

Adverse events as potential predictive factors of activity in patients with advanced HCC treated with atezolizumab plus bevacizumab

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**RUNNING HEADER: adverse events in HCC patients treated with atezolizumab plus
bevacizumab**

MALE	657 (79.8%)
FEMALE	166 (20.2%)
≤ 70	339 (41.2%)
> 70	484 (58.8%)
VIRAL	442 (53.7%)
NO VIRAL	381 (46.3%)
AT LEAST ONE LOCAL THERAPY	569 (69.1%)
NO LOCAL THERAPY	205 (24.9%)
CP A	769 (93.4%)
CP B	54 (6.6%)
BCLC B	335 (40.7%)
BCLC C	488 (59.3%)
PS 0	615 (74.7%)
PS ≥ 1	208 (25.3%)
PVT	175 (21.3%)
NO PVT	648 (78.7%)
AFP < 400 ng/mL	578 (70.2%)
AFP ≥ 400 ng/mL	240 (29.2%)
EHD	305 (37.1%)
NO EHD	517 (62.8%)
ALBI 1	752 (91.4%)
ALBI 2	66 (8.0%)
NLR ≤ 3	435 (52.8%)
NLR > 3	304 (36.9%)

Supplementary Table 1. Baseline characteristics of study population. AFP: alpha-feto-protein; ALBI: Albumin-Bilirubin; BCLC: Barcelona Clinic Liver Cancer; CP: Child-Pugh; EHD: extrahepatic disease; NLR: neutrophil-lymphocyte ratio; PS: performance status; PVT: portal vein thrombosis.

	IMMUNOTOXICITY 111 (13.5%)	NO IMMUNOTOXICITY 712 (86.5%)	P	HYPOTHYROIDISM 44 (5.3%)	NO HYPOTHYROIDISM 779 (94.6%)	P
MALE	83 (74.8%)	574 (80.6%)	0.16	36 (81.8%)	621 (79.7%)	0.85
FEMALE	28 (25.2%)	138 (19.4%)		8 (18.2%)	158 (20.3%)	
≤ 70	46 (41.4%)	293 (41.1%)	1.00	15 (34.1%)	324 (41.6%)	0.35
> 70	65 (58.5%)	419 (58.8%)		29 (65.9%)	455 (58.4%)	
VIRAL	60 (54.0%)	382 (53.6%)	1.00	25 (56.8%)	417 (53.5%)	0.76
NO VIRAL	51 (45.9%)	330 (46.3%)		19 (43.2%)	362 (46.5%)	
AT LEAST ONE LOCAL THERAPY	73 (65.8%)	496 (69.7%)	0.24	35 (79.5%)	534 (68.5%)	0.48
NO LOCAL THERAPY	33 (29.7%)	172 (24.1%)		9 (20.4%)	196 (25.2%)	
CP A	103 (92.8%)	666 (93.5%)	0.68	44 (100.0%)	725 (93.1%)	0.11
CP B	8 (7.2%)	46 (6.5%)		0 (0.0%)	54 (6.9%)	
BCLC B	38 (34.2%)	297 (41.7%)	0.15	22 (50.0%)	313 (40.2%)	0.21
BCLC C	73 (65.8%)	415 (58.3%)		22 (50.0%)	466 (59.8%)	
PS 0	107 (96.4%)	698 (98.0%)	0.29	31 (70.4%)	584 (75.0%)	0.48
PS ≥ 1	4 (3.6%)	14 (2.0%)		13 (29.5%)	195 (25.0%)	
PVT	29 (26.1%)	146 (20.5%)	0.21	6 (13.6%)	169 (21.7%)	0.26
NO PVT	82 (73.9%)	566 (79.5%)		38 (86.4%)	610 (78.3%)	
AFP < 400 ng/mL	83 (74.8%)	495 (69.5%)	0.26	37 (84.1%)	541 (69.4%)	0.06
AFP ≥ 400 ng/mL	27 (24.3%)	213 (29.9%)		7 (15.9%)	233 (29.9%)	
EHD	43 (38.7%)	262 (36.8%)	0.75	12 (27.3%)	293 (37.6%)	0.20
NO EHD	68 (61.3%)	449 (63.1%)		32 (72.7%)	485 (62.2%)	
ALBI 1	100 (90.1%)	652 (91.6%)	0.45	42 (95.4%)	710 (91.1%)	0.57
ALBI 2	11 (9.9%)	55 (7.7%)		2 (4.5%)	64 (8.2%)	
NLR ≤ 3	33 (29.7%)	402 (56.5%)	0.12	21 (47.7%)	414 (53.1%)	1.00
NLR > 3	34 (30.6%)	270 (37.9%)		14 (31.8%)	290 (3.7%)	

