NICE National Institute for Health and Care Excellence

For public, AIC and CIC redacted

Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refactory diffuse large B-cell lymphoma

Lead team presentation

Lead team: Stephen Sharp, Sumithra Maheswaran, Richard Ballerand

ERG: KSR

Chair: Jane Adam

Technical team: Roshni Maisuria, Zoe Charles, Janet Robertson

Company: Roche

28th January 2020

Key issues: clinical

- What is the committee's view on the available results from the GO29365 trial?
- Is the comparator used in the trial (bendamustine with rituximab) a reasonable proxy for standard of care?
- Are the results generalisable to UK clinical practice?
- Is polatuzumab vedotin a curative treatment, and if so at what stage can cure be assumed?

[redacted]

Disease Background - Non-Hodgkin lymphoma (NHL)

- NHL: heterogeneous group of lymphoproliferative malignancies, 80–95% arising from B-cells, the remaining from T-cells. Diffuse large B-cell lymphoma (DLBCL), 40% of cases, is a high grade lymphoma
- Haematological Malignancy Research Network (HMRN) estimates 5,510 new cases of DLBCL pa in UK
- Approximately 600 pa treated for relapsed or refractory (R/R) DLBCL are not suitable for hematopoietic stem cell transplant (potentially curative option).
- R/R DLBCL has a poor prognosis - median survival 10 months. Approximately 41% survive for 12 months.
- Outcomes particularly poor for those refractory to first-line therapy. In the SCHOLAR-1 study, (largest pooled retrospective analysis of patients with refractory DLBCL), median overall survival was 6.3 months in refractory disease & 22% alive at 2 years.
- Age an important prognostic indicator: patients ≥65 years have a poorer prognosis than younger patients

