Selective estrogen receptor degraders (SERDs) are competitive estrogen receptor (ER) antagonists that block best overall responses in patients with measurable disease (n = 19) are shown in Table 1. Less than dose-proportional increases in G1T48 exposure were observed at doses above 400 mg. Substantial decreases in Food effect was determined by administration of a high-fat meal 30 minutes before a single 200 mg dose of G1T48 on either cycle 1 day –10 or 1 day –7 in a crossover fashion. Blood samples were collected pre-dose and at multiple time points for 72 hours following administration during cycle 2. Pharmacodynamic analysis was performed on F-fluoroestradiol positron emission tomography (F-FES PET) imaging was performed at baseline and on cycle 2 day 2 (±2 days) to assess estrogen receptor occupancy during cycle 2. Patients with the UGT1A 1*28 genetic variant had increased mean AUC during the dosing interval at steady-state (AUC0-τ) and increased by ~21%, and T1/2 increased by ~2 hours; enterohepatic recirculation appeared to increase exposure in patients with relatively low exposure in the fasted state, presumably due to enterohepatic recirculation. Muscle spasms appeared to increase exposure in patients with relatively low exposure in the fasted state, presumably due to enterohepatic recirculation. (n = 3) Median (range) number of prior lines of therapy for advanced disease was 6 (4–10) and 10 (7–14) for cycle 1 and cycle 2, respectively. After completion of the PK assessment period, patients may have received Cytotoxic chemotherapy. In advanced/metastatic setting; Figure 3. Treatment duration and response by dose (all patients). TEAEs are reproduced without written permission of the authors.

**CONCLUSIONS**

- SERDs are well-tolerated with manageable adverse events (AEs) considered related to study treatment (D1 0-14 AEs: 42%, D2 0-14 AEs: 38%, D2 0-14 DNT AEs: 21%)
- Safety, tolerability, DLTs
- Mean (SD) age: 60 (12) years; 74% female; 91% White
- Efficacy; CR, complete response; PR, partial response; SD, stable disease.
- Median progression-free survival (PFS) 6.8 months; 95% confidence interval (CI) 3.3–11.5 months
- OS 12.0 months; 95% CI 7.3–16.8 months
- 12-month OS probability 55.2% ± 12.2%
- 24-month OS probability 49.9% ± 14.2%
- 36-month OS probability 44.6% ± 15.2%

**RESULTS**

**Table 1: PK characteristics**

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**Figure 1:** G1T48 Dosing and Rebound in ER+ BCA patients. **Table 2:** PK parameters during and following study drug discontinuation.

**Figure 2:** OS in ER+ BC patients at baseline. **Figure 3:** Treatment duration and response by dose (all patients). **Table 3:** Best response by dose (all patients). **Table 4:** G1T48 related AEs (decreases ≥3 points). **Table 5:** Best dose: Dose Response (Control) in Patients with BRCA Genetic Mutations.