Dalpiciclib plus endocrine therapy as adjuvant treatment for HR+/HER2– early breast cancer: updated results from the phase 3, DAWNA-A trial

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Introduction

- Dalpiciclib (Dalp), a potent CDK4/6 inhibitor, when combined with endocrine therapy (ET) has been shown to improve survival outcomes in hormone receptor-positive, human epidermal growth factor receptor 2-negative (HR+/HER2-) advanced breast cancer (BC) across first- and subsequent-line settings. [1–2]
- In the phase 3 DAWNA-A trial of adjuvant Dalp plus ET for HR+/HER2– early BC, addition of Dalp showed a significant invasive disease-free survival (IDFS) benefit at the first interim analysis (IA).[3] We now report updated results from the prespecified second IA after longer follow-up.

Methods and Materials

- In this randomized, double-blind, phase 3 trial (NCT04842617), eligible women were randomized (1:1) to receive Dalp or placebo, both with ET (see **Fig.1** for details). The primary endpoint was IDFS.
- As of Jun. 30, 2025, 378 IDFS events had occurred and the preplanned second IA was performed.

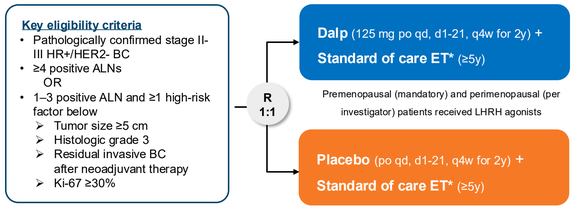


Figure 1. Study design

* ET regimen per protocol: letrozole 2.5 mg/anastrozole 1 mg/toremifene 60 mg QD or tamoxifen 10 mg BID. † Defined as time from randomization to the first invasive ipsilateral or contralateral BC recurrence, local or regional recurrence, distant recurrence, or death from any cause (ie. invasive breast cancer-free survival per STEEP 2.0). ALN, axillary lymph node; DDFS, distant disease-free survival; DFS, disease-free survival; LHRH, luteinizing hormone-releasing hormone; OS, overall survival.

Results

Patients

- A total of 5274 pts were randomized to receive Dalp + ET (n=2640) or placebo + ET (n=2634). Baseline characteristics are shown in **Table 1**.
- As of data cutoff, median follow-up was 27.0 mo; 70.4% of patients in the Dalp group and 72.1% in the placebo group had completed or discontinued Dalp or placebo.

Table 1. Baseline characteristics

	Dalp + ET (n=2640)	Placebo + ET (n=2634)		Dalp + ET (n=2640)	Placebo + ET (n=2634)
Age, years			**Histologic grade at time of surgery† , n (%)**		
Median (IQR)	50 (43–56)	49 (43–56)	Grade 1	69 (2.6)	89 (3.4)
<65	2462 (93.3)	2444 (92.8)	Grade 2	1774 (67.2)	1707 (64.8)
≥65	178 (6.7)	190 (7.2)	Grade 3	638 (24.2)	687 (26.1)
ECOG PS*, n (%)			**No. of positive lymph nodes† , n (%)**		
0	1953 (74.0)	1949 (74.0)	<4	597 (22.6)	596 (22.6)
1	675 (25.6)	678 (25.7)	≥4	2042 (77.3)	2038 (77.4)
Menopausal status, n (%)			**Prior therapy, n (%)**		
Premenopausal	1239 (46.9)	1263 (47.9)	Neoadjuvant chemo	896 (33.9)	907 (34.4)
Perimenpausal	366 (13.9)	338 (12.8)	Adjuvant chemo	1862 (70.5)	1858 (70.5)
Postmenopausal	1035 (39.2)	1033 (39.2)	ET	1776 (67.3)	1772 (67.3)
Hormone-receptor status, n (%)			Radiotherapy	2595 (98.3)	2583 (98.1)
ER+	2632 (99.7)	2624 (99.6)	**Ki-67‡ , n (%)**		
PR+	2102 (79.6)	2079 (78.9)	<20%	1057 (40.0)	1027 (39.0)
AJCC Stage† , n (%)			≥20%	1574 (59.6)	1607 (61.0)
Stage II	751 (28.4)	753 (28.6)	<30%	1500 (56.8)	1438 (54.6)
Stage III	1887 (71.5)	1881 (71.4)	≥30%	1131 (42.8)	1196 (45.4)

* Data were not collected for all patients due to COVID-19 pandemic. † Data were not collected for 1 patient due to randomization error. ‡ Provision of data was not mandatory for patients with ≥4 positive lymph nodes. AJCC, American Joint Committee on Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; ER, estrogen receptor; PR, progesterone receptor.

