# TRADE: Adjuvant Abemaciclib Tolerability at 6 Months After Initial Dose Escalation in Early HR+/HER2- Breast Cancer

Dana-Farber Cancer Institute

HARVARD MEDICAL SCHOOL

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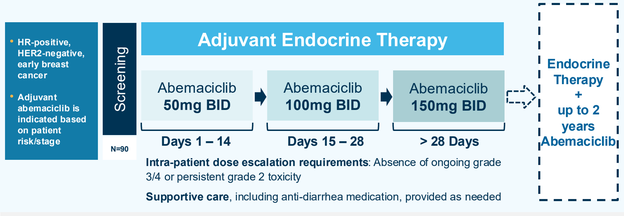
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## BACKGROUND

- Abemaciclib, a CDK4/6 inhibitor, reduces the risk of recurrence and improves overall survival in patients with high-risk HR+/HER2- early breast cancer. Its use is associated with toxicities, particularly diarrhea, which can impact patients' ability to maintain dose and/or remain on therapy.
- TRADE (NCT06001762) is a phase 2, investigator-initiated, single-arm trial designed to evaluate whether an initial dose-escalation strategy improves the tolerability of adjuvant abemaciclib**. The study met its primary endpoint, showing the dose escalation improved the ability to reach/maintain the target dose of 150 mg BID at 12 weeks, compared to historical controls.**
- **Here, we present the 6-month follow-up results from the TRADE study**.

## METHODS

**FIGURE 1:** STUDY SCHEMA




- The primary endpoint of the study was the composite adverse event rate at 12 weeks, which was defined as the discontinuation of adjuvant abemaciclib for any reason and/or inability to reach or maintain target dose of 150 mg BID. Here we present an exploratory endpoint.
- All patients initiated abemaciclib at 50 mg BID for 2 weeks, escalated to 100 mg BID for 2 weeks, and then to 150 mg BID onward for a planned 2-year course (**Figure 1**).

## RESULTS

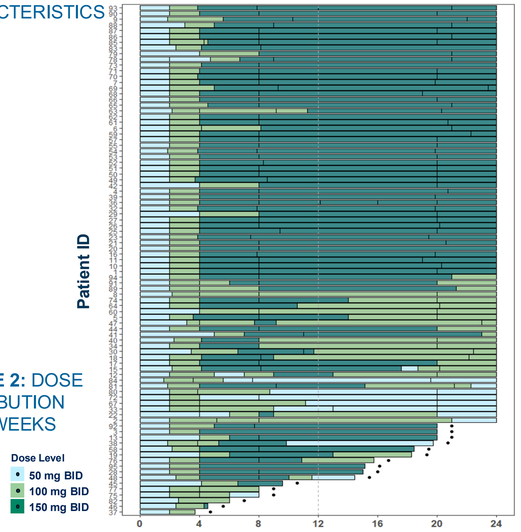
Patient characteristics are summarized in **Table 1**. At a median follow-up of 56 weeks, out of 89 evaluable patients, **73 (82%) remained on abemaciclib by 24 weeks.** (**Figure 2**):

**TABLE 1:** PATIENT CHARACTERISTICS

| | Overall (N=90) |
|---|---|
| **Age** | |
| Median | 58.0 |
| Range | 24.0 – 78.0 |
| **Race** | |
| White | 72 (80.0%) |
| Asian | 6 (6.7%) |
| Black/African American | 4 (4.4%) |
| Other | 8 (8.9%) |
| **Ethnicity** | |
| Hispanic/Latino | 3 (3.3%) |
| **Clinical Stage** | |
| II | 46 (51.1%) |
| III | 45 (48.9%) |
| **Endocrine therapy at therapy initiation** | |
| AI | 72 (80.0%) |
| AI and OS | 18 (20.0%) |
| **Prior neo/adjuvant chemotherapy** | |
| YES | 66 (73.3) |
| NO | 24 (26.7) |

*One patient had progression before 24 weeks

**FIGURE 2:** DOSE DISTRIBUTION BY 24 WEEKS




Abemaciclib discontinuation occurred in 6 patients (6.7%) during the first 12 weeks and in an additional 10 patients (11.2%) between weeks 12 and 24, resulting in a **cumulative discontinuation rate of 18% (n=16) by 24 weeks of exposure.** The most common reasons for discontinuation are summarized in **Table 2, and TEAEs are summarized in Table 3**.

