A Phase 1 Dose Escalation and Expansion Study of the Next Generation Oral SERD AZD9833 in Women with ER-Positive, HER2-Negative Advanced Breast Cancer

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Methods

n=12, 150 mg QD n=13, 300 mg QD n=13, 450 mg QD n=10 (Table 1).

In total, 60 patients were treated with AZD9833 across five doses; 25 mg QD n=12, 75 mg QD n=6, 150 mg QD n=24, 300 mg QD n=25, 450 mg QD n=6. Progression-free survival (PFS) were calculated.

Results

AZD9833 had notable antitumor activity in post-menopausal women, after ≥1 endocrine therapy and ≤2 prior chemotherapies for breast cancer. Endocrine therapy as a treatment for breast cancer has proven highly effective; however, resistance often develops and patients usually relapse. With AZD9833 monotherapy (B), and dose escalation and randomized dose expansion for patients pre-treated with endocrine therapy, AZD9833 has an encouraging efficacy and dose-dependent safety profile.

Pharmacokinetics after the first dose

After 15 days of once-daily dosing, exposure in terms of Cmax and AUC increased with dose, indicating a dose proportional pharmacokinetic profile.

Conclusion

AZD9833 demonstrates promising antitumor activity and a manageable safety profile. AZD9833 is an oral, next generation SERD with a novel mechanism of action, which selectively prevents estrogen receptor (ER) activity and is dependent on the expression of both ERα and ERβ. In this Phase 1 study, AZD9833 had notable efficacy in patients with ER+ breast cancer. AZD9833 has an encouraging efficacy and dose-dependent safety profile.