation?
  - What is the most plausible ICER for the intermediate cytogenetic subgroup?

Key issues

- Should the recommendation include the unknown cytogenetic subgroup who start treatment with gemtuzumab ozogamicin before cytogenetic tests are available?
  - Would a recommendation that excludes this subgroup be implementable in the NHS?
  - Is a stopping rule based on cytogenetic testing only appropriate (e.g. morphology and immunophenotyping)
  - How should the committee's preferred stopping rule be modelled - company's or ERG's approach?
  - What is the most plausible ICER?
- Should terms in the recommendation be clarified (e,g. favourable, intermediate)?
- Are there any potential equality issues?

NICE National Institute for Health and Care Excellence

Gemtuzumab ozogamicin for untreated acute myeloid leukaemia- PART 1

Chair's presentation

3rd appraisal committee meeting

Committee C

Lead team:**Derek Ward, Nigel Langford and David Chandler**

ERG: CRD and CHE, University of York

NICE technical team:Julia Sus and Nicola Hay

Company:Pfizer

22nd August 2018

Recap of comments on ACD from second meeting
Company's response to ACD and new evidence

Response to ACD

- Comments on implementability of the recommendation
- Comments on clinical evidence
- Comments on cost effectiveness

New evidence

- Changes to the economic model:
  - Quality of life in functionally cured patients
    - The company argued that utility value for functionally cured patients should be 0.76 or 0.77 and 0.74 for complete remission.
  - Hospitality inpatient days for veno-occlusive disease
    - The company considered 21 inpatient hospital days is more appropriate than 26.8 (based on clinicians' opinion which suggested a range of 14 to 28 days to be more plausible).
  - Update to mixture cured model (MCM) parameters
    - The company used more up-to-date version of the lifetable (ONS 2017).
- Scenario analysis: stopping rule for patients with unknown cytogenetics

[redacted]

Committee's decision at second meeting (2)
Company's revised cost effectiveness analyses

#	Company adjustment	Company's base-case population*	Patients with intermediate cytogenetics' profile
Single change ICERs:			
1	0.76 (with aging) utility for functionally cured patients	£16,279	£29,923
2	0.77 (with aging) utility for functionally cured patients	£15,960	£29,048
3	21 excess inpatient days for VOD	£16,833	£31,552
4	Updated MCM parameters	£17,006	£31,612
All change ICERs:			
ERG's original base case analysis		£16,910	£31,709
Company's revised base-case (2+3+4)		£15,977	£28,813
Company's revised base-case (1+3+4)		£16,296	£29,682
Company's revised base-case (2+4)		£16,050	£28,956
* patients not known to have unfavourable cytogenetics profile			

[redacted]

Committee's decision at second meeting (3) ERG‘s results: intermediate cytogenetics group

	Deterministic ICER (company)	Deterministic ICER (ERG-corrected)	Probabilistic ICER (95% CI)	P(CE) at £20,000	P(CE) at £30,000
ERG’s base-case	£31,709	£31,709	£34,681 (£30,070 - £40,768)	34%	47%
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Company’s revised base-case (1+3+4)*	£29,682	£30,091	£34,962 (£30,231 - £41,275)	33%	45%
Company’s revised base-case (2+4)*	£28,956	£29,556	£33,355 (£28,957-£39,149)	33%	47%

*1. 0.76 (with aging) utility for functionally cured patients
2. 0.77 (with aging) utility for functionally cured patients
3. 21 excess inpatient days for VOD
4. Updated MCM parameters

[redacted]

The committee decision making at the second meeting

- The committee had concerns regarding the potential impact of including the costs that would be incurred in all patients who require urgent treatment in cycle 1 while waiting for cytogenetic results and who were later found to have unfavourable cytogenetics.
- The committee agreed that 4 changes proposed by the company in their revised cost effectiveness analyses are reasonable and noted that it had little impact on the ICERs.
- The committee agreed that the cost-effectiveness estimates for the intermediate cytogenetic subgroup are higher than the range that NICE normally considers a cost-effective use of NHS resources.
- NICE agreed not to issue any post committee documentation and that further discussion should take place between NICE and the company regarding further analyses.

[redacted]

The committee decision making at the third meeting

- The company submitted further analyses incorporating:
  - a confidential patient access scheme and
  - a revised analysis
    - assumed all patients at presentation have unknown cytogenetics and require urgent treatment
    - 100% of patients treated with one cycle of induction therapy with gemtuzumab ozogamicin until cytogenetic status is known and only patients with favourable, unknown (because the cytogenetic analysis was unsuccessful) and intermediate cytogenetic status continue treatment with consolidation therapy.

[redacted]

Company's revised (probabilistic) analysis for 100% patients treated at presentation in cycle 1

Gemtuzumab ozogamicin list price, costs of treating patients in cycle 1 before cytogenetic status is known.

Analyses	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
ERG base-case settings (list price)			
100% Patients treated at presentation	[redacted]	[redacted]	£20,787
Company's revised analysis with adjustments* (list price)			
100% Patients treated at presentation	[redacted]	[redacted]	£19,556
*company's adjustments: MCM parameters updated and a 0.77 age adjusted utility value used for functionally cured patients.			

Patients known to not have unfavourable cytogenetic status will continue treatment with consolidation therapy.

[redacted]

Company's revised (probabilistic) analysis for intermediate cytogenetic subgroup

Gemtuzumab ozogamicin list price for treating patients with intermediate cytogenetic status.

Analyses	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
ERG base-case settings (list price)			
Intermediate subgroup only	[redacted]	[redacted]	£33,683
Company's revised analysis with adjustments* (list price)			
Intermediate subgroup only	[redacted]	[redacted]	£32,991
*company's adjustments: MCM parameters updated and a 0.77 age adjusted utility value used for functionally cured patients.			

[redacted]

ERG commentary on the company's revised analyses

- The ERG verified the additional analyses provided by the company and concluded that adjustments proposed by the company appeared reasonable.

[redacted]

End of life considerations

- The company and ERG agree that this intervention does not meet the end of life criteria.
- At 1st committee meeting and in the ACD: The committee noted that the results of ALFA-0701 showed that gemtuzumab ozogamicin could increase life expectancy compared with standard care by more than 3 months. However, the short life expectancy criteria were not met (company model standard of care life years gained: 6.02).
- No further evidence was submitted.

[redacted]

Key issues

- What are the most plausible ICERs for gemtuzumab ozogamicin
- Should gemtuzumab ozogamicin be recommended for routine commissioning and in which groups?

[redacted]