NICE National Institute for Health and Care Excellence

NICE guidance

Tisagenlecleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia in people 25 years and under

Technology appraisal guidance
Published: 15 May 2024

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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

This guidance replaces TA554.

1 Recommendations

1.1 Tisagenlecleucel is recommended, within its marketing authorisation, as an option for people 25 years and under for treating B-cell acute lymphoblastic leukaemia that is:

- relapsed after a transplant, or
- relapsed for a second or later time, or
- refractory.

It is only recommended if the company provides it according to the commercial arrangement.

Why the committee made these recommendations

This evaluation reviews the evidence for tisagenlecleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia (NICE technology appraisal guidance 554). It also reviews new evidence collected as part of the managed access agreement, which includes evidence from a clinical trial and from people having treatment in the NHS in England.

Usual treatment for B-cell acute lymphoblastic leukaemia that is refractory, relapsed after a transplant, or relapsed for a second or later time in people 25 years and under includes blinatumomab and chemotherapy.

There are no clinical trials directly comparing tisagenlecleucel with usual treatments. But an indirect comparison suggests that people having tisagenlecleucel live longer than people having blinatumomab or chemotherapy.

When considering the condition's severity, and its effect on quality and length of life, the most likely cost-effectiveness estimates are within the range that NICE considers an acceptable use of NHS resources. So, tisagenlecleucel is recommended for routine use in the NHS.

2 Information about tisagenlecleucel

Marketing authorisation indication

2.1 Tisagenlecleucel (Kymriah, Novartis) is indicated for 'paediatric and young adult patients up to and including 25 years of age with B-cell acute lymphoblastic leukaemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse'.

Dosage in the marketing authorisation

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

Price

2.3 The list price for tisagenlecleucel is £282,000 per infusion (company submission).

2.4 The company has a commercial arrangement. This makes tisagenlecleucel available to the NHS with a discount. The size of the discount is commercial in confidence.

3 Committee discussion

The evaluation committee considered evidence submitted by Novartis, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Relapsed or refractory B-cell acute lymphoblastic leukaemia

3.1 B-cell acute lymphoblastic leukaemia (B-ALL) is a rare haematological cancer characterised by the overproduction and accumulation of cancerous, immature white blood cells (lymphoblasts) that originate within the bone marrow. B-ALL develops rapidly and is one of the most common cancers to affect children and young adults. Around 15% to 20% of people with acute lymphoblastic leukaemia (ALL) experience relapse, typically within 2 years of having first-line treatment. Relapsed or refractory B-ALL has a very poor prognosis, which worsens with each successive relapse. The patient experts explained that people with B-ALL often report poor general and mental health and functional impairment. Children and young people with B-ALL experience a range of debilitating symptoms including fatigue, nausea or vomiting, feeling weak or breathless, sleeping problems, headaches, lower back pain and weight loss. The condition also significantly affects the ability of both the person and their caregivers to do daily tasks and maintain employment or education.

Clinical management

Existing treatment pathway

3.2 People with primary refractory B-ALL are usually offered blinatumomab (see NICE's technology appraisal guidance on blinatumomab for previously treated Philadelphia-chromosome-negative acute lymphoblastic leukaemia) or salvage chemotherapy, with the aim of bridging to an allogeneic stem cell transplant

(allo-SCT). Salvage chemotherapy includes FLA(G)-IDA (fludarabine, cytarabine and idarubicin, with or without granulocyte colony-stimulating factor). Inotuzumab ozogamicin is also available for adults with relapsed or refractory CD22-positive B-cell precursor acute lymphoblastic leukaemia (see NICE's technology appraisal guidance on inotuzumab ozogamicin for treating relapsed or refractory B-cell acute lymphoblastic leukaemia). People whose leukaemia responds to initial treatment but then relapses typically have treatment with the intention of later having an allo-SCT. This depends on their eligibility, health and the availability of a donor. For people who have had a second relapse, the treatment options are salvage chemotherapy or blinatumomab, depending on the previous treatment the person has had. Tisagenlecleucel is a chimeric antigen receptor (CAR) T-cell therapy that has been available in the NHS since 2018 through the Cancer Drugs Fund. The company submitted evidence for its use in people 25 years and under with refractory or relapsed B-ALL. The committee noted that tisagenlecleucel has been regularly used for treating B-ALL in the NHS since it became available through the Cancer Drugs Fund.

