Real-world second-line treatment pattern and disease burden of patients with unresectable or advanced hepatic carcinoma in China: A retrospective database study

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BACKGROUND & OBJECTIVES

- In China, the incidence of hepatic carcinoma (HC) is as high as 27.6 per 100,000 population, ranking fifth among the countries with the highest incidence of primary liver cancer.
- Treatment options for HC are stage-dependent, with systemic therapy being recommended as the first-line (1L) and second-line (2L) treatment of advanced HC patients who derive limited benefit from regional therapy.
- Starting from the end of 2017, the approval of various novel drugs for systemic treatment by the National Medical Products Administration (NMPA) and the further inclusion of these drugs into the National Reimbursement Drug List (NRDL) dramatically changed the treatment landscape for unresectable or advanced HC in China, especially for 2L treatment.
- Given the recent change in the novel HC-related drugs and their inclusion into the NRDL, it is paramount to evaluate clinical practice among Chinese unresectable or advanced HC 2L patients in the real-world setting after 2018.
- This study aims to describe the real-world 2L treatment patterns and disease burden of patients with unresectable or advanced HC in China.

METHODS

- **Study design**: Retrospective cohort study (**Figure 1**)
- **Study population**: Adult patients with unresectable or advanced HC and 2L treatment against HC. Definition of line of therapy (LoT) change is shown in **Figure 2**
- **Data source**: Tianjin Healthcare and Medical Big Data Platform, a regional electronic health record (EHR) database covering about 15 million residents in Tianjin, China

