Public observer slides – no ACIC information

Lead team presentation

Brodalumab for treating moderate to severe plaque psoriasis in adults [ID878]

1st Appraisal Committee meeting

Committee B

Chair: Amanda Adler

Lead team: Mark Chapman, Dani Preedy, Steve Smith

ERG: York Centre for Reviews and Dissemination

NICE technical team: Sharlene Ting, Ahmed Elsada

4th January 2018

Summary of evidence

Clinical effectiveness

AMAGINE randomised trials

- brodalumab *vs.* placebo and *vs.* ustekinumab: more people on brodalumab achieve PASI 75 at 12 weeks (and quicker) and maintain it up to 52 weeks

Network meta-analysis results after 10, 12 or 16 weeks depending on comparator

- brodalumab *vs.* all other treatments (apremilast, dimethyl fumarate, biologics): 2nd highest probability after ixekizumab of achieving PASI 75

Cost effectiveness

Presented in part 2 (confidential patient access schemes for apremilast, brodalumab, ixekizumab and secukinumab)

Background

Psoriasis

- common chronic inflammatory disease
- characterised by red, thick and scaly plaques on the skin
  - ❖ most common form: plaque psoriasis

Brodalumab (Kyntheum, Leo Pharma)

- recombinant, fully human monoclonal immunoglobulin IgG2 antibody
- binds to interleukin-17 receptor-A
- inhibits inflammation
- **Marketing authorisation:** "moderate to severe plaque psoriasis in adults who are candidates for systemic therapy“
- Administration by subcutaneous injection. Dose:
  - ❖ **Weeks 1-3:** 210 mg every week
  - ❖ **Weeks 4 onwards:** 210 mg every 2 weeks
    - ➢ If no response, stop treatment after 12 to 16 weeks
    - ➢ If partial response, may see improvement after 16 weeks

Patient and clinical perspective

Distressing and debilitating, need for a range of highly effective convenient treatments with minimal adverse reactions and impact on lifestyle

Impact of psoriasis

- can be distressing at all levels of severity
- affects all aspects of life: physical, psychological, social, financial
- topical medicines and phototherapy are inconvenient

People would like

- range of effective options (people respond differently to treatments)
- reduces symptoms immediately
- no adverse reactions
- limited impact on lifestyle
- targets high impact sites

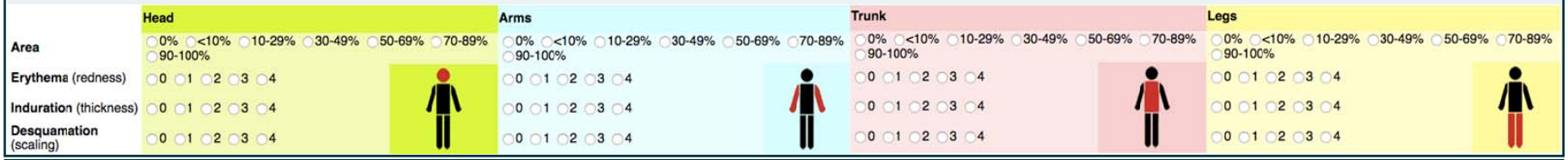
Brodalumab

- different mechanism of action
- very effective in clinical trials
- similar safety profile to other interleukin-17 inhibitors
- administration similar to other biologics

Measuring clinical effectiveness

Psoriasis Area and Severity Index (PASI)

- Weighted score (0 to 72) of 4 affected areas
  - ❖ 0 (no psoriasis); 10 (moderate); >10 (severe)
- Response considered as PASI 50, PASI 75, PASI 90, PASI 100
  - ❖ PASI 75: ≥75% reduction in PASI score from baseline (clinically important difference according to British Association of Dermatologists guidelines)
  - ❖ PASI 100: 100% reduction in PASI score (i.e. to 0)



Static Physician Global Assessment (sPGA)

- measure physician's impression of patient's psoriasis based on severity of induration, scaling and erythema
- score: 0 (clear), 1 (almost clear) to 5 (severe)

Dermatology Life Quality Index (DLQI)

- 10 questions scored 0 to 3 (worst impact): symptoms and feelings, daily activities, leisure, work and school, personal relationships and treatment
- range from 0 to 30
- 5 point improvement (clinically important difference)
- DLQI 0 or 1: psoriasis has no effect on life at a specific visit

Company's positioning of brodalumab

1st

Topical therapy
corticosteroid, vitamin D, vitamin D analogues, coal tar

2nd

Phototherapy
ultraviolet B (narrow and broad band), psoralen + ultraviolet A [PUVA]

3rd

Systemic non-biological therapy
methotrexate, ciclosporin, acitretin

4th

Systemic biological therapy
Severe (PASI ≥10 & DLQI >10)
adalimumab (TA146)
etanercept (TA103)
ixekizumab (TA442)
secukinumab (TA350)
ustekinumab (TA180)

Very severe
(PASI ≥20 & DLQI >18)
infliximab (TA134)

Severe (PASI ≥10 & DLQI >10)
apremilast (TA419)
dimethyl fumarate (TA475)

Brodalumab for moderate to severe psoriasis?

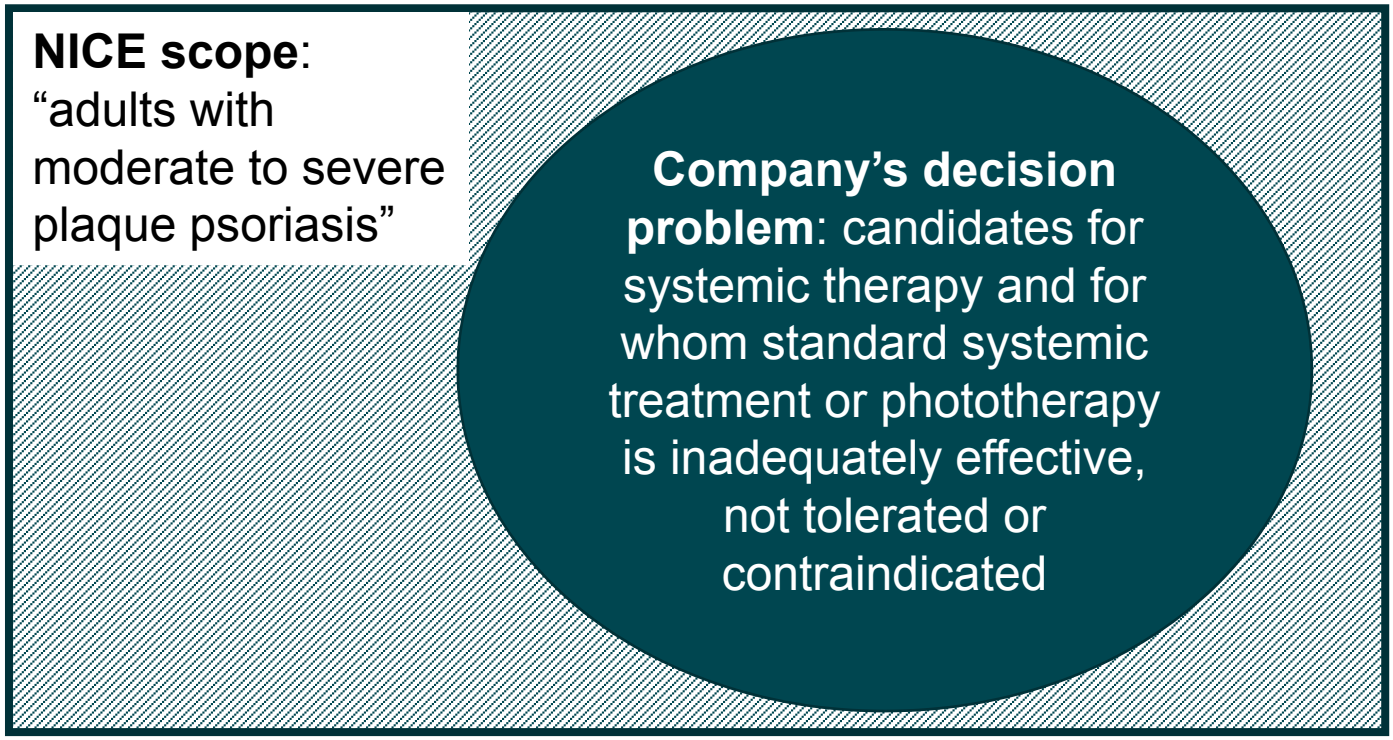
LEGEND
TNF-α inhibitor
IL-17 inhibitor
IL-12/IL-23 inhibitor
PDE-4 inhibitor
Th1 and Th17 → Th2

