# Avatrombopag for chronic immune thrombocytopenia

For committee, screen and public – does not contain ACIC information

**Chair:** Charles Crawley

**Technology appraisal committee B**

**Lead team:** Iolo Doull, Nigel Westwood, Peter Wheatley Price

**Evidence assessment group:** CRD and CHE Technology Assessment Group

**Technical team:** Emily Leckenby, Yelan Guo, Henry Edwards

**Company:** Swedish Orphan Biovitrum Ltd

10 August 2022 – 2nd meeting

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# Definitions for platelet response

| Technology & description | Definition | Notes |
|---|---|---|
| ***Avatrombopag*** | | |
| Durable platelet response, time to response (cumulative) | Median cumulative number of weeks of platelet response ≥50×$10^9$/L over 26 weeks | Primary endpoint of Study 302 |
| Proportion of patients with platelet response | Proportion of patients with platelet response (platelet count ≥50×109/L without rescue therapy) at Day 8 | Secondary endpoint of Study 302 |
| Durable platelet response rate* | Proportion of patients who had a platelet response for ≥6 of the last 8 weeks of treatment | Exploratory endpoint of Study 302; Binary outcome analysed in NMA presented to ACM1 and informed model* |
| *Mean platelet count ^* | *Change in mean platelet count from baseline versus comparators, at 26-week follow-up* | *Continuous outcome; used in company's additional NMA presented to ACM2 in response to ACD ^* |
| ***Eltrombopag*** | | |
| Proportion of responders* | Proportion of patients with a platelet count of 50–400 × $10^9$/L weekly during the first 6 weeks and at least once every 4 weeks thereafter, 24 week follow-up | Primary endpoint of RAISE study; Binary outcome, comparator analysed in NMA presented to ACM1 and informed model* |
| ***Romiplostim*** | | |
| Durable platelet response* | Proportion of patients with a platelet count > or =50x$10^9$/L during 6 or more of the last 8 weeks of treatment | Primary endpoint of Kuter 2008 study. Binary outcome, comparator analysed in NMA presented to ACM1 and informed model* |

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**Outcomes analysed and included in company's NMA presented to ACM1 and described as **durable platelet response rate** in ACD; ^ outcome used in company's additional NMA in response to ACD;*

# Key issues

- What is the committee's view of the company's additional NMA? Which response outcome does the committee consider to be more appropriate to be analysed in the network meta-analysis and to inform the model, durable platelet response, or mean platelet count?
- Does the committee consider the company's additional analysis on treatment duration resolves the uncertainties? Which treatment duration does the committee consider appropriate for decision making?
- Are the company's updated bleed-related unit costs suitable?

# Preliminary recommendation

**The committee was minded not to recommend avatrombopag as an option for treating primary chronic immune thrombocytopenia refractory to other treatments (for example, corticosteroids, immunoglobulins) in adults.**

**Requested further clarification and analyses, including:**

- A network meta-analysis with the mean platelet count as a continuous outcome;
- Scenario analyses for treatment duration based on Study 302, to compare with the company's model assumptions;
- Methods on company's market research and how bleed-related unit costs were derived
- Probabilistic sensitivity analysis for cost-effectiveness results

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# Clinical evidence recap

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# Chronic immune thrombocytopenia (ITP)

- Defined as a platelet count lower than 100 x $10^9$/L caused by abnormally high platelet destruction and impaired platelet production with normal bone marrow, in absence of other causes of thrombocytopenia

- Symptoms include fatigue, purpura, spontaneous bruising and regular bleeding episodes

  Episodes can range from minor bleeds to severe, life-threatening haemorrhages

  People with ITP also experience anxiety and fear about maintaining their platelet levels

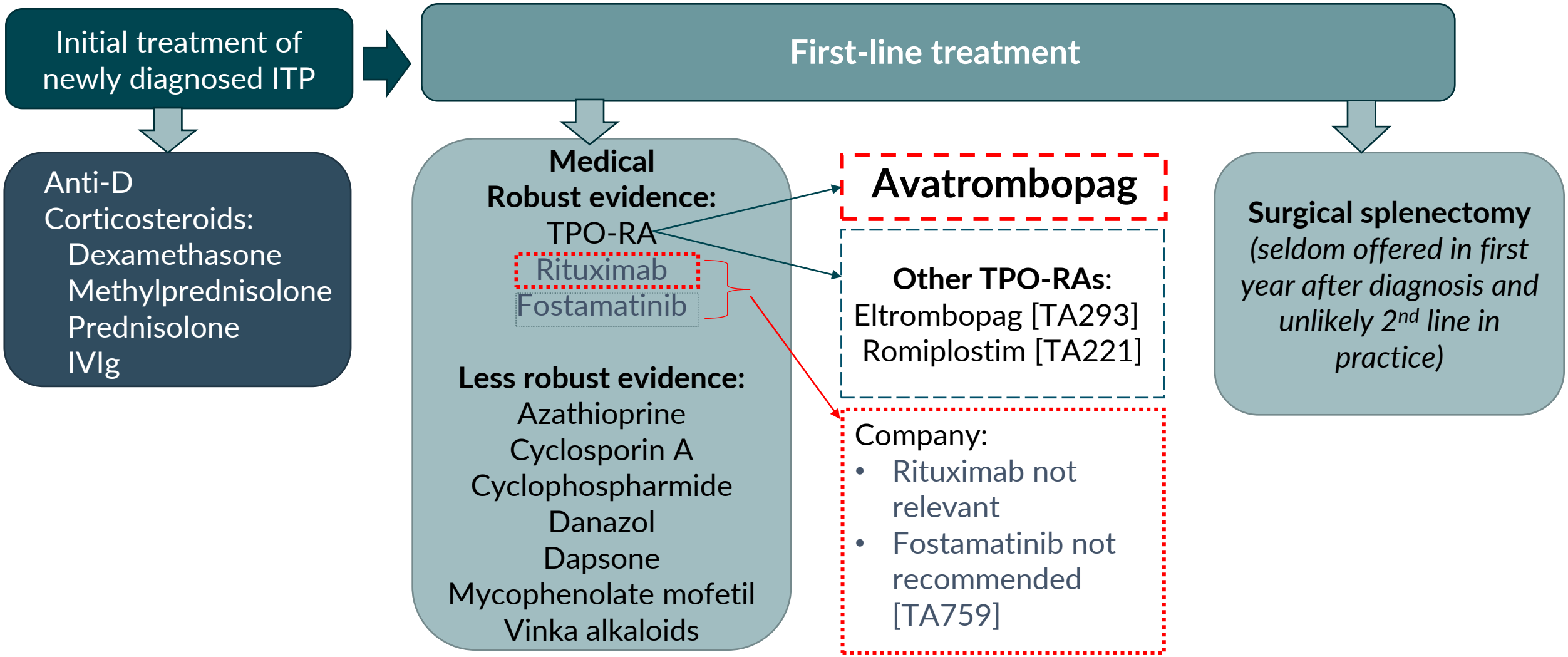
- Maintaining platelet count at ≥ 50 x $10^9$/L prevents clinically significant bleeding
- Treatment for ITP is usually required when platelet count is below 30 x $10^9$ per litre

**Appraisal Consultation Document (ACD):**

Chronic condition that significantly affects the lives of those affected by it

New treatment option for maintaining platelet counts would be welcomed by those with ITP

