A Phase I/II Study of CDX-1140, CAPOX and Pembrolizumab in Second-line Biliary Tract Cancer (trial in progress)

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Background

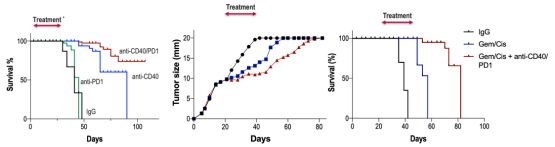
Advanced biliary tract carcinoma (BTC) carries a poor prognosis, and effective treatment options are limited in the second-line setting.

Our group conducts clinical trials evaluating different immunotherapy regimen in CCA.

We were the first to test anti-CTLA4 and anti-CTLA4 + anti-PDL1 in BTC.

While chemotherapy combined with PD-1 blockade has demonstrated modest clinical activity, primary and acquired resistance remain major challenges.

Preclinical studies indicate that CD40-mediated activation of antigen-presenting cells can enhance antitumor immunity and improve response to immune checkpoint inhibition, particularly when combined with chemotherapy.



Diggs,…, Greten (2021) Journal of Hepatology 74:1145-1154

Methods

This is an **ongoing Phase I/II, single-arm**, open-label study evaluating the safety and efficacy of the CD40 agonist antibody CDX-1140 in combination with capecitabine and oxaliplatin (CAPOX) and pembrolizumab in patients with advanced BTC who have progressed following prior systemic therapy. We have enrolled 15 patients on this trial.

The Phase I portion uses a dose-escalation design to determine the recommended Phase II dose (RP2D) of CDX-1140 in combination with CAPOX and pembrolizumab.

Phase II evaluates clinical efficacy at the RP2D.

The **primary Phase II endpoints** are 6-month progression-free survival (PFS) and overall response rate (ORR) per RECIST v1.1.

Secondary objectives include safety and overall survival.

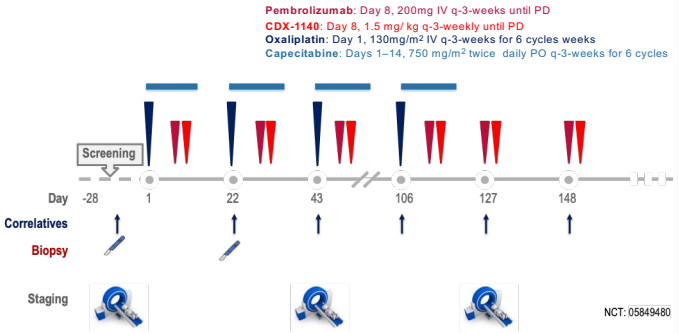
Exploratory endpoints include immune profiling of blood and tumor tissue, assessment of PD-L1 expression, cytokine analyses, multiplex immunohistochemistry, and genomic and transcriptomic analyses including ctDNA.

Key eligibility criteria
Histopathological confirmation of BTC
ECOG 0-1

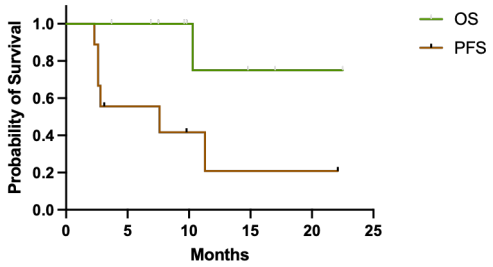
Study population
26 evaluable patients

I would like to thank the CCF foundation for support to two junior investigators in my group (for preclinical studies and protocol development)

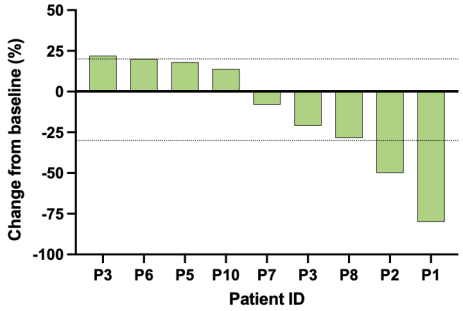
Trial outline



PFS and OS data (first 9 patients)



Tumor responses (preliminary)



All treatment emergent AEs in the first 13 patients:
Grade 4 lymphopenia, Rash (grade 2 & 3), Arthralgia (grade 2), CBC abnormalities

My group conducts clinical trials testing immunotherapy.

What was this study about?
This study looked at a new **combination of chemotherapy with immunotherapy** to treat biliary tract cancer.
The medicines used are: Capecitabine, Oxaliplatin, Pembrolizumab, CDX1140.
These drugs help the immune system fight cancer in different ways.

Why try this treatment?
We have conducted preclinical studies in mice and show that **combining these drugs might work better together** than using them alone in animals.

How is the treatment given?
Patients receive chemotherapy as a pill on day 1-14, and an infusion on day 1.
Followed by immunotherapy given as an infusion on day 14.
Treatment is given every **3 weeks**

Can I receive this treatment?
Yes, if you match all inclusion inclusion criteria for the study.
prior first line chemotherapy
please ask our team for further in/exclusion criteria.

⚠ **What are potential side effects?**
Most common site effects include joint pain and rash along with lab abnormalities.

How many patients have been treated in this trial and what are the results?
So far, we have started treatment in 15 patients.
👉 It is much too early to say how well the treatment works in every patient, but we have observed tumor shrinkage in some patients.

Where is this trial being conducted?
All patients are treated at the **National Cancer Institute in Bethesda, Maryland**.

Are there costs associated with treatment?
The Clinical Center does not charge patients for participation and treatment in clinical studies at NIH.
NCI pays for all travel for patients enrolled (from any destination within the United States).
In addition, in certain circumstances, you may qualify for help with hotel expenses.

Where can I get more written information about this trial?

Key takeaway

This is an ongoing clinical trial, which currently enrolls patients with cholangiocarcinoma, who have failed 1st line chemotherapy.

It may improve cancer control in some patients and is generally well tolerated.

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