

Supplementary Material

Supplementary Table 1. Intrahepatic cholangiocarcinoma cohort radiological characteristics and

summary. iCCA=intrahepatic cholangiocarcinoma; CT=computerised tomography; MRI=magnetic resonant imaging; Art=arterial phase; PV=portal venous phase

Supplementary Figure 1. A) Guidelines for clarification & standardization of data. B) Radiological definition for retrospective classification of iCCA. iCCA – intrahepatic cholangiocarcinoma; CT – computed tomography
*Includes iCCA/HCC Combined Tumours - a rare but distinct tumour based mainly on histology findings.

Supplementary Figure 2. A) Radiological example of intrahepatic cholangiocarcinoma (iCCA) demonstrating a dominant hypodense liver lesion and capsular retraction (arrows). B) Radiological example of bi-lobar liver metastases from a solid tumour primary.

Supplementary Figure 3: A) Kaplan-Meier curves for overall survival (OS) of all patients with liver-involvement who undertook systemic anti-cancer treatment (SACT). No significant difference in survival between groups. B) Kaplan-Meier curve for survival for the 15 patients who received carboplatin/paclitaxel chemotherapy, split by confirmed cancer of unknown primary (cCUP) or intrahepatic cholangiocarcinoma (iCCA) diagnosis. No significant difference in OS (Log-Rank (Mantel-Cox) test p-value=0.7387).

Supplementary Table 1: Intrahepatic cholangiocarcinoma cohort radiological review summary

Case ID	Radiology review		Hepatic tumour features										Associated radiological features				
	Oncologist review	Radiologists review	Radiology modality		Single dominant liver lesion?	Largest axial dimension (cm)	Mass description	Central hypointensity	Peritumoural enhancement	Capsule retraction	Dilated Intrahepatic Bile Ducts	Satellite liver nodules	Vascular encasement	Tumour Thrombus	Cirrhosis	Portal Hypertension	Extrahepatic metastatic sites
			Radiology modality	Phase of CT													
2	Possible ICCA	ICCA	CT	PV only	Present	5.1	Heterogenous mass with irregular margin	Present	Present	Absent	Absent	Present	Absent	Absent	Absent	Absent	Portal nodal mass
3	ICCA	ICCA	CT	Art, PV	Present	7	Heterogenous mass with irregular margin	Present	Present	Absent	Present	Present	Present	Absent	Absent	Absent	Portal, lung
4	Possible ICCA	Possible ICCA	CT	Art, PV	Present	14	Heterogenous mass with irregular margin	Present	Present	Absent	Present	Present	Present	Present	Present	Present	Bone, adrenal
5	ICCA	ICCA	CT and MRI	PV only	Absent	n/a	Heterogenous mass with irregular margin	Present	Present	Absent	Present	Present	Present	Absent	Absent	Absent	None
6	ICCA	ICCA	CT	PV only	Present	12	Heterogenous mass with irregular margin	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Nodes
8	ICCA	ICCA	CT	Art, PV	Present	15	Heterogenous mass with irregular margin	Present	Present	Absent	Present	Present	Present	Absent	Absent	Absent	Portal nodes
12	ICCA	Possible ICCA	CT	PV only	Present	14	Heterogenous mass with irregular margin	Present	Present	Absent	Present	Present	Present	Absent	Absent	Absent	Portal and mesenteric nodes
15	Possible ICCA	ICCA	CT	triple phase	Present	13	Heterogenous mass with irregular margin	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Portacaval nodes and perihaptic ascities
16	ICCA	ICCA	CT	PV only	Present	8	Heterogenous mass with irregular margin	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Bone, nodal, peritoneal nodules and small pelvic ascities
17	ICCA	ICCA	CT	Art, PV	Present	6	Heterogenous mass with irregular margin	Present	Present	Absent	Present	Present	Present	Absent	Absent	Absent	Bone, nodal, lung, peritoneal nodules and small pelvic ascities
24	Possible ICCA	Possible ICCA	CT	Art, PV	Present	5.6	Heterogenous mass with irregular margin	Present	Present	Absent	Present	Present	Present	Absent	Absent	Absent	Hilar nodes, small volume ascities
29	ICCA	ICCA	CT	Art, PV	Present	13	Heterogenous mass with irregular margin	Present	Present	Absent	Present	Present	Present	Absent	Absent	Absent	Nodes and perihaptic ascities
33	ICCA	ICCA	CT	PV only	Present	13	Heterogenous mass with irregular margin	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Pancreatitis from hypercalcaemia secondary to malignancy
34	ICCA	ICCA	CT	PV only	Present	14	Heterogenous mass with irregular margin	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Bone and nodes
35	Possible ICCA	Possible ICCA	CT and MRI	PV only	Absent	n/a	Heterogenous mass with irregular margin	Present	Present	Present	Present	Present	Present	Present	Present	Present	Nodes, peritoneal nodules and small volume ascities
41	Possible ICCA	ICCA	CT	Unenhanced	Present	8	Heterogenous mass with irregular margin	Present	n/a	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Portal nodes
45	ICCA	ICCA	CT	art, PV	Present	9	Heterogenous mass with irregular margin	Present	Present	Absent	Present	Present	Present	Absent	Absent	Absent	Nodes and lung
48	ICCA	ICCA	CT and MRI	pv only	Present	8	Heterogenous mass with irregular margin	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Bone, nodes, adrenal and small volume ascities
56	ICCA	ICCA	CT	art, PV	Present	8	Heterogenous mass with irregular margin	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Nodes
59	ICCA	ICCA	CT	pv only	Present	8	Heterogenous mass with irregular margin	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent	Peritoneal nodules and small volume ascities
60	ICCA	ICCA	CT	Art, PV	Present	5	Heterogenous mass with irregular margin	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Nodes, adrenal and peritoneal nodules
62	ICCA	ICCA	CT	art, PV	Present	5	Heterogenous mass with irregular margin	Present	Present	Present	Present	Present	Present	Absent	Present	Present	Nodes
67	ICCA	ICCA	CT	pv only	Present	9	Heterogenous mass with irregular margin	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Bone, nodes and adrenal
70	ICCA	ICCA	CT and MRI	pv only	Present	9	Heterogenous mass with irregular margin	Present on T1	Present	Present	Present	Present	Present	Absent	Absent	Absent	Nodal and adrenal

