Trial In Progress: A Phase 2 Study of CTX-009 in Adult Patients with Metastatic Colorectal Cancer who have received Two or Three Prior Systemic Chemotherapy Regimens

Abstract # TP281

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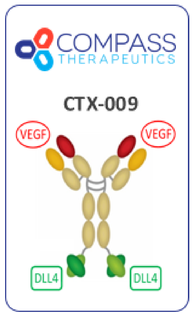
Background

Background of Disease

- Patients with unresectable locally advanced and unresectable metastatic colorectal cancer (CRC) are sequentially treated with various combinations or single agent courses of cytotoxic chemotherapy agents, as well as targeted therapies.[1]
- Despite the approval of multiple new agents in the past two decades, the goals of therapy are generally palliative, and in the cases of patients whose disease has progressed, or who have not tolerated 2 or 3 prior lines of therapy, the expectation for tumor response with the available treatments are less than 5% and the median overall survival is approximately 6 months (for 3rd line therapy) or less (for 4th line therapy).[2, 3]

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

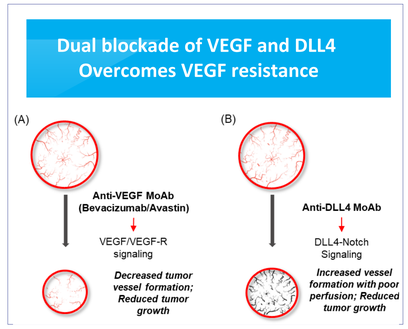
- Unique proprietary DLL4 binding epitope
- 2:2 valency effectively blocks both signaling pathways

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



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
- Of 6 patients with CRC treated in the 10.0 and 12.5 mg/kg cohorts in the Phase 1a monotherapy Study, 2 of these 6 had confirmed PRs (33% ORR)
- Patients had received a median of 3.5 prior lines of therapy; all had received bevacizumab
- Median PFS in these 6 patients was 6.7 months

A Phase 1b/2 study of CTX-009 in combination with irinotecan or paclitaxel revealed additional PRs in heavily pretreated patients with advanced solid tumors

Methods

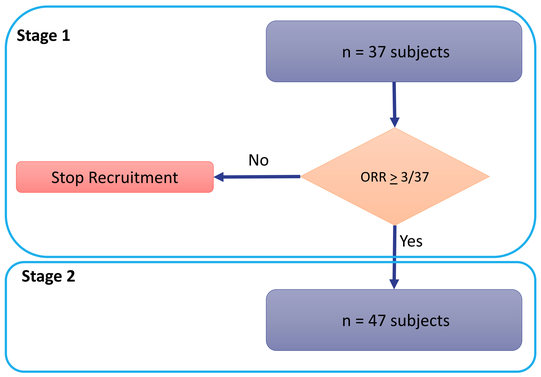
Study Rationale

- Presently, there is no consensus post-second-line therapy for patients with CRC in whom first- and second-line therapies have failed[3, 4]
- Phase 1 data shows encouraging results in a cohort of patients with CRC who had a median of 3.5 prior systemic therapies, and therefore warrants further exploration

Phase 2 Study Design

- CTX-009 is being evaluated in an **open-label, adaptive Simon Two Stage study** to evaluate the efficacy of CTX-009 in patients with metastatic CRC who have progression or relapse of the disease after receiving two or three systemic therapies for metastatic disease.
- The study design will enroll approximately 37 patients into Stage 1, and if criteria are met to move to Stage 2, an additional 47 patients will be enrolled.
  - ✓ To move to Stage 2 of the study, 3 or more Complete or Partial Responses must be confirmed via RECIST 1.1.
- Patients will be treated in 28-day cycles, with CTX-009 administration on Day 1 and 15.
- The study will open at approximately 10 sites across the United States.

Study Schema



Study Objectives

Primary Objective	Primary Endpoint
To assess the efficacy of CTX-009 in patients with colorectal cancer who have received two or three systemic therapies for metastatic 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

- ✓ Histologically or cytologically confirmed metastatic or recurrent colorectal cancer
- ✓ Primary tumor resected >3 months prior
- ✓ Progressive disease or relapse after two or three prior systemic therapies
- ✓ ECOG performance status 0-1
- ✓ Predicted lift expectancy of at least 12 weeks
- ✓ Adequate hepatic and renal function

Exclusion Criteria

- × Adequate wash-out period from prior regimens and/or procedures
- × Specific cardiovascular history including uncontrolled hypertension
- × Continuous use of NSAIDs or systemic corticosteroids
- × Infection requiring systemic antibiotics or antiviral drugs, etc. or other severe or uncontrolled illnesses
- × Clinically significant ECG findings

Additional Inclusion and Exclusion criteria as defined in the latest version of the study protocol.

Study Information

Protocol Number:
- CTX-009-003

Status:
- Active, recruiting, first patient dosed

ClinicalTrials.gov Identifier:
- NCT05513742

Contact: CTX-009-003@compasstherapeutics.com

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