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WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc*.

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ORIGINAL ARTICLE

Retrospective Study

Real-world clinical effectiveness of sorafenib among patients with unresectable hepatocellular carcinoma at two centers in the United States

Daneng Li, Stephen B Gruber, Shrividya Iyer, Sanjay Gupta, Mohamedtaki Tejani

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Abstract

BACKGROUND

In the United States, sorafenib monotherapy was approved in 2007 for first-line (1L) treatment of patients with unresectable hepatocellular carcinoma (uHCC). As other therapies have been approved in recent years for hepatocellular carcinoma treatment in later lines, it is essential to assess clinical effectiveness of older therapies in actual clinical practice to inform healthcare practitioners' decisions for better patient care.

AIM

To assess patient characteristics/clinical effectiveness of 1L sorafenib in uHCC patients treated in United States academic and community practice settings.

METHODS

A retrospective observational study was conducted among adult patients (≥ 18 years) in the United States initiating sorafenib monotherapy as 1L systemic therapy for uHCC with Eastern Cooperative Oncology Group status of 0 or 1 between January 2016 and December 2019 at City of Hope and Advent Health. Data were extracted by trained abstractionists from individual patients' electronic health records and captured in electronic case report forms. Institutional Review

Board approvals were obtained prior to study initiation. Data were captured from the time of sorafenib initiation until death or the end of follow-up. All data were de-identified prior to analyses. Clinical outcomes assessed included provider-reported best response, progression-free survival (PFS), and overall survival (OS). PFS and OS were estimated using Kaplan-Meier methods.

RESULTS

Among 134 uHCC patients treated with 1L sorafenib, majority were male (75%), and most were Caucasian (62%) or Asian (19%). Median patient age was 64 years. The most common etiologies of liver disease were hepatitis C (54%), alcohol-related liver disease (16%), and hepatitis B (11%). Most patients were reported to have Barcelona Clinic Liver Cancer stage B (19%) or stage C (70%) disease. Of 134 patients, 110 (82%) were reported to have discontinued treatment or died during follow-up. Primary reasons for sorafenib discontinuation were reported as progression (35%) and toxicity (30%). Best overall response was reported for 124 patients, of which 7.3% reported complete or partial response. Median time to treatment discontinuation was 2.3 mo. Overall, 103 patients (77%) had disease progression or died during sorafenib therapy. Median PFS was estimated to be 2.9 mo. At the end of follow-up, 82 patients (61%) were deceased. Median OS was 8.5 mo.

CONCLUSION

Newer therapeutic options that have reported higher PFS and OS in real-world clinical practice should be considered to enhance patient outcomes.

Key Words: Retrospective observational study; Sorafenib; Hepatocellular carcinoma; Clinical effectiveness

Core Tip: As treatment options evolve for hepatocellular carcinoma (HCC) it is important to assess and understand the clinical outcomes with older treatment options in diverse real-world clinical practice settings to inform clinical decision making and identify the right patient for the right drug. The current study aimed to assess the patient characteristics and clinical effectiveness of sorafenib as first-line therapy in unresectable HCC patients treated in both academic and community practice settings in the United States.

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INTRODUCTION

Primary liver cancer is the sixth most commonly diagnosed cancer and the third leading cause of cancer death worldwide in 2020, with approximately 906000 new cases and 830000 deaths[1]. Hepatocellular carcinoma (HCC) is the most common type of liver cancer and accounts for approximately 75% of liver cancer cases in the United States[2]. Systemic treatments may benefit patients with advanced-stage HCC. Sorafenib was the first systemic drug approved by the United States Food and Drug Administration in 2007 and was considered standard of care until 2018[3].

Sorafenib was approved for the treatment of unresectable HCC (uHCC) after two phase III trials [Sorafenib HCC assessment randomized protocol (SHARP) and Asia-Pacific] demonstrated significant improvements in overall survival (OS)[4,5]. However, rapid advances during the last four years have led to the approval of other molecular targeted drugs and several immune checkpoint inhibitors[3] for first- or second/later-line use. In the first-line (1L) setting, lenvatinib was approved in July 2018 for the treatment of advanced uHCC patients[6]. Additional systemic treatment options are currently available and approved for use in sorafenib-treated patients (in second or later lines), including the tyrosine kinase inhibitors regorafenib and cabozantinib, the vascular endothelial growth factor receptor inhibitor ramucirumab, and the programmed cell death protein 1 inhibitor pembrolizumab[7-11].