ICCA=intrahepatic cholangiocarcinoma; CT=computerised tomography; MRI=magnetic resonant imaging; Art=arterial phase; PV=portal venous phase

Supplementary figure 1.

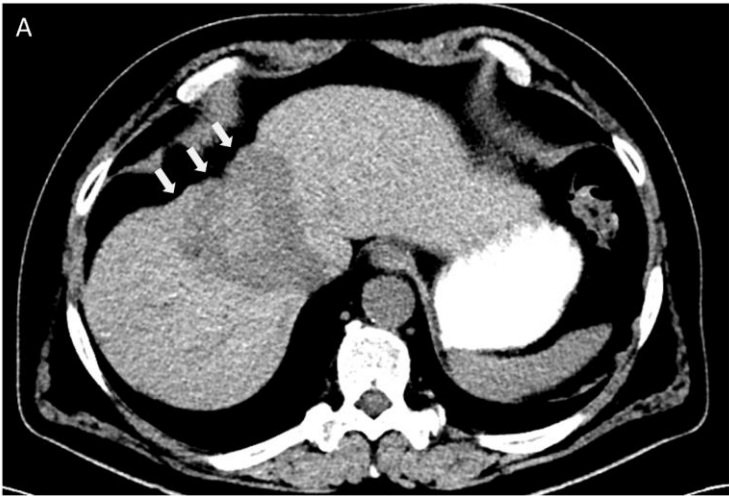
A

- (1) Where an accurate date of diagnosis was not available, in line with good practice, the date of biopsy or 15th of the month of diagnosis were used
- (2) Performance Status was collected according to the Eastern Cooperative Oncology Group (ECOG) definition, based on the patient's status at presentation, not subsequent statuses collected during treatment
- (3) Where the patient or physician concluded that chemotherapy was not appropriate or suitable, the patient was receiving Best Supportive Care
- (4) Where patients were receiving radical radiotherapy, this was considered a line of treatment and not inclusive of Best Supportive Care. Where patients were receiving Palliative Radiotherapy, this was included in Best Supportive Care strategy
- (5) To calculate survival, where the patient was not deceased, the date of last documented visit as of data lock was used

