607 **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**

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Background Tumor Treating Fields (TTFields) are electric fields that disrupt cancer cell survival, leading to immunogenic cell death and enhanced antitumor immune responses. TTFields therapy delivered by a noninvasive portable device is FDA-approved for glioblastoma and mesothelioma. The global pivotal LUNAR study (NCT02973789) 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 $\geq$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; NCT02973789

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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