Supplementary material

Supplementary Table 1. Description of analysed SNPs

Gene	SNP	Reported associations [ref]
VEGF	rs3025039	Risk of preeclampsia[1]; Risk of diabetic macular edema[2]; Risk of recurrent pregnancy losses[3,4]
	rs2010963	
	rs1570360	
	rs699947	
AGT	rs699	Risk of essential hypertension[5]
	rs4762	
PLA2G12A	rs2285714	Response to anti-angiogenesis in patients with age-related macular degeneration[6]
IL-18	rs1946519	Risk of acute myocardial infarction[7]
	rs360717	
	rs1834481	
	rs3882891	
AT1R	rs5186	Idiopathic recurrent spontaneous abortions[8]
ANGPT2	rs2442598	Vascular disorders[9]
TNF-alpha	rs1800629	Risk of dilated cardiomyopathy[10]; risk of HCC[11]; susceptibility to Chron's disease[12] or rheumatoid arthritis[13]
	rs1799724	
GNB3	rs5443	Stroke[14]; Hypertension[15]
IL-6	rs1800795	Coronary artery disease[16]; Diabetes mellitus[17]; risk of vasculitis[18]; susceptibility to liver diseases[19]
	rs1800797	
IL-23R	rs11209026	Risk of Crohn's disease and ulcerative colitis[20]; Immune-mediated diseases[21]; Primary immune thrombocytopenia[22]
	rs1884444	
	rs10889677	
	rs6682925	
IL-17	rs763780	HBV Infection[23]; response to biological drugs in psoriasis[24]; risk of cancer development[25]
	rs2275913	
FOXP3	rs3761549	

	rs3761548	Susceptibility to cancer[26];
	rs2280883	autoimmune disease susceptibility[27]; HBV-related HCC in China[28]

Supplementary Table 2. List of used assays.

SNP	Gene	Assay
rs 3025039	VEGF	C_16198794_10
rs 2010963	VEGF	C_8311614_10
rs 1570360	VEGF	C_1647379_10
rs 699947	VEGF	C_8311602_10
rs 699	AGT1	C_1985481_20
rs 4762	AGT2	C_1985480_20
rs 2285714	PLA2G12A	C_22271984_20
rs 1946519	IL-18	C_2898459_20
rs 360717	IL-18	C_2898462_10
rs 1834481	IL-18	C_2898467_30
rs 3882891	IL-18	C_12078232_10
rs 5186	AT1R	C_3187716_10
rs 2442598	ANGPT2	C_15803341_10
rs 1800629	TNF-a	C_7514879_10
rs 1799724	TNF-a	C_11918223_10
rs 5443	GNB3	C_21844734_10
rs 1800795	IL-6	C_1839697_20
rs 1800797	IL-6	C_1839695_20
rs 11209026	IL-23R	C_1272298_10
rs 1884444	IL-23R	C_11728603_10
rs 10889677	IL-23R	C_11283764_10
rs 6682925	IL-23R	C_1272359_10
rs 763780	IL-17	C_2234166_10
rs 2275913	IL-17	C_15879983_10
rs 3761549	FOXP3	C_27058744_10
rs 3761548	FOXP3	C_27476877_10
rs 2280883	FOXP3	C_15874601_20

Supplementary Table 3. Description of polymorphisms in BCLC cohort. Training cohort.

