PHASE I INTERIM STUDY RESULTS OF NOUS-209, AN OFF-THE-SHELF IMMUNOTHERAPY, WITH PEMBROLIZUMAB, FOR THE TREATMENT OF TUMORS WITH A DEFICIENCY IN MISMATCH REPAIR/ MICROSATELLITE INSTABILITY (dMMR/MSI)

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Background Defective DNA mismatch repair (dMMR) leads to high levels of microsatellite-instability (MSI-H) and insertions or deletions in coding regions, resulting in the generation of tumor-specific frameshift peptides (FSPs). We selected 209 shared FSPs among subjects with first- or second-line metastatic dMMR/MSI-H colorectal (CRC), gastric, and gastroesophageal junction (GEJ) cancers, to develop an off-the-shelf vaccine for the treatment of dMMR/MSI-H tumors. Selected FSPs were cloned into four proprietary Great Apes Adenoviral (GAd) and four Modified Vaccinia Ankara (MVA) vectors to generate a polyvalent viral vectored vaccine called Nous-209 [Leoni G., et al., Cancer Res. 2020]

Methods This phase 1 first in human (FIH) study (NCT04041310) was designed to evaluate safety and tolerability of two dose levels (one log difference for both GAd and MVA) of Nous-209 genetic polyvalent vaccine in combination with the programmed death receptor-1 (PD-1)-blocking antibody pembrolizumab, to assess immunogenicity of the combination and to detect preliminary evidence of anti-tumor activity. Nous-209 is administered intramuscularly, concomitantly with pembrolizumab (doses and schedule per approved label): one prime (GAd-209-FSP) at the 2nd pembrolizumab infusion and three booster (MVA-209-FSP) injections at subsequent infusions each 3 weeks apart. The study is composed of two sequential cohorts: dose escalation and dose expansion

Results Twelve evaluable subjects with first- or second-line metastatic dMMR/MSI-H cancers were evaluated as of May 28, 2021. Three subjects enrolled in dose level 1 (2 CRC and 1 GEJ cancer) demonstrated durable confirmed partial responses (PRs). In dose level 2 (6 CRC and 3 gastric cancers), 4 subjects had PRs, 2 had stable disease (SD) and 3 had progressive disease (PD). The median follow-up for subjects in dose level 1 is 17.9 months (range 15.3–20 months), and 8 months (range 3.8–12.5 months) for subjects in dose level 2 as of the above cut-off date. No dose limiting toxicities (DLTs) were observed, and the treatment combination was determined to be safe and tolerable. Vaccine immunogenicity was demonstrated by ex-vivo interferon-gamma ELISpot assay in 67% of subjects in dose level 1, and 100% of patients with evaluable samples in dose level 2

Conclusions The combination of the Nous-209 genetic polyvalent cancer vaccine and pembrolizumab has been demonstrated to be safe, immunogenic, and continues to show early signs of clinical efficacy, which may be attributed to the vaccine contribution

REFERENCE

- 1.. Leoni G, et al. A genetic vaccine encoding shared cancer neoantigens to treat tumors with microsatellite instability. *Cancer Res* 2020 July 20;80(18):3972–3982.

Ethics Approval The study was approved by The University of Texas MD Anderson Cancer Center, IRB number 2019–0651_MOD001. The study was approved by Feinstein Institute for Medical Research Northwell Health, IRB number 19–1086. The study was approved by WCG The Trusted Partner in Ethical Review, IRB number 20200155. The study was approved by Johns Hopkins Medicine, IRB number IRB00220323/CIR00053809. The study was approved by City of Hope, IRB number 19277/176947. The study was approved by Advarra Advancing Better Research. The study was approved by Dana-Faber Cancer Institute. The study was approved by Weill Cornell IRB. The study was approved by Roswell Park IRB.

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