Healthcare Resource Utilization and Costs in Patients Treated with Tyrosine Kinase Inhibitors as Treatment in Advanced Hepatocellular Carcinoma in the United States

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BACKGROUND

- Worldwide, hepatocellular carcinoma (HCC) is the 5th most common cancer among men (7th among women), and the 6th leading cause of cancer death[1]
- HCC remains an area of significant unmet medical need among patients who have progressed to advanced HCC [2-4]
- Second-line treatment options for advanced HCC includes two oral tyrosine kinase inhibitors (TKIs): regorafenib and cabozantinib [5-6]
- Limited real-world evidence exists on the healthcare resource utilization and costs for patients treated with second-line TKIs, regorafenib and cabozantinib. Additional evidence is needed to further evaluate the use the two therapies in advanced HCC
- The associated cost and burden of care is an increasingly important component of healthcare decision-making for both patients and payers

OBJECTIVES

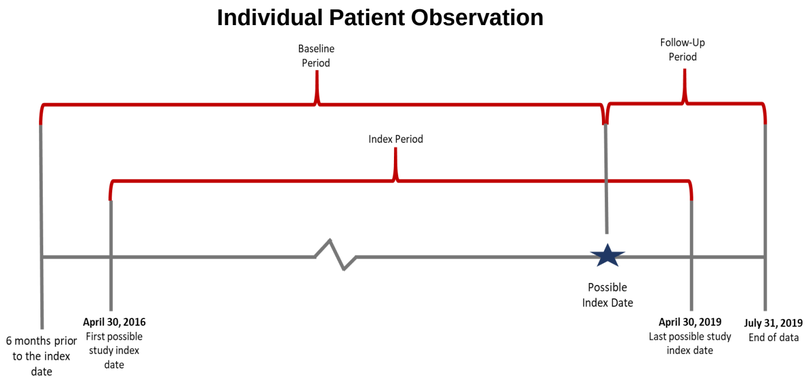
The primary objective of this observational study was to estimate the real-world health care costs and resource utilization associated with the use of tyrosine kinase inhibitors, regorafenib and cabozantinib for the treatment of advanced HCC. More specifically, this study aimed to achieve the following:

- To describe baseline clinical and demographic patient characteristics, including prevalence of clinically relevant comorbidities
- To describe the all-cause healthcare resource utilization and associated costs including number of inpatient admissions and length of stay, emergency room visits and outpatient visits and costs from the start to end of regorafenib or cabozantinib use
- To evaluate all-cause pharmacy costs (total, out-of-pocket and third-party payer) while persistent on regorafenib or cabozantinib use
- To describe treatment-related payer costs from the start to end of regorafenib or cabozantinib use
- To describe patient out-of-pocket costs from the start to end of regorafenib and cabozantinib use

METHODS

- A descriptive, retrospective observational study of patients who received regorafenib or cabozantinib for the treatment of HCC in the U.S. between April 30, 2016 and July 31, 2019
- Patients were identified from an administrative claims database, IBM MarketScan, representing Medicare and commercially insured patients from health systems and employers throughout the U.S.

Figure 1. Study Design



- **Baseline Period**: 6 months of continuous enrollment with no adjudicated prescription claim for regorafenib or cabozantinib prior to index date
- **Index Date:** Date of the first adjudicated prescription claim for regorafenib or cabozantinib
- **Index Period:** April 30, 2016 to April 30, 2019
- **Follow-up Period:** Index date until end of continuous enrollment
- **TKI Persistence Period:** Index date through the earliest of end of continuous enrollment, data cutoff or a gap of greater than 60 days
- **Medication Possession Ratio (MPR)** =

$$\frac{\text{Total days' supply of filled TKI}}{\text{Total numer of days from the first to last TKI dispense plus last days' supply}}$$

- Patients with an MPR ≥ 0.8 were considered adherent. Those with an MPR < 0.8 were considered non-adherent to therapy. Adherence was measured during the follow-up period

Statistical Analysis

- This retrospective analysis was primarily descriptive in nature. Descriptive statistics were generated for all study variables, demographics and measures of adherence.
- Healthcare resource use were summarized by medical service types during the period patients were persistent on regorafenib or cabozantinib
- Costs were summarized overall and per patient per month (PPPM) to account for variability in length of follow-up. PPPM costs were calculated for each medical service type. The consumer price index (CPI) medical care component was used to adjust costs for inflation over time and adjusted to the US dollar values in 2019

