PHASE 2 STUDY ASSESSING TOLERABILITY, EFFICACY AND BIOMARKERS FOR DURVALUMAB ± TRELIMEMAB AND GEMCITABINE/CISPLATIN IN CHEMO-NAÏVE ADVANCED BILIARY TRACT CANCER

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Introduction
- Biliary tract cancer (BTC) includes cholangiocarcinoma and intrahepatic cholangiocarcinoma (ICC), pancreatic adenocarcinoma (PA), gallbladder cancer (GB) and ampulla of Vater (Amp-V) cancer.
- BTC is most common in the extrahepatic ducts (EHD) as well as the gallbladder and ampulla of Vater (Amp-V).
- BTC has been regarded as an orphan disease for advanced treatment.
- Most BTC patients (BTC<50%) are positive for KRAS/Gem-Gem according to the personal treatment strategy.
- Early stages of advanced BTC patients have shown promising efficacy in some settings, albeit with SCV, and there is an opportunity for combining immunotherapy with standard chemotherapy.
- The study evaluated the tolerability and efficacy of Gem/Cis (Gem/Cis ± desmosumab) in patients with or without concurrent therapy (CT), as well as the role of programed death-1 (PD-1) inhibitors with or without concurrent gemcitabine/cisplatin (Gem/Cis) associated with survival in mullinal lung cancer and colorectal cancer as an effective combination.

Methods
- Study Design: The phase 2 study (NCT03958283) assessed the safety and efficacy of D+ with or without T+ and GEM in treatment-naive Korean patients with advanced BTC.
- Patients were enrolled in 3 cohorts (Figure 1). Table 1: Patient demographics and baseline characteristics

Results
- The study enrolled 112 patients with available data (Table 1).
- Median duration of follow-up OS: 13.3 months (95% CI: 2.5-19.3) months for the Gem/Cis + D cohort and 11.8 (95% CI: 7.4-19.4) months for the Gem/Cis + D + T cohort.

Key Conclusions
- These are the first clinical data of D+ T+ in Gem/Cis in chemotherapy-naïve and BTC patients.
- The addition of immunotherapy to chemotherapy was tolerable and showed very promising efficacy.
- We identified candidate biomarkers that may be indicative of response to these therapies in further analyses in the Gem/Cis + D and Gem/Cis + D + T cohorts.
- The combination of D+ Gem/Cis versus Gem/Cis is being investigated in the global Phase 3 TOPAZ-1 trial (NCT03887525), enrollment is ongoing.

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References
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Figure 4. Diagrammatic view of responses to: (A) Gem/Cis + D, (B) Gem/Cis + D + T, and (C) Gem/Cis + D + T during the first cycle of Gem/Cis + D + T in relation to the locoregional tumor burden.

Figure 5. Correlation between PD-L1 expression and first cycle of Gem/Cis and D + T in the BRC.

Figure 6. Schema of timelines and corresponding scales in the BRC.

Figure 7. Timeline of biomarker acquisition.

Figure 8. Bar graph of biomarkers in the BRC.

Figure 9. Time to tumor progression.

Figure 10. Kaplan-Meier curves of overall survival.

Figure 11. Kaplan-Meier curves of median duration of progression-free survival.

Figure 12. Kaplan-Meier curves of median duration of overall survival.

Figure 13. Kaplan-Meier curves of median duration of response.

Figure 14. Table of common adverse events (C2A; L0 in any cohort).