# GOBLET: A phase 1/2 multiple indication study in advanced gastrointestinal cancers treated with pelareorep and atezolizumab – preliminary safety and efficacy results in second-line or later unresectable anal carcinoma

**Dirk Arnold [1], Dominik Modest [2], Eray Goekkurt [3], Alexander Stein [3], Anke Reinacher-Schick [4], Nina Burkhart [1], Matt Coffey [5], Ruimei Li [6], Thomas Heineman [6]**

Asklepios Tumorzentrum Hamburg, AK Altona, Hamburg, Germany[1], Charité Universitätsklinikum Berlin, Campus Virchow, Med Klinik m. S. Hämatologie/Onkologie, Germany [2], Hematology-Oncology Practice Eppendorf (HOPE),Hamburg, Germany[3], St. Josef-Hospital, Klinikum der Ruhr-Universität Bochum, Abt. für Hämatologie, Onkologie u. Palliativmedizin,Germany [4],Oncolytics Biotech Inc., Calgary, Canada [5], Oncolytics Biotech Inc, San Diego, USA [6]

*IMACC 2023, Rome, Italy*

## Background and Study Design

Pelareorep (pela) is an intravenously administered, naturally occurring, non-genetically modified reovirus. Pela selectively kills tumor cells and promotes tumor-directed innate and adaptive immune responses resulting in increased T cell infiltration and PD-L1 expression in tumors, thereby priming the tumor for checkpoint blockade therapy (Samson et al., 2018) (Fig 1).

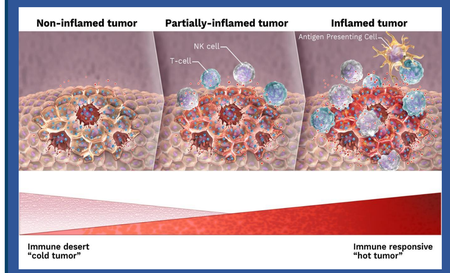



**Figure 1: Pelareorep mechanism of action**

Pelareorep selectively infects cancer cells leading to tumor cell lysis. In addition, its dsRNA genome is identified by pattern recognition receptors leading to the expression of interferons and inflammatory cytokines. This, in turn, results in immune cell recruitment and promotes the development anti-tumor innate and adaptive immune response.

GOBLET is an open-label, multiple-cohort, phase 1/2, Simon 2-stage study to assess the safety and efficacy of pela in combination with atezolizumab (atezo) +/- chemotherapy in different gastrointestinal cancers.

**Here we report interim results for GOBLET Cohort 4: 2nd-line or later unresectable squamous cell carcinoma of the anal canal (SCCA).**

Treatment options for squamous cell anal carcinoma following failure of first-line therapy are limited and include immune checkpoint inhibitors. In recent studies, objective response rates to checkpoint inhibitor therapy of previously treated SCCA patients ranged from 10-14%. Therapies that modify the tumor microenvironment may improve the susceptibility of tumors, including microsatellite stable (MSS) tumors, to immunotherapies. We hypothesize that pela will make the tumor microenvironment more immunologically active, in part by increasing T cell infiltration and PD-L1 expression, thereby enhancing the effectiveness of checkpoint inhibitors in 2nd-line or later SCCA. In support of this hypothesis, pelareorep-based combination therapies have demonstrated clinical activity in metastatic breast and pancreatic cancer.

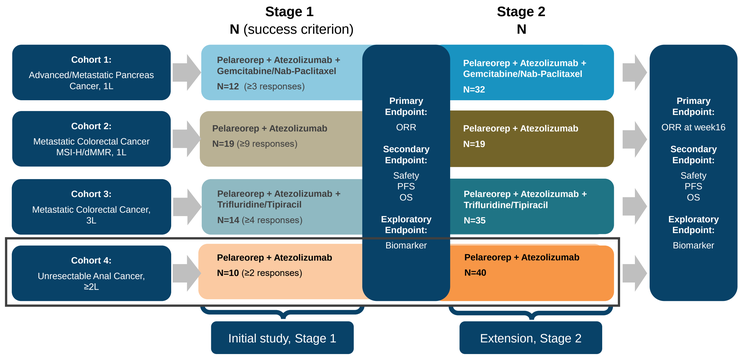
**Eudra-CT #**:2020-003996-16

**Coordinating Investigator:** Dirk Arnold, **Contact:** akupic@oncolytics.ca & Matthias.Lendner@aio-studien-ggmbh.de

## Study Design and Patient Characteristics

GOBLET Cohort 4 is enrolling patients with advanced/metastatic unresectable SCCA who failed prior systemic therapy. SCCA patients are treated with pela ($4.5x10^{10}$ $TCID_{50}$) on days 1, 8, 15 and 22, and atezo (840 mg) on days 2 and 16 of each 28-day cycle. Ten evaluable patients will be enrolled in Stage 1. The Stage 1 success criterion for expansion to Stage 2 (an additional 40 patients) is ≥2 responses.

