PS1-08-26: A Phase 1/2, Multi-Part, Open-Label Study of FWD1802, a Novel Oral Selective Estrogen Receptor Degrader (SERD), in Patients with ER+/ HER2- Locally Advanced or Metastatic Breast Cancer (BC)

Yanchun Meng[1], Fei Xu[2], Xiujuan Qu[3], Yehui Shi[4], Huihui Li[5], Yuping Sun[5], Xian Wang[6], Haifeng Liu[7], Sijuan Ding[8], Hai Hu[9], Hui Li[10], Jun Li[11], Min Yan[12], Yongmei Yin[13], Tao Sun[14], Weimin Xie[15], Xin Chen[16], Jiuwei Cui[17], Xinshuai Wang[18], Fanfan Li[19], Yueqing Feng[20], Jian Zhang[1], Chenggang Zhu[21]

1.Fudan University Shanghai Cancer Center; 2. Sun Yat-Sen University Cancer Center; 3. the First Hospital of China Medical University; 4. Tianjin Medical University Cancer Institute and Hospital; 5. Shandong Cancer Hospital; 6. Sir Run Run Shaw Hospital; 7. Jilin Cancer Hospital; 8. The Central Hospital of Yongzhou; 9. Zhejiang Cancer Hospital; 10. Sichuan Cancer Hospital; 11. Huizhou First Hospital; 12. Henan Cancer Hospital; 13. Jiangsu Province Hospital; 14. Liaoning Cancer Hospital & Institute; 15. Guangxi Medical University Cancer Hospital; 16. The Second People's Hospital of Yibin; 17. The First Hospital of Jilin University; 18. The First Affiliated Hospital of Henan University of Science & Technology; 19. The Second Hospital of Anhui Medical University; 20. Xinxiang Central Hospital; 21. Shenzhen Forward Pharmaceuticals Co. Ltd.

Background

- About 2/3 of BC patients are ER+/HER2-. Endocrine therapy (ET) is the mainstay treatment, despite rising resistance.
- FWD1802 has demonstrated potent anti-tumor effects in both wildtype and resistant ESR1-mutant xenograft tumors.

Objectives

- The primary objective is to determine the recommended Ph2 dose and/or maximum tolerated dose (MTD).
- Secondary objectives include safety, tolerability, pharmaco-kinetics and anti-tumor efficacy.

Study Design

- Trial (CTR20232130) design is illustrated in Fig 1.
- Key eligibilities include ≥1 prior ET, ≤1 prior CDK4/6i and ≤2 prior chemotherapies in advanced setting.
- Oral FWD1802 is administered daily in 28-day cycles.
- Current data cut-off: July 3, 2025

Fig. 1 Study Design

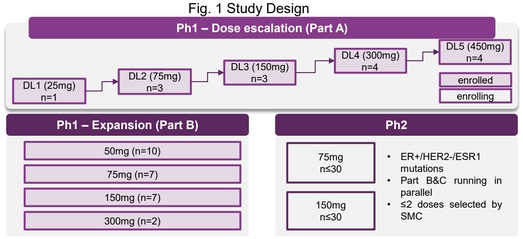


Table 1. Patient Characteristics

Characteristics	Overall N=69	75mg N=23	150mg N=24
Age, median (range)	56.0 (35.0-77.0)	58.0 (39.0-77.0)	55.0 (35.0-74.0)
ECOG 1, n (%)	59 (86%)	18 (78%)	23 (96%)
Post-menopausal, n (%)	44 (64%)	14 (61%)	14 (58%)
Visceral disease, n (%)	62 (89.9%)	21 (91.3%)	23 (95.8%)
Liver disease, n (%)	38 (55.1%)	11 (47.8%)	14 (58.3%)
Lung disease, n (%)	39 (56.5%)	12 (52.2%)	16 (66.7%)
Brain disease, n (%)	1 (1.4%)	1 (4.3%)	0 (0%)
mESR1+, n (%)	41 (59%)	16 (70%)	18 (75%)
# of lines of prior therapies, median (range)	2 (1-7)	2 (1-7)	2 (1-5)
Prior ET, n (%)	69 (100%)	23 (100%)	24 (100%)
# of lines of prior ET, median (range)	2 (1-5)	2 (1-4)	2 (1-4)
Prior fulvestrant, n (%)	32 (46%)	10 (43%)	11 (46%)
Prior chemo, n (%)	36 (52%)	12 (52%)	14 (58%)
# of lines of prior chemo, median (range)	1 (0-3)	1 (0-3)	1 (0-2)
Prior CDK4/6i, n (%)	49 (71%)	17 (74%)	16 (67%)

Patient Characteristics

- As of 2025/7/3, 69 patients were treated with FWD1802: 25mg (n=1), 50mg (n=10), 75mg (n=23), 150mg (n=24), 300mg (n=7) and 450mg (n=4). 75mg and 150mg were further explored in Ph2 part. Table 1 summarized key patient characteristics at baseline.
- Around 90% patients had visceral disease at baseline, >50% of patients had liver mets.
- Majority of patients were ECOG 1 at baseline.
- Majority of patients had undergone ET, CDK4/6i treatment before enrollment.