# Treatment pathway




**ACD**: company's positioning of avatrombopag in the treatment pathway appropriate; relevant comparators for avatrombopag are other TPO-RAs



**Source**: company submission figure 1. **Abbreviations**: ITP: immune thrombocytopenia; IVIg: intravenous immunoglobulin g; TPO-RA: thrombopoietin receptor agonist

# Avatrombopag (Doptelet, Swedish Orphan Biovitrum AB)

RECAP

**Marketing authorisation**

- Approved for "*treatment of primary chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments (e.g. corticosteroids or immunoglobulins)*
- EMA approved; granted January 2021

**Mechanism of action**

- TPO-RA that stimulates proliferation and differentiation of megakaryocytes from haemopoietic stem and progenitor cells; increases platelet production

**Administration**

- Oral: 20mg film coated tablet to be taken orally before, during or after food depending on individual patient platelet count
- Maintenance dose varies between 20mg weekly and 40mg daily

| | |
|---|---|
| Dose level 1 = 20mg once weekly | Dose level 4 (initial dose) = 20mg once daily |
| Dose level 2 = 20mg twice weekly<br>40mg once weekly | Dose level 5 = 40mg thrice weekly, 20mg on remaining 4 days |
| Dose level 3 = 20mg thrice weekly | Dose level 6 = 40mg once daily |

*Discontinue avatrombopag if*:

- platelet count does not increase to ≥ 50 x $10^9$/L after 4 weeks of dosing at maximum dose of 40mg once daily;
- platelet count greater than 250 x $10^9$/L after 2 weeks of dosing at 20 mg once weekly

**Price**

- 10x20mg tablets: £640; 15x20mg tablets: £960
- 30x20mg tablets: anticipated price, £1,920
- Subject to confidential patient access scheme

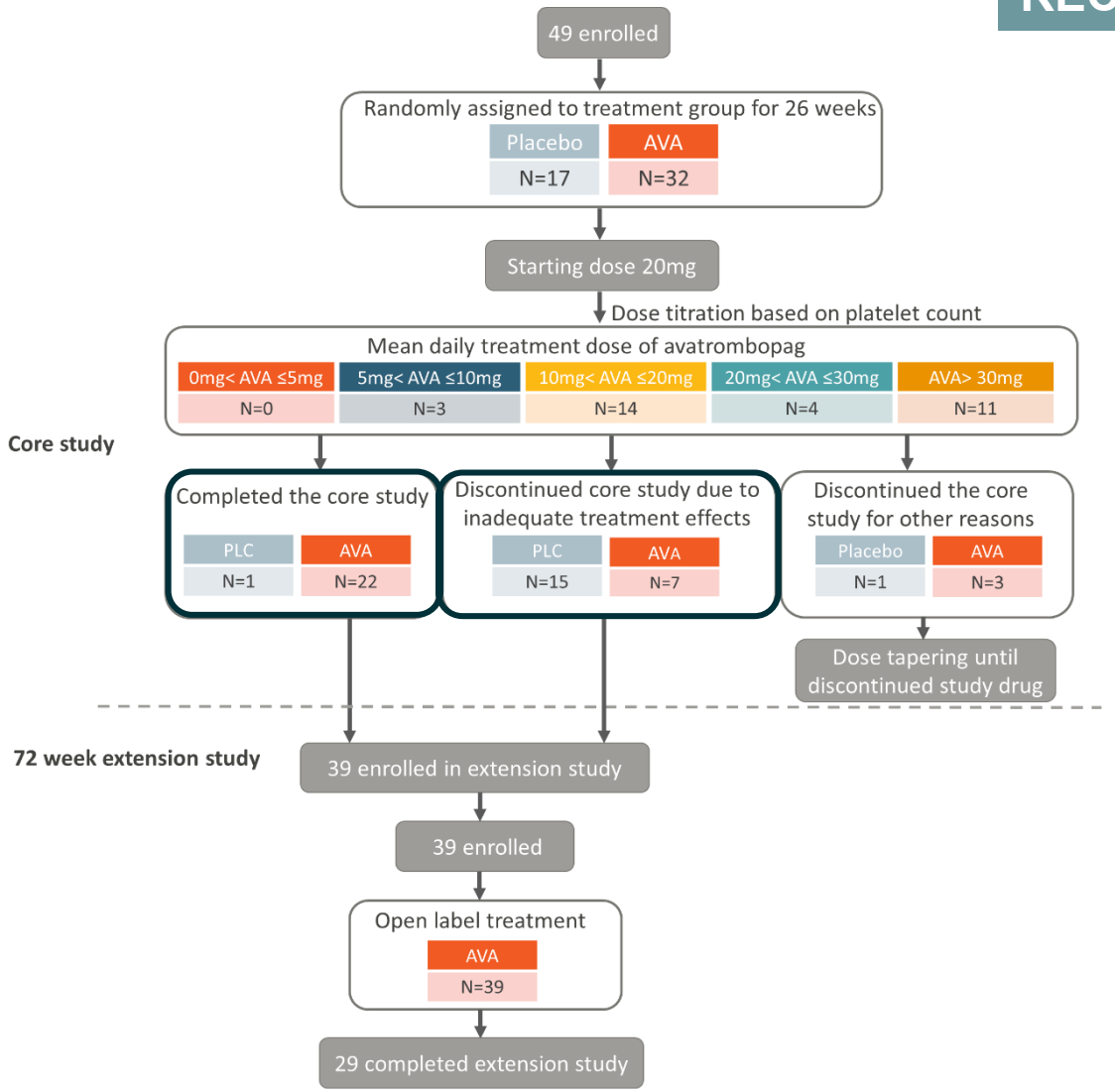
Annual cost of treatment (assuming 20mg daily): £21,983

NICE **Abbreviations**: L: litres; TPO-RA: thrombopoietin receptor agonist

RECAP

# Pivotal trial: Study 302

- The only clinical trial informed economic model
- Only 1 person on placebo completed the trial
  - Led to limitations when estimating durable placebo response in placebo group – affecting NMA results
  - **ERG**: concerned with robustness of efficacy/safety data due to imbalanced drop-out
  - **Clinical experts:** difficult to have a true "placebo" group for chronic ITP treatments




**ACD**: clinical trials of avatrombopag had recruitment and attrition issues, resulting in a limited evidence base

**Source**: company submission, figure 3. **Abbreviations**: AVA: avatrombopag; ITP: Immune thrombocytopenia; NMA: network meta-analysis; PLC: placebo

