Oral Presentations

Completed clinical trial

081 IMPOWER110: INTERIM OVERALL SURVIVAL (OS) ANALYSIS OF A PHASE III STUDY OF ATEZOLIZUMAB (ATEZO) MONOTHERAPY VS PLATINUM-BASED CHEMOTHERAPY (CHEMO) AS FIRST-LINE (1L) TREATMENT IN PD-L1-SELECTED NSCLC

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Background PD-L1/PD-1 inhibitors (CPI) as monotherapy or in combination with platinum-based doublet chemo ($\pm$ bevacizumab) are 1L treatment options in metastatic NSCLC, with choice of agent(s) determined by PD-L1 expression. For patients (pts) who may be ineligible for combination therapy, CPI monotherapy remains an attractive treatment choice. IMpower110 evaluated atezo as 1L treatment in PD-L1-selected pts independent of tumor histology.

Methods IMpower110 enrolled 572 chemo-naïve pts with stage IV nonsquamous (nsq) or squamous (sq) NSCLC, PD-L1 expression $\geq 1\%$ on TC or IC, measurable disease by RECIST 1.1 and ECOG PS 0-1. Pts were randomized 1:1 to receive atezo 1200 mg IV q3w (Arm A) or platinum-based

chemo (Arm B; 4 or 6 21-day cycles). Arm B nsq pts received cisplatin (cis) 75 mg/m² or carboplatin (carbo) AUC 6 + pemetrexed 500 mg/m² IV q3w; Arm B sq pts received cis 75 mg/m² + gemcitabine (gem) 1250 mg/m² or carbo AUC 5 + gem 1000 mg/m² IV q3w. Stratification factors were sex, ECOG PS, histology and tumor PD-L1 status (TC1/2/3 and any IC vs TC0 and IC1/2/3). The primary endpoint of OS is tested hierarchically in the wild-type (WT; EGFR/ALK-negative) population (TC3 or IC3 then TC2/3 or IC2/3 then TC1/2/3 or IC1/2/3).

Results The 3 primary efficacy populations included 554 TC1/2/3 or IC1/2/3 WT pts, 328 TC2/3 or IC2/3 WT pts and 205 TC3 or IC3 WT pts. Median follow-up was 15.7 months (range, 0-35) in TC3 or IC3 WT pts. In the TC3 or IC3 WT population, atezo monotherapy improved median OS by 7.1 months (HR, 0.595; P = 0.0106) compared with chemo (table 1). The safety population comprised 286 pts in Arm A and 263 in Arm B. Treatment-related AEs (TRAEs) and Grade 3-4 TRAEs occurred in 60.5% (Arm A) and 85.2% (Arm B), and 12.9% (Arm A) and 44.1% (Arm B), respectively.

Conclusions At this interim analysis, IMpower110 met the primary endpoint of OS with statistically significant and clinically meaningful improvement in the TC3 or IC3 WT population. The safety profile favored Arm A, with no new or unexpected safety signals identified.

Trial Registration NCT02409342

Ethics Approval The trial was conducted according to the principles of the Declaration of Helsinki. All patients provided written informed consent. Protocol approval was obtained from independent review boards or ethics committees at each site.

In-progress clinical trials

082 A PHASE 1 DOSE ESCALATION STUDY OF PRS-343, A HER2/4-1BB BISPECIFIC MOLECULE, IN PATIENTS WITH HER2-POSITIVE MALIGNANCIES

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Background Anticalin® proteins are recombinantly engineered human proteins based on lipocalins. PRS-343 is a first-in-class bispecific antibody-Anticalin fusion protein targeting the oncogenic tumor antigen HER2 and the costimulatory immune receptor 4-1BB on T and other immune cells. Here, we report the results of a phase 1 single-agent dose escalation trial in patients with HER2+ solid tumors.

Methods PRS-343 has been evaluated in sequential dose cohorts from 0.0005 to 8 mg/kg i.v. Doses were administered Q3W and the 8 mg/kg dose was also given Q2W. An

Abstract 081 Table 1

	Median OS					
	Arm A (atezo)		Arm B (chemo)		HR ^a	P value ^a
	n	Months	n	Months	95% CI	
TC3 or IC3 WT	107	20.2	98	13.1	0.595 (0.398, 0.890)	0.0106
TC2/3 or IC2/3 WT	166	18.2	162	14.9	0.717 (0.520, 0.989)	0.0416
TC1/2/3 or IC1/2/3 WT	277	17.5	277	14.1	0.832 (0.649, 1.067)	0.1481 ^b

IC, tumor-infiltrating immune cells; TC, tumor cells. PD-L1 expression was centrally evaluated with the VENTANA SP142 IHC assay. TC3 or IC3 = TC $\geq 50\%$ or IC $\geq 10\%$ PD-L1+; TC2/3 or IC2/3 = TC $\geq 5\%$ or IC $\geq 5\%$ PD-L1+; TC1/2/3 or IC1/2/3 = TC $\geq 1\%$ or IC $\geq 1\%$ PD-L1+. ^aStratified. ^bOnly for descriptive purposes.

accelerated titration design was utilized for the initial dose escalation followed by a modified 3+3 design and the option to back-fill cohorts. Dose-limiting toxicities (DLTs) were reported during the first cycle of each schedule. The primary study objectives include the safety profile and RP2D of PRS-343. Secondary objectives include ORR and DCR, PD biomarker response and PK profile. PD response was assessed in tumor biopsies (CD8+ T cell IHC) pre- and post- PRS-343 treatment.

