Efficacy of Durvalumab and Tremelimumab in HCC with High Tumor Burden and Vp4 Invasion

Yutaka Yata [1) 2) 6)], Takeshi Hatanaka [3) 6)], Satoru Kakizaki [4) 5) 6)], Atsushi Hiraoka [6)], Toshifumi Tada [6)], Kazuya Kariyama [6)], Joji Tani [6)], Ei Itobayashi [6)], Kunihiko Tsuji [6)], Hidenori Toyoda [6)], Atsushi Naganuma [6)], Kosuke Matsui [6)], Masaki Kaibori [6)], Hidekatsu Kuroda [6)], Shohei Komatsu [6)], Tomomitsu Matono [6)], Kazunari Tanaka [6)], Fujimasa Tada [6)], Kazuhiro Nouso [6)], Takashi Kumada [6)]

1) Department of Hepatology, Osaka Metropolitan University, Osaka, Japan
2) Department of Gastroenterology, Hanwa Memorial Hospital, Osaka, Japan
3) Department of Gastroenterology, Gunma Saiseikai Maebashi Hospital, Maebashi, Japan
4) Department of Clinical Research, NHO Takasaki General Medical Center, Takasaki, Japan
5) Department of Gastroenterology and Hepatology, Gunma University Graduate School of Medicine, Maebashi, Japan
6) Real-life Practice Experts for HCC (RELPEC) Study Group and HCC 48 (HCC experts from 48 clinics) Group, Japan

Key findings

- Dur/Tre demonstrated clinical efficacy even in patients with HTB, who generally have a poor prognosis.
- In Vp4-positive patients, who were excluded from the HIMALAYA trial, Dur/Tre showed a higher ORR and comparatively favorable outcomes.
- The frequency and severity of immune-related adverse events (irAEs) were similar between groups, indicating that Dur/Tre was safely administered in all patients.
- Responders achieved prolonged survival, and treatment response was strongly correlated with OS, emphasizing the importance of early response evaluation.

Conclusion

- Dur/Tre may represent a promising treatment option for patients with Vp4 invasion or HTB.

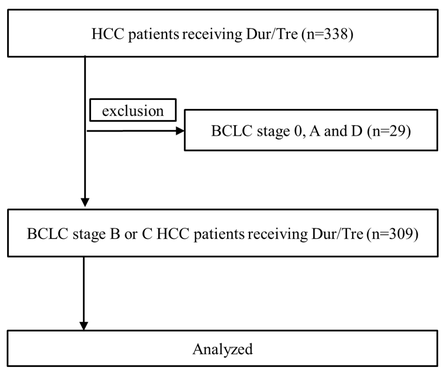
Objective

To evaluate the therapeutic efficacy of durvalumab and tremelimumab (Dur/Tre) in patients with HCC who had a high tumor burden (HTB) or tumor thrombus in the main portal vein trunk (Vp4).

Patients and Methods

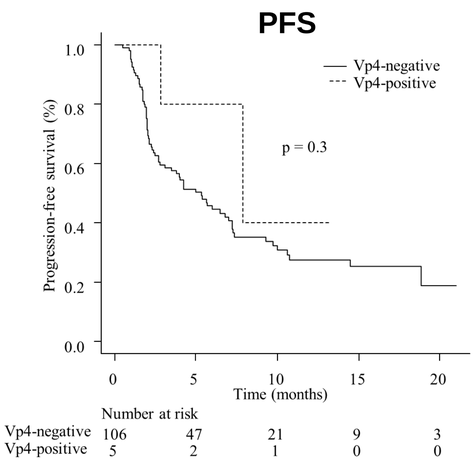
- A total of 309 patients with BCLC stage B or C HCC who received Dur/Tre between March 2023 and October 2024 were included.
- HTB was defined as the presence of at least one of the following radiological findings: (1) ≥50% liver involvement by HCC, (2) bile duct invasion, or (3) the presence of Vp4.

