immunotherapy of cancer

PHASE I STUDY OF NIVOLUMAB IN COMBINATION WITH IPILIMUMAB IN METASTATIC RENAL CELL CARCINOMA (mRCC)


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Aim: Nivolumab, a fully human IgG4 PD-1 immune checkpoint inhibitor antibody, has shown durable responses and encouraging overall survival (OS) data in mRCC. IPI, a fully human monoclonal antibody to CTLA-4, improved OS in melanoma and has antitumor activity in mRCC. The combination of these agents showed encouraging antitumor activity and an acceptable safety profile in advanced melanoma. We report preliminary results of this combination in mRCC.

Methods: Patients (pts) with mRCC were randomized to nivolumab 3 mg/kg + IPI 1 mg/kg (arm N3 + I1) or nivolumab 1 mg/kg + IPI 3 mg/kg (N1 + I3) IV every 3 wk for 4 doses then nivolumab 3 mg/kg IV every 2 wk until progression/toxicity (protocol-defined post-progression treatment allowed). The primary objective was to assess safety; secondary objective was to assess efficacy (RECIST 1.1).

Results: 21 and 23 pts were randomized to the N3 + I1 and N1 + I3 arms, respectively. Most pts (n = 35; 80%) had prior systemic therapy (N3 + I1: 17; N1 + I3: 18). Treatment-related adverse events (AEs) were seen in 39 pts (89%); 8 pts (18%; N3 + I1: 2; N1 + I3: 6) discontinued due to related AEs. Grade 3–4-related AEs occurred in 20 pts (46%; N3 + I1: 6; N1 + I3: 14), most commonly lipase (21%, n = 9), ALT (14%, n = 6), diarrhea (9%, n = 4), and AST (7%, n = 3). No grade 3–4 pneumonitis was seen. Objective response rate (ORR) was 43% (N3 + I1) and 48% (N1 + I3); median duration of response (DOR) was 31.1 wk (7 ongoing) in N3 + I1 and not reached (9 ongoing) in N1 + I3 (Table). Responses occurred by first tumor assessment (wk 6) in 44% of pts in the N3 + I1 arm and 55% of pts in the N1 + I3 arm. Stable disease (SD) as best overall response was seen in 5 (24%) (N3 + I1) and 8 (35%) (N1 + I3) pts.

Table: 10500

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<tr>
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<th>Arm N3 + I1</th>
<th>Arm N1 + I3</th>
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<tr>
<td>ORR, n (%)</td>
<td>9 (43)</td>
<td>11 (48)</td>
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<td>SD, n (%)</td>
<td>5 (24)</td>
<td>8 (35)</td>
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<td>DOR, range (wk)</td>
<td>4.1 - 42.1+</td>
<td>12.1 - 35.1+</td>
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<td>Median progression-free survival, wk (95% CI)</td>
<td>36.6 (6.0, )</td>
<td>38.3 (18.3, )</td>
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Conclusions: Nivolumab + IPI showed acceptable safety and encouraging antitumor activity in mRCC, with most responses ongoing. Studies are ongoing to explore this combination in a Phase III trial.

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