Pharmacokinetics, activity, and safety of ODM-201 in chemotherapy-naïve patients with metastatic castration-resistant prostate cancer: an open-label phase I trial with long-term extension

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Background

• ODM-201 is a novel second-generation AR inhibitor that demonstrated antitumor activity in vitro and in animal models and negligible penetration of the blood brain barrier in preclinical models (1,2).
• A significant PSA response was observed in the phase I ARADES study that evaluated the maximal tolerated dose, safety and activity of ODM-201 in men with metastatic chemotherapy-naïve castration-resistant prostate cancer (CRPC) (3). In ARADES the ODM-201 dosing form was a 100 mg capsule; thus patients on the higher daily doses (e.g., 700 mg bid) had to consume a large number of capsules.

Methods

• PK Component. Patients received a single 600 mg dose of ODM-201 capsules (n = 300 mg) in the fed state and one 600 mg dose of either TabA or TabB, 2 × 300 mg) in the fed and fasted state in a random order, with a ≥ 7 day wash-out between treatment administrations.
• Extension Component. Patients received ODM-201 (capsule formulation) 600 mg twice daily until disease progression or experiencing an intolerable adverse event (AE) (Figure 1).

Results

Table 1. Baseline characteristics. N = 30

<table>
<thead>
<tr>
<th>Age (median years, range)</th>
<th>48 (15-90)</th>
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<tr>
<td>Median Gleason score at diagnosis</td>
<td>9 (7-10)</td>
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<td>Disease localization</td>
<td>Bone only (n = 19), Bone and soft tissue (n = 11)</td>
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<tr>
<td>Median time from diagnosis to first dose (months)</td>
<td>36 (10-150)</td>
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<tr>
<td>Prior prostate cancer treatment</td>
<td>Androgen deprivation therapy (n = 25), Chemotherapy (n = 10)</td>
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<tr>
<td>Median months in study up to data cut-off date</td>
<td>15.3</td>
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Figure 1. The ARAFOR trial design and schedule of events.

Figure 2. Plasma concentration-time curve for ODM-201 following single dose administration of capsule, TabA and TabB.

PK Component.

• Concentration-time curves were similar for the ODM-201 capsule formulation and tablets, TabA and TabB, at fed state
• Absorption was slower and exposure was 2-fold greater when the ODM-201 tablets were administered in the fed vs. fasted state (Figure 2).

Figure 3. Percentage change in PSA at 12 weeks from baseline.

Figure 4. Time to PSA progression by PCWG2.

Figure 5. Time to radiologic progression.

References


Conclusions

• This trial showed that the ODM-201 tablet and capsule formulations had comparable single-dose pharmacokinetics
• ODM-201 at 600 mg bid dose level was well tolerated and showed substantial antitumor activity in metastatic chemotherapy-naïve CRPC patients
• A phase III trial of ODM-201 600 mg bid in men with non-metastatic CRPC is ongoing (ARAMIS NCT02000614)

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