IRENE study: Phase 2 study of INCMGA00012 (retifanlimab) and the oncolytic virus pela**reo**rep in metastatic triple **ne**gative breast cancer

Mridula George[1], Nicole Williams[2], Maryam Lustberg[2], Coral Omene[1], Nancy Chan[1], Nisha Ohri[1], Maria Kowzun[1], Lindsay Potdevin[1], Firas Eladoumikdachi[1], Shicha Kumar[1], Robert Wesolowski[2], Grey Wilkinson[3], Danielle Tang[1], Sinae Kim[4], Shridar Ganesan[1], Bruce Haffty[1] and Deborah Toppmeyer[1].

[1]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; [2]Ohio State University Comprehensive Cancer Center, Columbus, OH; [3]Oncolytics Biotech, Calvary, AB, Canada; [4]Rutgers School of Public Health, New Brunswick, NJ

BACKGROUND

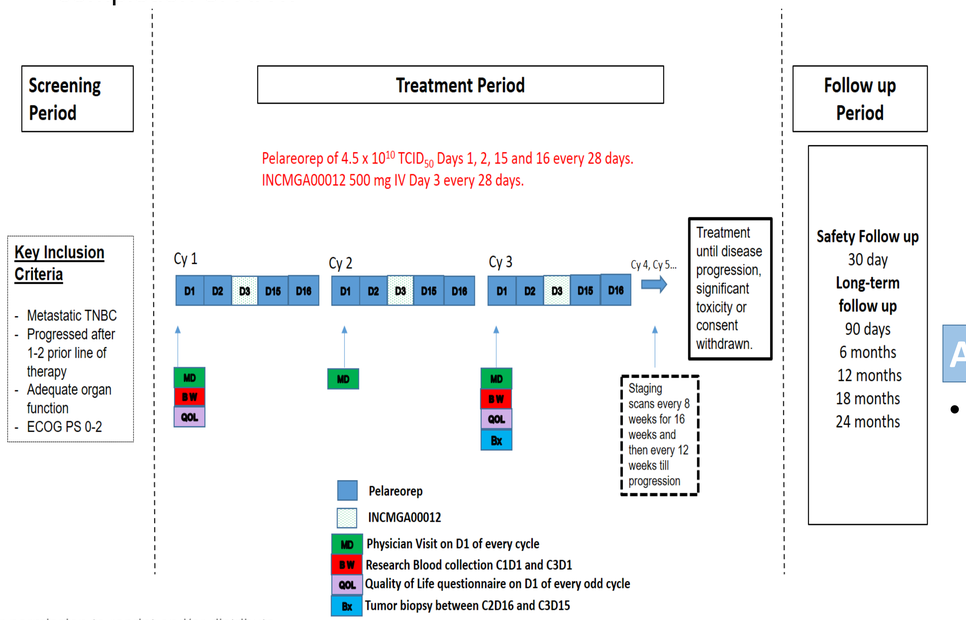
- Triple negative breast cancer (TNBC) is an aggressive subtype accounting for 15% of all breast cancer cases. Treatment with immunotherapy in combination with Abraxane, a taxane-based chemotherapy, is of benefit only in PD-L1 positive tumors, which represents a minority of patients.
- **Pelareorep**, 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	Exclusion Criteria
• Metastatic TNBC who have previously received 1-2 prior lines of chemotherapy in the metastatic setting	• Subjects who have received 3 or more lines prior treatment in the metastatic setting
• Measurable disease based on RECIST v1.1	• Prior therapy with Pelareorep.
• Age>18year with ECOG performance status of 0 or 1 with life expectancy ≥ 3 months with adequate organ function.	• History of immunodeficiency, interstitial lung disease, active pneumonitis or receiving chronic systemic steroids.
• Subjects with CNS metastases treated with radiation therapy (WBXRT or SRS) are eligible if stable, > 28 days following completion of XRT.	• 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.

ACCRUAL

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

Presenting Author: Mridula A. George. Email: mridula@cinj.rutgers.edu