HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
Focus
April 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

AVASTIN (bevacizumab), monoclonal antibody

In combination with fluoropyrimidine-based chemotherapy, no clinical benefit demonstrated in second-line treatment of metastatic colorectal cancer

Main points

- In colorectal cancer, AVASTIN has Marketing Authorisation, in combination with fluoropyrimidine-based chemotherapy, as second-line treatment of metastatic colorectal cancer in adults.
- In a new study, a low gain in overall survival (1.4 months) was observed, and in another study, a lack of gain was observed, with an increase in adverse events in both studies.
- No comparison to an anti-EGFR drug in case of wild-type RAS tumour is available.

Therapeutic use

- In a second-line treatment, in the event of progression with targeted therapy (bevacizumab or anti-EGFR), the choice is:
  - To change chemotherapy (oxaliplatin in crossover to irinotecan and vice-versa + fluoropyrimidines);

  AND/OR
  - In a patient with a tumour expressing wild-type RAS gene:
    - if an anti-EGFR was prescribed as first-line then use bevacizumab or aflibercept as second-line in combination with fluoropyrimidine-based chemotherapy with oxaliplatin or irinotecan;
    - if bevacizumab was prescribed as first-line, use an anti-EGFR monoclonal antibody second-line (cetuximab or panitumumab) in combination with fluoropyrimidine-based chemotherapy with oxaliplatin or irinotecan, or continue the treatment with bevacizumab + fluoropyrimidine-based chemotherapy with oxaliplatin or irinotecan.
- In a patient with a tumour expressing mutated RAS gene, bevacizumab is initiated or continued in second-line. Aflibercept may be used in second-line in case of oxaliplatin-based chemotherapy in first-line.

Role of the medicinal product in the therapeutic strategy

- A targeted therapy with AVASTIN or anti-EGFR (wild-type RAS) associated with a fluoropyrimidine-based chemotherapy is the preferred therapeutic option over chemotherapy alone in second-line treatment of metastatic colorectal cancer.

Clinical data

- During the initial assessment in 2009, the pivotal study comparing AVASTIN combined with the FOLFOX-4 protocol versus FOLFOX-4 alone in second-line treatment of metastatic colorectal cancer demonstrated an improvement in overall survival (primary endpoint) of 2.2 months (13 months in the AVASTIN + FOLFOX-4 group versus 10.8 months in the FOLFOX-4 alone group).
- The results of 2 new studies have demonstrated a gain in overall survival, in one study with a smaller extent (1.4 months) and a lack of gain in the other study. There are no data on quality of life from these two studies.
- The main adverse reactions on AVASTIN in studies were: hypertension, bleeding, proteinuria, arterial thromboembolism and gastrointestinal perforations.
- No data is available versus aflibercept (ZALTRAP), available as a second-line treatment of metastatic colorectal cancer.

Special prescribing conditions

- Medicinal product reserved for hospital use.
- Prescription restricted to specialists or doctors trained in oncology or cancer treatment

Benefit of the medicinal product

- The actual clinical benefit* of AVASTIN remains substantial.
- Considering that the results of the new clinical studies available have not demonstrated a relevant effect on overall survival from the addition of AVASTIN to chemotherapy, but have shown an increase in adverse events, AVASTIN, in combination with a fluoropyrimidine-based chemotherapy, does not provide an improvement in actual benefit** (IACB V) in second-line treatment of metastatic colorectal cancer including anti-EGFR.

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This document was created on the basis of the Transparency Committee Opinion of 20 April 2016 (CT-14881) and is available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a 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 ACB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

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