

Impact of body mass index in patients receiving atezolizumab plus bevacizumab for hepatocellular carcinoma

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Supplementary Table 1. Best radiological response evaluated per RECIST criteria version 1.1 stratified by BMI.....	4
Supplementary Table 2. Baseline characteristics of study population stratified by BMI class.....	5
Supplementary Table 3. Effects of BMI class and prognostic factors on overall survival after atezolizumab and bevacizumab in univariate and multivariate Cox regression models.....	7
Supplementary Table 4. Effects of BMI class and prognostic factors on progression-free survival after atezolizumab and bevacizumab in univariate and multivariate Cox regression models.....	8
Supplementary Table 5. Atezolizumab and bevacizumab treatment-related adverse events stratified by BMI class.....	9
Supplementary Figure 1. BMI association with baseline patient characteristics. <i>p</i> values shown for Pearson correlation coefficient for continuous variables and unpaired student t-test for categorical variables. Mean BMI (square) with 95% confidence interval (green) shown for categorical variables.	11
.....	11
Supplementary Figure 2. Kaplan-Meier curve showing overall survival (months) for underweight (BMI < 18.5), normal (18.5 ≤ BMI < 25), overweight (25 ≤ BMI < 30) and obese (BMI ≥ 30) patients with unresectable hepatocellular carcinoma patients after atezolizumab plus bevacizumab administration.....	12
Supplementary Figure 3. Kaplan-Meier curve showing progression-free survival (months) for underweight (BMI < 18.5), normal (18.5 ≤ BMI < 25), overweight (25 ≤ BMI < 30) and obese (BMI ≥ 30) patients with unresectable hepatocellular carcinoma patients after atezolizumab plus bevacizumab administration.....	13

Supplementary Table 1. Best radiological response evaluated per RECIST criteria version 1.1

stratified by BMI

	All patients (n=163 ^a)	BMI <25 (n=64)	BMI 25+ (n=59)	<i>p value</i>
Complete Response	0	0	0	
Partial Response	40 (24.5)	18 (22.0)	22 (27.2)	0.44
Stable Disease	79 (48.5)	41 (50.0)	38 (46.9)	0.69
Progressive Disease Rate	44 (27.0)	23 (28.1)	21 (25.9)	0.76

Notes: ^aRadiological response was assessed in 163 patients (85.3%);

Abbreviations: RECIST, response evaluation criteria in solid tumours.

Supplementary Table 2. Baseline characteristics of study population stratified by BMI class.

	Underweight (n=10)	Normal (n=87)	Overweight (n=51)	Obese (n=43)	<i>p value</i>
Centre					
Germany	3 (30.0)	9 (10.3)	9 (17.7)	9 (20.9)	
Austria	1 (10.0)	2 (2.3)	4 (7.8)	5 (11.6)	
United Kingdom	0	6 (6.9)	4 (7.8)	5 (11.6)	
Italy	0	6 (6.9)	4 (7.8)	2 (4.7)	0.02
United States of America	2 (20.0)	27 (31.0)	11 (21.6)	20 (46.5)	
Japan	4 (40.0)	31 (35.6)	14 (27.5)	2 (4.7)	
Taiwan	0	6 (6.9)	5 (9.8)	0	
	69.7	68.2	70.6	65.5	
Median Age (IQR)	(63.0-77.3)	(59.9-75.2)	(64.1-76.0)	(59.5-74.6)	0.26
Male Sex	8 (80.0)	75 (86.2)	43 (84.3)	35 (81.4)	0.98
Risk factors for chronic liver disease					
Non-alcoholic fatty liver disease	1 (10.0)	6 (6.9)	8 (15.7)	10 (23.3)	0.07
Alcohol related	4 (40.0)	32 (36.8)	15 (29.4)	22 (51.2)	0.19
Hepatitis B infection	0	25 (28.7)	10 (19.6)	2 (4.7)	0.004
Hepatitis C infection	5 (50.0)	35 (40.2)	14 (27.5)	18 (41.9)	0.32
Other	2 (33.3)	4 (7.1)	3 (8.1)	3 (7.3)	0.18
Child-Turcotte-Pugh class					
A	8 (80.0)	69 (79.3)	42 (82.4)	28 (65.1)	0.21
B	2 (20.0)	18 (20.7)	9 (17.7)	15 (34.9)	0.21
Varices present	1 (10.0)	14 (16.1)	14 (27.5)	10 (23.3)	0.33
Maximum Tumor Diameter (cm)	7.3 (6.2)	6.8 (5.3)	6.6 (4.7)	7.2 (3.8)	0.92

