HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
08 JANUARY 2020

dabrafenib / trametinib
TAFINLAR 50 and 75 mg hard capsules / MEKINIST 0.5 and 2 mg film-coated tablets

Reevaluation

Key points

Now favourable opinion for reimbursement in advanced non-small cell lung cancer (NSCLC) only in patients with a BRAF V600E mutation, as second or later-line treatment following the failure of chemotherapy and/or immunotherapy. This opinion is subject to the collection of observational data within a maximum period of 2 years with a view to reevaluation.

Unfavourable opinion for reimbursement in other situations as second or later-line treatment. As a reminder, unfavourable opinion for reimbursement in adult patients with advanced NSCLC with a BRAF V600 mutation as first-line treatment.

What therapeutic improvement?

No clinical added value.

Role in the care pathway?

The care pathway for advanced NSCLC must be defined in the context of multidisciplinary review meetings, based firstly on the presence of molecular abnormalities (in particular, EGFR mutation, ALK or ROS1 translocations), then PD-L1 tumour expression, as well as tumour histology (squamous or non-squamous), age, ECOG performance status and patient preferences.

Role of TAFINLAR / MEKINIST in the care pathway:

The TAFINLAR / MEKINIST (dabrafenib / trametinib) combination is a second and later-line treatment following the failure of chemotherapy and/or immunotherapy in adult patients with advanced NSCLC with a BRAF V600E mutation. The TAFINLAR / MEKINIST combination has no role in the treatment of adult patients with advanced NSCLC with a BRAF V600 mutation in other situations as second or later-line treatment.

As a reminder, the TAFINLAR / MEKINIST combination has no role as first-line treatment in adult patients with advanced NSCLC with a BRAF V600 mutation (including a V600E mutation).

01 COMMITTEE'S CONCLUSIONS

Clinical Benefit

◗ Advanced non-small cell lung cancer (NSCLC) is a serious, life-threatening condition.
◗ It is a curative treatment for NSCLC with BRAF V600 mutation.
◗ In the absence of any comparison with the available alternatives and considering the methodological weaknesses of the study provided, as well as uncertainties with respect to the prognostic value of the V600 mutation, the impact of TAFINLAR / MEKINIST on morbidity is difficult to quantify. The efficacy/adverse effects ratio of TAFINLAR / MEKINIST in the second or later-line treatment of advanced NSCLC is low in the event of BRAF V600E mutation and needs to be confirmed by new observational data. It is not established in other situations, in particular in the event of BRAF non V600E mutation, due to a lack of data.
◗ There are therapeutic alternatives as second and later-line treatment, which are chemotherapies and immunotherapies; however, the TAFINLAR / MEKINIST combination is the only authorised treatment targeting the BRAF V600 mutation.
◗ Pending new efficacy and safety data, the TAFINLAR / MEKINIST combination in the treatment of advanced NSCLC is a second and later-line treatment, only in the event of BRAF V600E mutation. TAFINLAR / MEKINIST has no role in the care pathway in other situations, due to a lack of data.

Public health impact:
Considering:
- the seriousness of NSCLC, particularly at the advanced stage,
- the low incidence of NSCLC patients with a BRAF V600 mutation,
- uncertainties with respect to the predictive and prognostic value of this mutation,
- the lack of quality of life data,
- the lack of any demonstrated impact on the organisation of care,
- uncertainties with respect to the response to the identified partially met medical need (particularly for the impact in terms of morbidity and mortality),

the TAFINLAR / MEKINIST combination is unlikely to have any impact on public health in this indication.

Considering all these elements, the Committee deems that the clinical benefit of the TAFINLAR / MEKINIST combination is:
- **low in the treatment of adult patients with advanced NSCLC only in patients with a BRAF V600E mutation, as second or later-line treatment following the failure of chemotherapy and/or immunotherapy. The Committee makes maintenance of the clinical benefit conditional on the collection of observational data in patients treated with the TAFINLAR / MEKINIST combination for advanced NSCLC with a BRAF V600 mutation with a view to reevaluation of the TAFINLAR / MEKINIST combination within a period of 2 years (see 010. Other Committee recommendations).**
- **insufficient to justify its funding by the French national health insurance system in other second and later-line treatment situations.**

As a reminder, in its opinion of 7 March 2018, the Committee considered that the clinical benefit in the first-line treatment of adult patients with advanced NSCLC with a BRAF V600 mutation was insufficient to justify its funding by the French national health insurance system.

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use only in the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600E mutation, as second or later-line treatment.

The Committee issues an unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in other second and later-line treatment situations.

As a reminder, in its opinion of 7 March 2018, the Committee issued an unfavourable opinion for reimbursement in adult patients with advanced NSCLC with a BRAF V600E mutation as first-line treatment.

Clinical Added Value

Considering:

- **the clinical results from a non-comparative, open-label phase 2 cohort study having demonstrated an overall response rate of 63% in patients with advanced NSCLC with a BRAF V600E mutation, as second and later-line treatment in patients having received chemotherapy;**
- **the absence of data in patients previously treated with immunotherapy;**
- **the absence of any direct comparison with current standard treatments (chemotherapy and immunotherapy), particularly versus chemotherapy, despite this being feasible;**

the Transparency Committee considers that the TAFINLAR / MEKINIST combination provides no clinical added value (CAV V) in the management of patients with NSCLC with a BRAF V600E mutation, as second or later-line treatment following the failure of chemotherapy and/or immunotherapy.