BSC

Best supportive care

Decision problem – population

Company focuses on narrower population than NICE scope which reflects likely position of brodalumab in NHS clinical practice



ERG comments:

- Company's decision problem appropriate and reflects likely position of brodalumab in NHS
- 17-35% of patients in AMAGINE trials had no prior systemic therapy or phototherapy

❖ ***Where would brodalumab fit in the treatment pathway?***

Decision problem – intervention and comparators

	NICE scope	Company's decision problem
Intervention	Brodalumab	Brodalumab in a treatment sequence followed by ustekinumab then secukinumab then BSC
Comparators	• TNF-alpha inhibitors (adalimumab, etanercept, infliximab) • IL-17 inhibitors (ixekizumab, secukinumab) • ustekinumab • apremilast • dimethyl fumarate • best supportive care (BSC)	9 treatment sequences changing what goes 1st; mostly ustekinumab is 2nd and secukinumab is 3rd

Sequence	1st	2nd	3rd	4th
1	**Brodalumab**	Ustekinumab	Secukinumab	BSC
2	Adalimumab	Ustekinumab	Secukinumab	BSC
3	Apremilast	Ustekinumab	Secukinumab	BSC
4	Dimethyl fumarate	Ustekinumab	Secukinumab	BSC
5	Etanercept	Ustekinumab	Secukinumab	BSC
6	Infliximab	Ustekinumab	Secukinumab	BSC
7	Ixekizumab	Ustekinumab	Secukinumab	BSC
8	Secukinumab	Ustekinumab	Adalimumab	BSC
9	Ustekinumab	Adalimumab	Secukinumab	BSC

❖ ***Is it more appropriate to compare***
- ➢ ***brodalumab to other individual treatments, or***
- ➢ ***specific sequences of treatments with and without brodalumab?***

Company clinical evidence

- **3 Phase III randomised controlled trials + open-label extension studies for all trials**
  - AMAGINE-1: brodalumab (140 mg *[not licensed]* or 210 mg) *vs* placebo
  - AMAGINE-2
  - AMAGINE-3

    ❖ identical in design
    ❖ brodalumab (140 or 210 mg) *vs* ustekinumab (45 or 90 mg) and placebo
- **Company**
  - reported results only for licensed brodalumab dose (210 mg)
  - did not use results from open-label studies in economic model
- **Network meta-analysis**
  - ustekinumab only drug in 'head-to-head' trials with brodalumab
  - brodalumab *vs*
    - ❖ apremilast, dimethyl fumarate, fumaric acid esters, biologics (adalimumab, etanercept, infliximab, ixekizumab, secukinumab, ustekinumab) and common comparators (placebo, acitretin, methotrexate)

AMAGINE trials

Adults (**18 to 75 years)** with **stable moderate to severe** plaque psoriasis for ≥6 months (**PASI ≥12**, sPGA ≥3, involved body surface area ≥10%)

Brodalumab 210 mg at weeks 0, 1, 2, 4, 6, 8 and 10 **(7 doses)**

Phase III, international, multicentre, randomised, double-blind, parallel group

No UK sites

- Placebo (all trials)
- Ustekinumab 45 or 90 mg at weeks 0, 4 and every 12 weeks (AMAGINE-2 & -3)

Key outcomes at 12 weeks

- Co-primary endpoints *vs* placebo:
  - ❖ PASI 75
  - ❖ sPGA 0 or 1
- Endpoint *vs* ustekinumab: PASI 100