# Study 302 results

*p<0.0001
†p=0.009

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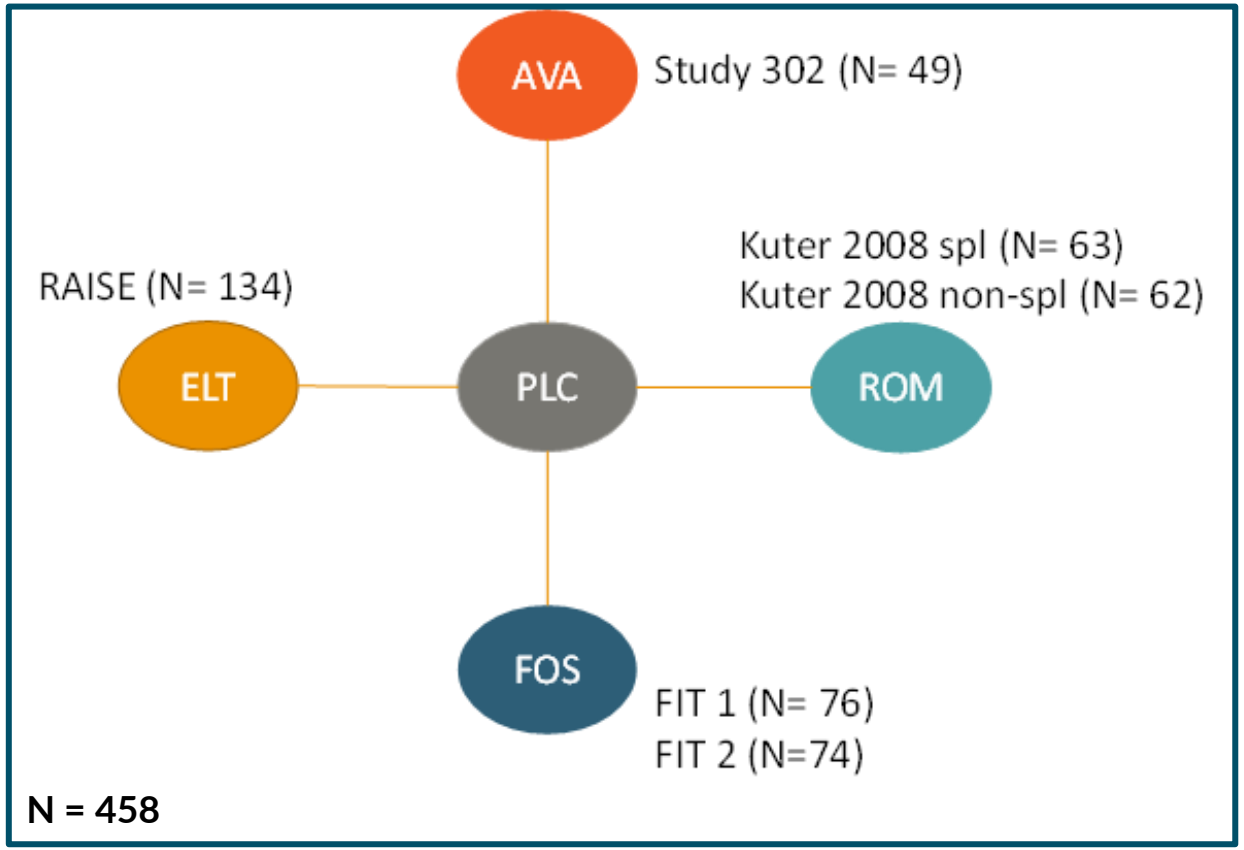
***ACD**: evidence from Study 302 suggested that avatrombopag improved cumulative platelet response and durable platelet response rate, but this was highly uncertain*

| | Result | |
|---|---|---|
| | AVA (n=32) | PLC (n=17) |
| **Primary endpoint** | | |
| Median cumulative number of weeks of platelet response ≥50×$10^9$/L over 26 weeks | 12.4* | 0 |
| **Outcome used to inform original NMA** | | |
| Durable platelet response rate (% of patients who had a platelet response for ≥6 of the last 8 weeks of treatment) | 34.4† | 0 |
| **Other secondary and exploratory endpoints** | | |
| % of patients with platelet response (platelet count ≥50×$10^9$/L without rescue therapy) at Day 8 | 65.6* | 0 |
| % of subjects with reduction in concomitant ITP medication use | 33.3 | 0 |
| % incidence of bleeding (any grade) | 43.8 | 52.9 |
| % Use of rescue therapy | 21.9 | 11.8 |

NICE **Source**: company submission, figure 6, table 15. **Abbreviations**: AVA: avatrombopag; ITP: immune thrombocytopenia; NMA: network meta-analysis; PLC: placebo

# NMA results – durable platelet response

Company conducted NMAs for 6 outcomes comparing avatrombopag's efficacy/safety with eltrombopag, fostamatinib*, romiplostim and placebo; frequentist approach; fixed effect models;




- Committee discussion focused on durable platelet response which informed model;

**Zero events correction methods**

- 3 RCTs (Study 302, Kuter 2008 SPL, FIT1*) had zero cell in placebo arm;
- During TE: company and ERG differed on continuity correction methods for zero events in NMAs;
- At ACM1: company accepted ERG's exploratory methods (adjustment values proportional to sample size added to "events" cells and "no event" cells, and total number of participants in each arm, as suggested by Sweeting 2004).

*Company and ERG agreed not necessary to include fostamatinib after ACM1. **Source:** company submission appendices, figure 2, company submission, table 24. **Abbreviations**: ACM: appraisal committee meeting; AVA: avatrombopag; ELT: eltrombopag; FOS: fostamatinib; PLC: placebo; RCT: randomised controlled trial; ROM: romiplostim; TE: technical engagement

# Comparative effectiveness estimates from NMA – durable platelet response (Study 302 as example)

RECAP

| Comparator vs. placebo | Company's NMA results for ACM1 (updated after TE) [1] | ERG base case NMA results[2] | ERG sensitivity analysis NMA results[3] |
|---|---|---|---|
| | Odds Ratio (no CI provided) | Odds Ratio, (95% CI) | Odds Ratio, (95% CI) |
| AVA | 27.49 | 18.72 (1.03, 340.54) | **26.91 (0.87, 835.27)** |
| ELT | 10.60 | 10.60 (3.64, 30.87) | **10.60 (3.64, 30.87)** |
| ROM | 33.56 | 29.61 (5.42, 161.58) | **33.39 (5.52, 201.98)** |
| ROM vs AVA | 1.22 | 1.58 (0.05, 45.57) | **1.24 (0.03, 59.99)** |

1. Derived directly from studies, CC proportional to sample size and applied to events only
2. Frequentist fixed-effects model, CC of 0.5 applied to both events and no events and with ITT RAISE data
3. **Frequentist fixed-effects model, CC according to the proportion of participants in each study arm applied to both events and no events, and total number of participants in each arm, and with ITT RAISE data**

**ACD**: ERG's sensitivity analysis may have been appropriate for correcting zero events in placebo groups. But any correction methods associated with high uncertainties.
**An alternative NMA with mean platelet count as a continuous outcome should be explored**

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**Source**: table 2, ERG response to TE. **Abbreviations**: CC: continuity correction; CI: confidence intervals; CrI: credible interval; ITT: intention to treat; NMA: network meta-analysis; TE: technical engagement;