Though previous retrospective and prospective real-world observational studies have evaluated clinical effectiveness of sorafenib[12-17], with the evolving landscape it is important to reassess clinical outcomes like OS in patients treated with 1L sorafenib, given there are many more options. Understanding OS with sorafenib becomes more critical given sorafenib is now a generic drug in the United States and progression-free survival (PFS)/OS are critical elements in assessing cost-benefit ratios of treatments, especially when comparing to novel branded therapeutic options. In our study we assess clinical outcomes of uHCC patients treated with 1L sorafenib at an academic cancer center and a community cancer practice.

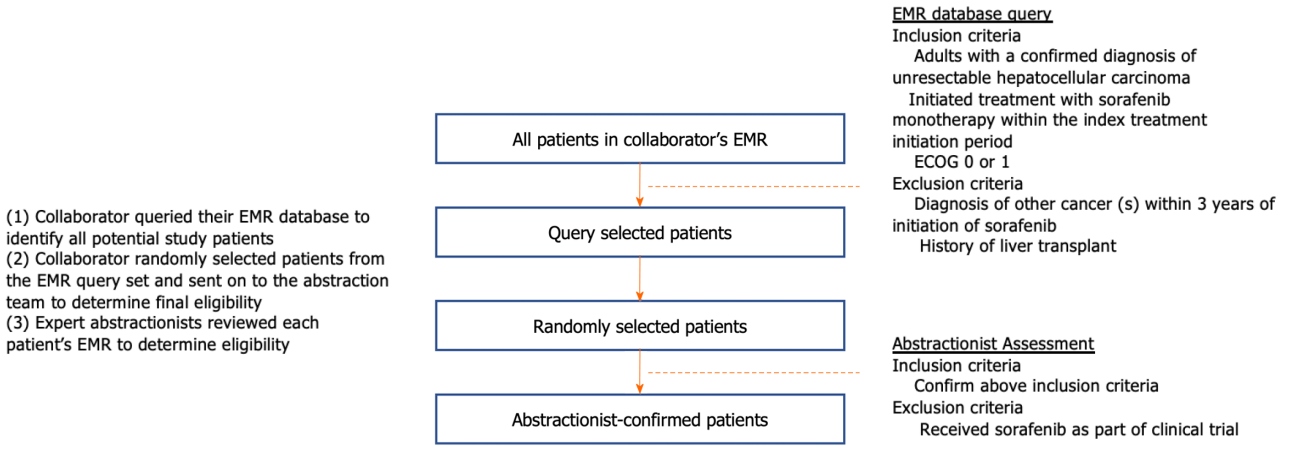

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Figure 1 Study overview. Flow diagram detailing patient record selection process. ECOG: Eastern Cooperative Oncology Group; EMR: Electronic medical record.

MATERIALS AND METHODS

Patient Population

A retrospective observational study was conducted among adult patients (≥ 18 years) in the United States who had initiated sorafenib monotherapy as 1L systemic therapy for uHCC with an Eastern Cooperative Oncology Group (ECOG) status of 0 or 1 between January 2016 and December 2019 at an academic cancer center (City of Hope) and a community cancer practice (Advent Health). City of Hope is an academic and National Cancer Institute-designated Comprehensive Cancer Center located in the state of California. Advent Health is a large regional community health system headquartered in Florida serving 5 million patients across 9 states (Colorado, Florida, Georgia, Illinois, Kansas, Kentucky, North Carolina, Texas, and Wisconsin). Patients were excluded if there was evidence of other malignant neoplasms within 3 years prior to initiation of sorafenib, liver transplant recorded at any point in their medical history, or if they had received sorafenib as part of a clinical trial. Each collaborating center had the study protocol reviewed and approved by their respective Institutional Review Board. All data transmitted from the data collaborators in support of the study were de-identified pursuant to Health Insurance Portability and Accountability Act Privacy Rule 164.514 (b) and (c).

Patient medical records were selected randomly in a three-part process as depicted in Figure 1. Each center used a database query to identify a superset of patients that contained all eligible patients (and likely some that were ineligible). Data were collected using a standard electronic case report form (eCRF) at both centers. Structured data were automatically collected from de-identified electronic medical records (EMR). Data explicitly stated in the EMR and not requiring any inference or clinical judgment were entered into the eCRF by expert oncology chart abstractionists trained on the study protocol at each center. Data abstracted by the abstractionists were reviewed by the study oncologist for completeness and quality assurance. Treating oncologists who were specifically trained on the study protocol also captured certain key data that were not expressly stated in the EMR but could be determined through clinical judgment from evidence in the patient EMR (including unstructured physician notes *e.g.*, response, progression).

Treatment

Sorafenib monotherapy initiated as 1L systemic therapy for uHCC between January 2016 and December 2019.

Follow-Up

Data on these patients were captured from the time of sorafenib initiation until their death, lost to contact, or the end of follow-up.

