NICE National Institute for Health and Care Excellence

Part 2a slides for website
Redacted

Venetoclax with a hypomethylating agent or low dose cytarabine for untreated acute myeloid leukaemia when intensive chemotherapy is unsuitable [ID4071]

Lead team presentation

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ERG: Aberdeen HTA Group

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Company: AbbVie

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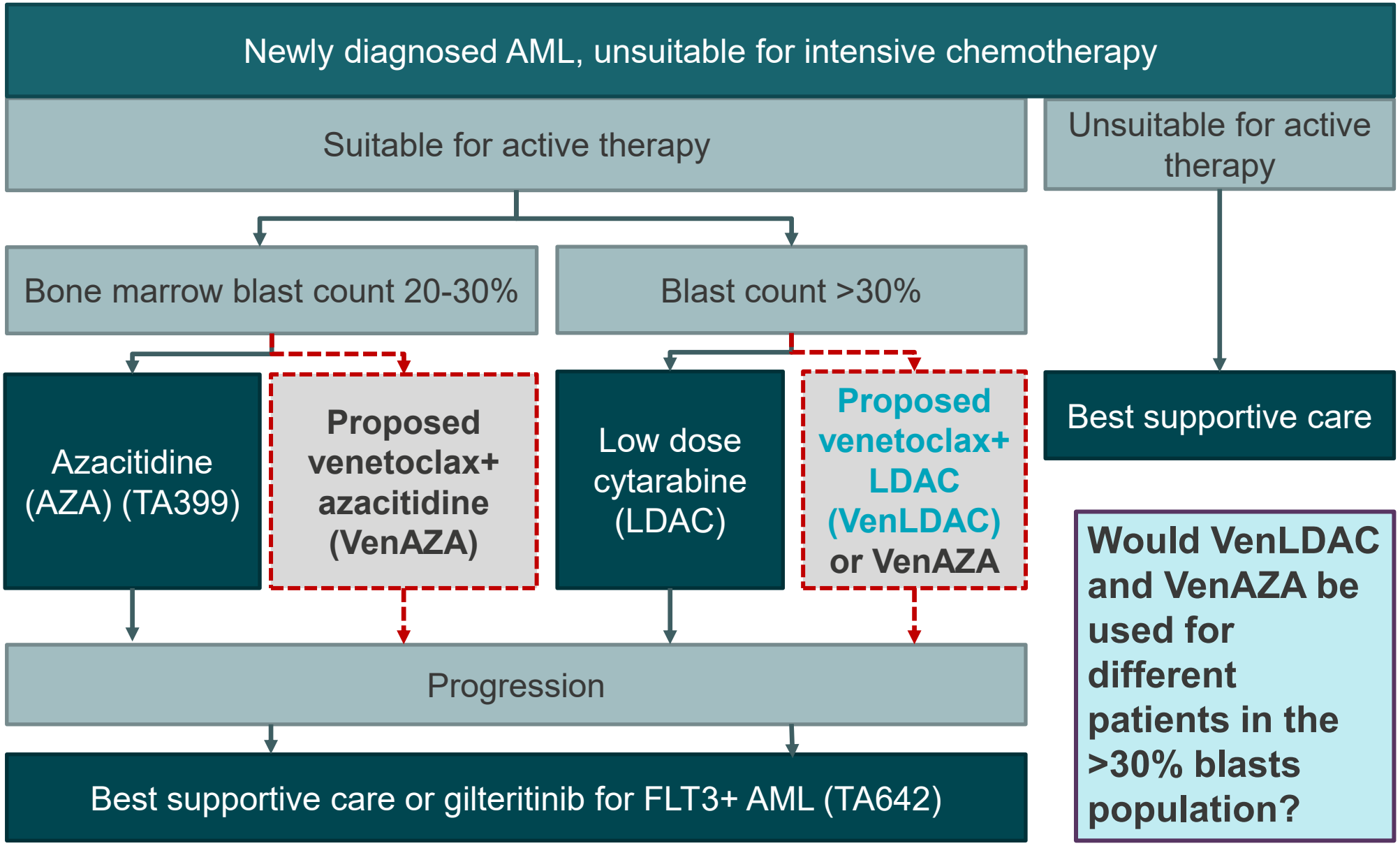
Variation to marketing authorisation

