Ritlecitinib for treating severe alopecia areata in people 12 years and over

For public – contains no ACiC information (redacted)

Technology appraisal committee A [16 January 2024]

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Company: Pfizer

Supplementary slides

Recap of ACM1

NICE

Recap ACM1 (September 2023): Conclusions

Ritlecitinib is not recommended for severe alopecia areata in people 12 years and over

Model input	Committee preferred assumption (ACM1)
Treatment included in BSC states	Non-pharmacological treatments only (wigs)
Source of utilities	• EQ-5D utilities mapped from mild, moderate and severe disease values in Bewley et al. 2022 (Adelphi data) • Scenarios using ALLEGRO LT and ALLEGRO EQ-5D needed
Carer disutilities	Include disutility for carers of young people with severe alopecia areata
AT/AU prevalence weighting	Weighting proportion of people with AT/AU in model according to proportion in clinical practice (9.52%)
Adults and adolescent prevalence weighting	Weighting proportion of young people in model according to proportion in clinical practice is needed
Long-term transition matrices	Average transitions over final year for which data was available to estimate long-term treatment effect
Discontinuation rates	Exponential model to extrapolate time to treatment stopping

Recap ACM1: Cost effectiveness results with committee's preferred assumptions

Committee's preferred assumptions most closely matched the EAG scenario: including all the EAG's preferred assumptions plus weighting the proportion of people with AT/AU

Committee did not have the full set of analyses it wanted to see:

- scenarios including the trial EQ-5D data, and
- scenarios weighting proportion of young people according to clinical practice

Scenario on EAG base case	Incremental costs (£) versus BSC	Incremental QALYs versus BSC	ICER (£) versus BSC
Weighted average according to expected distribution of AT/AU (9.52%) and non-AT/AU	[redacted]	[redacted]	43,461

Committee agreed acceptable ICER would be towards the top of the range usually considered a cost-effective use of NHS resources (£20,000 - £30,000 per QALY)

No confidential discounts included in the model other than intervention PAS

Additional information requested following ACM1

Committee requested:

- To review the longest available EQ-5D data from ALLEGRO trials, according to SALT score health states
- Scenario analyses using longest available EQ-5D data from ALLEGRO
- Further evidence that EQ-5D performs poorly on tests of content validity and responsiveness from synthesis of peer-reviewed literature
- Further evidence to demonstrate that generic and condition-specific preference-based measures of health-related quality of life are not suitable for estimating utility values for use in the model
- Estimate for proportion of people in clinical practice who are young people
- Scenarios to show impact of different estimates of proportion of young people in model

Response to draft guidance consultation

- Company
- Alopecia UK
- British Association of Dermatologists (BAD) and BAD guideline development group
- 131 web comments

Company's response

No changes to company's preferred assumptions from ACM1

- Additional evidence shows EQ-5D and other generic measures are not suitable for AA and should not be used in the model
- ALLEGRO-LT long term EQ-5D data provided
- No scenarios using the ALLEGRO EQ-5D trial data are presented
- Supporting evidence for the estimated utility values in the company's vignettes
- Commented that a number of committee's preferred assumptions are conservative and thus the resulting ICERs are also conservative
- Increased PAS

Responses continued

Alopecia UK

- people with severe depression and suicide ideation were excluded from the key trial
- EQ-5D is an inappropriate measure for quality of life in AA

BAD & BAD guideline development group

- BSC should include pharmacological treatments
- EQ-5D lack validity for AA
- most people will likely want to continue JAK inhibitor treatment if it is working well
- psychological support is inconsistent across England and Wales

Responses continued

Web comments

- The impacts and costs to the NHS of AA are being significantly underestimated
- EQ-5D is not sensitive for AA & the measure of BSC used is not accurate
- Mental health implications are underestimated. AA can lead to suicide.
- AA impact on teenage children affect their abilities to reach their full potential.
- Mental health of carers of children can also be severely affected.
- Physical health implications and comorbidities need to be considered too.
- NICE has discriminated against people with AA. People with AA are let down by the healthcare system. No treatments for AA are available.
- NICE draft recommendation is not fair. It also creates a two-tier health care system where some can afford to fund the treatment privately and some cannot.

Key issues

NICE

Key issue: Utilities 1/2

Supplementary slides

ACM1: Adelphi EQ-5D utilities are preferred for decision-making

Company:EQ-5D and other generic measures not suitable for AA

- EAG and committee accept limitations ALLEGRO 2b/3 EQ-5D data
- ALLEGRO-LT 24-36 months EQ-5D data consistent with ALLEGRO 2b/3 from ACM1
- Post hoc psychometric evaluation of ALLEGRO-2b/3 EQ-5D and SF-36 data show EQ-5D and SF-36 are unresponsive to changes in AA related HRQoL.
- No condition-specific preference-based utility measures exist. Dermatology Life Quality Index (DLQI) not suitable. Alopecia Areata Patient Priority Outcomes (AAPPO) not preference based.
- Company's vignette results are valid and suitable for AA:
    - Extension study in AA patients: comparable with original vignette estimates
    - Proxy review study: atopic dermatitis utilities overlap with vignette estimates
- Bewley utilities underestimate the full benefits of ritlecitinib and are highly conservative
- Utility values from the full-text publication (Vañó-Galván et al) describing the European cohort from the Adelphi Database, previously described only in abstract form by Bewley et al, results in a small reduction of ICER
- Requested scenarios with ALLEGRO EQ-5D data not provided as not appropriate