Study Variables and Endpoints

Patient demographics and clinical history were extracted from the EMR. Demographics of interest included age at sorafenib initiation, sex, and race/ethnicity. Clinical history included liver disease etiology (hepatitis B, hepatitis C, alcohol-related, and nonalcoholic fatty liver disease), cirrhosis severity (Child-Pugh score), ECOG performance status, and Barcelona Clinic Liver Cancer (BCLC) stage. Patients' treatment characteristics included receipt of treatments or procedures prior to and after sorafenib. Information about treatment with sorafenib start and end dates was ascertained. The reasons for discontinuation were captured at a category-level only (*e.g.*, toxicity, progression, patient preference, death, not reported).

After baseline tumor assessment, subsequent assessments by the treating oncologist recorded the tumor response as progressive disease (PD), stable disease (SD), partial response (PR), complete response (CR), not evaluable. When these observations were stated explicitly in the patient medical record, they were captured by the abstractionists. When the tumor response was not explicitly stated by the treating oncologist in the EMR the abstractionist recorded that an

Table 1 Patient demographics

Characteristic	Overall (*n* = 134)	Advent Health (*n* = 62)	City of Hope (*n* = 72)
Age at diagnosis (yr)			
Mean	65	64	65
Median (range)	64 (33-90)	63 (44-79)	66 (33-90)
Sex, *n* (%)			
Male	101 (75)	50 (81)	51 (71)
Female	33 (25)	12 (19)	21 (29)
BMI, *n* (%)			
< 18.5	4 (3)	4 (6)	-
18.5-24.9	48 (36)	20 (32)	28 (39)
25-29.9	38 (28)	14 (23)	24 (33)
≥ 30	34 (25)	21 (34)	13 (18)
Not reported	10 (8)	3 (5)	7 (10)
Race, *n* (%)			
Asian	25 (19)	3 (5)	22 (31)
African-American	15 (11)	11 (18)	4 (6)
Native Hawaiian or other Pacific Islander	1 (1)	-	1 (1)
Caucasian	83 (62)	41 (66)	42 (58)
Not reported	10 (7)	7 (11)	3 (4)
Ethnicity, *n* (%)			
Hispanic or Latino	34 (25)	16 (26)	18 (25)
Non-Hispanic or Non-Latino	94 (70)	45 (73)	49 (68)
Not reported	6 (5)	1 (1)	5 (7)

BMI: Body mass index.

assessment was done but tumor response was "not stated". The reviewing oncologist recorded the patients' best overall response (BOR) on sorafenib based on the treating oncologists' explicitly stated assessment or, if that was not available, by applying their clinical judgment based on the evidence in the EMR. The physician-reported criteria used to evaluate best clinical response [*e.g.*, Response Evaluation Criteria in Solid Tumors (RECIST) 1.1, modified (m) RECIST, or physician assessment, if no specific criteria were reported in patient charts] were collected. PFS was defined as time from sorafenib initiation to clinical progression or death during sorafenib treatment, and OS was defined as time from sorafenib initiation to death. For PFS, patients who did not progress during sorafenib treatment were censored at sorafenib treatment stop date; for OS, those who were still alive at the time of data collection were censored at the date of their last available medical record.

Statistical Analysis

Our study did not involve formal hypothesis testing or comparative analyses and was primarily descriptive; therefore, the sample size was based on available resources rather than a formal statistical power calculation. Descriptive statistics were reported for patients' demographic, clinical, and treatment characteristics as well as for physicians' characteristics. Missing data were not extrapolated or estimated and were calculated as percentage of patients of the total that had a particular characteristic as missing or not reported. Clinical outcomes are reported for the overall cohort. Real-world BOR (rwBOR) was calculated as percentage of patients who had a real-world best response reported as partial or complete. Disease control rate (DCR) was calculated as percentage of patients who had a rwBOR of SD, PR, or CR. Time-to-event outcomes (*i.e.*, PFS and OS) were estimated using the Kaplan-Meier method. PFS and OS between subgroups were compared using log-rank tests. A P value of $P < 0.05$ was considered statistically significant. The statistical methods of this study were reviewed by Shrividya Iyer from Eisai.

