Incidence of Neutropenia Adverse Events Identified in Electronic Health Care Records Among Initiators of CDK4/6 Inhibitors With Advanced Breast Cancer in the UK

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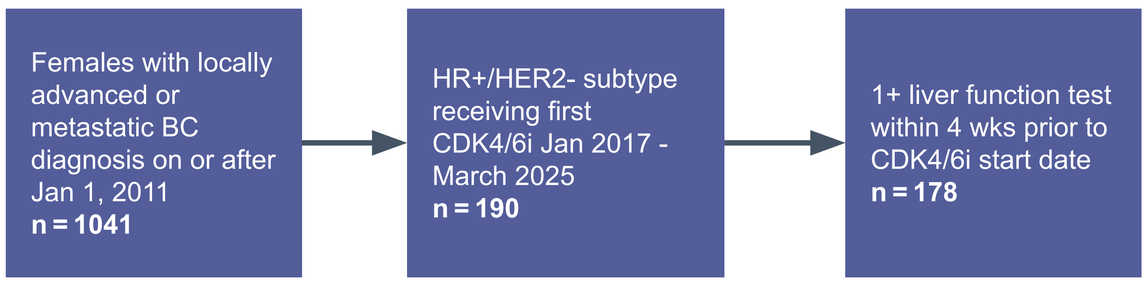
Background

- Establishment of robust safety surveillance capabilities requires that the underlying electronic health record (EHR) data be relevant and reliable. Lab-based adverse events (AEs), such as neutropenia identified from structured EHR data, may indicate an EHR system's ability to capture lab-based AEs more broadly
- The purpose of this study was to assess rates of neutropenia AEs derived from structured EHR lab data among CDK4/6 inhibitor (CDK4/6i)-treated women with advanced breast cancer (aBC) in the UK

Methods

- **Study design and data source:** Retrospective cohort study leveraging EHR data from the UK Flatiron Health Research Database
- **Study population:** The real-world cohort consisted of women who initiated CDK4/6is (palbociclib, ribociclib, abemaciclib) for locally advanced or metastatic HR+/HER2- breast cancer (BC) from January 1, 2017, through March 31, 2025
- **Study outcomes:** Patients were required to have a full blood count in the 4 weeks before treatment initiation. Neutropenia was defined based on absolute neutrophil count of <1500 cells/μL. AE grade for neutropenia (cells/μL) was categorised as follows: Grade 2, 1500-1000; Grade 3, <1000-500; Grade 4, <500. Presence of ICD-10 codes for neutropenia were also identified in the EHR.
- **Statistical analysis:** Cumulative incidence of neutropenia AEs was calculated, and supporting evidence of the AE, including ICD-10 coding and dose changes, were identified

Figure 1: Analytic Cohort of CDK4/6i Initiators Among Women with aBC in the UK Flatiron Health Research Database



Results

- After applying study population criteria, **178 women** with aBC who initiated one of the three CDK4/6is were included (**Table 1**).
- Median age at treatment was 57 years. Patients were predominantly White (>90%), and 87% were ECOG 0-1. Most women initiated palbociclib (60%) (**Table 1**).
- Over 30 and 90 days, 111 (63%) and 123 women (70%), respectively, experienced a neutropenia AE (**Table 2**).
- The 30-day cumulative incidence (95% CI) of Grade 2 and Grade 3+ neutropenia AEs was 48% (40%-55%) and 37% (29%-43%), respectively. The 90-day cumulative incidence increased to 66% (58%-72%) and 40% (32%-46%) for Grade 2 and Grade 3+ AEs, respectively (**Figure 2**).
- Among patients with a Grade 3 AE, 38% had evidence of a CDK4/6i dose reduction in the 30 days following the AE.
- About 61% of patients had neutropenia AEs based on the lab test results but no ICD code for neutropenia AE recorded in the database; only 3% had ICD code recorded but no lab-based neutropenia AE (**Table 3)**

