Abstract #TPS587

A Phase 2/3 randomized study of CTX-009 Combination in 2L Biliary Tract Cancer: COMPANION-002

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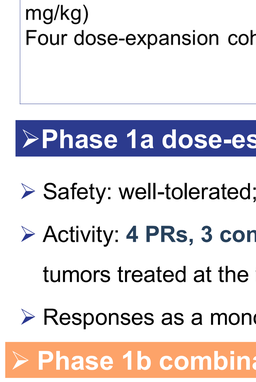
➢CTX-009: A Novel DLL4 x VEGF-A Bispecific Antibody



CTX-009 is a:

- bispecific antibody blocking DLL4 (Notch-1 ligand) and VEGF-A (soluble ligand)
- Does not lead to ADCC, Fc inactive
- Binds to its targets with 2:2 valency
- At 10 mg/Kg, CTX-009 has approximately the same VEGF-A capturing ability as bevacizumab (Avastin)
- The only DLL4 X VEGF bispecific that demonstrated monotherapy activity in the clinic in colorectal and gastric cancer

➢ 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*

➢CTX-009: Clinical Summary

Phase 1a: Dose Escalation Monotherapy Study	Phase 1b: Combination Study with Chemotherapy
N=45: Gastric, CRC, Other Nine dose-escalation cohorts (0.3-17.5 mg/kg) Four dose-expansion cohorts (7.5-15 mg/kg)	**N=17: 4 arms, multiple indications** 1. CTX-009 10.0 mg/kg + paclitaxel 2. CTX-009 10.0 mg/kg + irinotecan 3. CTX-009 12.5 mg/kg + paclitaxel 4. CTX-009 12.5 mg/kg + irinotecan

➢Phase 1a dose-escalation monotherapy**

- 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 with 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

➢Phase 2/3 CTX-009-002 (COMPANION-002) Study

➢Study Rationale

- Treatment options for patients with biliary tract cancer are limited, and the prognosis for these patients is poor. CTX-009 has demonstrated promising antitumor activity in patients with advanced cancer as monotherapy and in combination with chemotherapy. Combining CTX-009 with paclitaxel may therefore provide a benefit for patients with 2L biliary tract cancer.

➢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

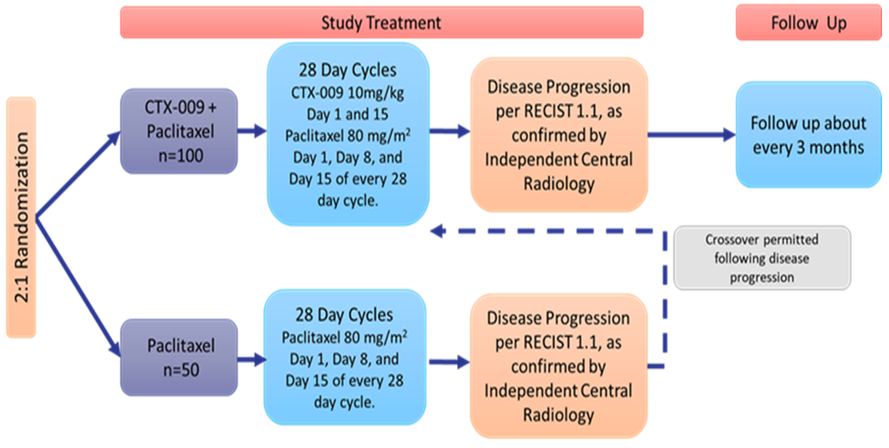
Patients will be stratified by:

➢**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

➢CTX-009-002 (COMPANION-002) Key Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
✓ Unresectable advanced, metastatic, or recurrent BTC (all four subtypes allowed)	× Percutaneous transhepatic biliary drains
✓ Radiologically documented progression after prior gemcitabine and platinum containing chemotherapy regimen	× Specific cardiovascular history including uncontrolled hypertension
✓ At least one measurable lesion	× A history of hemorrhage-related disease
✓ ECOG performance status 0-1	× Use of anticoagulants or thrombolytic agents for therapeutic purpose (prophylactic use of anti-coagulant and <=81mg aspirin use allowed)
✓ No evidence of ongoing infection and adequate biliary excretion	× Infection requiring systemic antibiotics or antiviral drugs, etc. or other severe or uncontrolled illnesses
✓ Adequate bone marrow, hepatic, and renal function	

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

➢CTX-009-002 (COMPANION-002) Active U.S. Sites as of 08-Jan-2024

➢Study Details and Contact Information

➢**Protocol Number:** CTX-009-002

➢**Status:** Active, recruiting

➢**ClinicalTrials.gov Identifier:** NCTC05506943

➢**Contact:** CTX-009-002@compasstherapeutics.com

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