KEYNOTE-365 COHORT C: PEMBROLIZUMAB + ENZALUTAMIDE IN PATIENTS WITH ABRIRATONE ACETATE–PRETREATED METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (mCRPC)—DATA AFTER MINIMUM OF 22 MONTHS OF FOLLOW-UP

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Background Previous data from cohort C of phase 1b/2 study KEYNOTE-365 (NCT02861573) showed that PD-1 inhibitor pembrolizumab + enzalutamide was well tolerated and showed antitumor activity in patients with abiraterone acetate–pretreated mCRPC. Updated data after a minimum of 22 months of follow-up are presented.

Methods Patients in the prechemotherapy mCRPC state who were intolerant to ≥4 weeks’ treatment with abiraterone acetate or for whom this treatment failed, had progressive disease ≤6 months before screening, and had ECOG PS 0–2 were enrolled. Patients received pembrolizumab 200 mg IV Q3W + enzalutamide 160 mg orally QD. Primary end points were PSA response rate (decrease ≥50% from baseline), confirmed ORR per RECIST v1.1 by blinded independent central review (BICR), and safety. Secondary end points were time to PSA progression; DCR (CR or PR of any duration + SD or non-CR/non-PD ≥6 months) and DOR per RECIST v1.1 by BICR; rPFS per PCWG3-modified RECIST v1.1 by BICR; and OS.

Results Of 103 enrolled patients, 102 were treated. Median age was 70.0 years (range, 43–87); 29.4% of patients were PD-L1+; 37.3% had RECIST-measurable disease. Median follow-up (time from enrollment to data cutoff) was 40.2 months (range, 22.3–49.9). Confirmed PSA response rate in patients with baseline PSA measurement (N = 101) was 23.8%. Median time to PSA progression was 4.0 months (95% CI, 3.5–4.4). In 38 patients with measurable disease, ORR was 10.5% (2 CR; 2 PR). Median DOR was 11.8 months (4.3 to 38.3+ months); 1 patient had a response ≥12 months. DCR for the total population was 33.3%. Median (95% CI) rPFS was 6.0 months (4.1–6.3); rPFS at 12 months was 30.1%. Median (95% CI) OS was 20.1 months (16.9–25.2); OS at 12 months was 76.2%. Treatment-related AEs (TRAEs) occurred in 92.2% of patients; most common (≥20%) were fatigue (39.2%), nausea (21.6%), and rash (21.6%). Grade 3–5 TRAEs occurred in 42.2%, most commonly rash (7.8%) and fatigue (5.9%). Four patients died of AEs: 1 death was treatment-related (unknown cause).

Conclusions After a minimum follow-up of 22 months, pembrolizumab + enzalutamide continued to show antitumor activity in abiraterone acetate–pretreated mCRPC. The safety profile of pembrolizumab + enzalutamide was generally consistent with individual profiles of each agent. There was a higher incidence than typically reported for the individual agents of all-grade (21.6%) and grade 3 (7.8%) rash, which is being further evaluated in the phase 3 study KEYNOTE-641.

Acknowledgements Medical writing and/or editorial assistance was provided by Matthew Gryzwacz, 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-SITC2021.347

Abstracts