HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
21 JULY 2021

The legally binding text is the original French opinion version

brentuximab vedotin
ADCETRIS 50 mg powder for concentrate for solution for infusion

Re-evaluation

Key points

Maintenance of the favourable opinion for reimbursement in the treatment of adult patients with CD30+ Hodgkin lymphoma (HL) at increased risk of relapse or progression following autologous stem cell transplant (ASCT).

What therapeutic improvement?

Therapeutic improvement in the management of the condition.

Role in the care pathway?

The first-line treatment of classic Hodgkin lymphoma (HL) in adult patients is based on chemotherapy protocols.

In the event of relapse after this first-line treatment, the favoured second-line treatment is high-dose ("salvage") chemotherapy, followed by autologous stem cell transplant (ASCT).

Autologous stem cell transplantation (ASCT) leads to durable complete remission in around 50% of patients. Post-ASCT relapse or progression generally occurs early on: in 70% of cases it occurs in the year following the transplant, and in 90% of cases it occurs within 2 years. In these patients presenting relapse/progression, the median survival is around 16 months and the 5-year survival rate is approximately 20%. Apart from ADCETRIS (brentuximab vedotin), there is currently no specific or recommended treatment to prevent post-ASCT relapse/progression.

As third-line treatment in refractory or relapsed patients post-ASCT, treatment with ADCETRIS (brentuximab vedotin) is recommended. In refractory or relapsed patients after brentuximab vedotin, salvage therapies with nivolumab or pembrolizumab may be envisaged (fourth line).

Role of the medicinal product in the care pathway

In the indication claimed, ADCETRIS (brentuximab vedotin) remains a first-line treatment for adult patients at increased risk of relapse or progression following ASCT, defined as those with:
- a history of disease refractory to chemotherapy, or
- relapse or disease progression within 12 months following first-line treatment, or
- extranodal involvement at the time of pre-ASCT relapse.

Its superiority has been established compared to placebo only in terms of progression-free survival. The absence of demonstration of an improvement in overall survival means that it is not possible to clearly define the advantage of preventive treatment for post-ASCT relapse or progression with brentuximab vedotin compared to treatment of relapse by brentuximab vedotin.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ CD30+ Hodgkin lymphoma is a serious, life-threatening disease.

◗ The proprietary medicinal product ADCETRIS (brentuximab vedotin) is a curative medicinal product.

◗ Its efficacy/adverse effects ratio is high.

◗ There are no therapeutic alternatives.

◗ ADCETRIS (brentuximab vedotin) is a first-line treatment for adult patients at increased risk of relapse or progression following ASCT, defined as those with:
- a history of disease refractory to chemotherapy, or
- relapse or disease progression within 12 months following first-line treatment, or
- extranodal involvement at the time of pre-ASCT relapse.

Public health impact

Considering:
- the seriousness of the condition,
- the unmet medical need for patients at increased risk of relapse or progression following autologous stem cell transplant, in the absence of a treatment having demonstrated an improvement in terms of the overall survival and quality of life of these patients,

But in view of:
- the lack of response to the identified medical need, due to:
    - the absence of any demonstrated additional impact on mortality compared to placebo. In fact, a difference compared to placebo was only demonstrated in terms of progression-free survival, an indicator of an impact on morbidity, whereas a statistically significant improvement in overall survival, an indicator of an impact on mortality, was expected. Robust new data on overall survival did not confirm a favourable impact on mortality.
    - the lack of demonstrated impact on quality of life given the availability of only initial exploratory data,
- the lack of demonstration of an improvement or absence of deterioration in the care and/or life pathway, since the data available concerning the use of medical resources or the patient's care pathway presented numerous methodological biases, preventing any formal conclusion from being reached,

ADCETRIS (brentuximab vedotin) is unlikely to have an impact on public health.

Given all these elements, the Committee deems that the clinical benefit of ADCETRIS (brentuximab vedotin) remains substantial in the MA indication.
The Committee issues a favourable opinion for maintenance of inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and dosages.

Clinical Added Value

Considering:
- initial data having demonstrated the superiority of ADCETRIS (brentuximab vedotin) compared to placebo, in a randomised, double-blind study in terms of progression-free survival assessed by an independent review committee, with an individual estimation of an absolute increase of 18.8 months, HR=0.57 CI95% = [0.4; 0.8];
- new updated data relative to progression-free survival beyond this follow-up period, interpretation of which is limited since it was assessed by the investigator, whereas the primary endpoint had been assessed by an independent review committee: this is therefore an exploratory analysis, without consideration of the multiplicity of analyses;
- the absence of demonstration of an increase in overall survival, the analysis having been non-conclusive for this criterion following a median follow-up of 7.7 years;

and despite:
- the identified need to have access to treatments improving the overall survival and quality of life of these patients;
- an excess toxicity, with, in particular, the occurrence of grade ≥ 3 adverse events in more than half of the patients (57%), and the development of peripheral neuropathy in 67% of patients;
- the absence of any formal conclusion that can be drawn based on the quality-of-life results;

the Transparency Committee considers that ADCETRIS (brentuximab vedotin) provides a minor clinical added value (CAV IV) in the care pathway for the treatment of patients at increased risk of relapse or progression following autologous stem cell transplant (ASCT), defined as those with:
- **a history of disease refractory to chemotherapy, or**
- **relapse or disease progression within 12 months following first-line treatment, or**
- **extranodal involvement at the time of pre-ASCT relapse.**