Background

- Fulvestrant is used after aromatase inhibitor (AI) failure in metastatic breast cancer but resistance develops quickly. We hypothesized that using anlotinib, a novel multi-target tyrosine kinase inhibitor, may delay fulvestrant resistance in patients (pts) and thus improve its efficacy.
- This single-arm, phase II trial (NCT05075512) aims to evaluate the efficacy and safety of fulvestrant in combination with anlotinib in pts with HR-positive and HER2-negative, previously AI treated, locally advanced or metastatic breast cancer.

Methods

- Eligible pts were women of any menopausal status aged 18-75 years; an ECOG performance status (PS) of 0-1; histologically confirmed HR-positive and HER2-negative breast cancer; and progression after at least 6 months of AI therapy for advanced disease.
- Eligible pts received 500 mg fulvestrant by intramuscular injection on days 1 and 15 of cycle 1 and then on day 1 of subsequent 28-day cycles. Pts were also given 12 mg oral anlotinib once daily for 2 weeks, followed by a week off in a 21-day cycle.
- The primary endpoints is progression-free survival (PFS) and the secondary endpoints include overall response rate (ORR), disease control rate (DCR), clinical benefit rate (CBR), overall survival (OS), and safety.

Results

- Twenty-seven pts have been enrolled from Aug 2021 to Sep 2023, the baseline characteristics were shown in Table 1. After a median follow-up time of 10.7 months (95% CI, 8.8-12.6), the overall median PFS was 7.6 months (95% CI, 3.1-12.1) and the mOS has not reached. In the 26 pts whose efficacy could be evaluated, the ORR was 19.2% (95% CI, 6.6-39.4) and the DCR was 78.9% (95% CI, 56.4-91.0), with partial response and stable disease recorded in 5 (19.2%) and 15 (57.7%) pts (Table 2, Figure 3). The CBR was 34.6% (95% CI, 17.2-55.7), with 4 pts reach SD for more than 6 months.
- Pts who have not received CDK 4/6 inhibitors previously had longer PFS (14.8 months, 95% CI 1.7-27.9) than those who have received CDK 4/6 inhibitors (4.6 months, 95% CI 2.6-7.9) in the subgroup analysis (HR=2.88, P=0.055). (Figure 2)

Conclusions

- TEAEs of any grade were observed in 96.2% of pts, and the frequent AEs (incidence ≥ 10%) included hypertension (50.0%), weight loss (23.1%), proteinuria (19.2%), increased TSH (19.2%), hand-foot syndrome (19.2%), and thrombocytopenia (15.3%). Grade 3 TEAEs occurred in 10 (38.5%) pts, the most common of which was hypertension (30.8%). There was no grade 4-5 TEAEs. Dose reductions of anlotinib occurred in 8 (30.8%) pts. (Table 3)
- Anlotinib combined with fulvestrant showed a promising efficacy with an acceptable safety profile for patients with metastatic breast cancer previously treated with AI. Further results are expected.