# Cost effectiveness evidence recap

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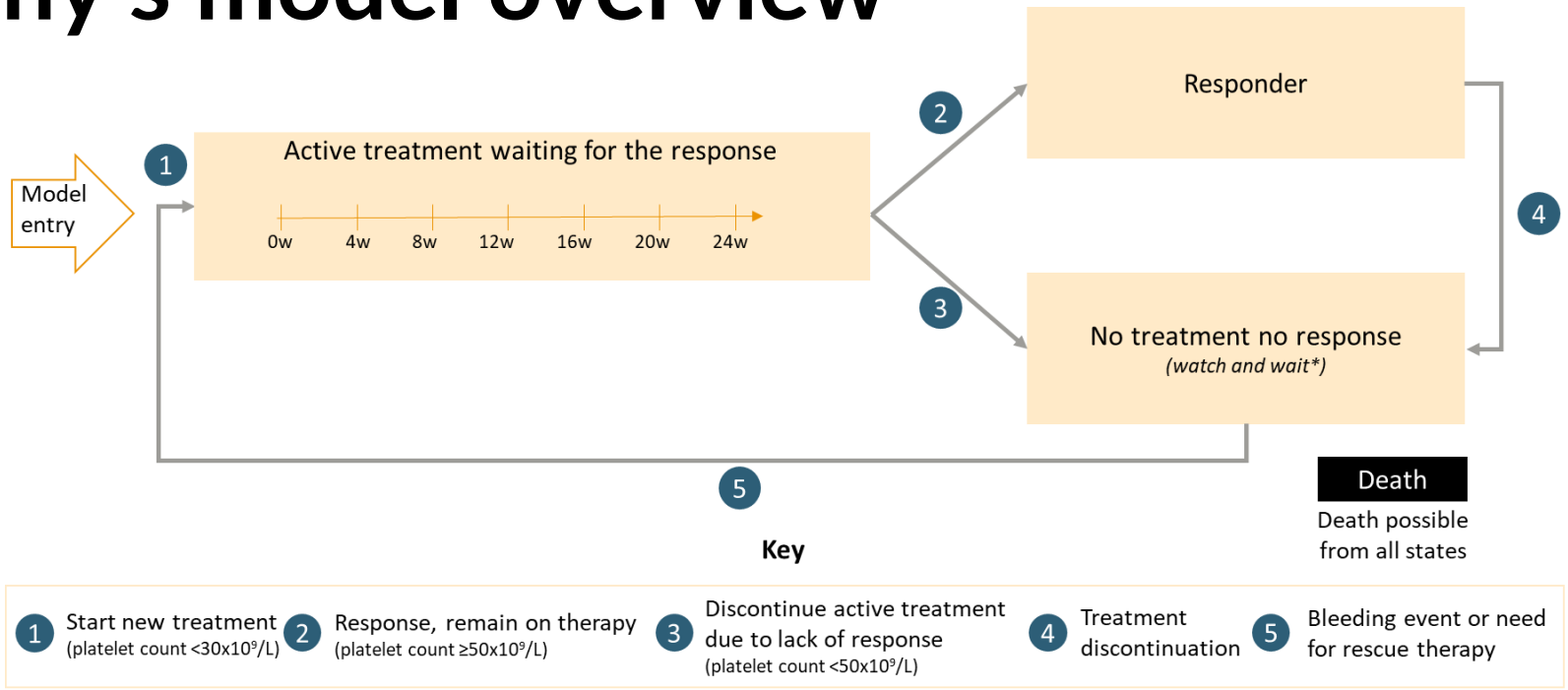
# Company's model overview



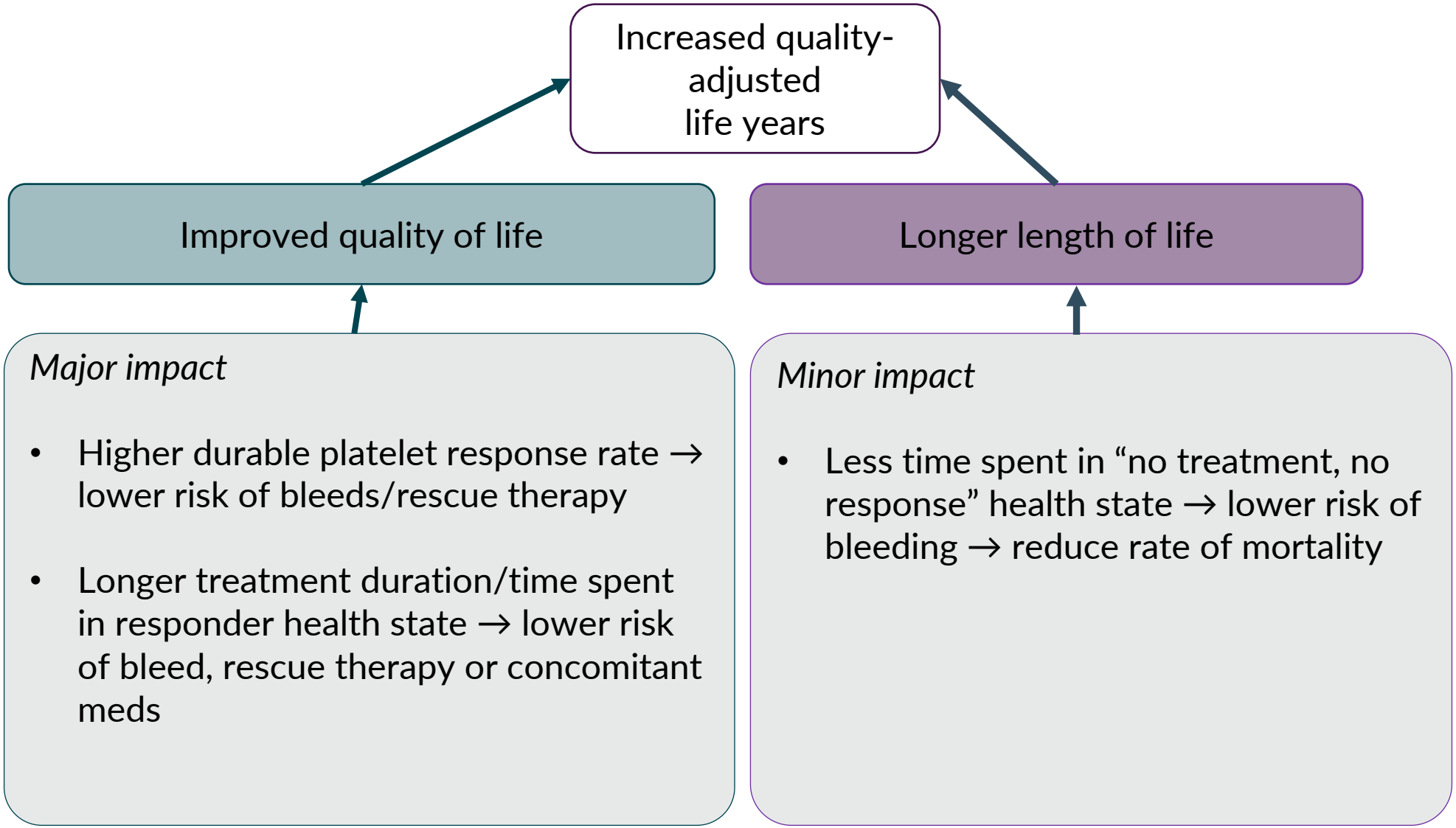

| | |
|---|---|
| **Model structure** | Markov cohort model consisting of 4 health states |
| **Perspective** | NHS and Personal Social Services (PSS) |
| **Time horizon** | 56 years (assumed to represent a lifetime horizon) |
| **Cycle length** | 4 weeks |
| **Discounting** | 3.5% per annum, applied to model long-term costs and QALYs |

**ACD**: company's economic model structure is appropriate for decision making

NICE **Source**: ERG report, figure 4. **Abbreviations**: L: litres; QALY; quality adjusted life year; w: weeks

