Obecabtagene autoleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia

Redacted committee slides – no confidential information

Technology appraisal committee HST [23rd October 2025]

3rd committee meeting – Part 2a

Chair: Paul Arundel

External assessment group: Birmingham Centre for Evidence and Implementation Science

Technical team: Janet Boadu, Victoria Kelly, Lorna Dunning

Company: Autolus Limited

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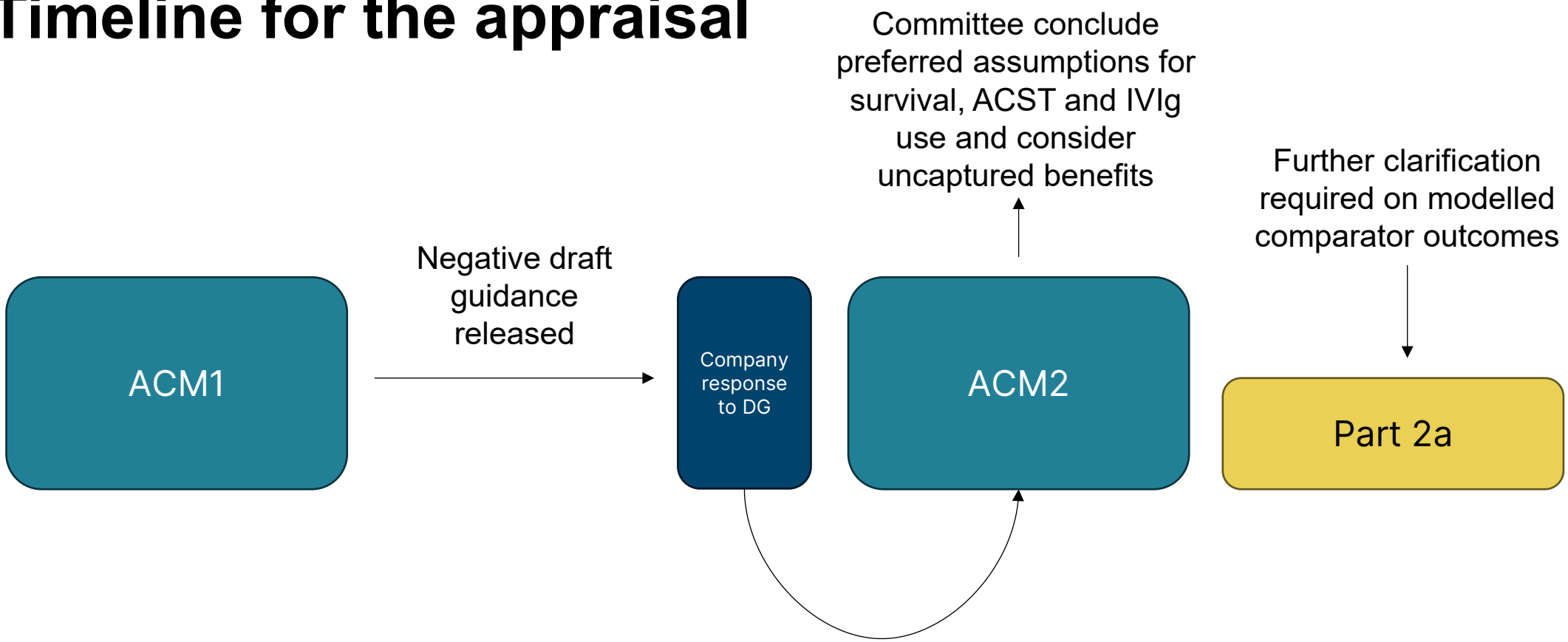
Timeline for the appraisal



- Company adopt committee preferred assumptions
- Company provide updated MAICs based on longer duration of follow-up for Obe-cel
- Company and EAG provide scenarios on IVIg and ASCT use after Obe-cel

Obecabtagene autoleucel (Aucatzyl, Autolus Limited)

