106P - The impact of alterations in cancer driver genes and other potentially targetable mutations on progression and overall survival in patients with biliary tract cancer treated on the randomised phase III multicentre BILCAP clinical trial.

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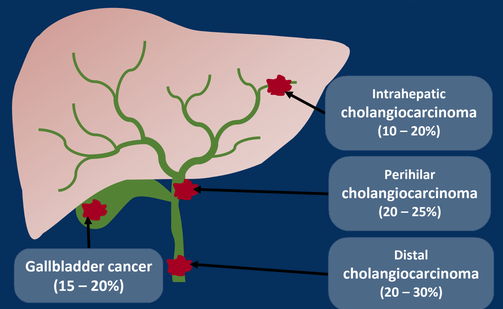
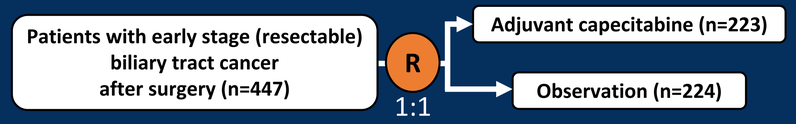
Background



Biliary tract cancer is cancer of the bile ducts (cholangiocarcinoma) and gallbladder.

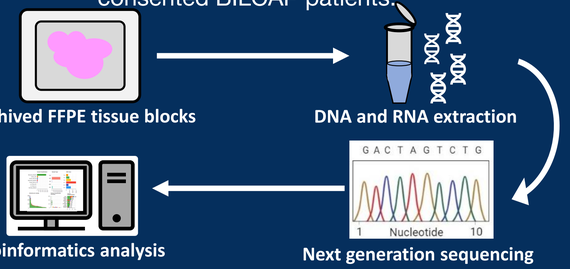
The BILCAP clinical trial established adjuvant capecitabine as the standard of care treatment in patients with resected biliary tract cancer.



Translational work to investigate the role of cancer driver genes and other potentially targetable mutations in patients enrolled on BILCAP was performed on a total of 204 patients.

Methods

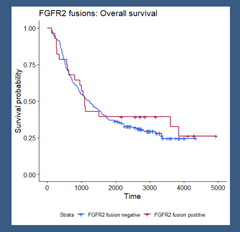
Archived fixed formalin (FFPE) tissue samples were collected from 204 consented BILCAP patients.

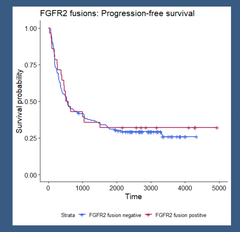


These samples underwent DNA and RNA extraction followed by low-pass whole genome sequencing (201 / 204), targeted gene sequencing (39 / 204) and RNA sequencing (204 / 204) for copy number analysis (amplification defined as copy number ≥ 4), mutation analysis and gene fusion analysis.

Conclusion

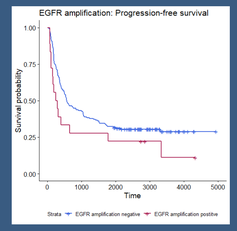
The BILCAP cohort shows a wide variety of driver and potentially targetable mutations in unselected biliary tract cancer patients, comparable to previous early-stage biliary tract cancer datasets.

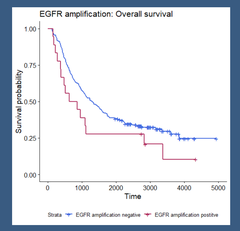




FGFR2 fusions had no effect on overall survival or progression-free survival.

EGFR amplification reduces overall survival and progression-free survival.





EGFR may be an important prognostic indicator in biliary tract cancer, and an attractive target for systemic anti-cancer therapy in biliary tract cancer.

FFPE blocks data from further patients from BILCAP (particularly patients with perihilar cholangiocarcinoma) is currently being processed and analysed.

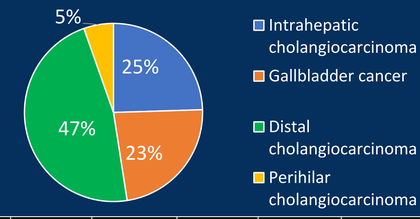
Data from other adjuvant clinical trials (JCOG1202: ASCOT investigating adjuvant S-1) and data from patients with metastatic biliary tract cancer at presentation are also being analysed.

