HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New indication
October 2016

SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

OPDIVO (nivolumab), anti-PD1 antibody

High clinical benefit for the treatment of advanced-stage clear cell kidney cancer or kidney cancer with a clear cell contingent after prior anti-VEGF therapy failure and moderate clinical added value compared to everolimus

Main points

- OPDIVO has been granted a marketing authorisation for monotherapy treatment of adults suffering from advanced renal cell carcinoma after prior treatment.
- Its superiority has been established over everolimus in terms of overall survival in patients with clear cell kidney cancer.
- It is a second-line treatment after failure of prior tyrosine kinase treatment.

Pre-existing indications*

OPDIVO has also been granted a marketing authorisation for the treatment of melanoma and non-small cell lung cancer (for more details, see marketing authorisation).

Therapeutic strategy

- The treatment of metastatic kidney cancer is essentially based on identifying the prognostic factors of the disease. Three prognostic groups have been defined: favourable, intermediate or poor, based on clinical and pathological criteria.
- For patients with a good or intermediate prognostic status, the first-line treatments are sunitinib (SUTENT), the bevacizumab (AVASTIN)/interferon combination and pazopanib (VOTRIENT).
  Cytokine monotherapy remains a potential treatment option for the first-line treatment of metastatic clear cell renal adenocarcinoma.
- For patients with a poor prognostic status, the recommended treatment is temsirolimus (TORISEL).
  After tyrosine kinase inhibitor failure, everolimus and axitinib are the recommended second-line treatments. Sorafenib has been granted a marketing authorisation solely for cases of cytokine (interferon or IL2) failure.
- **Role of the proprietary medicinal product in the therapeutic strategy**
  OPDIVO is a second-line treatment of advanced-stage clear cell kidney cancer after prior tyrosine kinase inhibitor (anti-VEGF) treatment failure. Its superiority has been established compared to an available alternative (everolimus) in terms of overall survival.

Clinical data

- A randomised, open-label phase III study compared nivolumab (n=410) versus everolimus (n=411) in adults with advanced or metastatic clear cell renal carcinoma or renal carcinoma including a clear cell contingent (ccRC) having received at least one prior anti-angiogenic treatment. Most patients (76.6%) had received a prior anti-angiogenic treatment line (sunitinib: 59.4%, pazopanib: 30.5%).
- In an intermediate analysis envisaged in the protocol after observing 398 events (70% of the number of events envisaged for the final analysis), the median overall survival (primary endpoint) was 25.0 months in the nivolumab

* This summary does not concern this indication.

group versus 19.6 months in the everolimus group, i.e. an absolute gain of 5.4 months in favour of nivolumab (HR = 0.73, 98.52% CI [0.57; 0.93]; p=0.0018). This value is probably overestimated due to an early discontinuation of the study.

- Analyses demonstrated that the overall survival with nivolumab was independent of the patients' PD-L1 status. No difference was observed between the nivolumab group and the everolimus group in respect of the median time to response (3.5 months versus 3.7 months respectively), the median response time (12 months in each of the groups) and the median progression-free survival (4.6 months versus 4.4 months).
- The quality-of-life analysis suggested a median rate of patients with disease-related symptom progression measured using the FKSI-DRS score of 41.2% in the nivolumab group and 54.2% in the everolimus group. Given the open nature of the study, no finding of an optimal level of evidence can be retained in respect of this endpoint.
- Treatment discontinuations due to adverse events (AEs) were 17.7% in the nivolumab group of which 7.6% were treatment-related versus 20.7% in the everolimus of which 13.1% were treatment-related. The frequency of grade 3-4 AEs was similar between the two groups (53.2% and 56.4% respectively). The only grade 3-4 AE observed with a frequency ≥ 5% in each of the two groups was anaemia (5.9% in the nivolumab group and 13.1% in the everolimus group).

Special prescription requirements

- Medicinal product for hospital use only.
- Prescription reserved for oncology, haematology and medical oncology specialists and departments.

Benefit of the medicinal product

- The actual clinical benefit* of OPDIVIO is high for the treatment of advanced-stage clear cell kidney cancer or kidney cancer with a clear cell contingent after prior anti-VEGF therapy failure.
- OPDIVO provides a moderate clinical added value** (CAV III) compared to everolimus only for patients subject to a high actual clinical benefit.
- Approval for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 5 October 2016 (CT-15277)
available at **www.has-sante.fr**

* The actual clinical benefit of a medicinal product (ACB) consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.

** The clinical added value (CAV) consists of the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the CAV rating from I, major, to IV, minor. A CAV rating of V (equivalent to "no CAV") denotes a "lack of clinical improvement".