ANALYSIS OF THE HR+/HER2- BREAST CANCER TUMOR MICROENVIRONMENT FOLLOWING IMMUNE PRIMING WITH PELAREOREP AND ATEZOLIZUMAB USING IMAGING MASS CYTOMETRY – RESULTS FROM THE AWARE-1 TRIAL

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Background Pelareorep (pela) is an intravenously delivered, non-modified oncolytic reovirus that shows anti-tumor activity through innate and adaptive immune responses as well as direct tumor lysis. Previous data from the window of opportunity AWARE-1 study demonstrated synergy between pela in combination with atezolizumab, demonstrating a favorable immunologic response in tumors from early breast cancer (eBC) patients.1 To understand the complex tumor microenvironment (TME) and immune responses in patients before and after treatment, we used imaging mass cytometry (IMC) to perform single cell, highly multiplexed, analysis of their tissue samples.

Methods Newly diagnosed HR+/HER2- eBC patients were enrolled into two cohorts: Cohort 1: pela + letrozole (n=10); and Cohort 2: pela + letrozole + atezolizumab (n=10). Pela was administered on days 1, 2 and 8, 9, and atezolizumab was given on day 3. Tumor biopsies (FFPE samples) collected pre-treatment (D1) and on days 3 (D3, prior to atezolizumab administration) and approximately on day 21 (when tumors were surgically removed) were examined by IMC. A marker panel of 37 antibodies conjugated to a unique metal isotope was assembled. Pixel-based classification was performed in Ilastik to generate cell probability masks and processed in Cellprofiler. RStudio was used to phenotype the data with PhenoGraph. Expression and neighborhood analysis was generated in RStudio.

Results Preliminary analysis with IMC reveals significant enrichment of cytotoxic T cells between D3 and surgery and between D1 and surgery. The Ki67+ subset of tumor shows a significant decrease in abundance between D1 and D3, D3 and surgery, and D1 and surgery. The general tumor subset shows a significant decrease in abundance between the D3 and surgery timepoints. Expression of PD-L1 significantly increases between the screening and D3 timepoints and significantly decreases between the D3 and surgery timepoints, conceivably explained by the immune-mediated destruction of tumor cells. Nearest neighbor distance analysis shows that cytotoxic T cells are significantly closer to tumor when comparing the screening and surgery timepoints.

Conclusions In accordance with the prior AWARE-1 results, IMC demonstrated an enhanced immune state of the tumors after treatment. IMC allows us to analyze the potent immune response and cellular interactions in the TME and characterization of these complex interactions provides a better understanding of the key mechanisms of action of these treatments in order to plan future clinical trials.

REFERENCES

1. Loghmani et al. SABCS 2022

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0582