NICE National Institute for Health and Care Excellence

NICE guidance

Polatuzumab vedotin in combination for untreated diffuse large B-cell lymphoma

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Polatuzumab vedotin with rituximab, cyclophosphamide, doxorubicin and prednisolone (R-CHP) is recommended for untreated diffuse large B-cell lymphoma (DLBCL) in adults, only if

- they have an International Prognostic Index (IPI) score of 2 to 5
- the company provides it according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with polatuzumab vedotin with R-CHP that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Standard treatment for untreated DLBCL is rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP). The company only provided evidence for polatuzumab vedotin with R-CHP for people with an IPI score of 2 to 5. This is narrower than polatuzumab vedotin's marketing authorisation, but clinical experts advised this is how it would be used in clinical practice.

Clinical evidence suggests that people with an IPI score of 2 to 5 having polatuzumab vedotin with R-CHP have more time before their cancer gets worse than people having R-CHOP alone. It is not clear if polatuzumab vedotin with R-CHP increases how long people live compared with R-CHOP.

The cost-effectiveness estimates for polatuzumab vedotin with R-CHP are likely to be within what NICE considers an acceptable use of NHS resources. So, polatuzumab vedotin with R-CHP is recommended for people with an IPI score of 2 to 5.

2 Information about polatuzumab vedotin

Marketing authorisation indication

2.1 Polatuzumab vedotin (Polivy, Roche) in combination with rituximab, cyclophosphamide, doxorubicin and prednisolone is indicated for 'the treatment of adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL)'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for polatuzumab vedotin.

Price

2.3 Polatuzumab vedotin costs £2,370 per 30 mg vial or £11,060 per 140 mg vial (excluding VAT, BNF online accessed December 2022).

2.4 The company has a commercial arrangement. This makes polatuzumab vedotin available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee considered evidence submitted by Roche, a review of this submission by the evidence review group (ERG), and responses from stakeholders. See the committee papers for full details of the evidence.

Clinical need and treatment pathway

There is a high unmet need for a first-line treatment that stops diffuse large B-cell lymphoma progressing

3.1 Diffuse large B-cell lymphoma (DLBCL) is an aggressive disease. Symptoms usually develop rapidly and progress quickly. The disease is treated with the aim of cure, but it is refractory to treatment or relapses after initial treatment in up to 50% of people. The clinical experts explained that current treatment for untreated DLBCL is rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP). They noted that first-line treatment has the best chance of cure. They explained there is an unmet need to stop the disease from progressing. This is because treatment options for relapsed or refractory disease are associated with significant burden and toxicity. The clinical experts explained that relapsed or refractory disease has poor survival rates. A patient expert submission to NICE explained that DLBCL is difficult to live with because of the symptoms of both the disease and treatment. Common symptoms include painless swellings at single or multiple sites (lymph node and non-lymph node), excessive night sweating, unexplained fever and weight loss. The patient expert submission also highlighted the psychological effects of relapsed or refractory disease for both patients and carers. People may have insomnia, anxiety and a constant fear of relapse and death. The committee agreed that DLBCL is an aggressive form of lymphoma that needs intensive treatment. It concluded that there is a high unmet need for first-line treatments that prevent disease progression.

Clinical evidence

It is appropriate to exclude DLBCL with an IPI score of 0 to 1 from this appraisal in line with the evidence available

3.2 The International Prognostic Index (IPI) risk group is usually used to predict DLBCL prognosis. IPI risk group is categorised based on independent predictors for outcomes like overall survival and progression-free survival. IPI risk group is determined by the number of predictors met: 0 or 1 is low risk, 2 is low-intermediate risk, 3 is high-intermediate risk, and 4 or 5 is high risk. The company positioned polatuzumab vedotin with rituximab, cyclophosphamide, doxorubicin and prednisolone (R-CHP) for DLBCL with an IPI score of 2 to 5. This is because the clinical trial excluded those with an IPI score of 0 to 1. However, the committee recalled that the marketing authorisation is 'adult patients with previously untreated DLBCL' and does not restrict by IPI risk group. The clinical experts explained that the outcomes for IPI 0 to 1 were usually very good and only a small proportion of people with DLBCL have an IPI score of 0 to 1. They noted that it was appropriate to exclude DLBCL with an IPI score of 0 to 1. The committee concluded that it was appropriate to exclude DLBCL with an IPI score of 0 to 1 for this appraisal, in line with the evidence available.