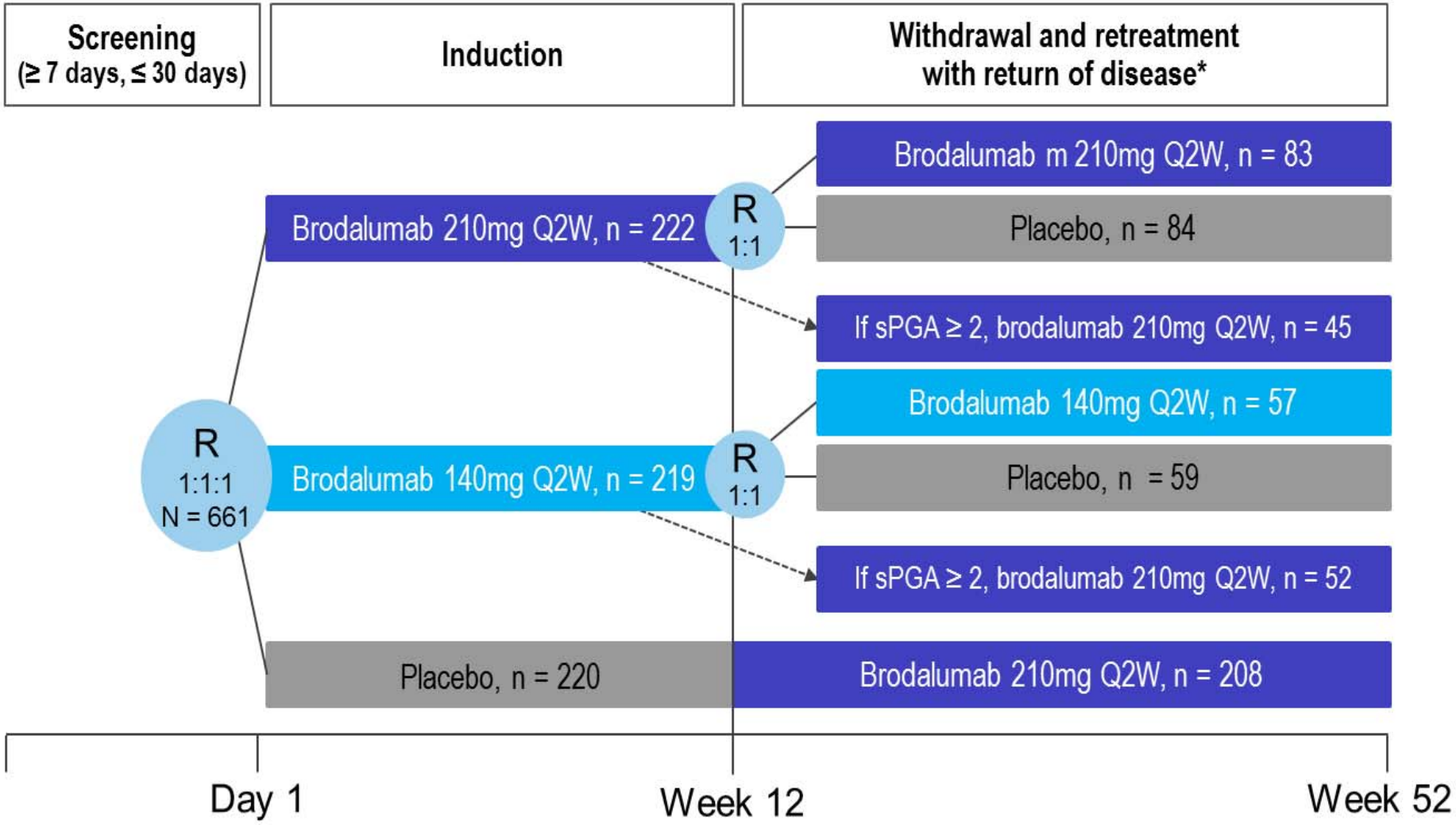
ERG comments

- Available drugs or sequencing differ in other countries
- NHS patients eligible for brodalumab unlikely to have stable psoriasis
  - ❖ likely to have more severe psoriasis which responds less well to treatment

❖ ***To what extent is response to treatment affected by whether or not psoriasis is stable?***

PASI, Psoriasis Area and Severity Index (0-72); sPGA, Static Physician Global Assessment (0-5)

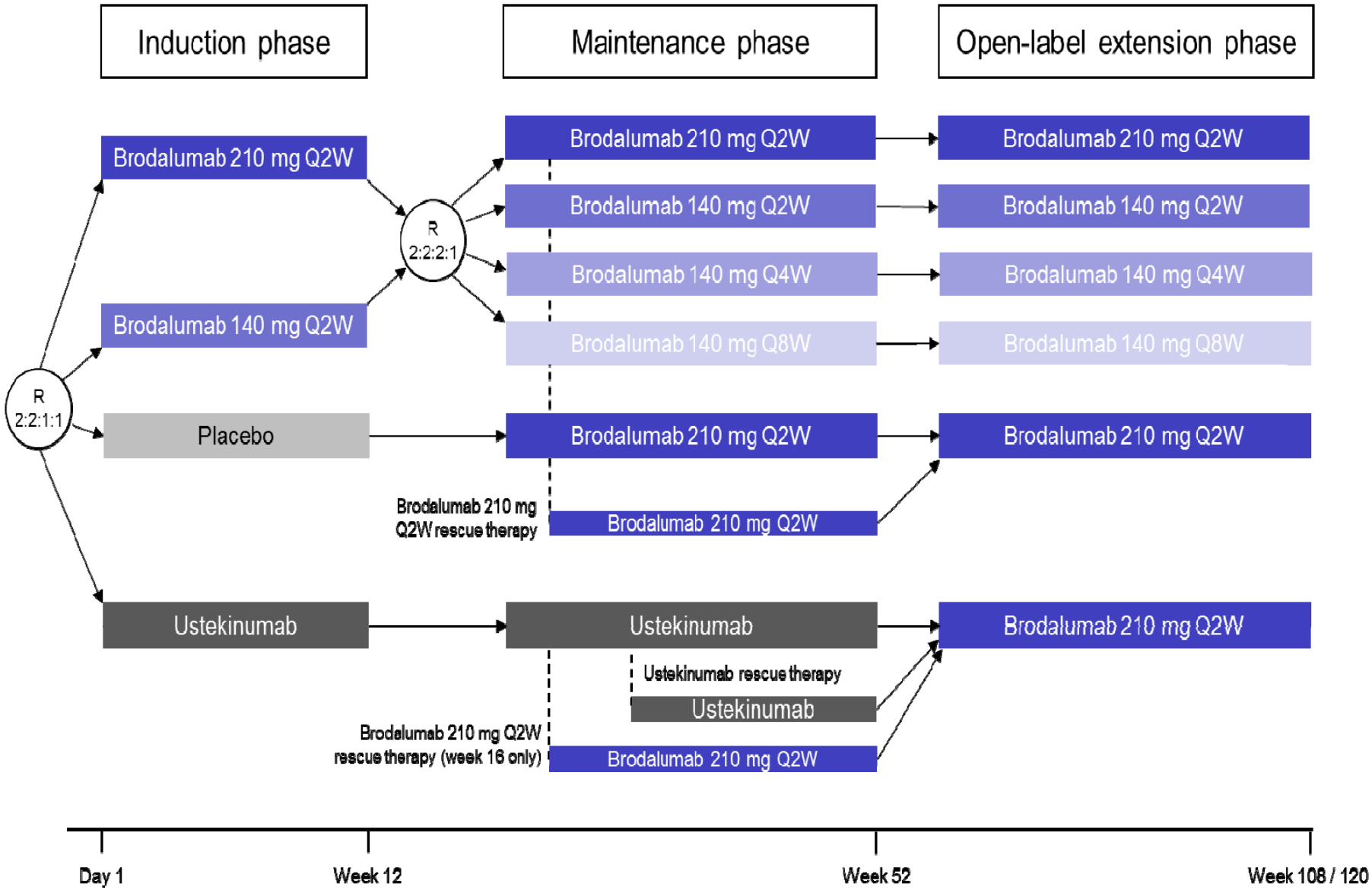
AMAGINE-1 trial design



At end of induction, patients on brodalumab re-randomised if they achieved sPGA 0 or 1
Patients re-randomised to placebo could get brodalumab 'rescue therapy' if psoriasis worsened (sPGA ≥3)

n, number of people; Q2W, every 2 weeks; R, randomisation; sPGA, Static Physician Global Assessment

AMAGINE-2 and -3 trial design



n, number of people; QnW, every n weeks; R, randomisation

ERG comments on trial design

- AMAGINE trials are of good quality and results likely to be reliable
- Re-randomisation design
  - cohorts at week 52 differ from week 12
  - no data on relapse rates → impossible to know if patients achieving PASI 75 response at end of induction:
    - maintained response or
    - stopped responding
  - At week 52, patients who discontinued were considered to be non-responders
- Discontinuation rates at 52 weeks for brodalumab were low (~20%)
  - similar to published rates for other biologics