Results 51 patients (median age 61.2 years, 61% female, 82% caucasian, 57% with more than three lines of prior therapy) with a variety of solid tumor indications [gastric/GEJ (n=19); BC (n=12); gynecological cancer (n=6); CRC (n=5); BTC (n=4); UC (n=2); melanoma, pancreatic and salivary duct (n=1 each)] have been treated with PRS-343. Based on pharmacokinetic analyses and observed kinetics of the CD8+ T cell expansion post-treatment, the low end of the active dose range is considered 2.5 mg/kg. 19 patients treated at active dose levels before the data cut-off on 09-06-2019 were evaluable for response [DCR 58% (11% confirmed PR) as per RECIST 1.1]. At the active doses, we observed significant and pronounced post-treatment expansion of CD8+ T cells particularly in the tumor nests, consistent with the MoA of PRS-343, while there was no increase in the doses below 2.5 mg/kg. The post-treatment expansion of CD8+ T cells was more pronounced in patients with a confirmed PR or prolonged SD. PRS-343 was very well tolerated, with no SAEs reported. The most frequent TRAEs were fatigue (9%), chills (6%) and diarrhea (5%) of mild to moderate severity. None qualified as a DLT.

Conclusions PRS-343 is the first molecule of its kind to demonstrate encouraging evidence of safety and clinical benefit with a correlative PD effect in a heavily pre-treated population. These initial data suggest that PRS-343, the first 4-1BB bispecific to enter clinical development, merits further investigation in clinical trials.

Trial Registration NCT03330561

083

PHASE 1 STUDY OF AN ANTI-CD27 AGONIST AS MONOTHERAPY AND IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH ADVANCED SOLID TUMORS

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Background MK-5890 is a humanized agonist monoclonal antibody that binds to CD27 to provide a costimulatory signal that enhances T-cell-mediated responses. This first-in-human phase 1 study of MK-5890 evaluated the safety and efficacy of escalating doses of MK-5890 as monotherapy and in combination with pembrolizumab in patients with advanced solid tumors.

Methods Key eligibility criteria included histologically or cytologically confirmed advanced solid tumor, measurable disease by RECIST v1.1, and ECOG PS ≤1. MK-5890 was tested

alone (dose range, 2-700 mg) or with pembrolizumab (fixed dose, 200 mg). Patients with disease progression following MK-5890 monotherapy were eligible to cross over to combination treatment. The primary objective was safety and tolerability. Objective response rate by investigator per RECIST v1.1 was also evaluated. The database cutoff for this analysis was May 30, 2019.

Results Of 44 patients enrolled, 25 received MK-5890 and 19 received MK-5890 plus pembrolizumab; their median age was 59.0 years, 61.4% were female, 47.7% had ECOG PS 1, and 13.6% previously received immune checkpoint inhibitor therapy. In the initial phase, dose-limiting toxicities (DLTs) were reported in 3 patients receiving MK-5890 and 1 patient receiving MK-5890 plus pembrolizumab; all DLTs were associated with infusion-related adverse events. Maximum tolerated dose was defined. Treatment-related adverse events (TRAEs) were reported in 40 patients (90.9%): 22 patients (88.0%) receiving MK-5890 and 18 patients (94.7%) receiving MK-5890 plus pembrolizumab. The most common TRAEs were fatigue (28.0%) and infusion-related reactions (28.0%) with MK-5890 and fatigue (36.8%) and pruritus (31.6%) with MK-5890 plus pembrolizumab. Grade 3-4 TRAEs were reported in 10 patients (22.7%): 6 patients (24.0%) receiving MK-5890 and 4 patients (21.1%) receiving MK-5890 plus pembrolizumab; no grade 5 events were observed. One patient (4.0%) achieved a partial response (PR) with MK-5890 and 1 patient (5.3%) achieved a PR with MK-5890 plus pembrolizumab. Fourteen patients entered the crossover phase to receive MK-5890 plus pembrolizumab. In the crossover phase, no DLTs were reported. TRAEs were reported in 12 patients (85.7%); the most common were pruritus (21.4%), rash (21.4%), and headache (14.3%). One patient (7.1%) reported grade 3-4 TRAEs of increased amylase and increased lipase; no grade 5 events were observed. Two patients (14.3%) achieved a complete response and 2 patients (14.3%) achieved a PR.

Conclusions Treatment with MK-5890, alone and in combination with pembrolizumab, demonstrated an acceptable safety profile. Early antitumor activity was observed in patients with advanced solid tumors in both monotherapy and combination therapy arms.

085

DURABLE RESPONSES IN ANTI-PD-1 REFRACTORY MELANOMA FOLLOWING INTRATUMORAL INJECTION OF A TOLL-LIKE RECEPTOR 9 (TLR9) AGONIST, CMP-001, IN COMBINATION WITH PEMBROLIZUMAB

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Background Intratumoral (IT) injection of CMP-001, a CpG-A TLR9 agonist packaged within a virus-like particle, is designed