Label	Variable	Category	Total cohort, n=82*
SNP_1_rs11209026_IL23R	SNP_1_rs11209026_IL23R	AA	2 (2.4)
		AG	10 (12.2)
		GG	70 (85.4)
SNP_2_rs1884444_IL23R	SNP_2_rs1884444_IL23R	GG	16 (19.5)
		GT	44 (53.7)
		TT	22 (26.8)
SNP_3_rs10889677_IL23R	SNP_3_rs10889677_IL23R	AA	7 (8.5)
		AC	34 (41.5)
		CC	41 (50.0)
SNP_4_rs6682925_IL23R	SNP_4_rs6682925_IL23R	CC	16 (19.5)
		CT	43 (52.4)
		TT	23 (28.0)
SNP_5_rs763780_IL17	SNP_5_rs763780_IL17	CT	7 (8.5)
		TT	75 (91.5)
SNP_6_rs2275913_IL17	SNP_6_rs2275913_IL17	AA	13 (15.9)
		AG	32 (39.0)
		GG	37 (45.1)
SNP_7_rs3761549_FOXP3	SNP_7_rs3761549_FOXP3	AA	7 (8.5)
		GG	75 (91.5)
SNP_8_rs3761548_FOXP3	SNP_8_rs3761548_FOXP3	TT	38 (46.3)
		TG	5 (6.1)
		GG	39 (47.6)
SNP_9_rs2280883_FOXP3	SNP_9_rs2280883_FOXP3	CC	42 (51.2)
		TC	6 (7.3)
		TT	34 (41.5)
VEGF +936C/T	rs3025039 VEGF	CC	68 (82.9)
		CT	14 (17.1)
VEGF -634G/C	rs2010963 VEGF	CC	5 (6.1)
		CG	39 (47.6)
		GG	38 (46.3)
VEGF -1154G/A	rs1570360 VEGF	AA	19 (23.2)
		AG	29 (35.4)
		GG	34 (41.5)
VEGF -2578C/A	rs699947 VEGF	AA	17 (20.7)
		AC	45 (54.9)
		CC	20 (24.4)
AGT M235T	rs699 AGT	AA	26 (31.7)
		AG	34 (41.5)
		GG	22 (26.8)
AGT T174M	rs4762 AGT	AA	5 (6.1)
		AG	16 (19.5)
		GG	61 (74.4)
PLA2G12A C/T	rs2285714 PLA2G12A	CC	34 (41.5)
		CT	42 (51.2)

		TT	6 (7.3)
IL-8 A/C	rs1946519 IL-8	AA	13 (15.9)
		AG	41 (50.0)
		GG	28 (34.1)
IL-8 A/G	rs360717 IL-8	AA	8 (9.8)
		AG	28 (34.1)
		GG	46 (56.1)
IL-8 C/G	rs1834481 IL-8	CC	47 (57.3)
		CG	26 (31.7)
		GG	9 (11.0)
IL-8 G/T	rs3882891 IL-8	GG	16 (19.5)
		GT	40 (48.8)
		TT	26 (31.7)
AT1R 1166A/C	rs5186 AT1R	AA	40 (48.8)
		AC	35 (42.7)
		CC	7 (8.5)
ANGPT2 C/T	rs2442598 ANGPT2	CC	53 (64.6)
		CT	24 (29.3)
		TT	5 (6.1)
G308A TNF-a	rs1800629 TNF-a	AA	1 (1.2)
		AG	24 (29.3)
		GG	57 (69.5)
C857T TNF-a	rs1799724 TNF-a	CC	63 (76.8)
		CT	18 (22.0)
		TT	1 (1.2)
GNB3 C825T	rs5443 GNB3	CC	25 (30.5)
		CT	43 (52.4)
		TT	14 (17.1)
IL-6 -174G/C	rs1800795 IL-6	CC	13 (15.9)
		CG	32 (39.0)
		GG	37 (45.1)
IL-6 -597A/G	rs1800797 IL-6	AA	12 (14.6)
		AG	32 (39.0)
		GG	38 (46.3)

*Expressed as absolute frequency (%).

Supplementary Table 4. distribution of patients with history of diabetes and arterial hypertension (AHT) who developed or not eDAE or DAE in each cohort.