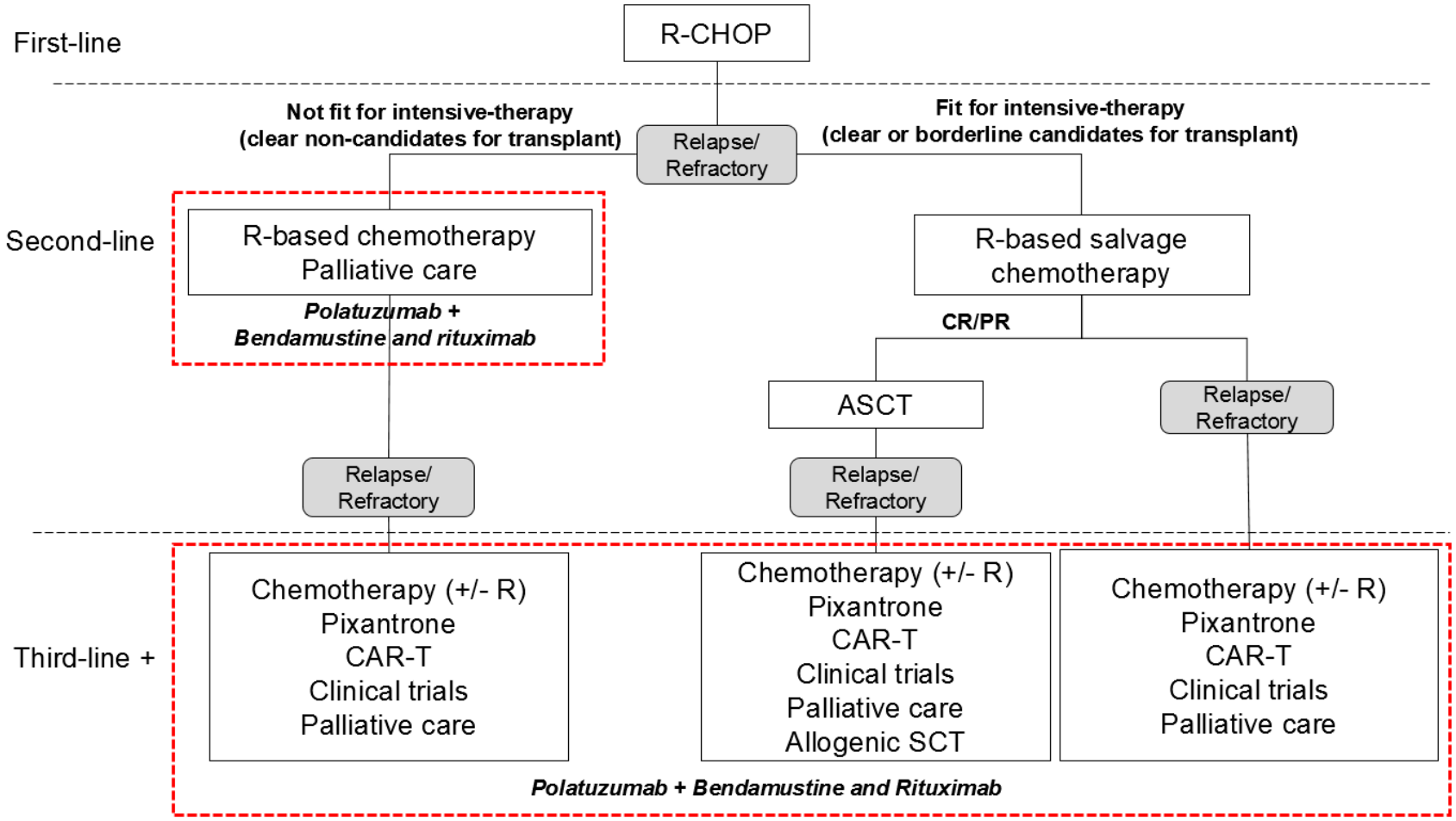
Polatuzumab vedotin

Polatuzumab vedotin: antibody-drug conjugate - binds to cell surface antigen CD79b which is expressed only on B-cells and in most B-cell Non-Hodgkin lymphomas

Conditional marketing authorisation, Jan 2020	In combination with bendamustine and rituximab for of adults with relapsed / refractory diffuse large B-cell lymphoma (DLBCL) ***who are not candidates for haematopoietic stem cell transplant.***
Additional tests	None
Administration and dosage	Polatuzumab vedotin • 1.8 mg/kg intravenously (IV) on day 1 over 1 hour • subsequent doses 30-minute infusion Bendamustine - 90 mg/m^2 IV on days 1 and 2 Rituximab - 375 mg/m^2 IV on day 1
Proposed Patient Access Scheme (PAS)	Proposed PAS submitted (not approved at present)

Treatment pathway and proposed positioning of polatuzumab vedotin in combination with bendamustine and rituximab

- No consensus on best treatment for R/R DLBCL
- Standard chemotherapy for first-line treatment of DLBCL is rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP)



Comparators defined in the NICE scope

Rituximab in combination with one or more chemotherapy agents such as:

- R-GemOx (rituximab, gemcitabine oxaliplatin)
- R-Gem (rituximab gemcitabine)
- R-P-MitCEBO (rituximab, prednisolone, mitoxantrone cyclophosphamide, etoposide bleomycin, vincristine)
- (R-)DECC (rituximab, dexamethasone, etoposide, chlorambucil, lomustine)
- BR (bendamustine, rituximab)

[redacted]

Patient perspective

- Most patients with DLBCL first notice rapidly-enlarging lumps, often in the neck, armpit or groin. Symptoms can vary depending on where the lymphoma is growing. Commonly systemic reported symptoms are reported, including fevers, night sweats, unexplained weight loss, fatigue, loss of appetite and severe itching.
- Patients report taking a year or more off work to recover from intensive chemotherapy regimens and stem cell transplants. Some side-effects, especially fatigue and peripheral neuropathy, can last for many years and have a significant impact on quality of life. Younger patients may experience fertility issues or early menopause.
- Patients report experiencing insomnia, anxiety and a ‘constant fear of dying’. Spending many weeks in hospital can have a detrimental effect on the patient and the family as a whole. Even after successful treatment, the relief of getting back into some kind of normal life is marred by the anxiety of relapse. Late effects of treatment are also a psychological and physical challenge.
- Caring for someone with DLBCL is emotionally challenging and time-consuming. Some carers take significant amounts of time off work to transport their loved one to-and-from hospital, care for dependants, collect medications and visit hospital. One patient reported preferring to stay in hospital if possible to try to spare their spouse worry.
- It can be very difficult for carers to understand what their loved one is experiencing. They often feel helpless, anxious and scared. One patient reported that their spouse turned to the GP for psychological support.
- Patients feel there is a definite unmet need for an effective, less demanding treatment with fewer side effects.

Clinical trial evidence – GO29365

Trial design	Phase Ib/II, multicentre, open-label study
Population	Patients with R/R DLBCL • Age ≥18 years • ECOG PS 0–2 • At least 1 measurable lesion ≥1.5 cm in its longest dimension • Adequate haematologic function • If received prior bendamustine, response duration >1 year
Intervention	Polatuzumab vedotin plus bendamustine and rituximab (pola vedotin+BR)
Comparator	Bendamustine with rituximab (BR)
Outcomes	• Complete response (CR) – primary outcome • Overall survival • Progression-free survival • Event-free survival • Duration of response • Adverse effects of treatment • Health-related quality of life Data for PFS and OS are from [redacted] data cut (submitted at clarification stage and used in model). For other endpoints 30th Apr 2018 data cut is reported

