Introduction of CTX-009 and COMPANION-002 Study

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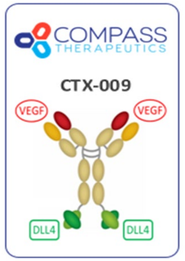
Introduction and Study Rationale

The purpose of the COMPANION-002 study is to define the safety and anti-tumor activity of a new research drug called CTX-009 in patients with biliary tract cancer (BTC). This study will also use paclitaxel, which is a chemotherapy drug. CTX-009 is an investigational drug, **which has not yet been approved by the FDA for medical use outside of a clinical trial.**

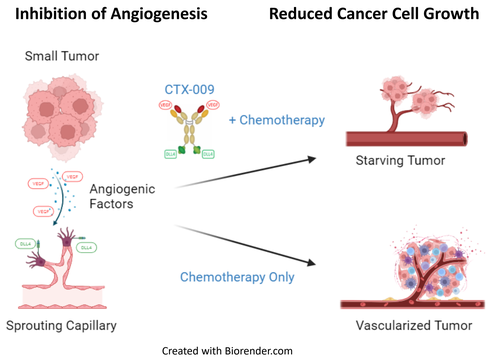
- Patients who received FOLFOX (folinic acid (leucovorin, FOL), fluorouracil (5-FU, F), and oxaliplatin (Eloxatin, OX), in the second line setting unfortunately, has only shown a 5% overall response rate in patients.[1]
- CTX-009 has demonstrated promising antitumor activity in patients with advanced cancer as monotherapy and in combination with chemotherapy.

What is CTX-009?

- CTX-009 is a bispecific antibody designed to target the immune system.
- CTX-009 can bind two targets simultaneously, VEGF-A and DLL4.
  1. VEGF-A (Vascular Endothelial Growth Factor-A) is a signal protein that helps new blood vessels form in a tumor and increases the amount of DLL4 expressed on cells that line your blood vessels.
  2. DLL4 (Delta Like Ligand 4) is a protein which uses VEGF-A expression to help blood vessels form and makes tumors grow.



- Preclinical and animal studies suggest the combined inhibition of both VEGF and DLL4 might synergistically disrupt blood vessel formation, know as angiogenesis, within tumors.



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Paclitaxel Phase 1B CTX-009 plus Irinotecan or Paclitaxel

- A Phase 1b study conducted in South Korea, evaluated CTX-009 in combination with chemotherapy (irinotecan or paclitaxel).
- In a Phase 1b study, 4 patients with BTC experienced a Partial Response, which means a patient's tumors decreased by more than 30%. Two of these patients who were on both CTX-009 at 10mg/kg and paclitaxel at 80mg/m^2 experienced tumor shrinkage of 41.4% and 61.6%.
- Both patients had multiple prior therapies, and were on study for more than a year, with durable responses for more than 9 months each.
- Data from this study led to a new Phase 2 study in patients with BTC, including cholangiocarcinoma, using paclitaxel.

Phase 2 CTX-009 plus Paclitaxel Data[2]

- A Phase 2 Study conducted in South Korea, enrolled 24 patients with BTC, these patients had received 1 or 2 prior lines of chemotherapy treatments. Patients received 10 mg/kg of CTX-009 on days 1 and 15 plus paclitaxel 80 mg/m^2 on days 1, 8, and 15 of a 28-day cycle.
- The primary endpoint of this study was the Overall Response Rate (ORR), which is the proportion of patients who have a partial or complete response to the therapy. Nine partial responses, for a 37.5% ORR were observed in patients treated in the second- and third-line settings.
- The median progression-free survival was 9.4 months and the survival rate at one year was 53%.

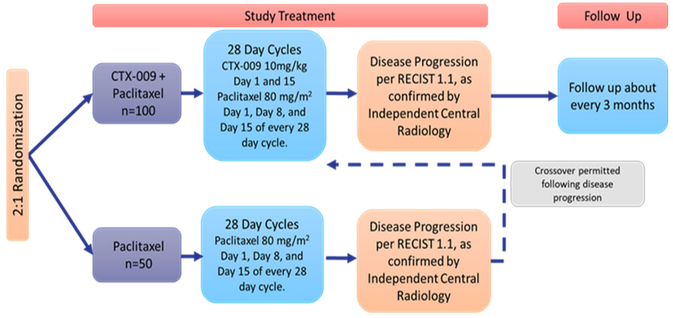
Safety and Adverse Reactions

- Adverse events were observed in ≥ 10% (more than 3 of 24) study participants who received CTX-009 in combination with paclitaxel
- Serious adverse events observed in this Phase 2 study included: neutropenia (low white blood cell count), anemia (low red blood cell count), hypertension (high blood pressure), and thrombocytopenia (low platelet blood count). Decreases in blood counts are a known side effect of paclitaxel and high blood pressure is a known effect for drugs that target VEGF-A.

