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CLAUDIO-01: A multicentric phase I/II trial to evaluate the safety and efficacy of SOT102 as monotherapy and in combination with standard of care (SoC) in patients with gastric, gastroesophageal junction (GEJ), and pancreatic adenocarcinoma

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Background

- SOT102 is an antibody-drug conjugate targeting CLDN 18.2, based on a highly specific monoclonal antibody conjugated to PNU-159682, an anthracycline derivative, using site-specific conjugation technology.
- Preclinical data support the development of SOT102 in the clinical setting.

Figure 1: SOT102 (CLDN 18.2 ADC)

A schematic representation of the molecular structure of SOT102

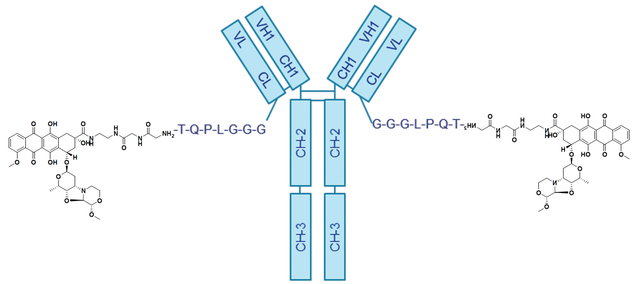
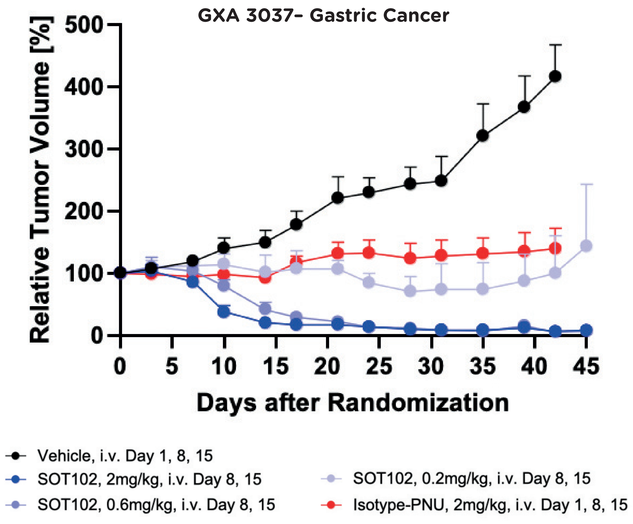


Figure 2: Efficacy/Tumor Growth



SOT102 led to tumor regression in gastric PDXs. Relative group mean (±SEM) tumor volumes over the duration of the study are shown for animals (n=3) administered with vehicle, SOT102 (2, 0.6 and 0.2 mg/kg) or isotype-PNU (2 mg/kg) via i.v. dosing on day 1, 8 and 15.

Trial design

CLAUDIO-01 (NCT05525286) is a multicenter, multimodular phase I/II trial in gastric/GEJ and pancreatic cancer patients in both advanced and first line. The trial consists of the following modules:

Patients with advanced/metastatic gastric/GEJ or pancreatic CA → **Part A** SOT102 monotherapy SOT102 iv q2w

Part B will start once monotherapy SOT102 dose level 3 in Part A is deemed safe

Patients with advanced/metastatic gastric/GEJ or pancreatic CA 1st line in combination with SoC → **Part B** SOT102 combined with SoC SOT102 iv q2w

Patients with advanced/ metastatic gastric/GEJ CA HER2-negative → SOT102 combined with SoC (mFOLFOX plus nivolumab)

Patients with advanced/ metastatic pancreatic CA → SOT102 combined with SoC (nab-paclitaxel plus gemcitabine)

The following expansion cohorts are planned upon identification of the recommended phase 2 dose (RP2D):

Patients with advanced/metastatic gastric/GEJ CA
3rd+ line
CLDN 18.2 positive

Patients with advanced/metastatic pancreatic CA
2nd+ line
CLDN 18.2 positive

→ **Part C** SOT102 monotherapy

Patients with advanced/metastatic gastric/GEJ CA
1st line
CLDN 18.2 positive, HER2-negative

Patients with advanced/metastatic pancreatic CA
1st line
CLDN 18.2 positive

→ **Part D** SOT102 combined with SoC

Key eligibility criteria

Key eligibility criteria for Part A:
- Normal organ function
- Gastric, GEJ, or pancreatic cancer with no better treatment option
- No prior CLDN 18.2-directed therapy
- Availability of tumor tissue for retrospective CLDN 18.2 analysis

Key eligibility criteria for Part B:
- Normal organ function
- First-line treatment of patients with advanced or metastatic gastric/GEJ cancer (SoC: mFOLFOX with nivolumab) or pancreatic cancer (SoC: nab-paclitaxel/gemcitabine)
- No prior CLDN 18.2-directed therapy
- Availability of tumor tissue for retrospective CLDN 18.2 analysis

→ **Study treatment SOT102 i.v alone or in combination with SoC on day 1 every 2 weeks**

Primary objectives and endpoints

- To determine the MTD and RP2D of SOT102 as monotherapy and in combination with first-line SoC treatment (Parts A and B)
- To assess the efficacy of SOT102 in monotherapy and in combination with first-line SoC treatment by ORR (Parts C and D)

Secondary objectives and endpoints

Parts A and B:
- To assess the safety and tolerability of SOT102 in monotherapy and in combination with first-line SoC treatment
- To characterize the PK of SOT102 (=conjugated antibody), total antibody and other metabolites
- To explore evidence of SOT102 activity in monotherapy and in combination with first-line SoC treatment in individual patients
- To explore whether patients develop any antibodies against SOT102

Parts C and D:
- To evaluate additional measures of efficacy of SOT102 in monotherapy and in combination with first-line SoC treatment
- To assess the safety and tolerability of SOT102 in monotherapy and in combination with first-line SoC treatment
- To assess quality of life (QoL) after treatment with SOT102 in monotherapy and in combination with first-line SoC treatment
- To characterize the PK of SOT102 (=conjugated antibody), total antibody and other metabolites
- To explore whether patients develop any antibodies against SOT102

Exploratory endpoints

- To assess the relationship between the intensity of CLDN 18.2 expression and clinical outcome

Status

- The trial is enrolling patients in Europe and USA.
- FPI was in March 2022.
- Dose escalation follows an accelerated modified Fibonacci scheme with cohort sizes of 3+3 and includes safety observation periods
- The current highest dose level for monotherapy is dose level 4 for Part A and dose level 1 in both cohorts of Part B.
- To date, 24 patients were treated in 4 escalating dose levels in Part A and 2 patients in first escalating dose level in Part B.
- The trial will proceed to reach a RP2D in both monotherapy and in combination with first-line SoC treatment in gastric/GEJ and pancreatic cancer patients.

Contact/Declaration of Interest

Contact: Dr. Radka Obermannova, obermannova@mou.cz

Dr. Obermannova's disclosures: Financial Interests: BMS (Advisory Board, Personal), Merck (Invited Speaker, Personal), MSD (Invited Speaker, Personal), Servier (Advisory Board, Personal) **Non-Financial Interests:** CZECRINonco (Leadership Role, Czech Clinical Trials Network in Oncology), Visegrad Funds (Leadership Role, Visegrad 4 educational grant for clinical trials staff)

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