CONFIDENTIAL

Baseline characteristics

Company argued population similar to BADBIR registry population (UK and Ireland)

	Age (years)^	Psoriasis duration (years)^	PASI^	DLQI^	% prior systemic therapy
AMAGINE-1					
Brodalumab* (n=222)	46 ± 12	20 ± 13	19.4 ± 6.6	14.2 ± 7.3	81
Placebo (n=220)	47 ± 13	21 ± 12	19.7 ± 7.7	13.9 ± 6.8	83
AMAGINE-2					
Brodalumab* (n=612)	45 ± 13	19 ± 12	20.3 ± 8.3	[redacted]	77
Ustekinumab (n=300)	45 ± 13	19 ± 13	20.0 ± 8.4	[redacted]	75
Placebo (n=309)	44 ± 13	18 ± 12	20.4 ± 8.2	[redacted]	74
AMAGINE-3					
Brodalumab* (n=624)	45 ± 13	18 ± 12	20.4 ± 8.3	[redacted]	68
Ustekinumab (n=313)	45 ± 13	18 ± 12	20.1 ± 8.4	[redacted]	70
Placebo (n=315)	44 ± 13	18 ± 12	20.1 ± 8.7	[redacted]	65

*210mg every 2 weeks, ^mean ± standard deviation

BADBIR, British Association of Dermatologists Biologic Interventions Register; DLQI, Dermatology Life Quality Index (0-30); PASI, Psoriasis Area and Severity Index (0-72); n, number of people

ERG comments on characteristics of populations in AMAGINE trials

- Similar baseline characteristics across different treatment groups
- AMAGINE-1 had more patients with psoriasis of longer duration, with psoriasis arthritis and who had previous treatments, than AMAGINE-2 and -3
- AMAGINE included patients with PASI ≥12 and mean baseline DLQI >12
  - higher than treatment threshold in current NICE guidance for severe psoriasis (PASI ≥10 and DLQI >10)
- 17-35% patients in AMAGINE had no previous systemic treatment or phototherapy and AMAGINE excluded patients on previous ustekinumab or anti-interleukin-17 therapy
  - inconsistent with proposed positioning of brodalumab

❖ ***Is AMAGINE population representative of moderate to severe psoriasis as defined in the NHS?***
❖ ***Are results from AMAGINE generalisable to target population of patients with prior systemic therapy?***

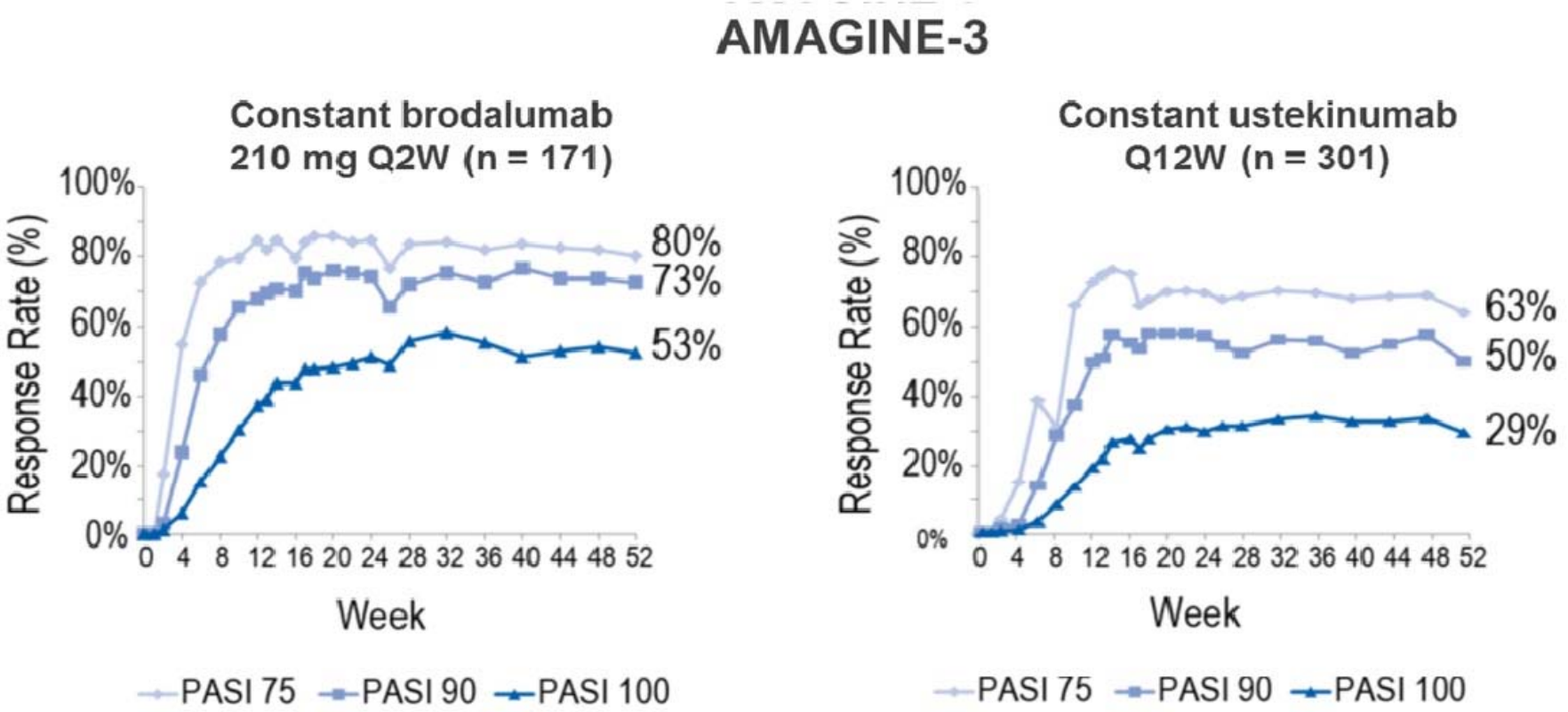
Key results at end of induction (12 weeks)

	% PASI 75 response^	% sPGA 0 or 1^	% DLQI 0 or 1^
AMAGINE-1			
Brodalumab (n=222)*	83 (78–88)	76 (70–81)	56 (NR)
Placebo (n=220)	3 (1–6)	1 (0, 4)	5 (NR)
AMAGINE-2			
Brodalumab (n=612)*	86 (83–89)	79 (75–82)	61 ([redacted])
Ustekinumab (n=300)	70 (65–75)	61 (55–67)	44 ([redacted])
Placebo (n=309)	8 (5–12)	4 (2–7)	4.5 (NR)
AMAGINE-3			
Brodalumab (n=624)*	85 (82–88)	80 (76–83)	59 ([redacted])
Ustekinumab (n=313)	69 (64–74)	57 (52–63)	44 ([redacted])
Placebo (n=315)	6 (4–9)	4 (2–7)	7 (NR)