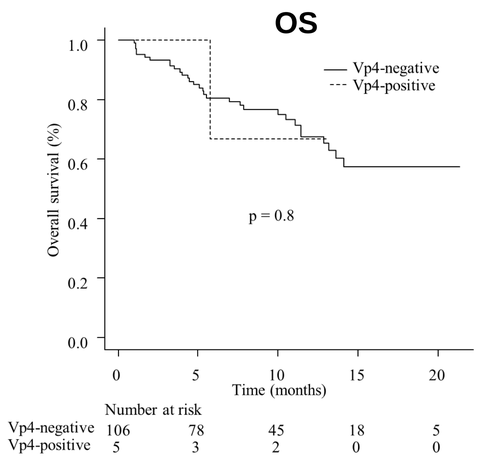
Patient Selection and Characteristics



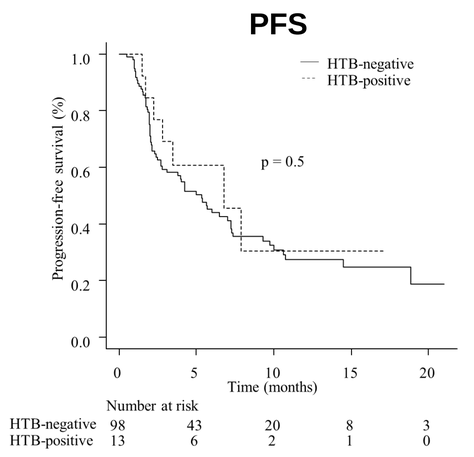
Factors		Entire cohort (n = 309)	Patients without HTB (n = 272)	Patients with HTB (n = 37)	P-value
Age (years)		73.0 [68.0,78.0]	73.0 [68.0,78.0]	72.0 [64.0,77.0]	0.4
Gender, n (%)	Male	258 (83.5)	225 (82.7)	33 (89.2)	0.5
Performance status, n (%)	0	236 (76.4)	208 (76.5)	28 (75.7)	0.9
	1	60 (19.4)	52 (19.1)	8 (21.6)	
	2	13 (4.2)	12 (4.4)	1 (2.7)	
Underlying liver diseases, n (%)	HCV	90 (29.1)	84 (30.9)	6 (16.2)	0.03
	HBV	55 (17.8)	47 (17.3)	8 (21.6)	
	HCV plus HBV	2 (0.6)	1 (0.4)	1 (2.7)	
	Alcohol	62 (20.1)	58 (21.3)	4 (10.8)	
	Others	100 (32.4)	82 (30.1)	18 (48.6)	
Viral-related disease, n (%)		147 (47.6)	132 (48.5)	15 (40.5)	0.4
BCLC stage, n (%)	Intermediate	92 (29.8)	88 (32.4)	4 (10.8)	0.007
	Advanced	217 (70.2)	184 (67.6)	33 (89.2)	
Child-Pugh score, n (%)	5	121 (39.2)	109 (40.1)	12 (32.4)	0.4
	6	122 (39.5)	108 (39.7)	14 (37.8)	
	≥7	66 (21.4)	55 (20.2)	11 (29.7)	
ALBI score		-2.18 [-2.56, -1.83]	-2.19 [-2.59, -1.85]	-2.06 [-2.36, -1.76]	0.2
mALBI grade, n (%)	1	70 (22.7)	64 (23.5)	6 (16.2)	0.4
	2a	65 (21.0)	58 (21.3)	7 (18.9)	
	2b	157 (50.8)	137 (50.4)	20 (54.1)	
	3	17 (5.5)	13 (4.8)	4 (10.8)	
Treatment settings, n (%)	First-line	111 (35.9)	98 (36.0)	13 (35.1)	1.0
	Later-line	198 (64.1)	174 (64.0)	24 (64.9)	
EHS, n (%)	Presence	137 (44.3)	125 (46.0)	12 (32.4)	0.2
Vp4, n (%)	Presence	14 (4.5)	0 (0.0)	14 (37.8)	<0.001
Liver involvement	≥50%	26 (8.4)	0 (0.0)	26 (70.3)	<0.001
Bile duct invasion	Presence	1 (0.3)	0 (0.0)	1 (2.7)	0.1
AFP, n (%)	≥100 ng/ml	145 (46.9)	126 (46.3)	19 (51.4)	0.6
DCP*, n (%)	≥100 mAU/ml	232 (75.8)	196 (72.9)	36 (97.3)	<0.001

