NICE National Institute for Health and Care Excellence

All confidential data redacted [redacted]

Slides for Public observer – Redacted

Mogamulizumab for treating mycosis fungoides or Sézary syndrome cutaneous T-cell lymphoma [ID1405]

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ACM 1 8th July 2020

Mycosis fungoides or Sézary syndrome

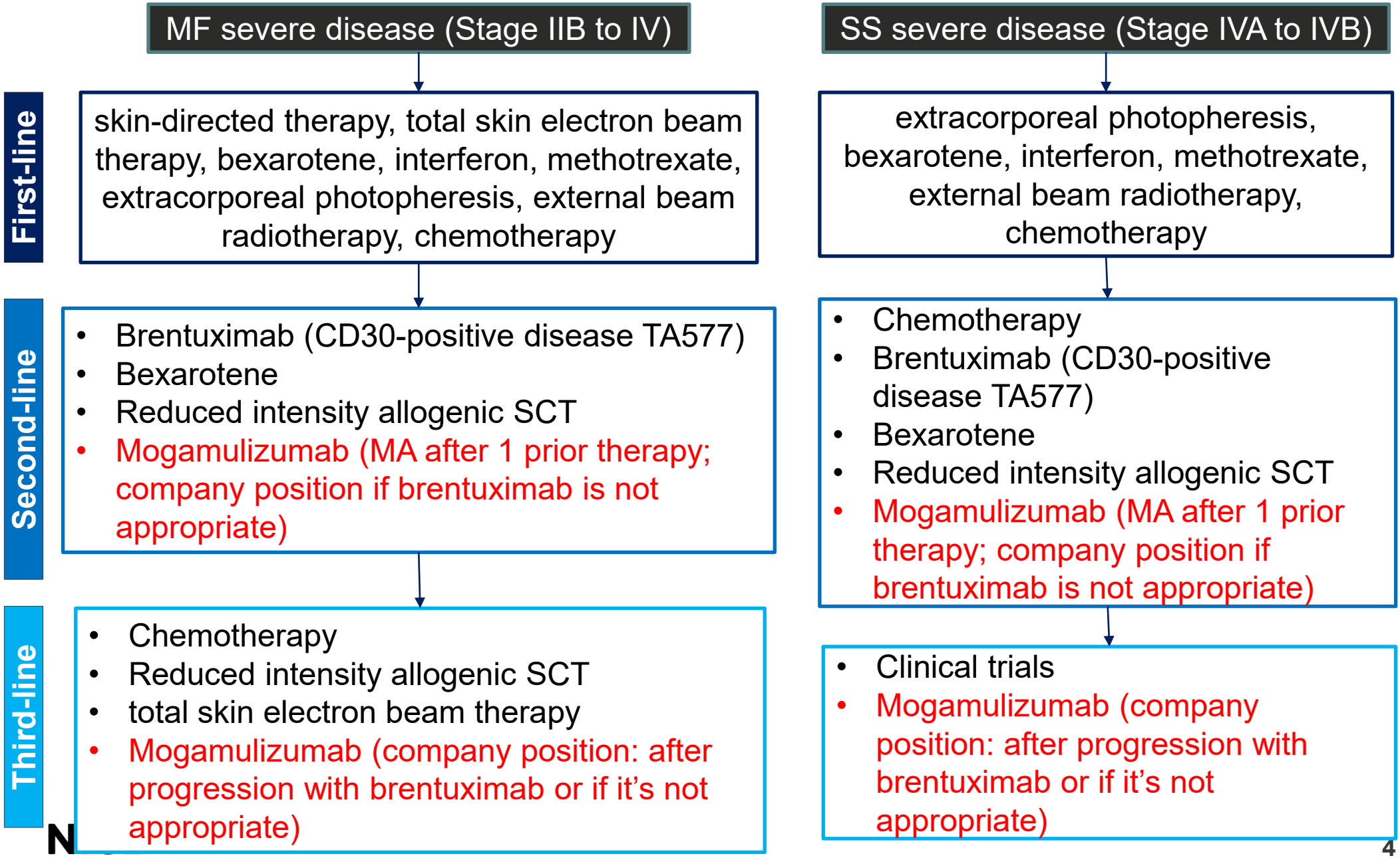
- Cutaneous T-cell lymphoma (CTCL) is a rare type of non-Hodgkin's lymphoma that affects the skin.
  - Mycosis fungoides (MF) is the most common type of CTCL
  - Sézary syndrome (SS) is closely related to MF and refers to a condition when cancerous T-cells (Sézary cells) are found in the blood as well as the lymph nodes
- It is caused by the uncontrolled growth of T-lymphocytes within the skin:
  - Many types of CTCL start as flat red patches or plaques on the skin, which progress to skin tumours, and may be itchy and sometimes painful
  - Some people experience swelling of the lymph nodes
- Between 2009 and 2013, 1,659 people were newly diagnosed with CTCL of which around 55% were MF
- The majority of people diagnosed with cutaneous T-cell lymphoma are over the age of 50 but it can also affect young people

Mogamulizumab (Poteligeo, Kyowa Kirin)

Company's proposed positioning is narrower than MA (severe disease after brentuximab or if it's not appropriate) see issue 1

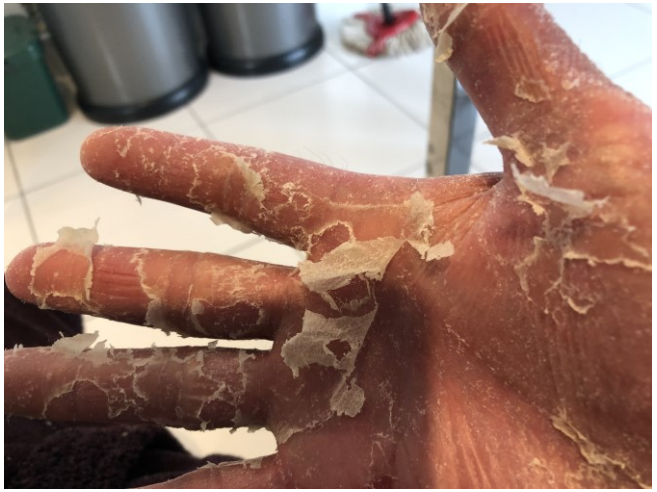
Marketing authorisation (received Jan 2019)	Treatment of adult patients with mycosis fungoides (MF) or Sézary syndrome (SS) who have received at least one prior systemic therapy.
Mechanism of action	Mogamulizumab is a defucosylated, humanized IgG1 kappa immunoglobulin that selectively binds to C-C chemokine receptor type 4 (CCR4), a G-protein-coupled receptor for C-C chemokines that is involved in the trafficking of lymphocytes to various organs including the skin, resulting in depletion of the target cells.
Administration	The recommended dose is 1 mg/kg mogamulizumab administered as an intravenous infusion over at least 60 minutes. Administration is weekly on days 1, 8, 15 and 22 of the first 28-day cycle, followed by infusions every two weeks on Days 1 and 15 of each subsequent 28-day cycle until disease progression or unacceptable toxicity.
Price	The list price is £1,329 per vial (20mg of mogamulizumab in 5ml, corresponding to 4mg/ml), the course of a treatment is £57,109. Simple discount PAS approved (updated post TE)