*210mg every 2 weeks; ^(95% confidence intervals); DLQI, Dermatology Life Quality Index (0-30); PASI, Psoriasis Area and Severity Index (0-72); sPGA, Static Physician Global Assessment (0-5); n, number of patients; NR, Not reported

Treatment effect up to 52 weeks

PASI response rates largely maintained up to 52 weeks

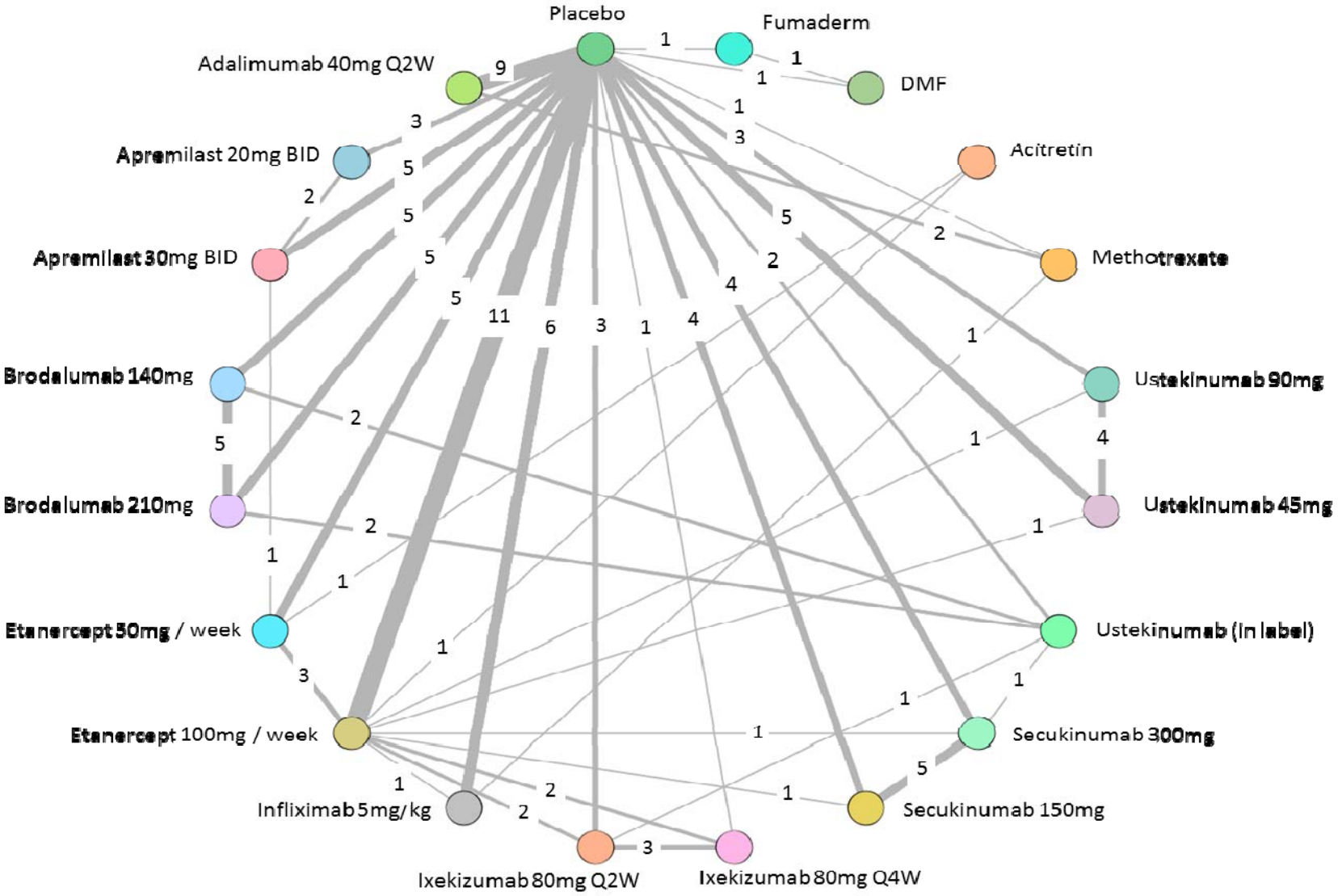


Similar results observed for AMAGINE-2 (not shown here)

n, number of patients; PASI, Psoriasis Area and Severity Index (0-72); Q2W, every 2 weeks

Base case network diagram

59 trials (n=28,346): moderate to severe plaque psoriasis, eligible for systemic therapy



BID, 2 times a day; DMF, dimethyl fumarate; QnW, every n weeks

Company's network meta-analysis – base case and sensitivity analyses

Base case: PASI response rates at induction

- Dosages and duration of induction therapy per licence of each treatment
- Company included unlicensed doses and (conventional) non-biologics only if contributed to evidence for relevant therapies
- Omitted comparators: non-biologics, best supportive care

Sensitivity analyses

Sensitivity analysis 1: Including EMA licensed dose recommended by NICE

Sensitivity analysis 2: 16 week outcomes from 1 of the 59 trials (CLEAR) used (primary endpoint of trial) *vs* 12-week outcomes used in base case

Sensitivity analysis 3: trials <100 patients randomised excluded

Sensitivity analysis 4: trials >30% randomised patients had previous biologics excluded (30% pragmatically chosen to include as many brodalumab trials as possible)

Sensitivity analysis 5: trials with mean baseline PASI >25 excluded

❖ ***Which analysis is most appropriate?***

EMA, European Medicines Agency; PASI, Psoriasis Area and Severity Index (0-72)

Company's network meta-analysis results

Results for unadjusted base case and sensitivity analyses are consistent

Treatment	Median probability of PASI 75 response		
	Company base case (unadjusted)	Sensitivity analysis 1 (licensed doses)	Sensitivity analysis 4 (exclude studies >30% previous biologics)
Ixekizumab 80mg Q2W	90.4%	89.4%	90.9%
Brodalumab 210mg	[redacted]	[redacted]	[redacted]
Secukinumab 300mg	83.6%	83.4%	84%
Infliximab 5mg/kg	79.2%	82.6%	80.6%
Ustekinumab 45mg	71.6%	72.9%	69.9%
Ustekinumab 90mg	75.3%	76.9%	74.8%
Ustekinumab (in-label dose)	71%	70.2%	71%
Adalimumab 40mg Q2W	66%	63.4%	67.3%
Etanercept 50mg / week	39.1%	41.2%	40.5%
Apremilast 30mg BID	27.3%	26.8%	29.2%
Dimethyl fumarate	19.3%	18.7%	20.4%
Placebo	5.7%	5.5%	6.3%

BID, 2 times a day; PASI, Psoriasis Area and Severity Index (0-72); Q2W, every 2 weeks