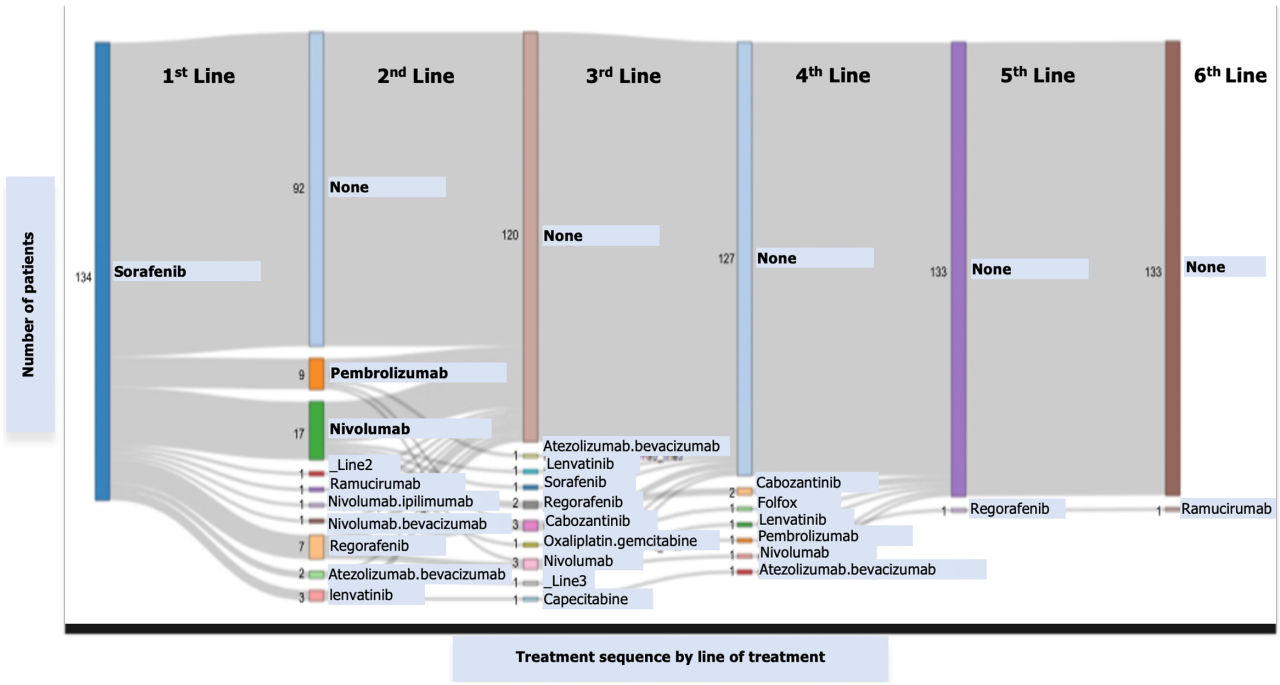

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Figure 2 Therapeutic sequences. Sankey plot detailing subsequent treatments received by patients.

RESULTS

Patient Demographics and Clinical Characteristics

Patient demographics and clinical characteristics of the 134 patients who received 1L sorafenib are shown in Table 1 and Table 2, respectively. Patients' median age was 64 years, and most patients were male (75%) and Caucasian (62%) or Asian (19%) (Table 1). Majority of the patients had either Child-Pugh class A cirrhosis (36%) or Child-Pugh class B cirrhosis (40%), with 9% showing more severe liver dysfunction with Child-Pugh class C cirrhosis. More than half (54%) of patients were diagnosed with hepatitis C and 11% with hepatitis B infection, whereas 16% of patients had alcohol-related liver disease and 8% had nonalcoholic fatty liver disease. Majority (70%) of patients were BCLC stage C, whereas 19% were BCLC stage B, and 9% BCLC stage A at initiation of 1L sorafenib (Table 2). Portal vein thrombosis was reported in 13% of patients.

Treatment Characteristics

Of the 134 patients treated with 1L sorafenib, 110 were known to have discontinued treatment or died during the observation period. Median real-world time to treatment discontinuation (rwTTD) was 69 d (2.3 mo) from initiation of 1L sorafenib. Among patients with Child-Pugh class A cirrhosis, median rwTTD was 2.4 mo; among patients with Child-Pugh class B cirrhosis, median rwTTD was 1.9 mo, while patients with Child-Pugh class C cirrhosis had a median rwTTD of 1 mo.

Reason for discontinuation of 1L sorafenib was available for 102 patients. For majority of patients, sorafenib was discontinued due to progression (35%) and toxicity (30%). Death (5%), patient preference (3%), and hospice or palliative care (2%) were other reasons listed as a reason for discontinuation.

Majority of the patients (69%) received only one line of therapy. Of those who went on to receive subsequent lines of therapy, 17 (40%) received second-line nivolumab and 9 (21%) received second-line pembrolizumab. Figure 2 shows the therapeutic sequences observed.

RWBOR and DCR

Of the 134 patients that received 1L sorafenib, 124 patients had response information captured from the EMR. The response findings were based on the treating physicians' assessment. Overall, 9 patients (7.3%) had best response reported as CR or PR on 1L sorafenib; 55 patients reported a best response as CR, PR, or SD with a DCR of 44.4%. BOR for subgroups are presented in Table 3.

