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P-49 GOBLET: A phase 1/2 multiple indication signal finding and biomarker study in advanced gastrointestinal cancers treated with pelareorep and atezolizumab — safety and preliminary response results

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Background: In GI cancers, checkpoint inhibitors are only effective in patients with high microsatellite instability (MSI-H) or deficient mismatch repair (dMMR) tumors. Oncolytic viruses may improve the susceptibility of microsatellite stable (MSS) tumors to immunotherapy by modifying the tumor microenvironment (TME). Pelareorep (pela) is an intravenously delivered, non-genetically modified, oncolytic reovirus that mediates cancer cell killing by activating innate and adaptive immune responses directed against the tumor as well as direct tumor oncolysis. Accordingly, treatment with pelareorep results in increased T cell infiltration and PD-L1 expression in tumors which primes the TME for responsiveness to checkpoint inhibitors. Pela has demonstrated activity in many cancers including colorectal and pancreatic cancer. The GOBLET study is designed to assess the efficacy of pela plus atezolizumab (atezo) with or without chemotherapy in multiple GI cancers.

Methods: GOBLET is a phase 1/2, open-label, non-randomized study in patients with advanced or metastatic GI cancers and utilizes a Simon two-stage design. In the first stage of the study, four treatment groups are being enrolled: Cohort 1 — First-line metastatic/advanced pancreatic cancer treated with pela plus atezo and chemotherapy (gemcitabine and nab-paclitaxel) (N=12); Cohort 2 — First-line MSI-H/dMMR metastatic CRC treated with pela plus atezo (N=19); Cohort 3 — Third-line metastatic CRC treated with pela plus atezo and chemotherapy (trifluridine/tipiracil) (N=14); and Cohort 4 — Second-line or later advanced squamous cell carcinoma of the anal canal treated with pela plus atezo (N=10). In Cohorts 1 and 3 (chemotherapy-containing cohorts) the first 3-6 patients enrolled comprise a safety run-in. The primary objectives of GOBLET are safety and efficacy measured by the objective response rate (ORR) at week 16. Based on pre-specified response thresholds, any cohort showing a positive ORR signal in Stage 1 may advance to the 2nd Stage and enroll additional patients.

Results: The three safety run-in patients in Cohorts 1 and 3 have been enrolled and their safety data reviewed by the independent Data Safety Monitoring Board (DSMB). The DSMB identified no safety signal and recommended that enrollment into these cohort continue without modification. Enrollment into Cohorts 2 and 4 is ongoing as these cohorts do not include safety run-ins. Tumor response results to date indicate that two of the three Cohort 1 patients had a partial response at week 8, the third Cohort 1 patient had a partial response at week 16.

Conclusions: No safety signal was observed in either the Cohort 1 (first-line pancreatic cancer) or Cohort 3 (third-line CRC) patients. This is consistent with the favorable safety profile observed in prior studies of pela in multiple cancer indications, and it supports the ability to safely treat patients with advanced GI cancers using pela in combination with checkpoint inhibitors and chemotherapy. Preliminary tumor responses to therapy in first-line pancreatic cancer patients are encouraging.

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P-50 RETRO-TAS, a retrospective observational study of rifluridine/tipiracil in chemorefractory metastatic colorectal cancer

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Background: Trifluridine/tipiracil (TAS-102) is an oral combination of an antineoplastic thymidine-based nucleoside analogue, trifluridine, and the thymidine phosphorylase (TPase) inhibitor, tipiracil hydrochloride, indicated for patients (pts) with metastatic colorectal cancer (mCRC) as third line therapy. The approved dose of TAS-102 in adults is 35 mg/m2/dose administered orally twice daily on Days 1 to 5 and Days 8 to 12 of each 28-day cycle as long as benefit is observed or until unacceptable toxicity occurs. We conducted an investigator initiated retrospective analysis in patients with chemorefractory mCRC treated with TAS-102 to record clinical practice and to collect real world data on the clinical efficacy of TAS-102 in the Greek population.

Methods: Clinicopathologic characteristics of patients treated in 8 Cancer Centres were collected to assess physician's choice of treatment in chemoresistant mCRC with TAS-102 in third line and beyond. In addition, the clinicopathologic features related to mCRC (focus on molecular profile), duration of treatment, dose modification and toxicity were analysed. The PFS, the OS, the 6-/8-month PFS rate and the disease control rate were calculated. Prognostic factors were evaluated by Cox regression model and Kaplan-Meier curves, along with log-rank tests using Stata/MP 16.0 for Windows.

Results: From October 2018 to October 2021, 200 patients with a median age at diagnosis of 63.7 years (IQR 54.2, 72.1) and at TAS-102 treatment initiation was 67.0 (IQR 58.0, 75.0). At the time of the analysis the median follow-up time was 14 months (IQR 7, 23), 158 PDs and 106 deaths were recorded. Of all patients 42% were females and 58% were metastatic at diagnosis. Molecular analysis revealed mutations in KRAS (52%), NRAS (5%), HER2 (3.5%), BRAF (3.5%) and MSI (9%). Adjuvant chemotherapy and radical surgery was delivered in 39.5% and 51.5% respectively. TAS-102 was administered as a third (70.5%), fourth (17.0%) or fifth line (12.5%) of therapy. Serious adverse events reported were neutropenia (4pts), anemia (2pts), thrombocytopenia (1pt), diarrhea (1pt), nausea (1 pt) and fatigue (8 pts). Dose reduction, delay of initiation of the next cycle and shorter duration of therapy was reported in 25%, 31% and 14.5% of patients. Patients received TAS-102 as monotherapy (71.5%), in combination with bevacizumab (24.5%) or with an anti-EGFR agent (4.0%). The median duration of TAS-102 therapy was 119.5 days and 81% of patients discontinued therapy due to progressive disease. Objective responses during TAS-102 therapy included 0.5% CR, 25% PR, 20% SD and 47% PD, while 7.5% of patients were not evaluable. The median PFS time was 4.8 and the median OS was 11.4 months. The 6 and the 8-month PFS rate was 41.4% and 31.5% respectively. In the multivariable analysis PS>1 and metastatic disease in the liver and lung were adversely associated with survival whereas tumor sidedness and mutational status were not.

Conclusions: This real-world observational study confirms and adds on the findings of the RECOURSE phase III study in relation to the toxicity and the effectiveness of TAS-102 in all subgroups of patients with chemotherapy refractory mCRC, regardless of mutational status and sidedness.

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Legal entity responsible for the study: The authors.

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P-51 Non-invasive HER2 status diagnosis in gastric cancer using surrogate DNA methylation markers

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Background: Gastric cancer (GC) is the fifth most common and fourth most lethal cancer worldwide. Unlike other cancer types, e.g., lung or breast cancer, very few targeted therapeutics have been developed for GC. HER2 (ERBB2) status is an essential biomarker for guiding the trastuzumab (Herceptin) therapy, which is the only molecularly targeted drug accepted as a first-line therapy, for the treatment of patients with advanced HER2-overexpressing GC. HER2 detection in GC often requires repeated testing to improve the accuracy of the result due to its high degree of