Stakeholders: agree EQ-5D is not suitable for AA

Key issue: Utilities 2/2

Supplementary slides

EAG: evidence does not show that EQ-5D is not appropriate measure for AA

EAG: agrees ALLEGRO EQ-5D data not suitable due to long average duration since diagnosis and exclusion of patients with psychiatric comorbidities

- Given data limitations, not surprising that the psychometric report did not show EQ-5D data sensitive to changes in AA related HRQoL. Same issues for SF-36. Note, no SF-6D data were presented. The EQ-5D-Y may underestimate HRQoL impacts of AA for the 12-17 year old patients.
- AQoL-8D instrument is a promising generic measure of HRQoL, the company have not identified any AQoL-8D based estimates in the literature that can be used.
- Vignette study is flawed: same issues as with the original study; unvalidated video conference method for TTO; general population valuation of vignettes is preferred.
- Adelphi data are sensitive to changes in AA related HRQoL: the usual activity domain was statistically significantly associated with physician rated AA severity. Also 29% participants scored ≥11 on the HADs scale for anxiety and 27% for depression.
- Did not critique proxy utilities in atopic dermatitis as EQ-5D utility from literature is suitable.
- Provided scenarios with EQ-5D data from ALLEGRO LT (large increase in ICERs)
- Used the published Adelphi data (Vañó-Galván) in its preferred base case

Does committee still consider the Adelphi EQ-5D Bewley utilities the most appropriate for decision-making?

Other issues: 1/3

Supplementary slides

Company: proportion of young people is a conservative assumption

ACM1	Weighting of young people according to clinical practice is needed.
Company	• The diagnosed point prevalence of AA is 0.58% and [redacted]% amongst adults and adolescents respectively (based on Oxford-Royal College of GPs estimates). This results in an estimate of 4.91% for adolescents with AA, and a scenario with this weighting is included. • But clinical experts at ACM1 advised that in clinical practice they have more adolescents than 14.6% observed in ALLEGRO 2b/3. If the ICER was weighted in line with the clinical experts' opinion, the ICER would be lower.
EAG	• Company's prevalence estimates for all AA and not severe AA – uncertainty remains in proportion of people with severe AA who are young people • Company did not provide any alternative estimates higher than 14.6%.

Is the value of 4.91% for adolescents with severe AA, reflective of what is seen in clinical practice?

Other issues: 2/3

Supplementary slides

Company: BSC without pharmacological treatments is a conservative assumption

ACM1	Given the inconsistent use of pharmacological treatments and the uncertainty around use after ritlecitinib, only non-pharmacological treatments were included (wigs) (Company stated only non-pharmacological treatment as comparator in CS)
Company	• Pharmacological treatments accepted in TA926 and in clinical opinion • Present new scenarios including 'basket' of pharmacological treatments (based on Adelphi Disease Specific Programme & UK Key Opinion Leader data). Some assume the same use in both arms and some assume less use after ritlecitinib.
Stake-holders	• Some agreed that BSC care should include pharmacological treatments • Data from ADAAGIO study are available
EAG	• ACM1 CS states most patients with severe AA have no pharmacological treatment • If high proportion have pharmacological treatments, then ALLEGRO placebo data not appropriate for estimating expected costs and benefits • Notes TA926 assumed the same BSC use in both arms. • All BSC scenarios uncertain, e.g. ADAAGIO data are different, 10-year treatment duration is too long, only cost and no effectiveness included for BSC.

NICE  Is BSC without pharmacological treatments suitable for decision making?

Other issues: 3/3

Supplementary slides

Company: time on treatment used in model is a conservative assumption

ACM1	Average transitions for patients remaining on treatment and exponential discontinuation rate
Company	• Prefers using stay in state and Weibull curve: • Average time on treatment <3 years inconsistent with ALLEGRO-LT • Scenarios with time on treatment [redacted] years based on stay in state effectiveness assumption and different discontinuation rates curves
Stakeholders	• Most people will likely want to continue treatment if it is working well
EAG	• Choice between steady state or average transitions rather than choice of discontinuation curve has large effect on ICERs • No new evidence submitted to support steady state, so no changes made • Using ACM1 assumptions, average time on treatment is 2.89 years - including all ritlecitinib patients, value for responders (about [redacted]) is higher. • Almost [redacted] participants in ALLEGRO-LT were recruited de novo

Does using the average transitions and exponential discontinuation rates best reflect time on treatment?

