HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

10 MARCH 2021

The legally binding text is the original French opinion version

durvalumab

IMFINZI 50 mg/ml concentrate for solution for infusion

New indication

Key points

Favourable opinion for reimbursement in combination with etoposide and either carboplatin or cisplatin for the first-line treatment of adults with extensive-stage small cell lung cancer (ES-SCLC).

What therapeutic improvement?

Therapeutic improvement compared to carboplatin/cisplatin + etoposide chemotherapy.

Role in the care pathway?

The treatment of extensive-stage small cell lung cancer (ES-SCLC) is based on a combination of chemotherapies, with several protocols having demonstrated similar efficacy.

The first-line treatment is the cisplatin/carboplatin + etoposide protocol for 4 to 6 cycles. For elderly, frail patients (ECOG ≥ 2) or in whom the use of cisplatin is contraindicated, the use of carboplatin is recommended.

The latest American NCCN (2020) and AURA (2020) guidelines recommend the use of immunotherapy, atezolizumab (TECENTRIQ) or durvalumab (IMFINZI), in combination with platinum salt-based induction chemotherapy then maintenance therapy.

Other protocols may also be used, particularly in the event of a contraindication to etoposide, such as combinations with irinotecan.

Complementary radiotherapy of the chest for PS (0-1) patients, demonstrating a significant response following chemotherapy and with a limited extrathoracic tumour mass may be discussed (stage IV).

Role of the medicinal product in the care pathway

IMFINZI (durvalumab), anti-PD-L1 immunotherapy, used in combination with carboplatin or cisplatin + etoposide chemotherapy, then alone as a maintenance therapy, is a first-line treatment option in adult patients with extensive-stage SCLC**.** Its efficacy in terms of overall survival has been demonstrated, in combination with etoposide and with either carboplatin or cisplatin as the platinum salt.

The Committee nevertheless highlights that:
- a subpopulation of “good responder” patients appears to benefit from long-term treatment, without it being possible to identify these patients,
- no data are available in patients with an ECOG performance score > 1, and
- data is limited in patients with brain metastases.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Extensive-stage small cell lung cancer (ES-SCLC) is a serious, life-threatening disease.

◗ This is a curative treatment.

◗ Considering the effect size, deemed to be modest but clinically relevant in view of the disease and the toxicity profile of combination of durvalumab with chemotherapy (carboplatin or cisplatin + etoposide), the Committee considers that the efficacy/adverse effects ratio is high.

◗ There are first-line medicinal alternatives, in particular chemotherapy protocols combining etoposide with a platinum salt.

◗ IMFINZI (durvalumab), used in combination with carboplatin or cisplatin + etoposide chemotherapy, then alone as a maintenance therapy, is a first-line treatment in adult patients with extensive-stage small cell lung cancer (ES-SCLC).

Public health impact

Considering:

- the seriousness of SCLC, particularly at extensive stages, with a life expectancy of 3 to 6 months without treatment and a median survival of 10 to 12 months for treated patients,
- the incidence of the disease,
- the medical need, considered to be partially met in first-line therapy by existing chemotherapies,
- the partial response to the identified medical need in view of demonstration of an additional impact deemed to be modest in terms of mortality of combining durvalumab with carboplatin or cisplatin + etoposide chemotherapy followed by maintenance monotherapy with durvalumab, compared to chemotherapy alone,
- the lack of elements supporting the absence of a deterioration in the care and/or life pathway in the absence of robust quality of life data,
- the lack of any demonstrated impact on the organisation of care (hospitalisation, AE, etc.),

IMFINZI (durvalumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of IMFINZI (durvalumab) is substantial in the new MA indication.
The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the new indication and at the MA dosages.

Clinical Added Value

Considering:

- **demonstration of the superiority of durvalumab combined with carboplatin or cisplatin + etoposide chemotherapy compared to chemotherapy alone, in a randomised, open-label study, in terms overall survival (OS, primary endpoint),**
- **the effect size, deemed to be modest but clinically relevant in view of the disease with an improvement in OS of 2.7 months; HR = 0.73; $CI_{98,22\%}$ [0.56; 0.95]; p=0.0047),**
- **the absence of robust data relative to progression-free survival considered to be exploratory given the interruption of the hierarchical analysis sequence,**

and despite:

- **the exploratory nature of the quality of life data,**

- **the acceptable safety profile of the durvalumab + carboplatin or cisplatin + etoposide combination compared to chemotherapy alone with a comparable frequency of grade ≥ 3 AEs (62.3% vs. 62.8%) and SAEs (32.1% vs. 36.5%) but marked by immune-mediated AEs (20% in the durvalumab + carboplatin/etoposide group),**
- **uncertainty concerning the effect of durvalumab given the difficulty in differentiating between the proportion attributable to the induction therapy in combination with chemotherapy and that attributable to maintenance therapy with durvalumab alone, and**
- **the impossibility of identifying "good responder" patients who appear to benefit from long-term treatment,**

the Committee considers that IMFINZI (durvalumab) in combination with carboplatin and etoposide, like TECENTRIQ (atezolizumab), provides a minor clinical added value (CAV IV) compared to chemotherapy alone, in the first-line treatment of extensive-stage small cell lung cancer (ES-SCLC).