Figure 1: Study design diagram

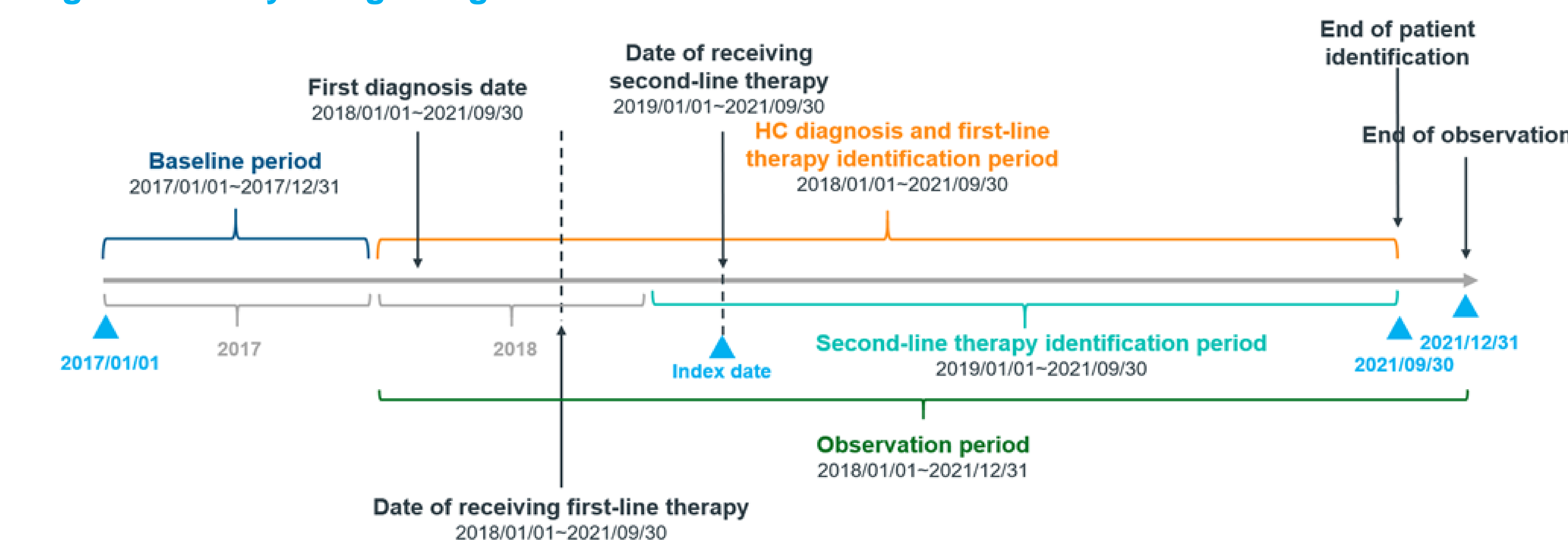
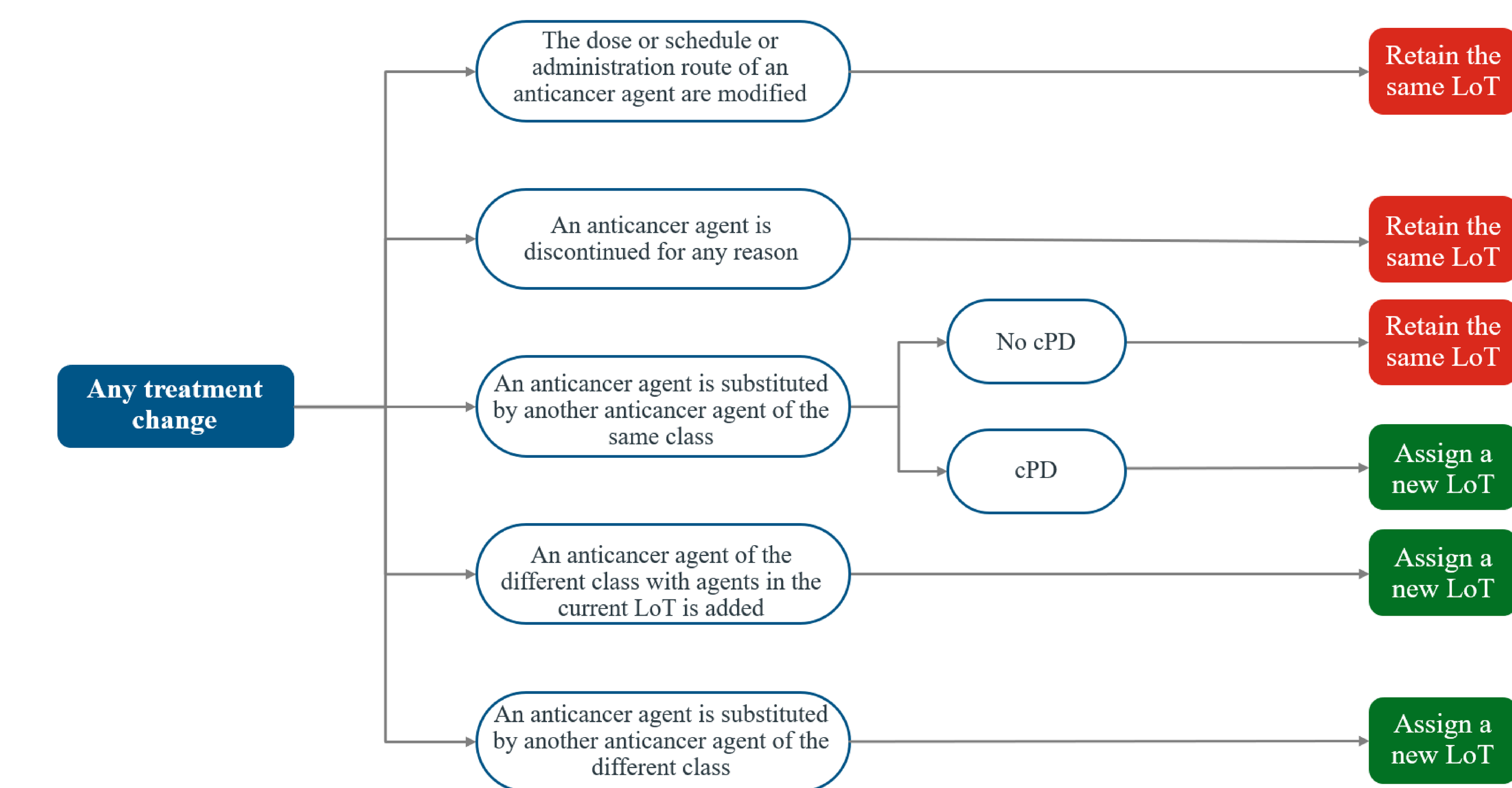


Figure 2. Definition of LoT change



RESULTS

- A total of **123 patients** were eligible for study inclusion (**Figure 3**). The patient characteristics, etiology, and extrahepatic metastasis of these patients are shown in **Table 1**.

