HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
30 MARCH 2022

The legally binding text is the original French opinion version

tafasitamab
MINJUVI 200 mg powder for concentrate for solution for infusion

First assessment

Key points

Pending confirmatory data:

Conditional favourable opinion for reimbursement in combination with lenalidomide followed by MINJUVI monotherapy for the treatment of adult patients with diffuse large B-cell lymphoma (DLBCL) only:

- as second-line treatment in patients who are not eligible for autologous stem cell transplant (ASCT),

- and as third and later-line treatment, only in patients who are not eligible for KYMRIAH and YESCARTA.

Unfavourable opinion for reimbursement in the third or later-line treatment of adult patients with diffuse large B-cell lymphoma (DLBCL) who are eligible for KYMRIAH and YESCARTA.

The Committee makes maintenance of this opinion conditional on the re-evaluation of MINJUVI (tafasitamab), in particular based on the final data that will be submitted to the EMA by the pharmaceutical company within the context of the conditional MA.

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

Role in the care pathway?

The choice of treatment is based on a systematic assessment of the main prognostic criteria for the disease. The IPI (International Prognostic Index) is used as a prognostic index for aggressive NHL. This takes into account the patient's age, the ECOG performance score, the lactate dehydrogenase (LDH) level, the disease stage and extranodal involvement.

According to the guidelines, the therapeutic options proposed for DLBCL are chemotherapy, immunotherapy with monoclonal antibodies and autologous T lymphocytes with an anti-CD19 chimeric antigen receptor (anti-CD19 CAR-T cells), radiotherapy and haematopoietic stem cell transplantation (primarily used at the time of relapse after salvage therapy).

The first-line treatment of choice is based on R-CHOP immunochemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristin and prednisolone) leading to recovery in more than half of patients.

As second-line therapy in patients not responding to first-line treatment (primary refractory disease) or who relapse following this treatment, the therapeutic approach depends on the patient's eligibility for high-dose chemotherapy (intensification) followed by autologous stem cell transplantation (ASCT). In patients aged under 65 to 70 years with an adequate performance status and no major organ dysfunction, it is recommended to administer salvage therapy combining rituximab and chemotherapy, generally based on platinum and/or gemcitabine (R-DHAP, R-ICE or R-GDP) followed, in the event of response (chemosensitive disease), by high-dose chemotherapy (intensification) and ASCT.

For patients who are not eligible for high-dose chemotherapy, in particular due to age, general condition and/or comorbidities, the same salvage chemotherapy protocols can be used (in particular R-DHAP) or adapted protocols (such as R-GemOx, R-mini-CYVE or R-Holoxan-VP16). None of these immunochemotherapies currently recommended in patients not eligible for intensive chemotherapy have a marketing authorisation.

From the third line of treatment, in patients not having responded following salvage chemotherapy or relapsing following second-line treatment (including with a history of ASCT), medicinal products based on CAR-T cells, YESCARTA (axicabtagene ciloleucel) and KYMRIAH (tisagenlecleucel), are currently recommended in eligible patients, in particular those whose life expectancy is compatible with the treatment timeframes (between apheresis and injection). In its re-evaluation opinions, the Committee considered that these two medicinal products provided an additional response and that the choice of one over the other should be made on the basis of the patient's condition, the availability of production slots, the expected clinical response and the safety profile.

In other cases, management is not standardised and the treatment options are limited. Depending on the clinical situation and the patient's preferences, the following may be envisaged:

o Various chemotherapies, in particular PIXUVRI (pixantrone) or the resumption of a treatment with immunochemotherapy protocols not previously used and adapted to the patient's age and comorbidities (for example, R-Bendamustine or R-Lenalidomide);

o A new intensive chemotherapy protocol with the objective of performing allogeneic haematopoietic stem cell transplantation if the patient is eligible (with the exclusion of refractory patients);

o The implementation of supportive care;

o Inclusion in a clinical trial.

Role of the medicinal product in the care pathway

MINJUVI (tafasitamab) in combination with lenalidomide followed by MINJUVI (tafasitamab) monotherapy is a therapeutic alternative in adult patients with diffuse large B-cell lymphoma (DLBCL) only:

- as second-line treatment in patients who are not eligible for ASCT,

- and as third and later-line treatment, only in patients who are not eligible for KYMRIAH and YESCARTA.