The appropriate population for decision making is people with DLBCL with an IPI score of 2 to 5

3.3 The main clinical evidence was from the POLARIX trial. This was a multicentre phase 3, double-blind, placebo-controlled study in adults with previously untreated DLBCL with an IPI score of 2 to 5. POLARIX compared polatuzumab vedotin plus R-CHP with R-CHOP. The primary end point was progression-free survival. People who had polatuzumab vedotin with R-CHP had a 24-month progression-free survival rate of 76.7 (95% confidence interval [CI] 72.7 to 80.8) compared with 70.2 (95% CI 65.8 to 74.6) for people who had R-CHOP. The hazard ratio for disease progression or death was 0.73 (95% CI 0.57 to 0.95, p=0.02). The company did pre-specified exploratory subgroup analyses, dividing by IPI risk group, among other things. For the IPI 3 to 5 subgroup the

hazard ratio for disease progression or death was 0.7 (95% CI 0.5 to 0.9). The committee noted that for some subgroups, such as IPI 2, age 60 or below, presence of bulky disease, and women, the 95% CIs for disease progression or death crossed 1. It noted that in the IPI 2 subgroup, which was 38% of the trial population, the hazard ratio for disease progression or death was 1.0 and 95% CIs ranged from 0.6 to 1.6, suggesting a lack of progression-free survival benefit in this group. The company noted in its submission that the subgroup analyses in the trial were exploratory and not confirmatory, and that POLARIX was not designed or powered to compare subgroups. It also explained that because IPI 2 disease is lower risk and progression or death occurs less often in this population the effect may not be picked up in the trial. The ERG explained that noise in the data could be a reason for the lack of effect shown in some of the subgroups. The clinical experts agreed with the company that IPI 2 disease is a lower risk group and that it is difficult to draw conclusions from the subgroup analysis when it is exploratory. In response to the appraisal consultation document, the company provided a scenario analysis for the IPI 3 to 5 subgroup. The committee noted that there was biological plausibility that people with IPI 3 to 5 disease would benefit more from treatment with polatuzumab vedotin plus R-CHP than people with IPI 2 to 5 disease. It noted that this is because they have more risk factors associated with poorer prognosis, which was supported by the exploratory subgroup analyses. However, the committee noted that the trial was designed to investigate the IPI 2 to 5 population and that the company had previously stated that the IPI 3 to 5 subgroup was only exploratory. The committee also noted that the company had not presented estimates of long-term survival for the IPI 3 to 5 population. Also, it did not have enough information on how the subgroup data had been used by the company to include it in its decision making. The committee concluded that people with an IPI score of 2 to 5 was the appropriate population for decision making.

An overall survival benefit for polatuzumab vedotin with R-CHP compared with R-CHOP cannot be determined using current data

3.4 People who had polatuzumab vedotin with R-CHP had a 24-month overall survival rate of 88.7% (95% CI 85.7 to 91.7) compared with 88.6% (95% CI 85.6 to 91.6) for R-CHOP. The hazard ratio for death was 0.94

(95% CI 0.65 to 1.37). The company explained that the overall survival results are immature and follow up is not long enough to capture the effect of polatuzumab vedotin with R-CHP on survival. The ERG explained that the POLARIX overall survival analysis did not show a statistically significant difference between polatuzumab vedotin with R-CHP and R-CHOP because the confidence interval crossed 1. The committee concluded that it was uncertain if there was an overall survival benefit of polatuzumab vedotin with R-CHP compared with R-CHOP.

Survival modelling

Progression-free and overall survival are extrapolated using a mixture-cure model

3.5 The company and ERG both used a mixture-cure model to extrapolate progression-free survival and overall survival. The mixture-cure model assumed the population consisted of 2 groups: a 'cured' population and a population whose disease would progress. The 'cured' population is assumed to have the same risk of death as the age- and sex-matched general population after 2 years. The committee concluded that a mixture-cure model was a reasonable approach.

