BRACELET-1 (PrE0113): A study to assess overall response rate by inducing an inflammatory phenotype in metastatic breast cancer with the oncolytic reovirus pelareorep in combination with anti-PD-L1 avelumab and paclitaxel

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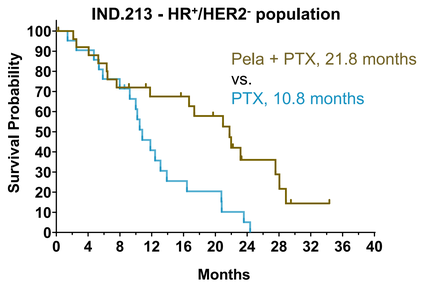
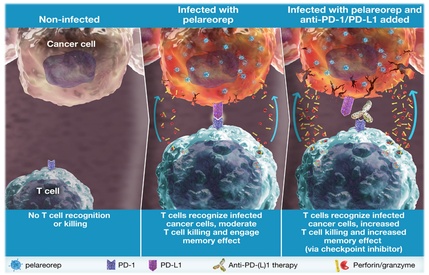
Background

- In a previous randomized phase 2 study (IND.213), intravenous treatment with the oncolytic virus, pelareorep (pela), in combination with paclitaxel (PTX) demonstrated a statistically significant improvement in overall survival (OS) from 10.4 months with PTX alone (n = 38) to 17.4 months with pela + PTX (n = 36, HR 0.65, 80% CI 0.46-0.91, p = 0.1) in metastatic breast cancer (mBC) patients[1].
- The greatest benefit in OS was seen in patients with hormone receptor-positive (HR$^+$)/human epidermal growth factor receptor 2-negative (HER2$^-$) disease where median OS was 21.8 months with pela + PTX (n = 26) compared to 10.8 months with PTX alone (n = 21, HR = 0.36; p= 0.003)[2].



- The addition of pela to PTX did not improve progression-free survival or tumor response suggesting its impact on OS was due to establishment of an adaptive immune response and raising the possibility of synergy with checkpoint blockade
- A subsequent window of opportunity study in early breast cancer with pela and anti-PD-L1 therapy has shown that pela can indeed promote an adaptive immune response in breast cancer tissue, enhancing CD8$^+$ T cell infiltration and upregulating PD-L1 expression, synergizing with checkpoint blockade therapy[3].

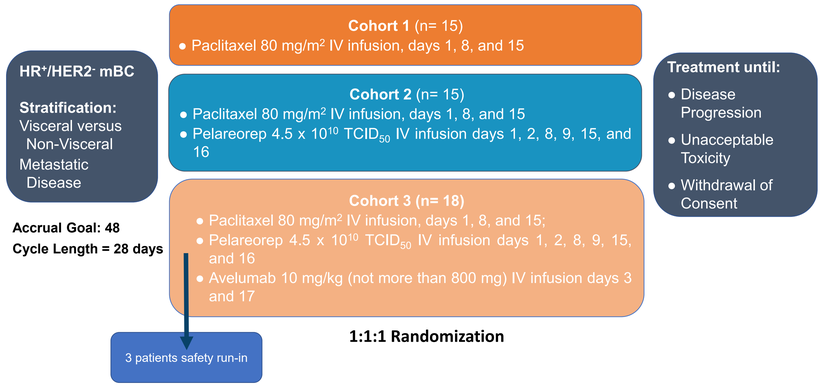


Pelareorep Mechanism of Action: Pela selectively infects cancer cells leading to tumor cell lysis. The virus also mediates anti-tumor immunity by activating both innate and adaptive immune response. Pelareorap can also increase the expression of PD-L/ PD-L1 on infected cancer cells and promote CD8$^+$ T cell trafficking to the tumor microenvironment.

- Moreover, high levels of peripheral T cell clonality (PTCC) have been identified as a candidate blood-based on-treatment biomarker for pela therapy in combination with checkpoint blockade therapy, further highlighting the role of an adaptive immune response in driving pelareorep mediated efficacy[3-4].

