HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
18 MARCH 2020

avelumab
BAVENCIO 20 mg/ml concentrate for solution for infusion

Reevaluation
MA amendment

Key points

Favourable opinion for reimbursement as monotherapy for the treatment of adult patients with metastatic Merkel cell carcinoma (MCC) previously treated with chemotherapy.

What therapeutic improvement?

No clinical added value in the treatment of patients with metastatic Merkel cell carcinoma (MCC) previously treated with chemotherapy, due to lack of direct or indirect comparison with the usual treatment.

Role in the care pathway?

At the metastatic stage of Merkel cell carcinoma (MCC), patients usually are treated with conventional chemotherapy. Two chemotherapy protocols are recommended from the first line of treatment: a carboplatin-etoposide combination, or a cyclophosphamide-doxorubicin-vincristine combination.

Cardiac toxicity of doxorubicin, or renal and neurological toxicity of platinum, significantly limit the use of these chemotherapies in previously treated elderly patients. After failure of chemotherapy at the metastatic stage or unacceptable toxicity, in the presence of contraindications to non-first-line

chemotherapy protocols in the population concerned, with a median age of about 75 years at the time of diagnosis and comorbidities, supportive care is considered.

Role of BAVENCIO (avelumab) in the care pathway:

Since the previous assessment, the care pathway has not been modified by the arrival of new treatments (only pembrolizumab obtained US marketing approval (MA) in July 2019 but it does not have MA in Europe). The role of BAVENCIO (avelumab) as second and later-line therapy in the treatment strategy is therefore not modified compared to the previous opinion. Despite persistent uncertainties related to the absence of comparative data versus the usual treatment of patients, BAVENCIO (avelumab) as monotherapy retains a role after failure of chemotherapy.

As a reminder, in accordance with the Transparency Committee opinion dated 19 September 2019, in the absence of clinical data versus the usual chemotherapy as first-line treatment of metastatic disease, BAVENCIO does not have a place as monotherapy for the first-line treatment of adult patients with metastatic Merkel cell carcinoma (MCC).

COMMITTEE'S CONCLUSIONS

Clinical Benefit

◗ Metastatic Merkel cell carcinoma (MCC) is a serious, life-threatening disease.
◗ It is a specific curative treatment.
◗ The efficacy/adverse events ratio remains moderate in patients previously treated with chemotherapy in view of the efficacy results (from a non-comparative phase II study and the CARADERM observational study) as well as its safety profile.
◗ Despite the absence of standard treatment, therapeutic alternatives are used in clinical practice in France as second and later-line treatment.

Public health impact

Considering:
- the seriousness of the disease,
- its low prevalence/incidence,
- the inadequately met medical need in patients previously treated with chemotherapy,
- preliminary andnon comparative data that demonstrate a confirmed overall response percentage of around 30% (primary endpoint) with updated follow-up in patients previously treated with chemotherapy, but,
- the absence of a comparative phase III study on mortality and quality of life, orat least, a robust indirect comparison with the usual treatment,
- the absence of demonstration of an impact on the organisation of health care,

BAVENCIO (avelumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of BAVENCIO (avelumab) remains substantial in the treatment as monotherapy of adult patients with metastatic Merkel cell carcinoma (MCC) previously treated with chemotherapy.

The Committee issues a favourable opinion for maintenance in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the treatment of patients with metastatic Merkel cell carcinoma (MCC) previously treated with chemotherapy and at the MA dosages.

Clinical Added Value

Considering:
- **the Committee's request in its initial opinion to have comparative data available for BAVENCIO (avelumab) versus the usual treatment of patients as second or later-line treatment in order to quantify its contribution,**
- **the lack of availability of these comparative data,**
- **the methodological limits of the follow-up data in the JAVELIN study and the preliminary, retrospective and observational data from the CARADERM database,**

the Committee is unable to assess the therapeutic contribution of BAVENCIO (avelumab) compared to the usual treatment. Consequently, it considers that BAVENCIO (avelumab) as monotherapy does not provide clinical added value (CAV V) in the treatment of patients with metastatic Merkel cell carcinoma (MCC) previously treated with chemotherapy.