# How quality-adjusted life years accrue in company's model

RECAP



# ACD consultation

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# Committee requests for further clarification and analyses

| ACD section | Committee request | Provided by company? | Changes to base case? |
|---|---|---|---|
| 3.9 to 3.11 | A network meta-analysis with the mean platelet count as a continuous outcome that, together with a distributional assumption, can be used to derive response probabilities | Yes | No – provided as scenario analyses |
| 3.16 | Scenario analyses for comparison with the company's model assumptions that estimate treatment duration or stopping rates based on the:<br>• patient-level data from Study 302<br>• empirical data from the extension of Study 302 | Yes | No – provided as scenario analyses |
| 3.17 | Details on the:<br>• methods of company's market research that informed costs in model<br>• how the bleed-related unit costs were derived | Yes | Yes - updated costs included |
| 3.19 | A probabilistic sensitivity analysis, including probabilistic incremental cost-effectiveness ratios, cost-effectiveness scatter plots and cost-effectiveness acceptability curves for £20,000 and £30,000 per quality-adjusted life year gained. | Yes, *but only for pair-wise comparisons* | - |
| **Company also provided commentary on the clinical efficacy of avatrombopag (ACD 3.6 and 3.7), and the time to treatment response in the model (ACD 3.13)** | | | |

# ACD consultation responses

**Responses received from:**

- Company: Swedish Orphan Biovitrum (Sobi)
- Clinical expert
- Patient group – ITP Support Association; joint response from CEO and patient expert



**Abbreviations:** ITP: immune thrombocytopenia

# Stakeholder comments

## Patient experts (ITP Support Association [ITPSA])

- **Overfocus on particular scientific elements of specific Sobi trial**
  - Avatrombopag has proven safety record and efficacy across all regions where it has approval
  - Already in use across the United States, Europe and Scotland
- **Not enough emphasis on wastage with current treatments, namely romiplostim**
  - Comes in fixed dose vials (300mcg) – residual drug lost once personalised dose prepared
- **Worst listed side effects of avatrombopag comparable to milder side effects of eltrombopag and romiplostim**
- **Many patients where current treatments do not produce good results, side effects are intolerable, or they do not fit lifestyle – with eltrombopag having significant food restrictions**
  - Provides healthcare professionals with another item in their 'toolbox of treatments'
- **Avatrombopag can be taken orally and without restrictions**
  - Recent ITPSA survey on patients' attitudes to treatment (TRAPeze study) highlighted preference of oral treatments; significant dislike of food restrictions
- **Provides a non-immunosuppressive option with a good response rate to those who cannot tolerate current TPO-RAs**

 **Source:** ACD comments form, ITP Support Association, **Abbreviations**: TPO-RA: thrombopoietin receptor agonist

# Updated clinical effectiveness evidence

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# Clinical efficacy of avatrombopag (ACD 3.6 and 3.7)

*Company: efficacy of avatrombopag demonstrated in both RCTs and real world settings*

**ACD:** Recruitment and attrition issues impacted certainty of clinical evidence for avatrombopag

## Company response at ACD consultation

- Pivotal trial for AVA demonstrated statistical and clinical significance, led to MA in Europe and UK
- Growing clinical experience of using AVA in Ireland and Scotland following approval
- Both the provided NMA and other responses draw on multiple published observational studies;
  - Positive real-world experience even in heavily pre-treated ITP populations or those previously treated with TPO-RAs

## ERG comments

- No comments

## Other considerations

- ITP Support Association
  - AVA has proven safety record and efficacy across all regions in which it has received approval
  - Medical advisors: AVA requested via IFR route a number of times in past year; approved for chronic ITP patients in NHS England

**Abbreviations**: AVA: avatrombopag; IFR: individual funding request; ITP: immune thrombocytopenia; MA: marketing authorisation; NMA: network meta-analysis; RCT: randomised controlled trial; TPO-RA: thrombopoietin-receptor agonist.

# Additional network meta-analysis (ACD 3.9 to 3.11) (1)

*Company: greater improvement in change in mean platelet count from baseline versus placebo but not versus comparators*

**ACD:** An alternative NMA, with mean platelet count as a continuous outcome, should be explored

**Company response at ACD consultation**

- Bayesian approach, fixed effect NMA conducted comparing AVA with PLC, ELT and ROM
- All treatments associated with significantly greater improvement in platelet count versus PLC
- Differences between active treatments not significant, AVA highest probability of being best (51%)
- All active treatments associated with very high likelihood of reaching target platelet count

| Mean difference for all comparisons ($\times 10^9$/L) (fixed effect model) | | | | | Probability of being best |
|---|---|---|---|---|---|
| | vs. PLC | vs. AVA | vs. ELT | vs. ROM | |
| PLC | PLC | *-56.73 [-83.13, -30.62]* | *-55.50 [-67.64, -43.27]* | *-46.34 [ -59.58, -33.08]* | 0% |
| AVA | 56.73 [30.62, 83.13] | AVA | *1.30 [-27.57, 30.24]* | *10.46 [-18.93, 39.92]* | 51% |
| ELT | 55.50 [43.27, 67.64] | -1.30 [-30.24, 27.57] | *ELT* | *9.18 [-8.81, 27.07]* | 42% |
| ROM | 46.34 [33.08, 59.58] | -10.46 [-39.92, 18.93] | -9.18 [-27.07, 8.81] | ROM | 7% |

**Source:** company response to ACD consultation, table 1. **Abbreviations**: AVA: avatrombopag; ELT: eltrombopag; L: litres; NMA: network meta-analysis; PLC: placebo; ROM: romiplostim

# Comparative effectiveness estimates from NMA – durable platelet response (Study 302 as example)

| Comparator vs. placebo | Company's NMA results for ACM1 (updated after TE) [1] | ERG base case NMA results[2] | ERG sensitivity analysis NMA results[3] |
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**ACD**: ERG's sensitivity analysis may have been appropriate for correcting zero events in placebo groups. But any correction methods associated with high uncertainties.
**An alternative NMA with mean platelet count as a continuous outcome should be explored**