Table 1. Demographic and Clinical Characteristics of CDK4/6i Initiators with Advanced BC in the UK, January 2017-March 2025

Characteristics	CDK4/6i initiators (N = 178)
Age, median (IQR), y	57 (48-67)
Race/ethnicity, n (%)	
White	118 (91)
Non-white	12 (9)
Unknown	48
ECOG, n (%)	
0	75 (43)
1	80 (46)
2+	18 (10)
Unknown	5
CDK4/6i drug received on start date, n (%)	
Abemaciclib	14 (8)
Palbociclib	107 (60)
Ribociclib	57 (32)

ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range

Table 2. Incidence of Neutropenia AEs Within 30 and 90 Days of Treatment Initiation Among CDK4/6i Initiators (n = 178) With aBC in the UK

	30 days		90 days	
	N	Incidence % (95% CI)	N	Incidence % (95% CI)
Any neutropenia AE	111	63 (55-69)	123	70 (62-76)
Grade 2 AE[a]	85	48 (40-55)	116	66 (58-72)
Grade 3+ AE[a,b]	65	37 (29-43)	70	40 (32-46)

[a] AEs by grade are not mutually exclusive as a patient may have had multiple AEs of varying grades during the at-risk period. [b] Grade 3+ includes Grade 3 and Grade 4

Figure 2. Time From CDK4/6i Initiation to First Neutropenia AE, by AE Grade Among Women With aBC in the UK

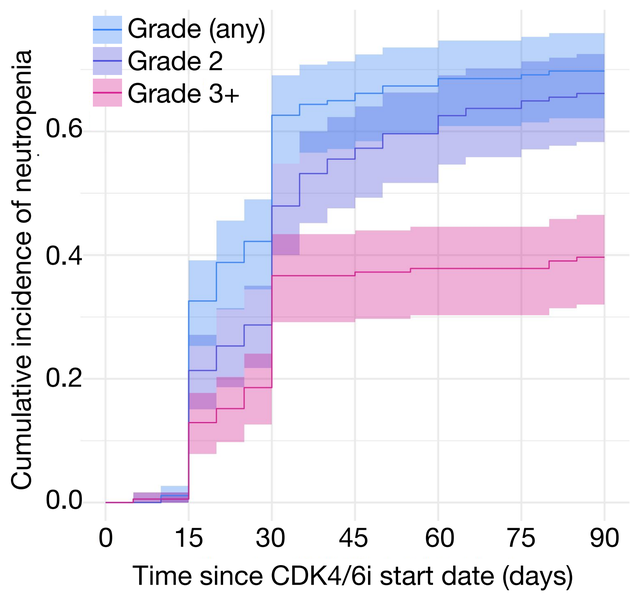


Table 3. Comparison of Lab Test-Identified Neutropenia AE vs Presence of ICD Code-Identified[a,b] AEs in CDK4/6i Initiators With aBC in the UK

	Lab result: Yes	Lab result: No
ICD code: Yes	6%	3%
ICD code: No	61%	30%

[a] ICD-10 codes for neutropenia: D70.X
[b] ICD-10 codes were identified within 30 days of the lab test result indicating neutropenia

- Cumulative incidence of neutropenia AEs among CDK4/6i initiators with aBC in the UK aligns with previously reported rates.[1-4]
- **Lab-based AE** identification from structured EHR data **is robust and has higher sensitivity** than ICD code-based analysis.

Conclusions and Future Directions

- Use of structured lab result data in the EHR can effectively identify neutropenia AEs within expected ranges in patients with aBC treated with CKD4/6is.
- Safety surveillance of lab-based AEs requires rich lab result and dosing data to ensure valid estimation of AE rates and capture of AE management among initiators of oncologic therapies.
- Future analyses will include lab-based AE assessments across other ex-US geographies as well as development and validation of large language models for AE capture in EHRs.

References
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