Figure 3. Patient flow diagram

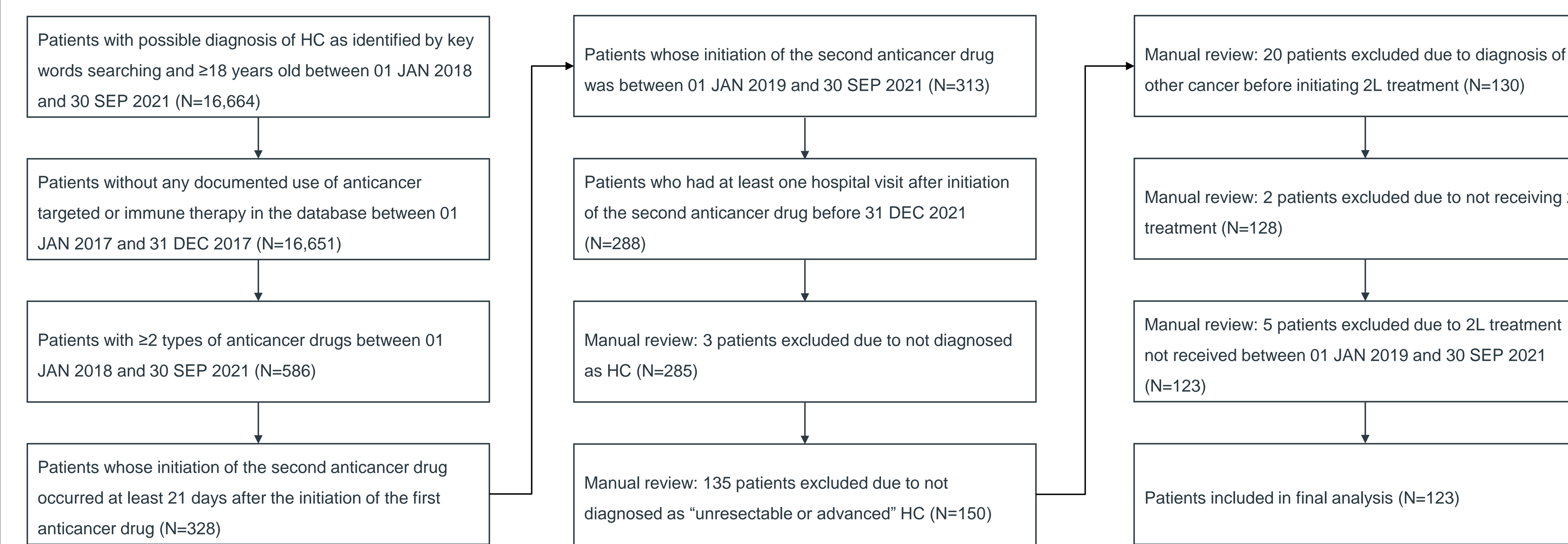


Table 1. Demographic and clinical characteristics

Variable	Overall (N=123)
Age, Mean (SD) (N=123)	61.5 (8.9)
Sex, Male (N=123)	102 (82.9%)
Medical insurance type (N=122)	
UEBMI[1]	54 (44.3%)
URBMI[1]	10 (8.2%)
Unspecified basic medical insurance	30 (24.6%)
Self-paid	23 (18.9%)
Off-site basic medical insurance	5 (4.1%)
Hepatic carcinoma etiology (N=101)	
Hepatitis B	80 (79.2%)
Hepatitis C	7 (6.9%)
Non-alcoholic fatty liver disease	2 (2.0%)
Others	12 (11.9%)
Extrahepatic metastasis site (N=37)	
Lung	17 (45.9%)
Regional lymph nodes	13 (35.1%)
Bone	12 (32.4%)
Adrenal glands	1 (2.7%)
Other or unspecific sites	5 (13.5%)
1L treatment patterns (N=123)	
Chemotherapy alone	6 (4.9%)
Targeted therapy alone	115 (93.5%)
Sorafenib	91 (74.0%)
Others	24 (26.0%)
Targeted therapy plus immune therapy	2 (1.6%)

