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PROCEADE PanTumor: A Phase 1b/2, multicenter study of precemtabart tocentecan (M9140), an anti-CEACAM5 ADC with exatecan payload, in patients with advanced solid tumors

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PROCEADE
PanTumor | PHASE 1b/2

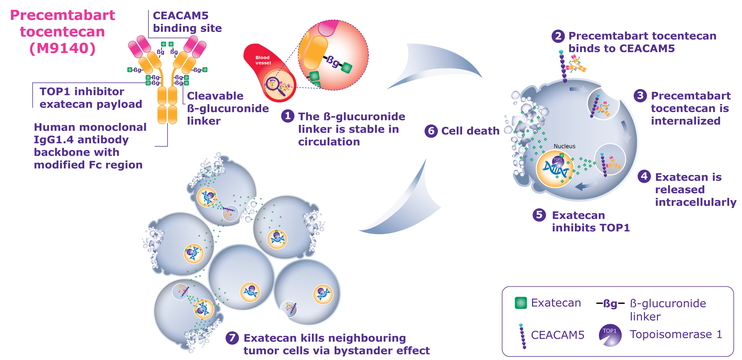
STUDY STATUS

The PROCEADE PanTumor Phase 1b/2 study plans to enroll ≈250 patients with advanced/ metastatic GC/GEJC, NSCLC, or PDAC in North and South America, Europe, and Asia

INTRODUCTION

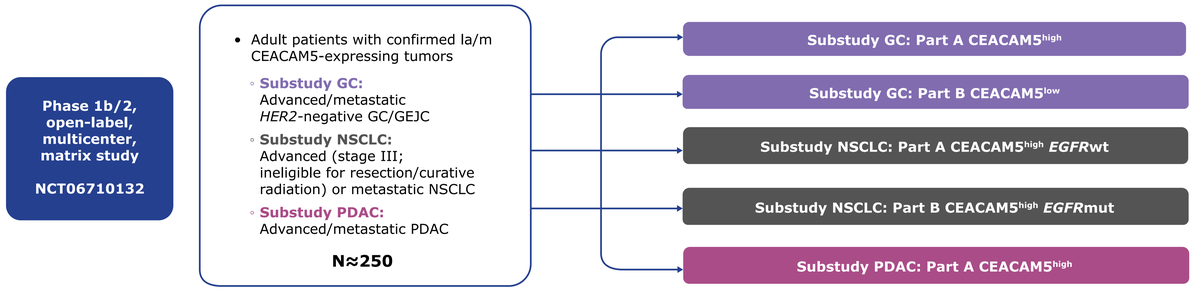
- **CEACAM5** is a cell surface glycoprotein overexpressed in various cancers, including **GC**, **NSCLC**, **PDAC,** and **CRC**, with limited expression on healthy adult cells[1-4]
- **Precemtabart tocentecan (precem-TcT) is an investigational anti-CEACAM5 ADC** (drug to antibody ratio: 8) that utilizes a unique linker-payload combination to selectively deliver the TOP1 inhibitor, **exatecan**, to CEACAM5 overexpressing tumor cells (**Figure 1**)[5-7]
- Precem-TcT has shown **promising preliminary efficacy and a manageable and predictable safety profile in 40 heavily pretreated patients with metastatic CRC** in the ongoing Phase 1 PROCEADE-CRC-01 study (NCT05464030)[6,7]
- We present the design of the **Phase 1b/2 PROCEADE PanTumor study (NCT06710132)**

Figure 1. Precem-TcT mechanism of action



STUDY DESIGN

Figure 2. Study design



METHODS

- This is a Phase 1b/2 study to assess the antitumor activity, tolerability, safety, and PK of precem-TcT monotherapy in patients with advanced/ metastatic GC/GEJC, NSCLC, or PDAC
- Each indication is represented by its respective substudy protocol within the framework of a master protocol

Table 1. Study endpoints of Phase 1[a]

Endpoints	
Primary	
	• Objective response (complete response or partial response)[a]
Secondary	
All substudies	• Adverse events and treatment-related adverse events
All substudies	• Duration of response[a] (time from first documentation of OR to PD or death) • Time to response[a] (date of first study intervention to first documentation of OR)[a] • Progression-free survival (date of first study intervention to PD)[a]
All substudies	• Disease control (CR, PR, SD, or non-CR/non-PD at Week 12 or later prior to documented PD)
All substudies	• Concentrations or PK parameters (e.g. C_{trough}, C_{eoi})
GC	• CEACAM5 expression analysis using IHC (Day 1)