Study design

Study Schema



BRACELET-1 is an open-label randomized phase 2, three-cohort study in HR$^+$/HER2$^-$ mBC. Patients must be refractory to endocrine therapy and have received prior treatment with a CDK4/6 inhibitor.

Study cohorts include: Cohort 1, a control group receiving PTX (n = 15); Cohort 2, treatment with pelareorep added to PTX (n = 15); Cohort 3, treatment with pelareorep, PTX, and avelumab (n = 18). The study includes a three patient safety run-in for Cohort 3.

BRACELET-1 will test the hypothesis that pelareorep mediated priming of an adaptive immune response will be synergistic with checkpoint blockade therapy in HR$^+$/HER2$^-$ mBC. Moreover, BRACELET-1 will further assess PTCC as an on-treatment biomarker. The overall goal of this study is to expand the number of mBC patients who can benefit from immunotherapy.

Study Objectives

- Evaluation of efficacy in terms of overall response rate (ORR) at week 16, according to RECIST v1.1.
- Examination of the safety of the study treatments (adverse events, lab parameters and treatment dose modifications and reasons of discontinuation).
- Examination of biomarkers to determine the immunological changes within the tumor microenvironment (TME) and peripheral blood in patients treated with paclitaxel alone, in combination with pelareorep, and in combination with pelareorep and avelumab.

Study information

Key inclusion criteria

- ✓ Metastatic breast cancer patients with ER$^+$ and/or PgR$^+$ and HER2$^-$ disease
- ✓ Patients must have progressed on at least 1 hormone-based therapy with a CDK4/6 inhibitor.
- ✓ ECOG performance status ≤1
- ✓ Measurable disease as defined by RECIST Version 1.1

Key exclusion criteria

- × No prior chemotherapy in the metastatic setting
- × No prior therapy with checkpoint inhibitors, agonists and other active immunotherapy in breast cancer
- × No major surgery within 21 days prior to beginning study
- × No radiation treatment within 14 days of beginning study
- × No history of autoimmune disease

Current active sites

Center	Location	Investigator
Carle Cancer Center	Urbana, Illinois	Kendrith Rowland, MD
Fox Chase Cancer Center	Philadelphia, Pennsylvania	Elias Obeid, MD
Indiana University Melvin and Bren Simon Comprehensive Cancer Center	Indianapolis, Indiana	Kathy Miller, MD
Montefiore Medical Park	Bronx, New York	Della Makower, MD
Ochsner Clinic Foundation	Jefferson, Louisiana	John Cole, MD
Ohio State University Comprehensive Cancer Center	Columbus, Ohio	Sagar Sardesai, MD
Rutgers Cancer Institute of New Jersey	New Brunswick, New Jersey	Mridula George, MD
Thomas Jefferson University Hospital, Sidney Kimmel Cancer Center	Philadelphia, Pennsylvania	Maysa Abu-Khalaf, MD
University of Miami Sylvester Comprehensive Cancer Center	Miami, Florida	Elisa Krill-Jackson, MD
University of South Alabama Mitchell Cancer Institute	Mobile, Alabama	Teja Poosarla, MD
University of Rochester Medical Center	Rochester, New York	Carla Falkson, MD
West Virginia University	Morgantown, West Virginia	Mohamad Salkeni, MD

Anticipated number of sites: 20
Protocol Number: registered on clinicaltrials.gov: NCT04215146
Status: The study is currently recruiting patients. The 3 patient safety run-in, in cohort 3 has been completed with no safety concerns identified. Therefore, the study is currently recruiting patients in all cohorts.
Current enrollment = 3; Target enrollment = 48.
Conducted through: PrECOG, LLC and Oncolytics Biotech, Inc.
Study contact information: PrE0113@precogllc.org

References

[1] Bernstein et al. Breast Cancer Res Treat, 2018. 167(2): p. 485-493.
[2] Gutierrez, A.A., et al. Annals of Oncology. 28 (suppl_5): v403-v427. 10.1093/annonc/mdx376, 2017.
[3] Manso et al. Annals of Oncology (2020) 31 (suppl_2): S15-S41.
[4] Mahalingam et al. Clinical Cancer Research (2020) 26, 71-81.