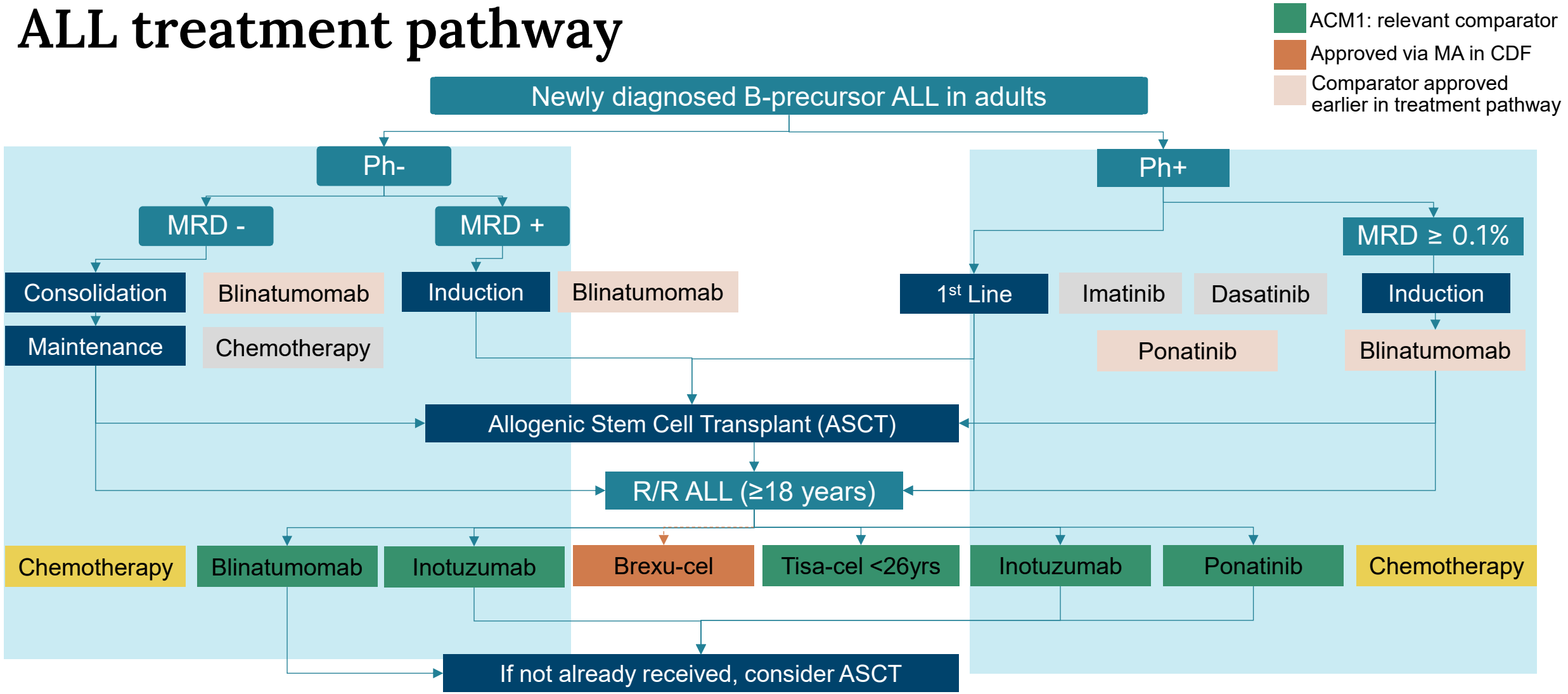
Marketing authorisation (MHRA, April 2025)	• Obecabtagene autoleucel is indicated for the treatment of adult patients (≥18 years) with relapsed or refractory B cell precursor acute lymphoblastic leukaemia
Mechanism of action	• Obecabtagene autoleucel is an autologous cancer therapy which involves reprogramming a patient's own T cells with a transgene encoding a chimeric antigen receptor (CAR) to identify and eliminate CD19 expressing cells
Administration	• Intravenous infusion
Price	• The list price for obecabtagene autoleucel £372,000.00 as a one-off cost • There is a confidential patient access scheme • NHSE has a tariff for delivering CAR T-cell therapies

Abbreviations: MHRA, medicines and healthcare products regulatory agency; CAR-T, chimeric antigen receptor T-cell; ALL, acute lymphoblastic leukaemia

Key issues

Key Issue	ICER impact
Treatment pathway	Unknown
FELIX and comparator trial generalisability	Unknown
Comparator trial outcomes	Unknown
MAIC results	Large
Severity estimates	Large

ALL treatment pathway



- What proportion of people would have the relevant comparators for R/R ALL without Brexu-cel in the pathway?
- What is the impact on Blinatumomab moving to earlier in the pathway for how R/R disease is treated?
- What proportion of people would have ASCT after treatments for R/R ALL?
- Are outcomes expected to be different across comparators?