RESULTS

Table 1. Patient Attrition

Inclusion/Exclusion Criteria	Number Excluded	Number Remaining
Starting Population: ≥ 1 ICD-10 diagnostic code for HCC	N/A	22,893
Included: ≥ 1 adjudicated prescription claim for regorafenib or cabozantinib during the index period	22,577	316
Included: ≥ 1 ICD-10 diagnostic code for HCC during the six-month baseline period or on the index date	113	203
Included: Continuous enrollment during baseline period through three months post index date	69	134
Included: Age ≥ 18 years	0	134
Excluded: Presence of one or more ICD-10 diagnostic codes for gastrointestinal stromal tumor or metastatic colorectal cancer when regorafenib was identified as the index drug	7	127
Excluded: Presence of one or more ICD-10 diagnostic codes for renal cell carcinoma when cabozantinib was identified as the index drug	14	113
Excluded: Adjudicated prescription claim for regorafenib or cabozantinib present during the baseline period	4	109
Excluded: Liver Resection or Transplant or Radio Frequency Ablation present during the follow-up period	0	109
Final Study Population		**109**
Number of patients that received regorafenib on index date		96 (88.8)
Number of patients that received cabozantinib on index date		13 (11.9)

Table 2. Demographic and Baseline[a] Clinical Characteristics

	All Patients (N=109)
Age	
Mean (SD [b])	61.8 (10.59)
Median (IQR [c])	61.0 (56.0-68.0)
Gender (N, %)	
Male	77 (70.6)
Female	32 (29.4)
Geographic Region (N, %)	
South	43 (50.6)
Midwest	17 (20.0)
Northeast	15 (17.7)
West	4 (4.7)
Employment Status on Index Date (N, %)	
Active Full Time	37 (33.9)
Active Part Time or Seasonal	1 (0.9)
COBRA[d] Continuee	1 (0.9)
Early Retiree	9 (8.3)
Long Term Disability	3 (2.8)
Medicare Eligible Retiree	29 (26.6)
Other/Unknown	23 (21.1)
Retiree (status unknown)	1 (0.9)
Surviving Spouse/Dependent	5 (4.6)
Charlson Comorbidity Index Score	
Mean (SD [b])	2.75 (1.8)
Median (IQR [c])	2 (2-4)
Secondary Metastasis HCC [g] (N, %)	40 (36.7)
Etiology of Liver Disease (N,%)	
Hepatitis B Infection	3 (2.8)
Hepatitis C Infection	24 (22.0)
Unspecific Hepatitis Infection	1 (0.9)
Alcoholic Liver Disease	3 (2.8)
Non-Alcoholic Liver Disease	11 (10.1)
Unknown	67 (61.5)
Procedures (N,%)	
Receipt of Concomitant Anticancer Drug Therapy	40 (36.7)
Receipt of TACE [e] or TAE [f] During Baseline Period	15 (13.8)
Receipt of TACE [e] or TAE [f] During the Follow-up Period	5 (4.6)
Unknown	49 (44.9)

[a] Baseline = determined in the 6 months prior to and leading up to index date; [b] SD = standard deviation; [c] IQR= interquartile range; [d] COBRA= consolidated omnibus budget reconciliation act; [e] TACE= Transarterial chemoembolization; [f] TAE= Transarterial embolization; [g] HCC= Hepatocellular carcinoma

Table 3. Measures of Persistence[a]

	All Patients (N=109)
TKI [d] Persistent (n, %)	34 (31.2)
TKI [d] Length of Persistency (day)	
Mean (SD [b])	154.3 (80.0)
Median (IQR [c])	133.5 (94.5-200.5)
TKI [d] Length of Persistency (month)	
Mean (SD [b])	5.1 (2.6)
Median (IQR [c])	4.4 (3.1- 6.6)

[a] Persistence= the time period starting on index date until earliest of TKI discontinuation, end of continuous enrollment, or data cutoff date; [b] SD = standard deviation; [c] IQR= interquartile range; [d] TKI= tyrosine kinase inhibitor (regorafenib or cabozantinib)

References

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Table 4. Healthcare Resource Utilization

Medical Service	Costs (N= 34)	
	n/Mean	*%*/SD
Inpatient Services		
Hospitalization Length of Stay (day; mean, SD [b]))	7.89	8.80
Patients with at Least One Inpatient Admission (n, %)	9	26.47%
Number of Inpatient Admissions PPPM (mean, SD [b])	0.38	0.74
Outpatient Services		
Patients with at Least One Outpatient Admission (n,%)	30	88.24%
Number of Outpatient Admissions PPPM [a] (mean, SD [b])	11.35	11.07
Emergency Department Services		
Patients with any Emergency Department Visits (n,%)	8	23.53%
Number of Emergency Department Visits PPPM (mean, SD [b])	0.35	0.81

[a] PPPM = determined while persistent on regorafenib or cabozantinib; [b] SD = standard deviation; [c] IQR= interquartile range