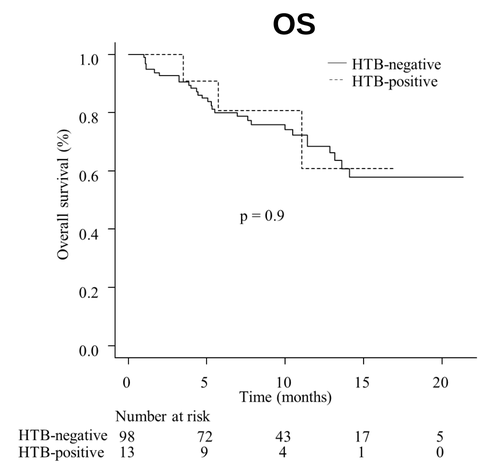
First-Line Dur/Tre with Vp4 *A Subgroup Analysis*



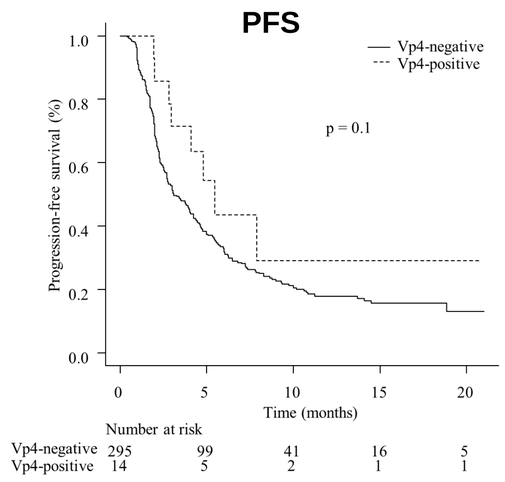


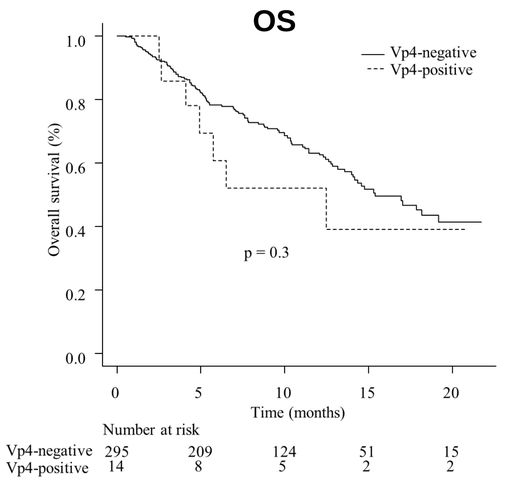
First-Line Dur/Tre with HTB *A Subgroup Analysis*





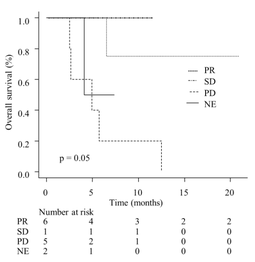
PFS and OS (Vp4)