ERG comments on network meta-analysis

- Trials similar enough to pool
- Network meta-analysis well conducted
- Quality of life in AMAGINE poorer than comparator trials and higher proportion received previous biologics
- Company presented only PASI response rates
- PASI response rates of placebo groups varied significantly across 49 trials:
  - PASI 50 response rates: 5.1–33.3%
  - PASI 75 response rates: 0–20% (AMAGINE trials: 2.7–8.1%)
- Results for placebo-adjusted and placebo-unadjusted models consistent
  - However, ERG prefers placebo-adjusted model
    - ❖ this reduces difference between studies and ensures that relative treatment outcomes across trials are not biased

❖ ***Which model is preferred? Unadjusted or placebo-adjusted?***

NMA results – ERG placebo-adjusted model

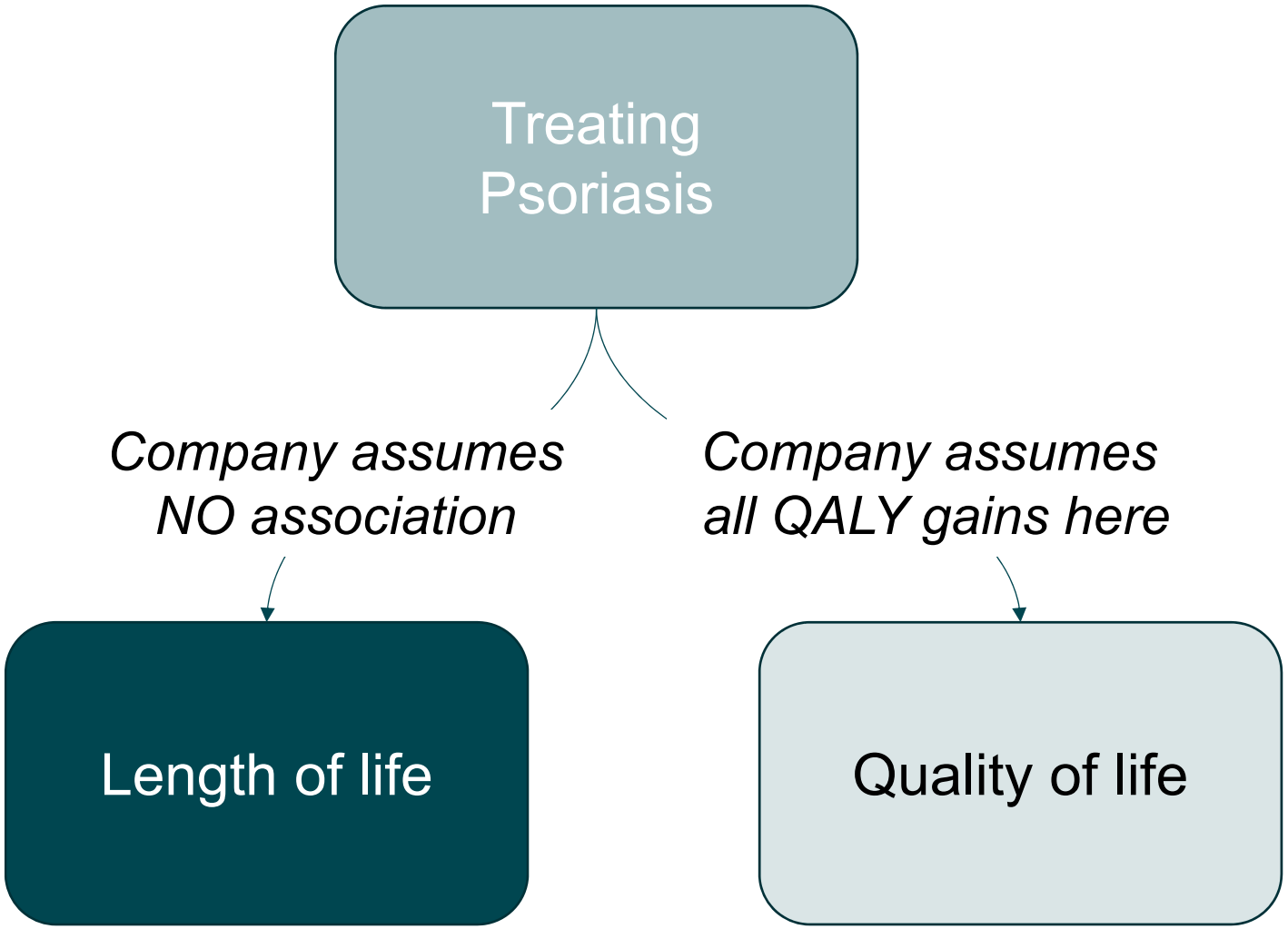
Treatment	Median probability of PASI response				Ranking
	PASI 50	PASI 75	PASI 90	PASI 100	
Ixekizumab (80 mg Q2W)	96.1%	89.1%	71.5%	41.1%	1
Brodalumab (210 mg)	[redacted]	[redacted]	[redacted]	[redacted]	2
Secukinumab (300 mg)	92.5%	81.8%	59.7%	29.2%	3
Infliximab (5 mg/kg)	90.9%	78.9%	55.6%	25.7%	4
Ustekinumab (90 mg)	87.0%	72.5%	47.4%	19.5%	5
Ustekinumab (in-label dose)	85.8%	70.6%	45.2%	18.1%	6
Ustekinumab (45 mg)	85.2%	69.7%	44.2%	17.4%	7
Adalimumab (40 mg)	85.0%	69.5%	43.9%	17.2%	8
Etanercept (100 mg/week)	71.2%	51.2%	26.4%	7.7%	9
Etanercept (50 mg/week)	59.8%	39.0%	17.3%	4.1%	10
Apremilast (30 mg)	51.9%	31.5%	12.6%	2.6%	11
Dimethyl fumarate	50.4%	30.2%	11.9%	2.4%	12
Placebo	14.7%	5.7%	1.3%	0.1%	13

BID, 2 times a day; PASI, Psoriasis Area and Severity Index (0-72); Q2W, every 2 weeks