Cohort	DAE	AHT		DM	
		No	Yes	No	Yes
BCLC1 cohort	No	27 (67.5)	13 (32.5)	29 (72.5)	11 (27.5)
	Yes	18 (42.9)	24 (57.1)	31 (72.8)	11 (26.2)
BCLC2 cohort	No	29 (56.9)	22 (43.1)	31 (60.8)	20 (39.2)
	Yes	14 (50)	14 (50)	20 (71.4)	8 (28.6)
Northern Italy cohort	No	131 (69.3)	58 (30.7)	142 (75.1)	47 (24.9)
	Yes	25 (78.1)	7 (21.9)	18 (56.3)	14 (43.8)
Naples cohort	No	18 (42.9)	24 (57.1)	27 (64.3)	15 (35.7)
	Yes	6 (22.2)	21 (77.8)	19 (70.4)	8 (29.6)
BCLC1 cohort + BCLC2 Cohort + Naples Cohort	No	74 (55.6)	59 (44.4)	87 (65.4)	46 (34.6)
	Yes	38 (39.2)	59 (60.8)	70 (72.2)	27 (27.8)

Cohort	eDAE	AHT		DM	
		No	Yes	No	Yes
BCLC1 cohort	No	29 (59.2)	20 (40.8)	34 (69.4)	15 (30.6)
	Yes	16 (48.5)	17 (51.5)	26 (78.8)	7 (21.2)
BCLC2 cohort	No	30 (52.6)	27 (47.4)	33 (57.9)	24 (42.1)
	Yes	13 (59.1)	9 (40.9)	18 (81.8)	4 (18.2)
Northern Italy cohort	No	133 (68.9)	60 (31.1)	144 (74.6)	49 (25.4)
	Yes	23 (82.1)	5 (17.9)	16 (57.1)	12 (42.9)
Naples cohort	No	19 (43.2)	25 (56.8)	29 (65.9)	15 (34.1)
	Yes	5 (20)	20 (80)	17 (68)	8 (32)
BCLC1 cohort + BCLC2 Cohort + Naples Cohort	No	78 (52)	72 (48)	96 (64)	54 (36)
	Yes	34 (42.5)	46 (57.5)	61 (76.3)	19 (23.7)

DAE: Dermatologic Adverse Events; eDAE: early Dermatologic Adverse Events; AHT: Arterial Hypertension; DM: Diabetes Mellitus.

Supplementary Table 5. Association between DAE and AHT in each cohort.

	Cohort	DAE		eDAE	
		HR (95%CI)	p-value	HR (95%CI)	p-value
AHT (Yes vs No)	All patients	**1.61 (1.14 - 2.28)**	**0.007**	1.31 (0.90 - 1.92)	0.16
	BCLC1 cohort	**1.96 (1.05 - 3.65)**	**0.04**	1.34 (0.67 - 2.65)	0.4
	BCLC2 cohort	1.12 (0.53 - 2.34)	0.8	0.77 (0.33 - 1.79)	0.5
	Northern Italy cohort	0.63 (0.27 - 1.46)	0.3	0.5 (0.19 - 1.31)	0.5
	Naples cohort	2.31 (0.93 - 5.73)	0.07	2.59 (0.97 - 6.91)	0.06
	BCLC1 cohort + BCLC2 Cohort + Naples Cohort	**1.62 (1.07 - 2.44)**	**0.02**	1.31 (0.84 - 2.04)	0.2
DM (Yes vs No)	All patients	1.09 (0.75 - 1.58)	0.6	0.9 (0.6 - 1.37)	0.6
	BCLC1 cohort	0.84 (0.42 - 1.67)	0.6	0.64 (0.28 - 1.48)	0.3
	BCLC2 cohort	0.59 (0.26 - 1.33)	0.2	0.34 (0.12 - 1.01)	0.052
	Northern Italy cohort	**2.25 (1.12 - 4.54)**	**0.02**	1.83 (0.85 - 3.95)	0.13
	Naples cohort	0.74 (0.33 - 1.71)	0.5	0.86 (0.37 - 1.99)	0.7
	BCLC1 cohort + BCLC2 Cohort + Naples Cohort	0.71 (0.45 - 1.1)	0.12	**0.58 (0.35 - 0.98)**	**0.04**

DAE: Dermatologic Adverse Events; eDAE: early Dermatologic Adverse Events; AHT: Arterial Hypertension; DM: Diabetes Mellitus.