**Figure 2: GOBLET study design**




### Primary endpoints:

- Tolerability of the study treatment
- Objective response rate (ORR) at week 16 (per RECIST v1.1)

### Secondary endpoints:

- Overall ORR
- Progression-free survival (PFS)
- Duration of response (DOR)
- Overall survival (OS)
- Disease control rate (DCR)

### Exploratory Objectives:

- Immunologic effects of treatment
- Biomarker exploration

As of the data cut-off, 8 evaluable SCCA patients have been enrolled. Baseline characterizes are summarized in Table 1.

**Table 1: Baseline characteristics of evaluable patients**

| | |
|---|---|
| **Average age in years (range), 70 (48-73)** | |
| ≥65 | 6 (75%) |
| <65 | 2 (25%) |
| **Sex** | |
| Male | 1 (13%) |
| Female | 7 (87%) |
| **Eastern Cooperative Oncology Group performance status (ECOG)** | |
| 0 | 4 (50%) |
| 1 | 4 (50%) |
| **Ethnicity** | |
| Hispanic or Latino | 0 |
| Not Hispanic or Latino (White) | 8 (100%) |
| **Previous radiation therapy** | |
| Yes | 7 (87%) |
| No | 1 (13%) |
| **Number of previous lines of chemotherapy** | |
| 1 | 4 (50%) |
| 2 | 3 (37%) |
| ≥3 | 1 (13%) |
| **Baseline PD-L1 expression*** | |
| Positive | 3 (38%) |
| Unknown | 6 (62%) |

*Baseline PD-L1 assessment is not mandatory

## Results

- To date, no safety signal has been identified by the independent Data Safety Monitoring Board. The most common adverse events (AEs) are listed in Table 2. There have been no Grade 4 events and no serious AEs related to the investigational drugs.
- Of the 8 SCCA patients are currently evaluable for tumor response, one has achieved a complete response (ongoing at 12 months) and 2 patients have achieved partial responses (one at week 8 and one ongoing at week 16). Five patients had a best response of progressive disease. The interim ORR is 37.5%. Final ORR, median PFS, and median OS are pending.
- The SCCA cohort has met the Stage 1 criteria for expansion to Stage 2 enrollment.

**Figure 3a: Patient enrolment flowchart**

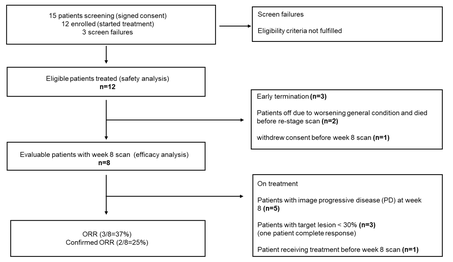



**Figure 3b: Tumor responses over time**

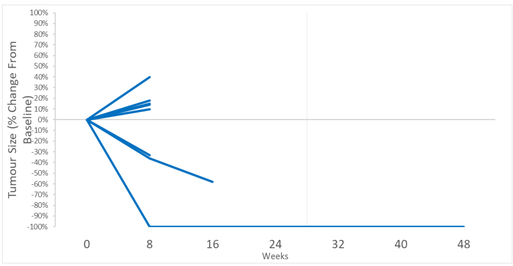
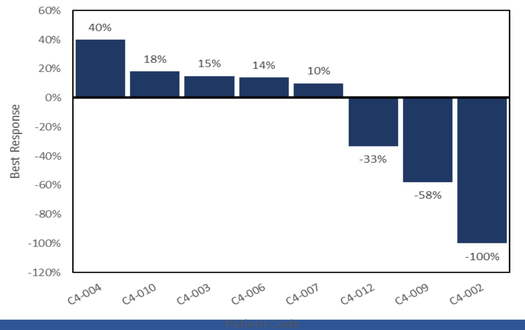



**Table 2: Most frequent (>1 patients) AEs**

| MedDRA Preferred Term | All TEAEs N= 12, n (%) | Grade 3/4 TEAEs N= 12 ,n (%) |
|---|---|---|
| Pyrexia | 7 (58.3%) | 0 (0.0%) |
| Fatigue | 5 (41.7%) | 0 (0.0%) |
| Chills | 4 (33.3%) | 0 (0.0%) |
| Alanine aminotransferase increased | 3 (25.0%) | 1 (8.3%) |
| Aspartate aminotransferase increased | 3 (25.0%) | 2 (16.7%) |
| Constipation | 2 (16.7%) | 0 (0.0%) |
| Diarrhoea | 2 (16.7%) | 0 (0.0%) |
| Disease progression | 2 (16.7%) | 0 (0.0%) |
| Dyspnoea | 2 (16.7%) | 0 (0.0%) |
| Nausea | 2 (16.7%) | 0 (0.0%) |
| Oedema peripheral | 2 (16.7%) | 0 (0.0%) |
| Urinary tract infection | 2 (16.7%) | 0 (0.0%) |
| Vomiting | 2 (16.7%) | 0 (0.0%) |

**Figure 3c: Best tumor responses**




## Conclusions

- The ≥2nd-line SCCA cohort of the GOBLET study, which is ongoing, has met the criteria for expansion to Stage 2 enrollment.
- No safety signal has been observed in SCCA patients treated with pela and atezolizumab.
- Preliminary tumor responses to combination therapy with pela and atezo in second-line or later SCCA patients are encouraging.