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Abstract #2108

276P - Dalpiciclib, a novel CDK4/6 inhibitor, combined with pyrotinib for HER2+ advanced breast cancer: Interim results of a phase II trial

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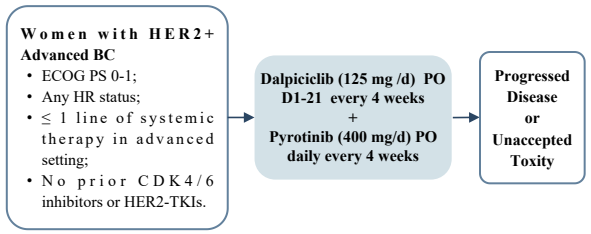
Background

- Given that nearly all patients(pts) with human epidermal growth factor receptor 2-positive (HER2+) breast cancer (BC) would develop resistance to trastuzumab eventually, novel approaches were urgently needed;
- This study aimed to evaluate the efficacy and safety of a novel CDK4/6 inhibitor dalpiciclib combined with pyrotinib, a HER2-targeted tyrosine kinase inhibitor (TKI), in HER2+ advanced BC.

Methods

- This was a single-arm, open-label, Simon's two-stage, prospective, phase II clinical study (NCT04293276).
- HER2+ advanced BC pts who had not received more than 1 line of systemic therapy in advanced setting were recruited. Prior CDK4/6 inhibitors and HER2 targeted TKIs were not allowed.
- Eligible pts received dalpiciclib 125 mg daily for 3 weeks, followed by 1 week off, and pyrotinib 400 mg daily in 28-day cycles.
- Enrollment into stage 2 was based on a determination that ≥ 13 of 23 evaluable pts enrolled in stage 1 were responders. The study was deemed to meet its primary endpoints if confirmed responses were observed in ≥23 pts out of a total of 37 response-evaluable pts.

Figure 1. Study design



Results

Patients

- As of the cutoff date (August 11, 2021), 41 pts were enrolled, of whom 40 were evaluable for efficacy, while 1 pt was withdrawn before her first efficacy assessment. Baseline characteristics are shown in Table 1

Table 1. Baseline Characteristics

	Patients (n=41)
Age, median (range), years	53(28-68)
ECOG PS, n (%)	
0	4 (9.8)
1	37 (90.2)
Hormone receptor status, n (%)	
HR+	18 (43.9)
HR-	23 (56.1)
Metastatic sites at screening, n (%)	
Visceral	38 (92.7)
Brain	14 (34.1)
Lung	22 (53.7)
Liver	17 (41.5)
Non-visceral	3 (7.3)
Number of metastatic sites, n (%)	
1	7 (17.1)
2	10 (24.4)
≥3	24 (58.5)
Lines of prior systemic treatment for advanced disease, n (%)	
0	20 (48.8)
1	21 (51.2)
Previous trastuzumab therapy, n (%)	
Yes	28 (68.3)
No	13 (31.7)
Resistance to trastuzumab*, n (%)	
Yes	5 (12.2)
No/Un#	36 (87.8)
Previous chemotherapy, n (%)	
Yes	38（92.7）
No	3（7.3）
Previous endocrine therapy, n (%)	
Yes	12(29.3)
No	29(70.7)

* Resistance to trastuzumab defined as relapse during or within 12 months after (neo)adjuvant trastuzumab, or progression within 3 months of trastuzumab treatment for metastatic disease.

Pts without prior trastuzumab, or pts previously treated with trastuzumab and without the evidence of trastuzumab resistance.

Primary Efficacy Endpoint

- 28 of 40 evaluable pts had achieved objective responses, and the ORR was 70% (1CR, 27PR, 9SD, 3PD). The subgroup ORR analyses were performed by HR status, prior lines of systemic therapy in the advanced-cancer setting and site of metastasis (Table 2).

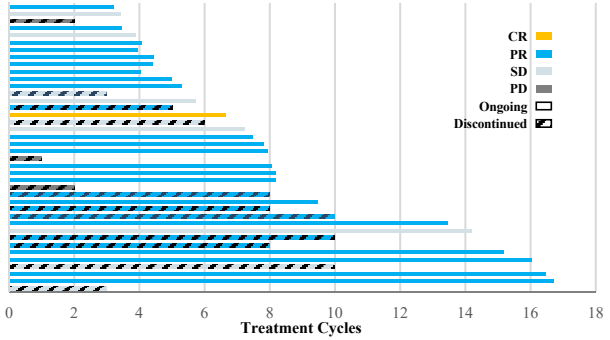
Table 2. Best overall response in evaluable pts

	Evaluable pts
Objective response in overall pts (n=40), n (%)	
CR	1 (2.5)
PR	27 (67.5)
SD	9 (22.5)
PD	3 (7.5)
ORR (95% CI)	70.0 (55.2 - 84.8)
Objective response in different subgroups, n (%)	
HR status	
HR+ (n=18)	10 (55.6)
HR- (n=22)	18 (81.8)
Pior line for advance disease	
Pior 0 line (n=20)	15 (75.0)
Pior 1 line (n=20)	13 (65.0)
Previous trastuzumab therapy	
Trastuzumab - treated (n=27)	18 (66.7)
Resistant to trastuzumab (n=5)	4 (80.0)
Trastuzumab - naive (n=13)	10 (76.9)
Metastatic sites	
Visceral metastasis (n=37)	26 (70.3)
Brain metastasis (n=13)	11 (84.6)
Without visceral metastasis (n=3)	2 (66.7)

Other Efficacy Endpoint

- During a median follow-up of 7.4 months, 12 PFS events occurred, and the median PFS had not been reached. Treatment duration and best response for each evaluable pt are shown in Figure 2.

Figure 2. Treatment duration for each evaluable pts



Safety

- All pts experienced treatment - related AEs (TRAEs), but most were tolerable. 9 pts (22.0%) needed dose reduction, and no treatment discontinuations happened due to AEs.
- 31 pts (75.6%) experienced grade 3/4 TRAEs, and the most common grade 3/4 AEs were neutropenia, leukopenia and diarrhea.

Table 3. Treatment-related AEs reported in ≥15% of pts (N=41)

	Any grade	Grade ≥3
Diarrhea	40 (97.6)	7 (17.1)
Leukopenia	39 (95.1)	23 (56.1)
Neutropenia	39 (95.1)	24 (58.5)
Anaemia	22 (53.7)	3 (7.3)
Nausea	21 (51.2)	0
Stomatitis	15 (36.6)	0
Vomiting	14 (34.1)	0
Blood creatine increased	10 (24.4)	0
Hypokalaemia	9 (22.0)	0
Hypertriglyceridemia	8 (19.5)	0
Mouth ulceration	8 (19.5)	0
Platelet count decreased	8 (19.5)	1 (2.4)
Blood alkaline phosphatase increased	7 (17.1)	0

Data were presented as n (%).

Conclusion

- **The results preliminarily suggested that the study met its primary endpoint. Dalpiciclib combined with pyrotinib showed promising efficacy and manageable toxicity, and could be considered as a completely oral, chemo-free regimen for pts with HER2-positive advanced breast cancer.**

Declaration of interests: The first and presenting author of this poster declares no conflict of interest. Contact: Prof. Min Yan (*ym200678@126.com*).