1159P Phase I/II study of spartalizumab (PDR001), an anti-PD1 mAb, in patients with advanced melanoma or non-small cell lung cancer

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Background: Spartalizumab is a humanized IgG4 anti-PD1 mAb, which has previously shown favorable PK and safety, and preliminary clinical activity.

Methods: This Phase I/II, open-label, dose escalation/expansion study (NCT02404441) characterized the safety and efficacy of spartalizumab in patients (pts) with advanced solid tumors. In dose escalation, the recommended Phase II dose was declared as 400 mg Q4W (alternative: 300 mg Q3W). Here, we present expansion data for anti-PD(L)1-naïve cohorts with advanced melanoma and NSCLC. PD-L1 expression was assessed centrally (Dako PD-L1 IHC 22C3 pharmaDx).

Results: As of Nov 13, 2017, 61 pts with melanoma received 400 mg spartalizumab Q4W; 36% of pts were treatment-naïve, 20% had ≥2 prior therapies, and all were anti-PD(L)1-naïve. Suspected-related AEs (all grades, ≥5%) were fatigue (15%), decreased appetite (11%), hypothyroidism (8%), rash (8%), asthenia (7%), vitiligo (7%). ORR (confirmed responses) was 26% (16/61), including 1 CR. 41 pts (67%) had baseline PD-L1 data: 63% were PD-L1– (TPS <1%). ORR was 40% (6/15) for PD-L1 + (TPS ≥1%) and 19% (5/26) for PD-L1– pts. 118 pts with NSCLC received 400 mg Q4W (n = 59) or 300 mg Q3W (n = 59); all pts had received prior treatment, 27% had ≥2 therapies. Suspected-related AEs (≥5%) were diarrhea, nausea, decreased appetite, hypothyroidism (5% each). ORR (confirmed responses) was 9% (11/118). 77 pts (65%) had baseline PD-L1 data: 61% were PD-L1–. More Q3W than Q4W treated pts were PD-L1– (70% vs 52%). ORR was 6% (3/47) in PD-L1–, 11% (1/9) in PD-L1 1–49%, and 19% (4/21) in PD-L1 ≥50%. ORR was lower in Q3W (5%; 3/59) than Q4W treated pts (14%; 8/59) but was higher in PD-L1+ pts in both groups (Q3W: 18.2% vs 3.8%, Q4W: 15.8% vs 9.5%). PK analyses confirmed flat dosing (Q3W or Q4W) achieved drug exposure comparable with weight-based dosing.

Conclusions: Spartalizumab was well tolerated with a manageable safety profile. Efficacy was observed in pts with NSCLC (Q3W and Q4W) and melanoma (Q4W), and was as expected given the high proportion of pts with PD-L1– disease. ORRs were higher in PD-L1+ pts, corroborating previous findings that PD-L1 expression enriches for response to anti-PD1 agents in certain tumor types.

Clinical trial identification: NCT02404441, CPDR001X2101.

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