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

1Ticiana Leal*, 2Raphael Bueno, 3Libor Havel, 4Jeffrey Ward. 1Carbone Cancer Center Univ. of Wisconsin, Madison, WI, USA; 2Brigham and Women’s Hospital, Boston, MA, USA; 3Thomayer Hospital, Prague, Czech Republic; 4Washington University, Saint Louis, MO, USA

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 pemtrexed 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 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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A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED PHASE III STUDY EVALUATING PERIOPERATIVE TORIPALIMAB COMBINED WITH PLATINUM-BASED DOUBLET CHEMOTHERAPY IN RESECTABLE STAGE III NSCLC

Wenxiang Wang, 1Lin Wu*, 2Wei Zhang, 3Shun Lu, 4Haoqiu Fang, 5Guohua Yu, 6Ming Zhou, 7Wenzun Xing, 8Qian Chen, 9Xingya Li, 10Nong Yang, 11Minhua Ye, 12Wentao Fang, 13Yunchao Huang, 14Jichen Liu, 15Jiye Tan, 16Xiaohong Hang, 17Wengang Zhang, 18Luei Zhang, 19Jun Chen, 20Xun Zhang, 21Yu Zhang, 22Jie Jiang, 23Aihong Zhong, 24Shanqing Li, 25Yunpeng Liu, 26Guowu Wu, 27Xiaoyan Kang, 28Ying Tian, 29Tao Xu. 1Hunan cancer hospital, Changsha, China; 2The First Affiliated Hospital Of Nanchang University, Nanchang, China; 3Shanghai Chest Hospital Shanghai Jiaotong University, Shanghai, China; 4Anhui Chest Hospital, Hefei, China; 5Welfare People’s Hospital, Wefang, China; 6Cancer Center of Guangzhou Medical University, Guangzhou, China; 7Henan Cancer Hospital, Zhengzhou, China; 8Cancer Hospital of the University of Chinese Academy of Sciences (Zhong Hai Cancer Hospital), Hangzhou, China; 9The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; 10Taichou Hospital Of Zhejiang Province, Taizhou, China; 11Yunnan Cancer Hospital, Kunming, China; 12The Second Affiliated Hospital Of Nanchang University, Nanchang, China; 13Zhongshan Hospital, Shanghai, China; 14Affiliated Hospital Of Jianguan University, Wuxi, China; 15Tonghua Central Hospital, Tonghua, China; 16The First Affiliated Hospital Of Xinjiang Medical University, Urumqi, China; 17Tianjin Medical University General Hospital, Tianjin, China; 18Tianjin Chest Hospital, Tianjin, China; 19Nanjing Chest Hospital, Nanjing, China; 20The First Affiliated Hospital Of Xiamen University, Xiamen, China; 21Fuzhou Pulmonary Hospital Of Fujian, Fuzhou, China; 22Peking Union Medical College Hospital, Peking, China; 23The First Affiliated Hospital Of China Medical University, Shenyang, China; 24Mehou People’s Hospital, Meizhou, China; 25Shanghai Junshi Biosciences Co., LTD, Shanghai, China

Background Surgery remains the mainstay of treatment for resectable stage III non-small cell lung cancer (NSCLC). The preliminary results from some pilot trials have shown that neoadjuvant immunotherapy in NSCLC is safe and tolerable. 1Hypothesizing that neoadjuvant toripalimab (a humanized anti-PD-1 antibody) plus chemotherapy can improve the outcome in resectable NSCLC, we are conducting a randomized, double-blind, placebo-controlled, phase III study to evaluate the efficacy and safety of toripalimab plus platinum-based doublet chemotherapy as neoadjuvant/adjuvant therapy for patients with resectable stage III NSCLC.

Methods This ongoing study enrolls patients aged 18–70 years with treatment-naive, histopathologically confirmed resectable stage III NSCLC without EGFR mutation or ALK translocation, ECOG PS 0–1, and adequate organ function. Eligible subjects are randomized (1:1) into experimental or control group, to receive perioperative toripalimab 240 mg or placebo combined with chemotherapy for 4 cycle in total (Docetaxel 60–75 mg/m2 or Paclitaxel 175 mg/m2 with platinum [squamous histology] or Pemetrexed 50 mg/m2 with platinum [non-squamous histology]) every 3 weeks for 6 cycles. One more cycle after surgery, then one more cycle after surgery, then monotherapy of toripalimab 240 mg or placebo every 3 weeks up to 13 cycles is delivered. Adjuvant radiotherapy is allowed. Randomization is stratified by tumor stage (IIIA vs IIIB), pathological type (squamous vs non-squamous), PD-L1 expression (PD-L1>1% vs <1% or not evaluable) and planned surgical procedure (pneumonectomy vs lobectomy). Radiographic response is assessed within 4–6 weeks after last dose of neo-adjuvant therapy, at 30 days after surgery and every 12 weeks thereafter. Primary endpoints are major pathologic response (MPR) rate evaluated by blind independent central pathology review (BIPR-MPR) and event-free survival evaluated by investigator (INV-EFS). Secondary endpoints include pathologic complete response (pCR) rate evaluated by BIPR and investigators (BIPR-pCR and INV-pCR), disease-free survival (DFS), 2–3 years OS rate, OS, safety, and feasibility of surgery.

REFERENCES

1. N/A

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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

Background Activation of the Stimulator of Interferon Genes (STING) pathway within immune and tumor cells of the tumor microenvironment (TME) results in durable anti-tumor effects via induction of innate and adaptive immunity. SB 11285 is a next-generation immunomodulatory 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. In preclinical studies using multiple tumor types (such as Melanoma, Head and Neck Squamous Cell Carcinoma) at the RP2D in combination with atezolizumab. SB 11285 will be administered as monotherapy weekly on Days 1, 5, 8, and 15, and 22 of repeated 28-day cycles in escalating doses and in combination with atezolizumab administered Q4W.

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. Bempagoladesleukin (BEMPREG) 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 BEMPREG 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 BEMPREG (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 (RP2D). 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 BEMPREG. 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% 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