OPINION ON MEDICINAL PRODUCTS

ribociclib
KISQALI 200 mg,
film-coated tablet
Reassessment

Adopted by the Transparency Committee on 4 January 2023

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement of KISQALI (ribociclib) in association with letrozole for the treatment of locally advanced or metastatic HR+/HER2- breast cancer, as initial hormone therapy-based treatment or after previous hormone therapy treatment with an interval of more than 12 months in menopausal women, in the absence of life-threatening visceral involvement in the short term.

Therapeutic improvement?

Therapeutic improvement with respect to letrozole alone.

Role in therapeutic strategy?

While at the localised stage, the objective of treatment is curative, at the locally advanced or metastatic stage and despite the treatments available, HR+/HER2- breast cancer is still a practically incurable, systematically life-threatening disease, impacting patients' quality of life.**Erreur ! Signet non défini.**

At the advanced stage (locally advanced or metastatic), the objective of treatment must be to prolong overall survival while maintaining or improving quality of life.

In the absence of life-threatening symptomatic visceral metastases in the short term, the therapeutic strategy is based on hormone therapy.

According to the most recent European Society for Medical Oncology[Erreur ! Signet non défini.] (ESMO) and the National Comprehensive Cancer Network[Erreur ! Signet non défini.] (NCCN) guidelines from 2021, the addition of a CDK4/6 inhibitor (IBRANCE (palbociclib), KISQALI (ribociclib) or VERZENIOS (abemaciclib)) to an aromatase inhibitor is recommended as a first-line approach for women initially diagnosed at an advanced stage or experiencing late or early recurrence in respect of adjuvant hormone therapy. Association with fulvestrant is also a first-line therapeutic option for women initially diagnosed at an advanced stage or experiencing late or early recurrence in respect of adjuvant hormone therapy (NCCN). ESMO specifies that this alternative should only be preferred if an interval of less than 12 months has elapsed since the last anti-aromatase dose was taken.

Moreover, the NCCN states that non-steroidal aromatase inhibitors alone (anastrozole or letrozole) remain first-line alternatives at the advanced stage (for women initially diagnosed at an advanced stage or experiencing late recurrence in respect of adjuvant hormone therapy) unless they were previously administered in the context of an adjuvant treatment discontinued less than 12 months previously (early recurrence) and concomitant non-steroidal aromatase inhibitor treatment with fulvestrant is also a therapeutic option.

The latest guidelines of the Ile-de-France breast care network[Erreur ! Signet non défini.] and the American Society of Clinical Oncology[Erreur ! Signet non défini.] (ASCO) are strictly comparable to those of the ESMO mentioned above.

However, the ASCO specifies that CDK 4-6 inhibitor treatment must be limited to patients who have never been exposed to this therapeutic class in a metastatic context.

Role of the medicinal product:

KISQALI (ribociclib) is a first-line treatment for locally advanced or metastatic HR+ and HER2- breast cancer, in the absence of life-threatening symptomatic visceral involvement in the short term, following an initial diagnosis at this stage or in the event of late recurrence after more than 12 months.

Committee's conclusions

Actual Clinical Benefit

- Locally advanced or metastatic HR+/HER2- breast cancer is a serious life-threatening disease.
- This product is a specific curative cancer treatment.
- For menopausal women, the efficacy/adverse effect ratio of the ribociclib association is significant in association with letrozole in the absence of life-threatening symptomatic visceral involvement in the short term, following an initial diagnosis at this stage or in the event of late recurrence after more than 12 months.
- Therapeutic alternatives are available.
- For menopausal women and in the absence of life-threatening symptomatic visceral involvement in the short term, associating ribociclib with letrozole is a first-line treatment option at the advanced stage (in cases of initial diagnosis or for late progressions after 12 months).

- **Public health benefit:**

Considering:

- the severity of locally advanced or metastatic HR+/HER2- breast cancer and its incidence at the advanced stage;
- the partially met medical need;
- the additional response provided by KISQALI (ribociclib), in association with letrozole, to the identified medical need with an impact on mortality;
- the lack of data enabling formal conclusions to be drawn in terms of quality of life;
- the lack of additional impact on delivery of care;
- the additional impact on the care and/or life pathway has not been studied.

KISQALI (ribociclib) is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the actual clinical benefit of KISQALI (ribociclib) remains significant in association with letrozole.

The Committee approves continued inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary products approved for community use in association.

Clinical Added Value

Considering:

- the evidence of superiority of ribociclib on the ranked secondary outcome measure which is overall survival with a median gain of 12.5 months (HR=0.765 ($CI_{95\%}$: [0.628; 0.932], p=0.004) in a cohort of menopausal female patients with no life-threatening symptomatic visceral involvement in the short term at the advanced stage (34% *de novo* and 66% experiencing late recurrence after more than 12 months);

and despite:

- a known safety profile particularly marked by haematotoxicity and a risk of QT interval prolongation;
- increased toxicity with the addition of ribociclib, particularly marked by grade 3 and 4 adverse events (71.6% versus 39.1% and 17.4% versus 3.3%);
- the lack of robust quality-of-life data;
- a substantial number of subjects lost to follow-up, but balanced between the two groups during the first 24 months,

the Committee deems that KISQALI (ribociclib) in association with letrozole provides moderate clinical added value (CAV III) versus letrozole alone for the treatment of locally advanced or metastatic HR+/HER2- breast cancer, as initial hormone therapy-based treatment or after previous hormone therapy treatment with an interval of more than 12 months in menopausal women, in the absence of life-threatening visceral involvement in the short term.