ILCA 2020
11-13 SEPTEMBER
INTERNATIONAL LIVER CANCER ASSOCIATION
VIRTUAL CONFERENCE

Efficacy And Safety Of Lenvatinib As A Salvage Therapy Of Transarterial Treatment For Unresectable Hepatocellular Carcinoma

J Lee[1,2], PS Sung[1,3,*], H Yang[1,2], SK Lee[1,3], SH Yoo[1,4], HL Lee[1,5], HY Kim[1,6], JH Kwon[1,4], HC Nam[1,2], SW Lee[1,5], JW Jang[1,3], CW Kim[1,6], SW Nam[1,4], SH Bae[1,2], JY Choi[1,3], SK Yoon[1,3]

1 The Catholic University Liver Research Center, College of Medicine, The Catholic University of Korea, Seoul
2 Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, Eunpyeong St. Mary's Hospital
3 Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, Seoul St. Mary's Hospital
4 Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, Incheon St. Mary's Hospital
5 Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, Bucheon St. Mary's Hospital
6 Division of Gastroenterology and Hepatology, Department of Internal Medicine, College of Medicine, Uijeongbu St. Mary's Hospital

CATHOLIC UNIVERSITY OF KOREA

INTRODUCTION

Treatment of interemediate to advanced HCC has been studied widely due to heterogeneity of its characteristics. Sorafenib has traditionally been used as a salvage treatment option since SHARP trial of 2008. Lenvatinib is a multikinase inhibitor that has been recently demonstrated to be non-inferior to sorafenib in a phase 3 randomized controlled trial (REFLECT trial)

Since it is being administered in intermediate to advanced HCC, large percentage of patients uses molecular targeted agent as a subsequent therapy to loco-regional treatment
such as TACE.

AIM

This study was designed to elucidate the clinical features and role of lenvatinib and compare them with those of sorafenib as a salvage treatment for HCC after transarterial treatment.

METHOD

Patient and study design

- This was a retrospective, multicenter study conducted at five Korean centers. Between January 2019 and June 2020.
- uHCC who underwent lenvatinib or sorafenib treatment after transarterial treatment were retrospectively analyzed
- Patients without follow-up visits after the start of the treatment are excluded

Evaluation of antitumor response

- Radiologic responses were classified according to the mRECIST
- 1st response evaluation was performed at 4 to 8 weeks after drug administration.

RESULTS

Initially, 66 patients with lenvatinib treatment and 108 with sorafenib treatment were reviewed. After the exclusion of patients without prior transarterial treatment or follow up visit, a total of 38 and 56 patients treated with lenvatinib and sorafenib treatment as salvage treatments for transarterial treatments, respectively, were enrolled.

There was no significant difference in etiology and epidemiology of each group.

The median PFS was 4.1 months for lenvatinib and 2.4 months for sorafenib (P = 0.012, by a log-rank test). ORR were significantly higher in the lenvatinib group (18.4%) than in the sorafenib group (3.6%, P = 0.028). Usage of the lenvatinib over sorafenib (hazard ratio: 0.264, 95% confidence interval: 0.127-0.550, P < 0.001) was the most significant factor associated with favorable PFS after failure of transarterial treatments in all enrolled patients.

There were no significant differences in safety issues between the two groups.

Baseline characteristics of the enrolled patients who received lenvatinib or sorafenib as a salvage treatment after transarterial treatment failure.

