459 PHASE 3 STUDY OF FIRST-LINE PEMBROLIZUMAB WITH AND WITHOUT VIBOSTOLIMAB (ANTI-TIGIT) IN PATIENTS WITH PD-L1–POSITIVE METASTATIC NSCLC

[1]Matthew Hellmann*, [2]Byoung Cho, [3]Rosalyn Juergens, [4]Ying Cheng, [5]Gilberto de Castro, [6]Mustafa Erman, [7]Jessica Bauman, [8]Toshiaki Takahashi, [9]Paul Schwarzenberger, [9]Pingye Zhang, [9]M Catherine Pietanza, [10]James Chih-Hsin Yang. *[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; [3]McMaster University, Juravinski Cancer Centre, Hamilton, ON, Canada; [4]Jilin Cancer Hospital, Changchun, China; [5]Instituto do Câncer do Estado de São Paulo, São Paulo, Brazil; [6]Department of Medical Oncology, Hacettepe University Cancer Institute, Ankara, Turkey; [7]Fox Chase Cancer Center, Philadelphia, PA, USA; [8]Shizuoka Cancer Center, Sunto-gun, Japan; [9]Merck and Co., Inc., Kenilworth, NJ, USA; [10]National Taiwan University Hospital and National Taiwan University Cancer Center, Taipei City, Taiwan, Province of China*

Background Vibostolimab (MK-7684) is a humanized monoclonal antibody (mAb) that binds to the T-cell immunoreceptor with immunoglobulin and ITIM domains (TIGIT), blocking the interaction between TIGIT and its ligands, CD112 and CD155. Pembrolizumab, an anti–PD-1 mAb, significantly improves OS versus chemotherapy in patients with PD-L1–positive advanced non–small-cell lung cancer (NSCLC). In the first-in-human study (NCT02964013), the combination of vibostolimab plus pembrolizumab had a manageable safety profile and showed promising antitumor activity in patients with advanced NSCLC naive to anti–PD-(L)1 therapy; ORR was 31% and 25% in patients with PD-L1 tumor proportion score (TPS) $\geq$1% and <1%, respectively. The current phase 3 study (NCT04738487) is comparing first-line treatment with MK-7684A, a co-formulation of vibostolimab plus pembrolizumab, versus pembrolizumab monotherapy in patients with PD-L1–positive metastatic NSCLC.

Methods This randomized, multicenter, double-blind study is enrolling adults with pathologically confirmed, previously untreated, metastatic NSCLC with PD-L1 TPS $\geq$1% (centrally confirmed). Patients must have measurable disease per RECIST v1.1, an ECOG PS of 0–1, have no *EGFR* mutations or *ALK* or *ROS1* gene rearrangements, and have no active or untreated CNS metastases. Patients are randomized 1:1 to receive intravenous treatment with vibostolimab 200 mg plus pembrolizumab 200 mg Q3W or pembrolizumab 200 mg Q3W for up to 35 cycles (approximately 2 years) or until PD, unacceptable AEs, intercurrent illness, or investigator decision. Patients who stop treatment after a CR or after completing 35 cycles and subsequently have PD can receive up to 17 additional cycles (approximately 1 year) of their randomized therapy. Randomization is stratified by ECOG PS (0 vs 1), PD-L1 TPS (1%–49% vs $\geq$50%), and region of enrollment (East Asia vs non-East Asia). The dual primary endpoints are PFS, per RECIST v1.1 by blinded independent central review (BICR), and OS. Secondary endpoints include ORR and DOR per RECIST v1.1 by BICR, patient-reported outcomes, and safety. Radiographic imaging occurs at baseline, Q9W from randomization through week 54, and then Q12W until PD, the start of new anticancer treatment, withdrawal of consent, or death. Health-related quality of life is assessed using validated patient-reported outcome instruments including the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30. AEs are graded according to National Cancer Institute Common Terminology Criteria for Adverse Events v5.0. Approximately 598 patients will be randomized. Enrollment began in April of 2021, and is ongoing at 42 sites in 11 countries.

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Trial Registration ClinicalTrials.gov, NCT04738487

Ethics Approval An independent institutional review board or ethics committee approved the protocol at each study site, and the trial is being conducted in compliance with Good Clinical Practice guidelines and the Declaration of Helsinki. All patients are required to provide informed consent prior to participation in the study.

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