EFFICACY AND SAFETY OF LENVATINIB IN PATIENTS WITH RECURRENT HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION

K. BANG[1], C. YOO[1], MH. RYU[1], SR. PARK[1], HD. KIM[1], and BY. RYOO[1]

1. Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

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INTRODUCTION

Lenvatinib is approved for use in patients with metastatic or recurrent hepatocellular carcinoma (HCC). However, its clinical outcomes in patients experiencing HCC recurrence after liver transplantation (LT), remain unclear.

Further, despite of immunotherapeutic advances (atezolizumab plus bevacizumab, pembrolizumab, and nivolumab) in the management of advanced HCC, patients with prior LT are not benefited because of the risk of allograft rejection, and they are also excluded in the most prospective clinical trials for novel agents.

Thus, we investigated the efficacy and safety of lenvatinib in patients with recurrent HCC after LT.

METHOD

Single center, retrospective study

Patients

22 patients who received lenvatinib for recurred HCC following LT at the Asan Medical Center, South Korea between November 2019 and March 2021 were included.

Treatment

Lenvatinib was administered per its standard dose for advanced HCC patients as described in the REFLECT trial (12 mg/day for bodyweight ≥ 60 kg and 8 mg/day for bodyweight < 60 kg)

Evaluation

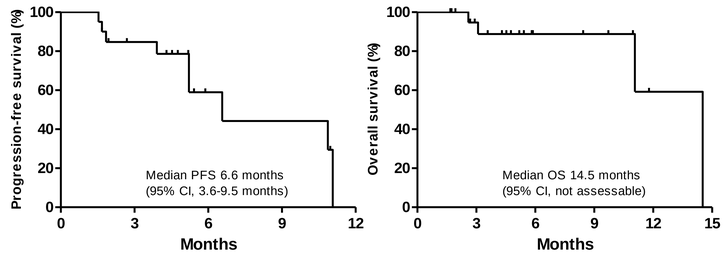
- Efficacy was measured using radiologic assessments, including CT or MRI, and graded according to the RECIST v1.1.
- Safety was graded according to the NCI-CTCAE v5.0.

RESULTS

Table 1. Baseline characteristics

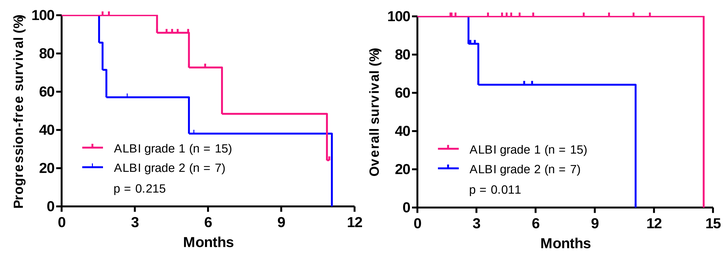
Variables	Total N=22
Age, years, median (range)	58 (20–69)
Sex, male	21 (95.5%)
ECOG performance status	
0	7 (31.8%)
1	15 (68.2%)
Etiology	
Hepatitis B	18 (81.8%)
Hepatitis C	2 (9.1%)
Alcohol	2 (9.1%)
Child-Pugh Score	
A	21 (95.5%)
B	1 (4.5%)
ALBI grade	
1	15 (68.2%)
2	7 (31.8%)
Site of recurrence or metastasis	
Liver	14 (63.6%)
Lung	11 (50.0%)
Peritoneum	5 (22.7%)
Bone	5 (22.7%)
Lymph node	3 (13.6%)
AFP, U/ml, median (range)	37 (1-373072)
< 400 U/ml	15 (68.2%)
≥ 400 U/ml	7 (31.8%)
Reason for LT	
HCC	22 (100.0%)
LT type	
LDLT	21 (95.5%)
DDLT	1 (4.5%)
Immunosuppressants	
Tacrolimus	21 (95.5%)
Everolimus	19 (86.4%)
Mycophenolate mofetil	3 (13.6%)
Interval between the LT and the start of lenvatinib, months, median (range)	12.0 (4.2-96.6)
BCLC stage	
C	22 (100.0%)
Treatment line of lenvatinib	
First	19 (86.4%)
Second	3 (13.6%)

Figure 1. Survival outcomes of lenvatinib



- With a median follow-up duration of 5.2 months (range, 1.7–14.5 months), the median progression-free survival (PFS) was 6.6 months (95% CI: 3.6-9.5) and overall survival (OS) was 14.5 months (95% CI: not assessable).
- The 6-month PFS and OS rates were 59.8% and 88.8%, respectively.

Figure 2. Survival outcomes according to the Albumin-Bilirubin grade at the time of lenvatinib initiation



- Patients with ALBI grade 2 showed significantly poorer OS [11.1 months (95% CI: not assessable)] compared to patients with ALBI grade 1 [14.5 months (95% CI: not assessable)] (p=0.011).

Table 2. Effectiveness of lenvatinib

Variables	Total N=22
Best response	
Complete response (CR)	0 (0.0%)
Partial response (PR)	3 (13.6%)
Stable disease (SD)	16 (72.7%)
Progressive disease (PD)	1 (4.5%)
Not evaluable (NE)	2 (9.1%)
Overall response rate	13.6%
Disease control rate	86.4%
Time to response, months (range)	1.7 (1.5-2.2)

Table 3. Adverse events in response to lenvatinib

Adverse Events	Total N=22	
	Any grade	Grade 3-4
All, n (%)	19 (86.4%)	10 (45.5%)
Neutropenia, n (%)	6 (27.3%)	4 (18.2%)
Anemia, n (%)	6 (27.3%)	0 (0.0%)
Thrombocytopenia, n (%)	7 (31.8%)	0 (0.0%)
Hypertension, n (%)	8 (36.4%)	4 (18.2%)
Hand foot syndrome, n (%)	4 (18.2%)	0 (0.0%)
Proteinuria, n (%)	1 (4.5%)	1 (4.5%)
Fatigue, n (%)	6 (27.3%)	3 (13.6%)
Anorexia, n (%)	4 (18.2%)	1 (4.5%)
Oral mucositis, n (%)	2 (9.1%)	0 (0.0%)
Diarrhea, n (%)	2 (9.1%)	0 (0.0%)

- Hypertension (n = 8, 36.4%) was the most frequently observed AE, followed by thrombocytopenia (n = 7, 31.8%) and fatigue (n = 6, 27.3).
- The most common grade 3-4 AEs were neutropenia (n = 4, 18.2%) and hypertension (n = 4, 18.2%).

CONCLUSIONS

Lenvatinib was effective and showed manageable toxicities in patients with recurrent HCC after LT.

These outcomes are comparable to those from the pivotal REFLECT trial where patients with LT were excluded.

Better baseline liver function (ALBI grade 1) at lenvatinib initiation correlated with better survival outcomes.

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CONTACT INFORMATION

Kyunghye Bang
Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea
Email: rudgp529@naver.com

Changhoon Yoo
Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea
Email: yooc@amc.seoul.kr

4. Therapy & Miscellaneous
KyungHye Bang
P-60
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