Real-World PFS (rwPFS)

Overall, 103 of 134 patients had disease progression or died during sorafenib therapy. Median rwPFS was 88 d (2.9 mo) from initiation of 1L sorafenib (Figure 3A). Median rwPFS was estimated to be 3.1 mo among patients with Child-Pugh class A cirrhosis, 2.6 mo among patients with Child-Pugh class B cirrhosis, and 1.4 mo among patients with Child-Pugh class C cirrhosis. RwPFS was observed to be significantly lower in Child-Pugh C patients compared to Child-Pugh A patients [hazard ratio (HR) = 3.27, 95% confidence interval (CI): 1.57-6.79, $P < 0.05$] and in patients with an ECOG status

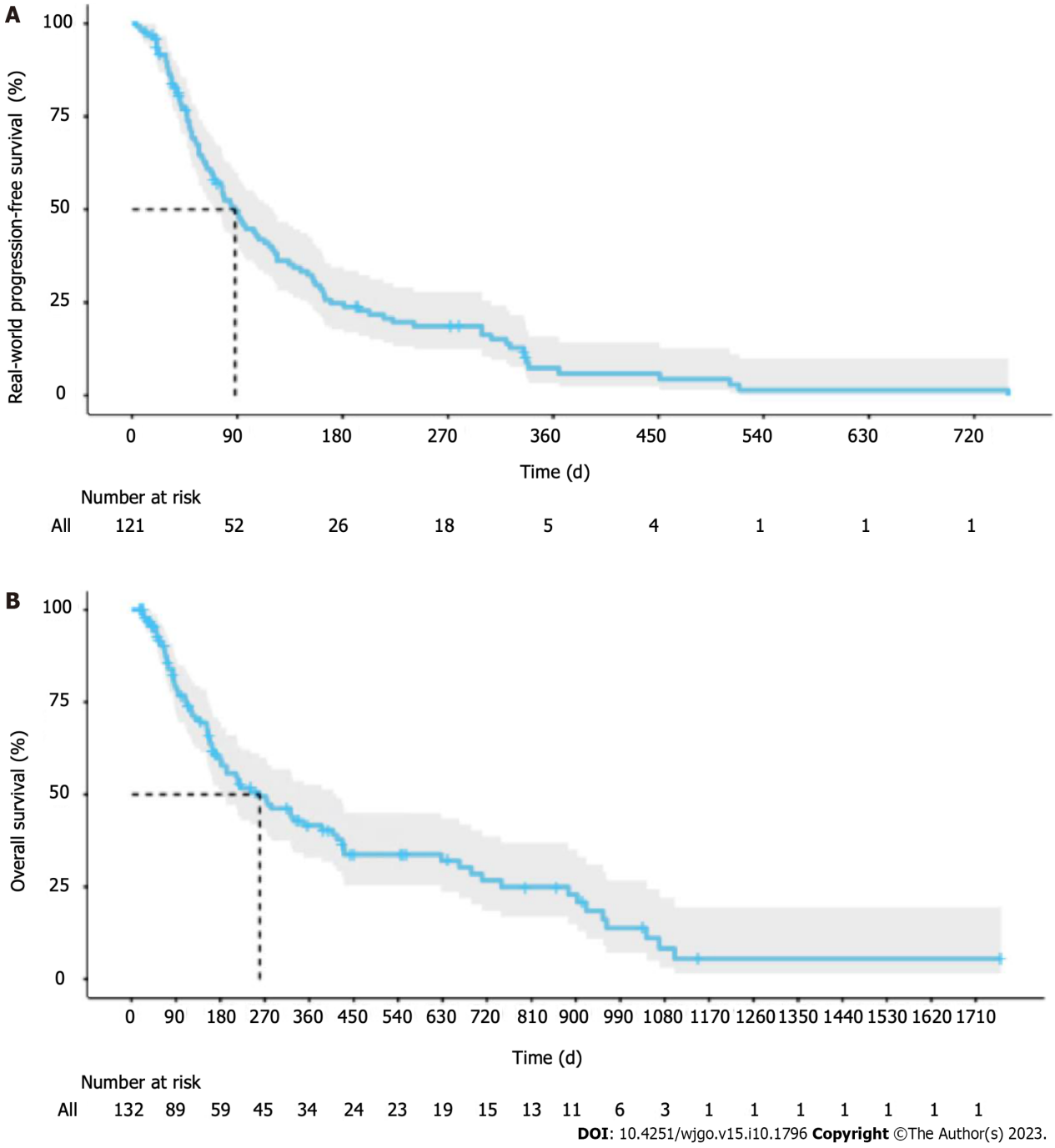

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Figure 3 Real-world progression-free survival and overall survival. A: Kaplan-Meier plot of Real-world progression-free survival (rwPFS), median rwPFS (88 d) is shown as a dashed line; B: Kaplan-Meier plot of overall survival (OS), median OS (258 d) is shown as a dashed line.

of 1 compared to patients with an ECOG status of 0 (HR = 1.70, 95% CI: 1.03-2.83, $P < 0.05$) (Table 3).