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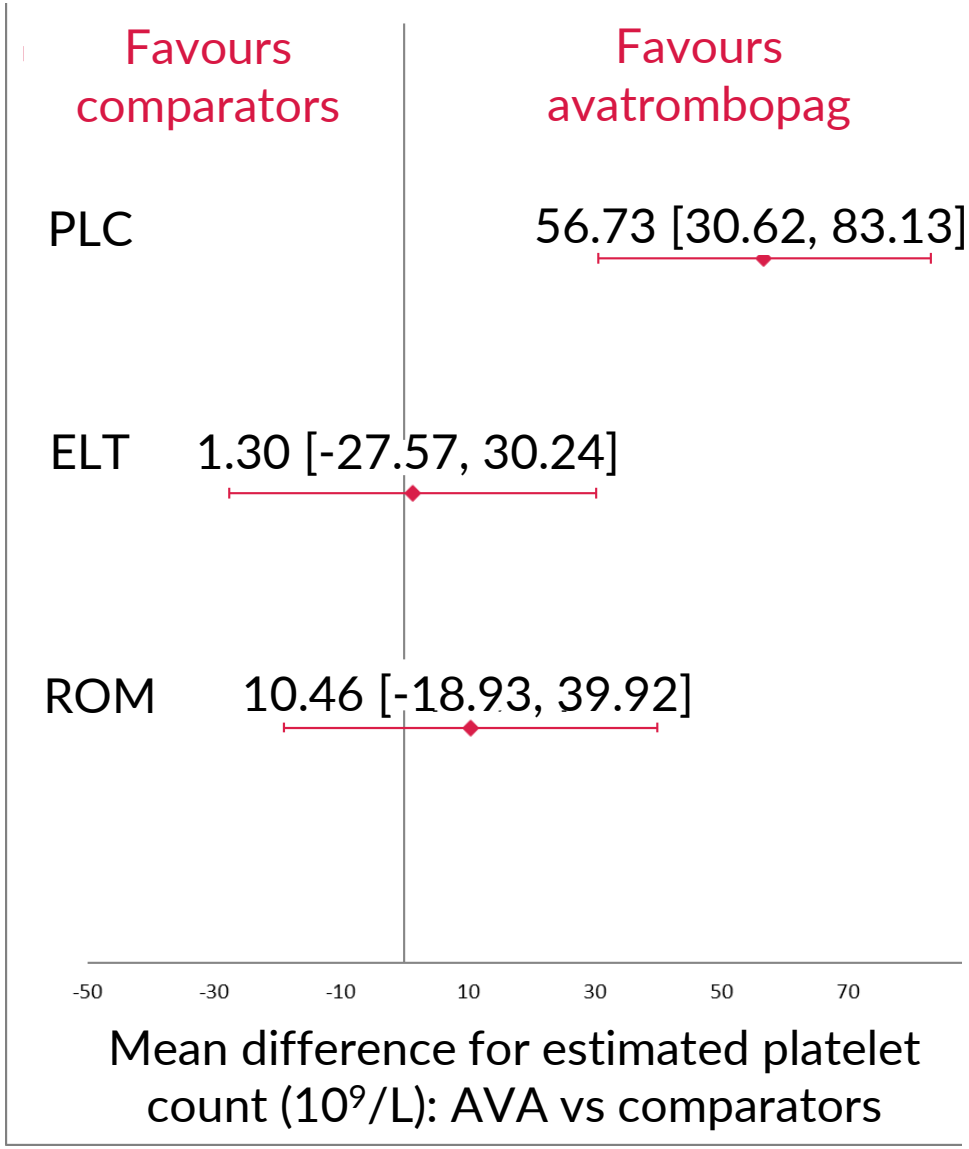
**Source**: table 2, ERG response to TE. **Abbreviations**: CC: continuity correction; CI: confidence intervals; CrI: credible interval; ITT: intention to treat; NMA: network meta-analysis; TE: technical engagement;

# Additional network meta-analysis (ACD 3.9 to 3.11) (2)




## Company response at ACD consultation

- Marginal differences between AVA and ELT: may be due to differences in study design around titration of treatments
- Titration of AVA: platelet target range of 50-150 x $10^9$/L; primary end point required a platelet count ≥50 x $10^9$/L
- Titration of ELT: patients assessed over a wider platelet range for response (defined as a platelet count of 50–400 × $10^9$/L)
- For AVA, likely clinically meaningful response achieved in more patients than what's suggested by primary end point

## ERG comments

- Company used a single 'last observation carried forward' (LOCF) method to input missing data for mean change from baseline in mean platelet count, which was estimated based on last observations before early drop out
- Company does not provide justification for its choice of continuous outcome; alternative outcomes could have been explored, for example:
  - Bayesian repeated measure NMA model accounting for multiple time points; or NMA model adjusting for baseline imbalances;

**Source:** company response to ACD consultation, figure 1. **Abbreviations**: AVA: avatrombopag; ELT: eltrombopag; L: litres; NMA: network meta-analysis; PLC: placebo; ROM: romiplostim

# Additional network meta-analysis (ACD 3.9 to 3.11) (3)

*ERG: does not consider additional NMA resolves uncertainties in clinical effectiveness vs TPO-RAs*

**ERG comments**

- Only one person in the placebo arm completed Study 302; only LOCF used to input missing data
  - Less conservative approach to replace missing outcome data than used in original submission
  - Not statistically valid; leads to serious bias/small standard errors - failure to account for uncertainty
- Mean platelet count fluctuates over time, providing restricted view of treatment response over time compared to durable platelet response modelled previously
- Unclear why NMA for change in mean platelet count from baseline at 12 weeks not presented
  - Analysis at 12 weeks would align with company's response around time to treatment response
  - Added advantage of fewer missing data points (fewer drop outs at week 12 versus week 26)
- Results of updated NMA markedly different from results from company's original NMA/ERG's NMA in terms of ranking efficacy of TPO-RAs
  - Estimates for probabilities of reaching platelet count of >50x$10^9$/L very close to 100% for all treatments

| | **Probability of being the best treatment** | | |
|---|---|---|---|
| | Company's NMA for ACM1 **(updated after TE)** | ERG's NMA (ACM1) | Company's additional NMA (after ACM1) |
| Avatrombopag | 58% | 44% | 51% |
| Eltrombopag | 3% | 31% | 42% |
| Romiplostim | 32% | 55% | 7% |

**Source:** LOCF: last observed carried forward; NMA: network meta-analysis; TPO-RA: thrombopoietin receptor agonist

# Additional network meta-analysis (ACD 3.9 to 3.11) (4)

What is the committee's view of the company's additional NMA?

Which response outcome does the committee consider to be more appropriate to be analysed in the NMA and to inform the model, durable platelet response, or mean platelet count?

# Updated cost effectiveness evidence

NICE National Institute for Health and Care Excellence

# Time to treatment response in model (ACD 3.13)

*ACD: 24-week timeframe to assess non-response does not reflect clinical practice, minor impact on cost-effectiveness results but uncertainty in model*

## Company response at ACD consultation

- Clarified that company had previously accepted ERG's views on time to treatment response during TE
- Altered base-case analysis by correcting it to a 3-cycle duration for assessment response (corresponding to a 12-week timeframe)
- 12-week duration aligns with evidence provided by clinical experts at ACM1

## ERG comments

- ERG's base case did not use a 12-week timeframe, although ERG highlighted issue around people remaining on treatment for 24 weeks before assessing response to treatment;
- ERG conducted exploratory analysis using 8-week timeframe to assess response to first-line TPO-RAs
  - Did not form part of ERG's preferred assumptions because 8-week (or 12-week) timeframes do not align with definition of durable platelet response used for response probabilities in model, which was defined at least 6 weekly platelet counts >$50x10^9$/L in final 8 weeks of a 24-26 week study
- Therefore, company's updated base case results in response to TE did not include 12-week timeframe for time to treatment response

**Abbreviations**: ACM: appraisal committee meeting; TE: technical engagement; TPO-RA: thrombopoietin receptor agonist

# Treatment duration: scenario analysis (ACD 3.16) (1)

*ACD: treatment duration might be similar between TPO-RAs, but requested scenario analyses based on Study 302*

**Background:** company originally assumed long-term treatment duration of 109 cycles (436 weeks/8.4 years) for all TPO-RAs