Safety

- No patients experienced DLT, so MTD was not reached in the study.
- Most treatment-emerged adverse events (TEAEs) were Grade 1-2, and 88% of events were Grade1.
- Zero SAE due to treatment was observed.
- 10% out of all patients experienced Grade 3 AEs due to treatment, 0 Grade 4 or 5 AEs.
- 12% experienced dose interruption, while 0 experienced dose reduction and only 1 patient discontinued the drug due to AE.
- Table 2 includes any treatment related AE occurred in more than 10% of total patient population.
- Sinus bradycardia were all Grade 1-2, 95% being Grade 1.
- Sinus bradycardia typically occurs in the first Cycle, and trend of adaptation was observed. In most cases, no intervention was provided or needed.
- QTc prolongation was not associated with specific symptoms.
- One patient discontinued treatment due to Grade 3 QTc prolongation. The prolongation was not associated with symptoms, and the AE was recovered within one week off the drug.

Table 2. Treatment-related adverse events occurred in more than 10% of patients

Preferred Term, n (%)	25mg N=1	50mg N=10	75mg N=23	150mg N=24	300mg N=7	450mg N=4	Total N=69
Any TRAE	1 (100%)	10 (100%)	22 (95.7%)	24 (100%)	7 (100%)	4 (100%)	68 (98.6%)
Sinus bradycardia	0 (0%)	4 (40.0%)	11 (47.8%)	16 (66.7%)	7 (100%)	4 (100%)	42 (60.9%)
ALT increased	0 (0%)	2 (20.0%)	9 (39.1%)	8 (33.3%)	2 (28.6%)	0 (0%)	21 (30.4%)
ECG QT prolonged	0 (0%)	2 (20.0%)	4 (17.4%)	5 (20.8%)	5 (71.4%)	4 (100%)	20 (29.0%)
Hypertriglyceridaemia	1 (100%)	2 (20.0%)	7 (30.4%)	7 (29.2%)	1 (14.3%)	0 (0%)	18 (26.1%)
AST increased	0 (0%)	3 (30.0%)	5 (21.7%)	8 (33.3%)	1 (14.3%)	0 (0%)	17 (24.6%)
Anaemia	1 (100%)	4 (40.0%)	6 (26.1%)	5 (20.8%)	0 (0%)	1 (25.0%)	17 (24.6%)
Hypercholesterolaemia	0 (0%)	3 (30.0%)	3 (13.0%)	5 (20.8%)	2 (28.6%)	0 (0%)	13 (18.8%)
WBC count decreased	0 (0%)	2 (20.0%)	4 (17.4%)	5 (20.8%)	1 (14.3%)	0 (0%)	12 (17.4%)
GGT increased	0 (0%)	3 (30.0%)	2 (8.7%)	4 (16.7%)	1 (14.3%)	1 (25.0%)	11 (15.9%)
Photopsia	1 (100%)	0 (0%)	3 (13.0%)	1 (4.2%)	2 (28.6%)	4 (100%)	11 (15.9%)
Hyperglycaemia	0 (0%)	1 (10.0%)	3 (13.0%)	4 (16.7%)	2 (28.6%)	0 (0%)	10 (14.5%)
Blood creatinine increased	0 (0%)	0 (0%)	2 (8.7%)	4 (16.7%)	2 (28.6%)	1 (25.0%)	9 (13.0%)
Neutrophil count decreased	0 (0%)	1 (10.0%)	3 (13.0%)	4 (16.7%)	1 (14.3%)	0 (0%)	9 (13.0%)
Hypocalcaemia	0 (0%)	0 (0%)	3 (13.0%)	6 (25.0%)	0 (0%)	0 (0%)	9 (13.0%)
Hypoalbuminaemia	0 (0%)	0 (0%)	2 (8.7%)	4 (16.7%)	0 (0%)	2 (50.0%)	8 (11.6%)
Hyperuricaemia	0 (0%)	2 (20.0%)	1 (4.3%)	4 (16.7%)	0 (0%)	1 (25.0%)	8 (11.6%)
Vision blurred	1 (100%)	2 (20.0%)	1 (4.3%)	2 (8.3%)	2 (28.6%)	0 (0%)	8 (11.6%)
Hyponatraemia	0 (0%)	1 (10.0%)	2 (8.7%)	2 (8.3%)	2 (28.6%)	0 (0%)	7 (10.1%)

Efficacy

- Out of all enrolled population, 60 patients were evaluable by the time of data cut-off.
- Overall ORR was 23.3%, with 14 patients reaching partial response (confirmed and unconfirmed): 1 in 50mg, 9 in 75mg, 3 in 150mg, and 1 in 300mg (Fig 2 and Table 3)
- For mESR1+ population under Ph2 doses, total ORR reached 41%. 8 out of 16 in 75mg reached PR, and 3 out of 11 in 150mg reached PR (Table 4).

