Comparison of background characteristics of patients receiving lenvatinib vs atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma

Shinji Itoh[1], Masafumi Ikeda[2], Daisuke Onozuka[3], Ryosuke Tateishi[4], Tatsuya Yamashita[5], Takuji Okusaka[6], Naoya Kato[7], Junji Furuse[8], Masatoshi Kudo[9]

Department of Surgery and Science, Kyushu University[1]
Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital East[2]
Department of Oral Microbe Control, Osaka University[3]
Department of Gastroenterology, The University of University[4]
Department of Gastroenterology, Kanazawa University Hospital[5]
Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital[6]
Department of Gastroenterology, Chiba University[7]
Department of Gastroenterology, Kanagawa Cancer Center[8]
Department of Gastroenterology and Hepatology, Kindai University[9]

PRISM

Background:

Systemic therapy is one of the most important treatment modalities for unresectable hepatocellular carcinoma (HCC).
At present, eight regimens, including Atezolizumab+Bevacizumab, Durvalumab+Tremelimumab, Durvalumab, Sorafenib, Lenvatinib, Regorafenib, Ramucirumab and Cabozantinib, are reimbursable for the treatment of HCC in Japan.
In clinical practice, there are various patient backgrounds and patterns in the treatment sequence of systemic therapy.
Therefore, a prospective, observational, large-scale multicenter study of systemic therapy for HCC (PRISM) was conducted to establish real-world evidence from real-world data in Japan.

Unresectable HCC pts who will receive first-line systemic therapy with written informed consent