In the absence of comparative data with the CAR-T cell-based medicinal products currently recommended as third-line treatment, which were the subject of concomitant development, the role of MINJUVI (tafasitamab) remains to be demonstrated in the third and later-line treatment of patients eligible for CAR-T cell-based medicinal products, i.e. in patients for whom at least two lines of systemic treatment have failed, with a history of autologous transplantation for eligible patients.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ Diffuse large B-cell lymphoma (DLBCL) is a serious, life-threatening disease.

◗ MINJUVI (tafasitamab) is a curative medicinal product.

◗ Its efficacy/adverse effects ratio is:
- high in combination with lenalidomide followed by MINJUVI monotherapy for the treatment of adult patients with diffuse large B-cell lymphoma (DLBCL):
• as second-line treatment in patients who are not eligible for ASCT,
• and as third and later-line treatment, only in patients who are not eligible for CAR-T cell-based medicinal products
- not determined in view of the purely descriptive data in the third or later-line treatment of adult patients with diffuse large B-cell lymphoma (DLBCL) who are eligible for CAR-T cell-based medicinal products.

◗ There are therapeutic alternatives.

◗ MINJUVI (tafasitamab) is a therapeutic alternative in adult patients with diffuse large B-cell lymphoma (DLBCL):
- as second-line treatment in patients who are not eligible for ASCT,
- and as third and later-line treatment, only in patients who are not eligible for KYMRIAH and YESCARTA.
In the absence of comparative data with the CAR-T cell-based medicinal products currently recommended as third-line treatment, which were the subject of concomitant development, the role of MINJUVI (tafasitamab) remains to be demonstrated in the third and later-line treatment of patients eligible for CAR-T cell-based medicinal products, i.e. in patients for whom at least two lines of systemic treatment have failed, with a history of autologous transplantation for eligible patients.

Public health impact

Considering:
- the seriousness and low prevalence of relapsed or refractory DLBCL, not eligible for autologous stem cell transplant (ASCT),
- the inadequately met medical need,
- the lack of additional response to the identified need in the absence of any demonstrated additional impact on morbidity and mortality and quality of life,
- the absence of data enabling assessment of the additional impact on the organisation of care,

MINJUVI (tafasitamab) is unlikely to have an additional impact on public health.

Given all of these elements, the Committee considers that, pending confirmatory data, the clinical benefit of MINJUVI (tafasitamab) is:

- **SUBSTANTIAL in combination with lenalidomide followed by MINJUVI monotherapy for the treatment of adult patients with diffuse large B-cell lymphoma (DLBCL):**
  - as second-line treatment in patients who are not eligible for ASCT,
  - and as third and later-line treatment, only in patients who are not eligible for KYMRIAH and YESCARTA.

- **INSUFFICIENT to justify public funding cover in the third or later-line treatment of adult patients with diffuse large B-cell lymphoma (DLBCL) who are eligible for KYMRIAH and YESCARTA.**

The Committee makes maintenance of this opinion conditional on the re-evaluation of MINJUVI (tafasitamab), in particular based on the final data that will be submitted to the EMA by the pharmaceutical company within the context of the conditional MA.

The Committee issues a conditional favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use only in combination with lenalidomide followed by MINJUVI monotherapy for the treatment of adult patients with diffuse large B-cell lymphoma (DLBCL):

- as second-line treatment in patients who are not eligible for ASCT,

- and as third and later-line treatment, only in patients who are not eligible for KYMRIAH and YESCARTA.

The Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the third or later-line treatment of adult patients with diffuse large B-cell lymphoma (DLBCL) who are eligible for KYMRIAH and YESCARTA.

Clinical Added Value

As second-line treatment in patients with DLBCL who are not eligible for ASCT, and as third and later-line treatment in patients who are not eligible for CAR-T, considering:

- the overall response rate of around 60% in the non-comparative phase 2 L-MIND study conducted in 80 patients with R/R DLBCL having mainly received one or two prior therapies and not eligible for autologous stem cell transplantation, over a median follow-up period of 17.3 months,
- the limitations of the indirect comparisons made, not enabling any conclusions to be reached with respect to the role of tafasitamab in the care pathway,
- the absence of robust direct comparative data, concerning, in particular, the response duration, progression-free survival and overall survival in the context of a serious, life-threatening disease,
- the absence of a quality of life assessment,
- and despite the inadequately met medical need,

The Committee considers that, on the basis of currently available data, and pending the final data that will be submitted to the EMA, MINJUVI (tafasitamab) provides no clinical added value (CAV V) compared to the current management.