OS

At the end of the observation period, 82 patients (61%) were deceased. Median OS was 258 d (8.5 mo) from initiation of 1L sorafenib (Figure 3B). Median OS was 10.6 mo among patients with Child-Pugh class A cirrhosis, 6.3 mo among patients with Child-Pugh class B cirrhosis, and 3 mo among patients with Child-Pugh class C cirrhosis. Median OS was significantly lower in Child-Pugh C patients compared to Child-Pugh A patients (HR = 4.49, 95% CI: 1.87-10.8, $P < 0.05$). No statistically significant differences in OS were observed between other subgroups (Table 3).

DISCUSSION

Our retrospective real-world study evaluated clinical outcomes among a demographically and clinically diverse adult uHCC patient population treated at an academic cancer center and a community health care system, thus including

Table 2 Patient clinical characteristics

	Overall (*n* = 134)	Advent Health (*n* = 62)[1]	City of Hope (*n* = 72)
Child-Pugh class, *n* (%)			
A	48 (36)	26 (42)	22 (31)
B	54 (40)	25 (40)	29 (40)
C	12 (9)	7 (11)	5 (7)
Not reported	20 (15)	4 (6)	16 (22)
BCLC stage, *n* (%)			
0	1 (1)	1 (2)	-
A	12 (9)	2 (3)	10 (14)
B	25 (19)	22 (35)	3 (4)
C	94 (70)	36 (58)	58 (81)
D	1 (1)	-	1 (1)
Not reported	1 (1)	1 (2)	0
ECOG, *n* (%)			
0	28 (21)	10 (16)	18 (25)
1	103 (77)	49 (79)	54 (75)
Not reported	3 (2)	3 (5)	0
Etiology, *n* (%)			
Hepatitis B	15 (11)	5 (8)	10 (14)
Hepatitis C	72 (54)	35 (56)	37 (51)
Alcohol-related liver disease	21 (16)	10 (16)	11 (15)
Nonalcoholic fatty liver disease	11 (8)	4 (6)	7 (10)
Not reported/none of the above	15 (11)	8 (13)	7 (10)

[1]Due to rounding, percentages may not add to 100%.
BCLC: Barcelona Clinic Liver Cancer; ECOG: Eastern Cooperative Oncology Group.

uHCC patients treated with 1L sorafenib in diverse health care settings from multiple states in the United States.

The clinical outcomes observed in our study were similar to previously published real-world data studies as well as the sorafenib arm clinical outcomes in major clinical trials. The results of the SHARP study demonstrated the clinical effectiveness of sorafenib in the treatment of uHCC. Compared to the placebo group, the sorafenib treatment group had significantly prolonged median OS (10.7 *vs* 7.9 mo)[4,5]. In the Asia-Pacific study, patients treated with sorafenib had a longer median OS (6.4 *vs* 4.2 mo) and median time to progression (2.8 *vs* 1.4 mo) compared to placebo[5]. Notably, the patient population in our real-world study had Child-Pugh scores ranging from A to C, while the majority (> 95%) of patients in SHARP had Child-Pugh A scores[4].

In line with previous clinical and prospective real-world data studies, median PFS and median OS in patients treated with sorafenib in our study were shorter in Child-Pugh B patients compared with Child-Pugh A patients[13,14]. In a multi-center phase 2 trial, the median PFS (range) for the total patient population was 3.9 (0.1-35.3) mo; median PFS (range) for patients with Child-Pugh A or B cirrhosis was 4.3 (0.1-35.3) mo and 2.1 (0.3-27.3) mo, respectively (log-rank $P < 0.001$). In the multivariate analysis in the same trial, Child-Pugh B patients had a greater risk of disease progression or death compared to Child-Pugh A patients (HR 1.87, 95%CI: 1.41-2.48, $P < 0.001$)[14].

