AVASTIN (bevacizumab), monoclonal antibody

RENAL CELL CARCINOMA

Significant clinical interest without demonstrated clinical benefit in combination with interferon in the first-line management of advanced and/or metastatic renal cell carcinoma, in the absence of data versus clinically relevant comparators (sunitinib and pazotinib)

Main points

- In renal cell carcinoma, AVASTIN has marketing authorisation in combination with interferon alpha-2a, in the first-line treatment of patients with advanced and/or metastatic renal cell carcinoma.
- The addition of bevacizumab to interferon improves progression-free survival by 4.8 months relative to interferon alone. No conclusion on the contribution of AVASTIN to overall survival is possible.
- New comparative efficacy data versus interferon alone, which is no longer a standard strategy, do not allow quantifying its contribution in this indication.
- In combination with interferon, it is a treatment option in the first-line management of advanced and/or metastatic renal cell carcinoma with a good or intermediate prognosis.

Therapeutic use

- The management of metastatic renal cell carcinoma is based mainly on the identification of the prognostic factors for the disease. This enables three prognostic groups (good, intermediate or poor) to be defined from clinical and laboratory criteria. These guidelines apply mainly to clear cell renal cell carcinomas.
- In patients with a good or intermediate prognosis, the first-line treatments are: sunitinib (SUTENT), pazopanib (VOTRIENT) and the bevacizumab (AVASTIN) / interferon combination. Cytokines as a monotherapy remain a possible first-line treatment option in the management of metastatic clear cell renal cell adenocarcinoma.
- In patients with a poor prognosis, the recommended treatment is temsirolimus (TORISEL), an mTOR inhibitor.

Role of the medicinal product in the therapeutic strategy

AVASTIN (bevacizumab), in combination with interferon, is a treatment option in the first-line management of advanced and/or metastatic renal cell carcinoma with a good or intermediate prognosis.

Clinical data

- The initial data relied on the interim results of the AVOREN randomised, double-blind study conducted in 649 patients with advanced and/or metastatic renal cell carcinoma as a first-line treatment. The overall survival results (primary endpoint) were not interpretable because the overall survival median was not reached in the bevacizumab + interferon group. The absolute increase in median progression-free survival (secondary endpoint) was + 4.8 months with the bevacizumab + interferon combination compared to interferon alone (10.2 months versus 5.4 months; HR=0.63; 95% CI [0.52; 0.75]; p=0.0001)
- The results of the final analysis of the AVOREN study have not shown that the addition of bevacizumab to interferon provided any benefit in overall survival.
- The new data rely on the final results of this study and on comparative study CALGB 90206 versus interferon alone.
- Another randomised study, conducted in 732 patients with locally metastatic renal cell carcinoma as a first-line treatment, did not show that the addition of bevacizumab to interferon provided any benefit on overall survival (primary endpoint) relative to interferon alone. Progression-free survival was improved by + 3.3 months as an absolute value: 8.5 months versus 5.2 months (HR=0.72; 95% CI [0.61; 0.83], p<0.0001).
- The main adverse reactions observed on AVASTIN in studies were: severe hypertension and proteinuria.
In all, these new comparative efficacy data versus interferon alone, which is no longer a standard strategy, do not permit quantifying the improvement in treatment of AVASTIN (bevacizumab) in the current first-line management of advanced and/or metastatic renal cell carcinoma.

The Committee regrets the absence of comparison of AVASTIN (bevacizumab) + interferon with tyrosine inhibitors (sunitinib and pazotinib), the only clinically relevant comparators.

Special prescribing conditions

- Medicinal product for hospital use
- Prescription restricted to certain specialists

Benefit of the medicinal product

- The actual benefit* of AVASTIN in combination with interferon is substantial.
- AVASTIN, combined with interferon, provides no clinical added value (CAV V) in the first-line management of advanced and/or metastatic renal cell carcinoma given:
  - the lack of comparative data versus clinically-relevant comparators, especially sunitinib,
  - and the only available comparative data versus monotherapy interferon, which is no longer a standard strategy,
- Recommends continued inclusion on the list of reimbursable products for hospital use.

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* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.

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