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BREAST CANCER, METASTATIC

273O nextMONARCH: Final overall survival analysis of abemaciclib monotherapy or in combination with tamoxifen in patients with HR+, HER2- metastatic breast cancer

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Background: Abemaciclib, an oral, continuously dosed cyclin-dependent kinase 4 & 6 (CDK 4 & 6) inhibitor, improves progression free survival (PFS) in combination with endocrine therapy (ET) in patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), metastatic breast cancer (MBC) in the phase III MONARCH2 and 3 studies. In the phase II nextMONARCH study, primary analysis of PFS and ORR confirmed the robust single-agent activity of abemaciclib in heavily pretreated HR+, HER2- MBC with no significant improvement by addition of tamoxifen. We here report the final 24-month overall survival results.

Methods: nextMONARCH was a multicenter, randomized, open-label phase II trial of abemaciclib in women with heavily pretreated HR+, HER2- MBC whose disease progressed on or after ET and chemotherapy. Patients were randomized 1:1:1 to abemaciclib 150 mg + tamoxifen 20 mg (A+T), or abemaciclib 150 mg (A-150) or abemaciclib 200 mg plus prophylactic loperamide (A-200). Final OS analysis occurred 24 months after the last patient entered treatment. OS was a preplanned secondary endpoint.

Results: At the time of data cutoff (28-June-2019), 12 of the 234 patients enrolled were still ongoing on study treatment. Median follow-up was 27.2 months. Median OS was 24.2 months in the A+T arm, compared to 20.8 months in A-150, and 17.0 months in A-200 (A+T vs. A-150: HR 0.620 (95% CI [0.397, 0.969] p=0.034); A-150 vs. A-200: HR 0.956 (95% CI [0.635, 1.438] p=0.832)). The primary PFS endpoint and ORR were unchanged at the 24-month analysis. Common treatment-emergent adverse events (TEAEs) across all abemaciclib arms occurring in ≥25% of patients included diarrhea (61.1%), neutropenia (49.6%), anemia (40.6%), nausea (36.3%), leukopenia (30.8%), fatigue (29.9%) and abdominal pain (27.4%).

Conclusions: Addition of tamoxifen to abemaciclib provided a statistically significant median OS improvement compared to abemaciclib monotherapy in this heavily pretreated HR+, HER2- MBC patient population. PFS was consistent with the primary results of nextMONARCH with no significant difference. No new safety findings were observed.

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274O Health-related quality of life (HRQoL) changes with veliparib in patients (pts) with metastatic or locally advanced breast cancer in the phase III BROCADE 3 study

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Background: Veliparib, a poly (ADP-ribose) polymerase 1/2 inhibitor, was evaluated in the phase III BROCADE 3 study (NCT02163694) for efficacy and safety in combination with paclitaxel/carboplatin (VPC) in pts with HER2-negative metastatic or locally advanced unresectable gBRCA-associated breast cancer, in which VPC significantly prolonged progression-free survival (hazard ratio=0.71 [95% CI 0.57, 0.88], P=.002) compared with placebo plus paclitaxel/carboplatin (PPC) (Dieras VC et al. *Ann Oncol*. 2019:30[suppl 5]:LBA9). In this analysis we investigated the impact of veliparib on HRQoL.

Methods: This double-blind study examined the effect of veliparib (120 mg oral twice daily for 7 days out of each 21-day cycle) added to paclitaxel/carboplatin vs. PPC. HRQoL measures were EORTC-QLQ -C30 and breast cancer (BR23), EQ-5D-5L, and Brief Pain Inventory-Short Form (BPI-SF). Responses were obtained on Day 2 Cycle 1, Day 1 Cycle 2, and every other cycle thereafter starting from Cycle 4 plus final and follow-up visit. Data were analyzed only through Day 1 Cycle 30 due to attrition. For each HRQoL domain, mean change in baseline scores, % responders (improved, stable, declined), and median time to symptom worsening were analyzed across study arms.

Results: 504 pts (VPC 334, PPC 170) were included in the analysis. Improvement from baseline in function, disease and treatment symptom burden, and health state was observed for both study arms, with greater benefits for VPC vs. PPC for pain, pain interference, and breast symptoms. Greater proportion of PPC vs. VPC pts declined in global health status, pain, arm symptoms, breast symptoms and pain interference, but here differences were not significant. Median time (months) to symptom worsening was significantly longer (P<0.05) for VPC vs. PPC pts for role functioning (8.2 vs. 6.5), physical functioning (8.8 vs. 7.1), constipation (7.7 vs. 6.2), and future perspectives (10.2 vs. 9.0).

Conclusions: Overall, addition of veliparib to paclitaxel/carboplatin has no detrimental effect on quality of life in pts with gBRCA mutation-associated advanced breast cancer and may be beneficial in some areas of functioning and symptom experience.