Equality considerations

Supplementary slides

ACM1: Committee considered

- some people with severe alopecia areata may be more affected by the psychological impact of hair loss because of the religious significance of hair
- severe alopecia areata can have a particularly high impact on psychosocial health and quality of life for young people

Alopecia UK, BAD and web comments

- severe AA is three times more likely in those with Asian/African ethnicity
- severe AA is associated with ‘severe physical disfigurement’ (UK Disability and Equality Act 2010)
- AA incidence is higher in patients from areas of social deprivation and non-white ethnicity groups, whose hair can have a cultural significance
- women with autoimmune skin conditions including alopecia are at higher risk of spontaneous abortions than controls

Cost effectiveness results

Supplementary slides

Company: updated base-case and key scenarios

Using the company's original assumptions but with new PAS

Company's deterministic result with updated PAS (comparisons versus BSC)	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Company base case: **1. vignette utilities** **2. staying in state until discontinuation** **3. Discontinuation rates: Weibull curve** **4. no weighting (AT/AU prevalence or age)**	[redacted]	[redacted]	8,294
• using new vignette TTO of patients with AA	[redacted]	[redacted]	7,767
• using atopic dermatitis utilities	[redacted]	[redacted]	17,973
• with carers for adults	[redacted]	[redacted]	7,685
• adolescents only population	[redacted]	[redacted]	7,986
• BSC: pharmacological txt - same in both arms	[redacted]	[redacted]	6,322 to 6,743
• BSC: pharmacological txt - less use ritlecitinib	[redacted]	[redacted]	74 to 5,105

Supplementary slides

Company: committee's ACM1 preferred assumptions with new PAS

Deterministic result with updated PAS (comparisons versus BSC)	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Committee's ACM1 preferred base case: **1. Bewley abstract utilities** **2. long-term transition: average transition matrices** **3. Discontinuation rates: exponential curve** **4. Weighted by AT/AU prevalence (9.52% AT/AU)***	[redacted]	[redacted]	25,626
• **Weighted by age (4.91% adolescent)***	[redacted]	[redacted]	29,988
• **Unweighted (no AT/AU prevalence or age)**	[redacted]	[redacted]	28,633
• **Bewley published utilities & unweighted**	[redacted]	[redacted]	28,367
• time on treatment [redacted] years based on **stay in state and different discontinuation rates curves**, unweighted (no AT/AU prevalence or age)	[redacted]	[redacted]	23,914 - 28,633

***Note:** it is not possible to weight ICER by age + AT/AU prevalence status simultaneously

EAG's preferred base case and scenarios

Supplementary slides

Deterministic result with updated PAS (comparisons versus BSC)		Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
EAG's ACM2 preferred base case: **1. Bewley published manuscript utilities** **2. average transition matrices** **3. Discontinuation rates: exponential curve** **4. Weighted by AT/AU prevalence (9.52% AT/AU)**		[redacted]	[redacted]	25,406
• **Weighted by age (4.91% adolescent)**		[redacted]	[redacted]	29,679
• **Weighted by age PROBABILISTIC**		[redacted]	[redacted]	30,407
• Unweighted (no AT/AU prevalence or age)		[redacted]	[redacted]	28,367
• Adolescents only subgroup (100% adolescent)		[redacted]	[redacted]	25,665
• BSC: pharmacological txt - same in both arms – Adelphi scenario & unweighted	10 years	[redacted]	[redacted]	24,145
	2 years	NR	NR	27,726
• EQ-5D ALLEGRO LT utilities & weighted by AT/AU		[redacted]	[redacted]	£130,335

Summary – key questions

Cost-effectiveness results

Supplementary slides summary

Utilities:

- Does it still consider the Adelphi EQ-5D Bewley utilities the most appropriate for decision-making? link to issues slides

Are committee's preferred assumptions conservative:

- Is the value of 4.91% for adolescents with severe AA, reflective of what is seen in clinical practice? link to issues slides
- Is BSC without pharmacological treatments suitable for decision making? link to issues slides
- Does using the average transitions and exponential discontinuation rates best reflect time on treatment? link to issues slides

Summary – key questions

Supplementary slides

- Recap ACM1: slides 24 & 25
- Recap key clinical trials: slides 26-28
- Summary of company's new evidence: slide 29
- Recap of the company's original vignettes study: slides 30 & 31
- Utilities: slides 32 – 34
- Proportion of young people: slide 35
- BSC: slide 36 & 37
- Time on treatment: slides 38 - 41

