Real-world characteristics and outcomes of durvalumab + gemcitabine + cisplatin in patients with cholangiocarcinoma in the US

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Objective

- To characterize the demographics, clinical characteristics, treatment patterns, and outcomes in patients with cholangiocarcinoma (CCA) treated with first-line (1L) durvalumab + gemcitabine and cisplatin (GemCis), particularly for those patients with autoimmune conditions (AICs) and with no autoimmune conditions (NAICs)

Conclusions

- Although the number of patients with AICs treated with durvalumab + GemCis is small, the data suggest that AICs do not restrict its use
- The median real-world overall survival (rwOS) for durvalumab + GemCis is consistent with TOPAZ-1 and previous global real-world studies

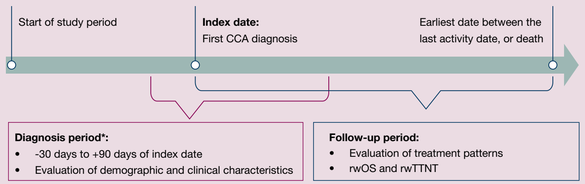
Introduction

- TOPAZ-1 demonstrated that durvalumab + GemCis was superior to GemCis in the 1L treatment of advanced biliary tract cancers.[1,2] Durvalumab + GemCis has become a guideline-recommended 1L regimen[1–4]
  - However, patients with CCA who have underlying AICs were excluded from TOPAZ-1 and often do not receive immunotherapy regimens[5,6]
- Real-world data are lacking[7] in a US cohort of patients with CCA with AICs or with NAICs who have received durvalumab + GemCis

Methods

- This is a retrospective observational study of adult patients (≥18 years old) diagnosed with CCA in the US, enrolled in the International Cholangiocarcinoma Patient Registry (ICPR) and receiving 1L treatment on / after January 2020, including those treated with 1L durvalumab + GemCis between 2021 and 2023
  - The ICPR contains de-identified data from medical records obtained directly from consenting patients and caregivers
  - The study cohort was enriched for patients treated with durvalumab, enabling a more comprehensive follow-up for this subgroup
- Patients were followed from the index date (initial date of CCA diagnosis) until the last activity date in the database or death, whichever occurred first (**Figure 1**)
- Demographics and tumor characteristics (primary objective; assessed at initial CCA diagnosis), comorbidities (assessed at any time point), second-line (2L) treatment modalities, median rwOS, and median real-world time to next treatment (rwTTNT; assessed between initiation of 1L treatment and last activity in the database or death) are reported
- AICs of interest included: autoimmune disease, autoimmune hepatitis, autoimmune pancreatitis, celiac disease, colitis, Crohn's disease, Graves disease, Hashimoto's thyroiditis, inflammatory bowel disease, lupus erythematosus, multiple sclerosis, psoriasis, psoriatic arthritis, rheumatoid arthritis, Sjögren's syndrome, type 1 diabetes mellitus, and ulcerative colitis

Figure 1. Study design



*A diagnosis period spanning from -30 to +90 days relative to the index date was used to mitigate any reporting discrepancies and ensure thorough identification of patient records.
CCA, cholangiocarcinoma; rwOS, real-world overall survival; rwTTNT, real-world time to next treatment.

Acknowledgments

This study was sponsored by AstraZeneca. Medical writing support under the direction of the authors was provided by Ksenia Vlasov, PhD. and Alexus Shirk, PhD, Publications and Medical Affairs Division of Omnicom Health Medical Communications, and was funded by AstraZeneca in accordance with Good Publication Practice (GPP 2022) guidelines.

Disclosures

NSA, RTS, SII, and SKM report a consulting or advisory role for AstraZeneca. MMJ reports consulting or advisory roles and honoraria from AstraZeneca. MJB reports research funding or grants from AstraZeneca. JWV reports a consulting or advisory role for, and research funding or grants from, AstraZeneca. NK, YJ, SLD, and SJV are employees and / or shareholders of AstraZeneca.

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Results and interpretation

Patient and clinical characteristics of patients receiving durvalumab + GemCis (Table 1)

- The ICPR dataset consisted of 500 patients with CCA; 314 received 1L treatments on / after January 2020, of which 70 patients received 1L treatment with durvalumab + GemCis
  - 13 (18.6%) patients had ⩾1 AIC and 57 (81.4%) patients had NAICs
- Median age at diagnosis in the patients treated with 1L durvalumab + GemCis was 56.0 years
  - Patients treated with 1L durvalumab + GemCis with AICs vs NAICs: 52.0 vs 56.0 years
- Among patients treated with 1L durvalumab + GemCis, 68.6% were female
- Mean number of comorbidities per patient in patients treated with 1L durvalumab + GemCis was 10.9
  - Patients treated with 1L durvalumab + GemCis with AICs vs NAICs: 16.7 vs 9.6
  - Patients treated with 1L durvalumab + GemCis with ⩾1 liver-related condition with AICs vs NAICs: 46.2% vs 70.2%

Table 1. Patient and clinical characteristics

	Patients with AICs (n=13)	Patients with NAICs (n=57)	Patients treated with 1L durvalumab + GemCis (n=70)	All patients treated on / after Jan 2020 (N=314)
Median (Q1–Q3) age, years	52.0 (44.0–65.0)	56.0 (46.0–66.0)	56.0 (46.0–66.0)	59.0 (50.0–66.0)
Female patients, n (%)	11 (84.6)	37 (64.9)	48 (68.6)	196 (62.4)
CCA subtype, n (%)				
Intrahepatic	12 (92.3)	47 (82.5)	59 (84.3)	213 (67.8)
Extrahepatic	⩽5	⩽5	⩽5	65 (20.7)
CCA not otherwise specified	0 (0)	⩽5	⩽5	25 (8.0)
Perihilar	0 (0)	⩽5	⩽5	10 (3.2)
Distal	0 (0)	0 (0)	0 (0)	⩽5
ECOG PS, n (%)				
0	6 (46.2)	31 (54.4)	37 (52.9)	141 (44.9)
1	⩽5	>10–⩽20	21 (30.0)	84 (26.8)
2	⩽5	⩽5	⩽5	11 (3.5)
Not recorded	⩽5	⩽5	10 (14.3)	76 (24.2)
Number of comorbidities per patient, mean (SD)	16.7 (9.2)	9.6 (5.4)	10.9 (6.8)	10.1 (6.2)
Patients with ⩾1 liver-related conditions,* n (%)	6 (46.2)	40 (70.2)	46 (65.7)	207 (65.9)
Time from CCA diagnosis to last activity date or death, months, median (Q1–Q3)	8.3 (6.7–16.2)	9.3 (4.9–14.6)	9.3 (5.2–15.3)	13.8 (8.1–22.0)

To minimize risk of identification, patient and clinical characteristics treatment modalities were consolidated into ⩽5 and >10–⩽20 and other values were not reported.
*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, non-alcoholic steatohepatitis, portal hypertension, primary biliary cholangitis, and primary sclerosing cholangitis.
1L, first-line; AIC, autoimmune condition; CCA, cholangiocarcinoma; ECOG PS, Eastern Cooperative Oncology Group performance status; GemCis, gemcitabine and cisplatin; Q, quartile; SD, standard deviation.

2L treatment patterns of patients receiving durvalumab + GemCis (Table 2)

- Median (Q1–Q3) time from diagnosis to start of any 1L therapy on / after January 2020 was 1.2 (0.8–2.6) months
- Median (Q1–Q3) time from diagnosis to start of 1L treatment in patients receiving durvalumab + GemCis (n=70) was 1.0 (0.7–1.7) months
- In the overall cohort of patients with CCA who initiated any 1L therapy on / after January 2020 (N=314), 107 patients received 2L treatment, of which 35 (32.7%) received targeted therapy alone
- Among patients treated with 1L durvalumab + GemCis (n=70), 17 received 2L treatment, of which 11 (64.7%) received targeted therapy alone
  - Among patients treated with 1L durvalumab + GemCis with AICs (n=13), ⩽5 received 2L treatment, all of whom received chemotherapy alone
  - Among patients treated with 1L durvalumab + GemCis with NAICs (n=57), >10–⩽20 received 2L treatment: 11 (73.3%) patients received targeted therapy alone

Real-world overall survival among patients treated with 1L durvalumab + GemCis

- Among patients treated with 1L durvalumab + GemCis (n=70), the median (95% CI) rwOS was 15.5 (15.1–not evaluable [NE]) months (**Figure 2**)

Real-world time to next treatment among patients treated with 1L durvalumab + GemCis

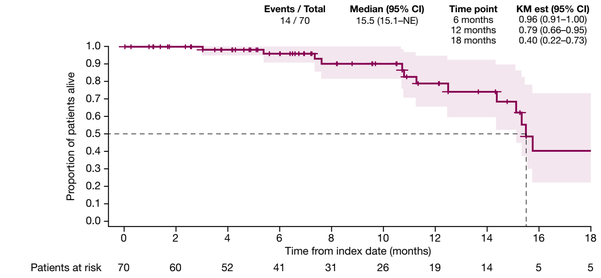
- Among patients treated with 1L durvalumab + GemCis (n=70), median (95% CI) rwTTNT was 10.8 (10.4–15.7) months
  - In a sensitivity analysis with death removed as an event and instead treated as a censoring event, median (95% CI) rwTTNT was 20.8 (10.4–NE) months
- Among patients treated with 1L durvalumab + GemCis with AICs (n=13) or NAICs (n=57), median (95% CI) rwTTNT was 10.7 (5.3–NE) months and 10.8 (9.0–NE) months, respectively (**Figure 3**)

Table 2. Reason for end of 1L treatment and 2L treatment patterns

	Patients treated with 1L durvalumab + GemCis (n=70)	All patients treated on / after Jan 2020 (N=314)
Reason for end of 1L treatment, n (%)		
Remained on treatment at the end of follow-up	34 (48.6)	105 (33.4)
Progression / metastasis	17 (24.3)	122 (38.9)
Medication end (unconfirmed)	15 (21.4)	47 (15.0)
Discontinuation	⩽5	26 (8.3)
Resection	⩽5	14 (4.5)
2L treatment regimen category		
Total number receiving treatment, n	17	107
Targeted therapy* alone, n (%)	11 (64.7)	35 (32.7)
Chemotherapy alone, n (%)	6 (35.3)	43 (40.2)
Chemotherapy + targeted therapy, n (%)	0 (0)	7 (6.5)
Durvalumab + GemCis, n (%)	0 (0)	6 (5.6)
Other, n (%)	0 (0)	16 (15.0)

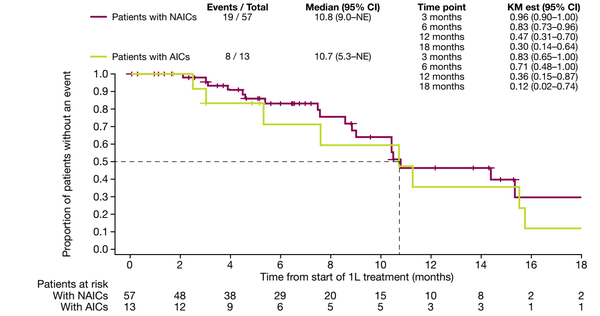
To minimize risk of patient identification, treatment modalities involving 5 or fewer patients were consolidated into ⩽5 and other values are not reported.
*Targeted therapies included devimistat, pertuzumab, silmitasertib, talazoparib, and trastuzumab.
1L, first-line; 2L, second-line; GemCis, gemcitabine and cisplatin.

Figure 2. Median rwOS among patients treated with 1L durvalumab + GemCis



1L, first-line; CI, confidence interval; GemCis, gemcitabine and cisplatin; KM, Kaplan-Meier; NE, not evaluable; rwOS, real-world overall survival.

Figure 3. Median rwTTNT among patients treated with 1L durvalumab + GemCis with AICs or NAICs



1L, first-line; AIC, autoimmune condition; CI, confidence interval; GemCis, gemcitabine and cisplatin; KM, Kaplan-Meier; NAIC, no autoimmune condition; NE, not evaluable; rwTTNT, real-world time to next treatment.

Plain language summary

Background: Why did we perform this research?

- Cholangiocarcinoma (CCA) is a cancer of the bile ducts and the biliary tube and is often diagnosed in the advanced stage when it can no longer be removed with surgery. Patients with autoimmune conditions, such as inflammatory bowel disease, are at higher risk of developing CCA
- Previously, gemcitabine and cisplatin (GemCis) was the standard treatment given to patients with CCA; however, immunotherapies (drugs that target the immune system to help the body fight cancer) have been recently approved for treating CCA in combination with GemCis
- 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 between 2019 and 2023. We looked at data for all adult patients with CCA who started first-line treatment on or after January 2020 as well as 70 adult patients diagnosed with CCA who had received durvalumab, a type of immunotherapy, in combination with GemCis as the first-line treatment

Results: What were the findings of this research?

- Of the 70 adult patients diagnosed with CCA who had received first-line durvalumab + GemCis, 13 patients had autoimmune conditions
- Of the patients who received first-line durvalumab + GemCis, the time point at which half of the patients were still alive after starting treatment was 15.5 months. The time point at which half of the patients moved onto the next line of treatment was 10.8 months for those who received first-line durvalumab + GemCis

Conclusions: What are the implications of this research?

- While data is limited for patients with CCA and autoimmune conditions, durvalumab is still being used in these patients, suggesting that these conditions may not prevent its use
- The length of time patients were alive for after starting treatment was similar to a previous clinical trial as well as other global, real-world studies

This study was funded by AstraZeneca
Poster presented at the Cholangiocarcinoma Foundation (CCF) Annual Conference 2026 by Nilofer S. Azad

Poster

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Poster presented at the Cholangiocarcinoma Foundation (CCF) Annual Conference 2026, Salt Lake City, UT, USA, May 1–3, 2026
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