The overall survival extrapolations are highly uncertain

3.6 The company explained that it was not possible to estimate long-term survival from the overall survival data in POLARIX because the overall survival data was immature (see section 3.4). Because of this, the overall survival mixture-cure model was informed by the progression-free survival cure fraction. The ERG explained that the approach seemed logical given the immaturity of the overall survival data in POLARIX. However, it noted that the company's overall survival extrapolations were highly uncertain. After consultation, the ERG presented a scenario showing how assuming no overall survival benefit with polatuzumab vedotin with R-CHP compared with R-CHOP affects the cost-effectiveness results. It explained that this was in line with the evidence from POLARIX which had not shown any difference in overall survival at

24-month follow up (see section 3.4). The committee noted that the overall survival extrapolations were highly uncertain. But, based on the benefits in progression-free survival seen in POLARIX (see section 3.3), it was plausible that there would be an overall survival benefit with polatuzumab with R-CHP, meaning the ERG's scenario analysis was conservative. The company noted that more overall survival data will be available in the future from data cuts in August 2022 and 2024. The committee noted that given the overall survival event rate seen in the POLARIX trial, it is unlikely that a meaningful number of overall survival events will have occurred at these data cuts to meaningfully address the overall survival uncertainty. The committee concluded that the ERG's scenario assuming no overall survival benefit with polatuzumab vedotin with R-CHP was likely an underestimate of overall survival. It further concluded that the company's overall survival extrapolation was broadly appropriate but highly uncertain, and that forthcoming clinical trial data is unlikely to meaningfully address the uncertainty.

It is not appropriate to include treatment effect waning

3.7 POLARIX showed no statistically significant survival benefit for polatuzumab vedotin with R-CHP compared with R-CHOP (hazard ratio 0.94; 95% CI 0.65 to 1.37). However, the company's extrapolation (based on the mixture-cure model, see section 3.5) assumed a continued survival benefit for polatuzumab vedotin with R-CHP over R-CHOP. The company explained that because DLBCL is curable in first line, a waning effect should not be applied. The company considered that because overall survival estimated in the model is informed by progression-free survival from POLARIX, the long-term efficacy of polatuzumab vedotin with R-CHP is likely to be underestimated. The ERG explained that there is uncertainty in the overall survival benefit from POLARIX (see section 3.4 and section 3.6) and other subsequent treatments would affect long-term survival. So the ERG applied a waning effect to overall survival to try to account for some of the uncertainty. After consultation, the ERG updated its approach to treatment waning by assuming equal overall survival in each treatment arm after 60 months. The company also presented evidence from first-line and relapsed and refractory DLBCL trials to support a continued survival benefit. The ERG noted that the additional trial evidence provided by the company supported a continued

overall survival benefit in DLBCL. But it explained that these trials had different treatment regimens, patient characteristics and study lengths, which limited how applicable this evidence was to polatuzumab vedotin with R-CHP. The ERG highlighted that the waning effect is in the context of a mixture-cure model. This means waning is applied to the whole population, even those whose disease is cured, which is a more conservative approach than the company's. The clinical experts explained that most death and relapse would occur within 2 years and that subsequent treatments are associated with significant toxicity. The committee noted that applying treatment waning to the whole population in the context of the mixture-cure model, meant that there is a 'cured' population initially, whose disease is then considered 'uncured' later. It noted that the company's approach favoured polatuzumab vedotin with R-CHP and was associated with uncertainty. But it considered the company's approach to be more clinically plausible than the ERG's. Because of this, the committee concluded that treatment effect waning should not be included, but took account of uncertainty about the modelled overall survival estimates in its decision making.

It is unclear if the company's correction to the progression-free survival modelling is appropriate

3.8 In response to the appraisal consultation document, the company highlighted a technical error in the model. It corrected the model at consultation so that at the point progression-free survival extrapolation estimates meet and exceed overall survival extrapolation estimates, they are capped in line with the overall survival extrapolation. The ERG suggested that the company's correction provides counter-intuitive results when changes are made to overall survival. It explained that this is because the mixture-cure model is inflexible to changes such as the correction the company had made. The ERG also explained that based on the information provided by the company, it had been unable to scrutinise this issue adequately. After requests for clarification by the committee at the second appraisal committee meeting, the nature of the error and the appropriateness of the correction was still uncertain. After the second committee meeting, the company provided further explanation on the correction. But the ERG noted that without further scrutiny it remained unclear if the correction was valid. The committee

concluded that it was unclear if the company's correction to the progression-free survival modelling was appropriate.

Economic modelling

The company's model structure is suitable for decision making

3.9 The company used a 3-state partitioned survival model to estimate the cost effectiveness of polatuzumab vedotin with R-CHP compared with R-CHOP. It had 3 health states: progression-free, progressed disease and death. The committee considered that the partitioned survival model is a standard approach to estimating the cost effectiveness of cancer drugs and concluded that it was appropriate in this instance.

