**PEMBROLIZUMAB + VIBOSTOLIMAB IN PATIENTS WITH
ADENOCARCINOMA METASTATIC CASTRATION-
RESISTANT PROSTATE CANCER (MCRPC) OR
TREATMENT-EMERGENT NEUROENDOCRINE MCRPC:
PHASE 1B/2 KEYNOTE-365 COHORTS G/H**

¹Neal Shore*, ²Johann De Bono, ³Gero Kramer, ⁴Anthony Joshua, ⁵Xin Tong Li, ⁶Christian Poehlein, ⁷Charles Schloss, ⁸Evan Yu. ¹Carolina Urologic Research Center, Myrtle Beach, SC, USA; ²The Royal Marsden NHS Foundation Trust, London, UK; ³Medical University of Vienna, Vienna, Austria; ⁴Saint Vincent's Hospital Sydney, Sydney, Australia; ⁵Merck and Co., Inc., Kenilworth, NJ, USA; ⁶University of Washington, Seattle, WA, USA

Background Frontline treatment for patients with adenocarcinoma mCRPC includes docetaxel, radium 223, or the next-generation hormonal agents (NHAs) abiraterone or enzalutamide. For patients with disease progression on these therapies, approximately 20% will develop treatment-emergent neuroendocrine mCRPC (t-NE) after diagnosis of prostate adenocarcinoma. The PD-1 inhibitor pembrolizumab showed antitumor activity when combined with olaparib in cohort A of the phase 1b/2 KEYNOTE-365 trial, and the TIGIT inhibitor vibostolimab showed antitumor activity in preclinical models. Combining PD-1 and TIGIT inhibition may have enhanced benefit in adenocarcinoma mCRPC or t-NE.

Methods KEYNOTE-365 is a nonrandomized, open-label, multicohort study (NCT02861573) to assess several pembrolizumab combination therapies in patient populations with adenocarcinoma mCRPC or t-NE. In each of cohorts G and H, 40–100 adults with Eastern Cooperative Oncology Group performance status (ECOG PS) 0/1 who received docetaxel for mCRPC will be enrolled. Prior therapy with ≤ 2 NHAs and 1 other chemotherapy for adenocarcinoma mCRPC is permitted. Patients in cohort G must have adenocarcinoma of the prostate without small cell histology at study entry. Patients in cohort H must have t-NE ($\geq 1\%$ 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 prostate cancer and progressed within 6 cycles of docetaxel for mCRPC. All patients will receive MK-7684A, a coformulation of pembrolizumab 200 mg and vibostolimab 200 mg intravenously every 3 weeks until disease progression, consent withdrawal, or other discontinuation event. Adverse events will be monitored through 30 days after discontinuation (90 days if serious) and graded per CTCAE v4.0. Computed tomography or magnetic resonance imaging will be performed at screening, every 9 weeks through week 54, and every 12 weeks thereafter. 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 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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