The global investigation of therapeutic decisions in HCC and of its treatment with sorafenib trial was a large prospective, observational cross-regional registry study undertaken to evaluate the real-life use, safety, and effectiveness of sorafenib in HCC patients; it included patients with baseline Child-Pugh B (21%) and C (2%) liver function[13]. Median OS was longer in Child-Pugh A patients (13.6 mo) than in Child-Pugh B patients (5.2 mo) and Child-Pugh C patients (2.6 mo)[13]. In a smaller retrospective real-world study of patients treated with sorafenib in Portugal ($n = 36$), median OS was reported to be 6.8 mo (95%CI: 3-10.6). Median OS differed according to Child-Pugh class [Child-Pugh A: 17.3 mo (95%CI: 5.3-29.4) *vs* Child-Pugh B: 3.2 mo (95%CI: 0.9-5.5); $P = 0.001$][17]. In the same study by Cardoso *et al*[17], two patients (6%) had PR, nine patients (25%) were classified as SD, and seven patients (19%) reported PD. Sixteen patients were also evaluated according to mRECIST criteria; one patient reached CR, four patients (11%) had PR, three patients (8%) had SD, and eight patients (22%) reported PD.

Table 3 Clinical outcomes by subgroup

Cohort/subgroup	Best overall response, % (CR + PR)	N (PFS)	Median PFS (Q1, Q3), months	HR (95%CI)	N (OS)	Median OS (Q1, Q3), months	HR (95%CI)
Overall	7.3	121	2.9 (1.5, 5.6)		134	8.5 (3.6, 24.6)	
Age group (yr)							
< 65[1]	7.7	61	3.5 (1.8, 7.1)		69	8.5 (3.6, 23.4)	
65-75	9.8	42	2.3 (1, 10.3)	1.40 (0.90-2.15)	45	10.6 (4, 29.7)	0.87 (0.53-1.44)
> 75	0	18	3.8 (1.5, 7.9)	0.85 (0.48-1.52)	18	6 (3.1, 31.6)	1.09 (0.58-2.02)
Sex							
Male[1]	7.4	91	2.8 (1.6, 5.4)		92	7.1 (3.6, 21.8)	
Female	6.9	30	3.6 (1.3, 7.9)	0.84 (0.53-1.32)	31	14.2 (3.7, 30.3)	0.68 (0.41-1.15)
Race							
Asian[1]	12.0	25	3 (1.5, 5.4)		25	10.6 (5.4, 23.4)	
African-American	7.7	12	4.5 (1.9, 6.7)	0.90 (0.43-1.89)	15	13.7 (1.8, 36.2)	1.03 (0.47-2.27)
Native Hawaiian or other Pacific Islander	0	1	2.8 (2.8, 2.8)	1.37 (0.18-10.3)	1	2.8 (2.8, 2.8)	6.52 (0.82-51.7)
Caucasian	6.4	77	2.6 (1.5, 6.4)	0.89 (0.54-1.47)	82	9.3 (4, 29.7)	1.05 (0.59-1.84)
Child-Pugh Class							
A[1]	9.1	43	3.1 (1.9, 5.4)		47	10.6 (5.2, 24.6)	
B	10.2	50	2.6 (1.5, 5.6)	1.23 (0.79-1.93)	54	6.3 (2.8, 14.2)	1.36 (0.84-2.19)
C	0	11	1.4 (0.7, 2.5)	3.27 (1.57-6.79)[a]	12	3 (1.7, 4.2)	4.49 (1.87-10.8)[a]
BCLC stage							
0	0	1	1 (1, 1)	NA	1	Not reached	NA
A[1]	9.1	10	10.8 (1, 14.8)		12	23.4 (23.4, -)	
B	21.7	23	2.9 (1.5, 9.8)	1.64 (0.68-3.96)	24	9 (3.1, 22.6)	4.67 (1.08-20.1)
C	3.4	85	3 (1.6, 5.3)	1.79 (0.80-3.98)	93	7.1 (3.6, 24.6)	4.35 (1.06-17.8)
D	0	1	2.1 (2.1, 2.1)	NA	1	5.4 (5.4, 5.4)	NA
ECOG							
0[1]	12.5	25	5.1 (3, 10.5)		27	29.1 (6, 30.3)	
1	6.2	94	2.4 (1.4, 5.2)	1.70 (1.03-2.83)[a]	102	6.3 (3.1, 14.2)	2.02 (1.13-3.60)
Hepatitis B							
No[1]	6.5	106	3 (1.5, 6)		116	7.9 (3.6, 29.7)	
Yes	13.3	14	3 (1.9, 7.3)	0.90 (0.48-1.70)	15	9 (5.4, 21.8)	1.31 (0.70-2.42)
Hepatitis C							
No[1]	5.5	54	2.8 (1.5, 5.4)		60	7.9 (5, 21.8)	
Yes	8.8	66	3 (1.5, 7.1)	0.94 (0.63-1.39)	71	9.3 (3.6, 29.1)	0.85 (0.54-1.32)

Alcohol-related liver disease							
No[1]	7.8	102	3 (1.5, 6.4)		110	9 (3.7, 29.1)	
Yes	4.8	18	2.6 (2.1, 4.1)	1.17 (0.68-2.00)	21	7.1 (3.1, 13.4)	1.46 (0.81-2.61)
Nonalcoholic fatty liver disease							
No[1]	7.1	110	3 (1.6, 5.6)		120	7.9 (3.7, 23.4)	
Yes	10.0	10	2.8 (1.4, 10.6)	0.79 (0.38-1.63)	11	10.6 (3.1, 29.7)	0.71 (0.31-1.64)

[1]Reference. The subgroup within a categorical variable (*e.g.* age) that the other subgroup/s (within the same variable) are compared to for calculation of the Hazard Ratios reported.

