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

- Diffuse large B-cell lymphoma (DLBCL) is an aggressive non-Hodgkin lymphoma with an unfavourable prognosis in the event of multiple relapses and disease refractory to at least two treatment lines, as reported by patient and user associations.
- KYMRIAH (tisagenlecleucel) is a curative treatment for relapsed or refractory diffuse large B-cell lymphoma after two or more lines of systemic therapy.
- The new data available is not of a nature to modify the Committee's previous conclusions. The efficacy/adverse effects ratio of KYMRIAH (tisagenlecleucel) remains high in the short term only and is still to be determined in the longer term, particularly in terms of maintenance of clinical remission and achievement of full recovery.
- There are therapeutic alternatives (see Section 05 of this opinion)
- KYMRIAH (tisagenlecleucel) remains a third or later-line treatment, in relapsed or refractory patients, in good general condition, with a life expectancy and disease progression compatible with the waiting time before administration.

Public health benefit

Considering:

- the seriousness of the disease, particularly in relapsed or refractory patients after two or more lines of systemic therapy, which is life-threatening in the short term, as reported by patient and user associations,

- its prevalence,
- the inadequately met medical need at this stage of the disease prior to the arrival of CAR-T cell-based medicinal products,
- the partial response to this need, due to:
  - the additional impact on morbidity and mortality in the short term, but which remains to be determined in the long term, particularly in terms of full recoveries;
  - the lack of demonstrated impact on quality of life in the absence of relevant data;
  - the limitations of the indirect comparisons, making precise quantification of the clinical effect difficult, and the limitations of indirect comparisons with YESCARTA (axicabtagene ciloleucel);
  - the long time frame between eligibility of patients and reinjection of CAR-T cells, estimated to be 5 to 7 weeks based on real-world data, and persistent uncertainties with respect to the clinical consequences, in particular in terms of efficacy, of the different phases in the procedure (from eligibility to administration);
- the absence of an improvement in the care pathway of patients due to:
  - hospitalisations, including in the ICU (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), whereas the third and later-line treatment of lymphoma can be administered in an outpatient context in a day hospital,
  - hospitalisation of patients far from their homes,
  - the need to remain close to this hospital for monitoring for at least 4 weeks following infusion,
- the impact on the organisation of care, despite the logistical advantage of being able to freeze the apheresis product with KYMRIAH (tisagenlecleucel), considering the need for
  - accreditation of hospitals based on precise criteria,
  - coordination between the various departments of centres authorised to treat patients with CAR-T 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 remains substantial in "the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy" and at the MA dosages.

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 "treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy" and at the MA dosages.

Clinical Added Value

Considering:

- additional experience with respect to the real-world data for KYMRIAH (tisagenlecleucel) in the French DESCAR-T registry (26 activated centres, 388 treated patients, median follow-up of 15 months since eligibility), which are consistent with the clinical data (JULIET),

- the role of KYMRIAH (tisagenlecleucel) compared to YESCARTA (axicabtagene ciloleucel), which remains difficult to determine given the major methodological limitations of the indirect comparison provided,
- the safety profile marked by significant short-term toxicity,
- and the initial uncertainties identified, which persist despite the Transparency Committee's requests, particularly with respect to:
  - the exact effect size compared to historic management, in the absence of any robust comparison,
  - maintenance of the clinical efficacy in the medium and long term, particularly concerning achievement of full recovery for patients in lasting remission,
  - and the absence of medium and long-term safety data,

the Committee considers that its previous conclusions are not liable to be modified. On the basis of currently available data, the Committee deems that KYMRIAH 1.2 x 10^6 – 6 x 10^8 cells (tisagenlecleucel) dispersion for infusion provides a minor clinical added value (CAV IV) in terms of efficacy compared to the historic management of relapsed or refractory diffuse large B-cell lymphoma after two or more lines of systemic therapy, based on various chemotherapies.