Abbreviations

AAPPO

Alopecia areata patient priority outcomes

AE

Adverse event

AIC/BIC

Akaike/Bayesian information Criterion

AFT

Accelerated failure time

AT

Alopecia totalis

AU

Alopecia universalis

BSC

Best supportive care

CI

Confidence interval

EBA

Eyebrow assessment

ELA

Eyelash assessment

FDG

Final draft guidance

ICER

Incremental cost effectiveness ratio

KM

Kaplan Meier

RCT

Randomised controlled trial

SALT

Severity of Alopecia Tool

TEAEs

Treatment-emergent adverse events

TTO

Time trade off

VAS

Visual analogue scale

ACM1: Innovation and uncaptured benefit conclusion

ICER would be towards the top of the range

- No licensed treatments for severe alopecia areata available on the NHS.
- A large unmet need for a new treatment that specifically targets the condition.
- Ritlecitinib is innovative in that it has a different mechanism of action to other treatments used in the NHS. Also, unlike other treatments, it targets hair regrowth in areas of the body other than the scalp, which is an important outcome for people with the condition.
- The committee accepted that there were likely to be uncaptured benefits in any measure of health-related quality of life for severe alopecia areata.
- Agreed that an acceptable ICER would be towards the top of the range usually considered a cost-effective use of NHS resources.

ACM1: Equality considerations

3.22 The committee considered that some people with severe alopecia areata may be more affected by the psychological impact of hair loss because of the religious significance of hair. Clinical and patient experts also explained that severe alopecia areata can have a particularly high impact on psychosocial health and quality of life for young people. Religion and age are protected characteristics under the Equality Act 2010. However, given that the cost-effectiveness estimates preferred by the committee were not within the range usually considered a cost-effective use of NHS resources, including those for the subgroup of young people aged 12 to 17 years, the committee was unable to make recommendations for these groups.

Recap: Key clinical trials: ALLEGRO 2b/3

Supplementary slides summary

	ALLEGRO 2b/3
Design	RCT
Population	• People aged ≥12 with severe AA (SALT ≥50) • Current episode ≤10 years • No evidence of re-growth within previous 6 months
Intervention	Subgroup of interest: ritlecitinib 50mg (licensed dose) once daily (n=130)
Comparator	Placebo (2 arms: dose escalation [200/50mg] (n=65) + continuous dose [50mg]) (n=66)
Duration	Placebo controlled: 24 weeks; total: 48 weeks
Primary outcome	Response rate based on SALT ≤20 at week 24
Key secondary outcomes	SALT ≤20 at week 48; SALT ≤10 at week 24 and 48; patient's global impression of change; eyebrow and eyelash assessment; HRQoL
Locations	155 sites globally (10 in the UK)
Use in model	Informs health state occupancy for ritlecitinib (48 weeks) and best supportive care (24 weeks)

Recap: Key clinical trials: ALLEGRO-LT

Supplementary slides summary

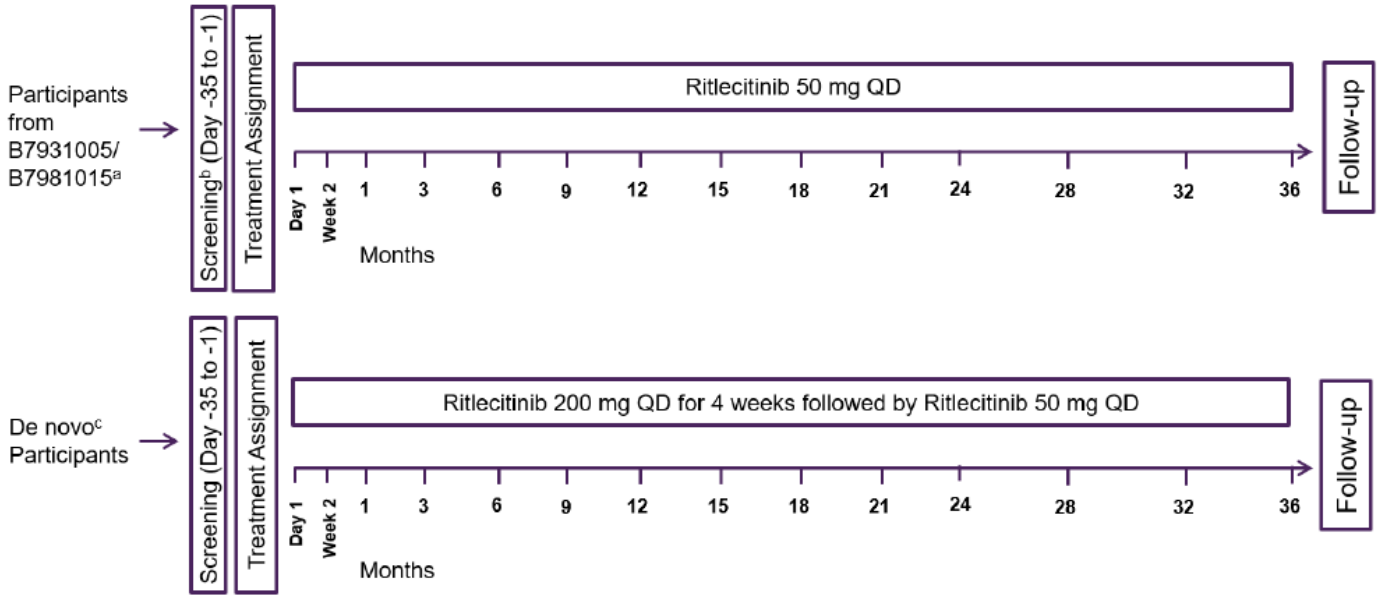
	ALLEGRO-LT
Design	Single-arm, open-label, long-term study
Population	• Participants exiting ALLEGRO 2a* or 2b/3 plus *de novo* participants • People aged ≥12 with SALT score ≥25 (*de novo* population) • Current episode ≤10 years
Intervention	ALLEGRO 2a or 2b/3 roll-over: ritlecitinib 50mg once daily De novo: ritlecitinib 200mg 4 week loading dose followed by 50mg once daily
Duration	36 months
Primary outcome	Incidence of adverse events (including serious AEs and AEs leading to discontinuation)
Secondary outcome	Response rate based on SALT ≤20
Locations	148 sites globally (4 in the UK)
Use in model	Informs health state occupancy from week 48 for those who continue ritlecitinib