Enroll

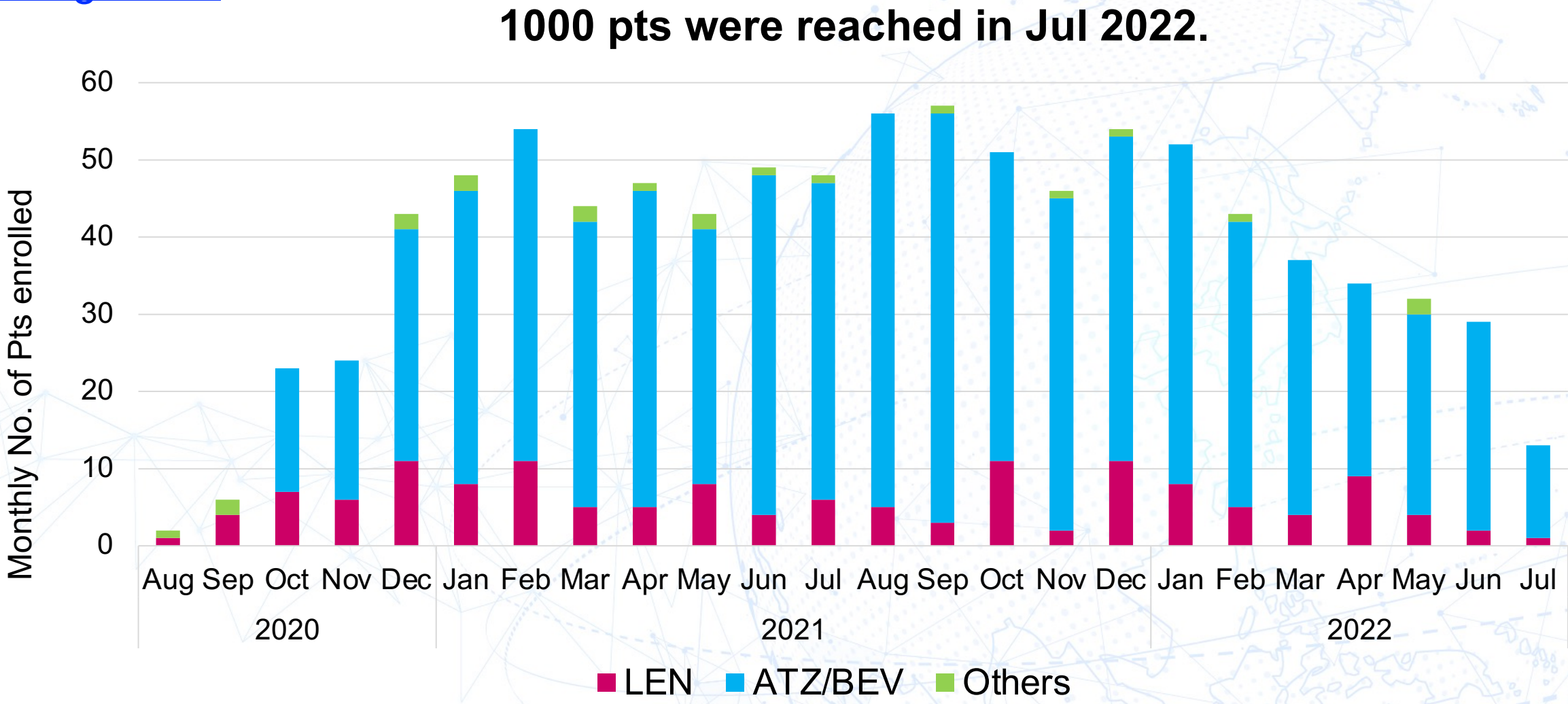
Data collection

1st, 2nd, 3rd, 4th… line therapy
Treatment methods: starting dose, continuous or intermittent, etc.
Efficacy: ORR, PFS, OS
Safety: Grade 3-4 AE, reason of discontinuation due to AE.

Enrollment: **2 years**
Planned enrolled: **1,000 pts**
Enrollment period: **Aug 2020-Jul 2022**

Clinical trial registration:
UMIN000040488

Background:



There are a certain number of patient who administrated LEN as the first-line systemic therapy.

Aim:

To identify the characteristics of patients with LEN administration at first-line systemic therapy in unresectable HCC.

Method:

- ✓ Of 1000Pts, 915 were included in this study, excluding those ineligible, untreated, mis-enrolled.
- ✓ We compared the background factors in patients who received LEN and atezolizumab plus bevacizumab (ATZ/BEV) as first-line systemic therapy by using the Wilcoxon rank-sum test, chi-square test, or Fisher's exact test.
- ✓ The two-sided significance level for all tests was $P < 0.05$.

Baseline characteristics between patients received ATZ/BEV vs LEN - 1

Characteristics		ATZ/BEV (n=774)	LEN (n=141)	P-value
Gender, n(%)	Male	617 (79.7)	114 (80.9)	0.757
Age (yrs)	Mean±S.D.	72.9±9.1	73.0±8.5	0.949
Hepatitis virus, n(%)	Present	395 (51.0)	67 (47.5)	0.442
HBsAg, n(%)	Positive	95 (24.1)	15 (22.1)	0.752
HCVAb, n(%)	Positive	248 (63.6)	45 (67.2)	0.573
Alcoholic liver disease, n(%)	Present	219 (28.3)	31 (22.0)	0.122
NASH/NAFLD, n(%)	Present	110 (14.2)	23 (16.3)	0.515
Prior treatment, n(%)	Present	517 (66.8)	100 (70.9)	0.336
Performance status, n(%)	0	590 (83.1)	98 (71.0)	0.007
	1	106 (14.9)	34 (24.6)	
	2	13 (1.8)	5 (3.6)	
	3	1 (0.1)	1 (0.7)	
Esophageal & gastric varices, n(%)	Present	207 (27.4)	39 (28.3)	0.831
Encephalopathy, n(%)	Mild	10 (1.3)	3 (2.1)	0.441

Baseline characteristics between patients received ATZ/BEV vs LEN - 2

Characteristics		ATZ/BEV (n=774)	LEN (n=141)	P-value
Ascites, n(%)	None	696 (89.9)	113 (80.1)	<0.001
	Mild	70 (9.0)	28 (19.9)	
	Moderate	8 (1.0)	0 (0.0)	
Total bilirubin (mg/dl), n(%)	<2	736 (95.2)	129 (92.1)	0.218
	2-3	30 (3.9)	10 (7.1)	
	>3	7 (0.9)	1 (0.7)	
Albumin (g/dl), n(%)	>3.5	495 (64.0)	66 (46.8)	<0.001
	2.8-3.5	258 (33.3)	64 (45.4)	
	<2.8	21 (2.7)	11 (7.8)	
Prothrombin (%), n(%)	>70	699 (90.5)	118 (84.3)	0.067
	40-70	63 (8.2)	20 (14.3)	
	<40	10 (1.3)	2 (1.4)	