Patient weight from the Western European, US, Canadian and Australian population in POLARIX is appropriate to use in the model

3.10 The model used patient weight distributions from the full population in the POLARIX trial. The committee noted that the mean patient weight from POLARIX was 75.92 kg, which is lower than calculated in the 2019 NHS Health Survey for England on overweight and obesity in adults and children (78.75 kg for adults). So the committee questioned if the weight distribution used in the model represented NHS clinical practice. It noted that this could affect the number of vials needed for each person, which would in turn influence costs. It was also aware that no vial sharing was assumed in the model, which may be a conservative approach. In response to the appraisal consultation document, the company explained that the mean patient weight from the subgroup of people in Western Europe, US, Canada and Australia (referred to from now as the Western subgroup) in POLARIX was 80.1 kg. It presented a scenario analysis using the height and weight distribution from the Western subgroup which increased the incremental cost-effectiveness ratio (ICER) by 11%. The committee noted that the average weight in the Western subgroup of POLARIX was more generalisable to the UK population than the weight in the full trial population. The company also presented evidence from a US study (O'Brian et al. 2015) predominantly in men (97%) who received a

DLBCL diagnosis between 1998 and 2008. The company explained that this evidence showed that on average, people with DLBCL have 5% weight loss in the year leading up to diagnosis. It explained that the average weight in the general population with 5% weight loss applied (74.8 kg) is generalisable to the weight in the full POLARIX population. The ERG explained that O'Brian et al. was done in a population that may not be generalisable to people who are having treatment for DLBCL in the NHS. The committee noted that the company's assumption that people with DLBCL would have 5% weight loss before diagnosis was based on 1 study in a population that is likely to have a different weight distribution to the population with DLBCL in the NHS. The committee concluded that it was appropriate to use the weight distribution of the Western subgroup in the model because this was most likely to be generalisable to the weight of people with DLBCL in the NHS.

The company's progressed disease supportive care costs are likely to be overestimated

3.11 Supportive care costs are applied to people in every weekly cycle in the model for the duration of the time the person is in the health state. For progressed disease, this is every year until the disease is cured or death occurs. In its original submission, the company used resource use data for progressed disease based on NICE's technology appraisal guidance on polatuzumab vedotin (TA649) which used progressed disease resource data from NICE's technology appraisal guidance on pixantrone monotherapy (TA306). In its original base case, the ERG preferred to estimate resource use based on NICE's technology appraisal guidance on rituximab (TA243). The committee concluded at the first appraisal committee meeting that neither the company nor ERG base cases represented supportive care resource use for DLBCL in the NHS. It further concluded that end of life costs, included in the company's progressed disease resource use, should be removed. In response to the appraisal consultation document, the company removed end of life costs from the progressed disease supportive care costs. Also in response to the appraisal consultation document, the company updated its approach to estimating progressed disease resource use and costs. The ERG highlighted that the company's approach assumed supportive care costs for progressed disease would apply indefinitely. However, many people

would have response to subsequent treatments and no longer incur these costs. Or, they may have end of life care only. The company explained that the same progressed disease costs were applied in every weekly cycle even though there are periods of high intensity treatment and lower intensity follow up. It explained that this meant that on average, the weekly costs included for progressed disease were appropriate. To inform its updated approach, the company did a survey with 3 clinicians to estimate resource use associated with second-line treatment for DLBCL. Based on this survey, it applied updated costs for the progressed disease state to its model. The company explained that the survey asked clinicians what the resource use was for people with DLBCL having second-line treatment only and did not ask about the off-treatment costs. People in the progressed disease state spend all their time after first progression in this state. So, the committee noted that the survey should have accounted for second-line treatment and all subsequent lines of therapy. The committee considered that this survey may have produced biased results, which reflected the costs of being on second-line treatment, but not the costs of being off treatment or on subsequent treatments. Further bias was possible because it was an opinion-based survey and not based on quantitative data. The committee noted that time off treatment should be considered when estimating the supportive care costs in progressed disease. It was not persuaded that this had been accounted for in the company's model. The committee concluded that the company's progressed disease costs are likely to be overestimated.

