**RESULTS**

**Efficacy**

In this 56-day single-臂 phase I study, 27 patients with stage ICI-3c-T4a, breast and endometrial cancers with PTEN/COH1 mutations showed partial response or stable disease. The partial response rate was 38.1% (10/26). The best tumor size change from baseline was 50% in breast cancer treatment and 42.5% in endometrial cancer treatment. One patient (0013) with PR was confirmed after 19 weeks on study treatment, resulting in 50 mg QD. The grade 3 rash on study day 53 was discontinued due to clinical disease progression after 24 weeks on study treatment. The median number (range) of prior treatment with a further tumor size reduction to 6.5% from baseline. Treatment with ARQ 751 was discontinued due to clinical disease progression after 24 weeks on study treatment.

**Pharmacokinetics (PK) and Pharmacodynamics**

- **ARQ 751 Mean Plasma Concentration-Time Profiles (preliminary)**: PK findings showed that ARQ 751 exhibited dose-proportional increases in Cmax and AUC following single oral doses of 12.5 mg QD to 100 mg QD. The mean plasma concentrations of ARQ 751 increased in a dose-proportional manner up to 100 mg QD. The PK profiles showed that ARQ 751 was rapidly absorbed with a mean maximum concentration (Cmax) ranging from 1.4 to 6.7 ng/ml at 1.5 to 3 hours post dose and a mean terminal elimination half-life (t1/2) ranging from 6 to 67 hours.

**CONCLUSIONS**

ARQ 751 demonstrated preliminary anti-cancer activity in tumors with PTEN/COH1 mutations and PTEN null. Two ER+ PR- and HER2+ stage IV breast cancer patients, one with PTEN/COH1 mutations and one with PTEN null, achieved a partial response after 6 weeks of treatment. In addition, one patient had stable disease at 15 weeks of treatment. Further development of ARQ 751 as a monotherapy or in combination with other anti-cancer agents is deemed feasible considering its manageable safety profile and preliminary evidence of biological activity.

**REFERENCES**


**ACKNOWLEDGEMENTS**

The authors thank the patients, clinicians, and investigators who participated in this study. The study was supported by ArQule, Inc. (Bedford, MA).