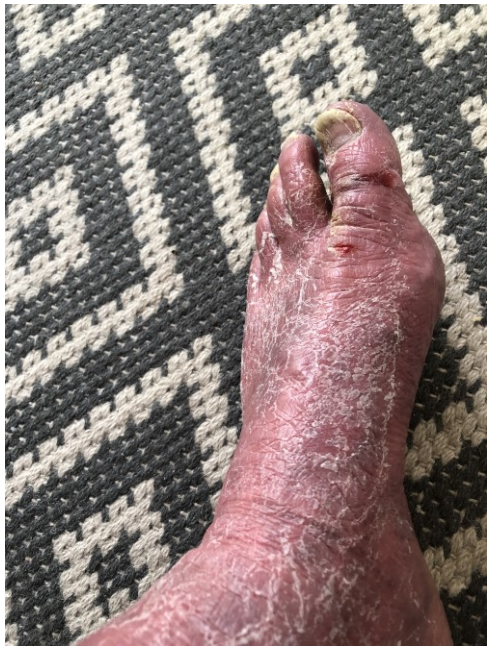
Treatment pathway for severe disease



Patient and carer perspectives

- People with CTCL usually live with their condition for many years, and experience symptoms flaring up
- Itching all the time can have a significant impact on quality of life. Skin may be painful, particularly if people have tumours or if areas of skin weep or become infected
- Psychological and social wellbeing are significantly affected, particularly at more advanced stages. Also applies to carers - often the main source of support and help with day-to-day activities
- There are many possible treatments for CTCL, but the effects are often short-lived and significantly affect patients' quality of life





The itching controls every aspect of my life. Very poor sleep patterns due to applying emollients 24 hours a day… I am not functioning as a human being

Open wounds all over my body but in particular my hands and feet…unable to hold pen or crockery and have to wear gloves filled with creams 24 hours a day

Mogamulizumab has transformed my life in recent months. Previous treatments like ECP and Interferon never really had any beneficial results in improving my condition whereas now mogamulizumab has.

Key clinical data sources

Primary data source used in model: MAVORIC

372 adults with stage IB-IVB relapsed or refractory MF or SS and ECOG ≤ 1

Mogamulizumab 1 mg/kg (n =186 in ITT)

Vorinostat 400 mg (n=186 in ITT)

136 (73%) crossed over to mogamulizumab (disease progression after at least 2 cycles or unable to tolerate)

Severe disease IIB-IVB (n=150)

Severe disease IIB-IVB (n=137) 72% crossed-over

Secondary data sources (not used in model)

ALCANZA

- Phase 3 trial brentuximab vs. physician's choice (methotrexate or bexarotene)
- 128 adults with ECOG 0-1 and:
  - CD30+ MF who had ≥1 previous systemic therapy, or
  - CD30+ primary cutaneous anaplastic large cell lymphoma (subtype of CTCL) who had ≥1 previous systemic therapy or radiotherapy
  - No patients with SS
- Main trial in TA577 brentuximab (results were confounded by treatment switching and no robust OS estimate for physician's choice was available)

Cross over adjustment

72% in vorinostat arm crossed over to moga so company, tech team & ERG all agree adjustment to OS estimates is appropriate to estimate what would have happened in comparator arm if no switching

Method	Assumptions	Company	ERG
RPSFTM	Common treatment effect (same treatment effect regardless of when it was received)	• Assumptions not met • Counter-intuitive HR as it favoured vorinostat	Agree results may not be clinically plausible
IPCW; Company preferred	No unmeasured confounders (that predict switching & prognosis)	Used stabilised weights obtained from a logistic regression model	• Most favorable estimates • Not possible to fully assess how weights obtained • If low % who did not switch despite being eligible IPCW may be biased
TSE; ERG preferred	No unmeasured confounders at secondary baseline (switching permitted after progression – all patients at similar disease stage)	Not appropriate because 1) OS extrapolations lacked plausibility compared with external data and 2) does not account for potential post-progression benefit	1) TSE should not be ruled out as OS estimates were as similar to the company's external data as the IPCW 2) No sufficient evidence to support this benefit

Abbreviations: IPCW, Inverse Probability of Censoring Weights; RPSFTM, Rank preserving structural time model; TSE, Two-stage estimation

