IRENE study: Phase 2 study of INCMGA00012 (retifanlimab) and the oncolytic virus pelareorep in metastatic triple negative breast cancer

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BACKGROUND

• Triple negative breast cancer (TNBC) is an aggressive subtype accounting for 15% of all breast cancer cases. Treatment with immunotherapy in combination with Abraxane, a taxane-based chemotherapy, is of benefit only in PD-L1 positive tumors, which represents a minority of patients.

• Pelareorep, a proprietary isolate of the unmodified, replication competent reovirus type 3 Dearing (T3D), has been shown to upregulate PD-L1 expression in tumor and inflammatory cells and downregulate intra-tumoral regulatory T-cells in the tumor microenvironment in pre-clinical and early clinical studies. Retifanlimab is a PD-1 inhibitor currently in development.

• The rationale for this clinical study is that the administration of pelareorep will prime the tumor microenvironment for enhanced tumor response to PD-1 inhibitor retifanlimab.

TRIAL DESIGN

• This is a phase II multi-site single-arm investigator-initiated clinical trial.

• Eligible patients will receive pelareorep 4.5x1010 TCID50 /day IV, on Days 1, 2, 15 and 16 and retifanlimab 500mg IV on day 3 of every 28-day cycle until disease progression or unacceptable toxicity.

• Tumor tissue, stool and blood samples will be collected while on treatment to evaluate changes in PD-L1 expression, gut microbiome and inflammatory cells induced by the study drugs. (ClinicalTrials.gov Identifier: NCT04445844)

ELIGIBILITY CRITERIA

Inclusion Criteria

• Metastatic TNBC who have previously received 1-2 prior lines of chemotherapy in the metastatic setting

• Measurable disease based on RECIST v1.1

• Age≥18year with ECOG performance status of 0 or 1 with life expectancy ≥ 3 months with adequate organ function.

• Subjects with CNS metastases treated with radiation therapy (WBXRT or SRS) are eligible if stable, > 28 days following completion of XRT.

EXCLUSION CRITERIA

• Subjects who have received 3 or more lines prior treatment in the metastatic setting

• Prior therapy with Pelareorep.

• History of immunodeficiency, interstitial lung disease, active pneumonitis or receiving chronic systemic steroids.

• Known history of HIV, hepatitis B or Hepatitis C infection.

ENDPOINTS

Primary Endpoints:

• Objective Response Rate (ORR) per RECIST v1.1

• Safety, tolerability and feasibility, determined by the number, frequency, duration, and severity of AEs using CTCAE v5.0;

Secondary Endpoints:

• Progression Free survival (PFS)

• Overall Survival (OS)

• Duration of Response (DOR)

Exploratory Endpoints:

• Assess changes in PD-L1 expression pre and post treatment and correlate with treatment response.

• Assess the role of TCR sequencing in predicting treatment response.

STATISTICAL DESIGN

• Simon's optimal 2-stage design will be used to calculate sample size. In the first stage, 14 patients will be accrued. If there are 1 or fewer responses in these 14 patients, the study will be stopped. Otherwise, 11 additional patients will be accrued for a total of 25 patients. The null hypothesis will be rejected if 4 or more responses are observed in 25 patients. The first 6 patients will be enrolled in a staggering interval for the safety run-in phase of the study.

ACCURAL

• The study will enroll up to 25 patients at Rutgers Cancer Institute of New Jersey and Ohio State University Comprehensive Cancer Center.

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