**TABLE 2:** REASONS FOR DISCONTINUATION

| Reason off treatment | # (% out of 89) |
|---|---|
| **Unacceptable adverse event** | **7 (7.9%)** |
| Pneumonitis | 2 (2.2%) |
| Elevated ALT | 1 (1.1%) |
| Diarrhea | 2 (2.2%) |
| Allergic reaction to Abemaciclib | 1 (1.1%) |
| Other (Vaginal dryness/otitis media/diarrhea/hot flashes/ headache/lymphedema) | 1 (1.1%) |
| **Physician decision** | **1 (1.1%)** |
| Unacceptable AE and patients' inability to comply with medical regimen | 1 (1.1%) |
| **Subject withdrew consent/patient preference** | **5 (5.6%)** |
| Traveling abroad so unable to comply with study requirement | 1 (1.1%) |
| Did not want to delay surgery | 1 (1.1%) |
| Grade 1 Diarrhea + additional AEs | 2 (2.2%) |
| Personal life issue + ongoing AEs | 1 (1.1%) |
| **Subject non-compliance** | **2 (2.2%)** |
| **Other** | **1 (1.1%)** |
| PI did not approve hold over 28 days | 1 (1.1%) |

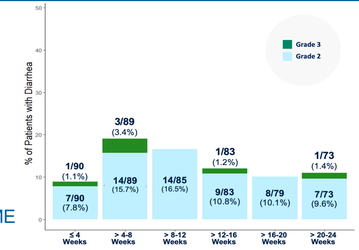
**TABLE 3:** TREATMENT EMERGENT ADVERSE EVENTS OCCURING IN ≥10% OF PATIENTS

| Toxicity | Grade 2 | Grade 3-4 | Total |
|---|---|---|---|
| **Any grade** | **51 (56.7%)** | **26 (28.9%)** | **77 (85.6%)** |
| Diarrhea | 25 (27.8%) | 5 (5.6%) | 30 (33.3%) |
| Neutrophil count decreased | 24 (26.7%) | 4 (4.5%) | 28 (31.1%) |
| Fatigue | 24 (26.7%) | 0 (0%) | 24 (26.7%) |
| Hypertension | 10 (11.1%) | 5 (5.6%) | 15 (16.7%) |
| White blood cell decreased | 14 (15.6%) | 1 (1.1%) | 15 (16.7%) |
| Lymphocyte count decreased | 8 (8.9%) | 3 (3.3%) | 11 (12.2%) |
| Abdominal pain | 9 (10%) | 1 (1.1%) | 10 (11.1%) |
| Nausea | 9 (10%) | 0 (0%) | 9 (10%) |

*One patient had a grade 4 adverse event (neutrophil count decreased)

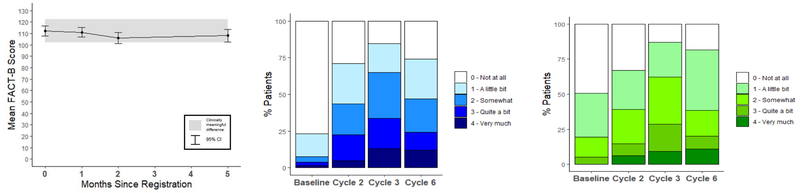
When analyzed by 4-wk intervals, rates of grade ≥2 diarrhea showed an early peak and gradual decline over time (**Figure 3**).

**FIGURE 3:** INCIDENCE AND SEVERITY OF DIARRHEA OVER TIME




Patient-reported outcomes indicated that quality of life remained stable throughout the study period (**Figure 4**).

**FIGURE 4:** TRENDS IN PATIENT REPORTED OUTCOMES OVER TIME




**FACT-B** | **"I HAVE DIARRHEA"** | **"I AM BOTHERED BY THE SIDE EFFECTS OF TREATMENT"**

## CONCLUSIONS

- In the TRADE study, after initial dose escalation, abemaciclib was generally well tolerated, with a cumulative discontinuation rate of 18% at 24 weeks, 7.9% for AE.
- 82% of patients remained on abemaciclib at 24 weeks.
- The incidence of grade ≥2 diarrhea peaked at month 2 and declined over time.
- The majority of patients maintained QOL and remained on therapy with manageable and expected toxicities.
- **These updated findings continue to support the feasibility of an initial abemaciclib dose-escalation approach to optimize drug exposure and reduce early discontinuation, while preserving therapeutic intensity.**

## ACKNOWLEDGEMENTS & REFERENCES


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