**RESULTS**

**Baseline Characteristics**

As of June 23, 2021, 77 patients were enrolled in the Phase II study. Median age was 58.0 years, and median duration of prior CDK4/6i therapy was 12.1 months (Table 1).

**Patient Disposition**

- All 77 patients were treated on-trial.

- Of 73 patients who discontinued study treatment, 43 (93.5%) were from group 1 and 30 (97.8%) from group 2.

- The ORR was 6.5% and 9.4% for groups 1 and 2, respectively.

- At data cutoff, 73 patients (92.4%) discontinued study treatment (43 [93.5%] in group 1; 30 [97.8%] in group 2).

- Disease progression inevitably occurs during CDK4/6i + ET treatment, highlighting the need for effective subsequent regimens.

**Efficacy**

- The objective response rate was 6.5% and 9.4% for groups 1 and 2, respectively.

- All Grade 3/4 AEs were stomatitis (54.3%), infections (42.4%), and fatigue (42.4%).

- Grade ≥3 adverse events occurring in ≥5% of the population:
  - Fever (18.8%)
  - Fatigue (18.8%)
  - Nausea (16.2%)
  - Diarrhea (14.3%)

- No grade > 2 corrected QT interval prolongation as assessed with the Fridericia formula was observed in the study.

**Duration of CDK4/6i Therapy**

- For patients with ≥ 12 months of prior CDK4/6i therapy, the median OS was 17.9 months in group 1 and 25.0 months in group 2.

- Patients with ≥ 6 months of prior CDK4/6i therapy had a median OS of 28.3 months in group 2.

**Safety**

- The most common grade 3/4 AE was stomatitis (54.3%), fatigue (42.4%), and infection (42.4%).

- Other (total, 2.5%; group 1, 4.3%; group 2, 0%)

- No grade > 2 corrected QT interval prolongation as assessed with the Fridericia formula was observed in the study.

**Key Findings & Conclusions**

- The first analysis of the TRINITI-1 trial confirms the promising efficacy and tolerability of RIB + ET. The study design will be updated to include a comparison between 1:1 dose escalation and dose reduction.

- No new safety signals observed; neuropathies and stomatitis were the most common grade 3/4 AEs.

- Grade 4 hospitalization was not observed. The latter typically results in rapid clinical decline culminating in death.

- There was a trend toward better outcomes in patients with longer duration of prior CDK4/6i treatment, with shorter CDK4/6i and Ki67 levels.

- Triplet therapy with RIB + ET + EXT is reasonably well tolerated and sufficiently active, with efficacy and safety consistent with that seen in patients with HR+ MBC, ABC directly following primary therapy, and in patients with HER2− disease.

**Acknowledgments**

Tara Sanft, Meghan Karuturi, Elizabeth Leverkus, and Elisa Franco were employed by Novartis, outside of the submitted work.

**References**

1. Breast Cancer Program at University of California Los Angeles.


3. POS2-13: safety and efficacy of the open-label, phase i study (PD13-03) of rbc1065 (ribociclib) plus exemestane (exemestane) (rib+ex) in patients with hormone receptor positive (hr+) or human epidermal growth factor 2 (her2) negative or unknown (hr+/her2−) advanced breast cancer (abc) who have received prior treatment with a non-her2 directed therapy: updated results from phase i. sano b, sasaki sh, matsuyama y, et al. j breast cancer 2019;22(3):151–63.

4. Acknowledgments: This study was sponsored by Novartis Pharmaceuticals Corporation. Presented at the 2021 San Antonio Breast Cancer Symposium December 7–10, 2021. This study was conducted at the Abramson Cancer Center, Philadelphia, PA; Memorial Sloan Kettering Cancer Center, New York, NY; and at the David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA; and at other institutions in the United States and Europe. This study was supported by an unrestricted educational grant from Novartis. Technical assistance was provided by the Novartis Central Lab, the Novartis Data Management, and the Novartis Medical Writing Services. For patients with HER2− disease, the need for more effective subsequent regimens is highlighted. **Figure 3a** shows the best percentage change from baseline in PFS by group. **Figure 3b** shows the ORR by group.

**Figure 1** A. PFS by Group

**Figure 2** shows the best percentage change from baseline in PFS by group. **Figure 3a** shows the ORR by group.