Fig. 2 Best change over baseline

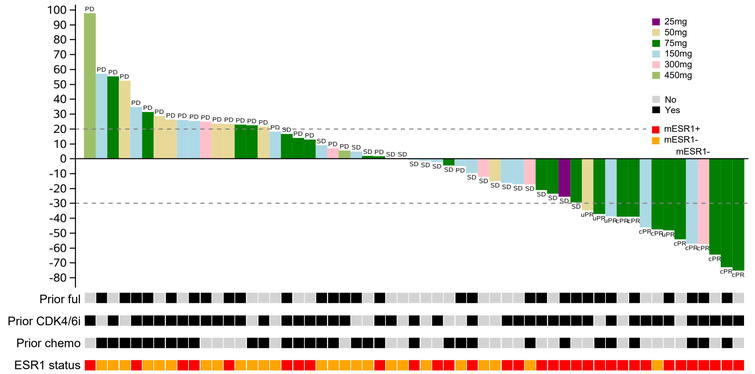


Table 3. Responses in total evaluable population

BOR, n (%)	25mg N=1	50mg N=10	75mg N=23	150mg N=17	300mg N=6	450mg N=3	Total N=60
PR	0 (0%)	1 (10.0%)	9 (39.1%)	3 (17.6%)	1 (16.7%)	0 (0%)	14 (23.3%)
Non-CR/Non-PD	0 (0%)	1 (10.0%)	0 (0%)	0 (0%)	0 (0%)	1 (33.3%)	2 (3.3%)
SD	1 (100%)	2 (20.0%)	7 (30.4%)	8 (47.1%)	3 (50.0%)	0 (0%)	21 (35.0%)
PD	0 (0%)	6 (60.0%)	7 (30.4%)	6 (35.3%)	2 (33.3%)	2 (66.7%)	23 (38.3%)
ORR	0 (0%)	1 (10.0%)	9 (39.1%)	3 (17.6%)	1 (16.7%)	0 (0%)	14 (23.3%)
DCR	1 (100%)	4 (40.0%)	16 (69.6%)	11 (64.7%)	4 (66.7%)	1 (33.3%)	37 (61.7%)
CBR	1 (100%)	1 (10.0%)	14 (60.9%)	3 (17.6%)	3 (50.0%)	1 (33.3%)	23 (38.3%)

Table 4. Responses in mESR1 patients under Ph2 doses

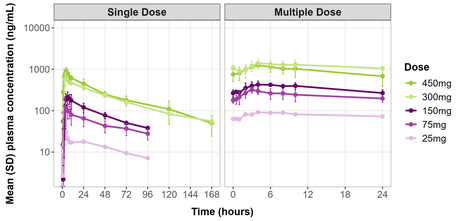
BOR, n (%)	75mg N=16	150mg N=11	Total N=27
PR	8 (50%)	3 (27%)	11 (41%)
Non-CR/Non-PD	0 (0%)	0 (0%)	0 (0%)
SD	5 (31%)	5 (45%)	10 (37%)
PD	3 (19%)	3 (27%)	6 (22%)
ORR	8 (50%)	3 (27%)	11 (41%)
DCR	13 (81%)	8 (73%)	21 (78%)
CBR	12 (75%)	3 (27%)	15 (56%)

CBR: PRs and SDs lasting for more than 24 weeks.

Clinical Pharmacokinetics

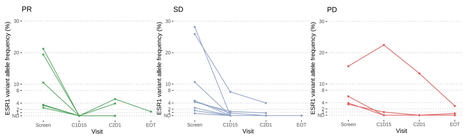
- FWD1802 demonstrated linear PK profile in the range between 25mg QD and 450mg QD.
- Half-life of FWD1802 was 46.8~72 hours.

Fig. 3 FWD1802 Plasma concentration after single and multiple dose



Biomarker Study

Fig. 4 ctDNA *ESR1* mutant allele frequencies



- ctDNA *ESR1* mutant allele frequencies showed decreases among patients with PR, SD and PD.

Conclusions

- FWD1802 showed a great safety profile, and trend of dose-dependency was observed.
- Highly encouraging ORR was observed in mESR1+ population under Ph2 doses.
- Clinical benefit was observed in all tested doses from 25mg to 450mg despite a heavily pretreated population.
- Ph2 part of the current study exploring efficacy in the mESR1+ population under 75/150mg is still ongoing.
- Ph1b/2 study of FWD1802 with multiple CDK4/6i and mTOR inhibitor is ongoing. (CTR20251995)

Disclosures and Notes

- References will be provided upon request.
- This research is sponsored by Shenzhen Forward Pharmaceuticals.
- The presenting author has no conflict of interest to declare.