Baseline characteristics: identified indirect comparison trials (1/2)

RECAP: Because FELIX is single-arm trial company did indirect treatment comparisons of obe-cel with inotuzumab (INO-VATE), blinatumomab (TOWER), and ponatinib (PACE)

- Company adjusted for several treatment effect modifiers see appendix
- No IPD so MAIC performed for obe-cel vs blinatumomab and inotuzumab. Naïve unadjusted comparison vs ponatinib (**At ACM2 committee concluded results of MIAC highly uncertain due to small sample sizes)**

EAG in its original report noted that:

- INO-VATE's had fewer lines of prior therapy
- Patients in TOWER more closely aligned to FELIX, (FELIX had a higher proportion of patients with >3 lines of therapy ([redacted] vs. 7.8%).
- Difference between FELIX and TOWER is less pronounced and causes less concern for adjustment compared to INO-VATE which did not include patients with 3 or more lines of prior therapy.
- INO-VATE involves a population earlier in the treatment pathway (prior induction), while TOWER is focused on salvage therapy, more aligned with FELIX.
- BM blasts significantly negatively impact patient outcomes, INO-VATE included more patients with high bone marrow blast counts (>50%)
- Missing data on primary refractory disease, bone marrow blasts, and remission status introduces uncertainty
- Disparity between FELIX and INO-VATE suggests that adjustments in the MAIC may face challenges due to limited overlap

Abbreviations: MAIC, matching adjusted indirect treatment comparison; IPD, individual patient data; EFS, event free survival; OS, overall survival.

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Baseline characteristics: identified indirect comparison trials (2/2)

Study Arm		FELIX (Obe-cel - mITT)	TOWER (Blinatumomab)	INO-VATE (Inotuzumab)	PACE (Ponatinib)
Population (N)		mITT n = 94	ITT n=271	ITT n=164	ITT n=32
Age, Median (Range)		50 (20 - 81)	41.0 (18-80)	46.5 (18-78)	62 (20-80)
Male:Female %		50.0%:50.0%	59.8%: 40.2%	55.5%: 44.5%	62.5%: 37.5%
Previous Lines of Treatment	1	**29 (30.9%)**	**114 (42.1%)**	**111 (67.7%)**	-
	2	**36 (38.3%)**	**91 (33.6%)**	**51 (31.1%)**	**≥2 TKI: 26 (81.3%)**
	3	**17 (18.1%)**	**45 (16.6%)**	-	**≥3 TKI: 12 (37.5%)**
	≥4	**12 (12.8%)**	**≥21 (7.8%)**	-	-
Refractory to 1st-line Therapy		24 (25.5%)	115 (42.4%)	-	27 (84.4%)
Relapse ≤12 Months		41 (43.6%)	76 (28.0%)	-	-
Previous SCT (%)		**36 (38.3%)**	**94 (34.7%)**	**29 (17.7%)**	**9 (28.1%)**
<50% BM Blasts at Screening (%)		47 (49.5%)	69 (25.5%)	53 (32.3%)	-
ECOG PS (%)	0	**35 (37.2%)**	**96 (35.4%)**	**62 (37.8%)**	**11 (31.9%)**
	1	**58 (61.7%)**	**134 (49.4%)**	**81 (49.4%)**	**17 (42.6%)**
	2	**0 (0.0%)**	**41 (15.1%)**	**21 (12.8%)**	**4 (25.5%)**

- What is committee's view of the similarities or difference across trials?
- What is the impact of any similarities or differences in trial population when comparing outcomes from the trials?

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Abbreviations: ORR, overall remission rate; -, not reported; SCT, stem cell transplant; : ECOG, Eastern Cooperative Oncology Group; PS, performance status

Clinical Outcomes of trials included in indirect comparison

	FELIX Obe-cel*	TOWER Blinatumomab (Ph-)	INO-VATE Inotuzumab (Overall)	PACE Ponatinib (Ph+)
Duration of follow up	[redacted]	11.7 months	29.6 months	5.4 months
Event-Free Survival	[redacted]	1.9 months (95% CI, 0.0 - 6.5)	-	-
Progression free Survival	-	-	5.0 months (95% CI, 3.9-5.8)	3.0 months (95% CI, 1.8 - 3.9)
Complete response	[redacted]	33.6%	73.8%	-
Overall Survival (Median)	[redacted]	7.7 months (95% CI: 5.6 - 9.6)	7.7 months (95% CI: 6.0- 9.2)	8 months

Trial based data	Obe-cel	Blinatumomab (Ph-)	Inotuzumab (Overall)	Ponatinib (Ph+)
Previous SCT (%)	[redacted]	34.7%	17.7%	28.1%
Subsequent SCT (%)	[redacted]	24.0%	48%	3.1%

*TA541: Committee concluded inotuzumab survival benefit is uncertain but it increases response rates and the rate of stem cell transplant

- What are committee considerations on the outcomes and the relevant trial populations?

