A Phase 2 Randomized Study of Dalantercept Plus Axitinib Versus Placebo Plus Axitinib in Advanced Renal Cell Carcinoma: Results from the Part 1 Dose Escalation and Expansion Cohorts

Michael B. Atkins,1, 2, 5 Martin H. Voss,1 Elizabeth R. Filimack,1 Brian I. Rini,1, 2 Robert Alter,2, 6 Nancy A. Dawson,1 J. Thaddeus Beck,2 Ravi Kumar,7 Matthew L. Sherman,8 Shuchi S. Pandya1

1Georgetown University Office of Clinical Research Coordination Center, Washington, DC; 2Memorial Sloan Kettering Cancer Center, New York, NY; 3The Ohio State University Comprehensive Cancer Center, Columbus, OH; 4Cleveland Clinic, Cleveland, OH; 5University of Texas MD Anderson Cancer Center, Houston, TX; 6Philadelphia, PA; 7Sloan-Kettering Memorial Cancer Center, New York, NY; 8University of Maryland Marcom School of Medicine, Baltimore, MD.

Study Design and Schema

**Key Eligibility Criteria (Part 1)**
- Advanced, pre-treatment clear cell RCC
- Measurable disease according to RECIST 1.1
- ECOG performance status grade 0–1
- No anti-angiogenesis therapy, with the exception of low dose aspirin
- No prior or active therapy targeting the VEGFR superfamily

**Results (Part 1)**
As of May 2016, 24 patients had enrolled in Part 1 at 0.6 mg/kg, 0.9 mg/kg, and 1.2 mg/kg dose levels.

<table>
<thead>
<tr>
<th>Dose Level (mg/kg)</th>
<th>Overall Dose Escalation (N = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.6</td>
</tr>
<tr>
<td>All Grades, n (%)</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>Grade ≥ 3, n (%)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**Objective Response Rate Analyses RECIST 1.1**

<table>
<thead>
<tr>
<th>Drug Arm</th>
<th>Overall (N = 26)</th>
<th>0.6 mg/kg (N = 26)</th>
<th>0.9 mg/kg (N = 26)</th>
<th>1.2 mg/kg (N = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose Escalation</td>
<td></td>
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<td></td>
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<tr>
<td>Partial Response, n (%)</td>
<td>22 (84.6)</td>
<td>1 (4.1)</td>
<td>13 (50.0)</td>
<td>8 (30.8)</td>
</tr>
<tr>
<td>Progression-Free Survival, n (%)</td>
<td>18 (69.2)</td>
<td>1 (4.1)</td>
<td>12 (46.2)</td>
<td>5 (19.2)</td>
</tr>
</tbody>
</table>

**Conclusions and Discussions**
- In this pretreated mRCC population, the combination of dalantercept and axitinib was well tolerated.
- The most frequent adverse events were generally low grade and included fatigue, diarrhea, elevated creatinine, peripheral edema, dyspnea, leucopenia, cough, and hypertension.
- Based upon the adverse events at the 1.2 mg/kg dose level and preliminary safety data at the 0.9 mg/kg dose level, dalantercept 0.9 mg/kg was selected as the RP2D dose level in part 2 of this study.
- Common toxicities associated with anti-VEGF therapy included hypertension, edema, hyperlipidemia, proteinuria, and thrombocytopenia.

**References**
6. www.accessdata.fda.gov/drugsatfda_docs/nda/2012/202053Orig1s0000.pdf
7. www.accessdata.fda.gov/drugsatfda_docs/nda/2012/202053Orig1s0001s0000.pdf