[redacted]

Results

Outcome	Pola vedotin+BR (n=40)	BR (n=40)
Complete response rate with PET-CT at primary response assessment (IRC-assessed)		
Complete response, n (%) 95% CI	16 (40.0), (24.86, 56.67)	7 (17.5), (7.34, 32.78)
Difference in response rates, n (%), (95% CI) p value	22.5, (2.62, 40.22) p=0.0261	
Progression-free survival (IRC-assessed)		
Patients with event, n (%)	[redacted]	[redacted]
Earliest contributing event, n Disease progression Death	[redacted]	[redacted]
Median time to event, months 95% CI	[redacted]	[redacted]
Stratified HR % (95% CI) p value (log-rank)	[redacted]	

[redacted]

Kaplan-Meier Curve for PFS by IRC, cut-off date [redacted]

[redacted]

Overall survival

Outcome	Polatuzumab vedotin+BR (n=40)	BR (n=40)
Patients with event, n (%)	[redacted]	[redacted]
Median time to event, months 95% CI	[redacted] [redacted]	[redacted] [redacted]
Stratified HR % (95% CI) p value (log-rank)	[redacted] [redacted] [redacted]	

[redacted]

Kaplan-Meier Curve for OS cut-off date [redacted]

[redacted]

Overview of issues

Issues	Summary
1. Formulation	Regulatory issue, no discussion needed
2. Relevant comparators	For discussion
3, Generalisability	For discussion
4. Is the treatment curative	For discussion
5. Cost assumptions	Resolved (subject to PAS approval), included for information
6. Modelling of non-cancer background mortality	For discussion
7. Health-related quality of life	For discussion
8. Time-Horizon	Considered under issue 6
9. End of life criteria	Agreed at engagement – meets criteria

[redacted]

Issue 2: Relevant comparators

Background

- No universally accepted standard of care for R/R DLBCL not suitable for transplant
- NICE scope: multiple comparators identified in addition to BR (trial comparator)
- Company: network could not be constructed for an indirect comparison with other comparators (ERG agreed)
- Company: BR is among the possible regimens for this patient population- no evidence to demonstrate superiority of one regimen over another
- ERG: Comparison with BR is consistent with scope but probably not the only suitable one

Stakeholder comments: clinical experts

- No standard of care in RR DLBCL
- BR not commonly used in UK (not routinely funded) but is SoC in other indications e.g. CLL and usually well tolerated
- Can cause cytopenia, but not expected to be worse than other regimens
- BR not expected to have worse efficacy/ tolerability than other comparators - no data to say that one regimen is better than another

Technical team: BR is a reasonable comparator in the absence of a standard of care

[redacted]

Issue 3: Generalisability and baseline imbalances

Background

- GO29365 relatively small (40 patients in each arm)- 3 UK patients
- ERG: non-white participants underrepresented & 84.7% had Eastern Cooperative Oncology Group (ECOG status) of 0 or 1 i.e. relatively fit
- More patients in the polatuzumab arm had low International Prognostic Index (IPI) score (22.5% compared with 7.5% had a score of 0- 1)
- More patients in the BR group had bulky disease (37.5%, compared with 25% in polatuzumab)
- Company adjusted for OS for both of these, but did not adjust PFS for bulky disease, which could favour polatuzumab

Stakeholder comments: clinical experts

- Ethnicity not a factor when considering efficacy or toxicity
- 14 out of 80 in trial had ECOG of 2. The use of polatuzumab is not rued out in these patients. ECOG 0-2 would be the range used
- Bulky disease is one of several relevant factors in DLBCL - difficult to determine the level of significance of the imbalances between arms given the small patient numbers
- No additional generalisability issues highlighted by experts

[redacted]

Adjustment for baseline imbalances

Company

- Acknowledged the imbalance of prognostic factors (bulky disease and IPI score). Therefore 2 analyses conducted: multivariable regression models & propensity score weighted regression models
- Both showed consistent treatment benefit for polatuzumab, with narrower 95% CI in the propensity score weighted model than multivariate models (indicating more precise estimates of treatment effect)
- Concluded: treatment benefit of polatuzumab not affected by the imbalance of some baseline prognostic factors

ERG

- Company methods appropriate, & range of methods tested in sensitivity analyses
- Adjustments to PFS and OS resulted in reduced calculated benefit for polatuzumab, but some benefit maintained, with no overlap of the 95% CIs
- Company used backward selection model for both PFS and OS in the economic analysis on the basis that it produced the least benefit for polatuzumab for OS (HR [redacted])
- Unclear why the propensity score weighted model was not used for PFS as it produced the least benefit in terms of PFS

Technical team: the results of trial GO29365 are generalisable to UK clinical practice

[redacted]

Issue 4: Is polatuzumab vedotin a curative treatment, and if so at what stage can cure be assumed?

