REAL-WORLD TREATMENT PATTERNS AMONG US ADULTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA (HCC) ELIGIBLE FOR LOCOREGIONAL THERAPY (LRT)

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BACKGROUND

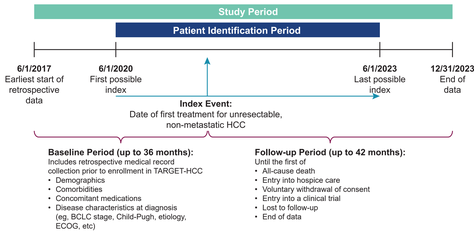
- Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer and is the third-leading cause of cancer-related death worldwide[1]
- Nearly one-third of patients with HCC are diagnosed at the intermediate stage (defined here as unresectable and non-metastatic) and are often ineligible for curative therapies[2]
- Treatment in unresectable, non-metastatic HCC has mostly relied on locoregional liver-directed treatment, such as transarterial chemoembolization (TACE) or radioembolization (TARE); however, due to the high variability in clinical characteristics among these patients with unresectable HCC (uHCC), not all patients respond to TACE/TARE alone. In such cases, clinicians may rely on systemic or multimodal therapy[2-4]
- The treatment landscape for unresectable, non-metastatic HCC is rapidly evolving; the objective of the study was to understand real-world, contemporary treatment patterns and clinical outcomes in patients with uHCC eligible for LRT

METHODS

Patient population identification and follow-up

- Unresectable, non-metastatic HCC patients (ie, eligible for LRT) enrolled in TARGET-HCC (a longitudinal, observational cohort of HCC patients receiving usual care at 40 academic and 10 community practice sites in the US) and initiated treatment between June 1, 2020, and June 1, 2023 were eligible for analyses if they met the inclusion and exclusion criteria (**Figure 1**)

Figure 1. Study schema



- **Inclusion criteria:**
  - Newly diagnosed with HCC
  - Age ≥18 years at the time of initial HCC diagnosis
  - Initiated first treatment for HCC between June 1, 2020, and June 1, 2023
  - Classified as having non-metastatic HCC at the time of initial HCC diagnosis
- **Exclusion criteria:**
  - Received curative HCC treatment (defined as ablation, resection, or transplant) as their first treatment following diagnosis
  - BCLC stage D at initial HCC diagnosis
  - Portal vein involvement present at initial HCC diagnosis
  - Enrolled in clinical trial within 12 months of first treatment for HCC
  - Newly diagnosed with or received treatment for a malignancy other than HCC on or within 12 months prior to the date of first treatment for HCC

Data abstraction:

- Patient and treatment information including narratives, imaging data used for staging, laboratory results, pathology reports, and other key variables such as comorbidities, medication use, and receipt/timing of HCC treatments was abstracted and curated from electronic health records using standardized guidelines

Treatment definitions:

- Index treatment was defined as the first treatment after initial diagnosis of unresectable, non-metastatic HCC, with a 30-day window for defining the index treatment(s) (**Table 1**)
- Subsequent treatment was defined as first treatment after the index treatment window
  - For systemic therapies, the subsequent treatment had to differ from the index treatment (ie, continuation of the first systemic therapy does not qualify as a subsequent treatment. A subsequent systemic therapy must be 30 days after the index therapy initiation AND differ from the index therapy)

METHODS

Table 1. Summary of procedures and/or medications included within each treatment type category

Treatment type	Procedure or medication
Locoregional therapy (LRT)	
Ablation	• Cryoablation • Microwave ablation (MWA) • Nanoknife/cyberknife ablation • Percutaneous ethanol injection (PEI) ablation • Radiofrequency ablation (RFA)
Embolization	• Particle embolization • Transarterial chemoembolization (TACE) • Transarterial embolization (TAE) • Transarterial radioembolization (TARE) • TARE-Y90
Other	• Intra-arterial chemotherapy
Radiation	
	• Stereotactic body radiotherapy (SBRT) • Image-guided radiation therapy (IGRT) • Intensity-modulated proton therapy (IMPT) • Conventional radiation therapy • Liver-directed radiation therapy
Systemic therapy	
Immuno-oncology (IO)	• Atezolizumab • Cemiplimab • Durvalumab • Ipilimumab • Nivolumab • Pembrolizumab • Tremelimumab
Anti-vascular endothelial growth factor (anti-VEGF)	• Ramucirumab • Bevacizumab
Tyrosine kinase inhibitors (TKI)	• Sorafenib • Lenvatinib • Regorafenib • Cabozantinib
Surgery	
	• Liver transplantation • Resection