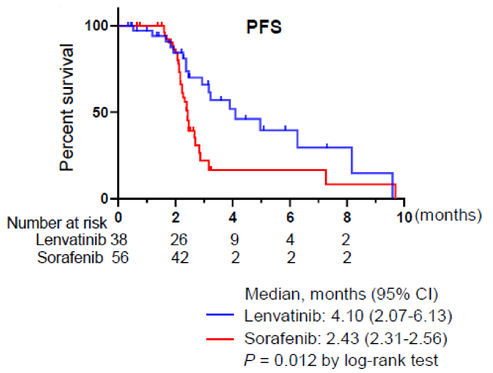
Parameters	Lenvatinib (N=38)	Sorafenib (N=56)	Total (N=94)	P
Epidemiology				
Sex, M/F (%)	33 (86.8)/5 (13.2)	43 (76.8)/13 (23.2)	76 (80.9)/18 (19.1)	0.343
Age, median (range)	59 (32-85)	63 (43–86)	62.5 (32-86)	0.136
Etiology				0.516
HBV, *n* (%)	28 (73.7)	39 (69.6)	67 (71.3)	
HCV, *n* (%)	1 (2.6)	6 (10.7)	7 (7.4)	
Alcohol, *n* (%)	7 (18.4)	8 (14.3)	15 (16.0)	
Others, *n* (%)	2 (5.3)	3 (5.4)	5 (5.3)	
Child-Pugh score				0.412
5, *n* (%)	22 (57.9)	35 (62.5)	57 (60.6)	
6, *n* (%)	11 (28.9)	18 (32.1)	34 (36.2)	
7, *n* (%)	5 (13.2)	3 (5.4)	3 (3.2)	
BCLC stage				0.449
A, *n* (%)	0 (0)	0 (0)	0 (0)	
B, *n* (%)	7 (18.4)	6 (10.7)	13 (13.8)	
C, *n* (%)	31 (81.6)	50 (89.3)	81 (86.2)	
D, *n* (%)	0 (0)	0 (0)	0 (0)	
ECOG				0.711
0, *n* (%)	12 (31.6)	21 (37.5)	33 (35.1)	
1, *n* (%)	26 (68.4)	35 (62.5)	61 (64.9)	
AFP, median (range), ng/mL	704.6 (1.4-115807)	708.8 (1.3-512682)	704.6 (1.3-512682)	0.639
PIVKA-II, median (range), mAU/mL	1648.5 (11-300000)	532.305 (14-52576)	806 (11-300000)	0.023
Macrovascular invasion, *n* (%)	17 (44.7)	26 (46.4)	43 (45.7)	1.000
Extrahepatic metastasis, *n* (%)	21 (55.3)	43 (76.8)	64 (68.1)	0.049
Previous treatments				
TACE, *n* (%)	35 (92.1)	55 (98.2)	90 (95.7)	
HAIC, *n* (%)	10 (26.3)	5 (8.9)	15 (15.9)	
Radiation therapy, *n* (%)	10 (26.3)	15 (26.8)	25 (26.6)	
Surgical resection, *n* (%)	5 (13.2)	11 (19.6)	16 (17.0)	
Radiofrequency ablation, *n* (%)	3 (7.9)	9 (16.1)	12 (12.8)	
Systemic chemotherapy, *n* (%)	6 (15.8)	2 (3.6)	8 (8.5)	

HBV, Hepatitis B virus; HCV, Hepatitis C virus; AFP, Alpha-fetoprotein; PIVKA-II, Protein induced by vitamin K absence-II; TACE, Transarterial chemoembolization; HAIC, Hepatic arterial infusion chemotherapy;

Treatment response in the enrolled patients

Treatment response	Lenvatinib, *n* (%)	Sorafenib, *n* (%)	*P*
CR	1 (2.6)	0 (0)	
PR	6 (15.8)	2 (3.6)	
SD	12 (31.6)	10 (17.9)	
PD	19 (50)	44 (78.6)	
ORR	18.4	3.6	0.028
DCR	50	21.4	0.007

uHCC, unresectable hepatocellular carcinoma; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate; DCR, disease control rate



CONCLUSIONS

In this real-world study, lenvatinib was demonstrated to be more efficacious than sorafenib as a salvage therapy for transarterial treatments in unresectable HCC.

Although there was no significant difference in OS, the lenvatinib showed superior ORR and PFS to sorafenib.

Also the prevelance of severe adverse events did not differ between those two groups.

Further prospective studies with larger populations and longer observational periods on lenvatinib efficacy in TACE-treated patients are needed to demonstrate the efficacy of lenvatinib over sorafenib as a salvage treatment, precisely.

REFERENCES

1. Ogasawara S, Ooka Y, Koroki K, Maruta S, Kanzaki H, Kanayama K, et al. Switching to systemic therapy after locoregional treatment failure: Definition and best timing. Clin Mol Hepatol. 2020;26(2):155-62.
2. Llovet JM, Ricci S, Mazzaferro V, Hilgard P, Gane E, Blanc JF, et al. Sorafenib in advanced hepatocellular carcinoma. N Engl J Med. 2008;359(4):378-90.
3. Kudo M, Finn RS, Qin S, Han K-H, Ikeda K, Piscaglia F, et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. The Lancet. 2018;391(10126):1163-73.
4. Kudo M. A New Treatment Option for Intermediate-Stage Hepatocellular Carcinoma with High Tumor Burden: Initial Lenvatinib Therapy with Subsequent Selective TACE. Liver Cancer. 2019;8(5):299-311.
5. Obi S, Sato T, Sato S, Kanda M, Tokudome Y, Kojima Y, et al. The efficacy and safety of lenvatinib for advanced hepatocellular carcinoma in a real-world setting. Hepatol Int. 2019;13(2):199-204.

ACKNOWLEDGEMENTS

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) and funded by the Ministry of Education (NRF-2019R1I1A1A01059642 and NRF-2020R1A2C3011569).

.

CONTACT INFORMATION

Dr. Jaejun Lee, pwln0516@gmail.com