Baseline characteristics between patients received ATZ/BEV vs LEN - 3

Characteristics		ATZ/BEV (n=774)	LEN (n=141)	P-value
Child-Pugh score, n(%)	5	409 (53.1)	52 (37.4)	<0.001
	6	246 (31.9)	47 (33.8)	
	7	85 (11.0)	23 (16.6)	
	8	22 (2.9)	12 (8.6)	
	9	7 (0.9)	3 (2.2)	
	10	2 (0.3)	2 (1.4)	
ALBI grade, n(%)	Grade 1	258 (33.4)	40 (28.6)	0.045
	Grade 2	498 (64.4)	92 (65.7)	
	Grade 3	17 (2.2)	8 (5.7)	
BCLC stage	Stage 0	5 (0.7)	0 (0.0)	0.307
	Stage A	40 (5.2)	7 (5.0)	
	Stage B	277 (35.8)	58 (41.1)	
	Stage C	449 (58.0)	74 (52.5)	
	Stage D	3 (0.4)	2 (1.4)	

Baseline characteristics between patients received ATZ/BEV vs LEN - 4

Characteristics		ATZ/BEV (n=774)	LEN (n=141)	P-value
Up-to-7 criteria, n(%)	Out	523 (67.6)	96 (68.1)	0.904
Maximum tumor size (cm)	Mean±S.D.	5.3±4.5	5.8±4.6	0.251
Intrahepatic lesion, n(%)	Present	705 (91.1)	138 (97.9)	0.006
location of intrahepatic lesion	bilobular	400 (56.7)	66 (47.8)	0.054
Portal vein invasion, n(%)	Vp0	562 (72.6)	99 (70.2)	0.593
	Vp1	23 (3.0)	8 (5.7)	
	Vp2	53 (6.9)	10 (7.1)	
	Vp3	53 (6.9)	13 (9.2)	
	Vp4 (main trunk)	67 (8.7)	11 (7.8)	
Hepatic vein invasion, n(%)	Vv0	712 (92.0)	120 (85.1)	0.067
	Vv1	12 (1.6)	5 (3.6)	
	Vv2	27 (3.5)	9 (6.4)	
	Vv3 (IVC)	23 (3.0)	7 (5.0)	

Baseline characteristics between patients received ATZ/BEV vs LEN - 5

Characteristics		ATZ/BEV (n=774)	LEN (n=141)	P-value
Bile duct invasion, n(%)	B0	728 (94.1)	132 (93.6)	0.555
	B1	8 (1.0)	3 (2.1)	
	B2	12 (1.6)	1 (0.7)	
	B3	14 (1.8)	4 (2.8)	
	B4	12 (1.6)	1 (0.7)	
Regional lymph node metastasis, n(%)	Present	87 (11.2)	15 (10.6)	0.835
Extrahepatic spread, n(%)	Present	212 (27.4)	34 (24.1)	0.420
AFP (ng/mL)	Mean±S.D.	10,677±61,369	6,020±24,740	0.188
AFP-L3 (%)	Mean±S.D.	27.4±30.2	29.3±31.5	0.566
PIVKA-II (mAU/mL)	Mean±S.D.	18,555±143,923	23,732±107,299	0.411

Conclusions:

This study revealed that LEN was selected in cases with poor general condition and liver function.
The PRISM study is a useful clinical study that can clarify the real-world data of systemic therapy for HCC in Japan.

Acknowledgements:

Patients, families, friends and 42 Centers contributing patients to PRISM study group:
Chiba University, Hiroshima University Hospital, Kurume University, Kanazawa University Hospital, Kumamoto University Hospital, The University of Tokyo Hospital, Yokohama City University Medical Center, Toho University Omori Medical Center, Tokushima University Hospital, Saitama Medical University Hospital, Kitasato University School of Medicine, Kindai University Hospital, Iizuka Hospital, National Cancer Center Hospital East, Kyusyu Cancer Center, Kanagawa Cancer Center, Japanese Red Cross Musashino Hospital, Aichi Cancer Center, Okayama University Hospital, Hokkaido University, Nara Medical University, Kyorin University, Iwate Medical University, Kyoto Prefectural University of Medicine, Kyusyu University, Ehime Prefectural Central Hospital, Yamaguchi University, National Cancer Center Hospital, Nagasaki University Hospital, Osaka University, Tokyo Medical and Dental University Hospital, Toranomon Hospital, Osaka International Cancer Institute, The Okayama City Hos pital, Osaka Metropolitan University, Hyogo Medical University Hospital, Niigata University, Toranomon Hospital Kajigaya, National Center for Globa l Health and Medicine, Kyusyu Medical Center, Ogaki Municipal Hospital, Juntendo University Shizuoka Hospital.
This study was funded by Eisai Co., Ltd. and Eli Lilly Japan. K.K., and supported by Japan Association of Molecular Targeted Therapy for HCC.