Macrovascular invasion (MVI)	1 (10.0)	32 (36.8)	22 (43.1)	23 (53.5)	0.06
AFP (ng/dL)					
≤400	9 (90.0)	59 (67.8)	31 (60.8)	27 (62.8)	0.32
>400	1 (10.0)	28 (32.2)	20 (39.2)	16 (37.2)	
Extrahepatic spread (EHS)	4 (40.0)	40 (46.0)	18 (35.3)	10 (23.3)	0.09
ECOG-PS					
0	6 (60.0)	58 (67.4)	33 (64.7)	22 (52.4)	0.24
1	4 (40.0)	23 (26.7)	18 (35.3)	19 (45.2)	
2	0	5 (5.8)	0	1 (2.4)	
Barcelona Clinic Liver Cancer Stage					
A	0	4 (4.7)	1 (2.0)	2 (4.8)	0.36
B	5 (50.0)	35 (40.7)	19 (38.0)	9 (21.4)	
C	5 (50.0)	47 (54.7)	30 (60.0)	31 (73.8)	
Previous locoregional treatment					
Resection	3 (30.0)	27 (31.0)	9 (17.7)	5 (11.6)	0.15
Radiofrequency ablation	3 (30.0)	17 (19.5)	8 (15.7)	10 (23.3)	0.68
Transarterial chemoembolization	4 (40.0)	27 (31.0)	14 (27.5)	12 (27.9)	0.86
Y90	1 (10.0)	6 (6.9)	8 (15.7)	6 (14.0)	0.39
External Beam Radiotherapy	0	4 (4.6)	2 (3.9)	0	0.49

Notes: n (%) for discrete variables; mean ± standard deviation for continuous variables

Abbreviations: AFP – alpha-fetoprotein; ECOG-PS – Eastern Cooperative Oncology Group Performance Status.

Supplementary Table 3. Effects of BMI class and prognostic factors on overall survival after atezolizumab and bevacizumab in univariate and multivariate Cox regression models

	Univariate models		Multivariable models	
	Hazard Ratio (95% CI)	<i>p</i> value	Hazard Ratio (95% CI)	<i>p</i> value
BMI Class				
Underweight vs Normal	1.41 (0.49-4.06)	0.52	2.19 (0.72-6.61)	0.17
Overweight vs Normal	0.84 (0.44-1.60)	0.60	0.73 (0.38-1.40)	0.34
Obese vs Normal	1.29 (0.70-2.39)	0.42	0.83 (0.42-1.64)	0.59
BCLC Stage (C vs A or B)	1.50 (0.89-2.52)	0.13	1.00 (0.54-1.86)	0.99
CTP Class (B vs A)	3.01 (1.77-5.13)	<0.0001	2.42 (1.32-4.45)	0.004
Tumour size > 7cm	1.30 (0.77-2.20)	0.32	1.06 (0.62-1.81)	0.84
MVI	2.51 (1.51-4.18)	<0.0001	2.04 (1.05-3.94)	0.03
Metastatic Disease	0.80 (0.47-1.36)	0.41	0.91 (0.51-1.63)	0.75
AFP > 400 ng/dL	1.32 (0.79-2.19)	0.29	1.21 (0.72-2.06)	0.47

Abbreviations: 95% CI – 95% Confidence Interval; BCLC – Barcelona Clinic Liver Cancer; CTP – Child-

Turcotte-Pugh; MVI – Macrovascular invasion; AFP – alpha-fetoprotein;

Supplementary Table 4. Effects of BMI class and prognostic factors on progression-free survival after atezolizumab and bevacizumab in univariate and multivariate Cox regression models