1. UEBMI: Urban Employee Basic Medical Insurance; URBMI: Urban Residents Basic Medical Insurance; 2. 01 Mar 2021 is the start date of the implementation of NRDL 2020

Treatment pattern:

- **Targeted therapy** (n=93, 75.6%) was the most commonly used 2L treatment category. **Regorafenib** (n=71, 57.7%) was the most commonly used 2L treatment type (**Table 2**).
- The percentage of patients using **2L treatment consistent with the recommendation of** 2020 Chinese Society of Clinical Oncology (CSCO) **guidelines** changed from 87.2% to 59.2%.
- Regarding **treatment flow**, before receiving 2L treatment, most patients used sorafenib as 1L treatment, and among patients receiving regorafenib as 2L treatment, sorafenib was the most commonly used first-line treatment **(Figure 4)**.
- The mean 2L **treatment duration** increased from 2.0 to 2.9 months after NRDL 2020 version implementation.

Figure 4. Treatment flow between 1L and 2L HC treatment

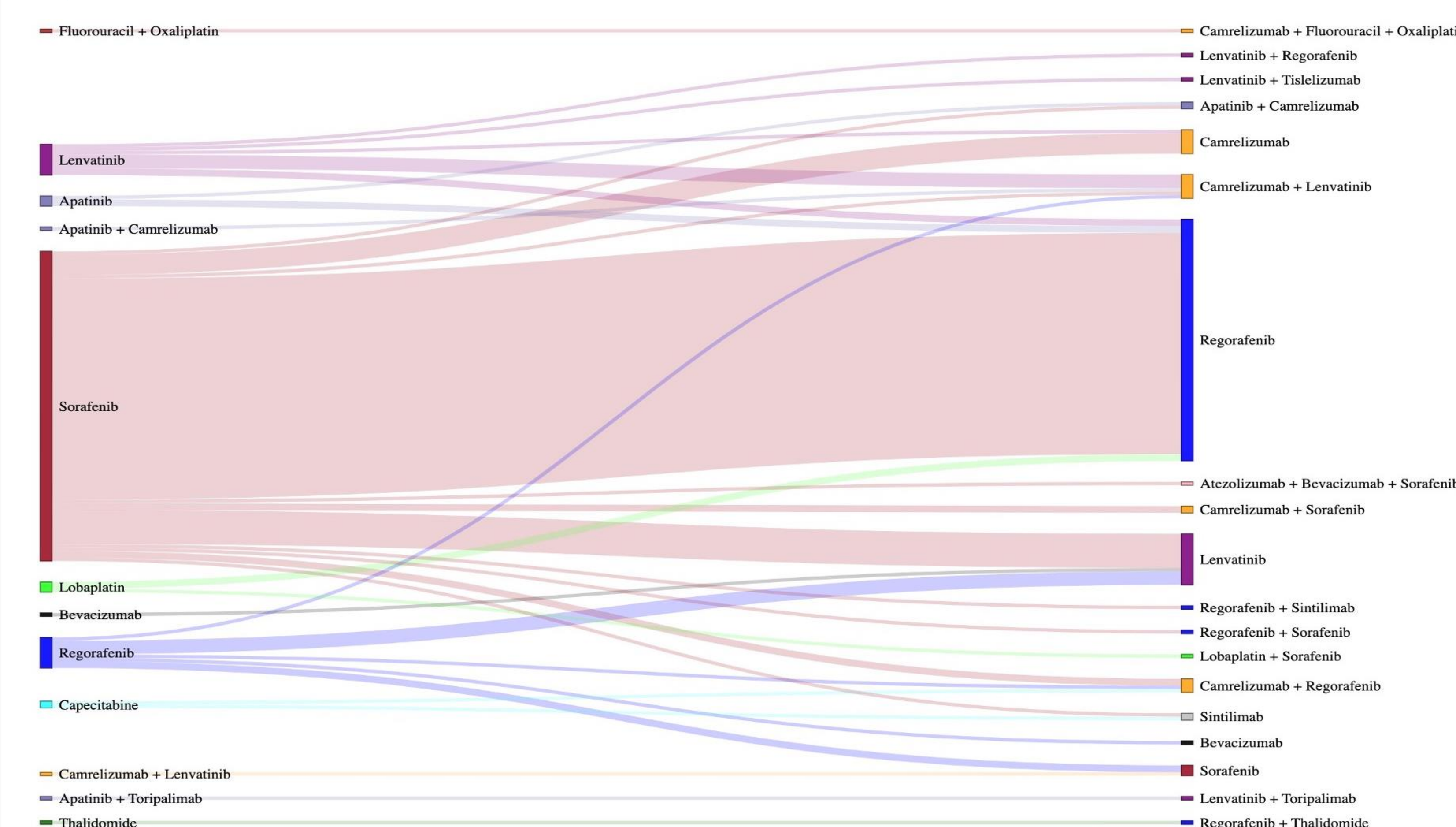


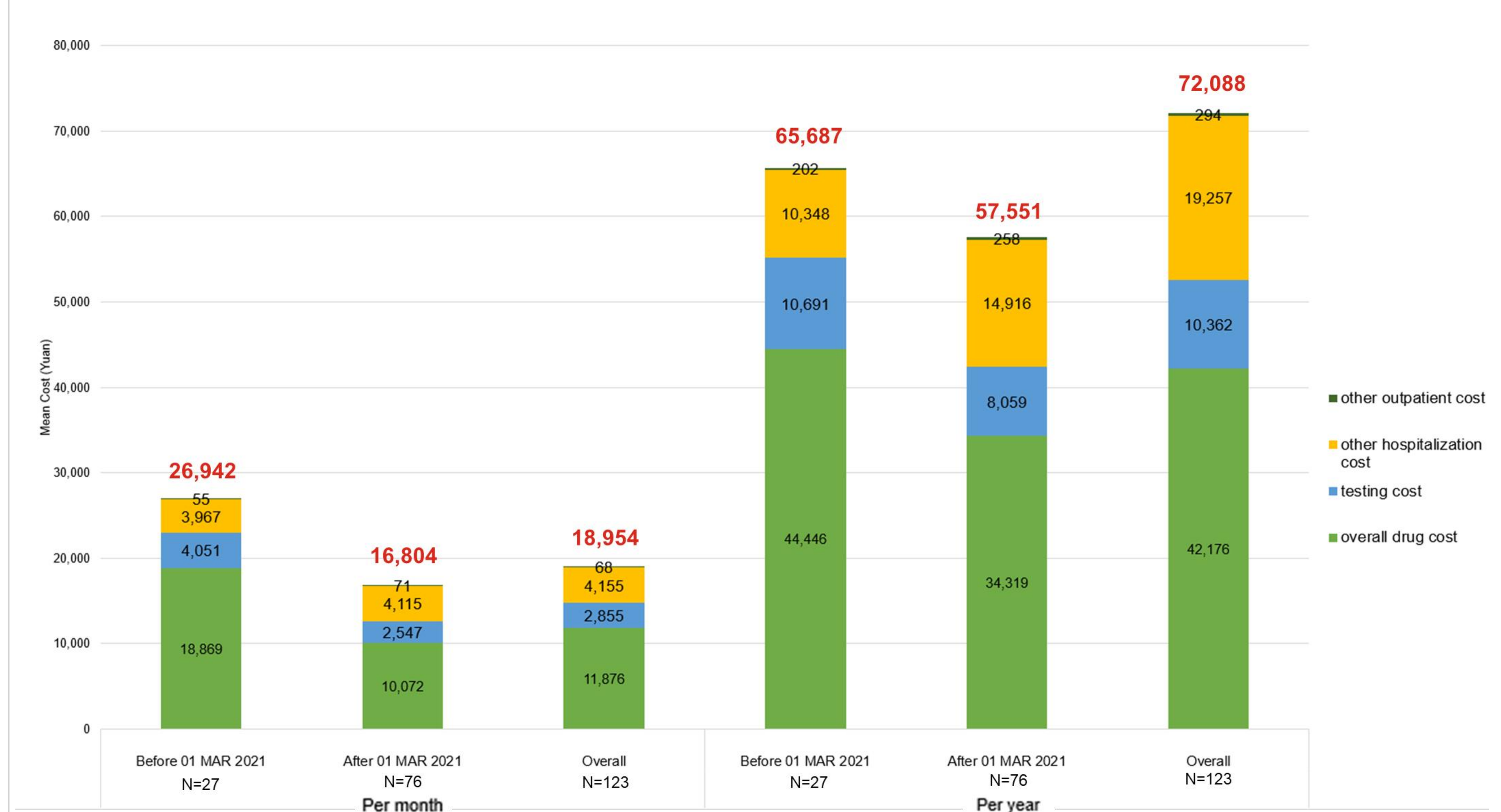
Table 2. HC 2L treatment patterns by category and type

