CTX-009 (tovecimig) with gemcitabine, cisplatin, and durvalumab as first-line therapy in patients with unresectable or metastatic biliary tract cancers

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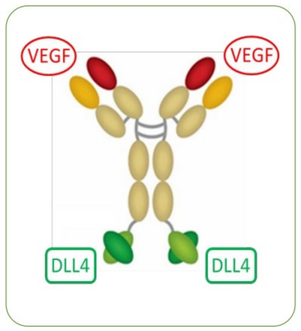
Background:

Advanced biliary tract cancers (BTCs) are notable for their aggressive nature, limited treatment options, and poor prognosis.[1] More treatment options are needed for first-line therapy of advanced BTCs.

CTX-009 (tovecimig): A Novel DLL4 x VEGF-A Bispecific Antibody

DLL4 upregulation in the tumor microenvironment mediates resistance to VEGF-targeted agents. Dual blockade of DLL4/NOTCH1 and VEGF signaling has been shown to be synergistic in preclinical models.[2] Tovecimig's 2:2 valency effectively blocks both signaling pathways.



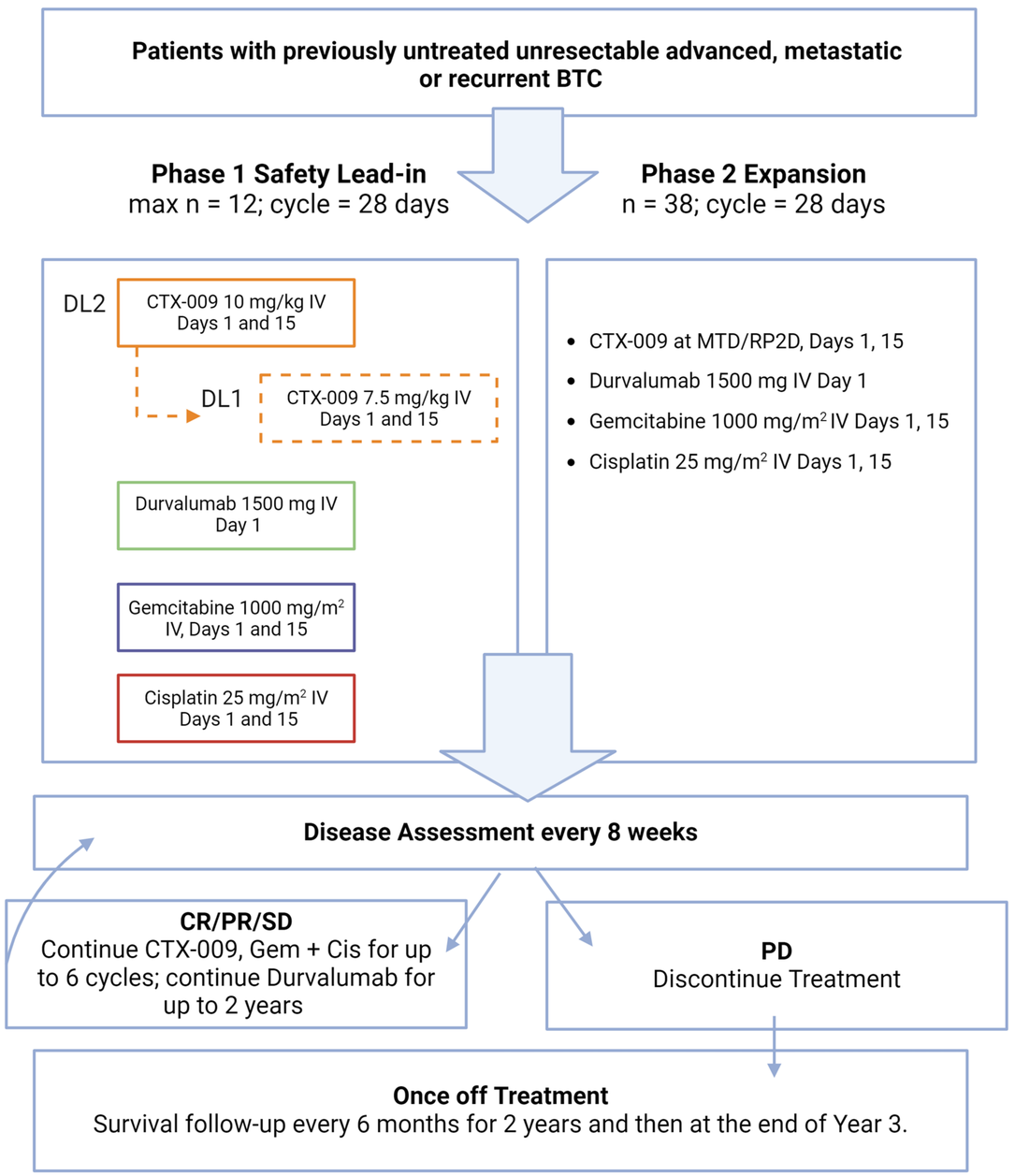
Study Design:

This is a phase 1/2 study evaluating the addition of CTX-009 (tovecimig), to the standard first-line therapy of gemcitabine/cisplatin/durvalumab (GCD) in patients with treatment-naïve unresectable or metastatic BTC.

GCD with CTX-009 will be given on Days 1 and 15 in a 28-day cycle.

There is a Phase 1 safety lead-in of 12 patients followed by a Phase 2 expansion of 38 patients.

Study Schema:



Key Eligibility Criteria:

Inclusion Criteria

- Histologically confirmed unresectable advanced, metastatic, or recurrent BTC
- Measurable disease
- Adequate hepatic and renal function

Exclusion Criteria

- History of uncontrolled hypertension
- Previous treatment of current malignancy. Patients who have received prior perioperative treatment (adjuvant or neoadjuvant) are eligible
- History of hemorrhagic disease
- History of active interstitial lung disease

Study Objectives:

Primary Objectives:

- Assess safety/tolerability of GCD + CTX-009 combination
- Assess 6-month progression-free survival

Secondary Objectives:

- Assess ORR, DOR, OS, PFS

Study Details and Contact Information:

Protocol Number: NCT06548412
Status: Active, recruiting
Site Email Contact:
GIClinicaltrials@mdanderson.org

References:
1. Kam AE, Masood A, Shroff RT. Current and emerging therapies for advanced biliary tract cancers. Lancet Gastroenterol Hepatol. 2021 Nov;6(11):956-969. doi: 10.1016/S2468-1253(21)00171-0. PMID: 34626563.
2. Yeom DH, Lee YS, Ryu I, Lee S, Sung B, Lee HB, Kim D, Ahn JH, Ha E, Choi YS, Lee SH, You WK. ABL001, a Bispecific Antibody Targeting VEGF and DLL4, with Chemotherapy, Synergistically Inhibits Tumor Progression in Xenograft Models. Int J Mol Sci. 2020 Dec 29;22(1):241. doi: 10.3390/ijms22010241. PMID: 33383646; PMCID: PMC7796106.