- Marketing Authorisation for VenAZA combination granted by EMA (and adopted by MHRA) but not VenLDAC combination.
- Company is seeking a variation to the MA from MHRA to include VenLDAC combination.
- Anticipated [redacted]
- Information relating to licence variation is not in public domain → part 2 discussion without public

Anticipated marketing authorisation	[redacted]

Treatment pathway



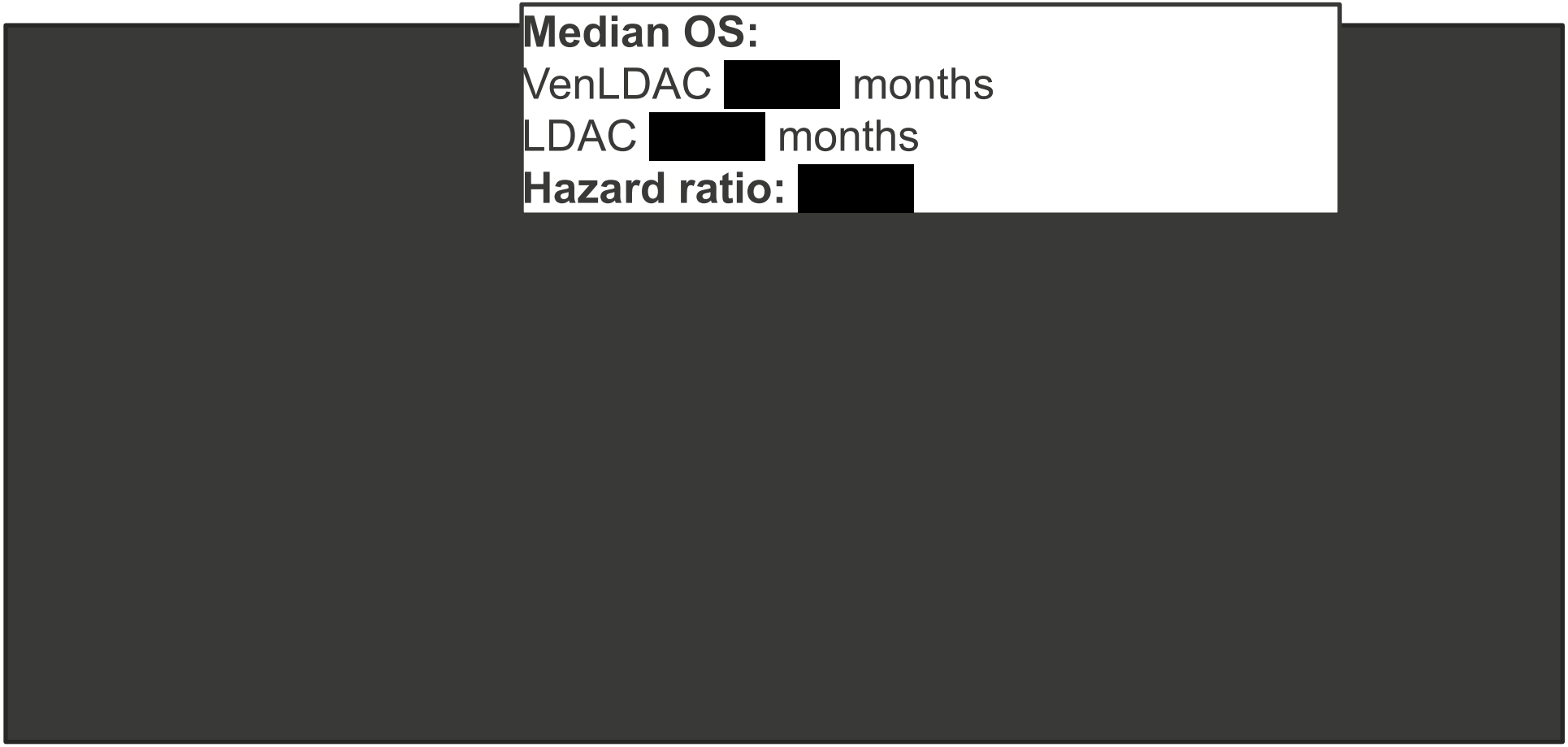
Same issues to resolve for VenLDAC combo