Reduction in the company's progressed disease supportive care costs by between 25% to 50% is appropriate

3.12 The ERG explained that to accurately estimate costs for the progressed disease state, on and off treatment costs should be included in the model, but the model was not structured to allow for this. The ERG estimated the time spent incurring costs in the progressed disease state in the model. It based its estimate on the number of subsequent treatments in POLARIX and an estimate of average time to progression on subsequent treatments for relapsed or refractory DLBCL, based on a study by Ohmachi et al. (2013). Based on this, it estimated that a 50% reduction in the company's progressed disease costs (see section 3.11)

was appropriate, accounting for minimal costs when off treatment. The committee noted that the ERG's estimate of a 50% reduction in the company's progressed disease costs was uncertain and based on an estimate of time to progression in relapsed and refractory DLBCL from a single study. It was also uncertain what costs were estimated for people who were off treatment in the ERG's analysis and considered that these may be too low. So, it agreed that a reduction in the company's estimate of progressed disease costs was appropriate, but the ERG's estimate of a 50% reduction in costs was likely too large. It noted that the ERG had also provided a scenario analysis including a 25% reduction in the company's progressed disease costs. But it was uncertain if this scenario analysis was appropriate because it may not reduce the costs enough. It concluded that the appropriate supportive care costs for progressed disease were likely to be somewhere between the ERG's scenario analysis reducing the company's costs by 25% and the ERG's preferred assumption of reducing the company's costs by 50%.

Utility for progressed disease may not have been fully accounted for

3.13 The company used utility values from the GOYA trial because it had a longer follow up than POLARIX. GOYA was a phase 3, open-label study of obinutuzumab plus CHOP compared with R-CHOP in adults with previously untreated CD20-positive DLBCL with an IPI score of 2 to 5. The company explained that 11 clinicians had confirmed that the GOYA utility values were more representative of DLBCL than the POLARIX utility values. The company presented several reasons why the POLARIX utilities were not representative of people with relapsed or refractory DLBCL seen in the NHS. Some people whose disease progressed did not report health-related quality of life (the exact number is considered confidential by the company and cannot be reported here) and those who did report had better health outcomes than those who did not. The company also explained that the timing of collection of the health-related quality of life data affected its applicability. The company considered the timing to be confidential so it cannot be reported here. The ERG noted that the GOYA utility values were similar to those used in NICE's technology appraisal guidance on polatuzumab vedotin (TA649) so agreed to use the GOYA utility values in the base case. The ERG also age

adjusted the progressed disease utility values using UK general population utility values from Ara and Brazier (2010). The committee queried the timing of the health-related quality of life data collection in the GOYA trial, which the company explained was before second-line treatment. The committee questioned whether the valuation of health-related quality of life data was overestimated because the GOYA data was collected before later line treatments were started. Clinical experts explained that the toxicity of later line treatments is significant and that they would expect this to contribute to quality of life. The committee noted it would have preferred to have seen GOYA utilities after second-line treatment was started. However, it concluded that the company's approach was acceptable for decision making but uncertain.

CAR-T therapies should not be included as subsequent treatments

3.14 In its initial submission, the company included 2 chimeric antigen receptor T-cell (CAR-T) therapies as subsequent treatments in the model. These CAR-T therapies are currently in the Cancer Drugs Fund; see NICE's technology appraisal guidance on axicabtagene ciloleucel (TA559) and NICE's technology appraisal guidance on tisagenlecleucel (TA567). NICE's position statement is that technologies with Cancer Drugs Fund recommendations cannot be considered as part of the treatment sequence in relevant appraisals because they cannot be considered established practice. The committee acknowledged the relevance of TA559 to this appraisal, and noted that it is currently being reviewed. At technical engagement, the company explained that CAR-T therapies have high costs, which may make polatuzumab vedotin with R-CHP more cost effective in the long term. But it agreed to remove CAR-T therapies as subsequent treatments from the model. The committee concluded that CAR-T therapies should not be included as subsequent treatments because they are not routinely commissioned.

Redistributing CAR-T therapy use to other subsequent treatments is acceptable

3.15 After technical engagement, in the model the company redistributed people having CAR-T therapies to have other subsequent treatments.

The ERG explained this meant the total use of subsequent treatments was more than 100%, which is implausible. Instead, the ERG did not adjust the proportion of people having each subsequent treatment when CAR-T therapies were removed at technical engagement. This made total subsequent treatment use 97%. The committee noted that use of subsequent treatments in the model was more than 100% before the redistribution of CAR-T therapies. The company explained that this was because chemotherapy and stem cell transplants were considered separately in the model (that is, if someone had chemotherapy and a stem cell transplant, this would be counted as 2 subsequent treatments, meaning the percentage would be higher than 100%). The committee concluded at the first appraisal committee meeting that people would have other treatments if CAR-T therapy was not available. After consultation, the ERG updated its base case to include redistribution of CAR-T therapies to other subsequent treatments. The committee concluded that the company's and updated ERG assumption about CAR-T therapy redistribution was appropriate.

