HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
11 DECEMBER 2019

talazoparib
TALZENNA 0.25 and 1 mg hard capsules

First assessment

Key points

Favourable opinion for reimbursement in HER2-negative locally advanced or metastatic breast cancer with germline BRCA1/2-mutations[1]

What therapeutic improvement?

No clinical added value compared to single-agent chemotherapy (capecitabine, vinorelbine, eribulin or gemcitabine).

Role in the care pathway?

The choice of systemic treatment in locally advanced or metastatic breast cancer is dependent on the histological characteristics of the tumour, predictive factors for response to treatments (hormone receptor and/or HER2 receptor expression), previously administered treatments and their tolerability, metastatic disease presentation, the time to relapse, the patient's general health status and comorbidities.
For patients with HER2-/RH- breast cancer, following treatment with anthracyclines and/or taxanes, there is no standard treatment in the advanced stage. Several single-agent chemotherapies are used

[1] For the precise indications, see page 3 or 4 of the opinion

sequentially: capecitabine or eribulin or vinorelbine. Gemcitabine, or retreatment with anthracyclines or taxanes and platinum-based therapies are other alternatives. Multi-agent chemotherapy is an alternative decided on a case-by-case basis.
For patients with HER2-/RH+ breast cancer, in case of of slow-progressing disease without any symptomatic and life-threatening organ involvement, the preferred treatment is endocrine-based therapy, potentially combined with a CDK4/6 inhibitor or a selective mTOR inhibitor. In the event of progression under various endocrine-based therapy lines or rapid progression of the disease (with, in particular, the development of organ metastases), chemotherapy becomes the standard treatment, with similar treatment to that in HER2-/RH- cancers.

Role of TALZENNA in the care pathway for HER2- advanced breast cancer
In patients having received (neo)adjuvant treatment with an anthracycline and/or a taxane for locally advanced or metastatic cancer, and whose cancer has germline BRCA1/2-mutations, monotherapy with oral TALZENNA (talazoparib) is a therapeutic alternative to the single-agent chemotherapies recommended in the first or later-line treatment of advanced HER2- breast cancer.
In the event of hormone receptor expression (RH+), given the absence of comparative data versus endocrine-based therapy combined with a CDK4/6 inhibitor, the role of TALZENNA is not determined compared to this treatment option that has recently been included in the care pathway. In accordance with the wording of the indication and the study inclusion criteria, the Committee considers that the role of TALZENNA comes after endocrine-based therapy, particularly in combination with a CDK 4/6 inhibitor, which can lead to use at a later treatment line.

No data is available to establish the optimal treatment sequence with single-agent chemotherapies used sequentially.

Given the concomitant development with LYNPARZA (olaparib) in this indication, the role of TALZENNA (talazoparib) compared to this other PARP inhibitor is not known. The choice between TALZENNA (talazoparib) and LYNPARZA (olaparib) should be made on a case-by-case basis taking into account the safety profile of each of these treatments.

In addition, in the absence of comparative data, the role of TALZENNA compared to platinum-based therapies is not known.

COMMITTEE'S CONCLUSIONS

Clinical Benefit

◗ Locally advanced or metastatic breast cancer is a serious, life-threatening disease.
◗ It is a specific curative treatment for advanced breast cancer.
◗ The efficacy/adverse effects ratio is high.
◗ Following (neo)adjuvant treatment with an anthracycline and/or a taxane for locally advanced or metastatic cancer and with an endocrine-based therapy in the event of hormone receptor expression (RH+), depending on eligibility, there are therapeutic alternatives.
◗ It is a first or later-line treatment for advanced HER2- cancer with germline BRCA1/2-mutations when single-agent chemotherapy is envisaged (see section 08 of the opinion - Role in the care pathway).

Public health impact:
Considering:
- the seriousness of locally advanced or metastatic HER2- cancer with germline BRCA1/2-mutations and its low prevalence,
- the partially met medical need,
- the absence of response to the identified medical need (due to a modest improvement in progression-free survival compared to single-agent chemotherapy, the absence of improvement in overall survival to date, the absence of demonstrative data on quality of life and the safety profile),
- the transposability that is not completely guaranteed given the profile of the patients included in the pivotal study and their previous treatments:
  - in contrast with the wording in the MA indication, according to the inclusion criteria of the pivotal study, patients were not required to have been treated with a prior endocrine-based therapy, if eligible, in the event of RH+ cancer;
  - the inclusion of new treatment regimens in the care pathway, such as combination of a CDK4/6 inhibitor with endocrine-based therapy in the event of RH+ cancer,
- the non-documented impact on the organisation of care.

TALZENNA is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of TALZENNA 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(s) and dosages.

◗ **Recommended reimbursement rate: 100%**

Clinical Added Value

Considering:
- **a demonstrated improvement in terms of median progression-free survival (primary endpoint) with talazoparib versus single-agent chemotherapy chosen by the investigator but the modest clinical relevance of 3 months (8.6 months versus 5.6 months, HR = 0.54 $CI_{95\%}$ [0.41; 0.71]; p <0.0001),**
- **the absence of any demonstrated improvement in overall survival following the interim analysis,**
- **the absence of any data on quality-of-life with a demonstrative value,**
- **the safety profile with, in particular, grade 3/4 adverse events occurring in 67.5% of patients in the talazoparib group (versus 63.5% in the chemotherapy group),**

the Transparency Committee considers that TALZENNA (talazoparib) provides no clinical added value (CAV V) compared to single-agent chemotherapy (capecitabine, vinorelbine, eribulin or gemcitabine).