Phase 1b/2 KEYNOTE-365 cohort J: Pembrolizumab plus belzutifan or belzutifan monotherapy in patients with docetaxel-treated metastatic castration-resistant prostate cancer

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Background: The hypoxia-inducible factor-2 alpha inhibitor belzutifan has demonstrated antitumor activity and manageable safety in patients with clear cell renal cell carcinoma. The PD-1 inhibitor pembrolizumab has demonstrated antitumor activity as monotherapy and combination therapy in patients with metastatic castration-resistant prostate cancer (mCRPC). The safety and efficacy of pembrolizumab plus belzutifan and belzutifan monotherapy in patients with docetaxel-treated mCRPC is being evaluated in cohort J of the multicohort, open-label, phase 1b/2 KEYNOTE-365 study (NCT02861573).

Methods: Eligible patients are adults with confirmed adenocarcinoma of the prostate without small cell histology who have an ECOG performance status of 0 or 1 and have received docetaxel for mCRPC. Prior treatment with 1 other chemotherapy and ≤2 next-generation hormonal agents are allowed. Approximately 20 patients will receive belzutifan monotherapy 120 mg by mouth once daily. If an efficacy signal is detected with belzutifan monotherapy based on a totality of evidence, an expansion phase will commence in which up to 180 patients will be randomly assigned 1:1 to receive pembrolizumab 200 mg IV every 3 weeks for ≤35 cycles plus belzutifan 120 mg by mouth once daily or belzutifan monotherapy. Randomization will be stratified by ECOG performance status (0 vs 1). Primary end points are safety and tolerability, prostate-specific antigen (PSA) response rate (PSA decline of ≥50% from baseline), and objective response rate (ORR) per RECIST version 1.1 by blinded independent central review (BICR). Secondary end points include time to PSA progression, ORR and radiographic progression-free survival per Prostate Cancer Working Group 3-modified RECIST version 1.1 by BICR, and overall survival. Enrollment is ongoing.

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Conflicts of interest disclosure:

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