Background

- Company: a proportion of patients have long-term remission and are likely to have the same survival as the general population (cured)
- At 30 months follow-up, 9/40 (23%) of patients in the polatuzumab arm in disease response (8 complete, 1 partial) vs 2/40 (5%) in the BR arm
- 8 responders in the polatuzumab arm had duration of response from 22+ months to 34+ months & 1 patient had received transplant
- Company: a high complete response (CR) rate is associated with improved outcomes in DLBCL

Stakeholder comments:

Clinical experts

- Too early to say if this will be a curative treatment
- Chance of cure is high in DLBCL with ongoing CR lasting >24 months and this is independent of the treatment used (e.g. no reason to be different from CAR-T therapies) as the disease itself and duration of response are the relevant factors
- However, might not be correct to assume that these patients have the same risk of mortality as general population as some patients will still relapse, and the treatments received themselves can impact on long term survival
- Estimate 5-15% 2 year survival with BR

Technical team: There is a lack of robust long-term evidence on long-term remission and cure. Is it plausible to assume that this is a curative treatment, and if cured will long term survival be the same as the general population?

[redacted]

Key issues: clinical

- What is the committee's view on the available results from the GO29365 trial?
- Is the comparator used in the trial (bendamustine with rituximab) a reasonable proxy for standard of care?
- Are the results generalisable to UK clinical practice?
- Is polatuzumab vedotin a curative treatment, and if so at what stage can cure be assumed?

[redacted]

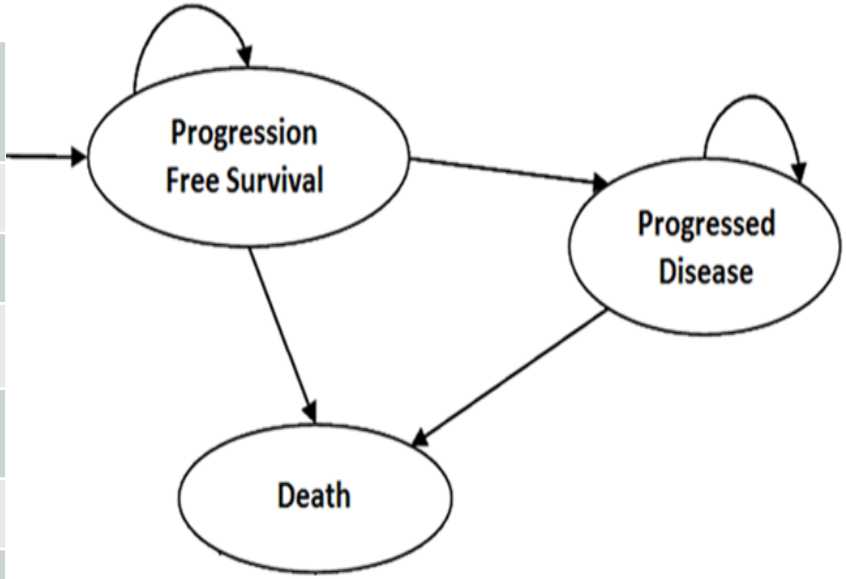
Key issues: cost effectiveness

- Which approach is most appropriate for extrapolation of PFS and OS – the company's cure-mixture model, or the ERG's independent parametric survival model?
- For modelling non-cancer background mortality, is an individual or cohort-based approach more appropriate?
- Do the utility values used in the model reflect the health-related quality of life of people with R/R DLBCL?

[redacted]

Cost-effectiveness model

Model type	Partitioned survival analysis model with three mutually exclusive health states
Health states	PFS, PD, Death
Population	Patients with R/R DLBCL ineligible for SCT
Intervention	Polatuzumab vedotin + BR (Pola+BR)
Comparators	BR
Time horizon	45 years
Model cycle	1 week
Discount rates	3.5% for both health and cost outcomes
Utility values	EQ-5D-5L data (ZUMA-1 study),cross-walked to 3L values



Progression free survival (PFS), Progressed disease (PD), Stem cell transplant (SCT), Bendamustine with rituximab (BR), Personal Social Services (PSS)

[redacted]

PFS cure-mixture extrapolation functions (adjusted analysis, COD March 2019)

Predicted cure fraction, generalised gamma extrapolation: [redacted] Pola+BR, [redacted] BR [redacted]

OS cure-mixture extrapolation functions (OS informed by PFS)

Predicted cure fraction, generalised gamma extrapolation [redacted] Pola+BR, [redacted] BR

[redacted]