[a]As assessed by investigators per RECIST v1.1

Table 2. Key eligibility criteria

Key inclusion criteria		
Overall study		
• Age ≥18 years • ECOG PS ≤1 • Adequate hematologic, hepatic, and renal function as defined in the master protocol • ≥1 lesion that is measurable using RECIST v1.1 • Archival FFPE tumor tissue is required. If archived tumor tissue is not available, a fresh biopsy is required • For all substudies, CEACAM5 expression levels are defined as follows based on an IHC test: ◦ CEACAM5^{high}: ≥50% of tumor cells (of ≥100 viable tumor cells present) exhibit moderate (2+) or strong (3+) membrane staining ◦ CEACAM5^{low}: <50% of tumor cells (of ≥100 viable tumor cells present) exhibit low (≥2+) membrane staining		
Substudy GC	**Substudy NSCLC**	**Substudy PDAC**
• Patients with documented histopathological diagnosis of advanced/metastatic, *HER2*-negative, gastric or GEJ adenocarcinoma, who are intolerant/refractory to or progressed after systemic therapies (must include a fluoropyrimidine, a platinum agent, and an ICI for MSI-H/PD-L1+ with CPS ≥1)	• Patients with histologically or cytologically documented advanced (Stage III not eligible for resection or curative radiation) or metastatic NSCLC with or without driver genomic alterations	• Patients with histologically or cytologically confirmed advanced/ metastatic PDAC, who were intolerant/refractory to or progressed after systemic therapies for the advanced/metastatic stage (must have included FOLFIRINOX, NALIRIFNOX, or Nab-paclitaxel/gemcitabine)
• Must have received and progressed[a] on ≥1 and ≤2 treatment lines for la/m disease	• Must have received and progressed[a] on ≥1 and ≤3 treatment lines for la/m disease	• Must have received and progressed[a] on ≥1 and ≤2 treatment lines for la/m disease
• Part A: CEACAM5^{high} GC/GEJC	• Part A: CEACAM5^{high} *EGFR*wt tumors (including patients with any driver genomic alterations other than *EGFR* mutations	• CEACAM5^{high} tumors only
• Part B: CEACAM5^{low} GC/GEJC	• Part B: CEACAM5^{high} known *EGFR* mutated tumors as assessed per local clinical practice	
Key exclusion criteria		
Overall study		
• History of malignancy ≤3 years before the date of enrollment • Known brain metastases • Diarrhea (liquid stool) or ileus grade >1 and/or active chronic inflammatory bowel disease (e.g., ulcerative colitis, Crohn's disease, intestinal perforation) and/or bowel obstruction • Cardiac arrhythmia, unstable angina, myocardial infarction, congestive heart failure (NYHA ≥II) or a coronary revascularization procedure ≤180 days of study entry. Calculated Fridericia-corrected average QTc >470 ms • Cerebrovascular accident/stroke (<6 months prior to enrollment)		
Substudy GC	**Substudy NSCLC**	**Substudy PDAC**
• Prior therapy with irinotecan	• Prior therapy with irinotecan	• None

[a]Per RECIST v1.1

STUDY CONTACT

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- For further information, please visit https://clinicaltrials.gov/ct2/show/NCT06710132.

For more information on this clinical trial, scan the QR code.

Abbreviations: ADC, antibody-drug conjugate; CEACAM5, carcinoembryonic antigen-related cell adhesion molecule 5; C_{eoi}, observed concentration at the end of the infusion period; CPS, combined positive score; C_{trough}, concentration observed immediately before next dosing (corresponding to predose or trough concentration for multiple dosing); CR, complete response; CRC, colorectal cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; *EGFR*, epidermal growth factor receptor; *EGFR*mut, epidermal growth factor receptor mutated; *EGFR*wt, epidermal growth factor receptor wild type; FFPE, formalin-fixed paraffin-embedded; GC, gastric cancer; GEJ, gastroesophageal junction; GEJC, gastroesophageal junction cancer; *HER2*, human epidermal growth factor receptor 2; ICI, immune checkpoint inhibitor; IHC, immunohistochemistry; IV, intravenous; la/m, locally advanced/metastatic; MSI-H, microsatellite instability-high; NSCLC, non-small cell lung cancer; NYHA, New York Heart Association; OR, objective response; PD, progressive disease; PDAC, pancreatic ductal adenocarcinoma; PD-L1, programmed death ligand-1; PK, pharmacokinetics; PR, partial response; Q3W, every 3 weeks; QTc, corrected QT interval; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TOP1, topoisomerase 1; SD, stable disease.

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