Tisagenlecleucel as a treatment option

3.3 The patient experts highlighted that allo-SCT and chemotherapy are associated with several debilitating side effects. These include hair loss, fatigue, infections arising from immunosuppression, mucositis, loss of fertility, loss of bone density, increased risk of secondary cancers, graft-versus-host disease and organ damage. Allo-SCT also carries a risk of transplant-related mortality (which can be 10% to 20% depending on the fitness of the donor and the person having the transplant). It also depends on the availability of a well-matched donor. The clinical expert said that allo-SCT is an important and effective treatment option. But limited availability and the risk of toxicity, which can occur even in the long term, means an alternative option in this area is much needed. Both the patient and clinical experts advised that tisagenlecleucel use in the NHS during its time in the Cancer Drugs Fund had transformed the way in which people with relapsed or refractory B-ALL have treatment. They explained that it represents a potential cure for people who often have no other option. The committee concluded that tisagenlecleucel would be an important addition to the treatment pathway for B-ALL if it were to be made available for routine commissioning.

Relevant comparators

3.4 The company considered blinatumomab and salvage chemotherapy to be the most relevant comparators. It did not consider inotuzumab ozogamicin to be a relevant comparator because it is only used in a very small proportion of the population relevant to this evaluation (adults with CD22-positive B-ALL). The committee discussed whether the main comparator would be blinatumomab, because of its established increased effectiveness compared with salvage chemotherapy. The clinical expert advised that blinatumomab is used increasingly as a second-line treatment and it is not usual practice to use it again at a later line. So, salvage chemotherapy remains an important option after a second relapse (as a third or later-line treatment). The NHS England Cancer Drugs Fund clinical lead (from here, Cancer Drugs Fund lead) also confirmed that salvage chemotherapy is commonly used for the population relevant to this evaluation. The committee concluded that blinatumomab is the main comparator because it is preferred by clinicians over salvage chemotherapy because it is more effective. But, salvage chemotherapy is also a relevant comparator because it is still commonly used after 2 or more relapses, particularly for people who have previously had blinatumomab.

Clinical effectiveness

Tisagenlecleucel data sources

3.5 In the company's submission for the original evaluation (NICE technology appraisal 554 [TA554]), the main evidence on the clinical effectiveness of tisagenlecleucel came from 3 single-arm studies:

- ELIANA, an international, multicentre, phase 2 study (n=97 enrolled, 79 had an infusion)
- ENSIGN, a US, multicentre, phase 2 study (n=73 enrolled, 64 had an infusion)
- B2101J, a US, single-centre, phase 1 and 2a study (n=67 enrolled, 57 had an infusion).

All 3 studies were presented as part of a pooled dataset, combining the sources together. In TA554, one of the reasons for tisagenlecleucel being recommended for use in the Cancer Drugs Fund rather than routine commissioning was because of the limited long-term data. After tisagenlecleucel entered the Cancer Drugs Fund, data on its use in the NHS was collected using the Systemic Anti-Cancer Therapy (SACT) dataset. Also, a real-world evidence study (Espuelas et al. 2022) collected evidence on its use in the NHS. This study shared a large proportion of its sample with people in the SACT dataset but used more clearly defined measures of key outcomes, particularly event-free survival (EFS). During this period, further data was collected in the ELIANA study, so for this evaluation it had the longest follow-up data available for tisagenlecleucel (79.4 months).

In this evaluation, the company chose to use data from the ELIANA study alone as a source of evidence for tisagenlecleucel's effectiveness. The EAG preferred the pooled dataset because it was used in the original evaluation (TA554) and allowed for more certain estimates of effectiveness because of the larger sample size. The EAG noted that there was no reason to use ELIANA alone. The company explained that it preferred ELIANA alone because in the original submission for TA554 the committee identified the lack of long-term data as a key area of uncertainty. It added that using ELIANA alone allowed for a longer median follow-up time than using the pooled dataset. The EAG highlighted that the later data cut from ELIANA would be included in the pooled dataset. It further explained that the pooled dataset had been used in its base case. The committee understood that the longer follow up from ELIANA would be accounted for in the pooled dataset and would also be augmented with additional data from 2 other studies. It concluded that the pooled dataset should be used to estimate tisagenlecleucel's effectiveness.

