OPINION ON MEDICINAL PRODUCTS

dabrafenib/trametinib

TAFINLAR 50 and 75 mg, MEKINIST 0.5 and 2 mg,

capsule and film-coated tablet

Reassessment

Adopted by the Transparency Committee on 5 October 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of continued reimbursement of the TAFINLAR (dabrafenib) / MEKINIST (trametinib) combination, only in the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) carrying a BRAF V600E mutation, in the second-line of treatment or beyond, after failure of the current standard treatments (chemotherapy and/or immunotherapy)

Therapeutic progress?

No progress, based on the data currently available.

Role in therapeutic strategy?

Apart from mutations or translocations for which targeted therapies are available, first-line treatment for non-small cell lung cancer is based on immunotherapy with or without platinum-salt-based chemotherapy regardless of BRAF status.

In a retrospective French case-control study, pemetrexed appeared to be the best doublet in terms of survival in BRAF-mutated patients. As a second line treatment, immunotherapy is recommended for patients who have failed to respond to chemotherapy alone. The use of immunotherapy for these patients can be considered under the same conditions as for non-mutated patients. In the ImmunoTarget study, patients with BRAF alteration had a 54% control rate on immunotherapy as a monotherapy, and seemed to be barely affected by PDL1 status. However, there is a clear numerical difference between patients with non-V600E BRAF mutations (median progression-free survival at 4.1 months) and V600E mutations (median progression-free survival at 1.8 months).

Role of TAFINLAR (dabrafenib) / MEKINIST (trametinib) in the treatment strategy:

The combination of TAFINLAR (dabrafenib) and MEKINIST (trametinib) remains an option for second-line treatment and beyond after failure of chemotherapy and/or immunotherapy in adult patients suffering from advanced NSCLC with the BRAF V600E mutation.

Committee's conclusions

Clinical Benefit

- Non-small cell lung cancer (NSCLC) is a serious and life-threatening disease.
- It is a specific treatment with curative intent for advanced NSCLC with a BRAF V600 mutation.
- In the absence of a comparison with the available alternatives and considering the methodological weaknesses of the data provided, the efficacy/adverse effect ratio of TAFINLAR (dabrafenib) / MEKINIST (trametinib) in the treatment of advanced NSCLC as a second-line treatment and beyond, is low in the case of BRAF V600E mutation
- Medicinal alternatives are available as second-line treatments and beyond, in the form of mono-chemotherapies used independently of BRAF status, however the TAFINLAR (dabrafenib) / MEKINIST (trametinib) combination is the only approved treatment targeting the BRAF V600 mutation.
- This is a second-line treatment and beyond.

Public health benefit

Considering:

- the severity of NSCLC, particularly at an advanced stage;
- the low incidence of NSCLC with a BRAF V600E mutation;
- the lack of evidence of a gain in overall survival or quality of life;
- the lack of a demonstrated impact on the delivery of care and the uncertain response to the partially met medical need identified;

the combination of TAFINLAR (dabrafenib) / MEKINIST (trametinib) is not likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the actual clinical benefit of TAFINLAR (dabrafenib) / MEKINIST (trametinib) remains low only in the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with a BRAF V600E mutation, as a second-line treatment or beyond, after the failure of current standard treatments (chemotherapy and/or immunotherapy).

The Committee approves continued inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary medicinal products approved for community use only for the treatment of adult patients suffering from advanced non-small cell lung cancer (NSCLC) with a BRAF V600E mutation, as a second-line treatment or beyond, after the failure of current standard treatments (chemotherapy and/or immunotherapy) and at the marketing authorisation dosages.

Proposed reimbursement rate: 100%

Clinical Added Value

Considering the new data added to the submission and based on:

- **follow-up data from the non-comparative pivotal study,**
- **data from retrospective studies,**

the Committee deems that the clinical added value (CAV) attributed to the TAFINLAR (dabrafenib) / MEKINIST (trametinib) combination in its opinion of 8 June 2020 remains unchanged, i.e. no improvement in clinical added value (CAV V) in the management of patients suffering from NSCLC with a BRAF V600E mutation, as a second-line treatment and beyond, after failure of chemotherapy and/or immunotherapy.