ERG analysis – PFS standard parametric lognormal extrapolation

Figure from ERG, R-Benda, bendamustine + rituximab; PFS, progression-free survival; Pola+BR, polatuzumab + bendamustine + rituximab

[redacted]

ERG analysis – OS standard parametric generalised gamma extrapolation

Figure from ERG, BR, bendamustine + rituximab; OS, overall survival; Pola+BR, polatuzumab + bendamustine + rituximab

[redacted]

Comparison of outputs: company's cure-mixture model vs. ERG's standard parametric model

Progression free survival comparison

Months	Pola + BR (ERG)	BR (ERG)	Pola + BR (CS)	BR (CS)	Pola + BR (KM)	BR (KM)
0	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
24	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
60	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
120	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Overall survival comparison

Months	Pola + BR (ERG)	BR (ERG)	Pola + BR (CS)	BR (CS)	Pola + BR (KM)	BR (KM)
0	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
24	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
60	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
120	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

BR, bendamustine + rituximab; Pola+BR, polatuzumab + bendamustine + rituximab

[redacted]

Issue 4: Is polatuzumab vedotin a curative treatment, and if so at what stage can cure be assumed? (economic modelling)

Background

- Company used a cure-mixture generalised gamma model to extrapolate PFS and OS. This assumes that a proportion of patients who are progression free at 2 years are "cured".
- In the cure-mixture extrapolation, the cured patients only have SMR-adjusted general population mortality risk from the start of the trial.
- In the economic model, the cured patients are assumed to use no healthcare resources after 2 years, and are assigned age/gender adjusted general population utilities.
- Instead of using a standard cure-mixture modelling software package (e.g. flexsurvcure in R), the company developed its own code, which was not transparent and clear enough for the ERG to assess the correctness of the implementation of the methods

Company comments

- Observed KM 2-year PFS rate (IRC) for pola+BR in GO29365 is [redacted].This estimate is robust and unlikely to change due to maturity of the data with 30 months median follow up.
- Plausible that approx. two-thirds of patients in PFS at 2 years are in long-term remission.
- In BR arm, long-term remission rates in adjusted analysis are [redacted] to [redacted] (depending on parametric model), this overlaps with range expected in clinical practice by experts (5-10%).
- Standard parametric models generally underestimate the observed 2 year PFS and predict that most patients in PFS at 2 years will progress or die by 5 years.

[redacted]

Issue 4: Is polatuzumab vedotin a curative treatment, and if so at what stage can cure be assumed? (economic modelling)

ERG comments

- Prefers independent standard parametric survival extrapolation due to lack of robust long-term evidence to be confident in a cure assumption.

- Agrees that PFS data are mature but difficult to see how one can infer the plausibility of long-term remission from [redacted] PFS at year 2 and [redacted] PFS at month 34.

- Main concerns about cure-mixture model:
  - Lack of a plateau in the KM curve for PFS. From months 24 to 32, PFS % falls from [redacted] to [redacted]
  - Smoothed hazard plots for OS and PFS from GO29365 do not suggest a “cure’ behaviour; details of how the smoothed hazards and OS/PFS extrapolations fitted to the empirical hazards were not presented.
  - Company model overestimates Pola+BR PFS and underestimates BR PFS towards the end of the follow-up.
  - In TA559 and TA567 of CAR-T therapies where cure mixture models were used, plateaus in the KM curves for PFS and OS were observed towards the end of follow-up.
  - Company’s justification for using the in-house code was not deemed to be persuasive. ERG prefers to use the flexsurvcure R package.
  - Cured patients have SMR-adjusted general population mortality risk from the start of the trial. In the model, 2-year timepoint is only relevant in terms of the healthcare resource utilisation and utilities.

[redacted]

Issue 5: Cost assumptions

Background

- Polatuzumab vedotin will initially be available only in a 140 mg vial size at a list price of [redacted] per vial. The 30 mg vial is in development and is planned to be available at an equivalent per mg price ([redacted] per 30 mg vial).
- The use of the 140 mg vial alone prior to the availability of the 30 mg vial could initially create waste for individual NHS Trusts due to a lack of flexibility in vial sizes to tailor the dose to patients' individual weights.
- Given an average dose of 143.9 mg based on the GO29365 study, nearly half is wasted when only 140 mg vials are available, and no vial sharing is assumed.
- After technical engagement, company revised their cost assumptions and submitted a PAS (not approved at present)
- In the model, no vial sharing is assumed
- Uncertainty about number of cycles of treatment: company model assumes a maximum of 6 cycles, but ERG noted that 5% patients had more than 6 cycles in trial.

