HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New indication
April 2017

SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

XALKORI (crizotinib), tyrosine kinase inhibitor

High clinical benefit for the treatment of ALK + non-small cell lung cancer and minor clinical added value compared to platinum salt-based chemotherapy

Main points

- XALKORI has been granted a marketing authorisation for the first-line treatment of adults with advanced ALK-positive non-small cell lung cancer (NSCLC).
- A study has demonstrated a gain in progression-free survival but with no impact on overall survival with XALKORI compared to platinum salt-based chemotherapy.
- It is difficult to transfer the findings of the study conducted to real-life conditions of use due to different treatment schedules between the two groups.
- This is a first-line treatment for advanced ALK+ NSCLC.

Pre-existing indications*

XALKORI has also been granted a marketing authorisation for the treatment of advanced ROS1+ NSCLC and for the second-line and subsequent treatments of ALK+ NSCLC.

Therapeutic strategy

- The therapeutic management of NSCLC differs according to the cancer stage. The conventional treatment for early stages is surgery. However, a large proportion of patients are diagnosed at an advanced stage of the disease (approximately 25 to 30% at the locally advanced stage and 40% at the metastatic stage); early stages merely represent approximately 25 to 30%. The management of these cancers is based on systemic treatment. The therapeutic strategy is guided based on the presence of genetic alteration or not.
- Other criteria are also involved in the therapeutic decision: tumour histology, the patient's performance status and comorbidities. ALK gene rearrangements are exclusive of other oncogenic mutations detected in NSCLC (in particular EGFR mutations, KRAS mutations, ROS rearrangements).
- Cytotoxic chemotherapy regimens such as cisplatin or carboplatin in combination with pemetrexed/vinorelbine/gemcitabine/docetaxel or paclitaxel are currently available for the first-line treatment of NSCLC. However, these therapies have no specific action on ALK rearrangements.
- **Role of the proprietary medicinal product in the therapeutic strategy**
  XALKORI is a first-line treatment for advanced ALK+ NSCLC. Failing data, its role compared to chemotherapy induction treatment followed by maintenance treatment with pemetrexed is not known.

Clinical data

- In a randomised open-label phase III study, the efficacy and safety of crizotinib were compared to platinum salt (cisplatin or carboplatin) chemotherapy plus pemetrexed as a first-line treatment, in patients with advanced ALK+ NSCLC. A total of 343 patients were randomised: 172 to the crizotinib group and 171 to the chemotherapy group.

* This summary does not concern these indications.

The median treatment duration was 47.4 weeks in the crizotinib group and 18.0 weeks in the chemotherapy group.
The median progression-free survival (primary endpoint) was 10.9 months in the crizotinib group versus 7 months in the chemotherapy group, i.e. an absolute gain of 3.9 months in favour of crizotinib (HR=0.454; 95% CI: [0.346-0.596]; p <0.0001).
On the date of analysis, no difference was observed between the two groups in respect of overall survival.

- The treatment schedules between the two groups were different in favour of the XALKORI group: treatment until progression in the XALKORI and not more than 6 cycles in the chemotherapy group corresponding to median treatment durations of 47.4 weeks versus 18.0 weeks, respectively. No data are available on the effect of XALKORI compared to chemotherapy induction treatment followed by maintenance treatment with pemetrexed.
- The main grade 3 or 4 adverse events more frequent in the crizotinib group than in the chemotherapy group were: transaminase elevation (14% versus 2.4%), diarrhoea (2.3% versus 0.6%), QT prolongation (2.3% and 0%). Conversely, leukopoenia (1.8% and 5.3%), hyponatraemia (0.6% and 2.4%), anaemia (0% and 8.9%), thrombocytopoenia (0% and 6.5%) were more frequent in the chemotherapy group.

Special prescription requirements

- Medicinal product subject to hospital prescription, reserved for medical oncology specialists or physicians with expertise in oncology.
- Medicinal product requiring monitoring during treatment.

Benefit of the medicinal product

- The actual clinical benefit* of XALKORI is high.
- XALKORI provides a minor clinical added value** (CAV IV) for the first-line treatment of advanced-stage ALK+ NSCLC.
- Approval for non-hospital pharmacy reimbursement and for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 5 April 2017 (CT-16041) 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".