Clinical effectiveness in the tisagenlecleucel studies

3.6 Evidence from the 3 phase 2 studies showed that tisagenlecleucel led to improvements in key clinical outcomes, including EFS and overall survival (OS). The median EFS was 24 months in ELIANA, 21 months in the pooled dataset and 22 months in Espuelas et al. (2022). The median OS in ELIANA and SACT had not

been reached but was 48 months in the pooled dataset. Rates of long-term EFS and OS were broadly comparable between the different data sources. But long-term OS was slightly higher in ELIANA than in the pooled dataset. Also, the real-world evidence showed slightly higher OS and EFS compared with the phase 2 trials (SACT reported data on OS at 36 months and Espuelas et al. [2022] reported on both EFS and OS at 24 months). The clinical expert advised that the real-world evidence was robust, particularly in Espuelas et al. (2022). This was because of the way in which key outcomes were recorded. The clinical expert noted that the real-word evidence supported the data from the key studies and produced remarkably similar results. But the data was not included in the modelling because it was not available in time. The committee concluded that the various sources of data gave generally similar results and the data generated in SACT supported the efficacy data from the key studies.

Adverse events

3.7 Adverse events were reported for the pooled dataset and showed that 51% of people experienced hypogammaglobulinaemia and 81% of people experienced cytokine release syndrome. The clinical expert explained that they would expect most people who have a tisagenlecleucel infusion to experience hypogammaglobulinaemia, and around 85% to have intravenous immunoglobulin treatment at some point in the future. The patient expert said that their experience with tisagenlecleucel was very positive. They explained that they had experienced long-term immunosuppression, which was easily treated with monthly intravenous immunoglobulin, and that they did not develop any subsequent issues from this or experience any other major adverse events. The clinical expert said that tisagenlecleucel causes less severe, shorter term and more manageable side effects than allo-SCT. The committee concluded that cytokine release syndrome and hypogammaglobulinaemia are important side effects of tisagenlecleucel and that rates of hypogammaglobulinaemia may have been underestimated in the key clinical studies.

Indirect treatment comparison

Matching-adjusted indirect comparison

3.8 Because tisagenlecleucel has only been studied in single-arm studies in the population relevant to this evaluation, the company did a matching-adjusted indirect comparison (MAIC) to estimate its relative effectiveness compared with blinatumomab and salvage chemotherapy for OS. To estimate blinatumomab's effectiveness, the company selected a study by von Stackelberg et al. (2016), a single-arm trial in 70 people aged up to 18 years in Europe and the US. For the comparator of salvage chemotherapy, the company used a study by Jeha et al. (2006) in which 61 people aged under 21 years had treatment with clofarabine. The company's clinical experts identified FLA(G)-IDA as being the more relevant chemotherapy regimen for this population, but in the absence of suitable evidence for this treatment, clofarabine was used as a proxy. The company used these sources to estimate the effectiveness of the comparators for both its original submission for TA554, and for this review, but focused on ELIANA data alone to estimate tisagenlecleucel's effectiveness (see section 3.5). The MAIC showed that, after adjustment for key baseline characteristics, tisagenlecleucel significantly improved OS compared with blinatumomab (hazard ratio 0.31, 95% confidence intervals 0.18 to 0.55) and salvage chemotherapy (hazard ratio 0.19, 95% confidence intervals 0.10 to 0.35). This data was almost identical when using the pooled dataset, but with slightly smaller confidence intervals. The committee concluded that the MAIC suggested that tisagenlecleucel improved OS compared with each comparator, and that clofarabine was a suitable proxy for FLA(G)-IDA.

Blinatumomab

3.9 The company used the von Stackelberg et al. study (2016) to estimate the effectiveness of blinatumomab (see section 3.8). The EAG disagreed with the selection of this study, suggesting that another study, RIALTO, was more appropriate. RIALTO was a study in 110 children and young people aged up to 18 years, with relapsed or refractory ALL who had treatment with blinatumomab. The EAG explained that the population in the von Stackelberg et al. study was likely to have a higher risk than people with ALL seen in the NHS, noting that 71%

