HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
3 FEBRUARY 2021
The legally binding text is the original French opinion version

atezolizumab
TECENTRIQ 1200 mg concentrate for solution for infusion

New indication

Key points

Favourable opinion for reimbursement in combination with bevacizumab for the treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC), who have not received prior systemic therapy only in patients with preserved hepatic function (Child-Pugh A), an ECOG score of 0 or 1, andnot eligible for locoregional therapies or in the event of failure of one of these therapies.

Unfavourable opinion for reimbursement in other situations.

What therapeutic improvement?

Therapeutic improvement compared to sorafenib.

Role in the care pathway?

The treatment of hepatocellular carcinoma (HCC) depends on the disease stage and general health status of patients.

Patients in whom HCC was diagnosed at an early stage (BCLC stage A) are generally eligible for curative treatment via surgery, transplantation or radiofrequency ablation. In the event of non-eligibility, treatment by transcatheter arterial chemoembolisation (TACE) may be proposed.

In patients in whom the disease has progressed, or who are diagnosed at the multinodular stage (BCLB stage B) with an ECOG score of 0 and preserved hepatic function (Child-Pugh A), TACE is recommended. In the event of a contraindication to TACE, or following the failure of TACE, a systemic treatment is recommended. Selective internal radiation therapy may be considered, but only concerns certain patients selected following a specific opinion reached at a multidisciplinary team meeting.

In patients in whom the disease has progressed, or who are diagnosed at the portal invasion and/or extrahepatic extension stage (BCLC C), with an ECOG score of between 0 and 2 and preserved hepatic function (Child-Pugh A), systemic treatment is recommended as first-line therapy (sorafenib). It should be noted that the adverse effects frequently associated with sorafenib are hand-foot syndrome, diarrhoea, alopecia, decreased appetite, fever and rash.

In patients in whom the disease has progressed, or who are diagnosed at a very advanced staged with impaired hepatic function and an ECOG stage of 3 or 4, only supportive care or inclusion in a clinical trial are recommended.

Role of the medicinal product in the care pathway

Considering demonstration of a clinically relevant benefit compared to sorafenib in terms of overall survival in a highly selective patient population (Child-Pugh A, ECOG 0 or 1), the Transparency Committee deems that TECENTRIQ (atezolizumab), in combination with bevacizumab, is a first-line treatment in patients with advanced or unresectable hepatocellular carcinoma, who have not received prior systemic therapy, with preserved hepatic function (Child-Pugh A), an ECOG score of 0 or 1, and not eligible for locoregional therapies or in the event of failure of one of these therapies. Outside these situations, this combination has no role in the absence of clinical data.

The safety profile of atezolizumab is marked by a lower incidence of hand-foot syndrome, diarrhoea, alopecia, decreased appetite, fever and rash (known to be associated with sorafenib), and by a more frequent occurrence of infusion reactions and immunological hypo and hyperthyroidism.

Uncertainties with respect to the level of efficacy depending on the various aetiologies persist, particularly in the event of non-viral aetiology, encouraging the implementation of follow-up of patients treated with TECENTRIQ (atezolizumab).

The Committee wishes to draw the attention of prescribers to the need for specific vigilance with respect to the risk of GI bleeding (cirrhotic patients and combination with an anti-angiogenic: bevacizumab).

It also wishes to remind prescribers that all patients with active hepatitis B (HVB) must be given concomitant anti-HVB therapy throughout the duration of treatment.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Hepatocellular carcinoma is a serious, life-threatening disease in the short term.

◗ The proprietary medicinal product TECENTRIQ (atezolizumab), in combination with bevacizumab, is a curative medicinal product.

◗ Its efficacy/adverse effects ratio is high in patients who have not received prior systemic therapy, with preserved hepatic function (Child-Pugh A), an ECOG score of 0 or 1, and not eligible for locoregional therapies or in the event of failure of one of these therapies. The transposability of the results to the French population (different aetiology profile) cannot be confirmed, however.

◗ There is an alternative in patients with BCLC stage B HCC, with preserved hepatic function and an ECOG score of 0, who have not received prior systemic therapy: transcatheter arterial chemoembolisation (TACE); and in patients with a good prognosis with Child-Pugh A hepatic cirrhosis and not eligible for first-line surgical or locoregional therapies or in the event of failure of these therapies: sorafenib (NEVAXAR).

◗ TECENTRIQ (atezolizumab), in combination with bevacizumab, is a first-line treatment in patients with advanced or unresectable hepatocellular carcinoma, who have not received prior systemic therapy, with preserved hepatic function (Child-Pugh A), an ECOG score of 0 or 1, and not eligible for locoregional therapies or in the event of failure of one of these therapies. It has no role in the other situations in the absence of clinical data.

Public health impact

Considering:

- the seriousness of advanced or unresectable hepatocellular carcinoma,
- the partially met medical need,
- the partial response provided by TECENTRIQ (atezolizumab), in combination with bevacizumab, to the partially met medical need, due to demonstration of its superiority compared to sorafenib on overall survival,
- the lack of demonstrated impact on quality of life,
- the absence of data enabling assessment of the additional impact on the organisation of care,

TECENTRIQ (atezolizumab) in combination with bevacizumab, 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, is:

- **substantial in the treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC), who have not received prior systemic therapy only in patients with preserved hepatic function (Child-Pugh A), an ECOG score of 0 or 1, and not eligible for locoregional therapies or in the event of failure of one of these therapies;**
- **insufficient in other situations to justify public funding cover.**

The Committee issues a favourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the indication "treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC), who have not received prior systemic therapy, with preserved hepatic function (Child-Pugh A), an ECOG score of 0 or 1, and not eligible for locoregional therapies or in the event of failure of one of these therapies" and at the MA dosages.

The Committee issues an unfavourable opinion for inclusion in the hospital formulary list of reimbursed proprietary medicinal products approved for use in the other situations.

Clinical Added Value

Within the reimbursement scope:

Considering:

- **demonstration of the superiority of TECENTRIQ (atezolizumab), in combination with bevacizumab, compared to sorafenib, in terms of overall survival (HR=0.58 [CI95%: 0.42-0.79] following median follow-up of 8.6 months, and a non-estimable individual estimate of an absolute improvement (median not reached in the atezolizumab + bevacizumab group), in a phase 3, randomised, open-label study, and**
- **the similar safety profile to that of sorafenib (although each drug has its own specificities, see care pathway),**

and despite:

- **uncertainties with respect to the transposability of the results of the pivotal study to French patients (patients predominantly native to Asia, in whom the distribution of hepatocarcinoma aetiologies does not correspond to French epidemiological conditions),**
- **the lack of demonstrated impact on quality of life,**

the Committee considers that TECENTRIQ (atezolizumab), in combination with bevacizumab, provides moderate clinical added value (CAV III) compared to sorafenib in the treatment of adult patients with advanced or unresectable hepatocellular carcinoma, who have not received prior systemic therapy, with preserved hepatic function (Child-Pugh A), an ECOG score of 0 or 1, and not eligible for locoregional therapies or in the event of failure of one of these therapies.