SUMMARY

tisagenlecleucel

KYMRIAH 1.2 x 10^6 – 6 x 10^8 cells

dispersion for infusion

Reassessment at the request of the TC

Original French opinion adopted by the Transparency Committee on 6 September 2023

The legally binding text is the original French opinion version

Transparency Committee's conclusions

Clinical Benefit

- B-cell ALL in paediatric and young adult patients is a serious blood disease. This disease is liable to be life-threatening to patients in the short term in the event of refractory disease, relapse post-transplant or second or later relapse.
- This is a curative treatment.
- The efficacy/adverse effects ratio remains high in the short and medium term.
- There are therapeutic alternatives.
- This is a first-line treatment in 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, in good general condition, with a life expectancy and disease progression compatible with the waiting time before administration of KYMRIAH (tisagenlecleucel).

- **Public health benefit**

Considering:

- the seriousness of B-cell ALL in patients with refractory disease, relapse post-transplant or second or later relapse, and its low prevalence,
- the inadequately met medical need at this stage of the disease,
- the partial response to this need, taking into account:

    - the additional impact on morbidity and mortality in the short term, with a transposability to routine practice not guaranteed due to the qualitatively weak data (not monitored and some parameters non-exhaustive) from the shared French CAR-T cell registry,
    - the lack of demonstrated impact on quality of life in the absence of relevant data,
    - the methodological limitations of the indirect comparison of tisagenlecleucel, making precise quantification of the clinical effect difficult,
    - and persistent uncertainties with respect to the clinical consequences, particularly in terms of efficacy and the exact composition of the bags,
- the absence of an improvement in the care pathway of patients due to:
    - hospitalisations in a qualified centre, sometimes far from the patient's home, with ICU stays possible (particularly during the first 10 days following infusion or in the event of the onset of early signs or symptoms of cytokine release syndrome and/or neurological effects),
    - the need to remain close to this hospital for monitoring for at least 4 weeks following infusion,
- the impact on the organisation of care, considering the need for:
    - accreditation of hospitals based on precise criteria,
    - close coordination between the various departments of centres authorised to treat patients with CART cells (laboratories, internal pharmacy, clinical departments, etc.),

KYMRIAH (tisagenlecleucel) is unlikely to have an impact on public health, on the basis of currently available data.

Considering all these elements, the Committee deems that the clinical benefit of KYMRIAH 1.2 x 10^6 – 6 x 10^8 cells (tisagenlecleucel) dispersion for infusion is substantial in the treatment of 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.

The Committee issues a favourable opinion for maintenance of inclusion of KYMRIAH 1.2 x 10^6 – 6 x 10^8 cells (tisagenlecleucel) dispersion for infusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the indication "treatment of 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" and at the MA dosages.

Clinical Added Value

Considering:

- the updated efficacy data from the ELIANA clinical study, confirming the results previously analysed, particularly in terms of complete remission percentage, with this remission remaining durable in some patients (approximately 1/3 to 1/2), following a median follow-up of 79.1 months between injection of KYMRIAH (tisagenlecleucel) and the database freeze for this last analysis in the ELIANA study,
- the overall survival results, with a median of 47.9 months (CI95% [19.4; NE]) in the 97 patients included (ITT population) in ELIANA, in clinical situations that are life-threatening in the short term and for which the available treatment options do not enable a complete recovery to be envisaged,
- the safety profile marked by significant short-term toxicity,

- additional experience with respect to the real-world data in the DESCAR-T registry (median follow-up duration since eligibility of 19.4 months, 19 activated centres, 99 patients treated with KYMRIAH (tisagenlecleucel)), suggesting results consistent with those of the clinical studies,
- despite the initial uncertainties identified, which persist, particularly with respect to:
  - the exact effect size compared to therapeutic management, in the absence of any robust comparison,
  - the qualitative weakness of the data in the DESCAR-T registry (data not monitored),
  - maintenance of the clinical efficacy in the long term, particularly concerning achievement of full recovery for patients in lasting remission,
  - and the absence of long-term safety data,

the Committee considers that its previous conclusions are not liable to be modified. On the basis of currently available data, KYMRIAH 1.2 x 10^6 – 6 x 10^8 cells (tisagenlecleucel) dispersion for infusion still provides a moderate clinical added value (CAV III) in the care pathway for the treatment of paediatric and young adult patients with B-cell ALL that is refractory, in relapse post-transplant or in second or later relapse.