AFT-38 PATINA: A Randomized, Open Label, Phase III Trial to Evaluate the Efficacy and Safety of Palbociclib + Anti-HER2 Therapy + Endocrine Therapy vs. Anti-HER2 Therapy + Endocrine Therapy after Induction Treatment for Hormone Receptor-Positive (HR+)/HER2-Positive Metastatic Breast Cancer

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Background: Based upon preclinical evidence that CDK4/6 inhibition could prevent resistance to both endocrine therapy (ET) and anti-HER2 therapy, the Phase III PATINA trial was designed to evaluate the addition of palbociclib to anti-HER2 and ET for patients with metastatic hormone receptor-positive (HR+) and HER2-positive (HER2+) breast cancer.

Methods: PATINA is a randomized, open-label, international Phase III trial assessing palbociclib in combination with anti-HER2 and ET during first-line treatment for HR+/HER2+ metastatic breast cancer (MBC) after completion of 6-8 cycles of induction chemotherapy plus trastuzumab plus pertuzumab (HP) or trastuzumab (H) without evidence of progression. Participants were randomized to palbociclib plus anti-HER2 therapy (H or HP) plus ET or anti-HER2 therapy plus ET alone. ET options included aromatase inhibitor (AI) or fulvestrant, with ovarian suppression required for premenopausal patients. The primary endpoint was investigator-assessed progression-free survival (PFS); key secondary endpoints were response rate (ORR), safety, tolerability, and survival (OS). The trial was powered to detect a hazard ratio (HR) of 0.667 for PFS with 90% power and 1-sided significance level of 0.025.

Results: Data cutoff for this analysis was on October 15, 2024. 518 participants were enrolled between June 2017 and July 2021, 261 to the palbociclib arm and 257 to the control arm. 97.3% of patients received dual anti-HER2 therapy and 90.9% received AI. The final PFS analysis was performed after 262 events with 53 months of median follow up. The addition of palbociclib significantly improved PFS with a HR of 0.74 (95% CI, 0.58–0.94; 1-sided p=0.0074). Median PFS was 44.3 months (95% CI: 32.4–60.9) in the palbociclib arm compared to 29.1 months (95% CI: 23.3–38.6) in the control arm. Confirmed ORR was 29.2% compared to 22.2% (p=0.0458), and clinical benefit rate (CBR) was 89.3% compared to 81.3% (2-sided p=0.0106), favoring the palbociclib arm.

As indicated in the table below, Grade 3 neutropenia was the most frequent adverse event in the palbociclib arm. Grades 2 and 3 fatigue, stomatitis and diarrhea occurred in more patients randomized to the palbociclib arm.

	Palbociclib Arm N=261			**Control Arm N=248***		
	Grade 2	**Grade 3**	**Grade 4**	**Grade 2**	**Grade 3**	**Grade 4**
Neutropenia		63.2%	4.6%		2.0%	0%
Fatigue	22.9%	5.4%		12.9%	0%	
Stomatitis	17.2%	4.2%		1.2%	0%	
Diarrhea	26.4%	11.1%		10.5%	1.6%	

*Excludes 9 patients who did not start treatment

The incidence of Grade ≥4 adverse events was similar across study arms (12.3% in the palbociclib arm vs. 8.9% in the control arm; 2-sided p=0.21). No treatment-related deaths were reported in either arm of the study.

The OS analysis remains immature, with only 119 of 247 planned events observed to date. The median OS was not reached (NE; 95% CI: 71.6–NE) in the palbociclib arm compared to 77.0 months (95% CI: 72.0–NE) in the control arm; 5-year survival rates were 74.3% compared to 69.8% (HR: 0.86; 95% CI: 0.60–1.24) in the palbociclib and control arm, respectively.

Conclusion: The AFT-38 PATINA Phase III trial demonstrated a clinically meaningful 15.2-month PFS improvement with palbociclib added to anti-HER2 plus ET, with a manageable toxicity profile, and may represent a new standard of care for patients diagnosed with HR+ HER2+ advanced breast cancer.