The changing landscape of advanced cholangiocarcinoma therapy at The Royal Free London NHS Foundation Trust between 2021 and 2025

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BACKGROUND

Systemic treatment options for advanced Biliary Tract Cancer (BTC) have evolved with the integration of Durvalumab into first line therapy. Additionally, the increasing availability of molecular profiling has enabled more personalised second line targeted treatments. While clinical trial data supports these developments, there is limited published data concerning their implementation and impact in the real-world setting.

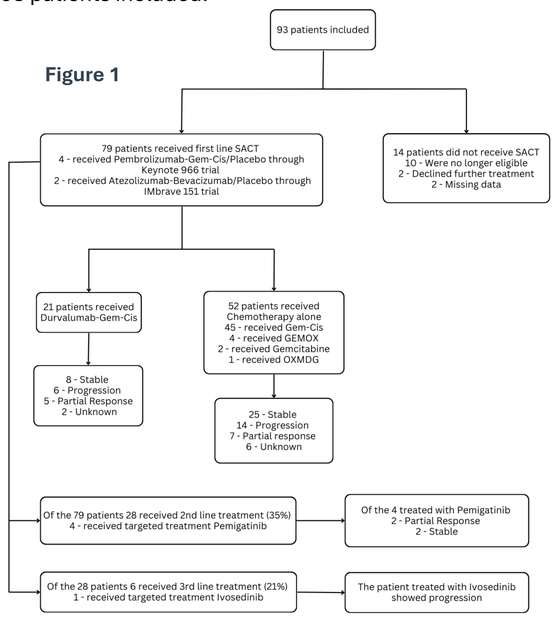
OBJECTIVES

1. Compare clinical outcomes between patients treated with Durvalumab-Gem-Cis and those treated with Chemotherapy alone.
2. Evaluate the proportion of patients undergoing molecular testing and identify the frequency of actionable mutations or fusions.
3. Assess the use of targeted therapies in eligible patients following molecular profiling.

METHODS

We retrospectively reviewed 93 patients with histologically confirmed BTC who were eligible for systemic anti cancer therapy (SACT) at the Royal Free London between 2021 and 2025. Medical records were reviewed and data collected on patient characteristics, molecular testing and treatment response assessed using RECIST criteria. All statistical analyses were carried out using Excel and IBM SPSS Statistics. Figure 1 shows a breakdown of the systemic treatment received by the 93 patients included.

Figure 1



RESULTS

Median Progression Free Survival was 5.5 months (95% CI 0-12.1) for the Durvalumab group versus 4.4 months for the Chemotherapy group (95% CI 3.3-5.5). This was based on 65 recorded progression events (15 in the Durvalumab group and 50 in the Chemotherapy group). Cox regression analysis yielded a hazard ratio of 0.145 (p=0.190).

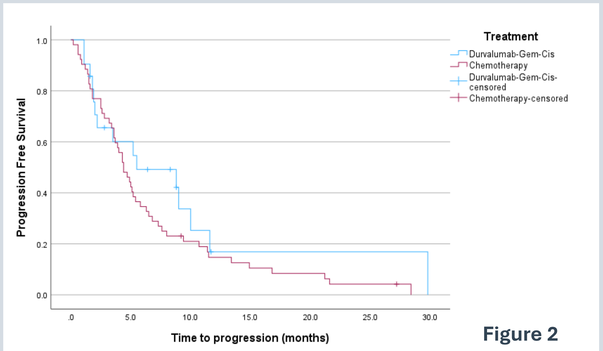


Figure 2

	Chemotherapy (Gem-Cis) n=52	Immunotherapy (Durvalumab-Gem-Cis) n=21
Sex		
Female	30 (58%)	17 (86%)
Male	22 (42%)	3 (14%)
Age, years	65 (37-84)	65 (42-82)
Subsequent lines of treatment		
One	19	5
Two	5	0
Eastern Cooperative Oncology Group Performance Status		
0	32	16
1	17	5
2	3	0
Extent of disease		
Locally advanced	7	2
Metastatic	45	19
Cholangiocarcinoma type at diagnosis		
Intrahepatic	27	13
Extrahepatic	12	5
Gallbladder	10	2
Combined HCC-cholangiocarcinoma	3	1

Figure 3

DEMOGRAPHICS

Figure 3 presents the baseline demographics and clinical characteristics in the Durvalumab and Chemotherapy groups. These were broadly comparable: the median age was 65 in both cohorts, most patients had metastatic disease, and intrahepatic cholangiocarcinoma was the most common subtype. Notably, a greater proportion of patients in the chemotherapy group received subsequent lines of treatment, potentially reflecting differences in tolerability and disease trajectory. This is further supported by the number of treatment cycles received by patients. On average, Chemotherapy patients received 5 cycles compared to 7 for Durvalumab patients. Only one patient in the Durvalumab group experienced immunotherapy toxicity.