Table 5. Total Costs

Medical Service	Costs (N= 34)			
	Mean	SD (±)	Median	IQR
All Cause Costs				
All Cause Total Costs	$17,781	$6,332	$16,106	$15,167- 19,792
All Cause Payer Costs	$15,406	$8,011	$15,696	$11,114- 18,726
All Cause Out of Pocket Costs	$235	$517	$112	$49- 183
Inpatient Costs				
Inpatient Total All Cause Medical Costs	$2,466	$5,301	$0	$0- $725
Inpatient Payer Medical Costs	$2,409	$5,216	$0	$0- $165
Inpatient Out of Pocket Medical Costs	$36	$155	$0	$0- $75
Outpatient Costs				
Outpatient Total All Cause Medical Costs	$589	$705	$360	$85- $837
Outpatient Payer Medical Costs	$376	$550	$183	$26- $595
Outpatient Out of Pocket Medical Costs	$85	$257	$15	$0- $65
Total Pharmacy Costs				
Total Costs	$14,725	$3,256	$15,091	$12,426- $16,475
Payer Costs	$12,620	$5,177	$14,674	$10,352- $15,755
Patient Out of Pocket Costs	$114	$268	$59	$9- $102
TKI [a] Pharmacy Costs				
Total Costs	$13,914	$3,742	$14,673	$11,152- $16,381
Payer Costs	$12,047	$5,110	$13,489	$9,500- $15,719
Patient Out of Pocket Costs	$84	$271	$15.68	$0- $47

[a] TKI= tyrosine kinase inhibitor (regorafenib or cabozantinib)

Figure 1. Total All Cause Costs

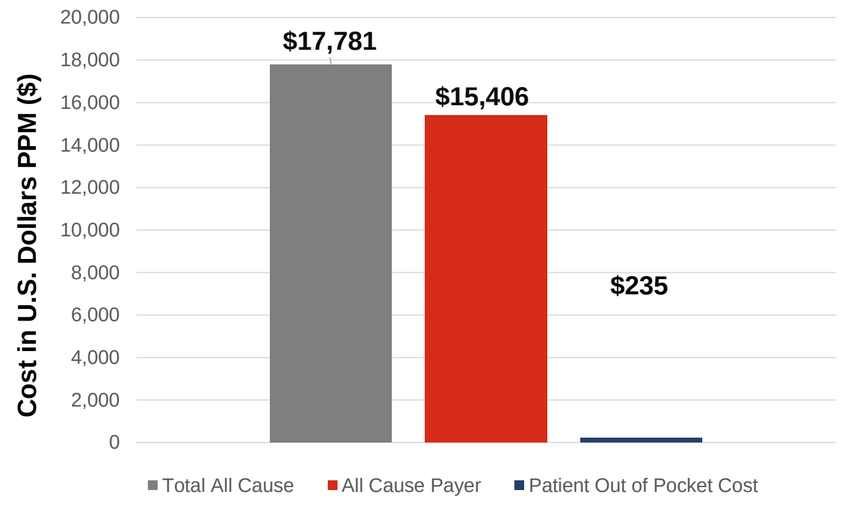
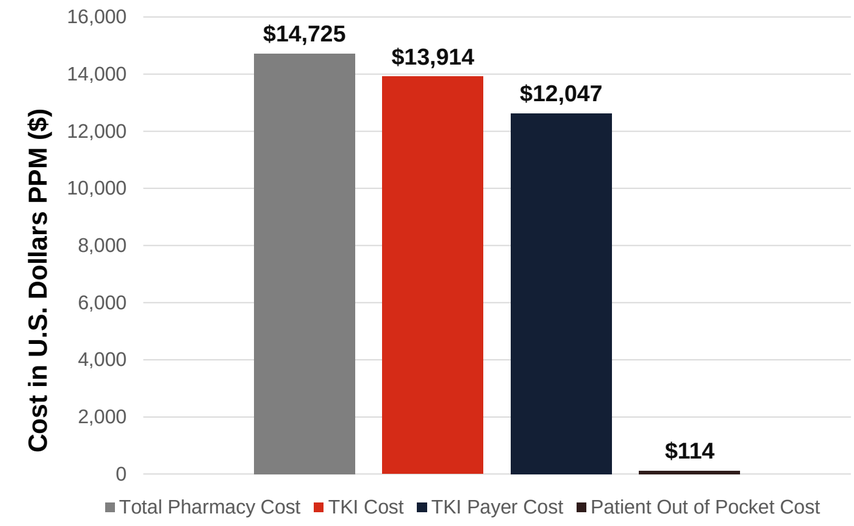


Figure 2. Pharmacy Costs



CONCLUSIONS

- Our findings show that the median all-cause cost to payers was $17,781, per patient per month (Figure 1). The principle driver of the total costs was the TKI pharmacy costs with payer costs at $13,914 per patient per month, (Figure 2) accounting for 78% of the total all-cause cost
- These real-world claims analysis demonstrates the substantial healthcare resource use and costs, driven primarily by the use of regorafenib or cabozantinib (pharmacy cost) in advanced HCC patients. These findings can inform future cost-effectiveness analysis, resource allocation and health care budgeting