Background Pelareorep (pela) is an intravenously administered, non-genetically modified oncolytic reovirus that selectively kills tumor cells and activates both innate and adaptive immune responses. In prior clinical trials, pela was shown to prime tumors for checkpoint inhibition by enhancing infiltration of lymphocytes into tumors and increasing PD-L1 expression. The GOBLET basket study was designed to assess the safety and efficacy of pela in combination with atezolizumab (atezo) +/- chemotherapy in multiple gastrointestinal cancer indications (PDAC, 1L MSI-H colorectal cancer, 3L MSS colorectal cancer, 2L anal carcinoma). Here we report the interim results for patients with advanced/metastatic PDAC.

Methods GOBLET is a phase 1/2 Simon two-stage study. PDAC patients enrolled in GOBLET are treated with pela, atezo and gemcitabine/nab-paclitaxel. They must have locally advanced/metastatic unresectable disease evaluable by RECIST v1.1, be ≥18 years old and have an ECOG score ≤1. The first stage enrolled 12 evaluable PDAC patients (evaluable patients must have at least one post-baseline tumor assessment). The primary objectives are safety and efficacy by investigator-assessed objective response rate (ORR). The protocol-specified Stage 1 success criterion for PDAC is ≥3 confirmed responses. In addition, blood samples collected at baseline (cycle 1 day 1 [c1d1]) and c2d1 of the 28-day treatment cycle will undergo T-cell receptor sequencing (TCR-seq) to assess treatment effect on the T-cell repertoire.

Results No safety signals have been observed in patients treated with pela, atezo and gemcitabine/nab-paclitaxel. Seven of 10 evaluable patients to date (28July2022) had a partial response at week 8 or later (3 confirmed, 4 currently unconfirmed), and 2 had stable disease for an objective response rate (ORR) of 70% and a clinical benefit rate (CBR) of 90%. TCR-seq revealed an expansion of T-cell clones, a decrease in clonal diversity, and an increase in T-cell fraction from c1d1 to c2d1 in all three patients for whom data are available. Updated tumor response and TCR-seq results will be presented.

Conclusions Consistent with previous studies in PDAC and other indications, pela in combination with chemotherapy and a checkpoint inhibitor is well-tolerated. The primary efficacy success criterion was met, and the high ORR and CBR observed in this study are very encouraging in comparison to tumor response rates observed in prior first-line PDAC treatment studies. The changes in T-cell repertoire observed in the first three patients are consistent with previous pelareorep/checkpoint inhibitor studies and will be further evaluated as possible biomarkers for response to therapy.

Trial Registration (Eudra-CT: 2020-003996-16)

Ethics Approval The study was approved by the ethic committee of Hamburg on February 22, 2021.