Treatment outcomes of patients with m*IDH1* cholangiocarcinoma in the United States

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Background

- Cholangiocarcinoma (CCA), categorized as intrahepatic (iCCA), perihilar (pCCA), or distal (dCCA), is often diagnosed at an advanced or metastatic stage[1]
- Approximately, 10–15% of patients with iCCA harbor mutations in the isocitrate dehydrogenase 1 (*IDH1*) gene
- Biomarker profiling and mutational analysis guide classification of cholangiocarcinoma and choice of targeted therapies[2,3]
- However, data on real-world treatment patterns and clinical outcomes remain limited
- This study aims to provide a real-world understanding of the management of patients with m*IDH1* CCA. It uses a dataset from **Citizen Health** based on electronic health records (EHRs) for study participants from over 3000 United States (US) healthcare institutions

Methodology

INCLUSION CRITERIA
- Patients diagnosed with CCA who completed a Citizen Health profile and provided the name of at least one institution where they have received care
- Patients who consented to share their de-identified data

DATA COLLECTION
- Data collection and digitalization of medical records from all providers seen by patients (average=7 health systems)

PROFILE
- Medical records and images scanned and uploaded to patient's account

DATA ANALYSIS
- Raw record processed by machine-learning engine + human QA to normalize and codify defined data elements

PRESENTATION
- De-identified data output is structured and ready to share for research. Counts and proportions are reported for categorical variables, and means, medians, standard deviations, interquartile ranges, and ranges are reported for continuous variables

Objectives
- **Describe the real-word journey of patients with m*IDH1* CCA**
- **Understand the biomarker testing patterns**
- **Analyze treatment outcomes**

Figure 1. Patient population

Results

- In total, **602** patients diagnosed with **CCA** between **2007 and 2025** from the **US** were included in this retrospective study. Baseline and biomarker testing characteristics are presented in **Table 1 and Table 2**
- Among **499 patients** who received the biomarker testing, **88 patients** (18%) had **m*IDH1*** CCA with **60 patients** (68%) diagnosed with advanced/ metastatic disease
  - **80 patients** (91%) received first-line (**1L**) systemic therapy for any stage, including gemcitabine-cisplatin (GemCis) (n=26, 33%) or GemCis-durvalumab (n=21, 26%) or GemCis-nab-paclitaxel (n=12, 15%), **Figure 2**. Treatment outcomes and disease control rate are presented in **Figure 3 and Table 3**
  - **63 patients** (72%) received second-line (**2L**) therapy including ivosidenib monotherapy (n=22; 35%) or in combination (n=7, 11%), **Figure 2**
  - In the **2L**, in patients who received **ivo-containing regimens** (n=29), **median progression-free survival (mPFS)** was **6.1 mo** and **median overall survival (mOS)** was **25.1 mo**; while in patients who received **other regimens** (n=34), **mPFS** was **4.1 mo** and **mOS** of **20.1 mo**. Treatment outcomes and disease control rate are presented in **Table 4**

Table 1. Baseline characteristics

	All (N=602)	Patients *with* m*IDH1* (N=88)
Age, Median [Min; Max]	59.5 [22.3, 85.8]	59.7 [33.9, 78.4]
Sex, n (%)		
Female	360 (60%)	67 (76%)
Male	242 (40%)	21 (24%)
CCA Subtype, n (%)		
iCCA	367 (61%)	73 (83%)
eCCA	156 (26%)	4 (5%)
NOS	79 (13%)	11 (13%)
Stage at Diagnosis, n (%)		
Early	114 (19%)	17 (19%)
Advanced/Metastatic	360 (60%)	60 (68%)
NOS	128 (21%)	11 (13%)

eCCA, extrahepatic cholangiocarcinoma; iCCA, intrahepatic cholangiocarcinoma NOS, not otherwise specified.

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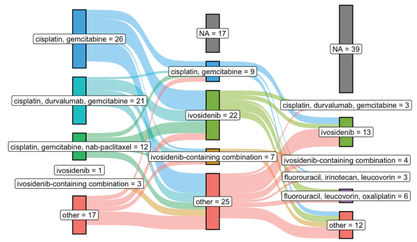
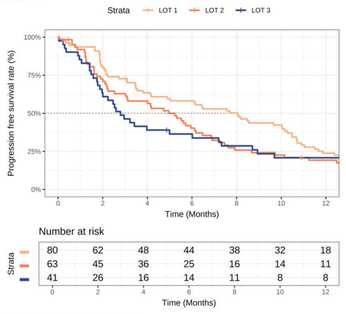
Figure 2. Lines of therapy by class received by patients with m*IDH1*



If less than 5% and was not ivosidenib/ivsidenib-containing combination, regimen was classified as 'other'.
'NA' indicates no further data.

