HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
1 APRIL 2020

ramucirumab
CYRAMZA 10 mg/mL concentrate for solution for infusion

New indication

Key points

Favourable opinion for reimbursement in the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) activating mutations, in combination with erlotinib.

What therapeutic improvement?

No clinical added value in the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with EGFR activating mutations, in combination with erlotinib.

Role in the care pathway?

The therapeutic arsenal for lung cancer has recently been expanded following the addition of specific treatments targeting this genome abnormality, as first-line therapy.

Hence, the current strategy for first-line treatment in the presence of an EGFR mutation in NSCLC is based on monotherapy with an anti-EGFR tyrosine kinase inhibitor (TKI) administered orally (IRESSA (gefitinib), TARCEVA (erlotinib), GIOTRIF (afatinib) and VIZIMPRO (dacomitinib)).

Due to evidence of a gain in terms of overall survival compared to erlotinib and gefitinib with a safety profile deemed to be acceptable, osimertinib is now the first-line option of choice when the use of an

anti-EGFR TKI is envisaged. It was assessed in patients with EGFR exon 19 deletion or exon 21 (L858R) activating mutations and T790M mutations.

Role of CYRAMZA (ramucirumab) in the care pathway:

On the basis of currently available data and pending overall survival data (immature data at the time of assessment by the Transparency Committee), the Committee deems that the ramucirumab + erlotinib combination is a treatment option for first or later-line therapy.

However, in the current context, given new first-line therapy developments, its precise role in the care pathway remains to be defined. The decision to prescribe CYRAMZA (ramucirumab) in combination with erlotinib or an anti-EGFR tyrosine kinase inhibitor must take into account the efficacy results, the safety profile of each drug and the patient's choice. The Committee reiterates that patients with EGFR mutations other than exon 19 deletion or exon 21 (L858R) activating mutations were not assessed in the RELAY having studied CYRAMZA (ramucirumab) in combination with erlotinib.

01 COMMITTEE'S CONCLUSIONS

01.1 Clinical benefit

◗ Non-small cell lung cancer (NSCLC) is a serious, life-threatening condition.
◗ The proprietary medicinal product CYRAMZA (ramucirumab) is part of a specific curative NSCLC treatment.
◗ The efficacy/adverse effects ratio of CYRAMZA (ramucirumab) in combination with erlotinib in the treatment of metastatic NSCLC with EGFR activating mutations is low due to the absence of a demonstrated improvement in terms of overall survival based on data from the interim analysis in view of the combination's safety profile (higher frequency of grade 3 or 4 adverse events with the combination compared to erlotinib alone).
◗There are medicinal alternatives.
◗ This is a first-line treatment in the management of adult patients with metastatic NSCLC with EGFR activating mutations (see section 09 of the opinion).

Public health impact

Considering:
- the seriousness of metastatic NSCLC with EGFR mutation,
- the low prevalence of EGFR mutation (10%),
- the medical need, which is considered to be partially met,
- the absence of a demonstrated impact on morbidity and mortality compared to current alternatives,
- the absence of conclusive quality of life data,
- the absence of data enabling assessment of the impact on the organisation of care,

CYRAMZA (ramucirumab) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of CYRAMZA (ramucirumab) is low in this MA indication extension.

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the MA indication(s) and dosages.

01.2 Clinical Added Value

Considering:
- **demonstration of the superiority of the ramucirumab + erlotinib combination compared to erlotinib alone in terms of progression-free survival (gain assessed by the investigator to be 7 months, HR = 0.591 ($CI_{95\%}$ = [0.461-0.760]), p<0.0001 and by the independent data monitoring board to be 5.4 months, HR = 0.671 ($CI_{95\%}$ = [0.518-0.869]), p=0.0022);**
- **the absence of any demonstrated improvement in overall survival (data immaturity at the time of the interim analysis);**
- **the absence of any formal conclusion that can drawn based on the quality of life results;**
- **the toxicity profile marked primarily by a higher incidence of grade 3 or higher treatment-related adverse events (infections) with the ramucirumab + erlotinib combination;**

the Committee considers that CYRAMZA (ramucirumab) provides no clinical added value (CAV V) in combination with erlotinib in the first-line treatment of adult patients with metastatic non-small cell lung cancer with epidermal growth factor receptor (EGFR) activating mutations.