THE ONCOLYTIC VIRUS PELAREOREP IN COMBINATION WITH IMMUNE CHECKPOINT INHIBITOR ACTIVATES T-CELL FUNCTIONING IN EARLY BREAST CANCER PATIENTS – IMMUNOPHENOTYPE RESULTS FROM AWARE-1 STUDY

Background Pelareorep (pela) is an intravenously delivered unmodified oncolytic reovirus demonstrating anti-tumor activity through innate and adaptive immune responses. Previous data from the window of opportunity AWARE-1 study demonstrated that pela, alone or in combination with atezolizumab (atezo), establishes a favorable immunologic response in tumors from HR+/HER2- early breast cancer (BC) patients. Here, we report additional translational flow cytometry results from peripheral blood of patients participating in the AWARE-1 trial.

Methods Treatment naïve HR+/HER2- early BC patients were enrolled in two cohorts: Cohort 1 (C1) – pela + letrozole (n=10); and Cohort 2 (C2) – pela + letrozole + atezo (n=10). Pela was administered on days 1, 2 and 8, 9, while atezo was administered on day 3. Blood samples were collected pre-treatment and on days 3 and 21. In this context, we investigated the immune cell composition of peripheral blood using a multicolor flow cytometry to describe different subsets of immune cells.

Results Flow cytometry analysis showed a significant increase in natural killer cells on day 21 in C2 compared to C1 (~2-fold, p value=0.0166). No differences were observed in B cells, T cells, monocytes or neutrophils. Interestingly, a statistically significant decrease in CD4/CD8 ratio was observed when C2 was compared to C1 on day 21 after normalization with D3 (~1.5-fold, p value=0.0142). Moreover, an increase in HLA-DR expression in CD8 population was detected in C2 vs C1 on day 21 (~1.5-fold, p value=0.0632). Regarding exhaustion markers, pela administration decreases CD39, LAG3 and TIM3 markers on day 3. However, low levels of these markers are only maintained at day 21 in patients who had received atezo on Day 3 (C2).

Conclusions These data suggest that combining pela with atezo may improve outcomes in HR+/HER2- BC by enhancing the cytotoxic and anti-tumor activity of T cells.

Trial Registration NCT04102618

REFERENCES

Ethics Approval The study was approved by Hospital Clínico de Valencia Ethics Board and Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) on February 8, 2019.