Issue	Impact	VenLDAC differences	Question for committee
1. Cure assumption		• Company's evidence for cure assumption focuses on VenAZA combination	• Is including a cure point plausible? If so, at how many years after remission? • If cure state removed, what extrapolation should be used for time-to-relapse curve?
6. Subsequent treatment distribution		• VenLDAC arm treated same as VenAZA arm (5% have subsequent gilteritinib)	• Is the company's updated proportion of people having subsequent gilteritinib appropriate? • Should stem cell transplant be included in model?
7. Dose of venetoclax		• Daily dose of VenLDAC in company model is 600mg (vs 400mg for VenAZA). • Relative dose intensity of [redacted] applied from VIALE-C.	• What dose of venetoclax should be considered for the cost-effectiveness results?
Other considerations		• None	• Are the end-of-life criteria met?

VIALE-C Overall survival results

Data cut-off August 2019, patients with >30% blasts

Kaplan–Meier plot of OS in the >30% blast subgroup in VIALE-C: Post-hoc analysis (N=160)



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Time-to-relapse extrapolations (3)

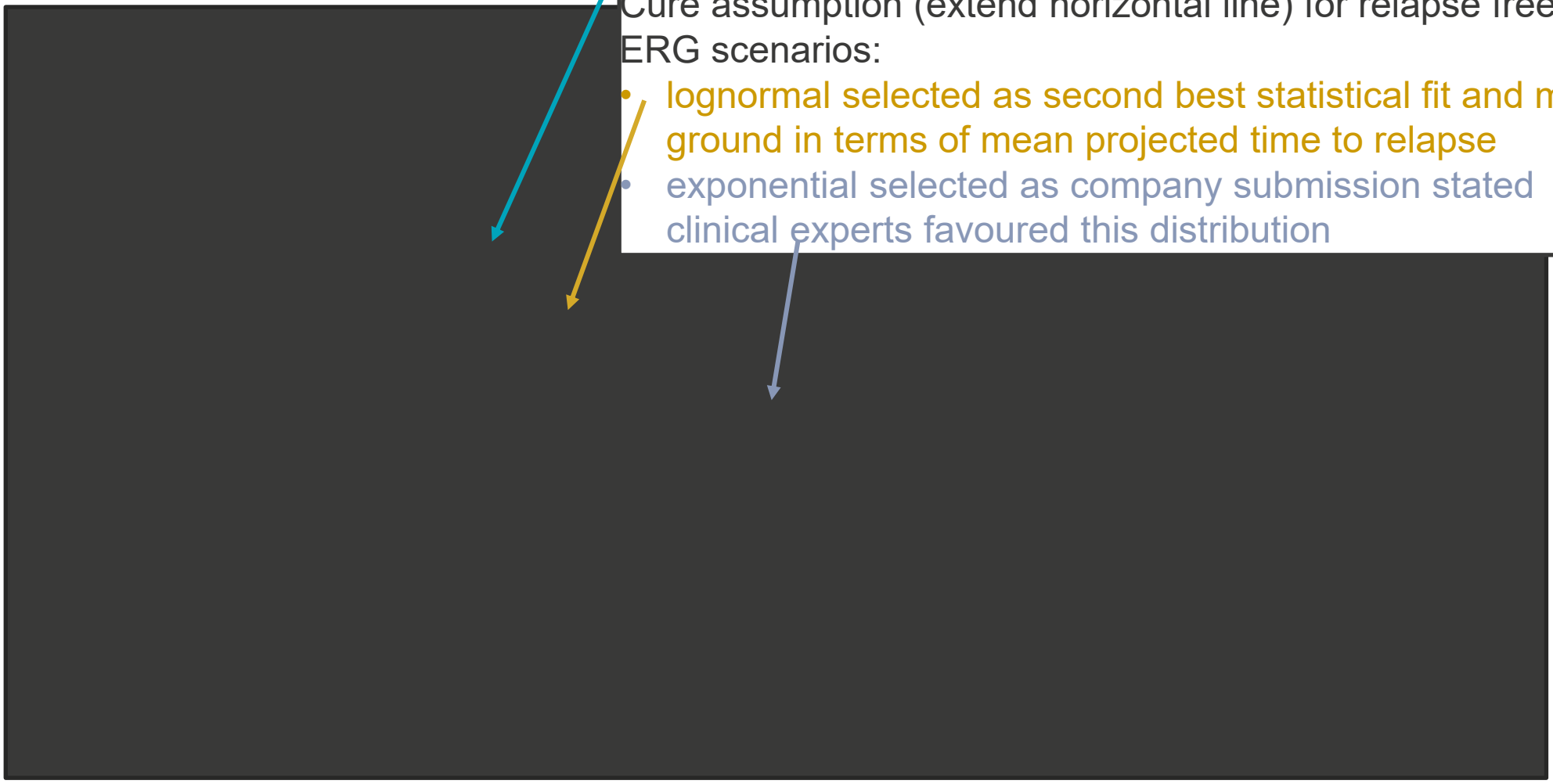
VenLDAC (>30% blasts)

