

INTERIM RESULTS FROM A PHASE IB, FIRST-IN-HUMAN STUDY OF A NOVEL COMPLEMENT FACTOR H INHIBITOR (GT103) IN PATIENTS WITH REFRACTORY NON-SMALL CELL LUNG CANCER (NSCLC)

¹Jeffrey Clarke*, ¹Thomas Stinchcombe, ¹Jeffrey Crawford, ²Hirva Mamdani, ¹Lin Gu, ¹Neal Ready, ¹Andrew Nixon, ¹Stephen Baleviic, ¹Michael Campa, ¹Liz Gottlin, ¹Ryan Bushey, ¹James Herndon, ¹Scott Antonia, ³Edward Patz, ⁴George Simon. ¹Duke University Medical Center, Durham, NC, USA; ²Maranos Cancer Institute, Detroit, MI, USA; ³Grid Therapeutics; Duke University, Durham, NC, USA; ⁴H Lee Moffitt Cancer Center, Tampa, FL, USA

Background Complement factor H (CFH) modulates immune self-recognition and complement mediated cytotoxicity by regulating the alternative pathway of the complement cascade. Overexpression of CFH can facilitate immune evasion and is associated with poor prognosis in NSCLC. Discovery of CFH autoantibodies in patients with early-stage lung cancer led to the development of GT103, a first-in-class IgG3 monoclonal antibody inhibitor of CFH which has demonstrated preclinical anti-tumor activity.

Methods We conducted a multi-institutional, first-in-human, phase Ib study of GT103 in patients with advanced, refractory NSCLC. A standard '3+3' dose escalation schema was utilized with four dose levels of GT103 (0.3, 1, 3, 10 mg/kg) administered IV every 3 weeks until disease progression or unacceptable toxicity. The dose limiting toxicity (DLT) observation period included cycle 1 and radiographic disease assessment using RECIST 1.1 was performed before every third cycle. Three additional patients were enrolled at the highest dose level to confirm the maximum tolerated dose. We present the interim results of the dose escalation portion of the trial.

Results Twenty-one patients were enrolled and received protocol treatment. Median age was 63 years (range 50-78). All 21 patients had stage 4 disease, 81% had received prior immunotherapy, 8 patients (38%) had known brain metastases, and a majority of patients had adenocarcinoma histology (67%). Median number of prior lines of therapy was 3 (range 2-8). DLT was observed in 2 patients; one patient at the 0.3 mg/kg dose level experiencing grade 3 acute kidney injury and one patient at 1 mg/kg dose level experiencing grade 2 colitis. No DLT was observed at the 3 and 10 mg/kg dose levels. Six patients (28%) experienced grade 2 or higher treatment-related adverse events. In addition to DLTs, treatment related grade 2-3 adverse events included grade 2 anorexia (n=1), grade 2 colitis (n=1), grade 2 and grade 3 lymphopenia (n=2), grade 2 creatinine increase (n=1), and grade 2 psoriasis flare (n=1). Stable disease was demonstrated in 5/21 (24%) patients and no objective responses were seen. The median progression-free survival observed was 42 days (95% CI: 40-NE) and the median number of cycles of treatment received was 2 (range 1-8). Updated pharmacokinetic data and correlative analyses of circulating biomarkers will be presented at time of the meeting.

Conclusions GT103 was well tolerated during dose escalation including at the 10 mg/kg level and demonstrated an acceptable safety profile in refractory NSCLC population. A separate phase 2 study of combination GT103 with anti-PD1 therapy is planned in NSCLC.

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Trial Registration ClinicalTrials.gov Identifier: NCT04314089

Ethics Approval All participants underwent informed consent and the study was approved by Duke University IRB with approval number Pro00104564.

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