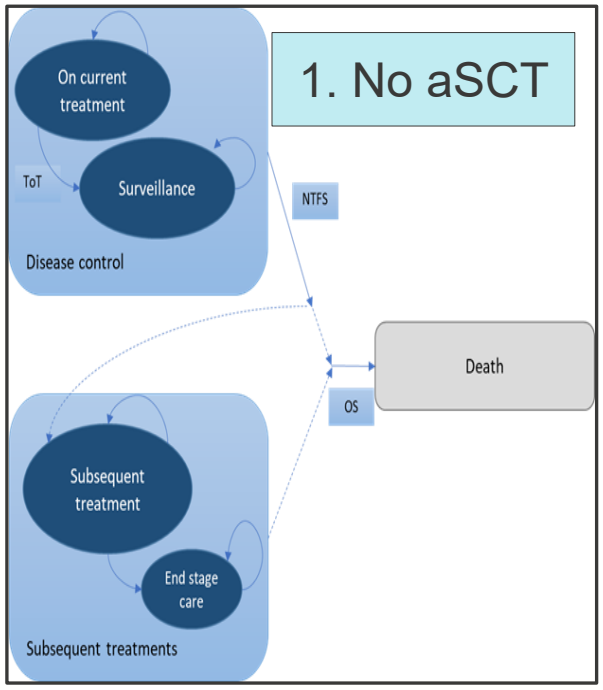
Slide amended post ACM 1

Key clinical evidence

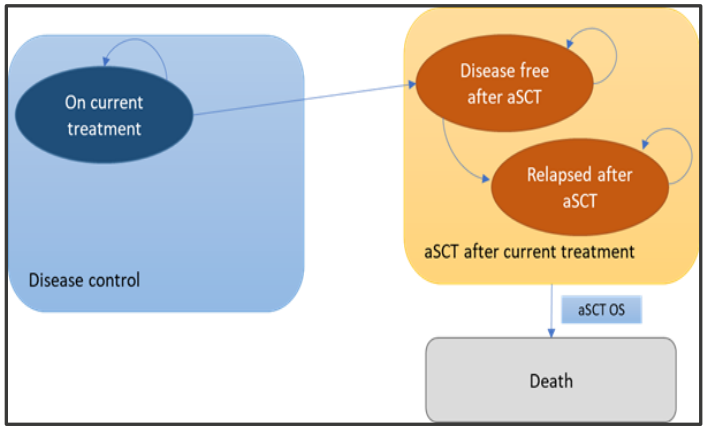
Outcome	MAVORIC ITT population (n=372)		MAVORIC severe disease (n=287)	
	Mogamulizumab	Vorinostat	Mogamulizumab	Vorinostat
Median PFS	7.70 (5.67 to 10.33)	3.10 (2.87 to 4.07)	9.4 (5.7 to 14.0)	3.1 (2.9 to 3.9)
PFS	HR 0.53 (0.41 to 0.69)		HR 0.43 (0.31 to 0.58)	
Median OS unadjusted	[redacted]	[redacted]	[redacted]	[redacted]
IPCW		[redacted]		[redacted]
TSE		[redacted]		[redacted]
OS unadjusted	[redacted]		[redacted]	
IPCW	[redacted]		[redacted]	
TSE	[redacted]		[redacted]	
Median NTFS	9.6 (7.0 to 11.8)	3.37 (3.1 to 4.0)	[redacted]	[redacted]
Median TOT	5.6 (4.4 to 7.1)	2.9 (2.4 to 3.3)	[redacted]	[redacted]

All OS data excludes patients who had an aSCT
Abbreviations: NTFS, next treatment-free survival; TOT, time on treatment; IPCW, Inverse Probability of Censoring Weights; TSE, Two-stage estimation

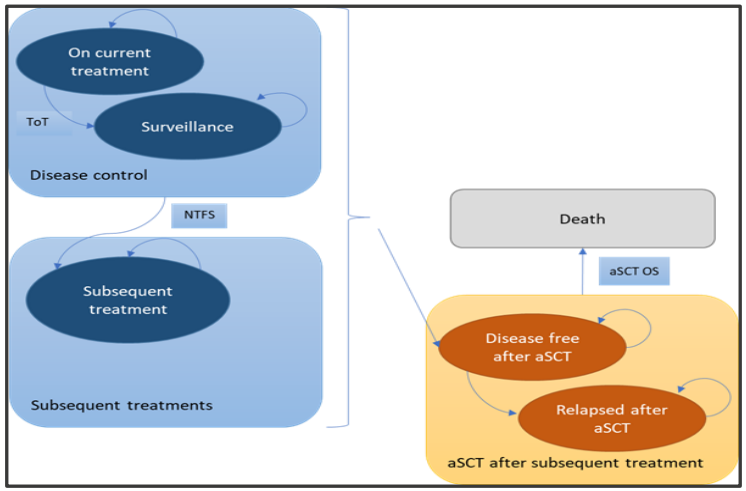
Summary of 3 modelled treatment pathways



1. No aSCT



2. aSCT after current treatment (occurs at 18 weeks)



3. aSCT after subsequent treatment (occurs at [redacted] weeks for moga & [redacted] weeks for SC)

- All patients start in the 'On current treatment' health state
- Can move to the dead state any time (based on OS and general population mortality)
- When treatment stopped, patients move to:
  - 'surveillance' health state if symptoms controlled without treatment
  - 'subsequent treatment' health state if disease progresses (based on NTFS) and have symptomatic care and increased monitoring
- In the last six months of life, end stage care modelled with ↑ resource use and ↓ quality of life

Issues resolved after technical engagement

	Summary	Stakeholder	Technical team	Base case?
4	Company use estimated aSCT after current treatment (not allowed in MAVORIC). Treatment effect may differ if aSCT had been allowed in trial so ERG prefer to remove aSCT – may not be in line with clinical practice but reduces bias	Company submitted weighted analyses but ERG suggest questionable	Agree with ERG and prefer to remove aSCT (minimal impact on ICER)	Company X ERG ✓
6	Company use cycle-specific utility values for first 12 weeks. The ERG suggest this is questionable because there were some counter-intuitive patterns, it's less robust & adds uncertainty to the model	Company use cycle-specific utility in revised base case	Prefer to include average 'on treatment' health-state specific utility	Company X ERG ✓
Other resolved issues in TR				
	Company preferred extrapolation: • next treatment-free survival (NTFS): generalised gamma both arms • DFS after aSCT: Gompertz ERG prefer lognormal for both NTFS & DFS	None	Agree with ERG (minimal impact on ICER)	Company X ERG ✓
	ERG corrected errors (2 related to the implementation of aSCT and 1 related to PFS utility used in TA577) & 45-year horizon			

Key considerations

Note: orange boxes for discussion; green is resolved (previous slide)

Model driver | Unknown impact | Small impact

Issue	Company revised base case	Technical team	Impact
1. Population	MAVORIC subgroup with severe disease (stage ≥IIB MF and all SS) after BV or if BV is not appropriate	Subgroup is in line with company positioning but there is uncertainty from mixed lines of treatment	
2. Comparator	Clinical effectiveness: Vorinostat Modelled: Bexarotene	Uncertain relative effectiveness as vorinostat not licensed/used in UK	
3a. Cross over	IPCW adjustment method	Both IPCW & TSE plausible	
3b. Extrapolation	OS: moga: lognormal; SC: exponential	OS: exponential for both arms	
	NTFS: generalised gamma	NTFS: lognormal for moga	
	DFS after aSCT: Gompertz	DFS after aSCT: lognormal	
4. aSCT	aSCT after current treatment is based on clinical advice	Accept ERG changes to assume no aSCT after current treatment	
5. Stopping rule	2-year stopping rule for moga	Prefer to remove as not in SPC/trial	
6. Utility values	Use cycle-specific utility values for first 12 weeks	Prefer average 'on treatment' health-state specific utility	
	Include caregiver utilities	Prefer to remove caregiver utilities	

Issue 1: Population

TE questions on clinical relevance of severe disease subgroup & MAVORIC generalisability

Background

The company's positioning of mogamulizumab is narrower than the full MA

MA & NICE scope	Company's proposed positioning	MAVORIC trial	Company base case
Adults with MF or SS who have had at least one prior systemic therapy	Adults with **advanced** MF or SS **(i.e. stage ≥IIB MF and all SS)** after at least one prior systemic therapy who are **clinically ineligible for or refractory to brentuximab vedotin**	Adults with MF or SS (Stage IB, II-A, II-B, III or IV) after at least 1 prior therapy with ECOG 0 or 1	MAVORIC severe disease subgroup (stage ≥IIB MF & all SS)

Company

Severe disease subgroup is in line with the expected use in clinical practice in the NHS and represents the population with the greatest unmet need

Tech team

- Severe disease subgroup is in line with company's positioning
- Unclear proportions for each line of treatment in modelled population

Uncertainty from mixed lines of treatment

Technical engagement response:

- 1 clinical expert: severe subgroup clinically relevant & MAVORIC results generalisable
- No new evidence from company around proportions at each line of treatment & no separate analyses by line of treatment or MF/SS

Issue 1: MAVORIC baseline characteristics

Characteristic	ITT (n=372, %)	Severe disease (n=287, %)	Prior BV (n=20, %)
Median age	[redacted]	65-67 (26-101)	[redacted]
Male	[redacted]	173 (60.3)	[redacted]
ECOG 0	[redacted]	155 (54.0)	[redacted]
ECOG 1	[redacted]	130 (45.3)	[redacted]
Stage IB–IIA	[redacted]	0	[redacted]
Stage IIB	[redacted]	55 (19.2)	[redacted]
Stage IIIA-IIIB	[redacted]	38 (13.2)	[redacted]
Stage IVA1	[redacted]	155 (54.0)	[redacted]
Stage IVA2	[redacted]	31 (10.8)	[redacted]
Stage IVB[a]	[redacted]	8 (2.8)	[redacted]
Median prior systemic therapies (range)	[redacted]	[redacted]	[redacted]
MF	[redacted]	[redacted]	[redacted]
SS	[redacted]	[redacted]	[redacted]

[a] two patients in the ITT population (one in each treatment group) were noted to have stage IVB disease at baseline but did not have measurable visceral disease at baseline

1 Clinical expert: BV is licensed for those with CD-30 positive disease (around 15 to 20%). Those with CD-30 negative disease would have Moga 2nd line

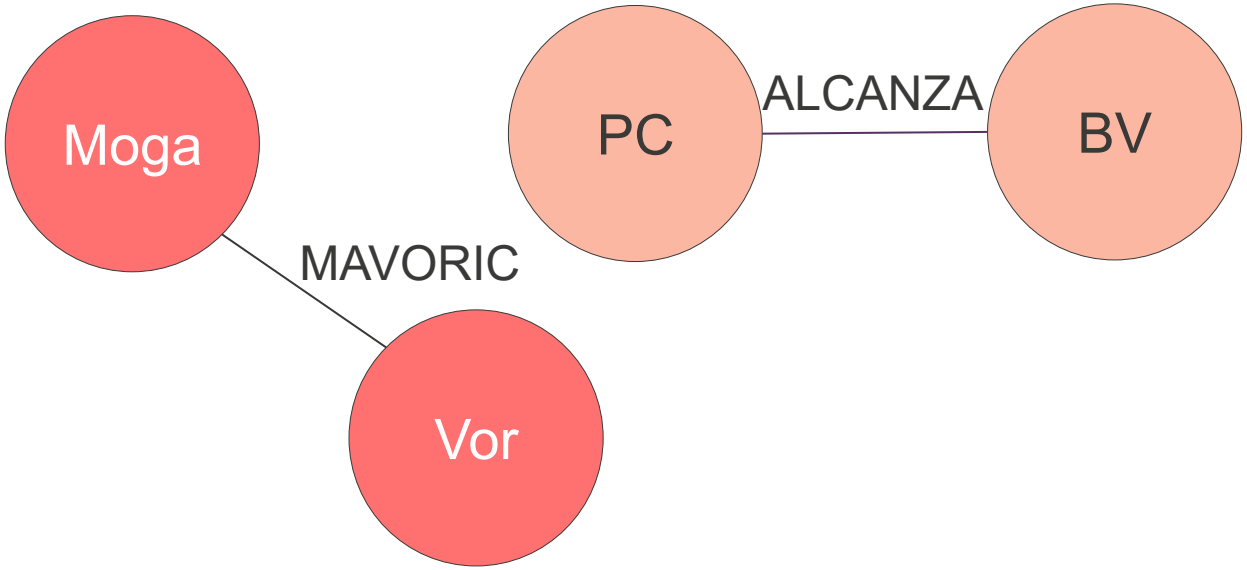
Do trial results adequately reflect the company's proposed severe disease subgroup?
Are results from MAVORIC generalisable to the NHS in England?
Is it acceptable to used a population that includes mixed lines of treatment?

Issue 2: Comparator

TE questions on current treatments used in NHS & use of vorinostat as a proxy

Background

- MAVORIC compared moga with vorinostat, a treatment that is not used or licensed in the UK
- Population in ALCANZA differs to MAVORIC & high level of cross-over in both trials
- Company do not have access to ALCANZA IPD to calculate adjusted OS in physician's choice arm
- No comparison of moga vs. physician's choice (methotrexate or bexarotene)



BV, Brentuximab vedotin; Moga, mogamulizumab; PC, physician's choice; Vor, vorinostat

Company

- Vorinostat is suitable proxy for standard care in NHS (similar PFS to physician's choice in ALCANZA)
- Clinical advice from 3 clinicians suggest bexarotene is most commonly used

Revised base case comparator: bexarotene

Tech team

Using MAVORIC to model moga vs. standard care in NHS results in uncertainty because vorinostat is not licensed in UK – this may be unresolvable because of a lack of evidence

Prefer mixed treatment to model SC

Issue 2: Company's TE response – new comparator

Company's original analyses		Company new analyses post TE		
Treatment	Base case	Base case	Scenarios	
Methotrexate	[redacted]	-	[redacted]	-
Bexarotene	[redacted]	100%	[redacted]	[redacted]
Interferon alfa-2a* (peginterferon)	[redacted]	-	-	[redacted]
Gemcitabine	[redacted]	-	-	-
CHOP	[redacted]	-	-	-
Liposomal doxorubicin	[redacted]	-	-	-
Etoposide	[redacted]	-	-	-
Prednisolone	[redacted]	-	-	-
PUVA	[redacted]	-	-	-
ECP	[redacted]	-	-	-
TSEBT	[redacted]	-	-	-

CHOP, Gemcitabine; cyclophosphamide plus doxorubicin, vincristine, prednisolone; ECP, Extracorporeal photopheresis; PUVA, Psoralen plus ultraviolet light therapy; TSEBT, Total skin electron beam therapy

Company

- Based on responses from 3 clinicians using moga
- Interferon not available in NHS & lack of efficacy data for pegylated interferon
- Methotrexate mostly used stage III erythrodermic disease (1st line)
- Bexarotene most common comparator but less clear in SS

ERG

Using a single comparator may be an over-simplification of treatment pathway, especially for SS but useful scenario analysis

Technical engagement response:

One clinical expert: would use chemo for all patients but this is not very effective & ↑ risk infection. Unable to comment on vorinostat as not available in UK.