of people relapsed within 6 months on previous treatment. Additionally, only 34% of people had subsequent allo-SCT in the study. But both the EAG's and company's clinical advisers estimated that around 50% of people having blinatumomab in the NHS would be expected to have subsequent allo-SCT, similar to the rates seen in RIALTO (53%). Allo-SCT is a primary driver of OS. So, it is possible that OS was underestimated for blinatumomab compared with what it would be in the NHS, so creating a bias in favour of tisagenlecleucel. The EAG also noted that a more recent study by von Stackelberg et al. (2023) did an indirect comparison between tisagenlecleucel and standard care, using person-level data from 3 real-world registry outcomes in Germany and Austria. The EAG explained that although it is unclear whether standard care in the study included blinatumomab, inotuzumab or chemotherapy, it showed that from around 5 to 7 years, OS was approximately 30%. This is closer to the cure fraction seen in the EAG's extrapolation of blinatumomab OS using RIALTO (23.4%) than the company's extrapolation (11.4%). The company noted that the von Stackelberg et al. (2016) study was used as the source of data in its original submission for TA554, and was accepted by the committee, although RIALTO was used in a scenario analysis. It explained that tisagenlecleucel is often used when allo-SCT would not be a suitable option (around 50% of people considered for tisagenlecleucel are estimated to have experienced a relapse after allo-SCT). This has changed the way in which blinatumomab is used in the NHS, with it being used primarily with the aim of achieving a complete response as a bridge to subsequent allo-SCT. The company was concerned about the use of RIALTO because this evaluation is attempting to model the effectiveness of blinatumomab in a hypothetical scenario in which tisagenlecleucel is unavailable. It explained that the enrolment period for RIALTO overlapped with tisagenlecleucel becoming available in the NHS. So, enrolment may have been biased by this, with allo-SCT being more suitable for people in RIALTO and so they may have been healthier. The clinical expert suggested that the rates of subsequent allo-SCT expected in clinical practice is uncertain, and the true figure probably lies between the rates reported in the 2 studies. The clinical expert also advised that there is a possibility that people in RIALTO could have tisagenlecleucel at a later line, which would confound results and potentially overestimate OS. The committee agreed that there was uncertainty as to which study best reflected expected clinical practice. It concluded that the von Stackelberg et al. (2016) study continued to be the best source for estimating blinatumomab outcomes in the absence of tisagenlecleucel and should be used

in its decision making.

Economic model

Company's modelling approach

3.10 The company used a partitioned-survival economic model for all treatments that included 3 states: event-free, progressed disease and death. Before entering the partitioned-survival part of the model, people having tisagenlecleucel also progressed through a decision tree to capture outcomes for people who stopped treatment or died before having tisagenlecleucel. The committee concluded that the model structure was appropriate for decision making.

Extrapolating overall survival for tisagenlecleucel

3.11 The company used a mixture-cure model to extrapolate OS. The company used estimates from its clinical experts on expected cure rates for people who have tisagenlecleucel, along with estimates of long-term OS. To extrapolate OS, the company chose the log-logistic distribution, based on good statistical fit and visual fit when compared with clinician estimates of cure. The EAG reiterated its preference for using the pooled dataset in place of ELIANA alone (see section 3.5). To extrapolate OS, the EAG selected the log-logistic distribution. The committee recalled its preference to use the pooled dataset to model tisagenlecleucel effectiveness (see section 3.5) and concluded that the EAG's approach to modelling OS for tisagenlecleucel was suitable for decision making.

NHS England CAR T-cell tariff

3.12 NHS England has established a single tariff to capture the costs of delivering CAR T-cell therapy. The tariff was developed after NICE recommended tisagenlecleucel (in TA554) through the Cancer Drugs Fund in 2018. The tariff includes all care costs, from the decision to have CAR T-cell therapy to 100 days after the infusion. Recent NICE evaluations of CAR T-cell therapies (such as

