NOVARTIS

KISQALI - Mechanism of action - HCP

Prescribing information

Image

Image

KISQALI® (ribociclib) mechanism of action

Indications:[1]

- KISQALI is indicated for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have received prior endocrine therapy

- In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist

KISQALI is not recommended to be used in combination with tamoxifen.

To learn more about the safety profile of KISQALI, visit our portal page here.

For full safety profile information, please refer to the KISQALI Summary of Product Characteristics.

Image

KISQALI selectively inhibits cyclin-dependent kinases 4 and 6 (CDK4/6) in eligible patients with HR+/HER2– aBC, thus potentially inhibiting tumour growth[1]

Information on this page is based on pre-clinical research. They should not be extrapolated to clinical response.

The role of CDK4/6 in HR+/HER2– aBC

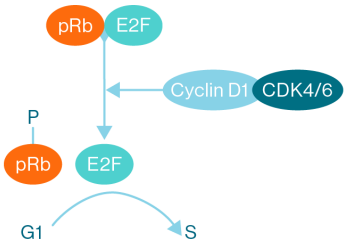
Image

CDK4 and CDK6 control of the cell division cycle

CDK4/6s are cell cycle checkpoint regulators that play a crucial role in the signalling pathways which lead to cellular proliferation.[1,2]

Once bound to D-cyclins, CDK4/6s are activated. The cyclin D-CDK4/6 complex can then regulate cell cycle progression (from phase G1 to S) via phosphorylation of the retinoblastoma protein (pRb).[2]

Regulation of the G1/S phase transition by cyclin D1 and CDK4/6:[3]



Adapted from Peurala E, et al. 2013.[3]

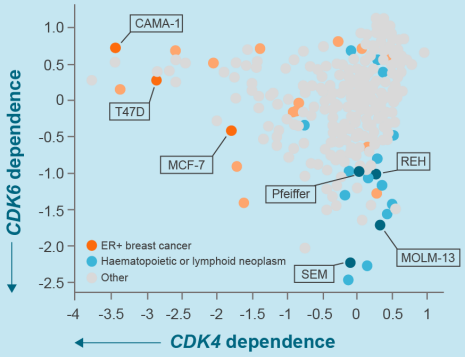
Patients with HR+/HER2– aBC have dysregulated levels of CDK4/6, leading to increased ER pathway activation, promoting cancer cell growth.[2,4]

Image

ER+ breast cancer cell dependency on CDK4/6

ER+ breast cancer cells are CDK4-dependent and show overexpression when compared to CDK6.[4]

Identification of cancer cell lines in which either CDK4 or CDK6 is dominant



Adapted from Kim S, et al. 2018 (and supplementary data).[4]

Image

References:

1. KISQALI® (ribociclib) Summary of Product Characteristics.
2. Pavlovic D, et al. *Ther Adv Med Oncol* 2023;15:17588359231205848.
3. Peurala E, et al. *Breast Cancer Res* 2013;15:R5
4. Kim S, et al. *Oncotarget* 2018;9(81):35226–35240 and supplementary data.

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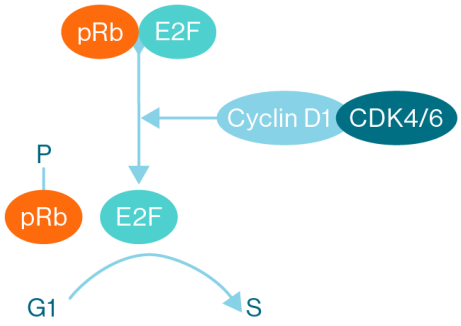

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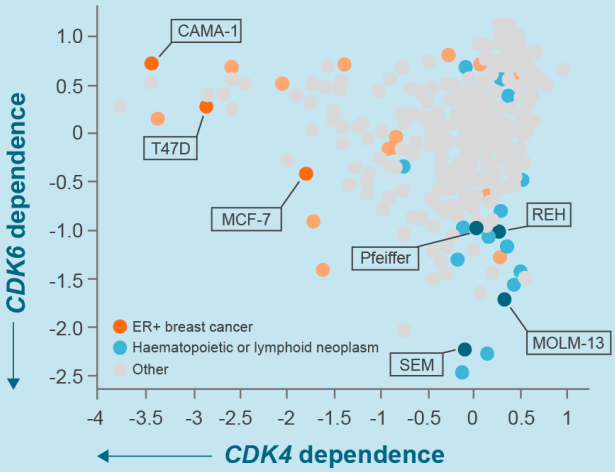

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Please use the arrows to navigate through the slideshow.

Mechanism of action of KISQALI

KISQALI is a selective inhibitor of CDK4 and CDK6[1,2]

KISQALI works by binding to the cyclin-CDK4/6 complex to inhibit the function of CDK4 and arrest the cell cycle, reducing the proliferation of cancer cells.[1,2]

Image

Adapted from Sammons SL, et al. 2017.[3]

In biochemical assays, KISQALI results in 50% inhibition (IC_{50}) values of 0.01 (4.3 ng/ml) and 0.039 µM (16.9 ng/ml) for CDK4 and CDK6, respectively.[1]

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aBC, advanced breast cancer; CDK4, cyclin-dependent kinase 4; CDK6, cyclin-dependent kinase 6; E2F, E2 transcription factor; ER, oestrogen receptor; HER2−, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; IC_{50}, half-maximal inhibitory concentration; pRb, retinoblastoma protein.

References

1. KISQALI® (ribociclib) Summary of Product Characteristics.

2. Kim S, et al. *Oncotarget* 2018;9(81):35226–35240 and supplementary data.

3. Sammons SL, et al. *Curr Cancer Drug Targets* 2017;17(7):637–649.

UK | March 2025 | 442145

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