**Company's response at ACD consultation**

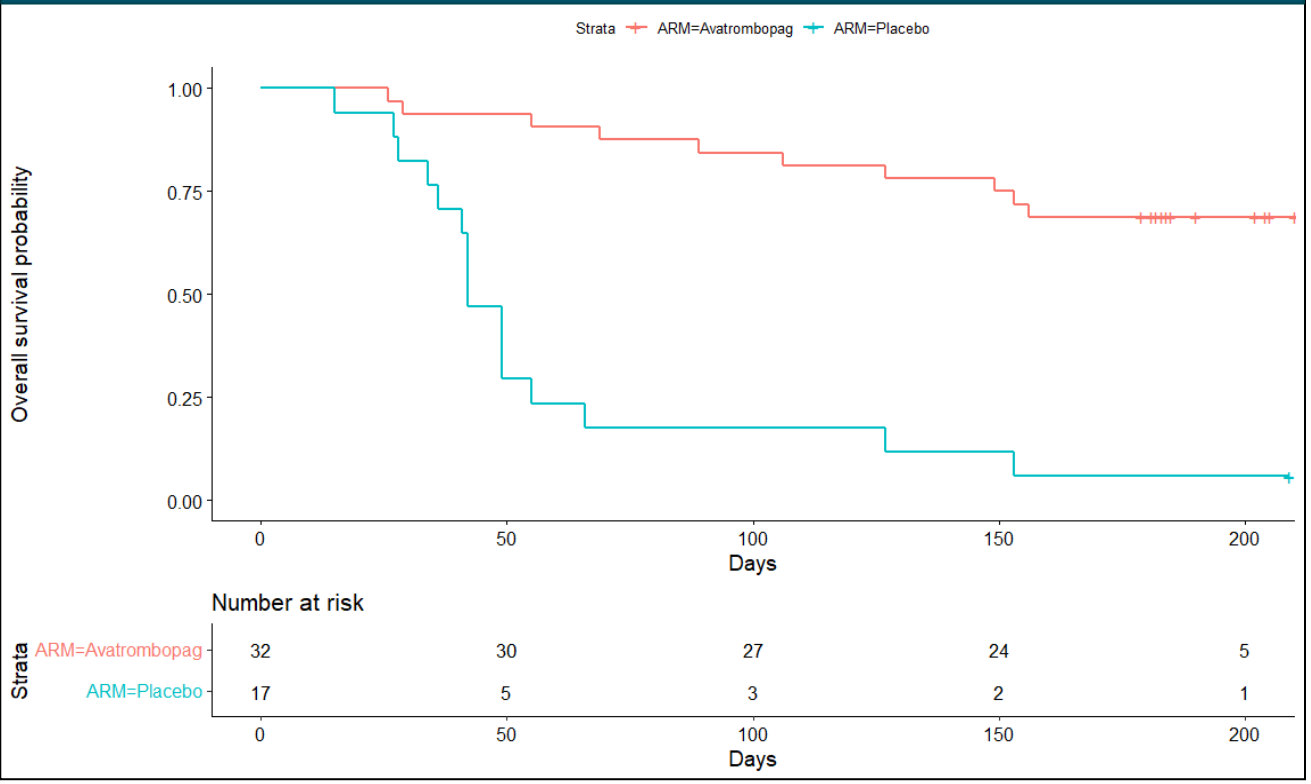
- Fitted log-normal distribution to Kaplan-Meier trial data to determine average duration of treatment
  - Estimated for 57.31 cycles based on Study 302, and 632.7 cycles with trial extension included
- 3 scenarios considered and ICERs provided:
  - Same duration of treatment for all TPO-RAs based on Study 302;
  - Same duration of treatment for all TPO-RAs based on Study 302 + extension
  - Different durations of treatment for ELT (109 cycles), ROM (393 cycles) and AVA (633 cycles)
- Results consistent with base case scenario of same treatment duration being assumed for all TPO-RAs

 **Abbreviations**: AVA: avatrombopag; ELT: eltrombopag; ROM: romiplostim; TPO-RA: thrombopoietin receptor agonist

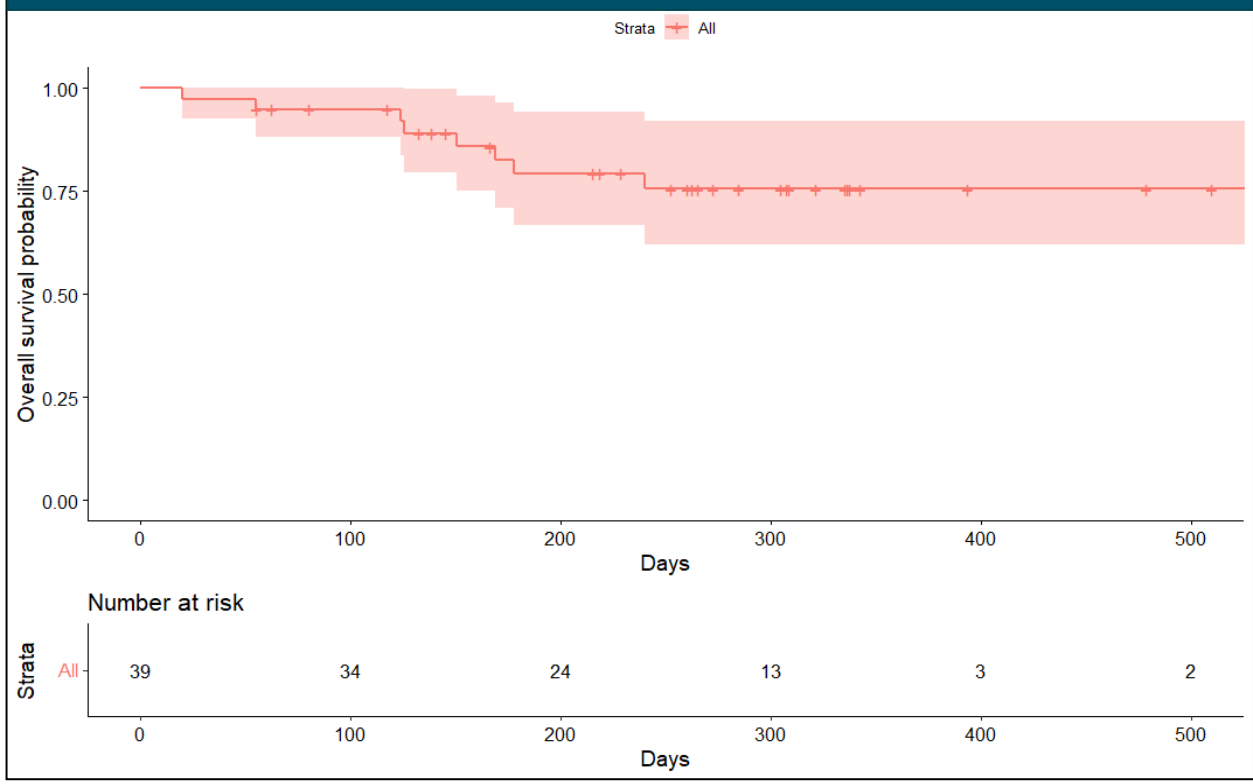
# Treatment duration: scenario analysis (ACD 3.16) (2)

*Company: provided analyses based on Study 302*

## Scenario analysis for patient-level data from Study 302
(1 cycle = 28 days)




## Scenario analysis based on extension of Study 302
(1 cycle = 28 days)




**Source:** company response to ACD consultation; figures 2 and 3.

# Scenario analysis for treatment duration (ACD 3.16) (3)

*ERG: company's additional evidence does not resolve uncertainties around average treatment duration*

