Treatment patterns among patients with extrahepatic cholangiocarcinoma with autoimmune conditions: a retrospective study

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Objective

- To characterize the demographics, clinical characteristics, and treatment patterns in patients with extrahepatic cholangiocarcinoma (eCCA) with autoimmune conditions (AICs) and with no autoimmune conditions (NAICs)

Conclusions

- More patients with eCCA received a first-line durvalumab-based regimen post-March 2022 vs the full study period, suggesting a shift in the treatment landscape after durvalumab was included in guidelines
- Patients with AICs were numerically more likely to be male and have more comorbidities and liver-related conditions than patients with NAICs
- Although the number of patients with eCCA and AICs is small, the use of durvalumab as first-line treatment in this subgroup may suggest that AICs do not restrict its use
- Future research will focus on clinical outcomes, which could inform clinical decision-making

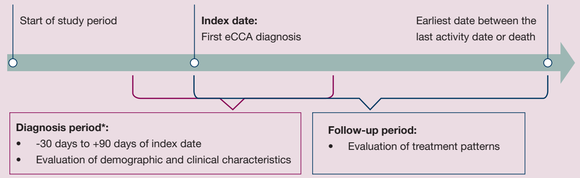
Introduction

- Findings from the TOPAZ-1 study support durvalumab and gemcitabine plus cisplatin (GemCis) as a standard of care treatment for advanced biliary tract cancer.[1] Durvalumab plus GemCis has become a guideline-recommended first-line regimen[2]
- Patients with eCCA often have underlying AICs such as inflammatory bowel disease,[3,4] which could restrict immunotherapy use
  - One study reported that 14.6% of elderly US adults with eCCA had a previously diagnosed AIC[4]
- Treatment patterns in patients with eCCA, including those with underlying conditions, have not been extensively studied[5,6]

Methods

- This subgroup analysis of the retrospective observational study included adult patients (≥18 years old) diagnosed with eCCA in the United States enrolled in the International Cholangiocarcinoma Patient Registry (ICPR) between 2019 and 2023
  - The ICPR contains de-identified data from medical records obtained directly from consenting patients and caregivers
- Patients were followed from the index date (date of eCCA diagnosis) until the last activity in the database or death (**Figure 1**)
- The study cohort was enriched for patients treated with durvalumab, enabling more comprehensive follow-up for this subgroup
- Demographics, clinical characteristics, biomarkers, treatment patterns, and adverse events (AEs) for patients with eCCA with AICs and NAICs were assessed
  - Treatment patterns were assessed for the full study period and post-March 2022, when durvalumab was added to National Comprehensive Cancer Network guidelines

Figure 1. Study design



*A diagnosis period spanning from -30 days to +90 days relative to the index date was used to mitigate any reporting discrepancies and ensure thorough identification of patient records, adhering to the recommendations provided by Citizen Health[7].

eCCA, extrahepatic cholangiocarcinoma.

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Disclosures

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Results and interpretation

Patient and clinical characteristics (Table 1)

- 500 patients with CCA were enrolled in the ICPR, of which 135 patients with eCCA were included in this analysis
  - 24 (17.8%) had ≥1 AICs and 111 (82.2%) had NAICs. The majority of patients had one AIC
  - AICs of interest included: autoimmune disease, autoimmune hepatitis, autoimmune pancreatitis, celiac disease, colitis, Crohn's disease, Graves disease, Hashimoto thyroiditis, inflammatory bowel disease, lupus erythematosus, multiple sclerosis, psoriasis, psoriatic arthritis, rheumatoid arthritis, Sjögren's syndrome, type 1 diabetes mellitus, and ulcerative colitis
- Median age at diagnosis in the overall population was 63.0 years
  - Patients with AICs vs NAICs: 63.5 vs 63.0 years
- Overall, 50.4% of patients were female
  - Patients with AICs vs NAICs: 41.7% vs 52.3%
- Mean number of comorbidities in the overall population was 10.1
  - Patients with AICs vs NAICs: 12.1 vs 9.7; 87.5% vs 78.4% with ≥1 liver-related conditions
- 121 (89.6%) of patients had at least one biomarker test at any time point
  - Biomarker testing methods included: next-generation sequencing, immunohistochemistry, cell-free DNA sequencing, RNA sequencing, DNA sequencing (general), fluorescence *in situ* hybridization, polymerase chain reaction, chromogenic *in situ* hybridization, germline DNA sequencing, *in situ* hybridization, quantitative proteomics
- PD-L1 positivity was noted in 12.6% of patients and HER2 positivity in 10.4% of patients