For further information, please contact Dr Valerie Crolley (v.crolley@ucl.ac.uk)

Valerie Crolley has no DOI to declare.

Results

A total of 204 patients were analysed: 50 had intrahepatic cholangiocarcinoma (iCCA), 47 had gallbladder cancer (GBC), 96 had distal cholangiocarcinoma (dCCA) and 11 had perihilar cholangiocarcinoma (pCCA).



Anatomical Subtype	FGFR2 Fusions	NTRK1 fusions	FGFR1 fusions	FGFR3 fusions	Treg > 0.05	CD4+ > 0.05	NTRK1 amplification	ERBB2 amplification	MET amplification	EGFR amplification	MDM2 amplification
iCCA	9	3	3	2	6	6	14	17	7	7	12
pCCA	0	0	0	0	2	0	3	7	0	0	5
GBC	14	1	1	0	11	6	13	11	8	9	9
dCCA	4	0	2	1	24	1	24	56	9	2	42

Overall Survival

Variable	N	Hazard ratio	p
FGFR2 fusions	28 / 204 (13.7%)	0.86 (0.51, 1.43)	0.6
NTRK1 fusions	4 / 204 (2.0%)	0.23 (0.03, 1.62)	0.1
FGFR1 fusions	6 / 204 (2.9%)	1.41 (0.56, 3.54)	0.5
FGFR3 fusions	3 / 204 (1.5%)	1.23 (0.30, 5.00)	0.8
Regulatory T-cell fraction > 0.05	43 / 204 (21.1%)	0.90 (0.60, 1.33)	0.6
CD4 T-cell fraction > 0.05	13 / 204 (6.4%)	0.83 (0.42, 1.67)	0.6

0.05 0.1 0.2 0.5 1 2 5

Variable	N	Hazard ratio	p
Known pathogenic IDH1 mutations	4 / 39 (10.3%)	0.55 (0.12, 2.42)	0.4

0.2 0.5 1 2

Variable	N	Hazard ratio	p
NTRK1 amplification	54 / 201 (26.9%)	0.74 (0.48, 1.15)	0.18
ERBB2 amplification	91 / 201 (45.3%)	1.13 (0.76, 1.68)	0.55
MET amplification	24 / 201 (11.9%)	0.70 (0.31, 1.58)	0.39
EGFR amplification	18 / 201 (11.9%)	2.54 (1.05, 6.14)	0.04
MDM2 amplification	68 / 201 (33.8%)	1.40 (0.89, 2.18)	0.14
MDM2 amplification - copy number > 8	6 / 201 (3.0%)	0.79 (0.28, 2.25)	0.66

0.5 1 2 5

Progression-free Survival

Variable	N	Hazard ratio	p
FGFR2 fusions	28 / 204 (13.7%)	0.87 (0.53, 1.44)	0.6
NTRK1 fusions	4 / 204 (2.0%)	0.23 (0.03, 1.66)	0.1
FGFR1 fusions	6 / 204 (2.9%)	1.34 (0.54, 3.30)	0.5
FGFR3 fusions	3 / 204 (1.5%)	1.00 (0.25, 4.04)	1.0
Regulatory T-cell fraction > 0.05	43 / 204 (21.1%)	0.78 (0.52, 1.18)	0.2
CD4 T-cell fraction > 0.05	13 / 204 (6.4%)	0.84 (0.41, 1.75)	0.6

0.05 0.1 0.2 0.5 1 2

Variable	N	Hazard ratio	p
Known pathogenic IDH1 mutations	4 / 39 (10.3%)	0.53 (0.13, 2.25)	0.4

0.2 0.5 1 2

Variable	N	Hazard ratio	p
NTRK1 amplification	54 / 201 (26.9%)	0.74 (0.48, 1.14)	0.17
ERBB2 amplification	91 / 201 (45.3%)	1.13 (0.77, 1.68)	0.53
MET amplification	24 / 201 (11.9%)	0.80 (0.39, 1.64)	0.53
EGFR amplification	18 / 201 (11.9%)	2.38 (1.08, 5.27)	0.03
MDM2 amplification	68 / 201 (33.8%)	1.33 (0.86, 2.05)	0.20
MDM2 amplification - copy number > 8	6 / 201 (3.0%)	0.78 (0.27, 2.22)	0.64

0.5 1 2 5