TTFIELDS THERAPY WITH AN IMMUNE CHECKPOINT INHIBITOR IN METASTATIC NON-SMALL CELL LUNG CANCER (mNSCLC) WITH PROGRESSION ON/AFTER PLATINUM-BASED THERAPY: HISTOLOGY SUBGROUPS IN THE PIVOTAL LUNAR STUDY

Jeffrey Ward, Thiciana A Leal, Rupesh Kotecha, Rodrigo Ramlau, Li Zhang, Janusz Milanowski, Manuel cabo dos, Jarami Rouble, Lubo Petrubelka, Ublor Havel, Sulth Kalmadi, Zoran Andric, Thiery Bergmann, David E Gerbe, Goetz Kloecker, Rajiv Panikkar, Joachim Aerts, Angelo Delmonte, Miklos Pies, Richard Grell, Christian Rolfo, Wallace Akerley, Michael Eaton, Mussavir Iqbal, Corey Langer. University of Louisville School of Medicine, St Louis, MO, USA; Emory University School of Medicine, Atlanta, GA, USA; Miami Cancer Institute, Baptist Health South Florida, Miami, FL, USA; Poznan University of Medical Sciences, Poznan, Poland; Sun Yat-sen University Cancer Center (SYSUCC), Guangzhou, China; Medical University of Lublin, Lublin, Poland; Medical Oncology Intercenter Unit, Regional and Virgen de la Victoria University Hospitals, IBIMA, Malaga, Spain; Nemocnice ADEL Ostrava-Vítkovice, Ostrava, Czech Republic; General University Hospital in Prague, Prague, Czech Republic; Thomayer Hospital, Prague, Czech Republic; Ironwood Cancer and Research Centers, Chandler, AZ, USA; Clinical Hospital Centre Banja Luka, Banja Luka, Bosnia & Hercegovina; Jules Bordet Institute, Hôpitaux Universitaires de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium; Harold C. Simmons Comprehensive Cancer Center, UT Texas Southwestern Medical Center, Dallas, TX, USA; University of Louisville, Louisville, KY, USA; Gesingter Cancer Institute, Danville, PA, USA; The Erasmus MC Cancer Institute, Erasmus University Medical Center, Rotterdam, Netherlands; IRCSS Institute Romagnolo per lo Studio dei Tumori “Dino Amadori” (IRST), Meldola, Italy; Kantonsspital Winterthur, Winterthur, Switzerland; Saarburg Cancer Research Institute-Center for Clinical Cancer and Immunology Trials (SCRI-CCCIT); Paracelsus Medical University, Salzburg, Austria; Cancer Cluster, Salzburg, Austria; Center for Thoracic Oncology, Tisch Cancer Institute at Icahn School of Medicine, New York, NY, USA; Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; St Francis Hospital, Indianapolis, IN, USA; College of Medicine, University of Saskatchewan, Saskatoon, SK, Canada; Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA

Background Tumor Treating Fields (TTFields) are electric fields that disrupt tumor cell survival, leading to immunogenic cell death and enhanced antitumor immune responses. TTFields, delivered by a noninvasive portable device, is FDA-approved for glioblastoma and mesothelioma. The global pivotal LUNAR study (NCT02973879) demonstrated improved overall survival (OS) for TTFields combined with investigator’s choice immune checkpoint inhibitor (ICI) or docetaxel (standard of care [SOC] at time of study design) vs SOC alone in patients with mNSCLC progressing on/after platinum-based therapy (HR 0.74; P=0.035).

Methods Adults with mNSCLC progressing on/after platinum therapy were randomized 1:1 to TTFields+ICI/docetaxel or ICI/docetaxel alone. TTFields (150 kHz) were delivered continuously until progression or intolerable toxicity. An exploratory analysis examined OS by histology and safety in the ICI subgroup.

Results Of 276 randomized patients, 134 (49%) assigned to receive an ICI had median age 65 years (range 23–86); 66% were male. 94% had received only one prior line of therapy. PD-L1 tumor proportion score (TPS; available for 76 patients) showed PD-L1-positive tumors (TPS ≥1%) were balanced between non-squamous and squamous subgroups (30/50 [60%] and 18/26 [69%]). TTFields+ICI vs ICI was also balanced for histology: non-squamous (37/66 [56%] vs 37/68 [54%]) and squamous (29/66 [44%] vs 31/68 [46%]). Median OS (mOS) was 18.5 months (mo) for TTFields+ICI vs 10.8 mo for ICI alone (HR 0.63 [95% CI 0.41–0.96]; P=0.03). mOS (95% CI) for TTFields+ICI vs ICI alone in patients with non-squamous disease was 19.7 (8.8–31.1) mo vs 9.9 (5.6–22.2) mo; HR 0.63 (95% CI 0.36–1.12) P=0.11, and for squamous was 15.4 (9.6–35.4) mo vs 12.9 (9.6–19.3) mo; HR 0.69 (95% CI 0.37–1.30) P=0.25. Adverse event (AE) rates (all-cause) were comparable between TTFields+ICI (99%) and ICI alone (91%) groups, including pneumonitis (5% vs 6%) and other immune-related AEs. TTFields-related AEs occurred in 73% of ICI-treated patients; most were grade 1/2 local skin irritation; 5% reported a grade 3 AE. No grade 4 AEs or deaths were attributed to TTFields.

Conclusions Analysis of OS benefit in patients receiving TTFields with an ICI for mNSCLC after progression on or after platinum therapy did not detect a difference between squamous and non-squamous disease. OS benefit occurred without exacerbating the toxicity of ICI therapy.

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Trial Registration ClinicalTrials.gov, NCT02973879

Ethics Approval All patients provided written informed consent. The study protocol and all amendments were approved by the relevant ethics committee and competent authority at each participating site. This study conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was conducted in compliance with good clinical practice guidelines (EN ISO 14155:2011) and all relevant national/regional regulations.

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