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* Jan 2025 data cut (enrolled- cohort 1A & IIA)

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Results of MAIC analyses

		Ponatinib (Ph+) † ESS = [redacted]	Blinatumomab (Ph-) ESS = [redacted]	Inotuzumab (Overall) ESS = [redacted]
EFS Hazard Ratio	Unadjusted	[redacted]	[redacted]	[redacted]
	Adjusted	[redacted]	[redacted]	[redacted]
OS Hazard Ratio	Unadjusted	[redacted]	[redacted]	[redacted]
	Adjusted	[redacted]	[redacted]	[redacted]
CR Odds Ratio		[redacted]	[redacted]	[redacted]

Subsequent SCT (%) for costs used in model	Obe-cel	Ponatinib (Ph+)	Blinatumomab (Ph-)	Inotuzumab (Overall)
	10%^	47%	13%	48%

Recap on extrapolation of EFS and OS in modelling:

- **At ACM2 committee preferred company OS and EFS extrapolations of obe-cel** noting difference between company and EAG preference had a negligible impact on the ICERs
- To inform effectiveness of comparators in modelling company applied the inverse hazard ratios from the MAIC to the obe-cel EFS and OS extrapolation (**committee at ACM2 considered this was highly uncertain but were not presented with alternative approaches**)

† HRs not applied in model
* HR applied in model
^ committee preferred value estimated by experts at ACM1&2

Whole population: EFS and OS using company preferred extrapolations

EFS: Obe-cel vs inotuzumab

OS: Obe-cel vs inotuzumab

Recap on modelling:

- Cure assumption, people in any treatment arm alive at 3 years.
- Cure assumption applies to both people who have not experienced an event and to people who have (those in the post-event health state)

PH- population: EFS and OS using company preferred extrapolations

EFS: Obe-cel vs inotuzumab & blinatumomab

OS: Obe-cel vs inotuzumab & blinatumomab

PH+ population: EFS and OS using company preferred extrapolations

EFS: Obe-cel vs ponatinib & inotuzumab

OS: Obe-cel vs ponatinib & inotuzumab

Severity estimates

Company's ACM2 base case* severity estimates:

Treatment	AS	PS	Modifier
Inotuzumab (Overall)	[redacted]	[redacted]	x 1.2
Blinatumomab (Ph-)	[redacted]	[redacted]	x 1.2
Ponatinib (Ph+)	[redacted]	[redacted]	x 1.2

Weighted average of company severity estimates:

Treatment	% weight	AS	PS	Modifier
Inotuzumab (Overall)	5%	[redacted]	[redacted]	x 1.2
Blinatumomab (Ph-)	74%			
Ponatinib (Ph+)	21%			

EAG's ACM2 base case severity estimates:

Treatment	AS	PS	Modifier
Inotuzumab (Overall)	[redacted]	[redacted]	x 1.2
Blinatumomab (Ph-)	[redacted]	[redacted]	x 1.2
Ponatinib (Ph+)	[redacted]	[redacted]	x 1.2

Weighted average of EAG severity estimates:

Treatment	% weight	AS	PS	Modifier
Inotuzumab (Overall)	5%	[redacted]	[redacted]	x 1.2
Blinatumomab (Ph-)	74%			
Ponatinib (Ph+)	21%			

Recap:

- Committee satisfied that 1.2 multiplier should apply
- EAG weighted analysis choice of 5% for inotuzumab was arbitrary and conservative to test previous company base case which suggested a 1.7 multiplier would apply (based on blin comparison only).

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* Company ACM2 base case is aligned with committee preferred values for survival (not costs) therefore the severity results from the company ACM2 base case represent the committee's preferred assumptions.

