HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New medicinal product
September 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

TAGRISSO (osimertinib), tyrosine kinase inhibitor

No clinical benefit demonstrated in the treatment of locally-advanced or metastatic non-small cell lung cancer with EGFR T790M mutation

Main points

- TAGRISSO has Marketing Authorisation in the treatment of locally-advanced or metastatic non-small cell lung cancer (NSCLC) with EGFR T790M mutation. This Marketing Authorisation is conditional on the results of a phase III comparative study (AURA3) in progress. The results of this study will be necessary to fully assess the extent of the effect and the role of osimertinib in the therapeutic strategy for NSCLC with EGFR T790M mutation.
- The only available data result from two non-comparative phase II studies performed in patients previously treated with anti-EGFR tyrosine kinase inhibitor (TKI).
- No data documents the safety and efficacy of osimertinib as a first-line treatment in patients carrying the T790M mutation from the outset (approximately 1% of cases).

Therapeutic use

- As a first-line treatment for EGFR mutated NSCLC, a monotherapy with an anti-EGFR TKI (gefinitib, erlotinib or afatinib) is recommended. The majority of patients will progressively acquire resistance to these treatments, especially due to the appearance of new mutations in the gene coding for the EGF receptor. The T790M mutation is therefore found in approximately 50 to 60% of patients who developed a resistance to anti-EGFR TKIs, while it is only present from the outset in approximately 1% of cases.
- In second-line, the standard treatment is a dual therapy combining a platinum salt with gemcitabine, vinorelbine, a taxane or pemetrexed. The addition of bevacizumab can be recommended in the absence of contraindication and in patients with a 0 or 1 performance index.
- **Role of the medicinal product in the therapeutic strategy**

  TAGRISSO may represent a first-line treatment in patients with locally-advanced or metastatic NSCLC carrying the EGFR T790M mutation who progressed during or after treatment with an anti-EGFR TKI. While awaiting comparative data, its role in relation to chemotherapy cannot be defined.

  In patients carrying the EGFR T790M mutation from the outset and not previously treated with anti-EGFR TKI, the role of TAGRISSO cannot be defined given the lack of clinical data.

  In all situations, treatment with TAGRISSO can only be initiated after documenting the EGFR T790M mutation. This mutation can be tested for in circulating tumour DNA and/or tumour biopsy.

Clinical data

- The evaluation of osimertinib relies on two non-comparative phase II studies of similar methodology analysed in a pooled manner. They were conducted in 411 patients with locally-advanced or metastatic NSCLC with EGFR T790M mutation who received at least one anti-EGFR TKI treatment.
  After a median treatment time of 13 months, the percentage of overall response (primary endpoint) was 66% among the patients who could be evaluated (n=397). The median duration of this response was 12.5 months. The median progression-free survival time was 11.0 months [9.6; 12.4] and the median overall survival time has not been reached.

- The percentage of patients who had at least one adverse event of grade 3 or higher was 36.3% and at least one serious adverse event was 26.0%. The most commonly reported adverse events of grade 3 or higher were: respiratory, thoracic and mediastinal disorders (8.3%), infections (5.8%) and haematologic and lymphatic system disorders (3.9%).

Special prescribing conditions

- Medicinal product requiring special monitoring during treatment.
- Medicinal product for hospital prescription, restricted to cancer treatment and clinical oncology specialists and departments.

Benefit of the medicinal product

- The actual benefit* of TAGRISSO is substantial.
- TAGRISSO does not offer any clinical added value** (CAV V, none) in the therapeutic strategy for locally-advanced or metastatic NSCLC with EGFR T790M mutation.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 21 September 2016 (CT-15113) and is available at **www.has-sante.fr**

* 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”.