Supplementary Table 2. Baseline characteristics of patients presenting and not presenting immunotoxicity and of patients presenting and not presenting hypothyroidism. AFP: alpha-feto-protein; ALBI: Albumin-Bilirubin; BCLC: Barcelona Clinic Liver Cancer; CP: Child-Pugh; EHD: extrahepatic disease; NLR: neutrophil-lymphocyte ratio; PS: performance status; PVT: portal vein thrombosis.

	DECREASED APPETITE 176 (13.5%)	NO DECREASED APPETITE 647 (86.5%)	P	FATIGUE 214 (26.0%)	NO FATIGUE 609 (74.0%)	P
MALE	141 (80.1%)	516 (79.7%)	1.00	169 (79.0%)	488 (80.1%)	0.77
FEMALE	35 (19.9%)	131 (20.2%)		45 (21.0%)	121 (19.9%)	
≤ 70	65 (36.9%)	274 (42.3%)	0.23	89 (41.6%)	250 (41.0%)	0.93
> 70	111 (63.1%)	373 (57.6%)		125 (58.4%)	359 (58.9%)	
VIRAL	77 (43.7%)	365 (56.4%)	<0.01	111 (51.9%)	331 (54.3%)	0.58
NO VIRAL	99 (56.2%)	282 (43.6%)		103 (48.1%)	278 (45.6%)	
AT LEAST ONE LOCAL THERAPY	113 (64.2%)	456 (70.5%)	0.76	144 (67.3%)	425 (69.8%)	0.57
NO LOCAL THERAPY	43 (24.4%)	162 (25.0%)		47 (22.0%)	158 (25.9%)	
CP A	162 (92.0%)	607 (93.8%)	0.39	199 (93.0%)	570 (93.6%)	0.75
CP B	14 (7.9%)	40 (6.2%)		15 (7.0%)	39 (6.4%)	
BCLC B	59 (33.5%)	276 (42.6%)	0.03	76 (35.5%)	259 (42.5%)	0.07
BCLC C	117 (66.5%)	371 (57.3%)		138 (64.5%)	350 (57.5%)	
PS 0	116 (65.9%)	499 (77.1%)	<0.01	150 (70.1%)	465 (76.3%)	0.08
PS ≥ 1	60 (34.1%)	148 (22.9%)		64 (29.9%)	144 (23.6%)	
PVT	42 (23.8%)	133 (20.5%)	0.35	57 (26.6%)	118 (19.4%)	0.03
NO PVT	134 (76.1%)	514 (79.4%)		157 (73.4%)	491 (80.6%)	
AFP < 400 ng/mL	116 (65.9%)	462 (71.4%)	0.13	150 (70.1%)	428 (70.3%)	0.86
AFP ≥ 400 ng/mL	60 (34.1%)	180 (27.8%)		64 (29.9%)	176 (28.9%)	
EHD	69 (39.2%)	236 (36.5%)	0.54	80 (37.4%)	225 (36.9%)	0.93
NO EHD	107 (60.8%)	410 (63.4%)		134 (62.6%)	383 (62.9%)	
ALBI 1	160 (90.9%)	592 (91.5%)	1.00	198 (92.5%)	554 (91.0%)	0.46
ALBI 2	14 (7.9%)	52 (8.0%)		14 (6.5%)	52 (8.5%)	
NLR ≤ 3	89 (50.6%)	346 (53.5%)	0.07	105 (49.1%)	330 (54.2%)	0.05
NLR > 3	80 (45.4%)	224 (34.6%)		93 (43.4%)	211 (34.6%)	

Supplementary Table 3. Baseline characteristics of patients presenting and not presenting decreased appetite and of patients presenting and not presenting fatigue. AFP: alpha-feto-protein; ALBI: Albumin-Bilirubin; BCLC: Barcelona Clinic Liver Cancer; CP: Child-Pugh; EHD: extrahepatic disease; NLR: neutrophil-lymphocyte ratio; PS: performance status; PVT: portal vein thrombosis.