Issue 2: Company's TE response – comparator treatment duration

Company

- Company submission used conservative assumption that the comparator treatment duration cannot be longer than the time on vorinostat
- Treatment duration with vorinostat is shorter than treatments used in UK therefore cost of comparator was underestimated
- Company's revised base case uses alternative mean duration of treatment

Treatment	Mean duration of treatment	Source	Implementation
Bexarotene	48 weeks	NHS England budget impact analysis submission	Exponential distribution fitted to the mean
Methotrexate	48 weeks		
Interferon alpha-2a	12 months		

ERG

- Although it's justified to adjust length of treatment to UK data where available, there are some concerns about this adjustment:
  - source of the data is not provided by the company
  - both adjustments using bexarotene & adapting length of treatment mean the modelled comparator effectiveness and costs refer to completely different treatments, around which there is a lot of uncertainty.
- Useful scenarios but ERG base case unchanged & difficult to assess relative effectiveness of moga in UK

Is it appropriate to use bexarotene alone as a comparator?

Issues 3a & 3b: Cross-over adjustment & OS extrapolation

TE questions on clinically plausible OS estimates for standard care in NHS

Background

- 72% in severe disease subgroup crossed over from vorinostat to mogamulizumab
- MAVORIC was not powered to detect OS differences (only 23% of patients had an OS event)

Company

- Prefer IPCW as produces clinically plausible results & accounts for potential post progression effect of moga
- Disease modifying effect of moga would result in longer tail for SoC

Cross over: IPCW is most appropriate;
OS: Exponential for SC, lognormal for moga

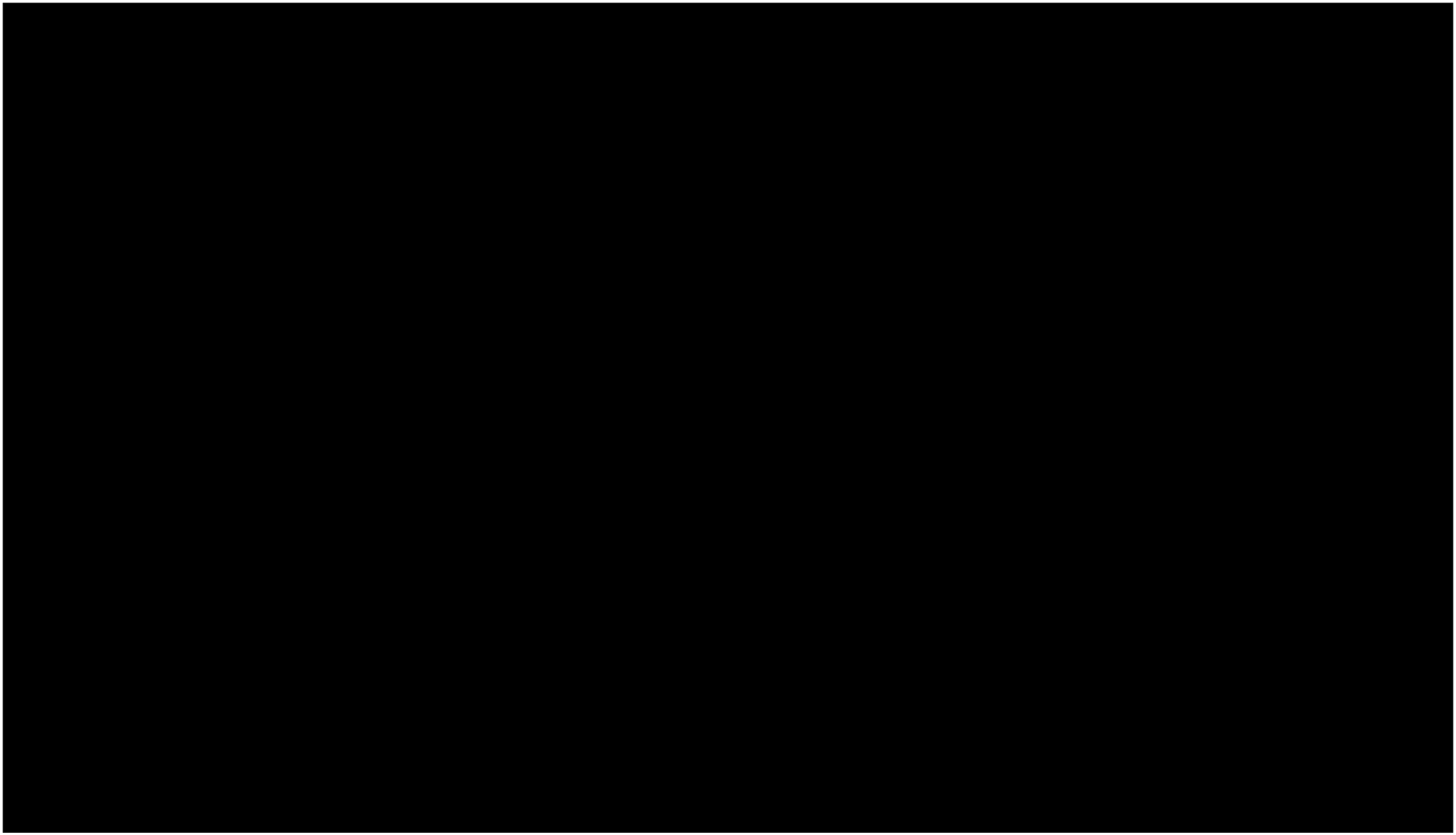
ERG

- There is substantial uncertainty because all adjustment methods are associated with bias
- Questionable that the main survival benefit of moga accrued on subsequent treatments
- Uncertain if moga is disease modifying

