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To the secretariat of COHERE,

Introduction

Ebvallo (tabelekleucel) is a promising new treatment for adults and pediatric patients aged 2 years and older with relapsed or refractory Epstein-Barr virus-positive post-transplantation lymphoproliferative disease (EBV+ PTLD) who have received at least one prior therapy. This condition is an ultra-rare and severe disease with a significant unmet need for effective treatments.

Clinical efficacy

The European Medicines Agency (EMA) has granted marketing authorization for Ebvallo based on its favorable benefit-risk profile. Despite the limited data from a small, single-arm study (ALLELE), the results are compelling. The study demonstrated that tabelekleucel significantly improves response rates and overall survival compared to current treatments available in Norwegian clinical practice. Given the ultra-rare nature of EBV+ PTLD, these findings are particularly noteworthy.

Safety profile

EMA's assessment indicates that the benefits of tabelekleucel outweigh the risks, especially considering the severe prognosis of untreated EBV+ PTLD. The safety profile of tabelekleucel is acceptable, with manageable side effects, making it a viable option for patients who have limited alternatives.

Challenges in clinical study design

Conducting a randomized controlled trial (RCT) against a placebo for tabelekleucel in this patient population is ethically and practically challenging. Patients with relapsed or refractory EBV+ PTLD have a very poor prognosis and limited treatment options. Assigning patients to a placebo group would mean denying them potentially life-saving therapy, which raises significant ethical concerns. Additionally, the rarity of the disease makes it difficult to recruit a sufficient number of participants for a traditional RCT. The ALLELE study, therefore, utilized a single-arm design, which, while not ideal, is justified given the circumstances and the urgent need for effective treatments.

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Small patient population

EBV+ PTLD is an ultra-rare condition, with an estimated incidence of only very few patients per year in Finland. This rarity inherently limits the number of patients available for clinical studies. Despite the small sample size, the data from the ALLELE study are robust and show a clear benefit of tabelekleucel over existing treatments. The small patient population also means that the overall budget impact of introducing tabelekleucel will be relatively limited, making it a feasible addition to the healthcare system. [redacted]

Economic considerations

While introducing tabelekleucel comes with a cost, the actual budget impact is expected to be relatively limited due to the small number of patients. [redacted]

Unmet medical need

EBV+ PTLD is a life-threatening condition with very few effective treatment options. The introduction of tabelekleucel addresses a critical gap in the current treatment landscape, providing hope for patients who have exhausted other therapeutic avenues. The ultra-rare nature of the disease would justify the acceptance of lower-quality evidence and higher resource use, as outlined in the prioritization guidelines for small patient groups with severe conditions.

Conclusions

Given the significant unmet medical need, the promising clinical efficacy, the ethical and practical challenges of conducting a placebo-controlled study, and the manageable budget impact, Ebvallo (tabelekleucel) would provide significant value if introduced into the Finnish healthcare system, at least for selected patient cohorts. This will provide a much-needed lifeline to patients suffering from this devastating disease and align with our commitment to offering cutting-edge treatments to those in dire need.

Yours Sincerely,

Erik Arver
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