Real-World Treatment Patterns of Early-Stage Hepatocellular Carcinoma (HCC) After Complete Resection or Ablative Therapy: Retrospective, Medical Chart Review in the United States

Poster #CO211

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Background

- Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver with an estimated annual incidence of 5.84 per 100,000[1,2]
- Despite potentially curative treatment options such as surgical resection or ablation for HCC patients at early stages, these treatments remain associated with high recurrence rates with approximately two-thirds of patients experiencing recurrence within 5 years of curative treatment with resection or radiofrequency ablation[3]
- Although recurrence is common after curative surgery or ablation, there are no adjuvant therapies approved by the Food and Drug Administration or recommended by clinical practice guidelines for patients with early-stage HCC
- The phase III Checkmate-9DX trial currently in progress aims to assess recurrence-free survival (RFS) and overall survival (OS) among early-stage HCC patients treated with adjuvant nivolumab, however, there is a dearth of evidence describing current real-world treatment patterns in clinical practice

Objective

- This study aimed to describe real-world characteristics and treatment patterns among patients with early-stage HCC who underwent curative resection or ablation

Methods

Study Design
- A US-based, retrospective chart review study in patients with early-stage HCC

Inclusion Criteria
- Initial diagnosis of early-stage HCC as determined by the Barcelona Clinic Liver Cancer (BCLC) staging system
- Underwent complete resection with no residual disease at resection margin (R0) or remainder of the liver or achieved a complete response after local ablation
- Identified as high-risk for HCC recurrence based on physician assessment
- Began post-resection or ablation follow-up between 01/01/18 and 12/31/2020

Exclusion Criteria
- Participated in any clinical trial for neoadjuvant/adjuvant therapy for early-stage HCC
- Diagnosed with fibrolamellar HCC, sarcomatoid HCC, or mixed cholangiocarcinoma HCC
- Patients who were receiving transplant drugs underwent liver transplant
- HBV and HCV co-infected patients

Data Collection and Analysis
- Data were collected from patient medical records abstracted by physicians in the Cardinal Health Oncology Provider Extended Network (OPEN); a community of >800 private practice and hospital-based oncologists/hematologists across the United States (US)
- Study Data were collected between 4/13/2022-5/23/2022
- All data were assessed using descriptive statistics

Results

Patient Demographics and Clinical Characteristics
- Among 300 eligible patients, the majority were male (60.0%) and White (60.7%) (**Table 1**)
- Majority of the population were non-Hispanic (87.7%) with Medicare (43.7%) or commercial (37.7%) insurance (**Table 1**)
- Mean age at HCC diagnosis was 63.2 years and 69% were identified as BCLC stage A1 or A2 (**Table 1**)
- All patients were considered to be at high risk of recurrence based on physician assessment; however, 80.0% met high-risk criteria based on a clinical definition* (**Table 1**)
- Approximately 59.0% and 41.0% underwent complete resection or local ablation, respectively (**Table 1**)
- Median study follow-up time after resection or ablation was 21.6 months (**Table 1**)

Table 1. Patient Baseline Demographic Characteristics

N=300	All patients
Age at initial diagnosis of early-stage HCC	
Mean (SD)	63.16 (8.98)
Min-max	36-84
Median (p25-p75)	63 (57.0-70.0)
Sex at birth, n (%)	
Male	180 (60.0)
Female	120 (40.0)
Race, n (%)	
White	182 (60.7)
Asian	30 (10.0)
Black/African American	74 (24.7)
Native Hawaiian or Other Pacific Islander	4 (1.3)
American Indian or Alaska Native	3 (1.0)
Ethnicity, n (%)	
Hispanic/Latino/Latina	37 (21.3)
Non-Hispanic/Latino/Latina	263 (87.7)
Insurance status at 1L initiation, categorical[1], n (%)	
Medicare	131 (43.7)
Medicaid	44 (14.7)
Commercial	113 (37.7)
Military	3 (1.0)
Self-pay	6 (2.0)
Unknown	3 (1.0)

[1]Not mutually exclusive

*Clinical definition based upon CheckMate-9DX criteria

Results (cont.)