Company original extrapolation: generalised gamma selected as lowest AIC/BIC and good visual fit

Cure assumption (extend horizontal line) for relapse free at 2y

ERG scenarios:

- lognormal selected as second best statistical fit and middle ground in terms of mean projected time to relapse
- exponential selected as company submission stated clinical experts favoured this distribution



End of life considerations

Criterion	Data source	Overall survival	
		Median	Mean
	VIALE: LDAC (>30% blasts)	[redacted]	-
	Undiscounted life years from model: LDAC (>30% blasts)	-	0.84 years
Extension to life, normally of a mean value of ≥ 3 months		Median increase (trial)	Mean increase (model)
	VenLDAC versus LDAC (>30% blasts)	[redacted]	0.41 to 1.51 years across all scenarios

Are the end-of-life criteria met?

Cost-effectiveness results

VenLDAC v. LDAC (>30% blasts)

NB. 3-way comparison with VenAZA (fully incremental) not presented

Scenario	ICER (£/QALY)		
	Licensed dose of venetoclax, [redacted] dose intensity	Licensed dose of venetoclax, 16.7% dose intensity	Licensed dose of venetoclax 11.8% dose intensity
Company base case	**£36,995**	**-**	**-**
ERG corrected subsequent treatment costs	**£36,781** **Probabilistic: £39,949**	**£10,958**	**£8,726**
1. ERG: AE costs updated	£36,652	£10,829	£8,597
1+2a. Removing VenLDAC cure assumption (generalised gamma time-to-relapse)	£77,743	£23,341	£18,638
1+2b. Removing VenLDAC cure assumption+lognormal time-to-relapse	£105,325	£36,256	£30,284
1+2c. Removing VenLDAC cure assumption+exponential time-to-relapse	£124,256	£45,237	£38,404

Is venetoclax cost-effective?

Issue 6: Subsequent treatment distribution

Company scenario analyses

- Company explored following scenarios for proportion of patients receiving subsequent gilteritinib:

	VenAZA/VenLDAC	AZA/LDAC
Original company base case	3%	0%
Scenario 1	5%	3%
Scenario 2	15%	10%

- Results based on original company base case, with error corrections
  - Company's updated base case includes scenario 1

Cost-effectiveness results	20-30% blasts	>30% blasts	
	VenAZA vs. AZA	VenAZA vs. LDAC	VenLDAC vs. LDAC
Original company base case	£16,638	£33,858	£27,182
Scenario 1	£16,234	£33,023	£25,534
Scenario 2	£21,905	£32,920	£24,521