*ALLEGRO 2a: proof of concept study

Supplementary slides summary

Recap: ALLEGRO-LT – design & participants flow

[redacted] of the participants in ALLEGRO-LT were newly recruited



QD = once daily

a. Participants originating from Study B7931005 or B7981015 were defined as those who received study intervention in one of these studies.

b. Participants with ≤30 days between the first study visit in B7981032 and the last dose in Study B7981015 did not require a screening period.

c. De novo participants are defined as those who did not previously receive study intervention in Study B7931005 or B7981015; this includes, but is not limited to, those consented and screened for Study B7931005 or B7981015 but who did not receive study intervention in one of these studies.

- [redacted] participants were assigned to treatment and treated.
- [redacted] participants were rolled over from ALLEGRO 2b/3 ([redacted]) and ALLEGRO 2a ([redacted])
- [redacted] participants were de novo

Summary of the additional evidence submitted in the company's response to the DG

- Long-term follow-up data from ALLEGRO LT for the EQ-5D
- EQ-5D from ALLEGRO 2b/3 and ALLEGRO LT stratified by SALT score to align with the definition of the health states in the economic analysis
- Assessment of the psychometric performance of EQ-5D and SF-36 from ALLEGRO
- Review of studies in AA reporting EQ-5D, SF-36 and DLQI
- Vignette study in a cohort of patients with AA
- A multicomponent scoping review to describe utility values for atopic dermatitis and their suitability for use as a proxy condition for utilities in AA
- Cost-effectiveness scenario analyses:
    - incorporating alternative utility values
    - exploring the impact of including pharmacological treatment within BSC
    - exploring different approaches to estimate time on treatment

Supplementary slides summary

Recap: Utilities – company's vignette approach 1/2

EAG: analysis based on vignette should be treated with caution

Company's vignette approach

1. Draft vignettes – informed by QoL data in ALLERGRO 2b/3, patient interviews (3 adults, 3 adolescents, 5 carers) and lit review

2a. Patient feedback on draft vignette (5 adults, 5 carers and 4 healthcare professionals)
2b. Vignettes for 4 SALT score ranges developed

3. Vignettes reviewed and rated by UK general public using TTO (n=120) and utilities estimated for each health state

EAG comments

Best practice methods for vignette development followed, but concerns around:

- vignettes don't report absence of symptoms unaffected by AA such as self-care and mobility - may lead to overestimation of importance of condition-specific symptoms by general public in TTO
- patients interviewed required to have had specific treatments or be interested in systemic treatment – doesn't capture people not actively seeking treatment who may have lower HRQoL impact from severe AA
- vignettes lack face validity compared with data in ALLEGRO 2b/3 (see next slide)

Supplementary slides summary

Recap: Utilities – company's vignette approach 2/2

EAG: vignettes lack face validity compared with ALLEGRO 2b/3 data

Comparison of vignette for person with SALT 50-100 and responses to HRQoL AAPPO questionnaire in ALLEGRO 2b/3 in SALT 50-100 population

Vignette SALT 50-100	ALLEGRO 2b/3 AAPPO item response SALT 50-100	
[redacted]	**Over the past week, how often did you feel embarrassed about your hair loss?**	Never/ rarely: [redacted] Sometimes: [redacted] Often/ always: [redacted]
[redacted]	**Over the past week, how often did you feel frustrated about your hair loss?**	Never/ rarely: [redacted] Sometimes: [redacted] Often/ always: [redacted]
[redacted]	**Over the past week, how much did you limit your exercise or other physical activity because of your hair loss?**	Not at all/ a little: [redacted] Moderately: [redacted] A great deal/ completely: [redacted]

Supplementary slides summary

ACM1: Utilities

Committee concluded Adelphi EQ-5D utilities are appropriate for decision-making, but asked for more evidence

Company

- general issues with EQ-5D as EQ-5D lacks content validity and is insensitive in AA
- issues with key trial EQ-5D: ceiling effect
- issues with Adelphi EQ-5D (Bewley et al 2022), e.g. not aligned with model states
- uses its vignette study to estimate utilities for each health state

ACM1 committee's conclusion:

- not sufficient evidence that EQ-5D is inappropriate measure for AA
- concerns about the validity of company's vignette study
- other types of utilities should be considered before vignettes
- based on the evidence presented, it considered that the utility values estimated from the Bewley et al. study were the most appropriate to include in the model.
- wants to see scenario analyses using EQ-5D from ALLEGRO LT and ALLEGRO trials.

