INAHTA Brief

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Title Tisagenlecleucel (Kymriah) for Pediatric Acute Lymphoblastic Leukemia and Diffuse Large B-Cell Lymphoma: A Health Technology Assessment

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Aim

The objective of this Health Technology Assessment (HTA) was to inform decisions on how to optimally structure the provision of tisagenlecleucel for pediatric and young adults with relapsed or refractory B-cell acute lymphoblastic leukemia (r/r B-cell ALL) and adults with relapsed or refractory diffuse large B-cell lymphoma (r/r DLBCL). The focus was to evaluate the clinical effectiveness and safety, cost-effectiveness, and budget impact on public funding, as well as implementation considerations and ethical issues.

Conclusions and Results

The HTA found that, in the short term, the majority of children and young adults with r/r B-cell ALL who were treated with tisagenlecleucel achieved significant overall remission rate and adults with r/r DLBCL also demonstrated responses on overall response rate and overall survival following treatment with tisagenlecleucel. However, long-term and direct comparative data were not available. Tisagenlecleucel has the potential to exert severe adverse events and its use is resource-intensive, requiring an established infrastructure to ensure patient safety during treatment. For r/r B-cell ALL, tisagenlecleucel had a 44.2% probability of being cost-effective at a willingness-to-pay (WTP) threshold of C$50,000 per quality-adjusted life-year (QALY) gained and a 99.1% probability at a WTP threshold of $100,000 per QALY gained. For r/r DLBCL, the probability of tisagenlecleucel being cost-effective was 0% at a WTP threshold of $50,000 per QALY gained and 1.8% at a WTP threshold of $100,000 per QALY gained. Price reductions of 45% and 65% would be required to achieve an ICUR of $100,000 and $50,000 per QALY, respectively. The results of the implementation analysis indicated that, in Canada, a centralized model may create geographic inequities. Important barriers included economic, social, physical, and psychological impacts associated with travel and the relocation of patients and caregivers to receive treatment. It was suggested that consideration be given to providing support services for travel, lodging, and the psychosocial needs of patients and carers. The ethics review highlighted the importance of informed choice and consent in treatment decision-making, given the uncertainty about safety and efficacy. It also called for the recognition of psychological and emotional benefits and burdens to patients, and the opportunity costs of therapy selection given that the high price of tisagenlecleucel may constrain resource allocation.

Based on the evidence from the review, the Health Technology Expert Review Panel (HTERP) recommended the provision of tisagenlecleucel in Canada for the following:

1. Pediatric and young adult patients three to 25 years of age with r/r B-cell ALL who are refractory, have relapsed after allogeneic stem cell transplant (SCT) or are otherwise ineligible for allogeneic SCT, or have experienced a second or later relapse, on the condition that there is a reduction in price.
2. Adult patients with r/r DLBCL after two or more lines of systemic therapy, including DLBCL, not otherwise specified, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma, on the condition that there is a substantial reduction in price.

Methods

The HTA was based on a systematic review of relevant literature identified through comprehensive searches of multiple databases and grey literature. The searches were performed by an information specialist using a peer-reviewed search strategy. The methodology for the review was guided by the criteria outlined in the checklist described in AMSTAR II and other relevant reporting guidelines such as the PRISMA statement and the PRISMA harms, and the report followed the CADTH standards for Optimal Use reviews. Economic assessments involved a reanalysis of the manufacturer-submitted economic evaluation to assess tisagenlecleucel in pediatric and young

adults with r/r B-cell ALL, and adults with r/r DLBCL, compared with salvage chemotherapy. Also, budget impact analyses were conducted to estimate the effect of reimbursing tisagenlecleucel on funding in Canada in the first three consecutive years. The implementation analysis involved a synthesis of information and results from a number of sources, and a rapid qualitative evidence synthesis. The ethics review included a review of existing analysis and a *de novo* analysis.

Further Research/Reviews Required

The primary gaps in the evidence were the absence of data that directly compare tisagenlecleucel with other treatments used in relapsed or refractory disease, as well as the lack of long-term data and uncertainty about how to handle tisagenlecleucel manufacturing failures for patients scheduled to receive treatment. More long-term follow-up and comparator data will be required to fully understand the benefit-risk profile of tisagenlecleucel and its place in therapy in pediatric and young adults with r/r B-cell ALL and adults with r/r DLBCL.

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