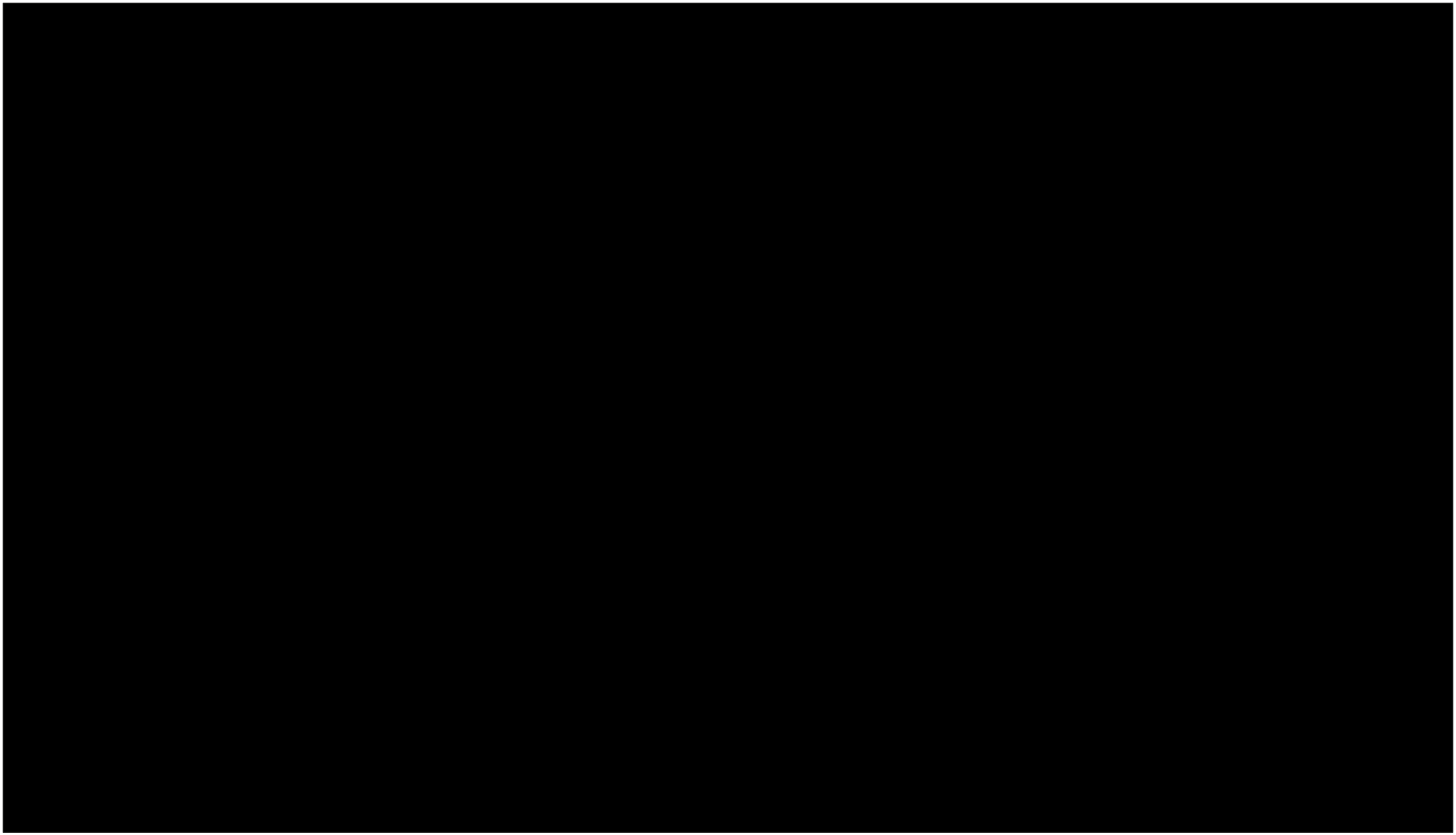
Cross over: IPCW and TSE - both uncertain;
OS: Exponential for both arms

Cross over adjustment	Median survival (months)		Hazard ratio
	Moga	Vor	
None	[redacted]	[redacted]	[redacted]
IPCW (Company preferred)		[redacted]	[redacted]
TSE (ERG preferred)		[redacted]	[redacted]

Issues 3a & 3b: Cross-over adjusted OS (severe disease from MAVORIC)



Issues 3a & 3b: Company preferred (IPCW, MOG: lognormal & SC: exponential)



Issues 3a & 3b: ERG preferred (TSE & exponential)

Slide amended post ACM 1

Issues 3a & 3b: OS for standard care arm

			Proportion alive, years (%)			
	Cross over	**Extrapolation**	**1**	**3**	**5**	**10**
MAVORIC	IPCW	Kaplan-Meier	44	39*	-	-
Company base case	IPCW	Exponential	67	31	14	2
Best statistical fit	IPCW	Generalised gamma	[redacted]	[redacted]	[redacted]	[redacted]
MAVORIC	TSE	Kaplan-Meier	78	51*	-	-
ERG preferred	TSE	Exponential	81	53	35	12
Observational data (table 27 in company submission)						
HES	NA	NA	57	31	25	-
Talpur 2012	NA	NA	91	68	51	34
Kim 2003	NA	NA	67	40	32	15
Agar 2010	NA	NA	-	-	37	22
Guideline	NA	NA			18-65	15-34

Company: Generalised gamma for standard care has long plateau – not realistic in UK

ERG: Clinical expert advice suggested TSE produced most clinically plausible OS estimates but all adjustment methods are biased (results vary vastly). Exponential best statistical fit for TSE. Population, treatment line & treatment differ in HES data

Company: HES data shows better expected survival compared with MAVORIC because there was a lower proportion with SS (47% in MAVORIC vs.7-15%) and stage IV disease (52% vs. 6-7%)

NICE

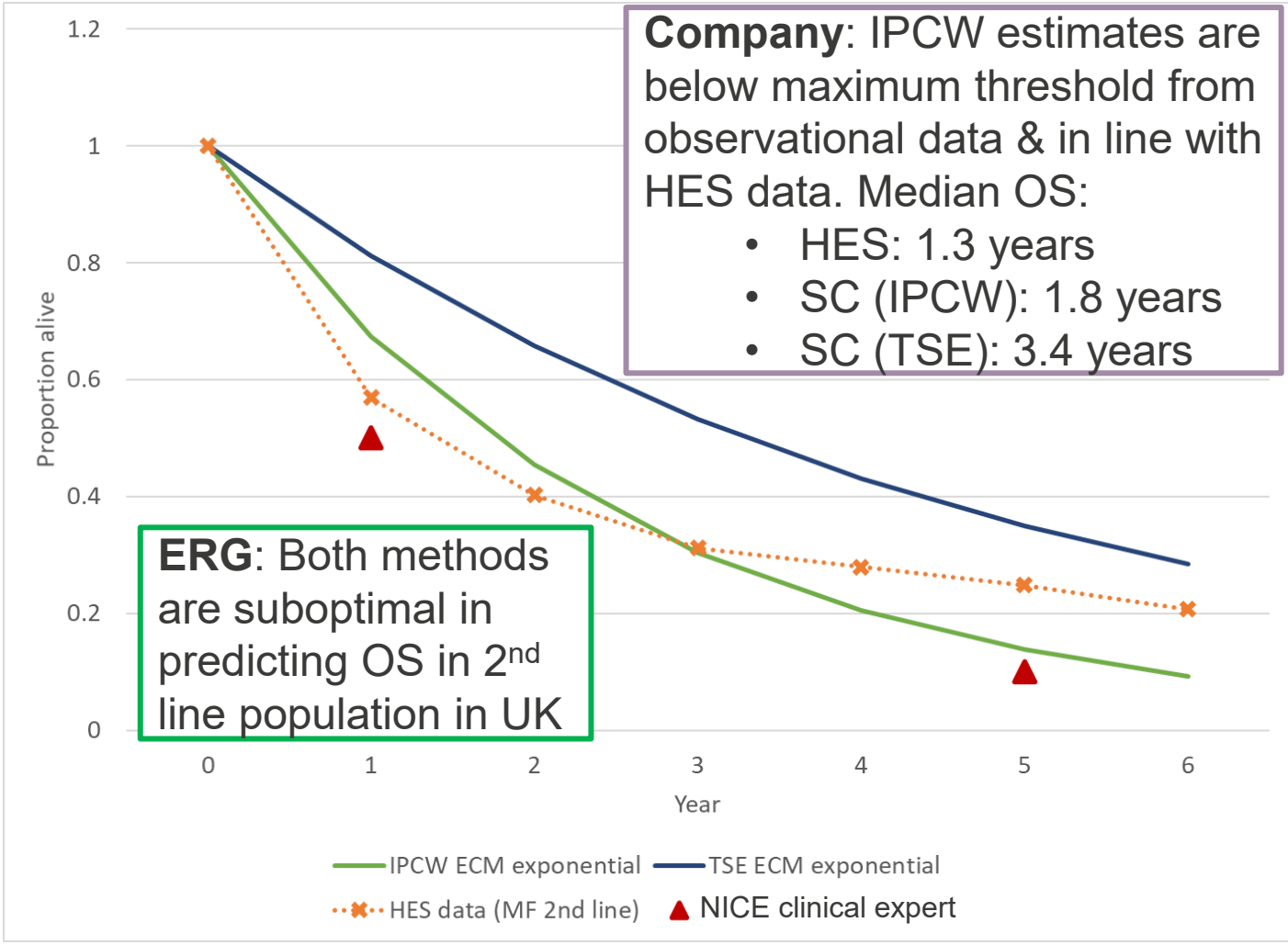
Which cross-over adjustment and OS extrapolation most closely estimates survival for people having standard care in NHS in England?

