Early use of CDK4/6 inhibitor combined with endocrine therapy plus anti-HER2 antibody may get more survival benefit in HR+/HER2+ advanced breast cancer: result from a phase II single-arm mini cohort study (CABC016)

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Background

Based on anti-HER2 therapy, the combination of CDK4/6 inhibitors proved to be a potential regimen, which can simultaneously inhibit the crosstalk between the ER and HER2 pathways. PATINA study showed a meaningful prolonged PFS after a chemo-based induction therapy when added Palbociclib to the maintaining treatment, same kind of de-chemo treatment which also achieve better efficacy is still expected to be the initial regimen during metastatic setting.

Methods

CABC016 is a phase II, single-arm, prospective cohort study (NCT05969184), assessing palbociclib combine with anti-HER2 antibody and endocrine therapy (ET) to treat HR+/HER2+ metastatic breast cancer (MBC). Patients are treated with palbociclib at a dose of 125 mg daily on days 1 - 21 of a 28 - day cycle, plus trastuzumab (H,trastuzumab or inetetamab) or trastuzumab plus pertuzumab (HP) intravenously on day 1 of each 21-day cycle. ET options include aromatase inhibitor (AI), tamoxifen or fulvestrant depend on endocrine sensitivity, with ovarian suppression if required. The primary endpoint is investigator-assessed progression-free survival (PFS); key secondary endpoints were safety, response rate(ORR), disease control rate (DCR), and survival (OS).

Trial design

Key Eligible Criteria (n=47)

- Pathologically and/or radiologically confirmed HR+HER2+ breast cancer
- ECOG PS 0 or 1
- No previous CDK4/6i treatment
- Allow stable brain metastasis

→ Trastuzumab ± Pertuzumab
→ Palbociclib (Qilu)
→ Endocrine: AI/SERM/SERD

Primary Endpoint:
- PFS

Secondary Endpoints:
- ORR,DCR,OS,safety

Results

Progression-free survival

- Analysis cutoff date is June 21, 2025.
- The mPFS of ITT population is 16.5 m(95%CI, 11.3 - 21.9), with 19.3 m (95%CI, 15.5 - 22.5) of median follow - up. The mOS is 34.9m(95%CI, 29.1 - 40.6), which is immature.
- Patients who were ET-naïve during metastatic setting had better mPFS (22.0 m[95%CI, 16.3 - 27.6], n = 26) than who had been treated by ET (8.3 m[95%CI, 3.2 - 13.5], n = 21) (P < 0.001).
- PFS is better in 1st- line treatment (18.9m[95%CI, 12.5 - 25.5; n = 17]) than in second/third - line (15.8 m[95%CI, 9.9 - 21.7; n = 18]), than fourth or later(up to 12 lines)treatment(7.7 m[95%CI, 1.5 - 13.9; n = 12]) (P = 0.008).
- No significant difference in mPFS was observed betweenthe inetetamab (13.9 m[95%CI, 9.3 - 18.5; n = 26]) and trastuzumab (14.5 m[95%CI, 7.4 - 21.6; n = 21]) (P = 0.28), or H and HP(11.3month[95%CI, 6.0 - 16.5] vs. 18.1m[95%CI, 11.0 - 25.1; P = 0.418).

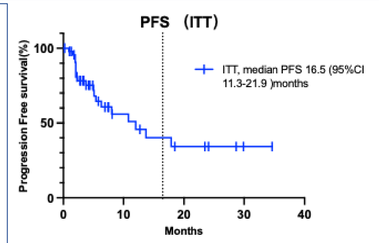


Fig1. progression-free survival of ITT population.

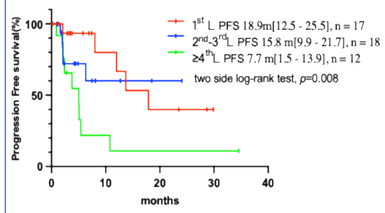


Fig 2. progression-free survival depend on treatment lines.

Overall response

- The ORR of ITT population is 34.1%, included 1 CR.
- The DCR is 87.8%.
- While in ET-naïve setting, the ORR rise to 45.5%, and DCR rise to 95.5%.
- For patients with stable brain disease, the longest survival reached 34.6 months.
- No significant difference in mPFS was observed between patients with or without brain disease (P= 0.293), with a 50%ORR and 62.5% DCR, respectively.

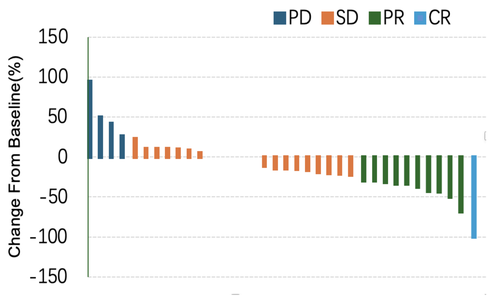


Fig 3. Estimation of target lesion (n=38)

Patient characteristics

Parameters Tatol ER ＞50% Ki67 ＞30%	BC patients (n, %) 47 34 (72.3) 32 (68.1)
Median age (Years, Range)	56 (32~74)
Metastatic site	
visceral	34 (72.3)
liver	14 (29.8)
brain	8 (17.0)
lung	23 (48.9)
Treatment status	
1st line	17 (36.1)
2-3 line	18 (38.3)
≥4 line(up to 12 lines)	12 (25.5)
At least one prior chemotherapy regimen	33 (70.2)
Single anti-Her2 target drug (H)	21 (44.7)
Due anti-Her2 target drugs (HP)	26 (55.3)
Endocrine therapy	125 (29.3)
AI	28 (59.6)
Fulvestrant	16 (34.0)
SERM	3 (9.4)
Prior anti-Her2 therapy	
TKI	31 (66.0)
ADC	8 (17.0)
H or HP	29 (61.7)
De novo disease	7 (14.9)
Endocrine resistance	29 (61.7)

Safety

- The overall safety profile was manageable.
- The most common grade 3-4 AEs were neutropenia (44.2%)and thrombocytopenia (20.9%).
- Dose reduction of palbociclib (from 125mg to 100mg) had occurred in 18 patients (38.3%) because ofmyelotoxicity.
- No patient fell out because of AEs.

Discussion

- Triple positive breast cancer exhibits distinct biological characteristics, demonstrating relatively lower sensitivity to chemotherapy compared to single-positive cases, while responding favorably to endocrine therapy.
- The current study data remain immature. Interim analysis indicates that the addition of CDK4/6 inhibitors resulted a acceptable long PFS, suggesting potential toward a chemotherapy-free era for TPBC.
- As a single-arm exploratory investigation, the findings of this study require further validation through larger sample sizes. Future research may incorporate randomized controlled designs and enroll more representative beneficiary populations.

Conclusions

This mini cohort study showed palbociclib plus ET plus anti-HER2 antibodycould be one of the optimal initial treatment options for metastatic setting of HR+/HER2+ breast cancer, especially for early use during ET-based regimen, even for stable brain disease.

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