End of life

End of life criteria are not met for polatuzumab vedotin with R-CHP

3.16 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's guide to the methods of technology appraisal 2013. The committee was aware that the mean life expectancy for people with untreated DLBCL who had R-CHOP was more than 24 months. So, it concluded that polatuzumab vedotin with R-CHP did not meet the end of life criteria.

Innovation

Polatuzumab vedotin with R-CHP is innovative

3.17 Clinical experts explained that POLARIX is the first international double-blind randomised controlled trial in over 20 years to show meaningful

improvement in the benefit-risk profile of another treatment over R-CHOP. The committee concluded that polatuzumab vedotin with R-CHP is innovative.

Cost-effectiveness estimates

An acceptable ICER is between £20,000 and £30,000 per QALY gained

3.18 NICE's guide to the methods of technology appraisal 2013 notes that above a most plausible ICER of £20,000 per quality-adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. The committee considered polatuzumab vedotin with R-CHP innovative but noted that the long-term overall survival estimates were highly uncertain (see section 3.6). It also took into account the likelihood of decision error and its consequences. So, it agreed that an acceptable ICER would be between £20,000 and £30,000 per QALY gained.

Polatuzumab vedotin with R-CHP is likely to be cost effective

3.19 The committee noted that its preferences were not fully reflected in either the company's or the ERG's base case at the second committee meeting. The committee's preferred assumptions included:

- considering the full POLARIX population (see section 3.3)
- the company's overall survival extrapolation approach (although noting this was highly uncertain; see section 3.6)
- no treatment effect waning (see section 3.7)
- the patient weight distribution from the POLARIX Western population subgroup (see section 3.10)
- excluding CAR-T therapies (see section 3.14)

- redistributing CAR-T therapy use to other subsequent treatments (see section 3.15).

The committee noted that the company provided a scenario analysis for the IPI 3 to 5 subgroup (see section 3.3). However, it was unclear how the subgroup data had been incorporated into the company's economic model in the scenario analysis. So the committee preferred to consider the full POLARIX population in its decision making. The committee noted that the utility values for progressed disease were uncertain but that the approach used in the company's and ERG's base case was acceptable for decision making (see section 3.13). It also noted that the company included a correction to the progression-free survival modelling after consultation. But it noted that it was unclear if this correction was appropriate and that including it lowered the ICER (see section 3.8). The committee also noted that the company's progressed disease supportive care costs were likely overestimated (see section 3.11). But it considered that the ERG's assumption of a 50% reduction in the company's costs was likely an underestimate and that reducing the company's progressed disease costs by between 25% to 50% is appropriate (see section 3.12). After the second appraisal committee meeting, the company provided an updated base case, including all of the committee's preferred assumptions, as well as:

- removal of the progression-free survival curve correction
- a reduction in the progressed disease costs by 30%
- an updated commercial arrangement for polatuzumab vedotin.

The committee agreed that the company's updated base case ICER was appropriate for decision making. Because of confidential commercial arrangements for cyclophosphamide, doxorubicin, prednisolone and rituximab, the exact ICERs are confidential and cannot be reported here. Taking into account all the confidential discounts, the company's updated base case ICER was at the lower end of the range of what NICE considers a cost-effective use of NHS resources. So, the committee concluded that polatuzumab vedotin with R-CHP is likely to be cost effective.

Conclusion

Polatuzumab vedotin with R-CHP is recommended for untreated DLBCL

3.20 The committee noted that when taking into account all its preferred assumptions and the commercial arrangement offered by the company, polatuzumab vedotin is likely to be a cost-effective use of NHS resources. So, it recommended polatuzumab vedotin with R-CHP for untreated DLBCL with an IPI score of 2 to 5, only if the company provides it according to the commercial arrangement.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

4.2 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for routine commissioning, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Interim funding will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early Access to Medicines Scheme designation or fast track appraisal), at which point funding will switch to routine commissioning budgets. The NHS England and NHS Improvement Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.

4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has diffuse large B-cell lymphoma and the doctor responsible for their care thinks that polatuzumab vedotin with rituximab, cyclophosphamide, doxorubicin and prednisolone is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee C.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

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Accreditation