HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
16 JUNE 2021

The legally binding text is the original French opinion version

trastuzumab deruxtecan
ENHERTU 100 mg powder for concentrate for solution for infusion

First assessment

Key points

Favourable opinion for reimbursement as monotherapy in the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens.

Maintenance of this opinion is conditional on the reevaluation of this medicinal product within a maximum period of 18 months from the date of this opinion based on the results of the phase 3 DESTINY-BREAST 02 study (results on PFS expected for March 2022 at the latest).

What therapeutic improvement?

No clinical added value in the therapeutic strategy on the basis of currently available data.

Role in the care pathway?

According to European (ESMO 2020) and French guidelines, the first-line treatment of metastatic HER2-positive breast cancer is based on the combination of two anti-HER2 agents: trastuzumab and pertuzumab combined with taxane-based chemotherapy (docetaxel or paclitaxel). As second-line therapy, KADCYLA (trastuzumab emtansine) is currently the option favoured by all the guidelines. Other options such as lapatinib/capecitabin and trastuzumab/lapatinib combinations are also considered to be alternatives at this stage of the disease.

Recently, the American NCCN 2021 guidelines included tucatinib (in combination with trastuzumab and capecitabin) as third-line treatment following the failure of tratuzumab/pertuzumab combined with a taxane then trastuzumab emtansine, with a level 1 grade of recommendations (high level of evidence), following the demonstration of its superiority in terms of progression-free survival and overall survival in a phase 2 study versus trastuzumab and capecitabin.

Role of ENHERTU (trastuzumab deruxtecan) in the care pathway:

ENHERTU (trastuzumab deruxtecan) is a third-line treatment option following the failure of trastuzumab/ pertuzumab combined with a taxane then trastuzumab emtansine. In the absence of any comparative data, its role compared to the available alternatives remains to be specified. It should be noted that the phase 2 non-comparative study having assessed the medicinal product only included patients in good general condition, with active brain metastases being of the exclusion criteria.

The Committee reiterates that in this same treatment line, there is an alternative with a better level of evidence, represented by tucatinib [TUKYSA] (MA obtained on 11/02/2021).

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Locally advanced or metastatic breast cancer is a serious, life-threatening disease.

◗ ENHERTU (trastuzumab deruxtecan) is a curative medicinal product.

◗ Its efficacy/adverse effects ratio is not adequately established based on current knowledge, due to:
- the weakness of the evidence of its short-term efficacy (phase 2 non-comparative study);
- the high toxicity.

◗ There are medicinal alternatives.

◗ It is a third-line treatment. In the absence of data, its role compared to the available alternatives remains to be specified.

Public health impact

Considering:
- the seriousness of the disease,
- the low incidence of metastatic HER2-positive breast cancer,
- the medical need partially met by the available alternatives following the failure of two anti-HER2 therapies,
- the lack of response to the identified need due to an impact on morbidity and mortality not demonstrated in view of preliminary, non-comparative data and the absence of quality of life data (see Section 07.5 Summary and discussion),
- the lack of additional impact on the care and/or life pathway,
- the absence of an impact on the organisation of care,

ENHERTU (trastuzumab deruxtecan) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that, on the basis of current knowledge, the clinical benefit of ENHERTU (trastuzumab deruxtecan) is moderate in the MA indication.

The Committee makes maintenance of the moderate clinical benefit conditional on the reevaluation of ENHERTU (trastuzumab deruxtecan) within a maximum period of 18 months from the date of this opinion based on the results of the phase 3 DESTINY-BREAST 02 study (results on PFS expected for March 2022 at the latest).

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 and dosages.

Clinical Added Value

Considering:

- **the not very robust quality of the research evidence for its efficacy in terms of tumour response derived from a non-comparative phase 2 study in a heterogeneous population (ranging from 2 to more than 5 previous treatment lines for the advanced stage),**
- **the absence of a quality of life assessment,**
- **the safety profile of trastuzumab deruxtecan marked, in particular, by the occurrence of serious adverse events (AEs) in more than a quarter of cases and of ≥ grade 3 AEs in more than two thirds of cases, and**
- **the existence of medicinal alternatives at this stage of the disease,**

the Committee considers that, on the basis of currently available data, ENHERTU (trastuzumab deruxtecan) provides no clinical added value (CAV V) in the treatment of patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens.