

Price Analysis of Cancer Therapies for the Treatment of Patients with Unresectable Hepatocellular Carcinoma

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Conflict of Interest Statement

- This study was completed with the support of Boston Scientific.
- Abimbola Williams, Nicholas Anderson, Young-Gwan Gwon, and Wendy Wifler are full-time employees of Boston Scientific.



Background

- Primary liver cancer is the 6th most frequently diagnosed cancer and was the 3rd leading cause of cancer death globally in 2020.¹
 - Primary liver cancer is the 6th leading cause of cancer death and represents 2.2% of all cancer cases in the United States.²
- Hepatocellular Carcinoma (HCC) is the most common type of liver cancer.³⁻⁵
 - HCC accounts for 75-90% of primary liver cancers.³⁻⁵
- The economic burden of HCC is substantial.⁶
 - The median cost was \$176,456, (interquartile range [\$84,489-\$292,192]) per patient regardless of HCC stage or treatment.⁶



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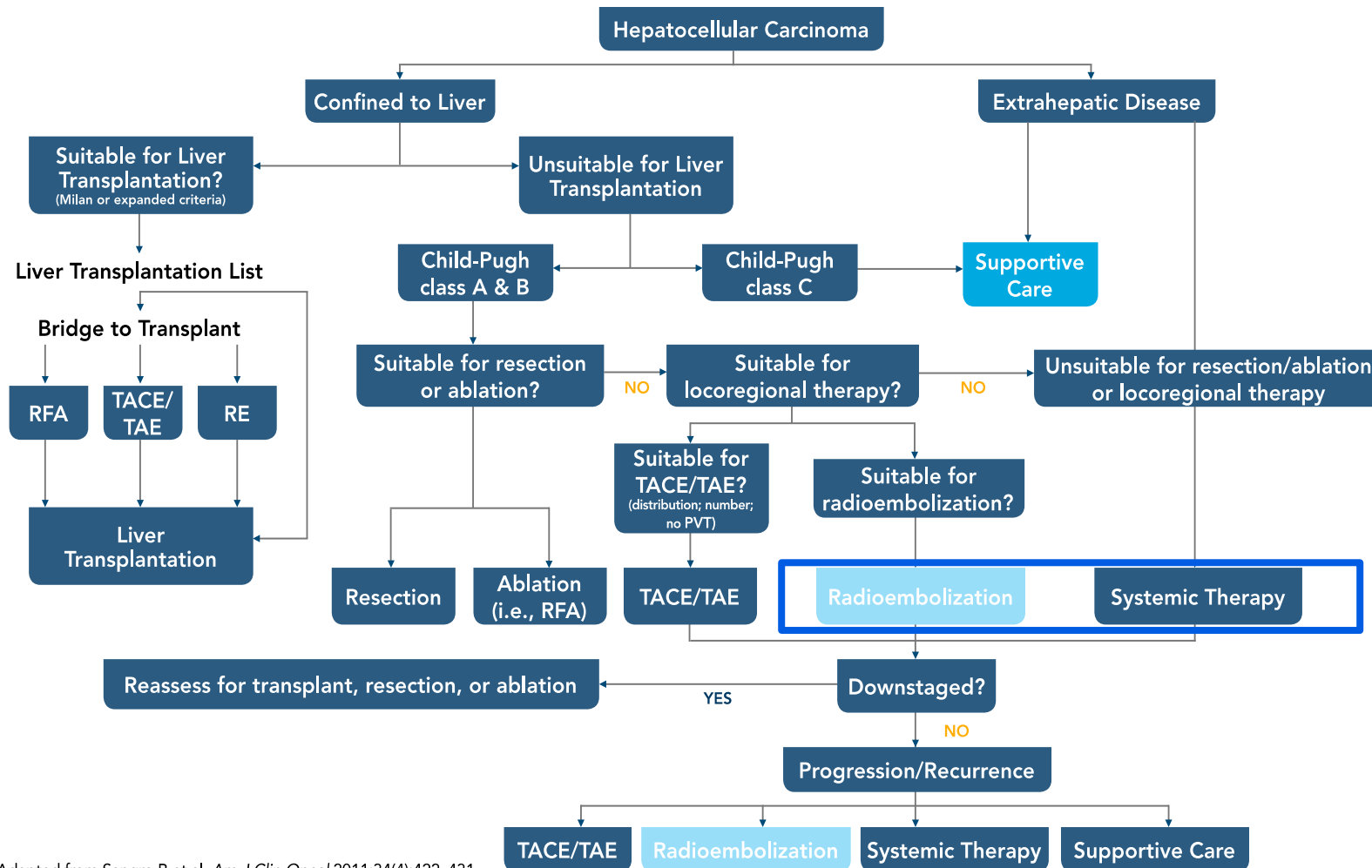
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TARE and the HCC Treatment Paradigm



- Patients with HCC receive a variety of treatment options, reflecting the heterogeneity of disease.¹
- HCC management is complex, with numerous treatment options at each stage of the disease.
- The price of cancer therapy for the treatment of adult US patients with HCC remains unknown.

Adapted from Sanaro B et al. *Am J Clin Oncol* 2011;34(4):422-431.

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Study Objectives & Methods

Objective: To estimate the price of systemic therapies (ST) compared to selective internal radiotherapy (SIRT) for the treatment of HCC from the payer and provider perspectives.

- The National Comprehensive Cancer Network Guideline for hepatobiliary cancers¹ was used as a framework to model the treatment strategies for adult HCC patients.
- An excel-based price analysis model was developed from a US payer (Medicare) and provider perspective.
- The prices of ST and SIRT were estimated over the treatment duration.

Methods

Data Source

- Drug regulatory information from US FDA
- Defined Daily Dosages (DDD) from NIH/NLM
- Costs (Medicare ASP/ASC/OPPS, Redbook AWP, Redbook WAC) and clinical parameters (treatment duration) from published literature

National Comprehensive Cancer Network (NCCN) Guideline for Hepatobiliary Cancers⁷: Principles of Systemic Therapy

- First-line systemic therapy
- Subsequent-line therapy if disease progresses

NCCN Guideline for Hepatobiliary Cancers⁷: Principles of Locoregional therapy

- Trans-arterial radio-embolization (TARE) (i.e., Selective Internal Radioembolization Therapy (SIRT))

Data Analysis

- Min-max price
- Summary statistics (median, mean, standard deviation)

ASP=Average Selling Price
FDA=Food and Drug Administration
NCCN= National Comprehensive Cancer Network

ASC=Ambulatory Surgical Care
NIH=National Institute of Health

AWP=Average Wholesale Price
NLM=National Library of Medicine
OPPS=Outpatient Prospective Payment System

DDD=Defined Daily Dosages
SIRT=Selective Internal Radiation Therapies



Methods - NCCN Guidelines Version 2.2021¹

A. Principles of Systemic Therapy^{HCC-G}

First-Line Systemic Therapy

Preferred Regimens

- Atezolizumab + Bevacizumab

Other Recommended Regimens

- Sorafenib
- Lenvatinib

Useful in Certain Circumstances

Subsequent-Line Therapy if Disease Progresses

Options

- Regorafenib
- Cabozantinib
- Ramucirumab
- Lenvatinib
- Sorafenib

Other Recommended Regimens

- Nivolumab
- Nivolumab + Ipilimumab
- Pembrolizumab

B. Principles of Locoregional Therapy^{HCC-6}

Clinical Presentation:

Liver-confined disease, inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease

Options:

Locoregional therapy preferred

- Ablation
- Arterially directed therapies
- External beam radiation therapy (EBRT)
- Clinical trial
- Systemic therapy
- Best supportive care

Progression on or after systemic therapy



Methods - Clinical Inputs

- Clinical parameters were derived from:
 - Treatment options guided by the NCCN guidelines version 2. 2021.¹
 - FDA-recommended defined daily dose (DDD) from FDA-approved labels - Orange Book² and Purple Book.³
 - For systemic therapy, the treatment duration was pulled from randomized controlled trials.⁴⁻¹²
 - For SIRT, the mean number of devices used per procedure was used as a proxy for treatment duration
- The total price/DDD was calculated for each treatment therapy and treatment duration over a short-term (<12 months) time horizon.

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Methods - Clinical Inputs (contd.)

Treatment Option	Treatment Duration
	Months
Systemic Therapy	
Atezolizumab ¹	7.4
Bevacizumab ¹	6.9
Sorafenib ²	3.7
Lenvatinib ²	5.7
Nivolumab ³	5.1
Cabozantinib ⁴	3.8
Regorafenib ⁵	3.6
Ramucirumab ⁶	3.0
FOLFOX ⁷	4.5
Ipilimumab ³	4.6
Pembrolizumab ⁸	3.2
SIRT	Mean number of procedures
TheraSphere ^{9,a}	1.28
SIR-Spheres ^{9,b}	1.28
QuiremSpheres ^{9,c}	1.28

^aTheraSphere is FDA approved SIRT and indicated for the treatment of unresectable HCC in the United States

^bSIR-Spheres is indicated for the treatment of unresectable metastatic liver tumors and available in the United States

^cQuiremSpheres is indicated for the treatment of unresectable liver tumors and not available in the United States

1. Chiang, C. L., Chan, S. K., Lee, S. F., & Choi, H. C. W. (2021). First-Line Atezolizumab Plus Bevacizumab versus Sorafenib in Hepatocellular Carcinoma: A Cost-Effectiveness Analysis. *Cancers* 2021, 13, 931.
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Methods - Cost Inputs

- Associated prices of 11 STs and 3 SIRTs were derived from:
 - The IBM Micromedex Redbook average wholesale price (AWP) and wholesale acquisition cost (WAC).
 - Medicare's allowable rates from approval date, which includes the average sale price (ASP) from Medicare payment limit (as of May 2021).
 - Clarivate's Decision Resources Group (DRG) 2021 Report ASP.
- One-way sensitivity analysis (OWSA) was conducted to explore the impact of treatment duration uncertainty on the model results.
 - Treatment duration was varied by $\pm 10\%$.

Treatment Option	Cost Parameters (in USD)		
	Medicare ASP ¹	Redbook WAC ²	Redbook AWP ²
Systemic Therapy			
Atezolizumab	\$78	\$9,470	\$11,364
Bevacizumab	\$73	\$797	\$956
Sorafenib	\$174	\$20,760	\$24,912
Lenvatinib	\$17,099	\$19,687	\$23,624
Nivolumab	\$28	\$6,679	\$8,015
Cabozantinib	\$17,218	\$21,663	\$25,995
Regorafenib	\$17,234	\$18,747	\$22,495
Ramucirumab	\$5,699	\$6,158	\$7,390
FOLFOX	\$5	\$296	\$1,058
Ipilimumab	\$7,359	\$7,614	\$9,137
Pembrolizumab	\$51	\$5,034	\$6,040
SIRT	Medicare OPPS ³	Medicare ASC ⁴	DRG ASP ⁵
TheraSphere ^a	\$17,092	\$17,092	\$17,088
SIR-Spheres ^b	\$17,398	\$17,398	\$16,653
QuiremSpheres ^c	\$17,092	\$17,092	\$17,088

^a TheraSphere is FDA approved SIRT and indicated for the treatment of unresectable HCC in the United States

^b SIR-Spheres is indicated for the treatment of unresectable metastatic liver tumors and available in the United States

^c QuiremSpheres is indicated for the treatment of unresectable liver tumors and not available in the United States

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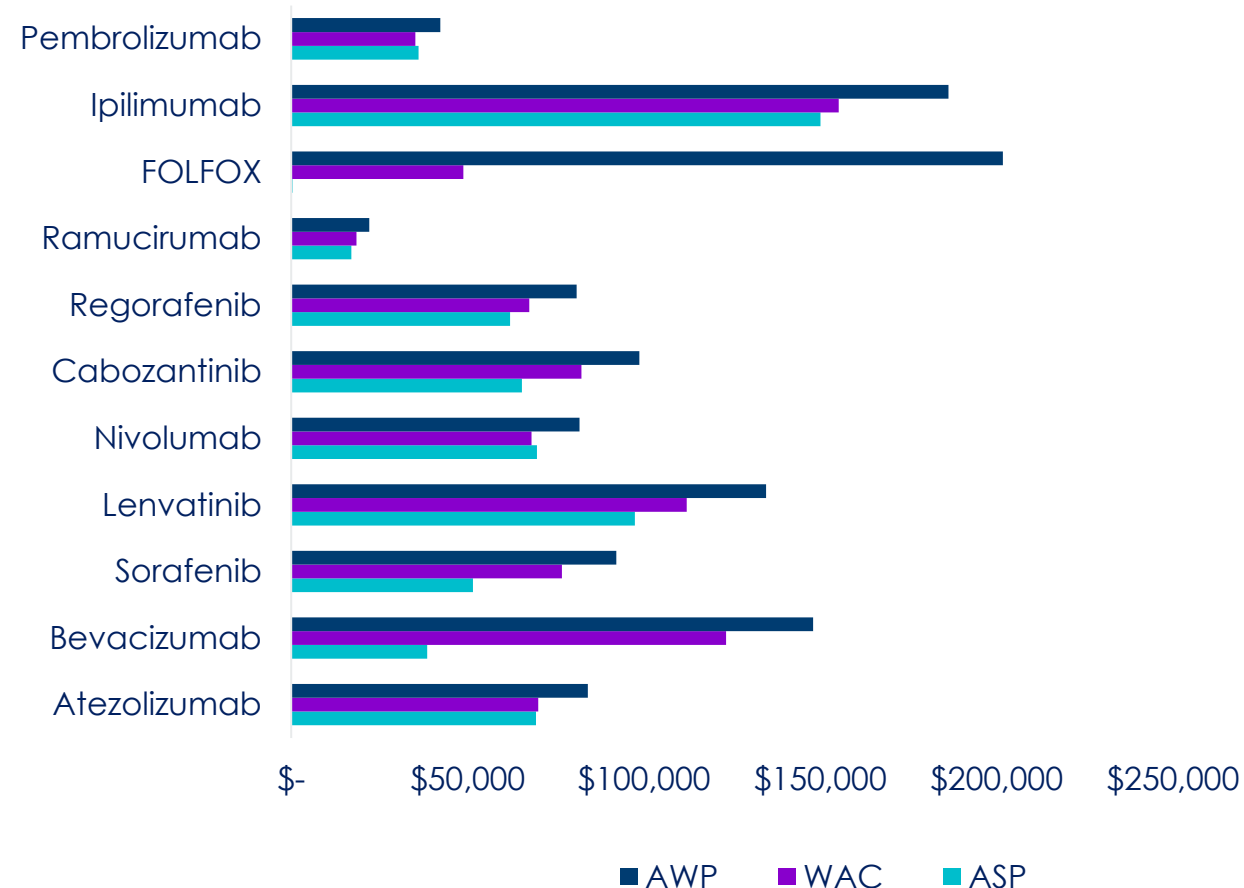
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Results - Base Case

- The median price/DDD of ST varied by perspective:
 - Provider AWP: \$92,174 (IQR: \$22,170-\$201,816).
 - Provider WAC: \$70,077 (IQR: \$18,475-\$155,324).
 - Medicare ASP: \$62,044 (IQR: \$341-\$150,127).