Supplementary slides summary

ACM2: new evidence from ALLEGRO-LT

Company:

- no difference in utility estimates overtime between the ALLEGRO 2b/3 (up to 48 weeks) and ALLEGRO-LT (24 months)
- results are inconsistent with the acknowledged impact on quality of life for patients with severe AA

Mixed model regression utility estimates ALLEGRO 2b/3 48 weeks (Adults only)

Covariate	Utility Weight	Standard error
SALT 50-100	[redacted]	[redacted]
SALT 21-49	[redacted]	[redacted]
SALT 11-20	[redacted]	[redacted]
SALT 0-10	[redacted]	[redacted]

Mixed model regression utility estimates ALLEGRO-LT 24 months (Adults only)

Covariate	Utility Weight	Standard error
SALT 50-100	[redacted]	[redacted]
SALT 21-49	[redacted]	[redacted]
SALT 11-20	[redacted]	[redacted]
SALT 0-10	[redacted]	[redacted]

Supplementary slides summary

ACM2: Alternative utility values applied in the model

EAG's scenario analyses – modified table 1 in critique of DG responses

Health state	Vignettes general populatio	Vignettes in patients with AA	Adelphi Bewley	Adeplhi Vañó-Galván	Allegro 2b/3 48 weeks	Allegro LT 24 months	Atopic dermatitis
SALT 50-100	[redacted]	[redacted]	0.78	0.77	[redacted]	[redacted]	0.67
SALT 21-49	[redacted]	[redacted]	0.85	0.85	[redacted]	[redacted]	0.78
SALT 11-20	[redacted]	[redacted]	0.90	0.89	[redacted]	[redacted]	0.83
SALT 0-10	[redacted]	[redacted]	0.90	0.89	[redacted]	[redacted]	0.83
Caregiver to adolescent	[redacted]	[redacted]	NR - values from the vignettes in general population used.				
ICER committee's DG preferences unweighted	£10,192	£9,320	£28,633	£28,367	£120,970	£142,860	£21,542
ICER committee's DG preferences weighted by AT/AU severity	NR	NR	NR	£25,406	NR	£130,335	NR

Supplementary slides summary

ACM2: EAG critique of company's updated analyses

- Small decrease in proportion of young people from 4.91% to 4.65% = ICER £30,000
- Upper limit to a threshold analysis (0% adolescents) = ICER £30,249

Result with updated PAS (comparisons versus BSC)	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Deterministic results (no AT/AU weighting included)			
Weighted by 4.91% adolescents	[redacted]	[redacted]	29,986*
Weighted by 4.65% adolescents	[redacted]	[redacted]	30,000
All ≥18 years (0% adolescents)	[redacted]	[redacted]	30,249
Probabilistic results (no AT/AU weighting included)			
Weighted by 4.91% adolescents	[redacted]	[redacted]	£30,407

*reported as £29,988 in company analyses

Supplementary slides summary

Company ACM2 scenarios: drug acquisition cost for BSC

Reduction to costs applied to patients receiving ritlecitinib	Ritlecitinib (£)	BSC (£)
Adelphi Disease Specific Programme (88% receiving BSC)		
0%	261.12	261.12
25%	195.84	261.12
50%	130.56	261.12
75%	65.28	261.12
UK Key Opinion Leader (87% receiving BSC)		
0%	328.27	328.27
25%	246.21	328.27
50%	164.14	328.27
75%	82.07	328.27

Supplementary slides summary

EAG: ACM2 scenario analyses around BSC

EAG's scenario analyses – modified table 2 in critique of DG responses

Scenarios in full population - not weighted by age or AU/AT severity:

Source of BSC treatment mix		difference between arms	10 years of BSC		2 years of BSC
			Unweighted	Weighted by AU/AT severity	
No pharmacological BSC		NA	£28,633	£21,457	£28,633
Adelphi Disease Specific Programme • 88% have pharmacological BSC		0%	£24,371	NR	£27,726
		25%	£14,158	NR	£25,553
		50%	£3,946	NR	£23,381
		75%	Dominates	NR	£21,207
UK key opinion leader • 87% have pharmacological BSC		0%	£23,213	NR	£27,480
		25%	£10,227	NR	£24,717
		50%	Dominates	NR	£21,954
		75%	Dominates	NR	£19,191
only 30% having BSC in both arms	Adelphi	0%	£27,180	NR	£28,324
	UK	0%	£26,764	NR	£28,235

