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Event-free survival (EFS), overall survival (OS), and safety of adding veliparib (V) plus carboplatin (Cb) or carboplatin alone to neoadjuvant chemotherapy in triple-negative breast cancer (TNBC) after ≥4 years of follow-up: BrighTNess, a randomized phase III trial

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Background

In BrighTNess, adding Cb with or without V to neoadjuvant chemotherapy significantly improved pathological complete response (pCR) with an acceptable safety profile in operable TNBC. We report EFS, OS, and second malignancies ≥4 years postsurgery.

Methods

Women with untreated stage II/III TNBC were randomized (2:1:1) to A) paclitaxel (P) 80 mg/m^2 (weekly, 12 doses) + Cb area under the curve 6 mg/mL (every 3 weeks, 4 cycles) + V 50 mg orally twice a day (PCbV); B) P + Cb + V placebo (PCb); or C) P + Cb/V placebo (P). All patients (pts) then received 4 cycles of doxorubicin + cyclophosphamide every 2–3 weeks. The primary (pCR) and secondary (EFS and OS) endpoints used a fixed testing procedure that ordered PCbV vs P, then PCbV vs PCb. Efficacy was assessed in all randomized pts and safety in all who received ≥1 dose. In primary pCR analyses, PCbV was superior to P but not PCb, so subsequent secondary analyses are descriptive with nominal P values.

Results

Overall, 634 pts were randomized to PCbV (n=316), PCb (n=160), and P (n=158). Median follow-up time was 4.5 years. Hazard ratio (HR) for EFS with PCbV vs P was 0.63 (95% confidence interval [CI] 0.43–0.92, *P*=0.016) and 1.12 (95% CI 0.72–1.72, *P*=0.620) for PCbV vs PCb. In post hoc analysis, HR for EFS with PCb vs P was 0.57 (95% CI 0.36–0.91, *P*=0.018). Deaths occurred in 38/316 (12%) with PCbV, 16/160 (10%) with PCb, and 22/158 (14%) with P. HR for OS was 0.82 (95% CI 0.48–1.38, *P*=0.452) for PCbV vs P, 1.25 (95% CI 0.70–2.24, *P*=0.455) for PCbV vs PCb, and 0.63 (95% CI 0.33–1.21, *P*=0.166) for PCb vs P. See table for myelodysplastic syndromes (MDS) and second malignancies.Table: 1190

Myelodysplastic syndromes and selected second cancers

n (%)	PCbVN=313[a]	PCbN=158[a]	PN=157[a]
Myelodysplastic syndrome[b]PancytopeniaMyelodysplastic syndrome	5 (1.6)4 (1.3)1 (0.3)	3 (1.9)3 (1.9)0	1 (0.6)01 (0.6)
Second malignancy[b]Acute leukemiaAcute myeloid leukemiaChronic myeloid leukemiaColon cancerLung cancerMalignant melanomaPancreatic cancer	6 (1.9)1 (0.3)2 (0.6)1 (0.3)01 (0.3)1 (0.3)0	6 (3.8)03 (1.9)01 (0.6)000	4 (2.5)01 (0.6)00002 (1.3)

[a]Patients who received ≥1 dose.[b]*Standardized Medical Dictionary for Regulatory Activities* (MedDRA) query.Cb, carboplatin; P, paclitaxel; V, veliparib.

Conclusions

Adding Cb to P improved pCR and EFS without increasing MDS or acute myeloid leukemia. Addition of V did not impact pCR or EFS. Mortality rate was low, but numerically higher with P than PCbV and PCb.

Clinical trial identification

NCT02032277.

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