NICE's technology appraisal guidance on brexucabtagene autoleucel for treating relapsed or refractory B-cell acute lymphoblastic leukaemia) used a CAR T-cell therapy delivery cost of £41,101. The Cancer Drugs Fund lead explained that these costs needed to be updated because they are for an adult population. They explained that CAR T-cell treatment in people who are under 18 years is more expensive. The clinical expert advised that this may be because children with ALL have a higher comorbidity rate than adults, need more support and need at least 2 weeks of inpatient hospital stay, which is often longer than adults. Also, children's CAR T-cell services cannot make the same cost savings that adult services make as a result of the economies of scale of treating multiple adult CAR T-cell indications. To account for this, a tariff price with 83% weighting for the under 18 years population and a 17% weighting for the 18 to 25 years population (using costs associated with treatment for adults) was supplied by NHS England for this evaluation. This resulted in a cost for tisagenlecleucel treatment of £95,194. The committee considered that NHS England was an appropriate source of information on the costs of delivering treatments in the NHS. But it would have preferred more information on the exact breakdown of the tariff cost, to ensure there was no double counting and that the costing exercise fully aligned with NICE's methods. The clinical expert suggested that, in future, a similar tariff should be considered for allo-SCT to make the comparison fair. The committee agreed that a tariff for allo-SCT may be useful, but it was satisfied that the model included the key costs associated with allo-SCT. It concluded that it would consider the tariff price supplied by NHS England in its decision making.

Intravenous immunoglobulin treatment

3.13 People having a tisagenlecleucel infusion often develop hypogammaglobulinaemia (see section 3.7) and typically have treatment with intravenous immunoglobulin, which can be prolonged and costly. The company's base case assumed that 30.4% of people having treatment with tisagenlecleucel go on to have intravenous immunoglobulin treatment. It assumed that intravenous immunoglobulin treatment lasts for a median of 11.4 months, based on data for the time to B-cell recovery in an earlier data cut of ELIANA. In the EAG base case, it also used a 30.4% likelihood of having intravenous immunoglobulin treatment but applied a longer median duration of 25.5 months. This was based on estimates of EFS at 5 years, adjusted for subsequent allo-SCT rates. The EAG

questioned if it was suitable for the company to model duration of treatment using an earlier data cut of ELIANA, when a later data cut shows a much longer average time to B-cell recovery. The EAG also noted that its estimates were similar to those seen in the SACT dataset and provided a scenario analysis based on rates reported in the SACT dataset in which 47% of people had intravenous immunoglobulin treatment, with a median duration of 18 months. The patient expert advised that intravenous immunoglobulin treatment did not have much of an impact on everyday life besides needing a monthly infusion, and that this was manageable. The committee recalled that the clinical expert said that rates of hypogammaglobulinaemia were likely underestimated in ELIANA and that most people having a tisagenlecleucel infusion would need intravenous immunoglobulin treatment (see section 3.7). The committee concluded that intravenous immunoglobulin treatment should be modelled using the data provided in the SACT dataset because this relates to actual use in the NHS, but requested further data from the Cancer Drugs Fund lead about this. After the committee meeting, NHS England provided more recent data on the rates and duration of intravenous immunoglobulin treatment in the NHS, which was not substantially different to the data used in the EAG scenario analysis based on the SACT data. But the committee continued to be concerned that the proportion of people needing intravenous immunoglobulin treatment and the average duration of intravenous immunoglobulin use could increase over time as the pool of people developing hypogammaglobulinemia and those having intravenous immunoglobulin treatment for long periods increases.

Discount rate

3.14 The company included a 3.5% per year discount rate for costs and benefits in its base case, but stated a preference for a 1.5% per year discount rate and included a scenario analysis for this. The NICE health technology evaluations manual states that the committee may consider a rate of 1.5% if it is satisfied that the following 3 criteria are met:

- the treatment must be for people who would otherwise die or have a very severely impaired life
- the technology is likely to restore people to full or near-full health

- the benefits must be sustained over a very long period of time.

The committee recalled testimony from the patient and clinical experts about the profound impact that B-ALL has on quality of life and its mortality risk (see section 3.1). It also noted that evidence from the clinical trials plus advice from experts suggested that for some people tisagenlecleucel represents a cure, although this would not apply to everyone, because some people still experience relapse. The clinical expert advised that it would only be possible to say safely that a person is cured from B-ALL if they had not had a B-ALL-related event for around 7 years after having treatment. They noted that only the ELIANA study had median follow-up data approaching this duration (see section 3.5 and section 3.6). The committee considered that there was uncertainty around how many people are cured by tisagenlecleucel, because B-ALL affects children and young adults, so the follow-up data is still limited. Also, some people still progress or die after treatment. It concluded that the first criterion was met, but that there was uncertainty around whether criteria 2 and 3 were met, and so a 3.5% per year discount rate should be applied to costs and benefits.

