419 PEMBROLIZUMAB + LENVATINIB IN PATIENTS WITH ADENOCARCINOMA METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCRPC) OR TREATMENT-EMERGENT NEUROENDOCRINE MCRPC: PHASE 1B/2 KEYNOTE-365 COHORTS E/F

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Background Treatment of adenocarcinoma mCRPC includes abiraterone, enzalutamide, or docetaxel but is not curative, and ~20% of patients develop treatment-emergent neuroendocrine mCRPC (t-NE) after diagnosis of adenocarcinoma. Monotherapy with the PD-1 inhibitor pembrolizumab showed promising antitumor activity in the phase 2 KEYNOTE-199 trial in adenocarcinoma mCRPC. The vascular endothelial growth factor (VEGF)/fibroblast growth factor receptor (FGFR) inhibitor lenvatinib inhibits proliferation and angiogenesis in mice models. Combined PD-1 and VEGF/FGFR inhibition may have enhanced benefit in adenocarcinoma mCRPC or t-NE.

Methods The nonrandomized, open-label, multicohort, phase 1b/2 KEYNOTE-365 study (NCT02861573) will be conducted to evaluate several pembrolizumab combination therapies in patient populations with adenocarcinoma mCRPC or t-NE. In cohorts E and F each, 40–100 adults with Eastern Cooperative Oncology Group performance status score of 0/1 who received docetaxel for mCRPC will be enrolled. Prior therapy with ≤2 next-generation hormonal agents (NHAs) and 1 other chemotherapy for mCRPC is permitted. Patients in cohort E must have confirmed adenocarcinoma of the prostate without small cell histology at study entry. Patients in cohort F must have t-NE (≥1% neuroendocrine cells in a recent biopsy specimen confirmed by central histology review) that progressed within 6 months of starting an NHA for mCRPC or hormone-sensitive metastatic prostate cancer and progressed within 6 cycles of docetaxel for mCRPC. Both cohorts will receive pembrolizumab 200 mg intravenously every 3 weeks + oral lenvatinib 20 mg daily until disease progression, consent withdrawal, or other discontinuation event. Computed tomography or magnetic resonance imaging will be performed at screening, every 9 weeks through week 54, and every 12 weeks thereafter. Adverse events will be monitored through 30 days after discontinuation (90 days if serious) and graded per CTCAE v4.0. Primary end points are safety and tolerability, prostate-specific antigen (PSA) response rate, and objective response rate (ORR) per RECIST v1.1 by blinded independent central review (BICR). Secondary end points are time to PSA progression; ORR and radiographic progression-free survival (rPFS) per Prostate Cancer Working Group 3 (PCWG3)–modified RECIST v1.1 by BICR; duration of response and disease control rate per RECIST v1.1 and PCWG3-modified RECIST v1.1 by BICR; and overall survival.

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Trial Registration ClinicalTrials.gov, NCT02861573

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

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