HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New indication
May 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

ALECENSA (alectinib), tyrosine kinase inhibitor

High clinical benefit and minor clinical added value compared to XALKORI as first line treatment of metastatic non-small cell lung cancer with ALK gene rearrangement.

Main points

- ALECENSA has been granted marketing authorisation for the first-line treatment in monotherapy of adults suffering from advanced metastatic non-small cell lung cancer (NSCLC) with ALK rearrangement.
- Its superiority over XALKORI (crizotinib) in terms of progression-free survival has been demonstrated, though it is impossible to draw any conclusions concerning overall survival due to the study methodology.
- Its tolerance profile is comparable to crizotinib.
- It is the preferred first-line treatment for this population.

Pre-existing indication*

ALECENSA has also been granted marketing authorisation for the second-line treatment of ALK+ NSCLC after crizotinib failure.

Therapeutic strategy

- The therapeutic strategy for metastatic NSCLC must be defined in the context of multidisciplinary review meetings, based on the presence of molecular abnormalities (in particular, EGFR mutation, ALK translocation or ROS1 rearrangement), PD-L1 tumour expression, tumour histology (squamous or non-squamous), age, ECOG performance status, comorbidities and patient preferences.
- For patients with NSCLC tumours presenting ALK gene rearrangement, crizotinib or ceritinib is recommended from the first line. No direct comparative data for these medicinal products are available.

Role of the proprietary medicinal product in the therapeutic strategy

Considering its demonstrated superiority over crizotinib, ALECENSA is the preferred option for the first-line treatment of NSCLC with ALK rearrangement.

Clinical data

- A randomised, open-label study, including 303 patients suffering from advanced ALK+ NSCLC, assessed the efficacy and safety of first-line alectinib versus crizotinib.
  As of the data lock date of 09 February 2017, median follow-up duration was 18.6 months in the alectinib group and 17.6 months in the crizotinib group.
- Median progression-free survival was 11.1 months (CI 95%: 9.1 - 13.1) in the crizotinib group and was not reached in the alectinib group (CI 95%: 17.7-NE).
  Alectinib reduced the risk of progression or death by 53% compared to crizotinib (HR=0.47 [$CI_{95\%}$: 0.34-0.65], p<0.0001]).

* This summary does not cover these indications.

- The results of the ranked secondary endpoints underlined the following points:
  - median progression-free survival improved by 15.3 months (25.7 months in the alectinib group versus 10.4 months in the crizotinib group, HR=0.50 [CI 95%: 0.36–0.70], p=0.0001).
  - reduced risk of initial brain progression on alectinib compared to crizotinib: 12% (18 patients) in the alectinib group versus 45% (68 patients) in the crizotinib group (specific cause HR = 0.16 [CI 95%: 0.10–0.28], p=0.0001).
- No differences were observed between the two treatment groups in terms of objective response rate.
  Considering the non-significant objective response rate results evaluated by the investigator, secondary endpoint hierarchical sequential testing was interrupted and, consequently, the overall survival comparison data cannot be considered as robust.
- There was a similar proportion of treatment discontinuations due to adverse events (AEs) in both groups (approximately 12%) and to serious AEs (approximately 29%).
- The only serious AEs reported with a higher incidence in the alectinib group (difference ≥2% between the 2 groups) were acute kidney failure (0% in the crizotinib group versus 3% in the alectinib group) and lung infections (0% versus 2% respectively). Conversely, cases of nausea were more frequent in crizotinib group patients (2% versus 0% respectively).

Special prescription requirements

- Prescription reserved for oncology specialists or physicians with oncology expertise.

Benefit of the medicinal product

- The actual clinical benefit* of ALECENSA is high.
- ALECENSA provides a minor clinical added value** (CAV IV) compared to crizotinib for its indication.
- Approved for non-hospital and hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 30 May 2018 (CT-16771) available at **www.has-sante.fr**

* The actual clinical benefit of a medicinal product (ACB) is 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"