Other factors

Equality

3.15 During the scoping consultation exercise for this evaluation, it was noted that people from ethnic minority backgrounds are less likely to find a suitable allogeneic stem cell match, and that access to tisagenlecleucel may address this. But the committee noted that a technology appraisal cannot change how suitable matches for allo-SCT are identified. Also, it was noted that because brexucabtagene autoleucel is now available through the Cancer Drugs Fund for relapsed or refractory B-ALL in people 26 years and over (see NICE's technology appraisal guidance on brexucabtagene autoleucel), there is a high unmet need for CAR T-cell therapies in people aged up to 25 years. The committee recognised that having continued access to tisagenlecleucel would help resolve an unmet need in this age range. Age and race are protected characteristics under the Equality Act 2010. But, because the recommendation does not restrict access to

treatment for some people over others, the committee concluded that there were no equalities issues relevant to this evaluation.

Uncaptured benefits

3.16 The committee recognised that tisagenlecleucel represents an effective treatment option for people with relapsed or refractory B-ALL who would otherwise have limited options. The evidence showed that it is associated with improvements in key clinical outcomes. The patient expert said that their quality of life improved considerably after treatment. They explained that side effects were manageable and that tisagenlecleucel is a potential cure for a condition with limited alternatives, which are less effective. The committee concluded that tisagenlecleucel is innovative in treating relapsed or refractory B-ALL and took this into account in its decision making.

Severity

3.17 The committee considered the severity of the condition (the future health lost by people living with the condition and having standard care in the NHS). The committee may apply a severity modifier (a greater weight to quality-adjusted life years [QALYs]) if technologies are indicated for conditions with a high degree of severity. The company provided absolute and proportional QALY shortfall estimates in line with NICE's health technology evaluations manual. Both the company and EAG's estimates for severity weighting indicated that a weighting of 1.7 should be applied to each comparison, when taking into account the committee's preference to use the von Stackelberg et al. (2016) study to model blinatumomab's effectiveness (see section 3.9). So, the committee concluded that a severity weight of 1.7 applied to the QALYs was appropriate.

Cost-effectiveness estimates

Acceptable incremental cost-effectiveness ratio

3.18 NICE's manual on health technology evaluations notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per QALY gained, decisions 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 noted several uncertainties, specifically regarding:

- comparative effectiveness
- the proportion of people having treatment with tisagenlecleucel who have intravenous immunoglobulin and the duration of intravenous immunoglobulin use.

Because of the uncertainty in the cost-effectiveness estimates, the committee agreed that an acceptable ICER would be around £20,000 per QALY gained when compared with blinatumomab, because this was the main comparator (see section 3.4).

Committee's preferred assumptions

3.19 The committee's preferred model assumptions were:

- using the EAG's corrections for model errors, updated eMIT (electronic market information tool) and BNF costs, and including end of life care costs
- using the pooled dataset to model tisagenlecleucel (see section 3.5)
- using the von Stackelberg et al. (2016) study as a source of data to model blinatumomab (see section 3.9)
- using the Jeha et al. (2006) study as a source of data to model salvage chemotherapy

- using updated SACT dataset to model the proportion of people having tisagenlecleucel infusion who have intravenous immunoglobulin treatment and the duration of intravenous immunoglobulin treatment (see section 3.13).

  The company's base-case ICERs for tisagenlecleucel compared with blinatumomab or salvage chemotherapy were around £20,000 per QALY gained, or lower (the exact ICERs are confidential and cannot be reported here). The ICERs remained within the range that NICE considers an acceptable use of NHS resources when the committee's preferred assumptions and NHS England CAR T-cell tariff costs were applied.

Conclusion

Recommendation

3.20 The clinical-effectiveness evidence showed that tisagenlecleucel improved key outcomes in people with B-ALL. The committee concluded that the ICER that included its preferred assumptions was within the range that NICE considers an acceptable use of NHS resources (see section 3.19). So, tisagenlecleucel is recommended for routine commissioning.

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 evaluation 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 cost comparison evaluation), at which point funding will switch to routine commissioning budgets. The NHS England 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 guidance 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 draft guidance.

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 relapsed or refractory B-cell acute lymphoblastic leukaemia and the healthcare professional responsible for their care thinks that tisagenlecleucel is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation 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 being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

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

Chair

Stephen O'Brien
Chair, technology appraisal committee C

NICE project team

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

Tom Jarratt
Technical lead

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Technical adviser

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Project manager

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