	Univariate models		Multivariable models	
	Hazard Ratio (95% CI)	<i>p</i> value	Hazard Ratio (95% CI)	<i>p</i> value
BMI Class				
Underweight vs Normal	1.23 (0.43-3.51)	0.70	1.84 (0.61-5.60)	0.28
Overweight vs Normal	0.76 (0.39-1.47)	0.42	0.69 (0.36-1.34)	0.27
Obese vs Normal	1.11 (0.60-2.06)	0.73	0.80 (0.41-1.56)	0.80
BCLC Stage (C vs A or B)	1.56 (0.92-2.64)	0.10	0.96 (0.51-1.82)	0.91
CTP Class (B vs A)	2.29 (1.35-3.87)	0.002	1.85 (1.01-3.39)	0.045
Tumour size > 7cm	1.28 (0.76-2.15)	0.36	1.04 (0.61-1.79)	0.88
MVI	2.30 (1.38-3.82)	0.001	2.07 (1.04-4.13)	0.04
Metastatic Disease	1.03 (0.60-1.75)	0.92	1.12 (0.62-2.03)	0.71
AFP > 400 ng/dL	1.35 (0.81-2.26)	0.24	1.22 (0.71-2.10)	0.47

Abbreviations: 95% CI – 95% Confidence Interval; BCLC – Barcelona Clinic Liver Cancer; CTP – Child-

Turcotte-Pugh; MVI – Macrovascular invasion; AFP – alpha-fetoprotein;

Supplementary Table 5. Atezolizumab and bevacizumab treatment-related adverse events stratified

by BMI class.

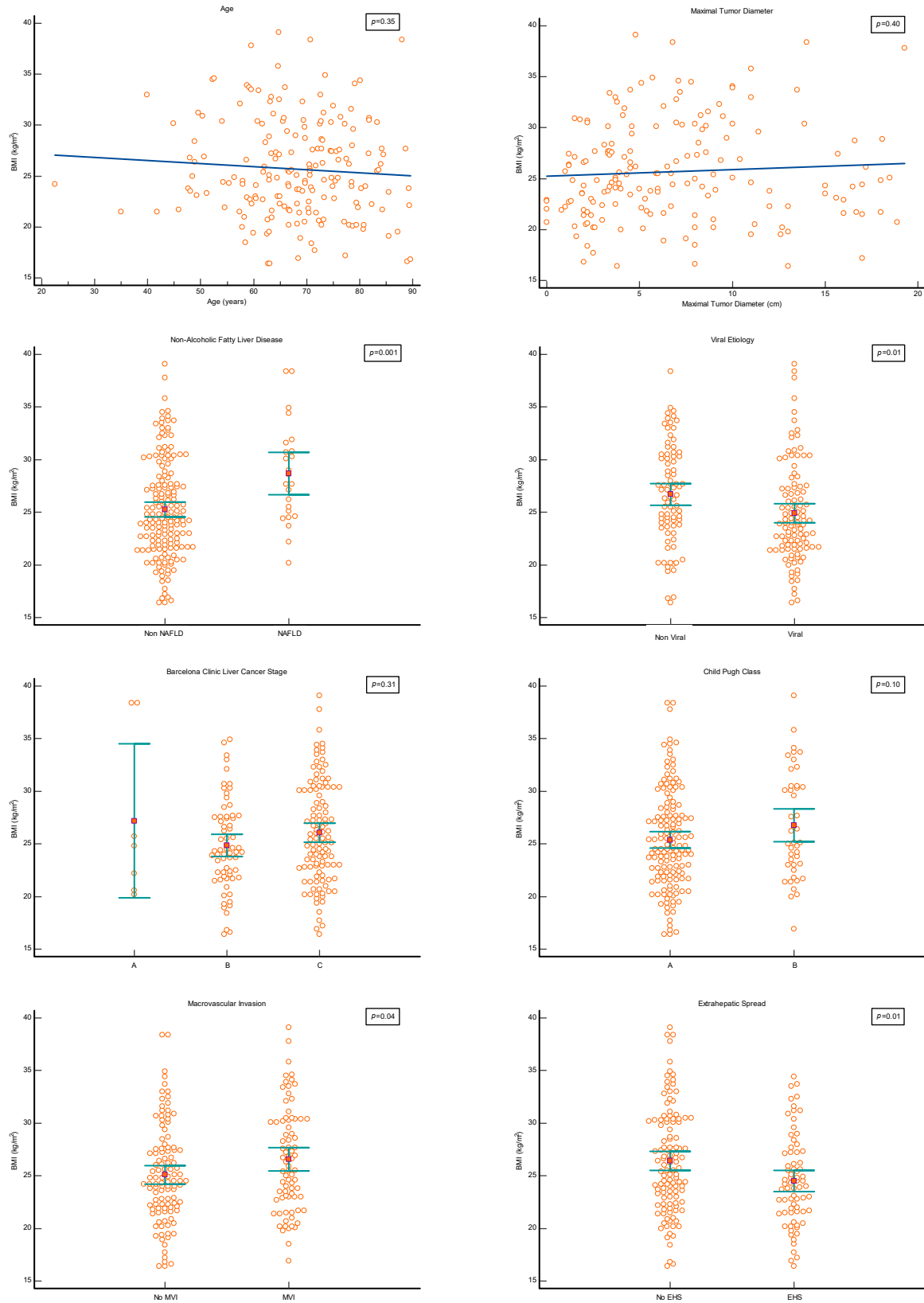
	Underweight (n=10)	Normal (n=87)	Overweight (n=51)	Obese (n=43)	<i>p value</i>
Any grade trAEs	7 (70.0)	55 (63.2)	32 (62.8)	33 (76.7)	0.42
Grade\geq3^a trAEs	2 (20.0)	19 (21.8)	10 (19.6)	8 (18.6)	0.97
Atezolizumab-related	2 (20.0)	9 (10.3)	2 (3.9)	2 (4.7)	0.21
Bevacizumab-related	1 (10.0)	11 (12.6)	8 (15.7)	6 (14.0)	0.95
trAEs requiring drug discontinuation	1 (10.0)	4 (4.6)	3 (5.9)	4 (9.3)	0.72
Atezolizumab trAEs					
Overall	4 (40.0)	38 (43.7)	19 (37.3)	33 (51.2)	0.60
Fatigue	2 (20.0)	8 (9.2)	10 (19.6)	11 (25.6)	0.09
Hepatotoxicity	1 (10.0)	15 (17.2)	8 (15.7)	4 (9.3)	0.64
Skin toxicity	1 (10.0)	2 (2.3)	3 (5.9)	3 (7.0)	0.49
Colitis	1 (10.0)	11 (12.6)	3 (5.9)	9 (20.9)	0.18
Thyroid dysfunction	2 (20.0)	6 (6.9)	1 (2.0)	0	0.02
Pneumonitis	0	1 (1.2)	1 (2.0)	2 (4.7)	0.58
Bevacizumab trAEs					
Overall	7 (70.0)	33 (37.9)	23 (45.1)	20 (46.5)	0.24
Bleeding	2 (20.0)	8 (9.2)	6 (11.8)	4 (9.3)	0.74

