Intrahepatic cholangiocarcinoma (iCCA) is found amongst the rarer primary tumours seen in UK patients. Common histological features include a paucity of tumour necrosis, an infiltrative growth pattern, and tumours which are often hypervascular on arterial phase imaging.

Aims: To identify frequency of iCCA amongst a provisional CUP (ICUP) cohort at a tertiary referral cancer centre.

Methods: All cases for patients referred with pCUP were reviewed, and data collected.
- Patients with liver involvement had radiology reviewed retrospectively independently by a gastrointestinal (GI) specialist radiologist and Hepatobiliary MPB (MPB) medical oncologist and determined as iCCA or 'possible iCCA' by the criteria outlined in Table 1.

Table 1: Radiological classification criteria

<table>
<thead>
<tr>
<th>Classification</th>
<th>Definition</th>
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<tr>
<td>Non-Evaluable</td>
<td>No scan available for patient</td>
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<tr>
<td>iCCA</td>
<td>Hypodense liver lesion with irregular margins, rim enhancement, biliary obstruction, capsular retraction or hepatic atrophy (Figure 1A)</td>
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<tr>
<td>Non-CCA</td>
<td>Small lesions within the lobes of liver in keeping with metastatic process</td>
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Figure 1A: Typical appearance of iCCA: domino-like mass forming lesion and capsular retraction

Figure 2: ▶ iCCA - primary tumour diagnosis or confirmed CUP (ICUP)

- Final diagnosis was determined for all patients depending on outcome of CUP pathway and retrospective radiological review (Figure 2).
- iCCA, primary tumour diagnosis or confirmed CUP (ICUP)

Figure 2: Consent diagram of cohort (final diagnosis highlighted in orange)

Results: A total of 158 patients with liver involvement from a provisional CUP cohort were included in the study.

- Median survival: 0.328542 years (p = 0.001172), log rank (Mantel-Cox) test p-value 0.001172 (Figure 4A)
- Patients with liver involvement and a non-CCA primary tumour diagnosis had a longer median OS (10.3 months) compared with patients with iCCA (3.8 months; log-rank (Mantel-Cox) test p-value 0.00277) (Figure 4A).

Figure 4A: Kaplan-Meier survival of overall survival (OS) of whole cohort split by liver involvement. B. Kaplan-Meier scores for OS of liver involvement cohort split by final diagnosis.

- Patients without liver involvement had significantly improved overall survival (OS) compared to non-liver involved patients (Median OS 10.3 months vs 4.4 months respectively). Log-rank (Mantel-Cox) test p-value ≤ 0.0001 (Figure 4A)
- Chemotherapy was delivered in 56% of patients with iCCA and 36% of patients with CUP; the most common chemotherapy given in both groups was carboplatin/paclitaxel and only one patient in the iCCA group received standard first-line chemotherapy cisplatin/gemcitabine

- Future work will involve retrospective molecular profiling on the liver-involved cohort to establish the frequency of potentially actionable mutations in these patients.

Conclusions: Intrahepatic cholangiocarcinoma is prevalent in patients referred with provisional CUP (11%) Patients with CUP now have treatable targets and patients identified as iCCA can have molecular profiling and access to alternative treatments.
- Diagnostic tissue should be assessed for molecular profiling, as increasing the number of iCCA markers performed does not definitively reveal diagnosis, and they are rarely positive.
- iCCA should be considered in all patients with liver involvement pCUP and compatible histology where liver tumour is found.
- Future work will involve retrospective molecular profiling on the liver-involved cohort to establish the frequency of potentially actionable mutations in these patients.

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References:

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