KEYNOTE-365 COHORT D: PEMBROLIZUMAB PLUS ABIRATERONE ACETATE AND PREDNISONE IN PATIENTS WITH CHEMOTHERAPY-NAIVE METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (mCRPC)

¹Josep Piulats*, ²Cristiano Ferrario, ³Mark Linch, ⁴Michael Stoeckle, ⁵Brigitte Laguerre, ⁶Jose Arranz, ⁷Tilman Todenhoefer, ⁸Peter Fong, ⁹William Berry, ¹⁰Urban Emmenegger, ¹¹Loic Mourey, ¹²Nataliya Mar, ¹³Leonard Appleman, ¹⁴Anthony Joshua, ¹⁵Henry Conter, ¹⁶Xin Tong Li, ¹⁶Charles Schloss, ¹⁶Christian Poehlein, ¹⁷Johann De Bono, ¹⁸Evan Yu. ¹Catalan Institute of Oncology, Barcelona, Spain; ²Jewish General Hospital, Montreal, Canada; ³University College London Hospital, London, UK; ⁴Saarland University Hospital, Homburg, Germany; ⁵Center Eugène Marquis, Rennes, France; ⁶Hospital Universitario Gregorio Marañon, Madrid, Spain; ⁷Studienpraxis Urologie, Nürtingen, Germany; ⁸Auckland City Hospital, Auckland, New Zealand; ⁹Duke Cancer Center Cary, Cary, NC, USA; ¹⁰Odette Cancer Centre, Toronto, Canada; ¹¹Insitut Universitaire du Cancer-Oncopole, Toulouse, France; ¹²UCI Medical Center, Orange, CA, USA; ¹³UPMC, Pittsburgh, PA, USA; ¹⁴Saint Vincent's Hospital Sydney, Sydney, Australia; ¹⁵University of Western Ontario, Brampton, Canada; ¹⁶Merck and Co., Inc., Kenilworth, NJ, USA; ¹⁷The Royal Marsden NHS Foundation Trust, London, UK; ¹⁸University of Washington, Seattle, WA, USA

Background Treatment with abiraterone acetate + prednisone can improve outcomes in mCRPC patients with or without prior chemotherapy. Cohort D of phase 1b/2 study KEYNOTE-365 (NCT02861573) evaluated safety and efficacy of PD-1 inhibitor pembrolizumab + abiraterone acetate and prednisone in patients who had not received chemotherapy for mCRPC.

Methods Patients were enrolled who had not received second-generation hormonal manipulation for mCRPC or failed/were intolerant to enzalutamide for mCRPC; had progressive disease ≤6 months before screening; and had ECOG PS 0/1. Patients received pembrolizumab 200 mg IV Q3W + abiraterone acetate 1000 mg orally QD and prednisone 5 mg orally BID. Primary end points: safety, PSA response rate (PSA decrease ≥50% from baseline), and confirmed ORR per RECIST v1.1 by blinded independent central review (BICR). Secondary end points: rPFS per PCWG3-modified RECIST v1.1, DCR, DOR, and OS.

Results One hundred three patients were treated. Median (range) age was 70.0 (46–89) years, 30.1% were PD-L1+, 35.9% had RECIST-measurable disease, 18.4% had visceral disease, and 26.2% had previously received enzalutamide only. Median (range) time from enrollment to data cutoff was 17.6 (9.7–27.0) months. Confirmed PSA response rate in patients with PSA measurement at baseline (n=103) was 56.3%. For 37 patients with RECIST-measurable disease, ORR was 16.2% (1 CR; 5 PRs); 2 patients with RECIST-nonmeasurable disease had CR. In total population, 5 patients had a response ≥6 months; DCR was 44.7%. ORR for RECIST-measurable patients was 7.7% for those who previously received enzalutamide only (n=13) and 21.7% for those who had not previously received NHAs (n=23); DCR was 11.1% in all patients who previously received enzalutamide (n=27) and 57.3% in all patients who had not received NHAs (n=75). Median (95% CI) rPFS was 15.1 (9.2–NR) months; rPFS at 12 months was 54.9%. Median (95% CI) OS was NR (23.3 months–NR); OS at 12 months was 82.9%. Sixty-nine patients (67.0%) discontinued treatment, mostly because of progressive disease (37.9%). Treatment-related AEs (TRAEs) were experienced by 90.3% of patients and most common (≥15%) were ALT increase (22.3%), AST increase (17.5%), asthenia (16.5%), and diarrhea (16.5%); 36.9% experienced grade 3–5 TRAEs. There were 18.4%/12.5% grade 3 or 4 ALT/AST laboratory elevations. Five patients died of AEs; 1 was treatment related (myasthenic syndrome).

Conclusions Pembrolizumab + abiraterone acetate and prednisone demonstrated antitumor activity in patients with chemotherapy-naive mCRPC. Safety was generally consistent with individual profiles of each agent. There was an increased incidence of grade 3–4 ALT/AST laboratory elevations.

Acknowledgements Medical writing and/or editorial assistance was provided by Matthew Grzywacz, PhD, of ApotheCom (Yardley, PA, USA). This assistance was funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. Funding for this research was provided by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Trial Registration ClinicalTrials.gov, identifier: NCT02861573

Ethics Approval The study and the protocol were approved by the Institutional Review Board or ethics committee at each site.

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.351>