HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
21 OCTOBER 2020

The legally binding text is the original French opinion version

atezolizumab

TECENTRIQ 1,200 mg concentrate for solution for infusion

Reevaluation

Key points

Favourable opinion for reimbursement in combination with bevacizumab, paclitaxel and carboplatin, only in the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) without EGFR mutant or ALK-positive tumours.

What therapeutic improvement ?

Therapeutic improvement compared to the bevacizumab, paclitaxel and carboplatin combination.

Role in the care pathway ?

In the absence of an activating EGFR or BRAF mutation and ALK or ROS gene rearrangement, the standard first-line treatment in patients with no major comorbidities and with an ECOG performance status of 0 to 2 is based on chemotherapy combining a platinum-based drug with one of the following drugs: paclitaxel, docetaxel, gemcitabine, vinorelbine or pemetrexed, depending on the patient's age (< or ≥ 70 years). The combination of bevacizumab with dual platinum-based chemotherapy is a first-line treatment option in certain patients, in the absence of contraindications and in the event of an ECOG performance status of 0 or 1.

Recently, immunotherapy has changed these standards. Hence pembrolizumab is a first-line treatment in metastatic non-squamous NSCLC :

- as monotherapy in patients whose tumours strongly express PD-L1 ligand with a tumour proportion score [TPS] ≥ 50% and not presenting a tumour EGFR mutation or ALK rearrangement,
- in combination with pemetrexed + platinum salt chemotherapy in patients with an ECOG status of 0 or 1, irrespective of PD-L1 expression rate, and whose tumours do not present EGFR or ALK mutations.

Role of the medicinal product in the care pathway

TECENTRIQ (atezolizumab) in combination with bevacizumab, paclitaxel and carboplatin, remains a first-line alternative for the treatment of patients with metastatic non-squamous NSCLC without EGFR mutant or ALK-positive tumours.

In the absence of a demonstrative analysis on the basis of expression of PD-L1 tumour proportion score [TPS], the efficacy of TECENTRIQ (atezolizumab) in combination with bevacizumab, paclitaxel and carboplatin according to PD-L1 status is not known. Furthermore, the Commission reiterates that the role of TECENTRIQ (atezolizumab) in combination with bevacizumab, carboplatin and paclitaxel compared to pembrolizumab (as monotherapy in patients with PD-L1 expression ≥ 50% or in combination with chemotherapy irrespective of PD-L1 expression status) is not known, in the absence of comparative data.

The choice of treatment between immunotherapy alone and immunochemotherapy must take into account validated data in terms of the efficacy and safety (benefit/risk) of each of the options.

The Committee issues a warning about the risk of vascular complications associated with the use of bevacizumab in certain patients (see product SPC) and reiterates the fact that bevacizumab can only be considered in the absence of contraindications (see Transparency Committee opinion of 25/05/2016 relative to AVASTIN).

As a reminder, in patients whose tumours have an EGFR mutation or ALK rearrangement, TECENTRIQ (atezolizumab) in combination with bevacizumab and chemotherapy has no role in the care pathway due to a lack of available clinical data (see opinion of 9 October 2019).

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers :

Clinical benefit

Metastatic non-squamous non-small cell lung carcinoma (NSCLC) is a serious, life-threatening disease.
TECENTRIQ (atezolizumab) in combination with bevacizumab, paclitaxel and carboplatin is a curative treatment.
Despite demonstration of a superiority of the atezolizumab + bevacizumab + chemotherapy combination compared to the chemotherapy + bevacizumab combination, an acceptable but not optimal comparator (see section 08.5 Summary and Discussion) in terms of overall survival in an open-label phase III study and taking into account both the safety data from the study, reporting a higher toxicity with the addition of atezolizumab, and the known toxicity of bevacizumab added to chemotherapy,
the efficacy/adverse effects ratio of this quadruple combination remains moderate in patients without EGFR mutant or ALK-positive tumours.
There are medicinal alternatives for the first-line treatment of metastatic non-squamous NSCLC (see section 06. Clinically relevant comparators).
In patients without EGFR mutant or ALK-positive tumours, TECENTRIQ (atezolizumab) in combination with bevacizumab, paclitaxel and carboplatin is a therapeutic alternative in metastatic non-squamous NSCLC (see section 09. Role in the care pathway).

Public health impact :
Considering :
the seriousness of non-squamous NSCLC, particularly at the metastatic stage,
the incidence of the disease,
the partially met medical need,
the partial response to the identified need (demonstrated superiority of the atezolizumab + bevacizumab + chemotherapy combination compared to the bevacizumab + chemotherapy combination in terms of progression-free survival and overall survival),
the lack of elements supporting the absence of a deterioration in the care and/or life pathway in the absence of robust quality of life data,
the absence of data enabling assessment of the additional impact on the organisation of care,
TECENTRIQ (atezolizumab) in combination with bevacizumab, paclitaxel and carboplatin is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of TECENTRIQ (atezolizumab) in combination with bevacizumab, paclitaxel and carboplatin remains moderate in the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) without EGFR mutant or ALK-positive tumours.

The Committee issues a favourable opinion for maintenance of inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the indication "in combination with bevacizumab, paclitaxel and carboplatin in the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) without EGFR mutant or ALK-positive tumours" and at the MA dosages.

As a reminder, in accordance with the opinion of 9 October 2019, the Committee considered that the clinical benefit of TECENTRIQ (atezolizumab) in combination with bevacizumab, paclitaxel and carboplatin is insufficient to justify its public funding cover in adult patients with EGFR mutant or ALK-positive (ALK+) metastatic non-squamous NSCLC, after failure of appropriate targeted therapies.

Clinical Added Value

Considering :
demonstration of the superiority of the atezolizumab, bevacizumab, paclitaxel and carboplatin combination compared to the bevacizumab, paclitaxel and carboplatin combination on progression-free survival assessed by the investigator (modest absolute increase of + 1.5 months),
new overall survival data (median of +4.8 months in favour of the addition of atezolizumab; HR=0.80; 95 % CI [0.67; 0.95]) following additional follow-up around 20 months (i.e., a total of 40 months of median follow-up), which demonstrates maintenance of the increase already demonstrated,
and despite :
the methodological limitations of the IMpower150 study impacting the robustness of the results, in particular the open-label nature of the study, the main analyses conducted in a non-stratified subpopulation of the study,
safety data reporting more grade 3 or 4 adverse events (65 % versus 60 %), AEs having led to treatment discontinuation (41 % versus 26 %) and AEs resulting in death (6.6 % versus 5.6 %),
the absence of robust quality of life data,
TECENTRIQ (atezolizumab) in combination with bevacizumab, paclitaxel and carboplatin, provides a minor clinical added value (CAV IV) compared to the bevacizumab, paclitaxel and carboplatin combination in the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) without EGFR mutant or ALK-positive tumours.