TUMOR TREATING FIELDS (TTFIELDS, 150 KHZ) CONCURRENT WITH STANDARD OF CARE TREATMENT FOR STAGE 4 NON-SMALL CELL LUNG CANCER (NSCLC) IN PHASE 3 LUNAR STUDY

Background Tumor Treating Fields (TTFIELDS) are a non-invasive, anti-mitotic treatment that disrupts the formation of the mitotic spindle and dislocation of intracellular constituents. TTFIELDS plus temozolomide significantly extended survival in newly diagnosed glioblastoma. Efficacy of TTFIELDS in NSCLC has been shown in preclinical models as well as safety in combination with pemetrexed in a pilot study. In the Phase 3 LUNAR study [NCT02973789], we investigated if the addition of TTFIELDS to immune checkpoint inhibitors or docetaxel increases overall survival (OS).

Methods Patients (N=534), with squamous or non-squamous NSCLC, are stratified by their selected standard therapy (immune checkpoint inhibitors or docetaxel), histology and geographical region. Key inclusion criteria are disease progression, ECOG 0–2, no electronic medical devices in the upper torso, and absence of brain metastasis. TTFIELDS (150 kHz) are applied to the upper torso for at >18 hours/day until progression in the thorax and/or liver. The primary endpoint is superiority in OS between patients treated with TTFIELDS in combination with the standard of care treatments versus standard of care treatments alone. Key secondary endpoints compare the OS in patients treated with TTFIELDS and docetaxel versus docetaxel alone, and patients treated with TTFIELDS and immune checkpoint inhibitors vs those treated with immune checkpoint inhibitors alone. An exploratory analysis will test non-inferiority of TTFIELDS with docetaxel compared to checkpoint inhibitors alone. Secondary endpoints include progression-free survival, radiological response rate, quality of life based on the EORTC QLQ C30 questionnaire. The sample size is powered to detect a HR of 0.75 in TTFIELDS-treated patients versus control group. In March 2020, an independent Data Monitoring Committee (DMC) performed a review of the LUNAR trial data collected to that point. The DMC concluded that no unexpected safety issues could be found in patients treated with the combination of immune checkpoint inhibitors and TTFIELDS, and recommended to continue the LUNAR study as planned.

Results N/A

Conclusions N/A

Acknowledgements N/A

Trial Registration NCT02973789

Ethics Approval The study was approved by participating centers’ Institution’s Ethics Boards, NCT02973789

Consent Not applicable

REFERENCE

1. N/A

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Abstracts

Exploratory endpoints are potential correlations between biomarkers and efficacy. A stratified Cochran Mantel Haenszel method will be used to assess binary endpoints. A Kaplan-Meier method, a stratified log-rank test and a stratified Cox proportional hazards model will be used to assess survival endpoints. Planned enrollment is 406 patients. The study is actively enrolling at 52 Chinese sites.

Results N/A

Conclusions N/A

Acknowledgements N/A

Trial Registration The Clinical trials. gov no NCT04158440

Ethics Approval This study was approved by the Ethics Board of all the involved sites; Approval number of Shanghai Chest Hospital: LS1936

Consent N/A

REFERENCES


2. Hellmann MD, Chaft JE, William WN Jr, et al. Tumor-derived cell lines, SB 11285 induced cytokines, such as interferon genes, consistent with TLR7/8 engagement. CD11c+ tumor microenvironment (TME) results in durable anti-tumor effects via induction of innate and adaptive immunity. SB 11285 is a next-generation immunotherapeutic cyclic dinucleotide that activates the STING pathway leading to stimulation of tumor-resident APCs, NK cells and priming of tumor antigen-specific CD8+ T cells. Preclinically, NKTR-262 plus BEMPEG combined innate immune signaling and enhanced antigen presentation, with sustained T-cell activation, resulting in tumor growth inhibition of treated and abscopal lesions.

Background

NKTR-262 is a small-molecule agonist of toll-like receptors (TLR) 7/8. Given by intratumoral (IT) injection, NKTR-262 is retained within the tumor microenvironment (TME) and promotes an immunostimulatory milieu and tumor antigen release. Bempegaldesleukin (BEMPEG) is a CD122-preferential IL-2 pathway agonist, which increases proliferation and tumor infiltration of CD8+ T cells and natural killer (NK) cells. Preclinically, NKTR-262 plus BEMPEG combined innate immune signaling and enhanced antigen presentation, with sustained T-cell activation, resulting in tumor growth inhibition of treated and abscopal lesions.

Methods

This phase 1 dose-escalation study enrolled patients with relapsed/refractory, advanced/metastatic solid tumors (REVEAL; NCT03435640). Patients received escalating doses of NKTR-262 (0.03 mg to 3.84 mg IT) followed 3 weeks later by BEMPEG (0.006 mg/kg IV) q3wk utilizing a 3+3 design. The primary endpoint was safety and tolerability, including definition of the recommended phase 2 dose (RPD). Other endpoints included antitumor activity, pharmacodynamics, and pharmacokinetics.

Results

As of June 15, 2020, 36 patients were enrolled. One dose-limiting toxicity, transient transaminase elevation, was observed at the highest NKTR-262 dose (3.84 mg). The most frequent treatment-related adverse events were flu-like symptoms, fatigue, nausea, and pruritus, consistent with the known profile of BEMPEG. Early evidence of clinical activity was observed in patients with metastatic melanoma, with a disease control rate (partial response [PR] + stable disease) of 41.2% (7/17 patients), including two patients with PRs after progression on two prior immunotherapy regimens. Preliminary analyses showed dose-dependent induction of CXCL10 and type 1 interferon genes, consistent with TLR7/8 engagement. CD11c+ target cells were significantly more abundant in baseline melanoma biopsies than other tumor types (p<0.001). Induction