[redacted]

Issue 5: Cost assumptions

Stakeholder comments

Company

- Does not expect more than 6 cycles to be given in clinical practice as this is not within the SmPC and not in the GO29365 protocol. No patients had more than 6 cycles in the study but the KM time to off treatment (TTOT) curve is not zero after 4.15 months (time point corresponding to 6 cycles) because of delayed cycles given to some patients.

ERG

- Not clear how the TTOT curve is constructed and how delayed doses were included in the company's calculations. New ERG base case includes the polatuzumab costs for the patients whom the drug was administered in delayed cycles. Company's approach was also tested in a scenario analysis.

[redacted]

Issue 6: Modelling of non-cancer background mortality

Background

- Background mortality in company's model was based on the age distribution in the trial rather than assuming a single-age cohort as preferred by the ERG in its base case.
- ERG prefers a cohort-based modelling approach for consistency with the modelling of PFS and OS.
- Company's individual modelling approach results in approx. 4% of patients still alive at age 105, which is implausible, and has implications for the choice of time horizon.
- ERG's cohort-based modelling approach results in no patients still alive at the end of the 45 year time horizon.

Company comments:

- Disagrees with using the ERG's cohort-based approach and believes the individual modelling approach is more realistic because it acknowledges that there is an age distribution in the trial cohort, as in clinical practice, and not all patients are 69. Company believes that to compare the OS outcomes in the trial cohort accurately with the survival of a general population control cohort, the actual age distribution needs to be considered.

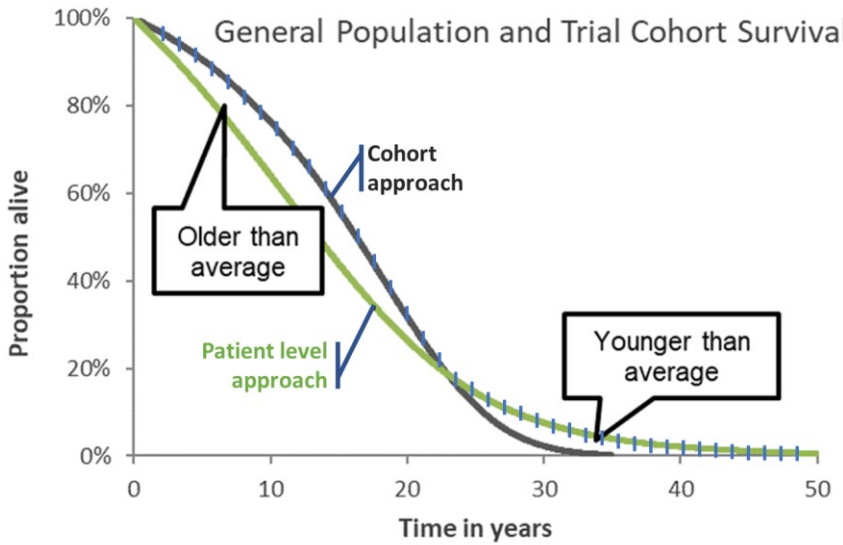
[redacted]

Issue 6: Modelling of non-cancer background mortality

Company comments

- Individual modelling approach is more reflective of clinical practice where a distribution of ages similar to the trial is expected.
- Short term survival is lower than in a cohort where everyone is the same age (69), as some people enter the model older than 69.
- Long term survival is higher, as some people enter the model younger than 69.
- Company adjusted background mortality after engagement to a standardised mortality ratio of 1.41 preferred by ERG, instead of 1 in original model.

Non-disease related mortality model



- The company selected cohort approach for cancer related mortality (*more dominant cause of death in the initial years*) and patient level approach for non-cancer related mortality (*more dominant cause of death in the later years*)

Technical team: Which method is the most appropriate for modelling non-cancer background mortality: individual or cohort-based?

[redacted]

Issue 7: Health-related quality of life

Background

- Health-related quality of life was not directly measured in trial GO29365
- Company justified using HRQL data collected in the ZUMA-1 trial of mixed histology lymphoma patients, on the basis that they were used in a previous NICE technology appraisal (TA559).
- Based on a small sample (34 patients provided 87 observations), using the EQ-5D-5L. The progressed disease value was based on a very small sample of 5 observations
- The utility values used in the base case were 0.72 for the progression-free health state and 0.65 for progressed disease (PD).
- The ERG identified alternative utility sources but did not consider these to be any better.

Stakeholder comments

- Clinical experts believe that this technology will increase health-related quality of life more than current care especially for those who achieve CR and improve lymphoma related symptoms.
- The company is not aware of more suitable estimates of utility values. The values selected in their base case were considered the most appropriate and also result in the most conservative ICER estimates for the sets identified.
- ERG state that the small variation in ICERs shows that the utility values themselves are not big drivers of model results.

Technical team: The company has used the best available data, but these are from a small sample that is not specific to R/R DLBCL and may not therefore be reliable.