**ERG comments**

- Company's approach of analysing Study 302 data reasonable
  - Similar to that used in Lee et al., (2013) for estimating mean treatment duration for eltrombopag and romiplostim;

- Study 302's extension data into the long-term have much fewer patients at risk (<10/year)
  - Extrapolations based on small numbers at risk gives an average duration approximately 48 years for avatrombopag;

- Even assuming identical treatment duration between all TPO-RAs, actual mean estimate used in model will have important impact on cost-effectiveness of avatrombopag relative to eltrombopag and romiplostim
  - Higher the treatment response rate between alternative TPO-RAs, the longer (greater mean time on treatment) or shorter (lower mean time on treatment) this response is maintained over time
  - Impacts 'no treatment no response' health state in model, where elevated risk of bleeding (higher costs)
- Lower discontinuation rates for more effective treatments only result in improved cost-effectiveness as:
  - Transition to 'no treatment no response' health state occurs late enough, and elevated risk of severe bleeding events/need for rescue therapy significantly discounted
  - Next subsequent line of therapy is less cost-effective than the TPO-RA



**Abbreviations**: TPO-RA: thrombopoietin receptor agonist

# Treatment duration (ACD 3.16) (4)

Does the committee consider the company's additional analysis on treatment duration resolves the uncertainties? Which treatment duration does the committee consider appropriate for decision making?

# Bleed-related unit costs (ACD 3.17) (1)

*Company: updated bleed-related unit costs to use NHS reference costs, but different cost codes to ERG*

**Company after TE:** used midpoint between NHS reference costs and market research data

**ERG**: preferred NHS reference costs

**ACD**: ERG's approach of using NHS reference costs more appropriate, recognised there may be additional resources not covered in these costs. Requested more information on company's market research methods, and how bleed-specific unit costs were derived from qualitative survey questions

**Company response at ACD consultation**

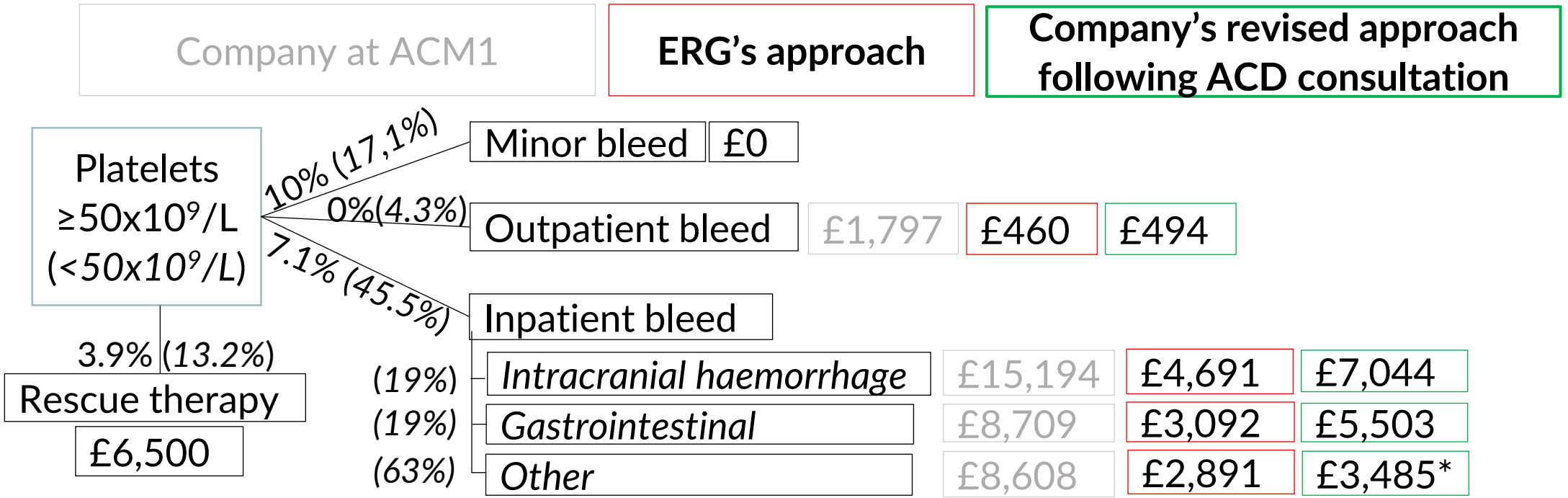
- Provided further details on how bleed-specific unit costs derived from survey
- Updated its costs associated with bleeding events to be in line with ERG's approach, but based on highest considered unit costs because clinical advice suggested that:
  - Duration of bleeds in ITP patients longer than general population
  - Takes longer to increase platelet count and stabilise bleeding
  - Severity of bleeds in patients with low platelet count tends to increase
  - Resource needs could be higher for ITP patients

**ERG comments**

- Considers proposed approach of uplifting NHS reference costs for bleeding events to be reasonable
- Company have selected highest unit cost for each type of bleed corresponding to those with highest complication and comorbidity score, rather than a weighted average

# Bleed-related unit costs (ACD 3.17) (2)

*Company: updated bleed-related unit costs to use NHS reference costs, but different cost codes to ERG*




Are the company's updated bleed-related costs suitable?

**Source:** company response to ACD consultation, table 2, ERG clarification of company's costing approach note. *corrected in ERG critique of company's response to ACD consultation. **Abbreviations**: ACM: appraisal committee meeting; L: litres

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# Thank you

# Back up slides

# Company's additional network meta-analysis (ACD 3.9 to 3.11) (2)

*Avatrombopag has lowest probabilities of reaching platelet count thresholds*

| | Probability of reaching ≥30×10$^9$/L (estimates using 'step' function) | | Probability of reaching ≥30×10$^9$/L (estimates using 'phi' function) | |
|---|---|---|---|---|
| | Proportion | SD | Median | 95% Credible interval |
| PLC | 0.00 | 0.00 | 0.00 | [0.00, 0.00] |
| AVA | 0.9997 | 0.0181 | 0.9997 | [0.9243, 1.000] |
| ELT | 1.00 | 0.00 | 1.00 | [1.00, 1.00] |
| ROM | 1.00 | 0.00 | 1.000 | [0.9993, 1.00] |

| | Probability of reaching ≥50×10$^9$/L (estimates using 'step' function) | | Probability of reaching ≥50×10$^9$/L (estimates using 'phi' function) | |
|---|---|---|---|---|
| | Proportion | SD | Median | Credible interval |
| PLC | 0.00 | 0.00 | 0.00 | [0.00, 0.00] |
| AVA | 0.9718 | 0.1656 | 0.9714 | [0.4778, 0.9999] |
| ELT | 0.9999 | 0.0089 | 0.9999 | [0.9706, 1.0000] |
| ROM | 0.9866 | 0.1148 | 0.9865 | [0.6004, 1.0000] |

**Source:** company response to ACD consultation, appendix A, tables 5 and 7. **Abbreviations**: AVA: avatrombopag; ELT: eltrombopag; L: litres; NMA: network meta-analysis; PLC: placebo; ROM: romiplostim; SD: standard deviation