N=300	All patients
Patients disposition at data collection, n (%)	
Alive	236 (78.7)
Deceased	64 (21.3)
Barcelona Clinic Liver Cancer stage at initial diagnosis of HCC, n (%)	
A1	116 (38.7)
A2	91 (30.3)
A3	46 (15.3)
A4	47 (15.7)
Patients that meet clinical criteria for high risk of HCC recurrence[1], n (%)	
Met clinical criteria for high-risk[1]	240 (80.0)
Did not meet clinical criteria for high-risk[1]	60 (20.0)
Surgical resection treatment, n (%)	
Patients who underwent complete resection with no residual disease at resection margin or remainder of the liver	177 (59.0)
Patients who achieved a completed response after local ablation	123 (41.0)
Months of follow-up following resection/ablation	
Mean, SD	24.0 (10.2)
Median, P25-P75th	21.6 (17.5-30.6)
Min, Max	0.0-49.8

[1]Patients meeting any of the following criteria were considered "high-risk" based on the Checkmate-9DX trial criteria: ≤3 tumors, at least one with diameter >5 cm, no evidence of Mvi; ≤3 tumors, ≤5 cm but confirmation of MVI or poorly/undifferentiated HCC (G3-G4); >3 tumors, none >5 cm, no evidence of Mvi; Single tumor >3 cm but ≤5 cm; Up to 4 tumors, none with diameter >5 cm

Pre-Recurrence Treatment Patterns

Among all patients (N=300):
- 100.0% did not receive neoadjuvant systemic therapy prior to resection/ablation (**Table 2**); and
- Very few (2.3%) received adjuvant systemic therapy after resection/ablation (**Table 2**)

Among those who did receive adjuvant systemic therapy after resection/ablation and prior to recurrence (n=7):
- Most received sorafenib (n=5); and
- Median duration of adjuvant systemic therapy was 6.2 months (**Table 2**)

Table 2. Early HCC Treatment Patterns

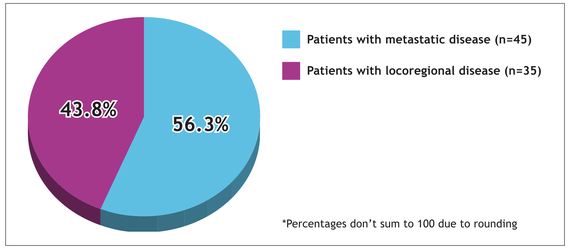
N=300	All patients
Neoadjuvant systemic therapy received prior to resection/ablation, n (%)	
No	300 (100.0)
Yes	0 (0.0)
Adjuvant systemic therapy received after resection/ablation and prior to recurrence, n (%)	
No	293 (97.7)
Yes	7 (2.3)
Regimen received[1], n (%)	
Sorafenib	5 (71.4)
Fluorouracil/Oxaliplatin (FOLFOX)	1 (14.3)
Ledipasvir-sofosbuvir	1 (14.3)
Duration of adjuvant systemic therapy received after resection/ablation and prior to recurrence, months[1]	
Mean	9.8, 6.2
Median, 25P-75P	6.2, 6.0-15.6
Min, max	2.9, 20.1

Post-Recurrence Characteristics and Treatment Patterns

Among all patients, 26.7% (n=80) experienced HCC recurrence within the 21.6-month median study follow-up period. Among those patients:
- 56.3% had a locoregional recurrence, and 43.8% had metastatic recurrence (**Figure 1**)
- 2.5% underwent resection for recurrent HCC, 23.8% received ablation therapy, and 61.3% received ≥1 line of systemic therapy post-recurrence (**Table 3**)

Among recurrent HCC patients who received systemic therapy (n=49):
- Median duration of first-line therapy was 8.5 months (**Table 3**)
- The majority received atezolizumab/bevacizumab (55.1%) followed by lenvatinib, (24.5%), and sorafenib (16.3%)
- 59.2% were still on first-line systemic therapy and 40.8% had discontinued first-line systemic therapy at the end of study follow-up (**Table 3**)
  - Among the patients who discontinued first-line therapy (n=20), 90.0% did so due to disease progression (**Table 3**)

Figure 1. Type of Recurrent HCC (n=80)*



*Percentages don't sum to 100 due to rounding

Results (cont.)