[redacted]

Company's cost effectiveness results

Revised base case deterministic results after technical engagement

Intervention	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£/QALY)
140 mg vial only							
Pola+BR	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
BR	21,061	[redacted]	[redacted]	-	-	-	-
140 mg and 30 mg vial							
Pola+BR	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
BR	21,061	[redacted]	[redacted]	-	-	-	-

Mean probabilistic results (assumes 140 mg vial only)

Intervention	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£/QALY)
Pola+BR	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
BR	36,776	[redacted]	[redacted]	-	-	-	-

BR, bendamustine + rituximab; ICER, incremental cost-effectiveness ratio; LYG, life years gained; Pola+BR, polatuzumab + bendamustine + rituximab; QALYs, quality-adjusted life years

Note: [redacted]

[redacted]

Impact of ERG's changes on ICER

Scenario	Pola+BR		BR		Incr. Cost (£)	Incr. QALY	ICER (£)
	Cost (£)	QALY	Cost (£)	QALY			
Company (BC)	[redacted]	[redacted]	21,061	[redacted]	[redacted]	[redacted]	[redacted]
Company (BC) + cohort modelling	[redacted]	[redacted]	21,169	[redacted]	[redacted]	[redacted]	[redacted]
Company (BC) + independent parametric extrapolation of OS and PFS	[redacted]	[redacted]	25,209	[redacted]	[redacted]	[redacted]	[redacted]
Company (BC) + delayed Pola doses included	[redacted]	[redacted]	21,197	[redacted]	[redacted]	[redacted]	[redacted]
ERG (BC) - all 3 of the above changes	[redacted]	[redacted]	25,162	[redacted]	[redacted]	[redacted]	[redacted]
ERG probabilistic BC	[redacted]	[redacted]	28,964	[redacted]	[redacted]	[redacted]	[redacted]

BR, bendamustine + rituximab; ICER, incremental cost-effectiveness ratio; Pola+BR, polatuzumab + bendamustine + rituximab; QALYs, quality-adjusted life years

[redacted]

[redacted]

Issues resolved during technical engagement

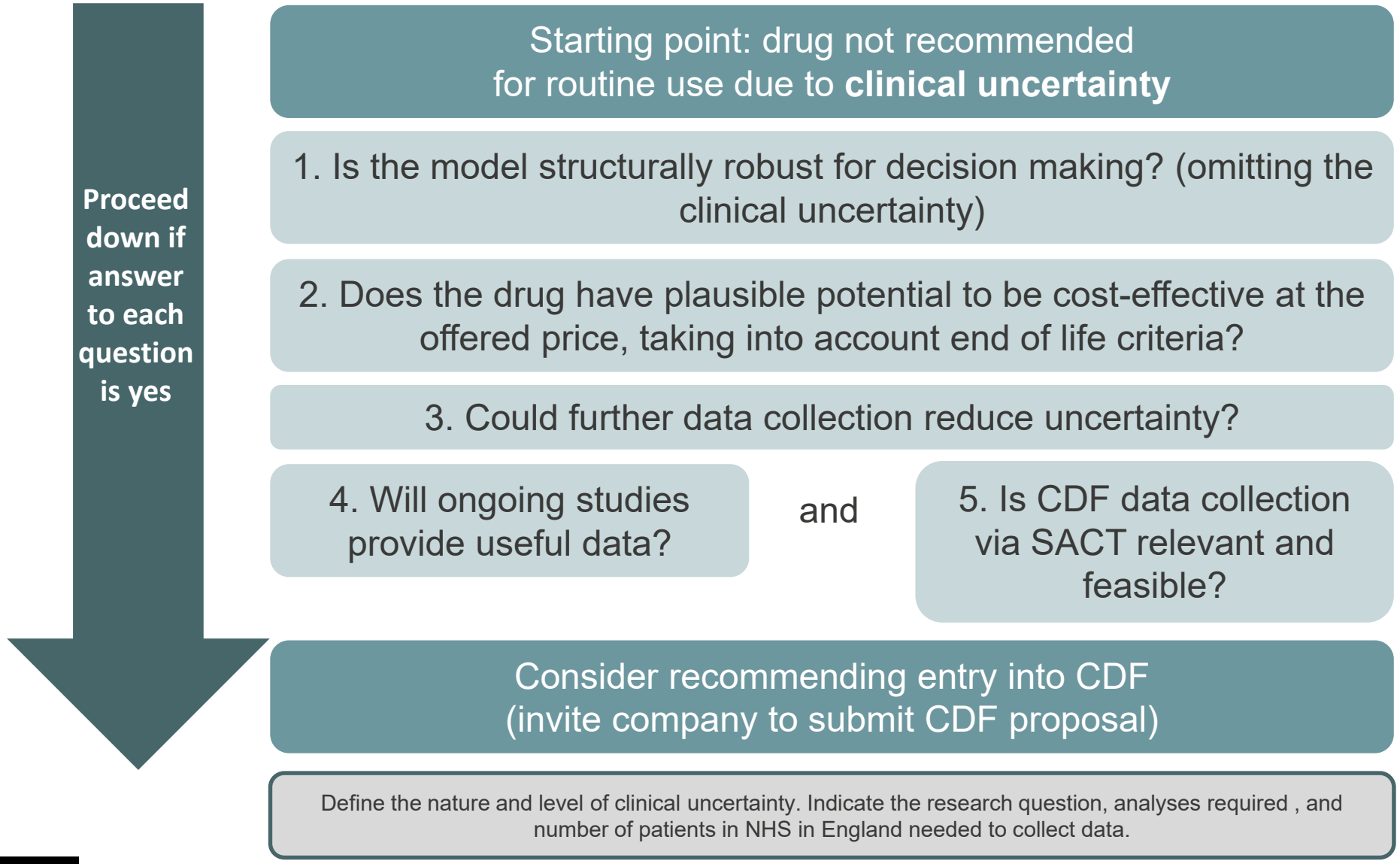
	Summary	Stakeholder responses	Technical team consideration
1	Issue 1- Formulation data from trial GO29365 was generated with a liquid formulation of polatuzumab; however the company is to supply polatuzumab vedotin in its lyophilised formulation.	Company believes there is no reason for there to be any difference in the safety and efficacy profiles of the liquid and lyophilised formulations.	Not aware any safety or efficacy issues and believes this is a regulatory issue that does not require discussion by the appraisal committee.
2	Issue 8 – Time horizon		Addressed under Issue 6
3	Issue 9 – End of life criteria	Company presented evidence in support of EoL criteria: **Life expectancy**: median OS for BR in GO29365 was [redacted] Average survival estimated in economic analysis was 12.2 months. **Extension of life**: difference in medians in GO29365 of 7.7 months. Estimated mean OS gain in original model was 4.1 years	ERG and NICE technical team are satisfied that the end of life criteria are met.

