Blocking Angiogenesis in Biliary Tract Cancer with CTX-009

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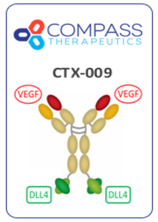
CTX-009: A Novel DLL4 x VEGF-A Bispecific Antibody



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

CTX-009 Phase 1 Study Design

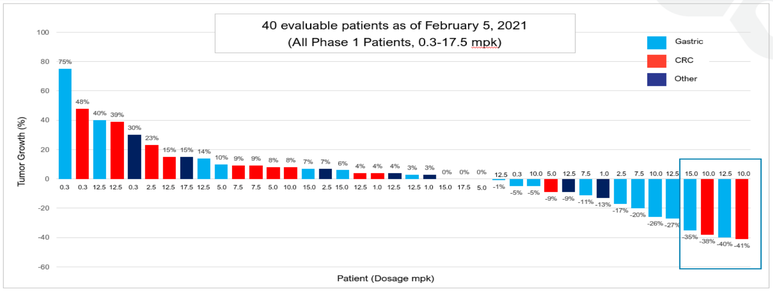
Phase 1a:
Dose Escalation Monotherapy Study

N=45: Gastric, CRC, Other
Nine dose-escalation cohorts (0.3-17.5 mg/kg)
Four dose-expansion cohorts (7.5-15 mg/kg)

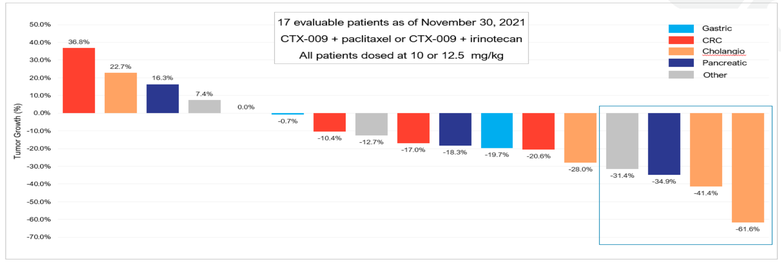
Phase 1b:
Combination Study with Chemotherapy

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 CTX-009 Monotherapy (all doses) *



Phase 1b CTX-009 Combination Study



Phase 1a and 1b CTX-009 Safety Data

Phase 1a Monotherapy (n= 45)

Drug-related adverse events observed in > 5% of patients	Total (n)	Total (%)	Grade 3 (n)	Grade 3 (%)
Hypertension*	17	38	7	16
General disorders (fatigue, fever, asthenia, edema, etc.)	7	16	1	2
Nervous system disorders (headache, dizziness)	7	16	1	2
Gastrointestinal disorders (nausea, vomiting, etc.)	6	13	2	4
Pulmonary hypertension	4	9	0	0
Proteinuria	3	7	0	0

Phase 1b Combination (n=17)

Drug-related adverse events observed in > 1 patient	Total (n)	Total (%)	Grade 3 (n)	Grade 3 (%)
Hypertension	8	47	4	24
Nausea	8	47	1	6
Fatigue	6	35	1	6
Neutropenia** Anemia** Thrombocytopenia**	6 4 2	35 24 12	2 3 2	12 18 12
Diarrhea	5	29	0	0
Anorexia	5	29	0	0
Proteinuria	5	29	0	0
Pulmonary hypertension (all grade 1)	5	29	0	0
Dyspnea	4	24	0	0
Gingival edema (mucositis)	2	12	0	0
Anal hemorrhage	2	12	0	0

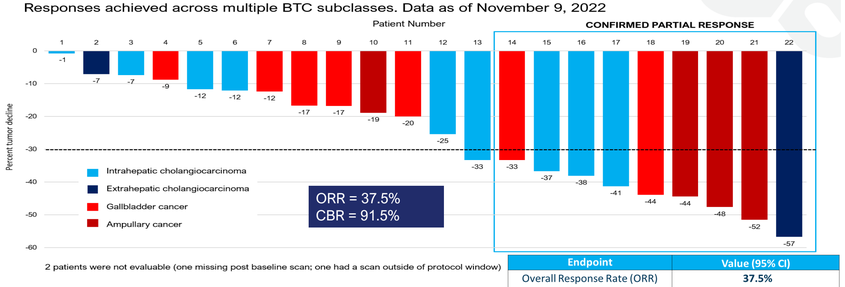
Phase 2 CTX-009 Combination Study – Patient Demographics**

	24 Total Patients
Age	
Median (years)	61.5
Gender, n(%)	
Male	14 (58%)
Female	10 (42%)
ECOG performance status, n(%)	
0	13 (54%)
1	11 (46%)

	24 Total Patients
Prior systemic therapies, n(%)	
1	11 (46%)
2	13 (54%)
Prior Gem/Cis regimen	23 (96%)
BTC subtype, n (%)	
Intrahepatic cholangiocarcinoma	9 (38%)
Extrahepatic cholangiocarcinoma	3 (13%)
Gallbladder cancer	7 (29%)
Ampullary cancer	5 (21%)

Phase 2 CTX-009 Data

Responses achieved across multiple BTC subclasses. Data as of November 9, 2022

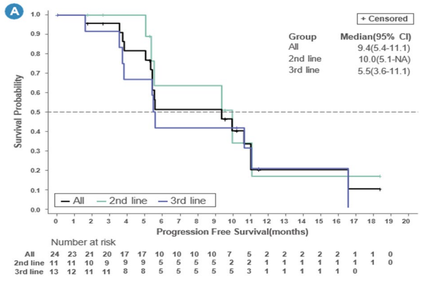


2 patients were not evaluable (one missing post baseline scan; one had a scan outside of protocol window)

- 9 partial responses (PRs) for a 37.5% ORR (defined in study objectives) in patients treated in the second-and third-line settings (64% ORR of patients treated in the second-line setting)
- Adverse event profile similar to Phase 1 studies

Endpoint	Value (95% CI)
Overall Response Rate (ORR)	**37.5%**
Stable Disease (SD)	**54.2%**
Progression Free Survival (PFS)	**9.4 m** (5.4 – 11.1)
Overall Survival (OS)	**12.5 m** (10.9 – NA)
Duration of Response	**6.9 m** (3.5 – NA)

Phase 2 CTX-009 Secondary Endpoints: PFS **

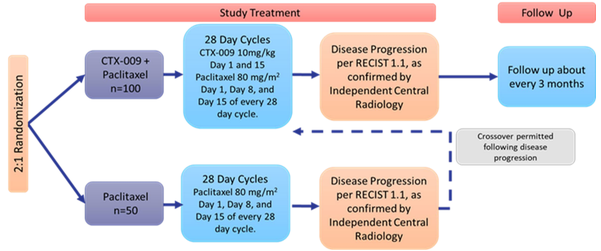


Phase 2: Treatment-Emergent ≥ Grade 3 Adverse Events (>10% pts)

Event	24 total Patients N (%)
Neutropenia	20 (83.3%)
Anemia	5 (20.8%)
Hypertension	4 (16.7%)
Thrombocytopenia	3 (12.5%)

TEAE leading to discontinuation: confusion, embolism, pneumonia (grade 5), biliary fistula, large intestine perforation, blood creatinine increased, and blood urea nitrogen increased

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



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)

CTX-009-002 (COMPANION-002) Active U.S. Sites as of 16-Oct-2023

Study Details and Contact Information

- **Protocol Number:** CTX-009-002
  Status: Active, recruiting
- **ClinicalTrials.gov Identifier** NCT05506943
- **Contact:** CTX-009-002@compasstherapeutics.com

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References:

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