Base Case Price Per Daily Drug Dosage of Systemic Therapy

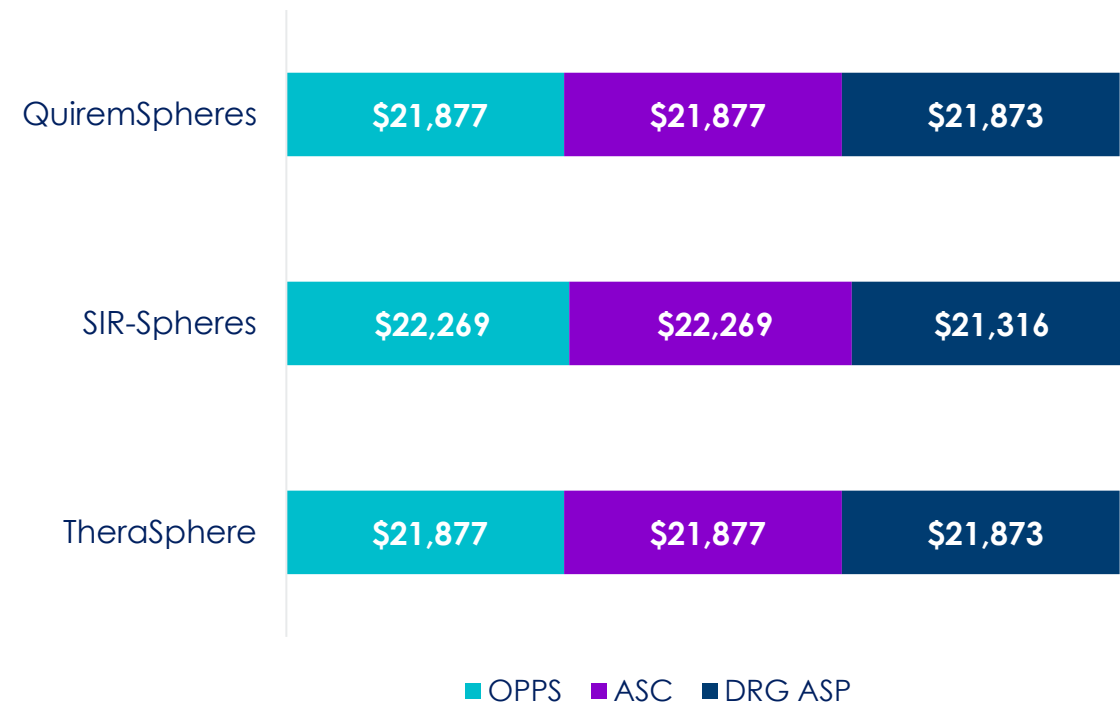




Results - Base Case

- The median price of SIRT was:
 - Medicare OPPS: \$21,877 (IQR: \$21,877-\$22,269).
 - Medicare ASC: \$21,877 (IQR: \$21,877-\$22,269).
 - DRG ASP: \$21,873 (IQR: \$21,316 –\$21,873).