Table 3. Post-Recurrence Characteristics and Treatment Patterns

N=80	Patients Experiencing HCC Recurrence
Resection/ablation following HCC recurrence, n (%)	
Patients who underwent resection for recurrent HCC	2 (2.5)
Patients who received ablation therapy for recurrent HCC	19 (23.8)
Type of locoregional treatment received following HCC recurrence	
No	61 (76.3)
Yes	19 (23.8)
Locoregional treatment received, n (%)	
Patients treated with Trans-arterial embolization (TAE)	1 (5.3)
Patients treated with Conventional trans-arterial chemoembolization (TACE)	2 (10.5)
Patients treated with Drug-eluting Beads (DEB)-TACE	2 (10.5)
Patients treated with Trans-arterial radioembolization (TARE, also called radioembolization; TheraSpheres)	12 (63.2)
Unknown	2 (10.5)
Systemic Therapy Received for Recurrent HCC, n (%)	
Yes	49 (61.3)
No	31 (38.8)
Lines of Systemic Therapy Received for Recurrent HCC[1], n (%)	
0	31 (38.8)
1	43 (53.8)
2	5 (6.3)
3	1 (1.3)
Systemic Therapy Regimen Received for 1L Treatment of Recurrent HCC[1] (n,%)	
Atezolizumab/bevacizumab	27 (55.1)
Lenvatinib	12 (24.5)
Sorafenib	8 (16.3)
Fluorouracil/oxaliplatin (FOLFOX)	1 (2.0)
Nivolumab	1 (2.0)
Median Duration of 1L Systemic Treatment for Recurrent HCC[1] (KM Median [months], 95% CI)	8.5 (6.1-21.8)
Status of IL Systemic Therapy Received for Recurrent HCC[1], n (%)	
Still on 1L therapy	29 (59.2)
Discontinued 1L therapy	20 (40.8)
Primary rationale for discontinuation, n (%)	
Disease progression (confirmed with scan)	14 (70.0)
Disease progression (defined clinically)	4 (20.0)
Patient choice	2 (10.0)

[1]Among patients who received 1 or more line of systemic therapy for the treatment of recurrent HCC (n=49)

Study limitations/strengths

Limitations
- This study utilized purposive sampling that selected physicians and patients based on pre specified selection criteria and thus, findings may not be representative of all patients with early HCC who underwent curative resection or ablation in routine clinical practice
- The accuracy and completeness of data collected in this study is limited by the quality of data in the patient's medical chart

Strengths
- Data were collected from unique sites and providers irrespective of hospital system, EMR systems, group purchasing organization or other criteria removing biases that may result from single-site or source datasets
- Data were abstracted by the patient's treating physician enabling collection of high-quality data independent of third-party abstractors' assumptions
- Providers use both structured data elements within the EMR and review unstructured patient clinical notes as necessary which allows for the capture of both the objective and subjective data points such as physician assessment of high-risk

Conclusions

- In this real-world study of patients with early-stage HCC who received curative resection or ablation, over a quarter of patients (n=80, 26.7%) had a locoregional or metastatic recurrence during the 21.6-month median follow up period
- Although recurrence was observed within the study follow up period, the majority of patients (95%) received no adjuvant therapy
- Patients who experienced disease recurrence, more often experienced a metastatic recurrence (56%) rather than a locoregional recurrence (44%)
- These findings highlight the need for adjuvant therapies to prevent recurrence in early-stage HCC patients after curative resection or ablation

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