SUMMARY

pembrolizumab

KEYTRUDA 25 mg/ml

concentrate for solution for infusion

Indication extension

Original French opinion adopted by the Transparency Committee 28 February 2024

The legally binding text is the original French opinion version

Summary of opinion

Favourable opinion for reimbursement of KEYTRUDA in combination with lenvatinib for the first-line treatment of adult patients with advanced clear-cell renal cell carcinoma only.

Unfavourable opinion for reimbursement of KEYTRUDA in combination with lenvatinib in the other situations covered by the MA indication.

Transparency Committee's conclusions

Clinical Benefit

- Clear-cell renal cell carcinoma (RCC) is a serious, life-threatening disease.
- KEYTRUDA (pembrolizumab) in combination with lenvatinib is a specific curative medicinal product for clear-cell renal cell carcinoma or with a clear-cell component.
- Its efficacy/adverse effects ratio is high only in clear-cell renal cell carcinoma or with a clear-cell component.
- Therapeutic alternatives are available.
- This is a first-line treatment, to be given in combination with lenvatinib, for advanced clear-cell renal cell carcinoma or with a clear-cell component.

Public health benefit

Considering:

- the seriousness of advanced clear-cell renal cell cancer, irrespective of the prognosis;
- its incidence estimated to be between 5,500 and 8,000 patients in France;
- the partially met medical need;

- the partial response to this medical need provided by KEYTRUDA (pembrolizumab) + lenvatinib, in the same way as the pembrolizumab/axitinib and nivolumab/cabozantinib combinations, in the first-line treatment of advanced clear-cell renal cell carcinoma or with a clear-cell component, due to:
  - evidence of an impact on morbidity and mortality in the short term compared to sunitinib, but without comparative data versus the other combinations including an immunotherapy due to their concomitant development, and
  - no evidence of an impact on quality of life due to a lack of probative data,
- the lack of evidence of an additional impact on the care and life pathway, as well as on the organisation of care (administration of KISPLYX (lenvatinib) by the oral route in combination with KEYTRUDA (pembrolizumab) by injection);

KEYTRUDA (pembrolizumab) in combination with lenvatinib is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of KEYTRUDA 25 mg/ml (pembrolizumab) in combination with lenvatinib is:

- **substantial in the first-line treatment of advanced renal cell carcinoma, only in clear-cell RCC or with a clear-cell component;**
- **insufficient to justify public funding in the first-line treatment of advanced renal cell carcinoma with a histological type other than clear-cell given the absence of robust data.**

The Committee issues:

- **a favourable opinion for inclusion of KEYTRUDA 25 mg/ml (pembrolizumab) in combination with lenvatinib in the list of covered drugs for inpatients approved for use only in the first-line treatment of advanced clear-cell renal cell carcinoma or with a clear-cell component, and at the MA dosages.**
- **an unfavourable opinion for inclusion in both the list of covered drugs for inpatients and the list of covered drugs for outpatients approved for use in the first-line treatment of advanced renal cell carcinoma with a histological type other than clear-cell.**

Clinical Added Value

In clear-cell renal cell carcinoma or with a clear-cell component

Considering:

- evidence of the superiority of the KEYTRUDA (pembrolizumab) + lenvatinib combination compared to sunitinib, considered to be an acceptable comparator at the time of implementation of the KEYNOTE-581 (CLEAR) study, for:
  - progression-free survival assessed by an independent review committee (primary efficacy endpoint): 23.9 months versus median of 9.2 months; HR = 0.39; 95% CI [0.32; 0.49]; p<0.0001,
  - overall survival (ranked secondary endpoint): the median was not reached in either of the two groups; HR=0.66; 95% CI [0.49; 0.88]; p=0.0049,

despite:

- an additional toxicity of this combination compared to sunitinib, particularly in terms of serious adverse events (50.6% vs 33.2%), grade ≥ 3 events (82.4% vs 71.8%) or events leading to discontinuation of treatment (37.4% vs 14.4%),
- exploratory quality of life data,

the Transparency Committee considers that the KEYTRUDA (pembrolizumab) + lenvatinib combination, like the pembrolizumab/axitinib combination and the nivolumab/cabozantinib combination, provides a moderate clinical added value (CAV III) compared to sunitinib in the first-line treatment of advanced clear-cell renal cell carcinoma or with a clear-cell component.

In renal cell carcinoma with a histological type other than clear-cell

Not applicable.