A Phase 2 Study of Vudalimab, a PD-1 × CTLA-4 Bispecific Antibody, Plus Chemotherapy or Targeted Therapy in Patients With Molecula...Resistant Prostate Cancer

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Aims: To explore the antitumor activity of vudalimab in combination with other checkpoint inhibitor (ICI) therapy in patients with mCRPC.

Background:
Vudalimab (XmAb21875) is a humanized bispecific monoclonal antibody that simultaneously targets PD-1 and CTLA-4, killing cancer via both PD-L1 and MHC class II pathways.

Methods:
Study Objectives:

Primary Study Objectives
- Characterize pharmacodynamics, based on cell surface markers on selected immune system cells in pretreatment and posttreatment biopsies
- Evaluate the safety and tolerability of vudalimab alone and in combination with other anticancer therapies in patients with mCRPC

Secondary Study Objectives
- Correlate clinical response with tumor and circulating tumor DNA mutation profiles, interferon transcriptional signature, and immune profiling characteristics of cells in the tumor microenvironment by transcriptomic exome sequencing of metastatic disease
- 5-Case study of best patients per cohort

Study Population:
- Eligible patients: Evaluable disease, based on PCWG3 criteria
- Documented cohort-specific genetic features in the study

Cohort Regimen Vudalimab Dose Combination Therapy Dose

Study Drug

Primary Study Outcome Measures:

Study Drug

Eligible patients received:
- Cabazitaxel
- Docetaxel
- Olaparib
- Axitinib
- Vudalimab

Treatment:
- Cabazitaxel 15 mg/m² or docetaxel 50 mg/m²
- Olaparib bid (Cohort C)
- Vudalimab Q2W IV in Cohort Regimen

Paclitaxel
- 10 mg/kg Q2W

Table 3. Investigator Assessment of Best Overall Response

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Best Overall Response</th>
<th>Number of Patients with Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: PARPi Naïve + HRD/ AVPC</td>
<td>SD</td>
<td>1</td>
</tr>
<tr>
<td>B: PARPi Naïve – HRD/ AVPC</td>
<td>SD</td>
<td>1</td>
</tr>
<tr>
<td>C: PARPi Naïve – HRD/ AVPC</td>
<td>SD</td>
<td>1</td>
</tr>
<tr>
<td>D: No Targetable Mutations</td>
<td>SD</td>
<td>1</td>
</tr>
<tr>
<td>E: MSI-H or MMRD</td>
<td>SD</td>
<td>1</td>
</tr>
</tbody>
</table>

Results:

Safety:

- Overall, 4 patients had adverse events resulting in discontinuation of study treatment
- No treatment-related severe adverse events (SAEs) occurring within the first cycle of therapy were reported for ≥ 2 of the 8 patients treated
- No treatment-related serious and/or severe adverse events leading to discontinuation of treatment
- In the absence of surgical orchiectomy, must be on and continue ADT

Table 1. Key Body Cytology

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</table>

Conclusions:

- The study met its primary endpoint of overall response rate (ORR) of ≥ 25% in ≥ 1 cohort
- The primary endpoint was achieved in ≥ 1 cohort
- A promising ORR of ≥ 25% was observed in ≥ 1 cohort
- The study met its secondary endpoint of clinical benefit rate (CBR) of ≥ 25% in ≥ 1 cohort
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Acknowledgments:

- With gratitude to the patients, their families, and caregivers and the XmAb21875-04 study team for their support in the conduct of this research.

References:

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