GEMINI Platform Study Design---BTC substudy

POPULATION

1L BTC Patient Population:

- Patients aged ≥ 18 years with histologically confirmed adenocarcinoma BTC
- Not ampullary carcinoma
- Unresectable advanced or metastatic stage
- No prior immunotherapy and locoregional therapy for BTC
- ECOG performance score 0–1

TREATMENT

Safety run in[1] (N=**6** evaluable pts/arm)	Expansion[2] (N=**24** evaluable pts/arm)
Cohort A	**AZD2936** (750 mg) → Q3W **Gemcitabine** (1000 mg/m^2) + **Cisplatin** (25 mg/m^2) → D1&D8 X 8 Cycles, Q3W
Cohort B	**MED5752** (750 mg) → Q3W **Gemcitabine** (1000 mg/m^2) + **Cisplatin** (25 mg/m^2) → D1&D8 X 8 Cycles, Q3W

ENDPOINTS

Primary Endpoint:
PFS6 and **Safety** by Inv (per RECIST1.1)

Secondary Endpoint:
ORR, DoR, DCR at 12w/24w, mPFS & PFS9 & PFS12, mOS & OS rate at 12m / 18m), PK, ADA

Exploratory Endpoint:
Efficacy (e.g ORR) by BICR (per RECIST 1.1), PD biomarker, predictive biomarker, ctDNA related to efficacy

Considerations

1. Study will have **SRC** for the first **6** evaluable pts / cohort.
2. Expansion to enroll **24** additional pts in each cohort to have a total of **30** evaluable pts / cohort
3. Provision of tumor samples – 1) mandatory baseline tissue-archival or fresh biopsy, 2) optional on-treatment and progression biopsy