NSCLC, metastatic

A RANDOMIZED, DOUBLE-BLIND, PHASE 2 TRIAL OF VELIPARIB (ABT-888) WITH CARBOPLATIN AND PACLITAXEL IN PREVIOUSLY UNTREATED METASTATIC OR ADVANCED NON-SMALL CELL LUNG CANCER


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**Aim:** Platinum-based regimens are the current standard of care for patients (pts) with metastatic non-small cell lung cancer (NSCLC). Veliparib (V) is a potent, orally bioavailable PARP inhibitor that (1) enhances the efficacy of platinum-containing DNA damaging therapies in preclinical models, and (2) has been safely combined with full dose carboplatin (C) and paclitaxel (P) in Ph 1 trials.

**Methods:** Pts with advanced or metastatic NSCLC were randomized 2:1 to V at 120 mg BID or placebo plus CP. Pts were stratified by histology and smoking history. The primary endpoint was progression-free survival (PFS, with 80% power and α = 0.05, assuming log-rank HR of 0.51). All data analyses were performed at the 78th PFS event except overall survival (OS, 90th event). In the case of a positive signal, continuation of the program to a phase 3 trial was planned.

**Results:** 158 pts were randomized; 64% of pts were male; 49% had squamous NSCLC; 60% smoked within 1 year of study entry. Adverse events (AE) in 20% or more pts were alopecia (39% VCP/42% CP), anemia (31/42), neutropenia (36/29), nausea (28/25) and peripheral neuropathy (24/25). Leukopenia was seen in 11% VCP vs. 1% CP. Grade 3/4 AEs in 10% or more pts were neutropenia (23/19) and anemia (10/10). Mean chemo cycles were 4.5 C/4.5 P with CP and 4.5 C/4.3 P with VCP.

**Table:**

<table>
<thead>
<tr>
<th>Efficacy (ITT Population)</th>
<th>CP n = 53</th>
<th>VCP n = 105</th>
<th>HR: VCP/CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS (mo, 95% CI)</td>
<td>4.2 (3.1-5.6)</td>
<td>5.8 (4.2-6.1)</td>
<td>0.71 (0.50-1.13)</td>
</tr>
<tr>
<td>Squamous</td>
<td>4.1 (2.8-NA)</td>
<td>6.1 (5.8-8.3)</td>
<td>0.50 (0.24-1.04)</td>
</tr>
<tr>
<td>Non-squamous</td>
<td>5.0 (2.8-6.6)</td>
<td>4.3 (2.8-6.0)</td>
<td>0.94 (0.52-1.71)</td>
</tr>
<tr>
<td>OS (mo, 95% CI)</td>
<td>9.1 (5.4-12.3)</td>
<td>11.1 (8.8-13.4)</td>
<td>0.77 (0.50-1.18)</td>
</tr>
<tr>
<td>Squamous</td>
<td>8.5 (5.0-11.4)</td>
<td>10.3 (8.3-13.2)</td>
<td>0.75 (0.41-1.34)</td>
</tr>
<tr>
<td>Non-squamous</td>
<td>11.1 (4.8-NA)</td>
<td>12.6 (8.0-NA)</td>
<td>0.79 (0.43-1.47)</td>
</tr>
<tr>
<td>Overall Response Rate (%)</td>
<td>28 (17-42)</td>
<td>31 (22-40)</td>
<td>-</td>
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<tr>
<td>Duration of Response (mo, 95% CI)</td>
<td>3.3 (2.7-4.3)</td>
<td>6.9 (4.4-7)</td>
<td>0.11 (0.03-0.50)</td>
</tr>
</tbody>
</table>

**Conclusions:** Estimated HR for progression and death from NSCLC favored VCP over CP, but results were not statistically significant. VCP was delivered without excessive toxicity. Based on results in the squamous histology subgroup, a Phase 3 pivotal trial has been initiated for patient with squamous cell cancer (M11-089).

**Disclosure:** S.S. Ramalingam: Has served as a consultant on scientific advisory board meetings for AbbVie and has received honorarium; Q. Qin: AbbVie employee and stock owner; J. Qian: AbbVie employee and stock owner; C. Nickner: AbbVie employee and stock owner; J. Dziubinski: AbbVie employee and stock owner; M.D. McKee: AbbVie employee and stock owner; V.L. Giranda: AbbVie employee and stock owner. All other authors have declared no conflicts of interest.