RESULTS

As shown by figure 4, the median Overall Survival was 12.2 months (95% CI 9.1-15.2) for the Durvalumab group versus 8.8 months (95% CI 4.8-12.8) for the Chemotherapy group. This was based on 51 deaths (9 in the Durvalumab group and 42 in the chemotherapy group). The hazard ratio was 0.706 (p=0.333).

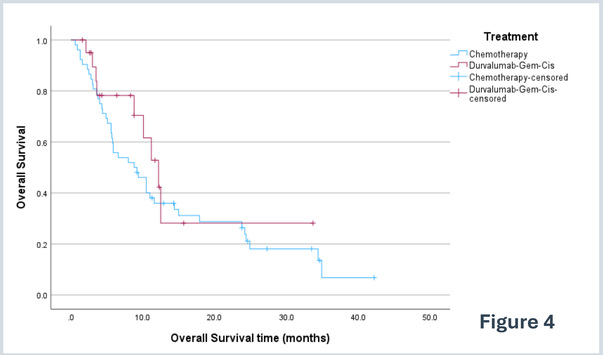


Figure 4

RESULTS

Among the 93 patients included in the study, molecular testing varied by target, as shown in Figure 5. MMR status was assessed in 65% of patients, while 53% underwent testing for IDH1 mutations, 63% for FGFR2 fusions and 55% for NTRK fusions. Of those tested, IDH1 mutations were identified in 13% and FGFR2 fusions in 9%.

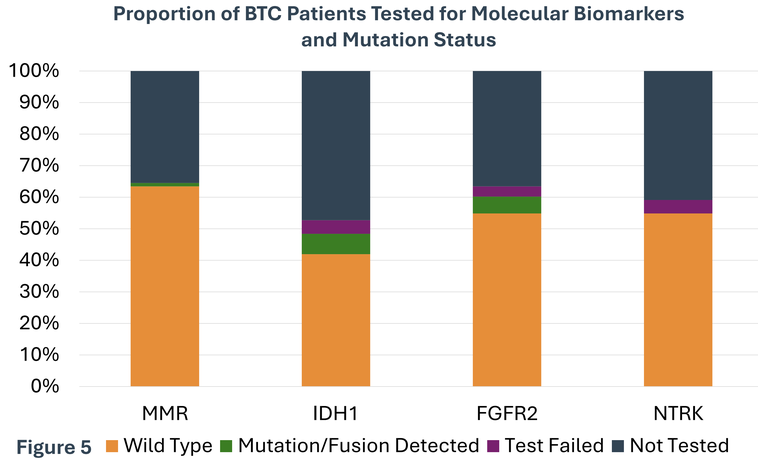
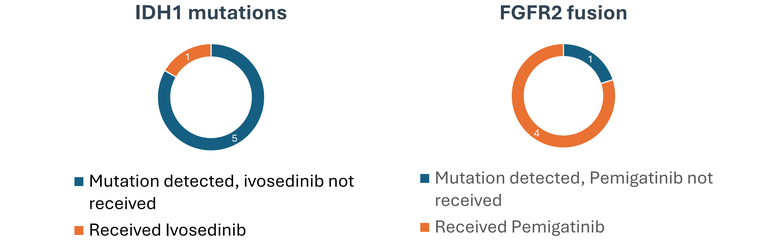


Figure 5

Of the 5 patients identified with an FGFR2 fusion, 4 received Pemigatinib. Among the 6 patients with an IDH1 mutation, 1 received Ivosedinib. The average number of cycles of Pemigatinib received was 6 (ranging from 1 to 11 cycles).



CONCLUSIONS

- Durvalumab-Gem-Cis was associated with improved outcomes compared to chemotherapy alone, though not statistically significant due to a small sample size.
- The results highlight the need for more upfront molecular testing to expand current treatment options.
- Over half of patients with an actionable target did not receive targeted therapy, predominantly due to a deteriorating performance status.
- The ABC-10 trial will assess the potential for earlier molecular targeted therapy.