Assumption		Committee preferred assumptions
Survival inputs	EFS Obe-cel	**Data source:** FELIX, pooled enrolled cohort IA + IIA, [redacted] **Curve selection:** Flexible - Normal - 2
	OS Obe-cel	**Curve selection:** Standard – Weibull
	Inotuzumab / Blinatumomab	Obe-cel curves with inverse HR applied (assumes proportional hazards)
	Ponatinib	**Data source:** PACE, N:32 **Curve selection OS:** Standard - Log-normal, **EFS:** Log-logistic
Cure assumption		• Assumes all cured at 3 years (regardless of event) • Assumes a standardised mortality ratio of 3 in cured state
IVIg usage		• Proportion receiving IVIg: [redacted]% [from Feb 24 data cut off] • Assume all patients receiving IVIg have it for 12 months • Applies this as upfront cost in model
ASCT	Subsequent treatment %	• Obe-cel – 10% • Inotuzumab – 48%, Blinatumomab – 13%, Ponatinib – 47%
	Costs	• Use base case costs aligned with TA893
CAR-T tariff		• Apply 25/26 tariff costs – consider uncaptured benefits of Obe-cel
Bridging therapies		• Applies correction factor to bridging treatment costs of <1.0
Severity		• Apply 1.2 severity weight for overall and subgroups

Cost-effectiveness results

All ICERs are reported in PART 2b slides

because they include confidential

comparator PAS discounts

Managed access

Criteria for a managed access recommendation

The committee can make a recommendation with managed access if:

- the technology cannot be recommended for use because the evidence is too uncertain
- the technology has the **plausible potential** to be cost effective at the **currently agreed price**
- new evidence that could **sufficiently support the case for recommendation** is expected from ongoing or planned clinical trials, or could be collected from people having the technology in clinical practice
- data could feasibly be collected within a reasonable timeframe (up to a **maximum of 5 years**) without **undue burden**.

No managed access proposals submitted by company

Would new evidence on uncertainties sufficiently support the case for recommendation? Could these be collected in clinical practice? E.g.,

- Subsequent SCT (small/moderate impact on ICER)
- IVIG usage (small impact on ICER)
- Comparative efficacy (large impact on ICER)

Obecabtagene autoleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia [ID6347]

Supplementary appendix

NICE National Institute for Health and Care Excellence

FELIX study design

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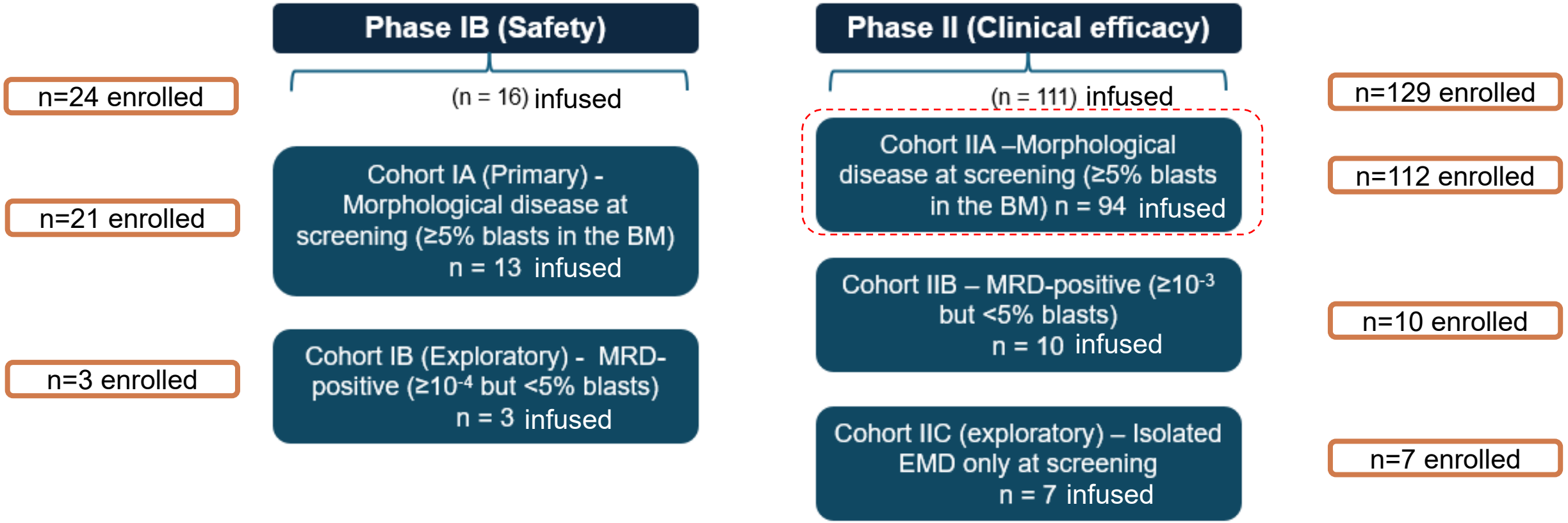
RECAP