❖ ***Is brodalumab clinically effective?***

Cost effectiveness

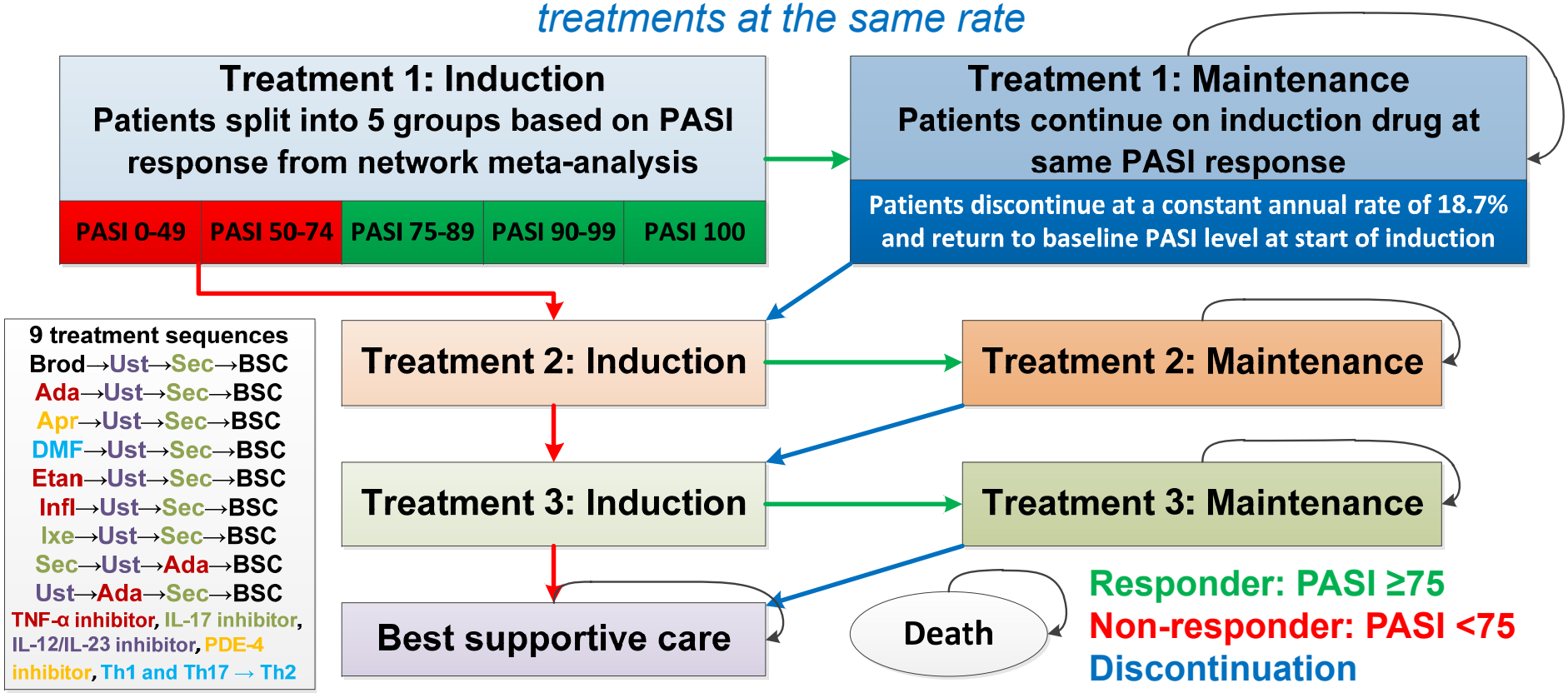
Where do QALY gains come from?



Increase in QALYs comes only from improvement in quality of life, rather than increasing length of life

Company model

ERG: model meets requirements of NICE reference case; high quality; similar to recent technology appraisals. Uncertainty in assuming that patients stop all treatments at the same rate



- Markov state transition model: 40 year time horizon, 2 week cycle length, treatment-specific duration of 'induction' (10, 12 or 16 weeks). Serious adverse events (infections) included. Perspective from NHS/PSS. 3.5% discount
- Baseline characteristics (similar to trials in network meta-analysis and AMAGINE): 45 years, mean weight 85.8kg, 68% men

Ada, Adalimumab; Apr, Apremilast; Brod, Brodalumab; BSC, Best supportive care; DMF, dimethyl fumarate; Etan, Etanercept; Infl, Infliximab; Ixe, Ixekizumab; PASI, Psoriasis Area and Severity Index (0-72); Sec, Secukinumab; Ust, Ustekinumab

Treatment sequences

Sequence	1st	2nd	3rd	4th
1	**Brodalumab**	Ustekinumab	Secukinumab	BSC
2	Adalimumab	Ustekinumab	Secukinumab	BSC
3	Apremilast	Ustekinumab	Secukinumab	BSC
4	Dimethyl fumarate	Ustekinumab	Secukinumab	BSC
5	Etanercept	Ustekinumab	Secukinumab	BSC
6	Infliximab	Ustekinumab	Secukinumab	BSC
7	Ixekizumab	Ustekinumab	Secukinumab	BSC
8	Secukinumab	Ustekinumab	Adalimumab	BSC
9	Ustekinumab	Adalimumab	Secukinumab	BSC

- Sequences based on: British Association of Dermatologists guidelines, expert opinion
- Therapies selected to have different mechanism of action
- Experts suggest likeliest 1st, 2nd & 3rd treatments: adalimumab, ustekinumab, secukinumab

TNF-α inhibitor, IL-17 inhibitor, IL-12/IL-23 inhibitor, PDE-4 inhibitor, **Th1 and Th17 → Th2**

BSC, Best supportive care

Treatment sequences – ERG comments

Limited number of sequences provides misleading cost-effectiveness estimates. ERG's alternative base case using net monetary benefit framework is preferred

- Modelling treatment sequences *vs* comparison of single lines of therapy followed by best supportive care → reflects clinical practice
- Limited number of sequences and positions of brodalumab
- Modelling selective sequences provide misleading cost-effectiveness estimates, especially if included treatments are also not cost effective
  - **ERG alternative approach:** net monetary benefit framework with rankings of each treatment compared with best supportive care
    - Treatment rankings from ERG's alternative base case are identical to company's base case → provides significant reassurance and confirmation on robustness of company's results

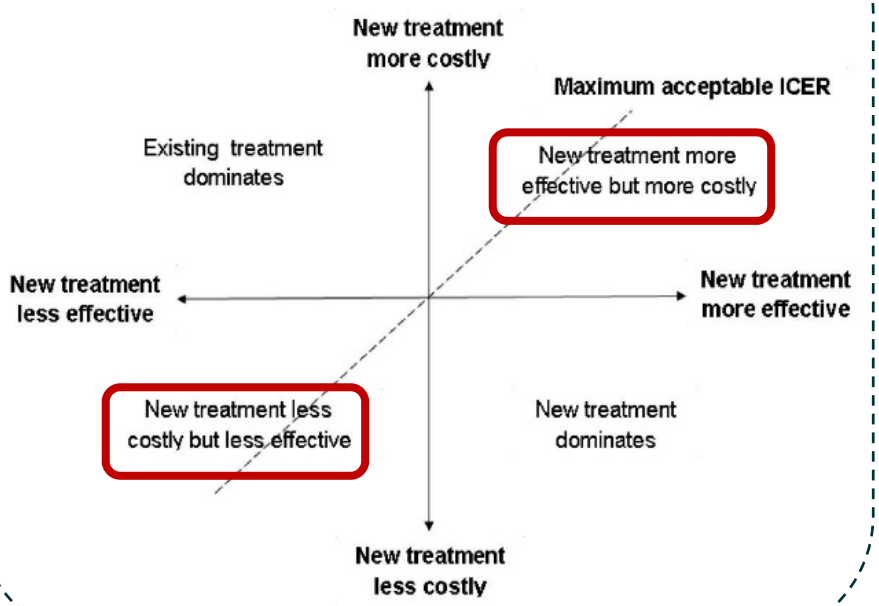
Incremental cost-effectiveness ratios (ICERs) vs net monetary benefit framework (NMB)

ICER: What is the extra cost per unit of extra benefit?

