HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
2 JUNE 2021
The legally binding text is the original French opinion version

tucatinib
TUKYSA 50 mg, 150 mg film-coated tablets

First assessment

Key points

Favourable opinion for reimbursement in combination with trastuzumab and capecitabine, for the treatment of adult patients with HER2-positive locally advanced or metastatic breast cancer who have received at least 2 prior anti-HER2 treatment regimens.

What therapeutic improvement?

Therapeutic improvement compared to the trastuzumab plus capecitabine combination used alone.

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/capecitabine and trastuzumab/lapatinib combinations are also considered to be alternatives at this stage of the disease. Chemotherapy, particularly with capecitabine (XELODA and generics), is also recommended in combination with trastuzumab (HERCEPTIN and biosimilars) based on validated guidelines (ESMO, St Paul de Vence, regional standards, etc.) 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.

Role of the medicinal product in the care pathway

Considering demonstration of the superiority in terms of overall survival of the addition of TUKYSA (tucatinib) to trastuzumab and capecitabine compared to the trastuzumab plus capecitabine combination used alone, the combination of TUKYSA (tucatinib) with trastuzumab and capecitabine is the treatment option to be favoured over the trastuzumab plus capecitabine combination as third-line treatment in adult patients following the failure of trastuzumab/pertuzumab combined with a taxane then trastuzumab emtansine. The Committee highlights the fact that these results were obtained in a population including patients with brain metastases (around half of the patients in the study).

The choice of third-line treatment in adult patients with HER2-positive locally advanced or metastatic breast cancer should consider, in particular, the level of evidence of the demonstration in terms of efficacy as well as the safety profile of the treatments available. In particular, as regards TUKYSA (tucatinib) in combination with trastuzumab and capecitabine, this choice should take into account demonstration of an increase in overall survival compared to the trastuzumab plus capecitabine combination used alone, as well as its specific safety profile, marked by very frequent gastrointestinal disorders (diarrhoea) and hand-foot syndromes.

COMMITTEE'S CONCLUSIONS

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

Clinical benefit

◗ Metastatic breast cancer is a serious, life-threatening disease.

◗ The proprietary medicinal product TUKYSA (tucatinib) is a curative medicinal product.

◗ The efficacy/adverse effects ratio of TUKYSA (tucatinib) in combination with trastuzumab and capecitabine is high, in particular in view of the demonstration of a statistically significant difference in terms of overall survival in a randomised, placebo-controlled study, with an increase of +4.5 months in favour of tucatinib, in combination with trastuzumab and capecitabine, with a safety profile marked by diarrhoea and hand-foot syndrome, nevertheless considered to be acceptable by the Committee.

◗ There are therapeutic alternatives (see chapter 5 Clinically relevant comparators).

◗ Considering demonstration of the superiority in terms of overall survival of the addition of TUKYSA (tucatinib) to trastuzumab and capecitabine compared to the trastuzumab plus capecitabine combination used alone, the combination of TUKYSA (tucatinib) with trastuzumab and capecitabine is the treatment option to be favoured over the trastuzumab plus capecitabine combination as third-line treatment in adult patients following the failure of trastuzumab/pertuzumab combined with a taxane then trastuzumab emtansine (see chapter 8 Role of the care pathway).

Public health impact

Considering:

- the seriousness of the disease,
- the low incidence of HER2-positive breast cancer,
- the medical need partially met by the available alternatives following the failure of two anti-HER2 therapies,
- the additional response to the identified need given a demonstrated additional impact on morbidity and mortality (demonstration of a benefit in terms of overall survival with an increase of +4.5 months compared to placebo in combination with trastuzumab and capecitabine) but without robust data in terms of quality of life,
- the absence of an impact on the organisation of care, given that TUKYSA is administered in combination with two other medicinal products, already recommended and used in clinical practice in this situation, one of which by the intravenous or subcutaneous route,

TUKYSA (tucatinib) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of TUKYSA (tucatinib) is SUBSTANTIAL in the MA indication.

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the marketing authorisation indication and dosages.

◗ **Recommended reimbursement rate: 100%**

Clinical Added Value

Considering:

- **demonstration of the superiority of TUKYSA (tucatinib) in combination with trastuzumab and capecitabine compared to placebo in combination with trastuzumab and capecitabine:**
  - **in terms of progression-free survival (absolute increase in median of +2.2 months) and overall survival (absolute increase in median of +4.5 months; HR= 0.66; CI95% [0.50 - 0.88]),**
  - **in a randomised, double-blind study in patients with HER2-positive locally advanced or metastatic breast cancer, including patients with brain metastases (approximately 50% of the population), who have received at least 2 prior anti-HER2 treatment regimens,**

and despite:

- **the safety profile of tucatinib in combination with trastuzumab and capecitabine deemed to be acceptable but marked by diarrhoea and hand-foot syndrome having led to dosage adjustments or even treatment discontinuations, and**
- **the absence of robust data on quality of life,**

the Transparency Committee considers that TUKYSA (tucatinib), in combination with trastuzumab and capecitabine, provides a moderate clinical added value (CAV III) compared to the trastuzumab plus capecitabine combination used alone.