Figure 3. Kaplan-Meier of PFS per line of treatment in patients with m*IDH1*



LOT, line of treatment; PFS, progression-free survival.

Table 2. Biomarker testing

	All (N=602)
Biomarker testing, n (%)	
YES	499 (83%)
NO	103 (17%)
	Patients tested (N=499)
Sample type*, n (%)	
Tissue	156 (26%)
Liquid biopsy	106 (21%)
NOS	11 (2%)
Test method*, n (%)	
NGS DNA	263 (53%)
IHC	194 (39%)
NGS RNA	12 (2%)
ISH	12 (2%)
Alterations, n (%)	
IDH1	88 (18%)
FGFR2 rearrangement	63 (13%)
TMB-H	30 (6%)
MSI	18 (3%)
HER2+ or amplification	14 (3%)

*Patients with multiple sample type and testing method
FGFR2, fibroblast growth factor receptor 2; HER2, human epidermal growth factor receptor 2; IDH1, isocitrate dehydrogenase 1; IHC, immunohistochemistry; ISH, in situ hybridization; MSI; microsatellite instability; NGS, next-generation sequencing; NOS, not otherwise specified; TMD-H, tumor mutational burden-high.

Table 3. Treatment outcomes in 1L in patients with m*IDH1*

	Patients with 1L regimens (N=80)
Progression-Free Survival, PFS (months)	
Median [95% CI]	8.0 months [4.2, 10.2]
Overall Survival, OS (months)	
Median [95% CI]	30.0 months [25.8, 38.8]
Disease Control Rate*, n (%)	
	67 (84%)

*Disease Control Rate includes Complete Response, Partial Response and Stable Disease
1L, first line; CI, confidence interval.

Table 4. Treatment outcomes in 2L in patients with m*IDH1*

	Patients with 2L Ivo-containing regimens (N=29)	Patients with 2L other regimens (N=34)
Progression-Free Survival, PFS (months)		
Median [95% CI]	6.1 months [2.2, 11.2]	4.1 months [1.6, 5.5]
Overall Survival, OS (months)		
Median [95% CI]	25.1 months [14.2, 39.5]	20.1 months [16.5, 24.4]
Disease Control Rate*, n (%)		
	20 (69%)	19 (56%)

2L, second line; CI, confidence interval.

Conclusions

- Most patients with CCA were diagnosed with advanced or metastatic disease and the majority of patients had access to biomarker testing
- Patients with m*IDH1* CCA received mainly GemCis or GemCis-durvalumab as 1L therapy and ivosidenib as 2L therapy, as recommended by current guidelines
- Median OS was longer than expected in each line of treatment, potentially due to survivorship bias, self-selection bias, and a limited number of patients harboring IDH1 mutations
- **This real-world study corroborates the efficacy finding from ClarIDHy[4,5] and supports ivosidenib as the 2L standard of care for patients with m*IDH1* CCA**

Patient summary

Cholangiocarcinoma (CCA) is a rare cancer that is often found late. About 10–15% of patients with an intrahepatic subtype of CCA have a change in a gene called *IDH1*. This study looked at how these patients are tested and treated in real life in the United States.

What the study did

Researchers looked at medical records from many hospitals to see:

- How patients were tested for biomarkers;
- What treatments they received; and
- How long they lived after treatment

Key findings

- **602 patients with CCA were included**, and most had advanced cancer when diagnosed
- About **83% underwent biomarker testing**, mostly with next-generation sequencing (NGS)
- Nearly **18% of patients** had an *IDH1* mutation
- **Most received standard first-line treatments** like gemcitabine–cisplatin (with or without durvalumab)
- Almost **one third of patients** with an *IDH1* alteration who received second-line treatment were administered ivosidenib
- **Patients treated with ivosidenib lived slightly longer** than those who received other second-line therapies

Conclusion

Most patients in our study were diagnosed late but had access to biomarker testing. Treatment patterns followed current guidelines, and the study supports ivosidenib as a valuable second-line option for patients with IDH1-mutated CCA.

This patient summary includes select illustrations designed by Freepik