HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
Update
September 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

TAGRISSO (osimertinib), tyrosine kinase inhibitor

Substantial actual benefit and minor improvement compared with chemotherapy combining a platinum salt with pemetrexed in patients who acquired the EGFR T790M mutation during a previous treatment with anti-EGFR TKI.

Main points

- TAGRISSO has Marketing Authorisation in the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with EGFR T790M mutation.
- The new data affect only patients who acquired the EGFR T790M mutation during their first-line treatment with anti-EGFR TKI.
- In this case, progression-free survival was improved compared with platinum-based chemotherapy (absolute gain of 5.7 months) in patients previously treated with an anti-EGFR TKI.
- No gain in overall survival has been demonstrated to date.
- The safety profile of osimertinib is more favourable than that of platinum salt-based chemotherapy.

Therapeutic use

- In the locally advanced or metastatic stage, therapeutic management is based on a systemic treatment guided by the EGFR mutational status.
- As a first-line treatment for EGFR mutated advanced NSCLC, a monotherapy with an anti-EGFR tyrosine kinase inhibitor (TKI) (IRESSA [gefitinib], TARCEVA [erlotinib] or GIOTRIF [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 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.
- As second-line, the reference treatment is dual therapy combining a platinum salt (cisplatin or, if contraindicated, carboplatin) with one of the following: gemcitabine, vinorelbine, taxanes (docetaxel and paclitaxel) or pemetrexed. The addition of bevacizumab (AVASTIN) can be recommended in the absence of contraindication and in patients with an ECOG performance index of 0 -1. Since the first assessment of this medicinal product in September 2016, TAGRISSO was recommended as a possible second-line alternative in patients who acquired the T790M mutation during their prior treatment with anti-EGFR TKI, but it was not possible, at the time, to specify its role compared with chemotherapy.
- **Role of the medicinal product in the therapeutic strategy**
  TAGRISSO is a second-line treatment for advanced or metastatic NSCLC with EGFR T790M mutation after failure of a prior treatment with an anti-EGFR tyrosine kinase inhibitor. Its superiority was established against an available alternative (platinum-based chemotherapy) in terms of progression-free survival. In patients carrying the EGFR T790M mutation from the outset and not previously treated with anti-EGFR tyrosine kinase inhibitor, the role of TAGRISSO cannot be specified due to a lack of clinical data.

Clinical data

- This reassessment is mainly based on data from the AURA3 study, a randomised, open-label, comparative study versus chemotherapy (platinum salt + pemetrexed +/- maintenance therapy with pemetrexed) conducted in 419 patients with locally advanced or metastatic NSCLC with EGFR T790M mutation and previously treated with anti-EGFR TKI.

- Osimertinib demonstrated its superiority compared with chemotherapy in the primary endpoint of progression-free survival determined by the investigator: a median of 10.1 months in the osimertinib group versus a median of 4.4 months in the chemotherapy group, i.e. an absolute gain of 5.7 months in favour of osimertinib: HR=0.30; 95% CI = [0.23; 0.41]; p<0.001. In the interim analysis of overall survival, no difference between the two groups was found in this criteria: HR=0.72; 99.96% CI = [0.34; 1.52]; p=0.121>0.04.
- Concerning safety, the number of AEs grade ≥3 (22.26% versus 47.1%) as well as the number of SAEs (17.9% versus 25.7%) was higher in the chemotherapy group than in the osimertinib group.

Special prescribing conditions

- Medicine for hospital prescription only, restricted to cancer treatment and clinical oncology specialists.

Benefit of the medicinal product

- The actual benefit* of TAGRISSO is substantial.
- TAGRISSO provides minor clinical added value** (CAV IV) compared with chemotherapy combining a platinum salt with pemetrexed in patients who acquired the EGFR T790M mutation during a previous treatment with anti-EGFR TKI
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

HAUTE AUTORITÉ DE SANTÉ
This document was created on the basis of the Transparency Committee Opinion of 13 September 2017 (CT-15996) 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”.