Hypertension	5 (50.0)	18 (20.7)	11 (21.6)	10 (23.3)	0.22
Proteinuria	4 (40.0)	19 (21.8)	10 (19.6)	5 (11.6)	0.20
Thrombosis	0	2 (2.3)	2 (3.9)	6 (14.0)	0.03

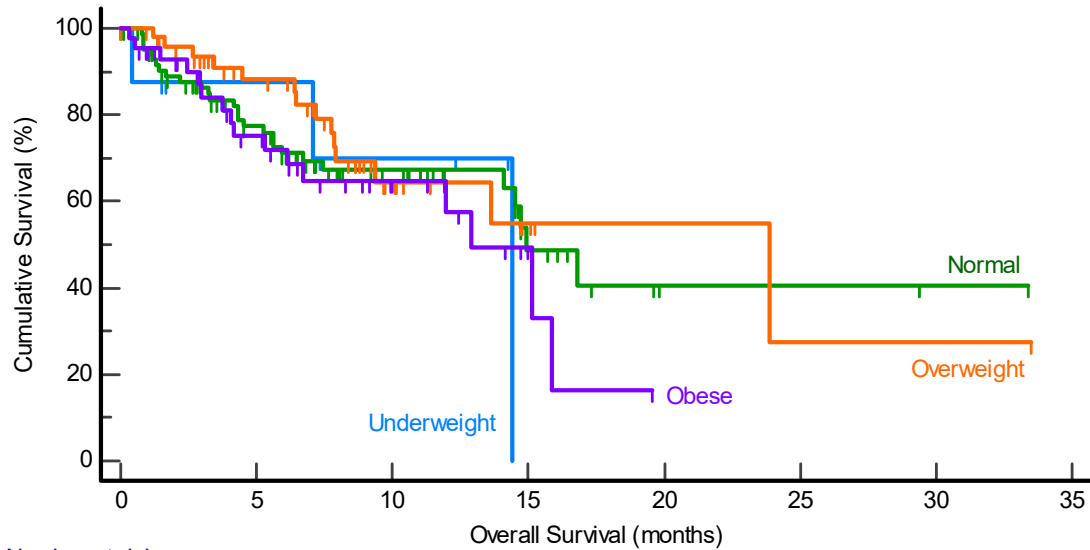
Notes: ^agraded as per the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE)