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

Study Design

- CTX-009 is being evaluated in an **open-label, randomized, controlled study** in patients with previously treated, advanced, or metastatic BTC (intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, gallbladder, or ampullary)
- **150 patients** will be randomized in a 2:1 ratio to receive either **CTX-009 plus paclitaxel or paclitaxel alone**. This means twice as many patients will receive the study drug CTX-009 combined with paclitaxel compared to those receiving paclitaxel alone.
- On treatment days, IV infusion times for CTX-009 and/or paclitaxel are each one hour.



Crossover Note:
Patients who are initially randomized to receive paclitaxel alone, have the option to 'crossover' into the study arm where patients receive both CTX-009 and paclitaxel if their disease worsens while on treatment. This decision will be discussed with the Investigator, Study Doctor, and the patient to determine if they are eligible.

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

- You have bile duct cancer that cannot be removed by surgery, has spread to other parts of the body, and has **progressed after 1L treatment with gemcitabine and platinum-containing chemotherapy.**
- You feel well enough to do most of your daily activities without help (ECOG performance status of 0 or 1).
- There is no active serious infection in your body, and your liver is working well enough to process bile properly.
- Your blood counts, liver function, and kidney function are all at levels that are considered safe for treatment.
- You do not have tubes placed in your liver to help with bile drainage (percutaneous transhepatic biliary drains).
- You do not have certain heart problems like uncontrolled hypertension.
- You do not have a history of disease that causes heavy bleeding.

Comprehensive Inclusion and Exclusion criteria can be found at ClinicalTrials.gov NCTC05506943

CTX-009-002 (COMPANION-002) Active U.S. Sites

Arizona
Mayo Clinic, Phoenix
University of Arizona, Tucson

California
University of Southern California Norris Comprehensive Cancer Center, Los Angeles
Stanford Medicine Cancer Center, Palo Alto
University of California San Francisco, San Francisco

Colorado
Rocky Mountain Cancer Centers, Aurora

Delaware
Medical Oncology Hematology Consultants, Newark

Florida
University of Florida, Gainesville
Mayo Clinic Jacksonville, Jacksonville
AdventHealth Orlando, Orlando

Illinois
Northwestern University, Chicago
University of Chicago, Chicago

Louisiana
Ochsner Clinic Foundation, New Orleans

Maryland
Johns Hopkins University, Baltimore

Massachusetts
Massachusetts General Hospital, Boston

Minnesota
Mayo Clinic Rochester, Rochester

Missouri
Washington University School of Medicine, Siteman Cancer Center, Saint Louis

New Jersey
Rutgers Cancer Institute, New Brunswick

New Mexico
The University of New Mexico, Albuquerque
Memorial Medical Center, Las Cruces

New York
Montefiore Medical Center, Bronx
Roswell Park, Buffalo
Columbia University, New York

Ohio
Grabrail Cancer Center, Canton
Cleveland Clinic, Cleveland

Tennessee
University of Tennessee Medical Center, Knoxville
SCRI Oncology Partners, Nashville

Texas
Texas Oncology, Austin
Texas Oncology, Baylor Charles A. Sammons Cancer Center, Dallas
Texas Oncology, Denison
Texas Oncology, San Antonio
Texas Oncology, Northeast Texas, Tyler
The University of Texas MD Anderson Cancer Center, Houston

Washington
Northwest Cancer Specialists, Vancouver

Study Contact Information

- **Protocol Number:** CTX-009-002
- **Status:** Active, recruiting
- **ClinicalTrials.gov Identifier:** NCTC05506943
- **Contact:** CTX-009-002@compasstherapeutics.com

Acknowledgments: We would like to thank the following Principal Investigators for their contribution to the study: Ursa Brown-Glaberman, Nashat Grabrail, Ian Hu, Olivia Aranha, Mohamedtaki Tejani, Aparna Kalyan, Chih-Yi Liao, Lingling Du, Howard Hochster, Umair Majeed, Nguyen Tran, Gregory Heesstand, Anthony El-Khoueiry, Priyadarshini Pathak, Saikrishna Gadde, Suneel Kamath, Efrat Dotan, Ilyas Sahin, Rachna Shroff, Renuka Iyer, Fernand Bteich, Meredith Pelster, Donald Richards, Vivan Cline, David P. Cosgrove, Amir Faridi, Sujatha Nallapareddy, and Nathan M. Shumway. Special thanks to Thomas Schuetz, Karin Herrera, Patricia Gonzalez, Sarah Pilgrim, Kelly Ocasio Norat, Anna Gifford, and Nicole Gampp. Most importantly, we would like to thank the patients and their families who have participated or are participating in these studies.

References:
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Presented at the Cholangiocarcinoma Foundation (CCF) Annual Conference 2024, April 17-19, Salt Lake City, UT, USA & Online