B

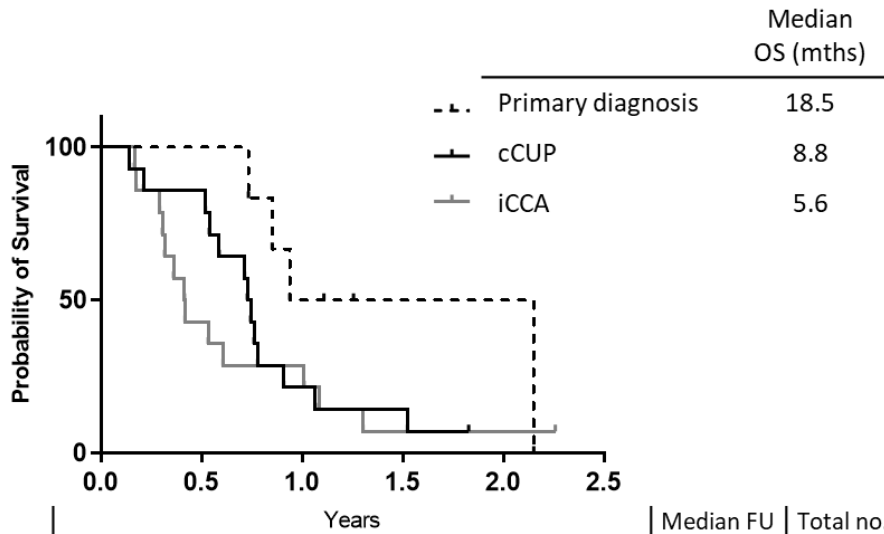
Classification	Definition
<i>Non-Evaluable</i>	No scan available for patient at time of review
<i>iCCA*</i>	"Hypodense hepatic mass in the unenhanced phase with irregular margins, peripheral rim enhancement in the arterial phase and progressive attenuation on venous and delayed phases. CT can also detect the level of biliary obstruction, capsular retraction or hepatic atrophy" (Bridgewater et al. 2014)
<i>Possible iCCA</i>	Review equivocal- unable to classify as strictly iCCA or no iCCA
<i>Non-iCCA</i>	Multiple small lesions within the lobes of the liver, in keeping with a metastatic process

Supplementary Figure 2



Supplementary Figure 3

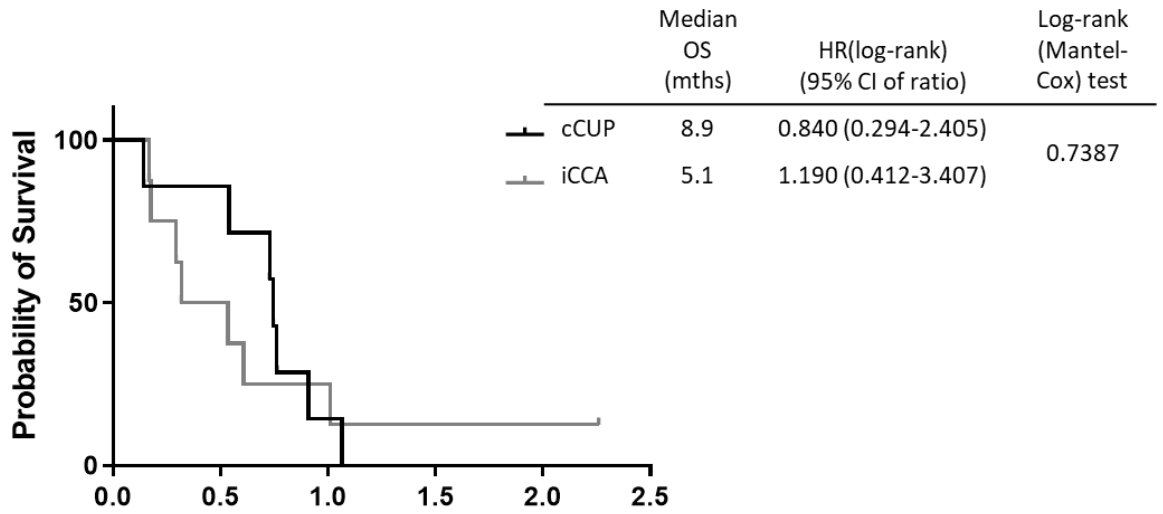
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Number at risk	Years					Median FU (mths)	Total no. of events
Primary tumour	6	6	4	2	2	15	4
cCUP	14	12	4	1	1	21.8	13
iCCA	14	7	3	2	2	27.1	13

	HR (logrank)	95% CI of ratio	Log-rank (Mantel-Cox) test p-value
iCCA vs CUP	1.344	0.968-6.579	0.462
iCCA vs Primary tumour	2.523	1.091-4.538	0.088

B



Number at risk	Years					Median FU (mths)	Total no. of events
cCUP	7	7	2	1	1	8.9	7
iCCA	8	4	2	2	1	6.4	7