HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New indication
December 2017

TRANSPARENCY COMMITTEE OPINION SUMMARY

ZYKADIA (ceritinib), tyrosine kinase inhibitor

High clinical benefit and minor clinical added value compared to chemotherapy combining a platinum salt and pemetrexed, followed by maintenance treatment with pemetrexed, as first line treatment of metastatic non-small cell lung cancer with ALK gene rearrangement

Main points

- ZYKADIA has been granted marketing authorisation for the first-line treatment of adults in monotherapy for advanced metastatic non-small cell lung cancer (NSCLC) with ALK gene rearrangement.
- Its superiority has been demonstrated over platinum salt-based chemotherapy in terms of progression-free survival, though without demonstrated impact on overall survival. This chemotherapy, however, is no longer the current treatment standard.
- Its safety profile is superior to that of chemotherapy.
- It is a first-line treatment for this population.

Pre-existing indication*

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

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 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**
  ZYKADIA is first-line treatment for ALK-positive NSCLC. Failing comparison with an optimum level of evidence, its position relative to crizotinib remains to be defined.

Clinical data

- A phase III open-label, randomised study compared the efficacy and safety of ceritinib (n=189) to standard first-line chemotherapy (n=187), including a platinum salt combined with pemetrexed, followed by maintenance treatment with pemetrexed, in adults suffering from locally advanced or metastatic ALK+ NSCLC.
- Most patients were at a metastatic stage (96.3% at stage IV). Median progression-free survival (primary endpoint) was 16.6 months in the ceritinib group and 8.1 months in the chemotherapy group, i.e. an absolute gain of 8.5 months. (HR=0.55; CI95% [0.42; 0.73], p<0.001).
- During the main analysis, no differences were observed between the two groups in terms of overall survival.
  To date, 60% of patients from the chemotherapy group had already crossed over to an ALK-inhibitor treatment.

* This summary does not cover these indications.

The evaluation of response in terms of brain metastases related to a limited number of study patients (11.7%). Consequently, no reliable conclusions can be drawn concerning this endpoint.

- As this was an open-label study, no robust conclusions can be drawn from the analysis of quality-of-life data.
- 11.1% of patients in the ceritinib group and 16.6% of patients in the chemotherapy group discontinued their treatment due to adverse events.
- The primary toxicities observed for ceritinib were digestive in nature (diarrhoea: 84.7% versus 10.9% and increased ALAT: 60.3% versus 21.7%, γ-GT: 37.0% versus 10.3%) and renal (increased creatinine: 22.2% versus 9.7%). Conversely, the primary toxicities in the chemotherapy group were haematological in nature (anaemia: 14.8% versus 35.4%, neutropoenia: 4.8% versus 21.7%).

Special prescription requirements

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

Benefit of the medicinal product

- The actual clinical benefit* of ZYKADIA is high.
- ZYKADIA provides a minor clinical added value** (CAV IV) compared to chemotherapy combining a platinum salt and pemetrexed, followed by pemetrexed maintenance treatment, 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 13 December 2017 (CT-16500) 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"