Table 1. Patient and clinical characteristics

	eCCA with AIC (n=24)	eCCA with NAIC (n=111)	Total eCCA (N=135)
Median (Q1–Q3) age, years	63.5 (55.0–68.0)	63.0 (55.0–70.0)	63.0 (55.0–70.0)
Female patients, n (%)	10 (41.7)	58 (52.3)	68 (50.4)
Number of comorbidities per patient, mean (SD)	12.1 (4.8)	9.7 (6.0)	10.1 (5.8)
Patients with ≥1 liver-related conditions,* n (%)	21 (87.5)	87 (78.4)	108 (80.0)
Time from eCCA diagnosis to death or last encounter date, median (Q1–Q3), months	16.3 (9.0–33.7)	16.3 (10.7–25.5)	16.3 (10.5–26.1)

*Liver-related conditions of interest included: abnormal liver enzyme levels, ascites, cholangitis, cholecystitis, choledochal cyst, cirrhosis, fatty liver, hemochromatosis, hepatic encephalopathy, hepatic failure, hepatic steatosis, hepatitis A / B / C virus, jaundice, liver enzymes outside reference range, liver fluke infection, metabolic dysfunction-associated steatohepatitis, portal hypertension, primary biliary cholangitis, and primary sclerosing cholangitis.

AIC, autoimmune condition; eCCA, extrahepatic cholangiocarcinoma; NAIC, no autoimmune condition; Q, quartile; SD, standard deviation.

Treatment patterns (Table 2 and Figure 2)

- Of 91 patients with eCCA who received first-line therapy in the full study period:
  - 34 (37.4%) received GemCis alone
  - 27 (29.7%) received chemotherapy alone
  - 7 (7.7%) received GemCis plus durvalumab
  - 7 (7.7%) received durvalumab as monotherapy or with any other chemotherapy regimen
- Of patients with eCCA with AICs who received first-line therapy in the full study period:
  - ≤5 of 18 patients received GemCis plus durvalumab
- Of patients with eCCA who initiated first-line therapy on / after March 2022 (n=20):
  - 12 (60.0%) received GemCis plus durvalumab or durvalumab as monotherapy or with any other chemotherapy regimen
  - 7 (35.0%) received GemCis alone

Table 2. Overall treatment patterns

Treatment patterns	eCCA with AIC (n=24)	eCCA with NAIC (n=111)	Total eCCA (N=135)
1L treatment regimen category, n (%)			
Total number receiving treatment	**18**	**73**	**91**
GemCis alone	9 (50.0)	25 (34.2)	34 (37.4)
Chemotherapy alone	6 (33.3)	21 (28.8)	27 (29.7)
GemCis plus nab-paclitaxel	≤5	>5–<10	9 (9.9)
GemCis plus durvalumab	≤5	>5–<10	7 (7.7)
Durvalumab as monotherapy or with any other chemotherapy regimen	≤5	>5–<10	7 (7.7)
Chemotherapy plus targeted therapy*	0 (0)	≤5	≤5
Chemotherapy plus other immunotherapy	0 (0)	≤5	≤5
Pembrolizumab monotherapy / combination	0 (0)	≤5	≤5

To minimize risk of patient identification, treatment modalities involving 5 or fewer patients were suppressed, and additional cell counts were also suppressed as necessary to prevent back-calculation of these small counts.

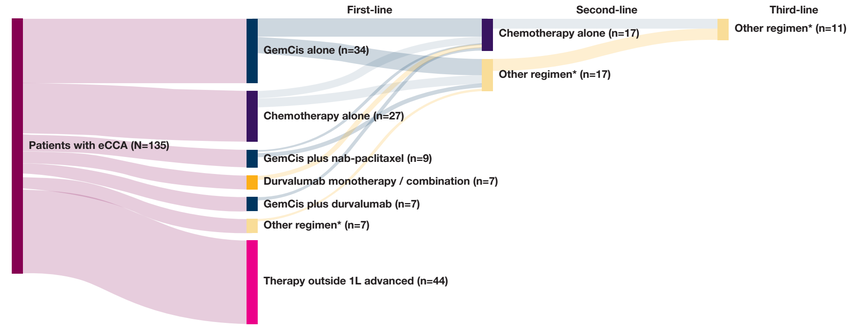
*Targeted therapies included devimistat, silmitasertib, talazoparib, pertuzumab, and trastuzumab.

1L, first-line; AIC, autoimmune condition; eCCA, extrahepatic cholangiocarcinoma; GemCis, gemcitabine plus cisplatin; NAIC, no autoimmune condition.

Safety (Table 3)

- A total of 129 patients (95.6%) had at least one AE; fatigue was the most common AE (71.1%)

Figure 2. Treatment modalities for patients with eCCA by line of therapy



*To minimize the risk of patient identification, treatment modalities involving 5 or fewer patients were consolidated into an 'Other regimen' category. This category included targeted therapies, immunotherapy alone, immunotherapy plus chemotherapy, chemotherapy alone, and chemotherapy plus targeted therapy.

1L, first-line; eCCA, extrahepatic cholangiocarcinoma; GemCis, gemcitabine plus cisplatin.

Table 3. Safety

	Total eCCA (N=135)
Diagnosis of AEs at any time point (not mutually exclusive), n (%)	
At least one AE	129 (95.6)
Fatigue	96 (71.1)
Nausea	71 (52.6)
Neutropenia	55 (40.7)
Anemia	45 (33.3)
Adverse reaction	44 (32.6)
Thrombocytopenia	37 (27.4)
Diarrhea	38 (28.1)
Constipation	24 (17.8)
Pain	29 (21.5)
Dose reduction	61 (45.2)
Treatment hold for AE resolution	59 (43.7)
Treatment discontinued due to AE (treatment not tolerated)	25 (18.5)

AE, adverse event; eCCA, extrahepatic cholangiocarcinoma.

Plain language summary

Background: Why did we perform this research?

- Cholangiocarcinoma (CCA) is a cancer of the bile ducts and the biliary tube. Extrahepatic CCA (eCCA; cancer that develops outside of the liver) is one of the most common forms of CCA in patients with inflammatory bowel disease and is often diagnosed in the advanced stage when it can no longer be removed with surgery
- The previous most appropriate treatment for advanced CCA was a combination of the chemotherapy drugs gemcitabine plus cisplatin (GemCis). Immunotherapies, drugs which target the immune system to help the body fight cancer, have recently been approved for treating CCA in combination with GemCis as the most appropriate treatment
- Studies are needed to understand how patients with CCA, particularly those with underlying autoimmune conditions, are treated in the US, including what kinds of treatments they receive and how well the treatments work

Methods: How did we perform this research?

- Patients were enrolled in the International Cholangiocarcinoma Patient Registry (ICPR) between 2019 and 2023. We looked at data for 135 adult patients diagnosed with eCCA between 2013 and 2023, with a focus on those treated with durvalumab, a type of immunotherapy

Results: What were the findings of this research?

- In the full study period, 14 of 91 (15%) patients took durvalumab alone or in combination with other drugs as their first treatment for cancer. After durvalumab became a guideline-recommended treatment in March 2022, 12 of 20 (60%) patients took durvalumab alone or in combination with other drugs as their first treatment for cancer
- Most patients had at least one adverse event, of which tiredness was the most common

Conclusions: What are the implications of this research?

- Increased use of durvalumab for eCCA since March 2022 suggests a change in treatment approaches
- While data are limited for patients with eCCA and autoimmune conditions, durvalumab is still being used in these patients, suggesting that these conditions may not prevent its use

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Poster presented at the Cholangiocarcinoma Foundation (CCF) Annual Conference 2026 by Sumera I. Ilyas

Poster

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