A phase 1/2 study of BDC-4182, a claudin18.2-targeting next-generation immune-stimulating antibody conjugate (ISAC), in patients with advanced gastric and gastroesophageal cancer

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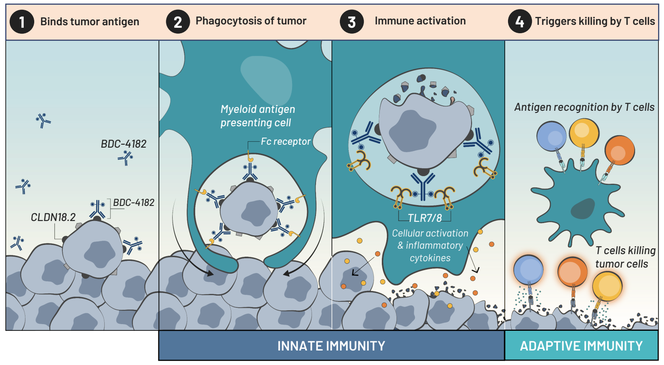
Mechanism of Action

- BDC-4182 is a next-generation ISAC with significantly enhanced immune activating capability

Tumor recognition → Innate activation → T cell priming → Tumor regression

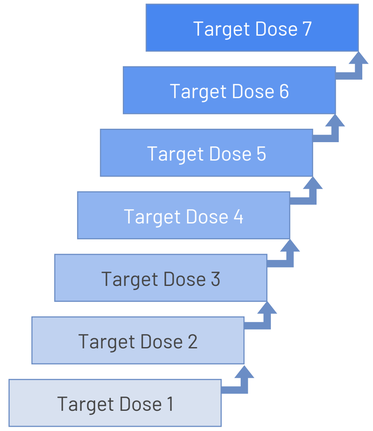


Study Design: Dose Escalation with Cycle 1 Step-Up Dosing

Dose Escalation with Step-Up Dosing
Monotherapy, 3 + 3 Design
(21 – 42 patients)

Step-Up Dosing | Target Dose

- Gastric and gastroesophageal cancer patients
- Open for enrollment in Australia, South Korea, and Taiwan (NCT06921837)



Backfill
(≤ 20 patients)

Backfill at dose levels cleared for safety

Key Eligibility and Exclusion Criteria

Key Eligibility

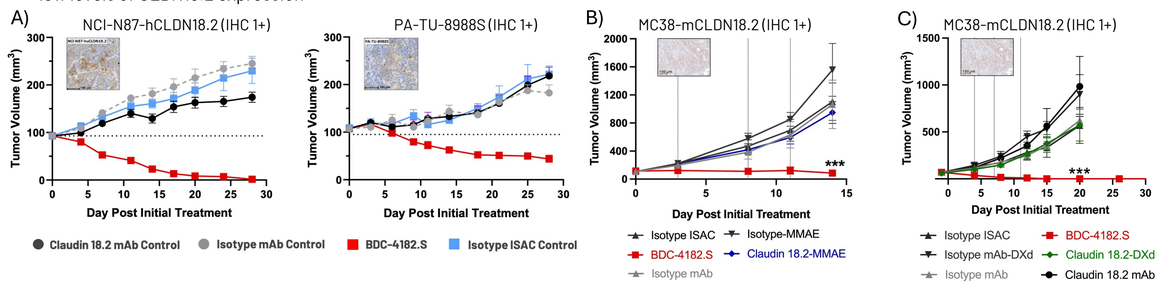
- Histologically or cytologically confirmed metastatic or unresectable gastric or gastroesophageal cancer
- Measurable disease by RECIST v1.1
- Received ≥ 1 prior lines of locally available standard therapies or intolerant of standard therapies
- CLDN18.2 expression of ≥ 1% of tumor cells scored as ≥ IHC 2+ if prior CLDN18.2 expression is known (may be enrolled if prior expression is unknown)
- Adequate organ function suitable for Phase 1 therapy
- Willingness to provide tumor biopsy prior to enrollment if clinically feasible

Key Exclusions

- Uncontrolled or symptomatic CNS metastases
- Clinically significant or uncontrolled cardiac, pulmonary, or hepatic disease
- Active infection or residual toxicity from a previous treatment
- Recent use of investigational agent or standard anti-cancer therapies

Biological Rationale

- BDC-4182 promotes tumor killing by several mechanisms, including:
  - Antibody-dependent cellular phagocytosis by tumor-associated myeloid cells
  - Activation and expansion of tumor-specific T cells
  - Cytotoxic T cell-mediated tumor cell killing with potential for durable anti-tumor immune memory
- A CLDN18.2-targeting ISAC surrogate (BDC-4182.S) elicited complete tumor regression in xenograft and syngeneic models with low levels of CLDN18.2 expression (IHC1+) & generated T cell-dependent immune memory that prevented outgrowth CLDN18.2-negative tumors
- Compared with cytotoxic ADCs, BDC-4182.S demonstrated superior anti-tumor efficacy at lower doses in CLDN18.2-high tumors and in tumors with low levels of CLDN18.2 expression[1]



CLDN18.2-targeting ISAC surrogates demonstrated tumor growth inhibition and improved activity relative to cytotoxic ADC controls in models with low CLDN18 expression. Data are shown as mean and SEM with dashed lines indicating the day of dosing.

Biomarker Assessment

- Serial blood collection will enable longitudinal analyses of circulating pharmacodynamic biomarkers, including cytokines and chemokines
- Baseline tumor tissue will be evaluated to assess CLDN18 expression and support exploratory biomarker analyses
- Exploratory blood- and tissue-based analyses may investigate relationships among:
  - Target expression
  - Pharmacodynamic activity
  - Safety
  - Anti-tumor activity

These analyses aim to inform exposure–response relationships and potential patient selection strategies

References
1. Fu et al. Preclinical Investigation of BDC-4182, a Claudin 18.2-Targeting ISAC to Support Clinical Development. SITC 2025. https://doi.org/10.1136/jitc-2025-SITC2025.0950

Primary Objective

Objective:
- Define safety, tolerability, and recommended Phase 2 dose (RP2D)

Endpoints:
- Incidence of AEs/SAEs (CTCAE v5.0)
- Dose-limiting toxicities

Secondary Objectives

Objectives:
- Evaluate preliminary anti-tumor activity
- Characterize pharmacokinetics and evaluate immunogenicity of BDC-4182

Endpoints:
- Evaluate according to RECIST v1.1 ORR, DOR, DCR, PFS, BOR, and OS
- PK parameters (Cmax, Cmin, AUC, CL, V, $t_{1/2}$)
- Incidence of anti-drug antibodies

Exploratory Objectives

Objectives:
- Investigate relationship between CLDN18 expression and clinical activity
- Explore potential blood and tumor biomarkers associated with exposure, efficacy, or safety

Endpoints:
- Correlation of CLDN18 expression and efficacy
- Biomarker associations (gene expression, protein, and tissue image analysis)

Summary

- BDC-4182 is a first-in-class CLDN18.2 immune-stimulating antibody conjugate (ISAC) being investigated in a Phase 1/2 study in patients with previously treated metastatic gastric or gastroesophageal cancer
- Preclinical studies demonstrate robust immune activation, including complete tumor regression, in low-CLDN18.2-expressing models and superior anti-tumor activity compared to cytotoxic ADCs in the same low-expression setting
- This study incorporates step-up dose escalation to enable assessment of biologically active exposures while maintaining tolerability
- Dose-escalation cohorts are open for enrollment in Australia, South Korea, and Taiwan (NCT06921837)

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