Analyses of patient characteristics, treatment patterns, and clinical outcomes:

- Radiological progression was defined as presence of one or more of the following changes in tumor size, location, and vascular involvement as noted in the medical record:
  - New lesion
  - New extrahepatic involvement (including new metastases)
  - New vascular invasion
  - Expansion of existing lesions (ie, >20% increase in tumor size from baseline imaging study)
- Time-to-event outcomes were calculated from date of index treatment to qualifying event(s) (**Table 2**)

Table 2. Definitions for time to event outomces

Outcome	Definition
Real-world Time to Progression (rwTTP)	Date of index treatment to date of radiological progression
Real-world Progression Free Survival (rwPFS)	Date of index treatment to first of radiological progression or death from any cause or hospice entry (if date of death unavailable)
Real-world Overall Survival (rwOS)	Date of index treatment to date of death from any cause or hospice entry (if date of death unavailable)

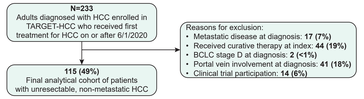
- Time-to-event and survival outcomes were presented using cumulative incidence curves (or its complement for survival) with overall proportions at clinically relevant intervals (ie, every 6 months) after index
- Patient characteristics and treatment patterns were assessed using descriptive statistics (eg, means, standard deviations, medians and interquartile ranges for continuous variables, and frequencies and percentages for categorical variables). Treatment patterns are summarized in **Figure 3**

RESULTS

Patient identification and baseline characteristics

- Among 233 adult HCC patients enrolled in TARGET-HCC who received their first treatment for HCC on or after June 1, 2020, we identified 115 eligible patients with unresectable, non-metastatic HCC from 7 academic and 4 community sites for inclusion in the current study (**Figure 2**)
- The most common reason for exclusion was receipt of curative therapy (19%), followed by portal vein involvement (18%) and metastatic disease (7%) at HCC diagnosis
- Median study study follow-up was 19.8 (Interquartile Range 10.3, 32.5) months

Figure 2. Study flow



- Mean age was 65.0 years, and 76.5% were male (**Table 2**)
- At diagnosis, 38.0% (n=41) of patients were BCLC stage A, 40.7% (n=44) BCLC stage B, and 14% (n=15) non-metastatic BCLC stage C. Patients with BCLC stage A were noted to have either a single lesion >5 cm, rapidly progressive disease, or other contraindications to LRT

Table 3. Baseline characteristics of patients with unresectable HCC eligible for LRT

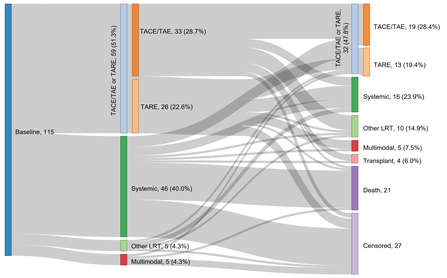
Characteristic	Category	N=115	%
Age (years)	18-64	59	51.3
	65+	56	48.7
	Mean (SD)	65.0	8.9
Sex	Male	88	76.5
Race	Non-Hispanic White	62	57.9
	Non-Hispanic Black	19	17.8
	Hispanic	21	19.6
	Asian	4	3.7
	Not reported/missing	8	*
BCLC stage at diagnosis	0	8	7.4
	A	41	38.0
	B	44	40.7
	C	15	13.9
	Indeterminate	7	*
Performance score (ECOG)	0	102	98.1
	1 or 2	2	1.9
	Unable to be determined	13	*
Etiology	Viral	49	55.7
	Nonviral	22	25.0
	Mixed	17	19.3
	Indeterminate	27	*
Comorbidities	Cardiovascular disease	17	23.3
	Diabetes	16	21.9
	Hypertension	36	49.3
	Chronic kidney disease	4	5.5
Index treatment (singular mode of treatment unless otherwise noted)	TACE/TAE or TARE	59	51.3
	TACE/TAE	33	28.7
	TARE	26	22.6
	Systemic treatment	46	40.0
	Other LRT	5	4.3
	Multimodal therapy[a]	5	4.3
Site type	Academic	103	89.6
	Community	12	10.4

*Patients with not reported, missing, or indeterminate data were excluded from estimation of percentages in this table.
[a]Multimodal therapy defined as TACE/TAE or TARE and systemic therapy within 30 days.