Abbreviations: trAE – treatment-related adverse event.

Supplementary Figure 1. BMI association with baseline patient characteristics. p values shown for Pearson correlation coefficient for continuous variables and unpaired student t-test for categorical variables. Mean BMI (square) with 95% confidence interval (green) shown for categorical variables.

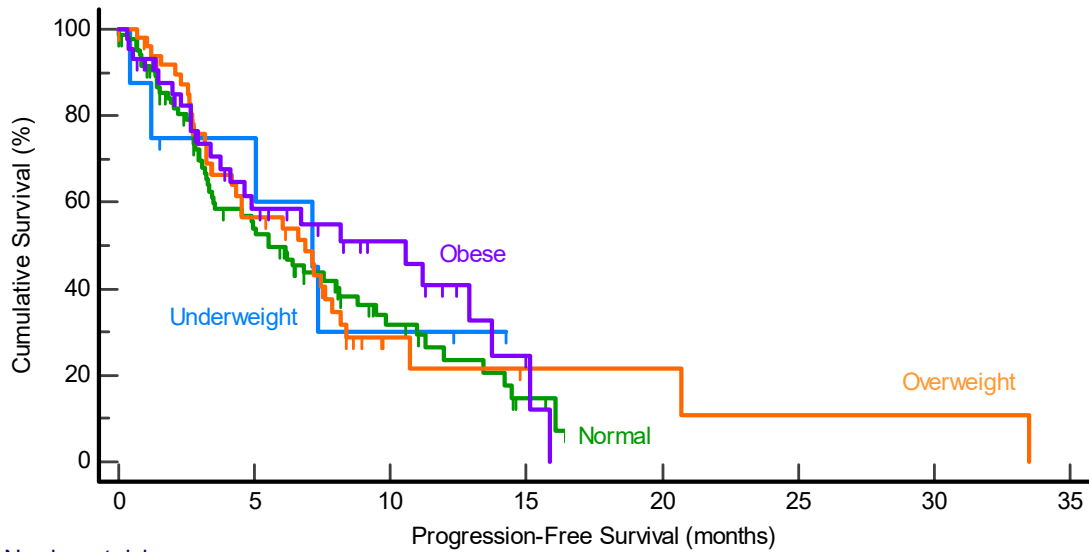


Supplementary Figure 2. Kaplan-Meier curve showing overall survival (months) for underweight (BMI < 18.5), normal (18.5 ≤ BMI < 25), overweight (25 ≤ BMI < 30) and obese (BMI ≥ 30) patients with unresectable hepatocellular carcinoma patients after atezolizumab plus bevacizumab administration.



	0	5	10	15	20	25	30	35
Number at risk								
Underweight	8	5	3	0	0	0	0	0
Normal	85	50	25	9	2	2	1	0
Overweight	50	32	11	4	2	1	1	0
Obese	43	24	11	3	0	0	0	0

Supplementary Figure 3. Kaplan-Meier curve showing progression-free survival (months) for underweight (BMI < 18.5), normal (18.5 ≤ BMI < 25), overweight (25 ≤ BMI < 30) and obese (BMI ≥ 30) patients with unresectable hepatocellular carcinoma patients after atezolizumab plus bevacizumab administration.



Number at risk	0	5	10	15	20	25	30	35
Group: Underweight	8	5	2	0	0	0	0	0
Group: Normal	84	38	14	3	0	0	0	0
Group: Overweight	50	23	4	2	2	1	1	0
Group: Obese	43	19	10	2	0	0	0	0