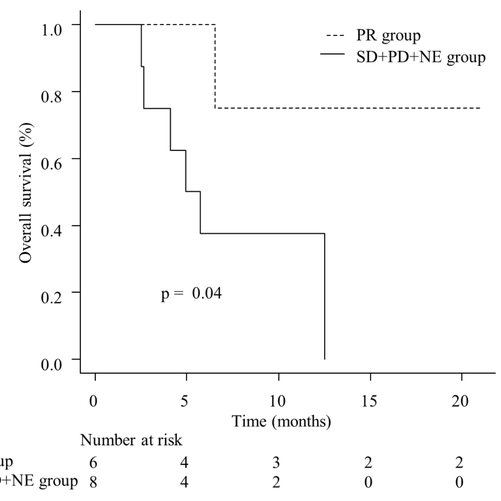




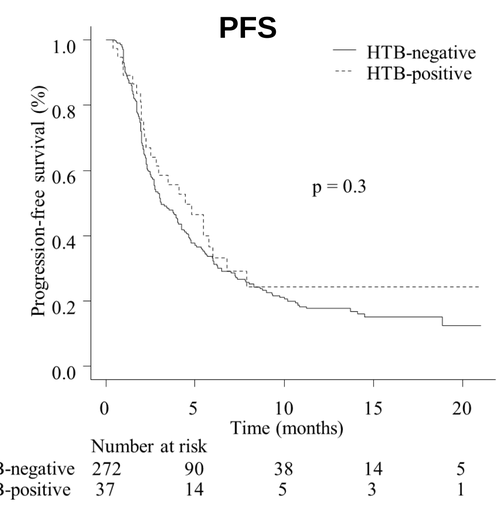
Tumor Response and OS (Vp4)

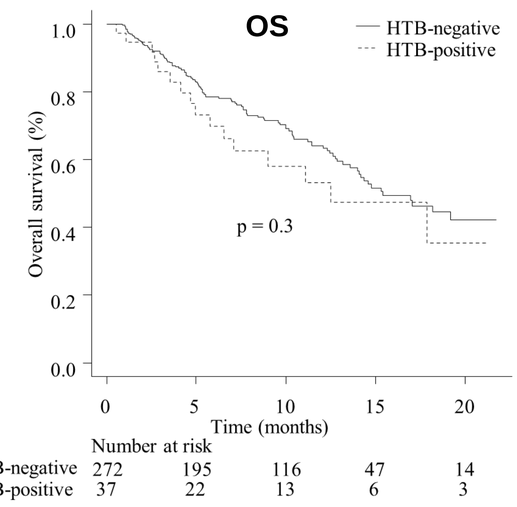
Factors	Patients without Vp4 (n = 295)	Patients with Vp4 (n = 14)	P-value
Best response, n (%)			0.04
CR	3 (1.0)	0 (0.0)	
PR	43 (14.6)	6 (42.9)	
SD	83 (28.1)	1 (7.1)	
PD	139 (47.1)	5 (35.7)	
NE	27 (9.2)	2 (14.3)	
ORR (%)	15.6	42.9	0.02
DCR (%)	43.7	50.0	0.8





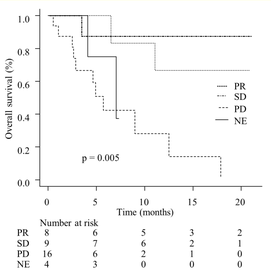
PFS and OS (HTB)

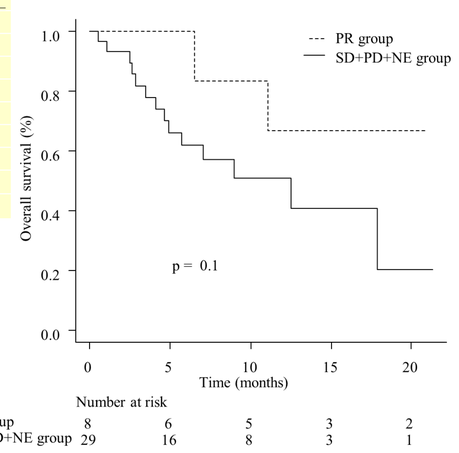




Tumor Response and OS (HTB)

Factors	Overall (n = 309)	Patients without HTB (n = 272)	Patients with HTB (n = 37)	P-value
Best response, n (%)				0.8
CR	3 (1.0)	3 (1.1)	0 (0.0)	
PR	49 (15.9)	41 (15.1)	8 (21.6)	
SD	84 (27.2)	75 (27.6)	9 (24.3)	
PD	144 (46.6)	128 (47.1)	16 (43.2)	
NE	29 (9.4)	25 (9.2)	4 (10.8)	
ORR (%)	16.8	16.2	21.6	0.5
DCR (%)	44.0	43.8	45.9	0.9





COI: All authors declare no conflicts of interest associated with this study.