MONARCH 3: Abemaciclib as initial therapy for patients with HR+/HER2- advanced breast cancer


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Background: Abemaciclib is an oral selective CDK4 & 6 inhibitor dosed on a continuous schedule and has demonstrated efficacy and tolerability as monotherapy and in combination with fulvestrant in patients (pts) with hormone receptor-positive (HR+) human epidermal growth factor receptor 2-negative (HER2-) advanced breast cancer (ABC). MONARCH 3 evaluates abemaciclib plus the non-steroidal aromatase inhibitors (NSAI) anastrozole (A) or letrozole (L) as initial therapy in HR+/HER2- ABC.

Methods: MONARCH 3 is a double-blind, Phase 3 study of abemaciclib + NSAI (A or L) vs placebo (P) + NSAI in postmenopausal women with HR+/HER2- ABC who have had no prior systemic therapy in the metastatic setting. Endocrine naive pts or pts with disease relapse >12 months after (neo)adjuvant endocrine therapy (ET) were randomized 2:1 and stratified by metastatic site (visceral, bone only, or other) and prior ET (A or L). The primary endpoint was investigator-assessed progression-free survival (PFS). Secondary objectives included objective response rate (ORR) and safety. The study was powered to 80% (HR 0.8) at 1-sided α=0.025 assuming a hazard ratio (HR) of 0.67 in favor of abemaciclib + NSAI, with analyses at 189 and 240 PFS events.

Results: 493 women were randomized to abemaciclib + NSAI (n = 328) or P + NSAI (n = 165). Pt characteristics were: visceral disease (52.9%), measurable disease (80.5%), prior (neo)adjuvant A (27.4%), and de novo ABC (39.8%). At the interim analysis, 194 PFS events were observed. The PFS analysis was significantly prolonged with a HR of 0.543 (95% CI 0.409 to 0.723, P = 0.00021; median PFS: not reached in abemaciclib arm, 14.7 months in placebo arm). In pts with measurable disease, the ORR was 59% in the abemaciclib arm and 44% in the P arm (P = 0.004). The most frequent adverse events were (abemaciclib vs P arm) diarrhea (81.3% [grade 3: 9.5%, no grade 4] vs 28.8% [grade 3: 1.2%, no grade 4]), neutropenia (41.3% [grade 3: 21.1%] vs 1.9% [grade 3: 4.2%]), and fatigue (40.1% [grade 3: 1.8%] vs 31.7% [grade 3: 0.9%]).

Conclusions: Abemaciclib + NSAI demonstrated a tolerable safety profile and was an effective initial treatment for pts with HR+/HER2- ABC, significantly improving PFS and ORR.

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