Background PD-L1/PD-1 inhibitors (CPI) as monotherapy or in combination with platinum-based doublet chemo (≥ bevacizumab) are 1L treatment options in metastatic NSCLC, with choice of agent(s) determined by PD-L1 expression. CPI monotherapy remains an attractive treatment choice. IMpower110 evaluated atezolizumab as 1L treatment in PD-L1–selected pts independent of tumor histology.

Methods IMpower110 enrolled 572 chemo-naive pts with stage IV nonsquamous (nsq) or squamous (sq) NSCLC, PD-L1 expression ≥ 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 chemotherapy (chemo) as first-line (1L) treatment options in metastatic NSCLC, with choice of agent(s) determined by PD-L1 expression. For zumab) are 1L treatment options in metastatic NSCLC, with PD-L1/PD-1 inhibitors (CPI) as monotherapy or combination with platinum-based doublet chemo (± bevaci-

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

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 onco-

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 onco-

Conclusions 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
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=3); 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 correlating 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

Ronnie Shapira-Frommer*, 1Marloes Gi van Dongen, 2Konstantin Dobrenkov, 3Elliot Chartash, 2Yang Liu, 3Claire Li, 2Richard Wnek, 3Manish Patel. 1Oncotherapy Institute, Sheba Medical Center, Ramat-Gan, Israel; 2Ramat-Gan, Israel; 3Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands, Amsterdam, Netherlands; 4Merck and Co., Inc., Kenilworth, NJ, USA, Kenilworth, NJ, USA; 5Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL, USA

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

Mohammed Milhem, 1Yousef Zakharia, 2Dwakar Davar, 3Elizabeth Buchbinder, 3Theresa Medina, 3Adi Daud, 4Antoni Ribas, 5Isaain Niu, 6Jeffrey Gney, 7Kim Margolin, 7Anthony Olszanski, 8Irenej Mehni, 9Takami Sato, 10Montaser Shaheen, 11Aaron Morris, 12David Mauro, 13Katie Campbell, 14Riyue Bao, 15George Weiner, 16Jason Luke, 17Arthur Krieg, 18John Kirkwood*, 1University of Iowa, Iowa City, IA, USA; 2University of Pittsburgh Medical Center, Pittsburgh, PA, USA; 3Dana Farber Cancer Institute, Boston, MA, USA; 5University of California San Francisco, San Francisco, CA, USA; 5University of California Los Angeles, Los Angeles, CA, USA; 5Banner MD Anderson Cancer Center, Gilbert, AZ, USA; 6Georgetown University, Washington, DC, USA; 6City of Hope, Duarte, CA, USA; 7Fox Chase Cancer Center, Philadelphia, PA, USA; 8Georgetown University, Philadelphia, PA, USA; 9University of Arizona, Tucson, AZ, USA; 10Checkmate Pharmaceuticals, Cambridge, MA, USA

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