Supplementary slides summary

ACM2: Company - time on treatment 1/2

Company:

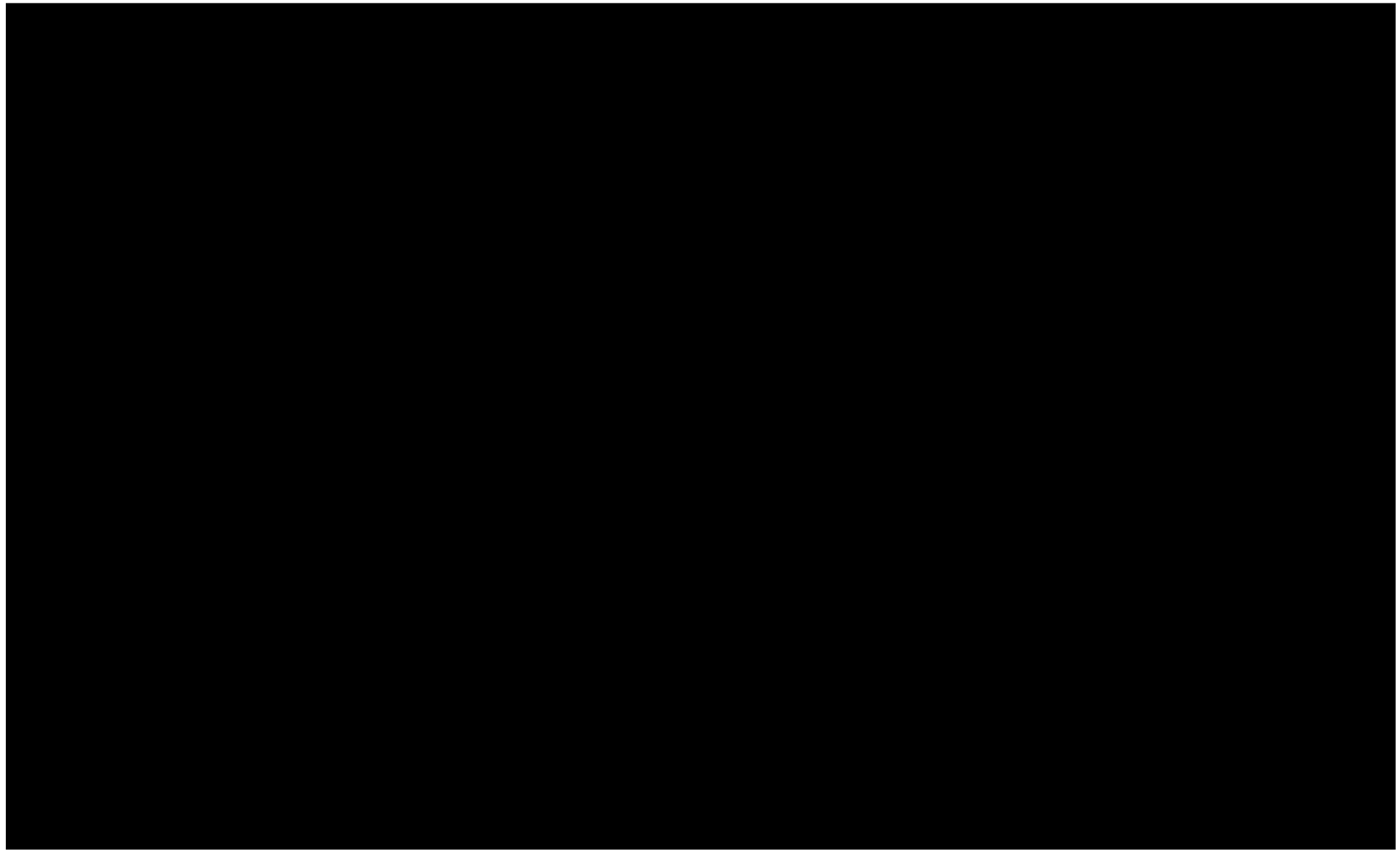
- Data from the ALLEGRO-LT study supports stabilisation of the proportion of patients achieving a response
- more appropriate estimation of time on treatment is stay in state as there is no evidence of treatment waning in patients who are responding and is the most appropriate assumption based on clinical opinion

Figure: ALLEGRO-LT: Response Based on SALT ≤ 20 up to Month 24 (Interim Analysis Selected cohorts, 50 mg dose).

Supplementary slides summary

ACM2: Company - time on treatment 2/2

Figure: Time on treatment based on assumption of treatment waning and long term discontinuation combined.