- Company prefer infused patients only from cohort IIA for modelling (n=94) - mITT
- EAG considers both Cohorts IA and IIA relevant (n=133): Cohort IA includes 21 enrolled of which 13 infused and cohort IIA includes 112 enrolled of which 94 infused - ITT
- EAG suggest ITT data set more representative of what happens to people during start of CAR-T in NHS practice

Abbreviations: BM, bone marrow; EMD, extramedullary disease; MRD, minimal residual disease; mITT, modified intention-to-treat; ITT, intention-to-treat; CAR-T, chimeric antigen receptor T-cell

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RECAP

Obe-cel study results: January 2025 date cut-off

	Cohorts IA and IIA – enrolled (n=133)		Cohorts IA and IIA – infused (n=107) [committee preferred]
Source of data	(clarification response A1) February 2024	Autolus_Data on file. January 2025	Autolus_Data on file. January 2025
ORR	[redacted]	[redacted]	[redacted]
CR	[redacted]	[redacted]	[redacted]
CRi	[redacted]	[redacted]	[redacted]
DOR	Without censoring	Without censoring	Without censoring
Median (months)	[redacted]	[redacted]	[redacted]
12 months	[redacted]	[redacted]	[redacted]
24 months	[redacted]	[redacted]	[redacted]
36 months	[redacted]	[redacted]	[redacted]
48 months	[redacted]	[redacted]	[redacted]

Abbreviations: ORR, overall remission rate; CR, complete remission; Cri, complete remission with incomplete haematological recovery; DOR, duration of remission ;NR, not reported

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Treatment effect modifiers used in ITC matching

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COMPANY: A logistic propensity score model was created including relevant TEMs and PFs, following which weights for the IPD were estimated such that the weighted mean baseline characteristics of interest for the population in FELIX was aligned with that reported in the comparator trials, using method of moments. Based on the clinical validation, the final list of prognostic factors and TEMs included in the feasibility assessment and subsequent ITC, in order of priority, is reported below:

- Primary refractory disease
- % Bone marrow blasts at screening
- Prior lines of therapy
- Extramedullary disease prior to lymphodepletion
- Duration of 1st remission ≤12 months
- Philadelphia chromosome
- Age at baseline
- Bridging chemotherapy
- Race
- Prior SCT
- ECOG status
- Sex

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Abbreviations: TEM, Treatment effect modifier; PFs Prognostic factors; ITC, indirect treatment comparisons; ECOG, Eastern Cooperative Oncology Group; SCT, stem cell transplant; ESS, effective sample size.

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Key issue: Appropriate costs associated with ASCT (obe-cel arm)

Committee at ACM1:

- Company at ACM1 included benefits of ASCT in OS for obe-cel but not the costs
- At ACM1 experts estimate proportion receiving ASCT after CAR-T likely less than 10%
- Committee concluded wanted range of scenarios exploring proportion <10% of people having ASCT after obe cel in the ITT population

Company response to DG

- Updated base case: [redacted]% ASCT for obe-cel; and explored lower proportions (5% and 2.5%) → minimal ICER impact. Explored alternate costs using report by Ernst & Young (2021) showing hospital resource use remained significant beyond 100 days and showed costs to be higher than what is used in company base case → [redacted]

EAG

- [redacted] in ICER from alternate costs due to increase in costs in comparator arms (as these costs applied in both arms)
- Updated base case to [redacted] to reflect expert and committee preference and explored lower proportions (5% and 2.5%)
- Agrees with company base case costs but acknowledges further investigation in alternate costs warranted

ASCT cost category	company base case (inflated to 2023 cost year)	Ernst & Young report (2021 cost year)
SCT costs	£115,591	£82,197
0-6 months follow-up	£34,347	£88,808*
6-12 months follow-up	£23,594	£35,963

- What is the most appropriate proportion to use when estimating number of patients receiving allo-SCT post CAR-T treatment?
- Are the base case costs appropriate?

*Calculated as the reported total per patient cost at ([initial transplant spell+ 0-100 days post transplant costs]-[transplant spell costs]+[100-200 days post transplant spell discharge costs]). Abbreviations: CAR T; chimeric antigen receptor T-cell; ASCT, allogeneic stem cell transplant