Key issues: cost effectiveness

- Which approach is most appropriate for extrapolation of PFS and OS – the company's cure-mixture model, or the ERG's independent parametric survival model?
- For modelling non-cancer background mortality, is an individual or cohort-based approach more appropriate?
- Do the utility values used in the model reflect the health-related quality of life of people with R/R DLBCL?

[redacted]

Committee decision making: CDF recommendation criteria



Summary of cost effectiveness results

Scenario	ICER (£/QALY)
Company base-case	[redacted]
ERG base case deterministic	[redacted]
ERG mean probabilistic results	[redacted]
ERG PFS - Cure-mixture generalised gamma	[redacted]
ERG PFS - Independent log-logistic	[redacted]
ERG PFS - Independent generalised gamma	[redacted]
ERG OS - Cure-mixture generalised gamma	[redacted]
ERG OS - Independent log-normal	[redacted]
ERG OS - Independent log-logistic	[redacted]
ERG - declining OS treatment effect from 30-120 months	[redacted]
ERG - declining PFS treatment effect from 30-120 months	[redacted]
ERG - declining OS and PFS treatment effect from 30-120 months	[redacted]
ERG - TTOT curve, excluding delayed doses given after 6th cycle	[redacted]
ERG - polatuzumab given to all patients who did not progress in the first 6 months	[redacted]

[redacted]

[redacted]

Cure-mixture model extrapolations

Predicted long-term remission (cure fraction) from PFS cure-mixture model extrapolations (adjusted analysis, cut-off date March 2019)

Parametric distribution	Cure fraction Pola+BR	Cure fraction BR
Exponential	[redacted]	[redacted]
Weibull	[redacted]	[redacted]
Gompertz	[redacted]	[redacted]
Log-normal	[redacted]	[redacted]
Generalised gamma	[redacted]	[redacted]
Log-logistic	[redacted]	[redacted]

Predicted long-term survival (cure fractions) from OS informed by PFS-IRC cure-mixture model extrapolations (adjusted analysis, cut-off date March 2019)

Parametric distribution	Cure fraction Pola+BR	Cure fraction BR
Exponential	[redacted]	[redacted]
Weibull	[redacted]	[redacted]
Gompertz	[redacted]	[redacted]
Log-normal	[redacted]	[redacted]
Generalised gamma	[redacted]	[redacted]
Log-logistic	[redacted]	[redacted]

BR, bendamustine + rituximab; Pola+BR, polatuzumab + bendamustine + rituximab

[redacted]