High-Risk, HR+, HER2- Early Breast Cancer:
Dose Modification Strategies to Manage AEs

CDK4/6i for High-Risk, HR+, HER2- EBC and Dose Modifications

Two CDK4/6i are currently approved by regulatory authorities (e.g. FDA and European Commission) for treating select patients with HR+, HER2- EBC who are at high risk of disease recurrence.[1-3]

To maximize therapeutic benefits and optimize clinical outcomes, patients should continue treatment for the full prescribed duration; this may require dose modifications to manage adverse events (AEs)[4,5]

In clinical trials investigating adjuvant CDK4/6i + endocrine therapy (ET) for patients with high-risk, HR+, HER2-, EBC, dose adjustments were common[6-9]:

62-73% of patients had dose interruptions

23-44% of patients had a dose reduction

19-20% of patients discontinued treatment

Monitoring and Managing AEs to Help Patients Stay on Treatment

Patients may experience **symptomatic** and/or **asymptomatic** AEs, which can result in premature discontinuation of therapy if not properly managed[5,6,10]

Symptomatic AEs
Felt and Reported by Patients[1,2]

- Diarrhea
- Fatigue
- Arthralgia
- Headache
- ILD/Pneumonitis
- Nausea
- Infection

Asymptomatic AEs
Detected by Routine Monitoring[1,2]

- Hepatotoxicity
- Cardiac arrythmia
- Neutropenia
- Anemia

Regular monitoring and timely dose adjustments are essential for managing AEs, maintaining patients on therapy, and optimizing clinical outcomes[6,8,11]

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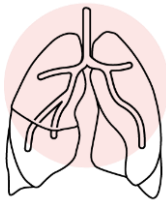
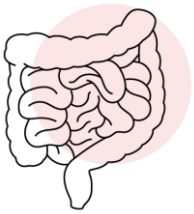
AE Management With Dose Modifications

While Grade 1 AEs do not typically require dose modifications, common Grade ≥2 CDK4/6i-associated AEs are generally manageable through dose-interruption and/or dose-reduction strategies[1,2,10]

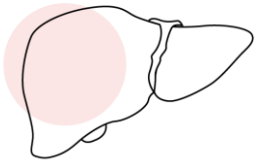
AEs associated with CDK4/6i include:



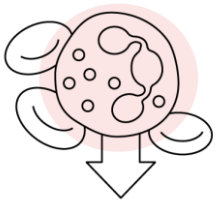
ILD/Pneumonitis



Diarrhea



Hepatotoxicity



Neutropenia

QT Prolongation

Consult appropriate drug labels and SmPC for AEs that may be CDK4/6i-specific; these can include severe cutaneous AEs, QT prolongation, and/or venous thromboembolic events and follow label guidance, which may include dose interruption, dose reduction, and/or discontinuation[1,2]

Dose reductions are an effective way to manage AEs and were **not associated with reduced efficacy** in analyzed studies of adjuvant CDK4/6is[8,10,11,12]

Implementing dose reductions **early and when needed** in a patient's treatment journey can effectively manage AEs and reduce the likelihood of treatment discontinuation[7]

Educating and increasing **patient awareness** of AE symptoms and expectations may inform dose modification strategies according to drug labels, improving patient experiences and treatment adherence[8]

Early monitoring and, if needed, dose modifications of adjuvant CDK4/6is are critical to manage the AEs of patients with high-risk, HR+, HER2- EBC to support their ability to stay on treatment and optimize clinical outcomes[8,11,12]

References: **1.** Abemaciclib [EU SmPC]. Amsterdam, The Netherlands: European Medicines Agency; Eli Lilly Nederland B.V. Last updated January 2026 **2.** Ribociclib [EU SmPC]. Amsterdam, The Netherlands: European Medicines Agency; Novartis Europharm Limited. Last updated January 2026 **3.** Freedman RA, et al. *J Clin Oncol.* 2024;42(18):2233-2235. **4.** Lau C, et al. *Breast Cancer Res Treat.* 2025. doi:10.1007/s10549-025-07701-x. **5.** Nabieva N and Fasching PA. *Cancers (Basel).* 2023;15(6):1763. **6.** Rugo HS, et al. *Ann Oncol.* 2022;33(6):616-627. **7.** Hortobagyi GN, et al. *Ann Oncol.* 2025;36(2):149-157. **8.** Goetz MP, et al. *NPJ Breast Cancer.* 2024;10(1):34. **9.** Fasching PA, et al. Oral presentation at: *ESMO 2024*. Abstract LBA13. **10.** Cazzaniga ME, et al. *Breast Cancer Res Treat.* 2019;176(3):483-494. **11.** Hamilton E, et al. Poster presentation at: *SABCS 2024*. Abstract P1-11-16. **12**. Hudson K, et al. Oral presentation at: SABCS 2024. Abstract P1-11-29.

Abbreviations: AE= adverse event; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; EBC=early breast cancer; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; HR=hormone receptor; ILD=interstitial lung disease; SmPC= Summary of Product Characteristics

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