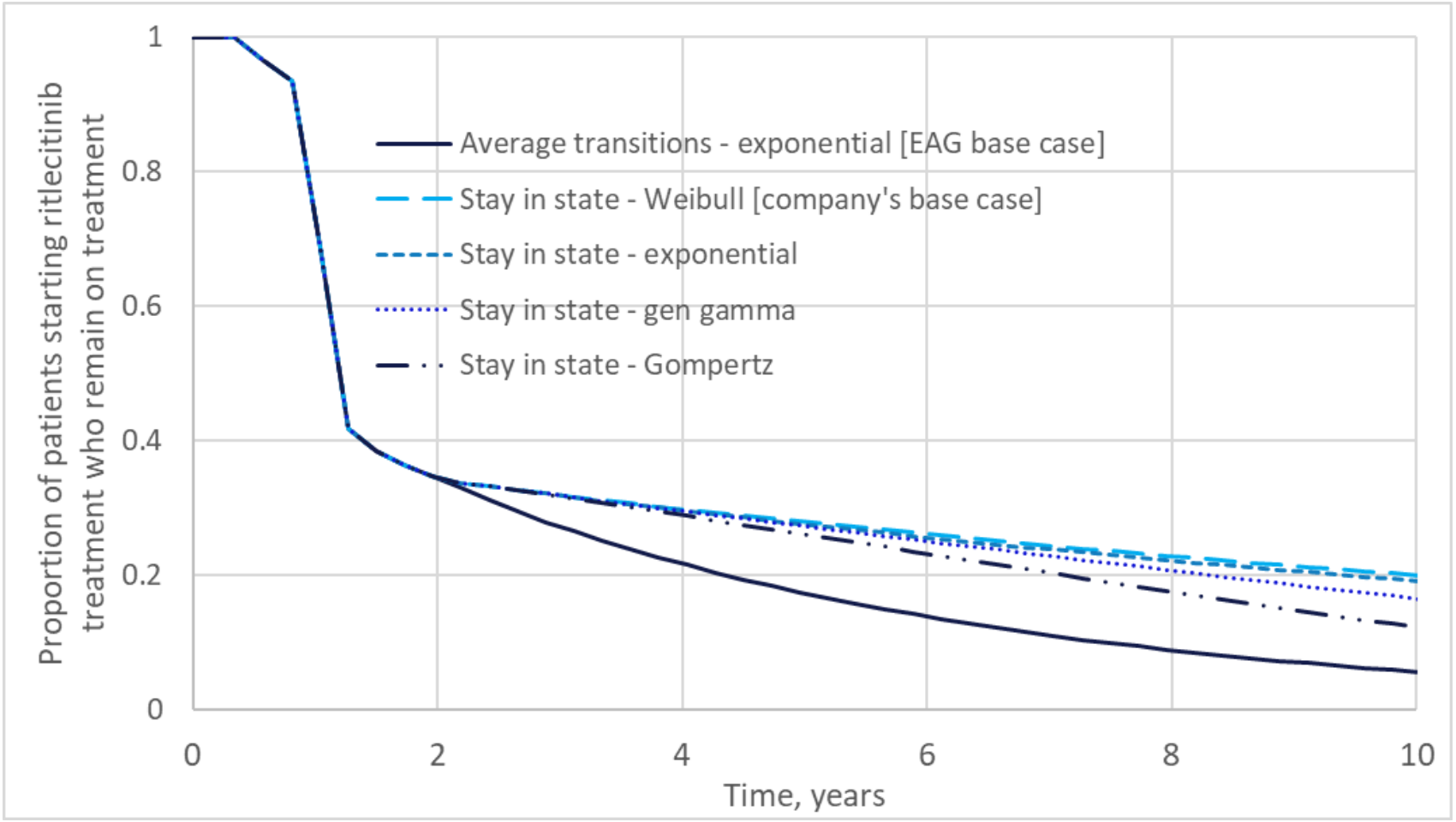


Supplementary slides summary

ACM2: EAG – company's scenarios time on treatment 1/2

Choice between steady state or average transitions, rather than choice of discontinuation curve has large effect on ICERs.

Figure: Proportion of patients remaining on ritlecitinib under different assumptions regarding treatment waning (steady state or average transitions) and discontinuation in those who continue to respond (various parametric extrapolations)



Supplementary slides summary

ACM2: EAG – company's scenarios time on treatment 2/2

Recap of critique of assumption of lack of waning (Key issue 3 in EAG report)

EAG

- No new evidence provided
- Stay in state approach assumes no treatment effect waning
- Assumption of no treatment waning is poorly supported
- Limited follow-up in ALLEGRO-LT so hard to verify long term effect
- Unclear how missing data has been dealt with in interim analysis – appears to be treated as missing at random
- High proportion of missing data at 24 months ([redacted] of cohort who started on 50mg dose missing) – less complete data beyond 24 months means if assume missing data is due to non-responders, proportion of responders falls after 24 months
- Prefers to use average transition matrices from second year of treatment to estimate long term outcomes for people remaining on treatment after 96 weeks