**Base Case Price Per the Mean Number of Treatments
Per Procedures of SIRT**



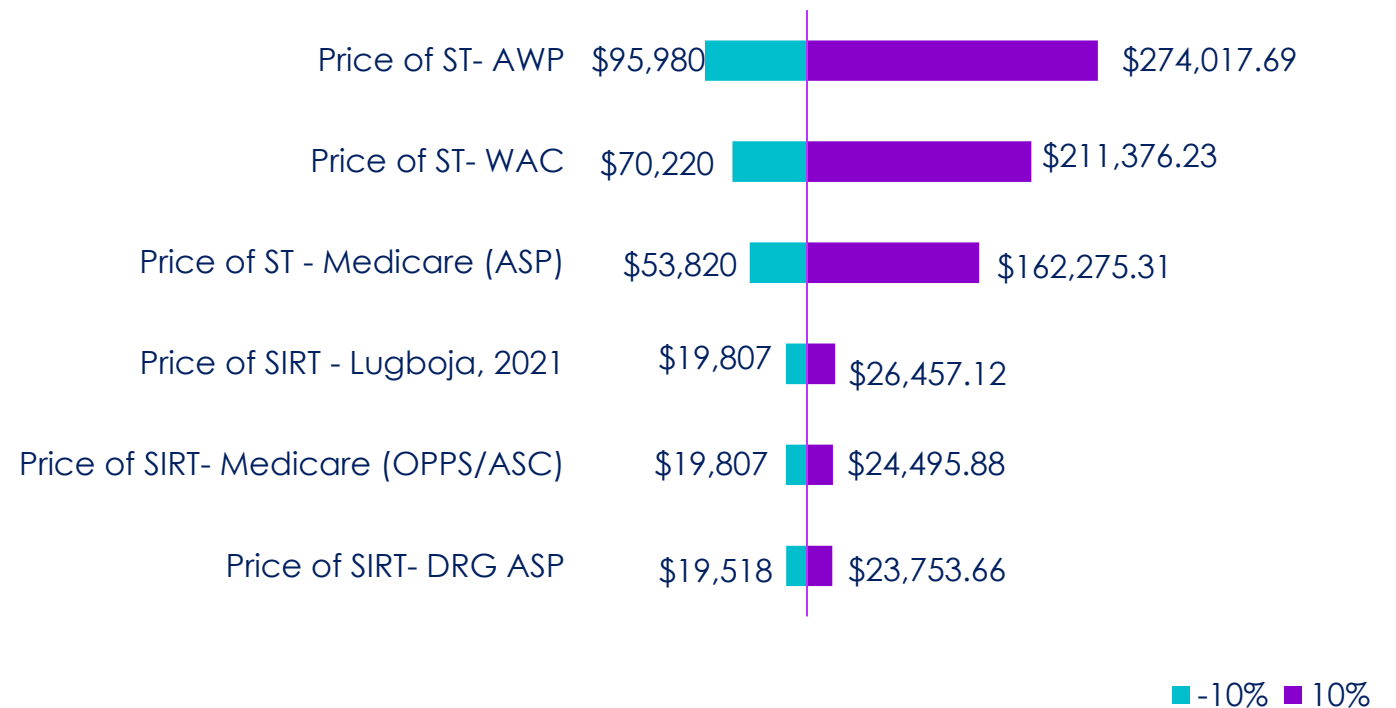
^a TheraSphere is FDA approved SIRT and indicated for the treatment of unresectable HCC in the United States
^b SIR-Spheres is indicated for the treatment of unresectable metastatic liver tumors and available in the United States
^c QuiremSpheres is indicated for the treatment of unresectable liver tumors and not available in the United States



Results - Tornado Diagram

- When compared to ST, SIRT remained cost saving when the treatment duration (ST) or the mean number of devices used per procedure (SIRT) was varied by $\pm 10\%$.
 - Price of SIRT remained lower when compared to ST.

Tornado Diagram: Impactful Parameters on Model Results





Strengths

- First study to undertake a price analysis of treatment options for HCC from two perspectives, payer and provider.
- Study models the treatment options for HCC using the NCCN guidelines.
 - Study generates comparable price estimates between ST and SIRT in the treatment options for HCC.
- Price estimates can serve as inputs for developing and prioritizing interventions to reduce the economic burden of HCC.



Study Limitations

- These price estimates did not account for drug rebates or patient assistance programs negotiated directly with manufacturers by benefit management entities.
- There is potential variability in the price of ST due to site of service where prescription is filled or plan coverage.
- Quantification of the total cost of care for ST and SIRT are not included in this analysis.
 - Indirect (e.g., societal cost) or direct costs (e.g., personnel, equipment, mapping for SIRT, and other consumables) were not estimated.
- All SIRTs were included in this model. However, not all are indicated/available within the United States for the treatment of HCC.
 - SIR-Spheres is indicated for the treatment of unresectable metastatic liver tumors and available in the United States.
 - QuiremSpheres is indicated for the treatment of unresectable liver tumors and not available in the United States.



Conclusion

- The price of cancer therapy for HCC varies widely by therapy and perspective (payer vs. provider).
 - This research provides real-world evidence on the comparative costs of HCC treatments utilized in prevailing NCCN guidelines.
 - The price differences of ST are greater than those of SIRT when considering patients who progress through first-line and second-line ST.
 - Findings provide compelling evidence for clinicians and payers on potential cost savings in the treatment of HCC.
- The availability of alternative cancer therapies, such as locoregional (non-surgical) approaches, may offer a clinically meaningful benefit and reduce the total costs of HCC care from the payer and provider perspective.
 - While all locoregional therapies were included in the study, TheraSphere is the only FDA approved SIRT for the treatment of unresectable HCC in the United States.
- Economic evaluations on the cost-effectiveness of ST vs. SIRT (alone or in combination) for the treatment of HCC are needed.

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