Treatment patterns

- Treatment choice for both index and subsequent treatment were heterogenous (**Figure 3**)
- Index treatment patterns:
  - Treatment with TACE/TAE or TARE was most common at 51.3% (n=59) followed by systemic therapy at 40% (n=46)
  - Among patients who initiated systemic therapy, 65.2% (n=30) received IO-based combinations such as IO+anti-VEGF, 26.1% (n=12) received IO only, and 8.7% (n=4) received a TKI only
- Subsequent treatment patterns:
  - 58% (n=67 of 115) patients received subsequent treatment, with 47.8% (n=32) receiving TACE/TAE or TARE, 23.9% systemic treatment (n=16), 14.9% other LRT (n=10), 7.5% multimodal therapy (n=5), and 6.0% transplant (n=4
- 18.3% (n= 21 of 115) patients died without receiving subsequent treatment and 23.5% (27 of 115) other patients were censored at data cutoff

Figure 3. Sankey diagram summarizing patterns of index and subsequent treatment



**Multimodal therapy was defined as TACE/TAE or TARE and systemic therapy for HCC received within 30 days.

Real-world clinical outcomes

- A total of 60 progression events were observed, resulting in a median rwTTP of 11.3 11.3 (95% CI: 6.7, 28.8) months (**Figure 4**)
- Median rwPFS was 7.9 (95% CI: 5.0, 13.3) months (**Figure 5**)
- Although we observed 33 deaths, the data were not mature enough to observe median rwOS; however, the 75th percentile was 15.7 (95% CI: 10.1, 28.4) months (**Figure 6**)

Figure 4. Real-world time to progression (rwTTP)

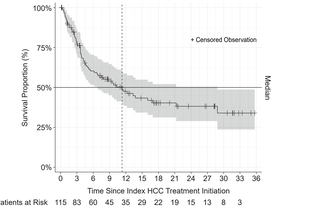


Figure 5. Real-world progression-free survival (rwPFS)

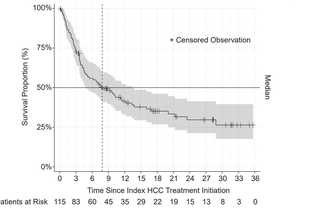
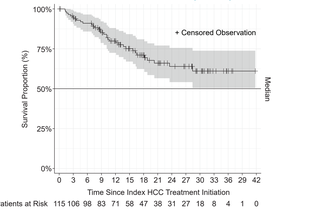


Figure 6. Real-world overall survival (rwOS)



CONCLUSIONS

- **In this real-world study, our results showed high variability in management of uHCC eligible for LRT; for index treatment, TACE/TARE was most commonly utilized while some patients received systemic therapy alone**
- **The study findings also emphasize that the prognosis of uHCC eligible for LRT remains poor, as consistent with evidence in the literature[5,6]**

LIMITATIONS AND FUTURE RESEARCH

- Treatment choice may be influenced by factors beyond staging criteria. Since real-world evidence studies are limited by the detail and completeness of electronic medical records not designed for research, more comprehensive characterization of treatment choice rationale (eg, impact of comorbidity burden, tumor size, treatment contraindications) was not available
- Study findings on subsequent treatments should be interpreted with caution, since identification of subsequent treatment in this real-world study was operationalized through a predefined treatment gap
- Target-HCC cohort is a convenience sample and may not fully represent the US HCC patient population. However, the longitudinal nature of the cohort allows for the description and evaluation of treatment sequences used in clinical practice
- Further research on adaptive, multimodal treatment strategies is needed to inform treatment guidelines and improve outcomes in this patient population

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https://bit.ly/4gs3dmH

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