Mitazalim, a CD40 agonist with best-in-class profile

- Mitazalim is a FcγR crosslinking dependent CD40 agonistic antibody (tgGT) with a tumor-directed immune activation.
- Mitazalim binds with high affinity to a unique binding epitope on the CD40 receptor allowing for high efficacy and potency.
- Mitazalim has the potential for superior clinical activity: mitazalim is the only FcγR-dependent CD40 agonist with tumor-directed activity that can be dosed at 1 mg/kg.

Mitazalim in pancreatic cancer

- Targeting CD40 with mitazalim kicksstart the cancer-immunity cycle, priming and activating tumor-specific T cells.
- Pancreatic ductal adenocarcinoma (PDAC) is characterized by a desmoplastic tumor stroma that creates a mechanical barrier that limits exposure to chemotherapy, hosts immune-suppressive macrophages and leads to poor immune infiltration.
- CD40 agonists promote degradation of the tumor stroma by myeloid cells, improving the influx of T cells and sensitivity to chemotherapeutic agents.

OPTIMIZE-1 study overview

OPTIMIZE-1 (NCT04888312) is a phase 1b/2, open-label, multicenter study designed to evaluate safety, tolerability, and efficacy of mitazalim in combination with mFOLFIRINOX in adults with previously untreated metastatic PDAC.

Study design

Part 1 (Phase 1b)
- Dose Level 2 300 µg/kg
- Dose Level 3 450 µg/kg
- N=5

Part 2 (Phase 2)
- N=38

Mode of Action

1. Mitazalim + mFOLFIRINOX = enhanced tumor cell killing
2. Enhanced T cell infiltration
3. Mitazalim activates Dendritic Cells (DCs) Enhanced processing of tumor specific T cells

Study Objectives

Phase 1b
- Primary objective: To determine the recommended Phase 2 dose (RP2D).
- Secondary objectives: Assessment of clinical activity (ORR), survival outcome.

Phase 2
- Primary objective: To assess the clinical activity of mitazalim in combination with chemotherapy as determined by ORR.
- Secondary objectives: include: Survival outcomes, best overall response, duration of response, disease control rate, time to next anti-cancer therapy, safety and PK analysis. PD biomarkers will be analyzed as exploratory endpoints.

At the interim analysis mitazalim in combination with mFOLFIRINOX demonstrated encouraging clinical activity and manageable safety in patients with previously untreated metastatic pancreatic ductal adenocarcinoma

Duration of treatment

Best Overall Response (n, %)

SD

5 (21.7)

ORR (n, %)

12 (52.2)

Disease Control Rate (n, %)

21 (91.3)

Time (months)

N=23

Patient Baseline Characteristics

Key Eligibility Criteria

Inclusion:
- Diagnosis of metastatic PDAC
- ECOG status of 0 or 1
- No previous chemotherapy for PDAC
- No prior abdominal radiotherapy
- Life expectancy ≥ 3 months
- Acceptable hematologic and clinical laboratory chemistry values

Exclusion:
- Other types of non-dual pancreatic tumor
- Known CNS, metastases or carcinomatous meningiomas
- Has other current cancer or history of cancer in the past 3 years

Safety

Biomarkers in peripheral blood confirm mitazalim's mode of action

Tumor shrinkage during treatment

(A) Changes in the sum of the diameters of the target lesions (%) (B) Changes in tumor size from baseline at the point of best tumor reduction. In two PR patients, all target lesions were resolved, but non-target lesions were still present. N=23

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Efficacy and Safety of mitazalim in combination with mFOLFIRINOX in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC): an interim analysis of the OPTIMIZE-1 phase 1b/2 study

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% Change in target lesions from baseline