Trial In Progress: A Phase 2/3 Randomized, Controlled Study of CTX-009 in Combination with Paclitaxel versus Paclitaxel Alon in Adult Patients with Unresectable Advanced, Metastatic or Recurrent Biliary Tract Cancers who have received One Prior Systemic Chemotherapy Regimen

Abstract # TPS640

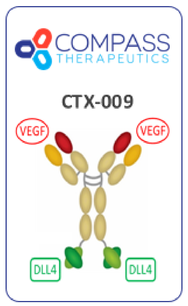
Marilyn Fontaine[1], Sarah Pilgrim[1], Thomas J. Schuetz[1]
[1] Compass Therapeutics Inc, Boston, MA 02135

Background

Background of Disease

- Biliary tract cancer (BTC) is a group of gastrointestinal tumors that are anatomically classified into four subtypes: intrahepatic cholangiocarcinomas, extrahepatic cholangiocarcinomas, gallbladder cancers, and ampullary carcinomas
- For locally advanced and metastatic BTC, first-line chemotherapy includes the use of gemcitabine and cisplatin. Recently, in the TOPAZ-1 study, the addition of durvalumab to gemcitabine and cisplatin improved OS in the first-line setting.[1]
- Presently, there is no consensus second-line therapy for patients with BTC in whom first-line therapy has failed[2]

CTX-009: A Novel DLL4 x VEGF-A Bispecific Antibody



Bispecific rationale

- Dual blockade of DLL4-Notch1 signaling is synergistic in preclinical models
- DLL4 upregulation in the tumor microenvironment mediates resistance to VEGF-targeted agents
- DLL4 expression is a negative prognostic factor in various malignancies including gastric, renal cell, ovarian, and colorectal cancers

Differentiation of CTX-009

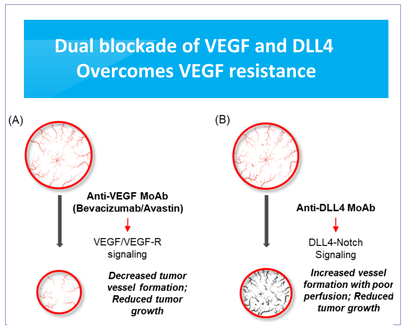
- Unique proprietary DLL4 binding epitope
- 2:2 valency effectively blocks both signaling pathways

VEGF/VEGFR inhibition

- Reduced blood vessel growth and expansion in tumors
- Regression of existing tumor vessels
- Loss of VEGF-mediated EC survival, and sensitizes ECs to effects of chemotherapy and radiation

DLL4/Notch inhibition

- Increased EC proliferation and sprouting, non-productive angiogenesis
- Blocks an essential pathway for cancer stem cells[3]



CTX-009 Clinical Summary

Phase 1a dose-escalation monotherapy, including cohort expansion at projected RP2Ds

- Safety: well-tolerated; MTD was not determined
- Activity: 4 PRs, 3 confirmed by RECIST in 16 patients with advanced solid tumors treated at the therapeutic doses
- Responses as a monotherapy: colorectal and gastric cancers

Phase 1b combination study with irinotecan or paclitaxel

- Confirmed PRs observed with CTX-009 in combination with paclitaxel in patients with cholangiocarcinoma and pancreas cancer
- These data led to the addition of a Phase 2 arm in patients Biliary Tract Cancer (BTC); Simon 2 Stage design
  - 24 patients enrolled; 22 patients evaluable for response
  - Phase 2 safety data are comparable to Phase 1 studies
  - Efficacy data presented at this meeting (Abstract #540)

Methods

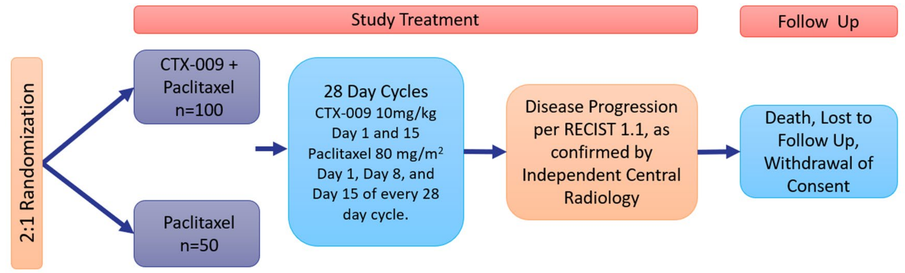
Study Rationale

- Combination chemotherapy regimens have demonstrated limited efficacy in patients with BTC in the second-line setting,[4] given the modest benefit and lack of durable efficacy of FOLFOX compared with best supportive care, it is unlikely that FOLFOX would be superior to single agent paclitaxel. There are data suggesting taxanes may have some activity in patients with BTC.[5]
- The contribution of CTX-009 needs to be confirmed in a randomized study

Phase 2/3 Study Design

- CTX-009 is being evaluated in an **open-label, randomized, controlled study** in patients with previously treated, advanced or metastatic BTC
- 150 patients will be randomized in a 2:1 ratio to receive either CTX-009 plus paclitaxel or paclitaxel alone
- The study will open at approximately 30 sites across the United States.
- Patients will be stratified by:
  - **Stage:** Locally advanced vs. Metastatic
  - **Anatomic subsite of primary tumor:** intrahepatic cholangiocarcinoma vs. other (extrahepatic cholangiocarcinoma, gallbladder, or ampullary)
  - **Eastern Cooperative Oncology Group (ECOG)** Performance status (0 vs. 1)

Study Schema



Study Objectives

Primary Objective	Primary Endpoint
To assess the efficacy of CTX-009 in combination with paclitaxel vs. paclitaxel alone in patients with biliary tract cancers (BTC) who have received one systemic therapy for advanced disease, as measured by Overall Response Rate (ORR) assessed by an Independent Central Radiology (ICR) review	Percentage of patients whose Best Overall Response (BOR) is assessed as Complete Response (CR), or Partial Response (PR) as assessed by RECIST 1.1

Secondary Objectives and Endpoints include **Disease Control Rate**, **Duration of Response**, **Progression Free Survival**, **Overall Survival**, **Safety**, **Quality of Life**, and **Exposure Response** through PK Analysis

Key Eligibility Criteria

Inclusion Criteria

- ✓ Unresectable advanced, metastatic, or recurrent BTC (all four subtypes allowed)
- ✓ Radiologically documented progression after prior gemcitabine and platinum containing chemotherapy regimen
- ✓ ECOG performance status 0-1
- ✓ Predicted lift expectancy of at least 12 weeks
- ✓ No evidence of ongoing infection and adequate biliary excretion
- ✓ Adequate bone marrow, hepatic, and renal function

Exclusion Criteria

- × Eligible to be treated with a molecularly targeted therapy after 1st line
- × Adequate wash-out period from prior regimen
- × Specific cardiovascular history including uncontrolled hypertension
- × Infection requiring systemic antibiotics or antiviral drugs, etc. or other severe or uncontrolled illnesses

*** Additional I/E criteria as defined in the latest version of the study protocol**

Study Information

Protocol Number:
- CTX-009-002

Status:
- Active, recruiting

ClinicalTrials.gov Identifier:
- NCTC05506943

Contact: CTX-009-002@compasstherapeutics.com

References

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