From publication to practice: How trial data translate to clinical use of CDK4/6 inhibitors in patients with HR+/HER2- advanced breast cancer

CDK, cyclin-dependent kinase; HR, hormone receptor; HER2, human epidermal growth factor receptor 2.

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What is the optimal approach to managing a patient on a CDK4/6 inhibitor?

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CDK, cyclin-dependent kinase.

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Quality of life: 4th ESO-ESMO guidelines for advanced breast cancer[1]

Strong consideration should be given to the use of **validated PROMs** for patients to record the symptoms of disease and side effects of treatment experienced as a regular part of clinical care[1]

Health professionals should be ready to **change and adapt treatment strategies** to disease status, treatment adverse effects and QoL, patients' priorities and life plans[1]

ESO, European School of Oncology; ESMO, European Society for Medical Oncology; PROM, patient-reported outcome; QoL, quality of life.

1. Cardoso F, et al. *Annals Oncol.* 2018;29:1634–57.

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Factors influencing QoL in patients prescribed a CDK4/6 inhibitor for ABC

Comorbidity considerations[1]

Previous treatment experience[2]

Managing AEs associated with CDK4/6 inhibitors[3]

ABC, advanced breast cancer; AE, adverse event; CDK, cyclin-dependent kinase; QoL, quality of life.

1. Battisti NML, et al. *Ther Adv Med Oncol.* 2018;10:1–26. 2. Brito C, et al. *BMC Cancer.* 2014;14:397. 3. Thill M, et al. *Ther Adv Med Oncol*. 2018;10:1–12.

PRO with CDK4/6 inhibitors in HR+/HER2- ABC

No difference in QoL between CDK4/6 inhibitor + endocrine therapy vs endocrine therapy alone in Phase III trials[1-3]

MONALEESA-3 trial

At the end of treatment in MONALEESA-3, the addition of ribociclib to fulvestrant **did not negatively impact QOL*** (mean change from baseline was -5.2 points with ribociclib vs -5.5 with placebo)[1]

PALOMA-3 trial

PRO† significantly improved for palbociclib + fulvestrant vs placebo + fulvestrant (66.1 vs 63.0; p=0.0313[2]

No significant differences were observed for other QLQ-BR23 functioning domains, breast or arm symptoms[2]

MONARCH-2 trial

Abemaciclib + fulvestrant **did not show statistically significant and clinically meaningful differences** in patient-reported global health, functioning or most symptoms‡ compared to placebo + fulvestrant[3]

Possible improvement in QOL for ribociclib vs placebo[4]

MONALEESA-7 trial

In MONALEESA-7, **median time to deterioration of QOL* was not reached** in the ribociclib arm vs 21.2 months in the placebo arm (hazard ratio 0.70; p=0.004)[4]

Providing first-line therapy that extends duration of response to treatment while maintaining QOL is critical for these patients[5]

*Global health status/quality of life scale score from EORTC QLQ-C30 questionnaire. †EORTC QLQ-C30 and QLQ-BR23. ‡Modified brief pain inventory short form, EORTC QLQ-C30 and QLQ-BR23.
ABC, advanced breast cancer; CDK, cyclin-dependent kinase; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; QLQ-BR23, Breast Cancer-Specific Quality of Life Questionnaire; QoL, quality of life; PRO, patient-reported outcomes.

1. Fasching PA, et al. *Ann Oncol.* 2018;29(Suppl.8):viii90–121.. 2. Harbeck N, et al. *Ann Oncol*. 2016;27:1047–54. 3. Kaufman PA, et al. *J Clin Oncol*. 2016;36 (Suppl):1049.
4. Tripathy D, et al. *Lancet Oncol.* 2018;19:904–15. 5. Mahtani RL, Vogel CL. *Cancer Manag Res*. 2019;11:513–24.

Persistence with treatment in stable ABC

AEs can result in a relevant number of treatment terminations that are not related to progression[1]

Monotherapy

AEs may still cause an issue with persistence for patients receiving monotherapy[1]

Combination therapy

It can be assumed persistence will be lower than with monotherapy, but real-world data is needed to capture this figure[1]

Prior non-compliance

Past non-compliance to any medication is a predictor for lower persistence with future treatment[1]

Good communication

Lack of physician–patient communication can be a contributing factor in treatment discontinuation due to AEs[2]

ABC, advanced breast cancer; AE, adverse event.

1. Wallwiener M, et al. *BMC Cancer*. 2019;19:611. 2. Wuensch P, et al. *J Cancer Res Clin Oncol.* 2015;141:55–60.

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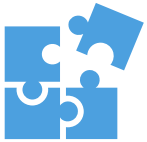
Optimizing treatment in patients with ABC prescribed a CDK4/6 inhibitor

Information and reassurance that AEs can be easily managed[1]



Integrated care plan that is personalized and optimizes health and QoL, while addressing clinical needs[2]

Clinical intervention to address AEs systematically and at an early stage[2]

Avoid unnecessary hospital visits and provide good outpatient care

ABC, advanced breast cancer; AE, adverse event; CDK, cyclin-dependent kinase; QoL, quality of life.
1. van Vilet LM, et al. *Front Psychiatry*. 2019;10:464. 2. Cardoso F, et al. *Annals Oncol.* 2018;29:1634–57.