ICER decision rule: recommend technology if

Δ Costs/ Δ QALYs < threshold

But, ICER > 0 can mean:



NMB

- Value of an intervention in monetary terms at a willingness-to-pay threshold (NHS opportunity cost)
- For NMB, ICER decision rule is rearranged:
  (Δ QALYs * threshold) – Δ Costs > 0
- Incremental NMB: difference in NMB between alternative interventions
- Positive incremental NMB: intervention is cost-effective compared with alterative at given willingness-to-pay threshold

❖ ***How should cost effectiveness of brodalumab be assessed?***

Key model parameters

Parameter	Company's source	ERG comment
PASI response achieved after induction and maintenance on an active treatment	Base-case network meta-analysis	ERG prefers placebo-adjusted network meta-analysis
PASI response achieved for best supportive care	Base-case network meta-analysis for placebo	
Mortality rate	UK life tables, age and sex specific adjusted for increased risk of death by 42% associated with psoriasis (based on UK GPRD study), not affected by treatment or level of PASI response	Appropriate

❖ ***Is a relative risk of death of 1.42 plausible?***

PASI, Psoriasis Area and Severity Index (0-72); GPRD, General Practice Research Database

Key model assumption

Assumption	ERG comment
Treatment effectiveness does not depend on previous use of therapies → placement of drug in sequence has no impact on drug's effectiveness	Consistent with previous appraisals
Treatment waning: same effect maintained with ongoing treatment until discontinuation	Consistent with previous appraisals
Discontinuation annual rate assumed to be the same for all treatments	Consistent with previous appraisals but uncertainty around the appropriateness of using a constant rate for all treatments
On best supportive care, patients continue until end of the modelled time horizon or death	Appropriate
Patients can move to the death state from any health state at any time	Appropriate

❖ ***How should treatment discontinuation be modelled?***

Utility values

- Utility values based on EQ-5D-3L data from AMAGINE-1 subgroup DLQI >10
  - change in EQ-5D-3L from baseline to week 12 stratified by PASI response
  - company explored relationship between change in EQ-5D-3L score, PASI response and baseline DLQI using regression model
- Utility decreased to account for serious infection (multiplier calculated using data from Diamantopoulos 2014 on utility for pneumonia, adjusted for expected duration of event, baseline age and sex of Sisk 1997 cohort)
- **Base case:** patients with PASI ≥12 and DLQ1 >10 (moderate to severe); regression model adjusted for baseline DLQI
- **4 scenario analyses** to address uncertainty of generalisability of data:
  1. all patients in AMAGINE-1
  2. 4th quartile of DLQI from TA103 (etanercept)
  3. DLQI >10 estimates from TA350 (secukinumab)
  4. median values from previous appraisals

DLQI, Dermatology Life Quality Index (0-30); PASI, Psoriasis Area and Severity Index (0-72)

Utility values – ERG comments

- Company should adjust regression model for baseline EQ-5D (better goodness of fit), not baseline DLQI
- Consistent results in DLQI >10 subgroup and all patients → data from AMAGINE-1 generalisable to AMAGINE-2 and -3
- Uncertainty about generalisability of utility values to other trials in network meta-analysis: other appraisals have higher baseline utility and smaller increments

PASI response	Adjusted for baseline DLQI		Adjusted for baseline EQ-5D (ERG's base case)		e.g. TA350 (secukinumab)[a]
	DLQI>10 (base case)*	All patients^	DLQI>10	All patients	DLQI >10
Baseline	0.5206	0.6105	0.5206	0.6105	0.6402
PASI <50	(0.0158)	(0.0044)	(0.0035)	(-0.0037)	(0.109)
PASI 50–74	(0.1898)	(0.1349)	(0.2337)	(0.1574)	(0.193)
PASI 75–89	(0.2946)	(0.2441)	(0.3411)	(0.2631)	(0.226)
PASI 90–99	(0.3552)	(0.2798)	(0.3608)	(0.2895)	NR
PASI 100	(0.3680)	(0.2897)	(0.3774)	(0.2986)	NR

Increments in parentheses; *n=401; ^n=621; [a]Used EQ-5D-3L as in AMAGINE-1, n=3,286; DLQI, Dermatology Life Quality Index (0-30); PASI, Psoriasis Area and Severity Index (0-72); NR, Not reported

❖ ***How should utility values be modelled? Adjusted for baseline DLQI or baseline EQ-5D?***

Resource use and costs

Cost parameter	Company assumption	ERG comment
Drugs	Brodalumab: 7 doses for induction (12 weeks) Other drugs: list price, lowest priced biosimilars if available	Brodalumab: 8 doses (unit packs of 2 cannot be split) Other drugs: appropriate
Administration	Only infliximab (intravenous infusion)	Previous appraisals include costs for subcutaneous treatments; little impact
Monitoring visits	Exclude additional resource use for dimethyl fumarate	Include additional 2 outpatient visits and associated blood tests for dimethyl fumarate
Non-responder	Exclude: already included in best supportive care costs	Include non-responder costs of £128 per 2 week cycle, based on TA475 (dimethyl fumarate) and TA442 (ixekizumab)
Best supportive care	Based on Fonia 2010 £5,283 per year	Appropriate
Adverse events	Based on 6 serious infections: £2,653	Appropriate

ERG base case

- Analysis: Net monetary benefit of each treatment vs best supportive care
  - addresses ‘misleading’ estimates of cost effectiveness from restricted treatment sequences that may include options that are **not cost effective**
- Clinical effectiveness input: derived from placebo-adjusted network meta-analysis
  - improved goodness of fit
- Utility: regression model adjusted for baseline EQ-5D for DLQI >10 subgroup
  - improved goodness of fit
- Brodalumab dosing assumptions for induction (12 weeks) from 7 to 8 doses
  - more appropriate given the inability to split packs
- Inclusion of non-responder costs
  - consistent with recent appraisals

Results in Part 2 only

- Confidential PAS for apremilast, brodalumab, ixekizumab and secukinumab

- Results for company's base case, scenario and sensitivity analyses are largely consistent

- Committee will see:
  - Company's base case deterministic and probabilistic results
  - ERG's base case probabilistic results

Company comments on innovation

- Brodalumab:
  - has the potential to deliver complete skin clearance for many patients
  - treats nail and scalp psoriasis
  - is associated with rapid responses
  - requires fewer induction doses than anti-TNF therapies
  - delivers sustained responses, even after interrupting treatment
  - provides clinicians and patients with a choice within the interleukin-17 class of biological therapies

❖ ***Is brodalumab innovative?***

Equality considerations

- As in previous appraisals, the following issues have been identified:
  - Psoriasis Area and Severity Index (PASI) may underestimate disease severity in people with darker skin as redness may be less evident (key component of PASI)
  - Dermatology Life Quality Index (DLQI) underestimates the impact of people who are not sexually active or older or socially isolated and does not capture anxiety and depression

❖ ***Are there any equality issues to consider?***

End of Part 1