Slide amended post ACM 1

Issues 3a & 3b: Company's TE response - HES data

TE: Company asked to provide details of HES data and breakdown of OS data

Characteristic	MF	SS
Mean age at diagnosis	[redacted]	[redacted]
Male	[redacted]	[redacted]
Second line therapy		
SACT	[redacted]	[redacted]
Radiotherapy	[redacted]	[redacted]
Allogenic SCT	[redacted]	[redacted]
Other SCT	[redacted]	[redacted]
Skin phototherapy	[redacted]	[redacted]
Skin surgery	[redacted]	[redacted]



Company: IPCW estimates are below maximum threshold from observational data & in line with HES data. Median OS:

- HES: 1.3 years
- SC (IPCW): 1.8 years
- SC (TSE): 3.4 years

ERG: Both methods are suboptimal in predicting OS in 2nd line population in UK

	Year	1	2	3	4	5	6	7	8
Hospital episode statistics (HES)	MF (n=82)	57%	40%	31%	28%	25%	21%	21%	21%
	SS (n=14)	57%	49%	40%	40%	40%	10%	10%	-

Issue 5: Mogamulizumab stopping rule

TE question on if a 2-year stopping rule is clinically appropriate

Background

- No stopping rule in SPC or MAVORIC trial
- In MAVORIC [redacted] of patients in the subgroup with severe disease and [redacted] in the ITT population having moga at 2 years

Company

- Apply stopping rule based on clinical input and clinical benefits from MAVORIC
- Moga treatment effect with a stopping rule is likely to be similar to MAVORIC as only small proportion having treatment at 2 years
- Moga is disease-modifying and clinical advice suggests potential benefit after progression

Use 2-year stopping rule

Tech team

- No robust estimate of treatment effect for moga after treatment is stopped at 2 years
- Using 2 year stopping rule introduces additional uncertainty

2-year stopping rule is not evidence based

TE response:

- **1 clinical expert**: appropriate for most patients but some have disease that responds well for longer
- **Company**: use of stopping rule is in line with clinical expert opinion

Issue 6: Carer utility values

TE question on impact of MF & SS on carers and how this compares to other cancers

Background

- EQ-5D-3L data collected in MAVORIC
- Company's vignette study (n=100) was used to evaluate carer utilities. Vignettes were informed by a targeted review of qualitative studies of people with cutaneous T-cell lymphoma and/or their caregivers and interviews with specialists. Vignettes were scored by people from the general population and valued using the van Hout mapping algorithm

Tech team

- Methods used to derive carer utilities may not be robust → based on vignette and not in line with NICE methods guide (adds uncertainty)
- Larger impact on ICER with TSE

Prefer to exclude carer utility

Is it appropriate to remove carer utilities?

Company

- Vignette showed caregiver utility values lower in third-line vs. second-line treatment
- Conservative approach used → apply in disease control state only
- Base case includes carer utility gain for time spent in the disease control health state in the Moga arm

Include utility values for carers

TE response:

- **1 clinical expert**: huge burden on carers. Patients have painful, itchy, disfiguring lesions, often involving hands/ feet so affecting function and fear of cancer diagnosis with no widely available cure
- **Company**: use conservative approach (only applied to disease control health state)

Slide amended post ACM 1

End-of-life

TE: Company asked to provide data to address EOL criteria as this was not in submission

	Mogamulizumab		Vorinostat		Standard care		
	Mean OS months	Median OS months	Mean OS months	Median OS months	Mean OS months	Median OS months	**OS gain months**
MAVORIC severe disease	NA	[redacted]	NA	[redacted]	NA	NA	[redacted]
Company base case (IPCW)	101	NA	NA	NA	37	21	**64**
Tech team preferred	78	NA	NA	NA	33 to 59	NA	**19 to 45**
HES data	NA	NA	NA	NA	NR	MF: 18 SS: 12	NA

ERG: evidence suggests life expectancy >24 months & uncertainty around whether moga could be associated with >3 month OS gain as vorinostat is used as a proxy for standard care

Cost-effectiveness results (updated PAS)

	Incremental			ICER (£/QALY)
	Costs (£)	LYGs	QALYs	
1. Company revised base case (bexarotene as comparator & ↑ treatment duration)				
Mogamulizumab vs. SC	£72,736	3.69	2.83	£25,724
2. Revert to mixed comparator and resolved issues (ERG corrected errors, NTFS & DFS extrapolations, no aSCT after current treatment & use single utility for 'on treatment')				
Mogamulizumab vs. SC	£96,116	3.84	2.91	£33,048
3. Apply 2) and TSE cross-over adjustment instead of IPCW				
Mogamulizumab vs. SC	£77,444	2.10	1.72	£44,993
4. Apply 2) and exponential extrapolation for OS (both treatment arms)				
Mogamulizumab vs. SC	£85,849	2.83	2.21	£38,764
5. Apply 2) and remove 2 year stopping rule				
Mogamulizumab vs. SC	£109,139	3.84	2.91	£37,526
6. Apply 2) and remove carer utility				
Mogamulizumab vs. SC	£96,116	3.84	2.73	£35,194
7a. Tech team preferred upper threshold using TSE adjustment (apply 2 to 6)				
Mogamulizumab vs. SC	£80,201	1.09	0.85	**£94,250**
7b. Tech team preferred lower threshold using IPCW adjustment (apply 2, 4-6)				
Mogamulizumab vs. SC	£98,872	2.83	2.04	**£48,533**

