Poster Session Abstracts

Abstract P4-22-02: Evaluation of veliparib (V) and temozolomide (TMZ) in a phase 2 randomized study of the efficacy and tolerability of V+TMZ or carboplatin (C) and paclitaxel (P) vs placebo (Plc)+C/P in patients (pts) with *BRCA1* or *BRCA2* mutations and metastatic breast cancer

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Abstract

Background: V is a potent, poly(ADP-ribose) polymerase (PARP) inhibitor that obstructs DNA damage repair. *BRCA1/2* tumors are defective in homologous recombination, which leads to more error-prone mechanisms of DNA repair and increased sensitivity to PARP inhibition. V enhances the antitumor activity of alkylating agents such as TMZ in preclinical models. In addition, V+TMZ showed promising activity in a single-arm phase 2 study in pts with *BRCA1/2* mutations. This phase 2 trial (NCT01506609) investigated the efficacy and tolerability of V+TMZ (or V+C/P) compared to Plc+C/P in pts with locally recurrent or metastatic breast cancer harboring a *BRCA1* or *BRCA2* mutation. Results from the primary analysis for the V+TMZ arm vs Plc+C/P are presented, and the V+C/P vs Plc+C/P results will be presented separately.

Methods: Male and female pts aged ≥18 years with histologically confirmed locally recurrent or metastatic breast cancer were randomized 1:1:1 to: 1) V 40 mg BID D1–7 + TMZ 150–200 mg/m^2 QD D1–5, 28-D cycle; 2) V 120 mg BID D1–7 + C AUC 6, D3 and P 175 mg/m^2, D3, 21-D cycle; 3) placebo BID D1–7 + C/P. Key eligibility criteria included known deleterious *BRCA1/2* mutation, ≤2 prior chemotherapies for metastatic disease, no prior platinum agent, and no CNS metastases. Randomization was stratified by hormone receptor status, prior cytotoxic therapy (yes vs no), and ECOG PS (0–1 vs 2). The primary endpoint was progression-free survival (PFS) per RECIST 1.1 by independent review. Overall survival (OS), objective response rate (ORR), and safety/tolerability were also evaluated.

Results: A total of 290 pts (284 *BRCA*+ per central lab) were randomized (V+TMZ, n=94 [91 *BRCA+]*). Baseline demographics and disease characteristics were comparable among treatment arms; 41.3% of pts had triple-negative breast cancer (TNBC) and 31.7% had received >2 prior regimens. Median study drug exposure was 6 cycles for the V+TMZ arm and 10 cycles for the Plc+C/P arm. Median PFS, median OS (interim), and ORR for V+TMZ were inferior to Plc+C/P (PFS 7.4 vs 12.3 mo, OS 19.1 vs 25.0 mo, and ORR 28.6% vs 61.3%). In pts with TNBC, median PFS was 5.5 (3.1–8.5) mo; 8.4 (6.8–10.6) mo for pts with non-TNBC. Treatment-emergent adverse events (AEs) of interest occurring differentially with V+TMZ are shown in Table 1. Grade ≥3 AEs in ≥30% of pts in the V+TMZ arm were thrombocytopenia (48%) and neutropenia (37%).

Conclusions: V+TMZ provided durable responses, with less neutropenia, alopecia, and neuropathy than Plc+C/P; however, PFS, OS, and ORR were inferior in the TMZ arm compared to C/P.

Treatment-Emergent AEs, n (%)	V+TMZ, n=93	Plc+C/P, n=96
Neutropenia	46 (50)	71 (74)
Alopecia	10 (11)	55 (57)
Peripheral neuropathy	11 (12)	56 (58)
Thrombocytopenia	73 (79)	67 (70)
Nausea	70 (75)	56 (58)

Table 1

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