Early AB-ITALY: Evaluating Real-World Use of Adjuvant Abemaciclib and Drug Interaction Risk in HR+/HER2- early Breast Cancer

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INTRODUCTION

Abemaciclib is a selective CDK4/6 inhibitor approved for adjuvant treatment in patients with high-risk hormone receptor-positive, HER2-negative (HR+/HER2-) early breast cancer (eBC). The MONARCH-E trial demonstrated significant increase in invasive disease-free survival (iDFS) when combined abemaciclib with endocrine therapy. Nonetheless, real-world data regarding safety, treatment adherence, and drug-drug interactions (DDIs),particularly among elderly and comorbid populations often excluded from clinical trials, remain limited. Evaluating these real-world factors is critical to optimizing treatment and patient outcomes in clinical practice.

PATIENTS AND METHODS

This retrospective study analyzed consecutive patients with HR+/HER2- eBC treated at 21 Italian oncology centers who received adjuvant abemaciclib combined with an aromatase inhibitor (AI). Comprehensive clinical data, medication usage, and adverse events (AEs) were collected. Drug-PIN®, a platform integrating clinical (age, sex, race, smoking and alcohol habits),laboratory (renal and hepatic function), and pharmacological parameters (chronic concomitant treatments), was utilized to assess DDIs, providing a numeric interaction score (Drug-PIN score) and qualitative risk tiers (green: none; yellow/dark yellow: intermediate; red: high risk). Statistical analyses, including univariate and multivariate approaches, identified predictors of AEs.

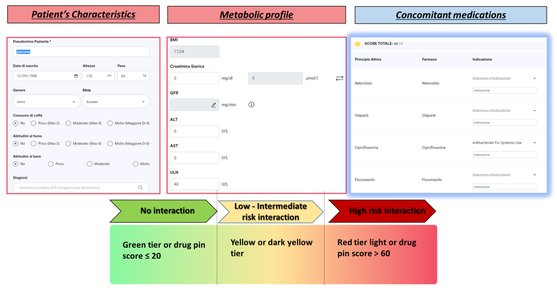


Fig.1.Drug-PIN platform

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RESULTS

We enrolled 714 patients with a median age of 56 years (range 30-86); 44% were premenopausal, and 51% had at least one comorbidity, while 13% had multiple comorbidities. Notably, 60 patients (8.4%) were aged ≥75 years. Genetic testing performed in 350 patients identified 29 mutated. Disease characteristics included node-positive (c/pN2) status in 389 (54%), carcinoma of no special type in 73%, lobular carcinoma in 14%, and high-grade tumors (G3) in 57%. Chemotherapy was omitted in 10% of cases. Oncotype DX testing was conducted in 42 patients (6%), with a mean recurrence score (RS) of 26 (range 8-50); 20 had an RS ≤25. With a median follow-up of 13.2 months (range1-33), 85% of patients experienced any-grade AEs, primarily diarrhea (76%), asthenia (41%), and neutropenia (27%). Grade ≥3 AEs occurred in 30%, with severe diarrhea reported in 11%, mostly during the first two cycles.

Characteristic	Value
Total patients	714
Median age, years (range)	56 (30–86)
Age ≥75 years	60 patients (8.4%)
Premenopausal	44%
≥1 comorbidity	51%
>2 comorbidities	13%
Genetic testing performed	350 patients
Germline mutation positive	29 patients
c/pN2 status	389 patients (54%)
Carcinoma of no special type (CDI)	73%
Lobular carcinoma (CLI)	14%
High-grade tumors (G3)	57%
No chemotherapy administered	10%
Oncotype DX performed	42 patients (6%)
Mean Recurrence Score (range)	26 (8–50)
Recurrence Score ≤25	20 patients

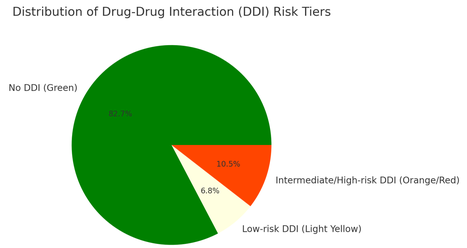
Table 1. Baseline Characteristics of the Study Population (N = 714)

RESULTS (continued)

Dose reductions were required in 47% and discontinuation due to toxicity occurred in 9.5%. Patients aged ≥75 showed comparable diarrhea rates (p=0.20) but a trend toward increased dose reductions (p=0.09). Concomitant medications were reported in 50% of patients, and 8% had polypharmacy. The median Drug-PIN interaction score was 12.0 (range 3-100), with at least one DDI identified in 17.3% of the patients, with 10.5% categorized in the intermediate-high or high-risk tiers. Notably, high-risk DDIs occurred more frequently among patients who discontinued treatment due to toxicity (25% vs 10%, p=0.04).

Adverse Event / Outcome	Value
Any-grade adverse events	85%
Diarrhea	76%
Asthenia	41%
Neutropenia	27%
Grade ≥3 adverse events	30%
Grade ≥3 diarrhea	11% (mostly in first 2 cycles)
Dose reduction	47%
Treatment discontinuation due to AEs	9.5%
Dose reduction in patients ≥75 y	trend toward higher (p = 0.09)
Discontinuation in patients ≥75 y	not reported as significant
Diarrhea rate in patients ≥75 y	similar (p = 0.20)

Table 2. Adverse events (AEs)



CONCLUSIONS

In this large, multicenter real-world cohort, adjuvant abemaciclib demonstrated a favorable and manageable safety profile, consistent with—though slightly higher than—rates reported in MONARCH-E, as expected in a less selected population. The treatment remained feasible even in older patients and those with multiple comorbidities, supporting its applicability across a broad spectrum of clinical scenarios routinely encountered in practice.The early onset of gastrointestinal AEs, particularly diarrhea, mirrors the kinetic pattern described in clinical trials and was effectively managed through supportive measures and dose adjustments. Notably, nearly half of patients required dose reduction, yet treatment discontinuation remained limited, underscoring the drug's overall tolerability.The Drug-PIN–based DDI assessment showed that most patients had no clinically relevant interactions, reflecting the intrinsically favorable pharmacokinetic profile of abemaciclib. However, the presence of intermediate-to-high–risk DDIs was associated with an increased likelihood of dose modification, suggesting that systematic DDI evaluation may help anticipate toxicity and optimize therapy.Together, these findings reinforce the robustness of abemaciclib's safety in the adjuvant setting and highlight the value of real-world evidence in complementing clinical trial data. Prospective studies integrating pharmacological interaction profiling may further refine patient selection and support personalized management strategies to maximize treatment adherence and outcomes.

Parameter	Value
Median Drug-PIN score (range)	12.0 (3–100)
Patients with ≥1 DDI	17.3%
Patients in intermediate-high/high-risk tier	10.5%
Drug-PIN score ≥6.5 associated with AEs	Any-grade and G≥3/4 AEs (AUC 0.629, p=0.001)
High-risk DDIs in patients who discontinued due to AEs	25% vs 10%, p=0.04

Table 3. Drug interactions and Drug-PIN score impact

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