

## VIBOSTOLIMAB PLUS PEMBROLIZUMAB WITH/WITHOUT DOCETAXEL VS DOCETAXEL IN NSCLC AFTER PLATINUM CHEMOTHERAPY AND IMMUNOTHERAPY

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**Background** Agents blocking interactions between the T-cell immunoreceptor with immunoglobulin and ITIM domains (TIGIT) and its ligands (CD112, CD155) have demonstrated preclinical antitumor activity. Anti-TIGIT humanized monoclonal antibody vibostolimab (MK-7684) showed promising antitumor activity and manageable toxicity in heavily pretreated patients across multiple tumor types, particularly when combined with the PD-1 inhibitor pembrolizumab (NCT02964013). Pembrolizumab has significantly improved OS versus chemotherapy in PD-L1–positive advanced non-small-cell lung cancer (NSCLC). However, many patients present with primary or acquired resistance to immunotherapy. This phase 2 study (NCT04725188) evaluates efficacy and safety of MK-7684A, a co-formulation of vibostolimab plus pembrolizumab, administered with/without docetaxel versus docetaxel alone in patients with previously treated metastatic NSCLC.

**Methods** This randomized, placebo- and active-controlled, multicenter, partial-blind study is enrolling adults with histologically/cytologically confirmed metastatic NSCLC with PD after platinum-doublet chemotherapy and 1 prior anti-PD-(L)1 therapy. Patients must have measurable disease per RECIST v1.1, ECOG PS of 0–1, and no known active CNS metastases (previously treated brain metastases allowed if radiologically/clinically stable). Tumor tissue from archival or newly-obtained core or excisional biopsies are evaluated centrally for PD-L1 expression before randomization, and local documentation of the absence of *EGFR* mutations or *ALK/ROS1* gene rearrangements must be provided. Patients are randomized 1:1:1 to receive intravenous vibostolimab (200 mg) plus pembrolizumab (200 mg) Q3W (open-label), vibostolimab plus pembrolizumab plus docetaxel (standard-of-care dose) Q3W (blinded), or docetaxel plus placebo Q3W (blinded). Randomization is stratified by ECOG PS (0/1), prior anti-PD-(L)1 therapy (immediate/no immediate prior therapy), and PD-L1 tumor proportion score (<50%/≥50%). Treatment continues for up to 35 cycles (approximately 2 years) of vibostolimab plus pembrolizumab, and per locally approved label for docetaxel, or until PD, unacceptable AEs, intercurrent illness, or investigator decision. Patients with SD/PR/CR may be eligible for up to 17 additional rechallenge cycles of vibostolimab plus pembrolizumab following BICR-verified radiographic PD by RECIST v1.1 after initial treatment or first course is completed or stopped for confirmed CR. Primary endpoint is PFS per RECIST v1.1 by BICR. Secondary endpoints are OS, ORR and DOR per RECIST v1.1 by BICR, and safety. Radiographic imaging occurs at baseline, Q6W through week 36, Q9W through week 54, and then Q12W until PD, start of new anticancer treatment, withdrawal of consent, or death. AEs are assessed by NCI CTCAE v5.0. Approximately 240

patients will be randomized. Enrollment began in April of 2021, and is ongoing at 42 sites in 10 countries.

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**Trial Registration** ClinicalTrials.gov, NCT04725188

**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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