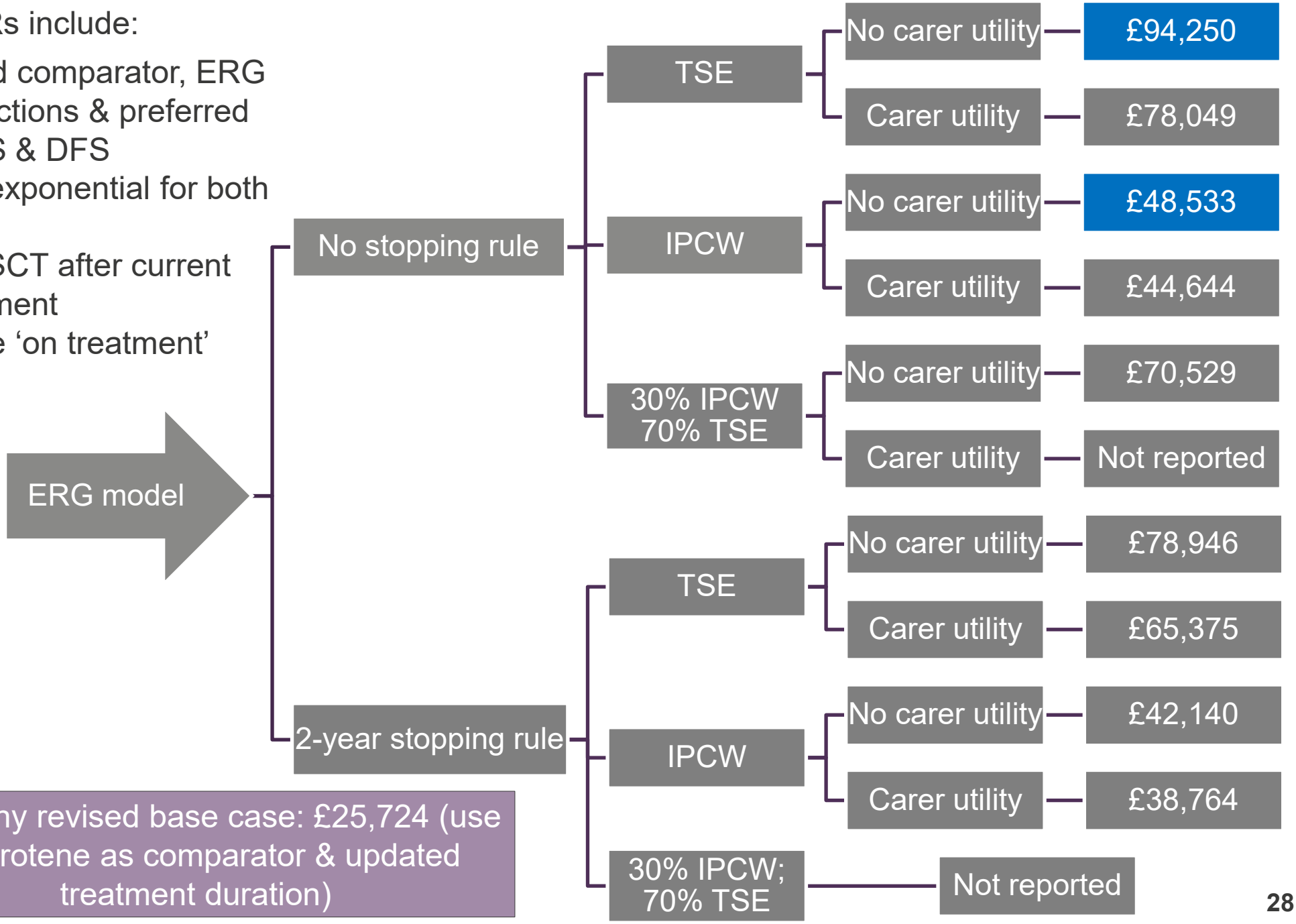
Company's new scenario post TE

- Company present new scenario in response to TE using alternative disease management costs:
  - Previously used a conservative approach with costs from TA577 but these could be overestimated
  - Lower costs used in HES database (no data for community-based costs)
  - **Scenario**: resource use from HES with updated current unit costs reduced the company's revised base case ICER from £25,724 to £22,512

Tech team scenarios

All ICERs include:

- Mixed comparator, ERG corrections & preferred NTFS & DFS
- OS: exponential for both arms
- no aSCT after current treatment
- single ‘on treatment’ utility



Company revised base case: £25,724 (use bexarotene as comparator & updated treatment duration)

Additional areas of uncertainty

From table 8 in technical report → these are areas of uncertainty that cannot be resolved. Committee should be aware of these when making its recommendations.

Issue	Why issue is important	Impact on ICER
Immature evidence base	Median overall survival in the trial has not yet been reached (23% of patients had OS event)	Unknown
Treatment effect for SC	The estimated treatment effect in the standard care arm is based on vorinostat (not licensed in the UK) – see issue 2	Unknown
Cross-over in MAVORIC	• 72% cross-over from vorinostat arm to Moga • Large variation in adjusted OS for SC • See issue 3a for details	The IPCW and TSE methods to adjust for cross-over are explored
Allogenic SCT	aSCT after current treatment was not allowed in MAVORIC and the treatment effect may differ if people had been allowed this. There are also issues around the use of fixed time points for aSCT and the clinical plausibility of the estimates used in the model.	Removing aSCT after current treatment has minimal impact on ICER but may not reflect clinical practice

Innovation, equality & CDF

Innovation

- The company considers mogamulizumab to be innovative.
  - The technical team considers that all relevant benefits associated with mogamulizumab are adequately captured in the model.

Equality

- The company submission does not identify any specific equalities considerations

Cancer Drugs Fund

- The company submission does not include CDF proposal
- CDF should be considered if:
  - Model is structurally robust for decision-making
  - There is plausible potential to be cost-effective
  - Further data collection would reduce clinical uncertainty

Key Issues

Model driver | Unknown impact | Small impact

Issue	Question for committee	Tech team	Impact
1. Population	• Do trial results adequately reflect company's proposed severe disease subgroup? • Are results from MAVORIC generalisable to the NHS in England? • Is it acceptable to use a population that includes mixed lines of treatment?	There is uncertainty from mixed lines of treatment	
2. Comparator	Is it appropriate to use bexarotene alone as a comparator?	Uncertain relative effectiveness as vorinostat not licensed/used in UK	
3a. Cross over	Which cross-over adjustment and OS extrapolation most closely estimates survival for people having standard care in the NHS in England?	Both IPCW & TSE plausible	
3b. Extrapolation		OS: exponential for both arms	
5. Stopping rule	Is a 2-year stopping rule appropriate?	Prefer to remove as not in SPC/trial	
6. Carer utility	Is it appropriate to remove carer utilities?	Prefer to remove caregiver utilities	
Other	End of life and Cancer drugs fund	-	