Background Tumor Treating Fields (TTFields) therapy is a loco-regional treatment modality approved for glioblastoma and malignant pleural mesothelioma. Effectiveness of TTFields (150 kHz) therapy plus pembrolizumab in recurrent non-small cell lung cancer (NSCLC) was previously demonstrated in a phase 1/2 study. TTFields therapy plus standard of care (SOC; docetaxel or immune checkpoint inhibitors) vs SOC alone is currently being evaluated in the large phase 3 LUNAR study (NCT02973789). Given that preclinical data show that TTFields induce immunogenic cell death and enhance efficacy of PD-1 inhibitors, investigation of this combination in a clinical population is warranted.

Methods EF-36/KEYNOTE B36 (NCT04892472) is a multicenter, phase 2, open-label study evaluating efficacy and safety of TTFields (150 kHz) therapy plus pembrolizumab for first-line treatment of advanced NSCLC. The study was approved by the institutional review board/ethics committee as required for each participating site. Patients (≥ 22 years) with Eastern Cooperative Oncology Group performance status 0–1 and treatment-naïve advanced or metastatic intrathoracic, PD-L1 positive (tumor proportion score [TPS] ≥ 1%) NSCLC are eligible. Patients with epidermal growth factor receptor-sensitizing mutations or anaplastic lymphoma kinase translocation NSCLC are ineligible. Patients stratified by PD-L1 expression (TPS ≥ 50% vs TPS 1–49%) will receive TTFields therapy (18 h/day, via the NovoTTF-200T System, with pembrolizumab 200 mg intravenously every 3 weeks [Q3W]), until disease progression per Response Evaluation Criteria in Solid Tumors v1.1. Follow-up is Q3W, with computerized tomography (CT) scans Q9W. Primary endpoint is objective response rate (ORR). Secondary endpoints include overall survival (OS), progression-free survival (PFS), duration of response, disease control rate, and safety. ORR, OS, and PFS in patients with TPS ≥ 50% and TPS 1–49% are also secondary endpoints. The device manufacturer will provide patients and caregivers with technical and lifestyle integration training, and guidance on preventing and managing skin effects, via Device Support Specialists and field personnel. Usage information from the device is provided to physicians to aid discussions with patients and maximize usage. This novel support framework helps ensure patients can confidently operate the NovoTTF-200T System and integrate TTFields therapy into daily life, improving usage duration and optimizing patient outcomes. A sample size of 66 is required to achieve 80% power to detect ORR of 40% at 1-sided alpha level 0.1, using 1-sample exact test for proportion, considering < 10% loss to follow-up. Recruitment is ongoing; planned interim analysis will occur after enrollment of 15 patients with ≥ 1 follow-up CT scan.

Trial Registration NCT04892472

Ethics Approval The study was approved by the institutional review board/ethics committee as required for each participating site