Variable	Overall (N=123)	Before 01 MAR 2021[2] (N=47)	After 01 MAR 2021[2] (N=76)
Category of 2L treatment			
Targeted therapy alone	93 (75.6%)	40 (85.1%)	53 (69.7%)
Targeted therapy plus immune therapy	19 (15.4%)	5 (10.6%)	14 (18.4%)
Immune therapy alone	9 (7.3%)	2 (4.3%)	7 (9.2%)
Chemotherapy plus immune or targeted therapy	2 (1.6%)	-	2 (2.6%)
Type of 2L treatment			
Regorafenib	71 (57.7%)	37 (78.7%)	34 (44.7%)
Lenvatinib	15 (12.2%)	1 (2.1%)	14 (18.4%)
Camrelizumab	7 (5.7%)	-	7 (9.2%)
Camrelizumab + Lenvatinib	7 (5.7%)	1 (2.1%)	6 (7.9%)
Camrelizumab + Regorafenib	4 (3.3%)	-	4 (5.3%)
Sorafenib	3 (2.4%)	-	3 (3.9%)
Apatinib + Camrelizumab	2 (1.6%)	2 (4.3%)	-
Camrelizumab + Sorafenib	2 (1.6%)	-	2 (2.6%)
Sintilimab	2 (1.6%)	2 (4.3%)	-
Atezolizumab + Bevacizumab + Sorafenib	1 (0.8%)	-	1 (1.3%)
Bevacizumab	1 (0.8%)	1 (2.1%)	-
Camrelizumab + Fluorouracil + Oxaliplatin	1 (0.8%)	-	1 (1.3%)
Lenvatinib + Regorafenib	1 (0.8%)	-	1 (1.3%)
Lenvatinib + Tislelizumab	1 (0.8%)	-	1 (1.3%)
Lenvatinib + Toripalimab	1 (0.8%)	1 (2.1%)	-
Lobaplatin + Sorafenib	1 (0.8%)	-	1 (1.3%)
Regorafenib + Sintilimab	1 (0.8%)	1 (2.1%)	-
Regorafenib + Sorafenib	1 (0.8%)	-	1 (1.3%)
Regorafenib + Thalidomide	1 (0.8%)	1 (2.1%)	-

Disease burden:

- The **mean direct medical cost** per month and per year related to 2L treatment was 18,954 and 72,088 Chinese Yuan (CNY), respectively. After the implementation of the NRDL 2020 version, the mean direct medical cost per month reduced from 26,942 to 16,804 CNY, and the mean direct medical cost per year reduced from 65,687 to 57,551 CNY (**Figure 5**).
- Assuming 60% of the drug cost and 100% of the non-drug cost could be reimbursed, the estimated **mean out-of-pocket cost** per month was 14,948 and 6,847 CNY before and after NRDL 2020 version implementation, and the estimated mean out-of-pocket cost per year was 35,343 and 23,343 CNY before and after NRDL 2020 version implementation.

Figure 5. Direct medical cost of patients with 2L HC treatment



CONCLUSION & DISCUSSION

- **Targeted therapy**, especially **regorafenib**, was the most common 2L treatment against unresectable or advanced HC in China.
- Due to increased innovative choices for HC treatment since **NRDL 2020 version implementation**, the percentage of patients using 2L treatment consistent with the recommendation of 2020 CSCO guidelines changed.
- There was a trend towards **increased treatment duration and reduced direct medical cost** after NRDL 2020 version implementation.

FUNDING: This study was sponsored by Bayer Healthcare Company Ltd, Beijing, China

DISCLOSURES: The authors declare no competing interests