Efficacy

- The IDFS benefit with Dalp + ET vs placebo + ET was maintained (HR, 0.60 [95% CI 0.49–0.74]; nominal 1-sided p <0.0001). The 3-yr IDFS rate was 90.6% with Dalp + ET vs 87.4% with placebo + ET, yielding an absolute difference of 3.2% (**Fig. 2A**).
- Improvement in IDFS with Dalp was consistent across randomization stratification factors and other baseline characteristics (**Fig. 2B**).
- DFS and DDFS were also prolonged with Dalp + ET (**Fig 3**).

Results

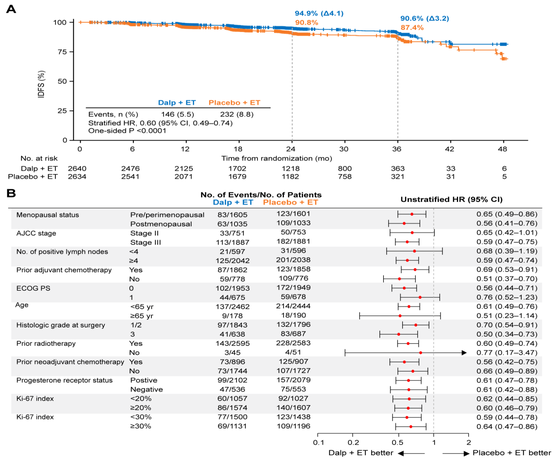


Figure 2. Kaplan–Meier curve (A) and forest plot (B) of IDFS.

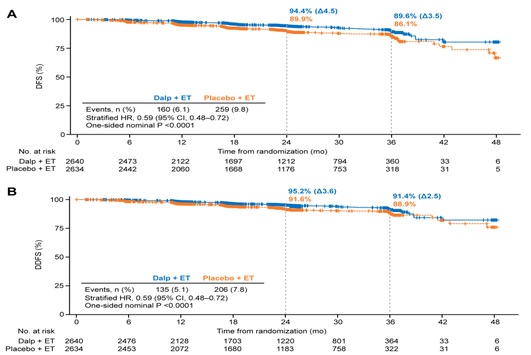


Figure 3. Kaplan–Meier curve of DFS (A) and DDFS (B).

Efficacy end points were compared using log-rank tests; HRs with 95% CIs were estimated using stratified Cox proportional hazards models. For IDFS in prespecified subgroups, HRs with 95% CIs were estimated using unstratified Cox proportional hazards models.

Results

Safety

- Safety data were consistent with previous report,[3] with no new safety signals noted (**Table 2**).
- Discontinuation of Dalp/placebo due to adverse events (AEs) were observed in 3.0% of patients in the Dalp group and 1.7% in the placebo group.
- No treatment-related deaths occurred.

Table 2. Common AEs

	Dalp + ET (n=2640)			Placebo + ET (n=2634)		
	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
Hematological toxicities						
Neutrophil count decreased	2570 (97.8)	1701 (64.7)	353 (13.4)	634(24.1)	56(2.1)	11(0.4)
White blood cell count decreased	2562 (97.5)	1779 (67.7)	69 (2.6)	823 (31.3)	34 (1.3)	1 (<0.1)
Anaemia	1465 (55.7)	56 (2.1)	0	228 (8.7)	7 (0.3)	0
Platelet count decreased	1141 (43.4)	114 (4.3)	25 (1.0)	173 (6.6)	10 (0.4)	4 (0.2)
Lymphocyte count decreased	646 (24.6)	239 (9.1)	11 (0.4)	198 (7.5)	17 (0.6)	0
Non-hematological toxicities						
Hypertriglyceridaemia	932 (35.5)	87 (3.3)	24 (0.9)	999 (38.0)	104 (4.0)	24 (0.9)
ALT increased	739 (28.1)	23 (0.9)	1 (<0.1)	736 (28.0)	18 (0.7)	0
AST increased	731 (27.8)	19 (0.7)	0	648 (24.6)	15 (0.6)	0
COVID-19 infection	568 (21.6)	15 (0.6)	0	477 (18.1)	10 (0.4)	0
Arthralgia	490 (18.6)	2 (0.1)	0	617 (23.5)	3 (0.1)	0
Urinary tract infection	481 (18.3)	8 (0.3)	0	514 (19.6)	5 (0.2)	0
Upper respiratory tract infection	467 (17.8)	19 (0.7)	0	411 (15.6)	13 (0.5)	0

Data are n (%). Listed are AEs of any grade in ≥15% of patients and grade ≥3 AEs in ≥2% of patients in either group. ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Conclusions

- Addition of Dalp to adjuvant ET continued to show clinically meaningful improvement in IDFS within and beyond the 2-yr treatment period, with a manageable safety profile.
- These findings support the adjuvant use of Dalp for HR+/HER2- early BC.

References: 1. Nat Med 2021;27(11):1904-1909. 2. Lancet Oncol 2023;24(6):646-657. 3. J Clin Oncol 2025; 43: 515-515.

Funding: Jiangsu Hengrui Pharmaceuticals

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