The oncovirous pelareorep primes the tumor microenvironment for checkpoint blockade therapy in early breast cancer patients

**RESULTS**

**T cell Repertoire Turnover**

**In all treated subjects** (Fig 2)

- A statistically significant increase in tumor and peripheral blood T cell diversity was seen post-treatment compared to baseline (Fig 3a).
- Diversity was also associated with a unique phenotype: rearrangements in a sample after contemporaneously decreasing to a common number of T cells to control for size and T-cell fraction. Lower values in diversity are associated with more expanded clones, while higher values indicate fewer expanded clones.

**CONCLUSION**

- Previous we showed that Cohort 2 met the study’s success criterion of ≥30% increase in CelTIL score in at least 50% of the patients.
- These data illustrate pela’s ability to induce an inflamed tumor phenotype and demonstrate its synergy with atezo. Moreover, they support the development of combo therapy for early breast cancer patients.

**References**

1. [Citation 1]
2. [Citation 2]
3. [Citation 3]

**STUDY DESIGN & METHODS**

- **AWARE-1** is a window-of-opportunity study designed to evaluate the safety and effect of pela on tumor microenvironment (TME) and peripheral blood T-cell populations in 28 women with early BC (HR+ HER2- – patients in Cohorts 1 and 2 fully enrolled), 6 patients in ER-, HER2+ population (on-going) (Fig 2)

**STUDY OBJECTIVES**

- **Primary objective:** To evaluate CelTIL score 3 weeks following initiation of treatment in each cohort.
- **Secondary objective:** To evaluate immunological changes within the tumor and peripheral blood.

**BACKGROUND**

- **Pelareorep** is an oncovirous (V17) delivered and systemically available oncolytic reovirus that can replicate in tumor tissue and induce a T cell inflamed phenotype. Previously reported data from AW AWARE-1 showed that pela combined with atezolizumab (atezo) resulted in CelTIL score increases of >30% in 60% of HR+/HER2- early BC patients, thereby meeting the study's primary endpoint. Patients who received pela without atezo showed increase of >30% in CelTIL score in 40% of patients.

- **Increased CelTIL scores were accompanied by a favorable immunologic response in both the tumor and the blood**. We hypothesized that the CelTIL score increases were associated with a unique phenotype indicating a more expanded clone diversity post-treatment.

**RESULTS**

- **In all treated subjects** (Fig 2)
  - A statistically significant increase in tumor and peripheral blood T cell diversity was seen post-treatment compared to baseline (Fig 3a). Diversity was also associated with a unique phenotype: rearrangements in a sample after contemporaneously decreasing to a common number of T cells to control for size and T cell fraction. Lower values in diversity are associated with more expanded clones, while higher values indicate fewer expanded clones.

**Figure 1:** Pelareorep mechanism of action. Pelareorep infects cancer cells leading to tumor cell lysis. This also activates and modifies tumor immunity by activating both innate and adaptive immune responses. We hypothesized that the pelareorep mediated immune responses would boost anti-CelTIL responses.

**Figure 2:** AWARE-1 study design

**Figure 3:** Comparative analysis of cohort 1 vs. cohort 2 (Fig 4)

- The addition of atezolizumab enhanced pela’s ability to generate and expand new T cell clones.
- A greater decrease in pre- vs. post-treatment changes in diversity (pre- vs post-treatment) (Fig 3b)

**Figure 4:** Pelareorep mechanism of action

- The oncolytic virus pelareorep primes the tumor microenvironment for checkpoint blockade therapy in early breast cancer patients.