[a]$P < 0.05$. BCLC: Barcelona Clinic Liver Cancer; CI: Confidence interval; CR: Complete response; ECOG: Eastern Cooperative Oncology Group; HR: Hazard ratio; NA: Not applicable; OS: Overall survival; PFS: Progression-free survival; PR: Partial response; Q1: Quartile 1; Q3: Quartile 3.

Our real-world study has a few limitations. Clinical data were entered directly into the eCRFs by data abstractionists based on medical records available at the time of data entry; therefore, the data are potentially subject to inadvertent entry, keying errors, or missing data. Review of the eCRFs by treating oncologists was enforced to minimize these errors. Frequency of scans in clinical practice might vary between patients and could be less frequent than commonly mandated in clinical trials. While published response criteria were provided as guidance in eCRFs, clinical responses were based on physician assessment and a criterion (if used) was asked to be reported. No safety data were collected. Our study may have also missed ascertainment of care received outside of the study clinics, and the convenience sample of United States-based centers likely limits the generalizability of our findings to other countries. Despite these limitations, our study provides useful information on the use and outcomes of sorafenib in real-world clinical practice in the United States.

CONCLUSION

To our knowledge, no other retrospective study has evaluated real-world outcomes of sorafenib in the United States combining data from an established academic cancer center and a multi-state community health care system. Real-world median PFS and OS of sorafenib in 1L uHCC were < 3 mo and < 9 mo, respectively. Newer therapeutic options that have reported higher PFS and OS in real-world clinical practice should be considered as 1L treatment choices to enhance uHCC patient outcomes.

ARTICLE HIGHLIGHTS

Research background

Sorafenib has been approved for use in unresectable hepatocellular carcinoma (uHCC) patients for more than a decade. As other therapies have been approved in recent years for uHCC treatment in later lines, it is essential to assess clinical effectiveness of older therapies in actual clinical practice to inform healthcare practitioners' decisions for better patient care.

Research motivation

Limited recent data on real-world clinical effectiveness of sorafenib in diverse clinical practice settings in the United States.

Research objectives

To assess clinical effectiveness of sorafenib as first-line (1L) therapy in uHCC patients treated in both academic and community practice settings in the United States.

Research methods

In a retrospective observational study we assessed clinical outcomes including best response, progression-free survival (PFS), and overall survival (OS) among adult uHCC patients (≥ 18 years) in the United States initiating 1L sorafenib monotherapy at City of Hope (academic) and Advent Health (community practice) between January 2016 and December 2019.

Research results

Median time to treatment discontinuation was 2.3 mo. Overall, 103 patients (77%) had disease progression or died during sorafenib therapy. Median PFS was 2.9 mo and median OS was 8.5 mo.

Research conclusions

Median PFS and OS of sorafenib in 1L uHCC were < 3 mo and < 9 mo, respectively.

Research perspectives

Newer therapeutic options that have reported higher PFS and OS in real-world clinical practice should be considered to enhance patient outcomes.

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FOOTNOTES

Author contributions: Li D, Gruber SB, and Tejani M contributed to study design, data collection, data interpretation, and manuscript development; Iyer S and Gupta S contributed to study design, data interpretation, and manuscript development; all authors read and approved the final version.

Institutional review board statement: The study was reviewed and approved by the Ethics Committees of Advent Health Orlando and City of Hope.

Informed consent statement: Informed consent was not required for this study as it was a retrospective analysis and data were de-identified prior to analysis. Waivers for informed consent were provided by each site's Institutional Review Board.

Conflict-of-interest statement: Dr.Li reports personal fees and other from AstraZeneca, other from Brooklyn ImmunoTherapeutics, personal fees from Adagene, personal fees from Coherus, personal fees from Delcath, personal fees from Eisai, personal fees from Exelixis, personal fees from Genentech, personal fees from Ipsen Biopharmaceuticals, personal fees from Merck, personal fees from Servier, personal fees from Sumitomo Pharma, and personal fees from TerSera Therapeutics, outside the submitted work.

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