Supplementary table 6. Cox regression models for Exitus by AGT1 (rs699)

Center	AGT1 (rs699)	HR (95%CI)	p-value	HR (95%CI) adjusted by BCLC + ECOG-PS	p-value	HR (95%CI) adjusted by BCLC + ECOG-PS + AHT + DM	p-value	HR (95%CI) adjusted by AHT + DM	p-value	HR (95%CI) adjusted by DM	p-value	HR (95%CI) adjusted by AHT	p-value
BCLC1 cohort	AA vs AG	0.6 (0.35-1.04)	0.07	0.59 (0.34-1.03)	0.06	0.53 (0.3 -0.94)	0.03	0.54 (0.31-0.96)	0.04	0.58 (0.33-1.01)	0.052	0.55 (0.31-0.97)	0.04
	AA vs GG	0.87 (0.47-1.6)	0.7	0.88 (0.48-1.63)	0.7	0.8 (0.42 -1.5)	0.5	0.79 (0.42-1.48)	0.5	0.83 (0.45-1.54)	0.6	0.79 (0.42-1.49)	0.5
	AG vs GG	1.44 (0.82-2.56)	0.2	1.48 (0.83-2.66)	0.2	1.51 (0.84 -2.7)	0.17	1.44 (0.82-2.56)	0.2	1.44 (0.81-2.55)	0.2	1.45 (0.82-2.57)	0.2
BCLC2 cohort	AA vs AG	1.13 (0.57-2.23)	0.7	1.11 (0.56-2.21)	0.8	1.13 (0.56 -2.24)	0.8	1.14 (0.58-2.24)	0.7	1.14 (0.58-2.25)	0.7	1.14 (0.58-2.25)	0.7
	AA vs GG	0.58 (0.27-1.23)	0.2	0.64 (0.27-1.51)	0.3	0.67 (0.28 -1.61)	0.4	0.59 (0.28-1.24)	0.16	0.59 (0.28-1.24)	0.17	0.58 (0.27-1.23)	0.16
	AG vs GG	0.51 (0.25-1.04)	0.07	0.57 (0.26-1.28)	0.2	0.6 (0.27 -1.34)	0.2	0.52 (0.25-1.05)	0.07	0.51 (0.25-1.05)	0.07	0.51 (0.25-1.04)	0.06
Northern Italy cohort	AA vs AG	1 (0.71-1.43)	0.9	1.06 (0.75-1.51)	0.7	1.01 (0.72 -1.41)	0.9	0.97 (0.69-1.35)	0.9	0.98 (0.7- 1.38)	0.9	0.95 (0.68-1.33)	0.8
	AA vs GG	0.86 (0.57-1.32)	0.5	0.9 (0.59-1.37)	0.6	0.81 (0.53 -1.24)	0.3	0.77 (0.5- 1.17)	0.2	0.81 (0.54-1.22)	0.3	0.77 (0.5- 1.17)	0.2
	AG vs GG	0.86 (0.57-1.29)	0.5	0.84 (0.56-1.27)	0.4	0.8 (0.54 -1.19)	0.3	0.8 (0.54- 1.18)	0.3	0.82 (0.56-1.21)	0.3	0.8 (0.55- 1.19)	0.3
Naples cohort	AA vs AG	0.81 (0.45-1.44)	0.5	0.84 (0.46-1.51)	0.6	0.77 (0.41 -1.44)	0.4	0.75 (0.41-1.37)	0.4	0.79 (0.43-1.42)	0.4	0.76 (0.42-1.37)	0.3
	AA vs GG	1 (0.42-2.39)	0.9	1.1 (0.44-2.76)	0.9	0.99 (0.39 -2.54)	0.9	0.95 (0.4- 2.28)	0.9	0.99 (0.41-2.36)	0.9	0.95 (0.4- 2.29)	0.9
	AG vs GG	1.24 (0.54-2.83)	0.6	1.31 (0.56-3.06)	0.5	1.29 (0.55 -3.01)	0.6	1.26 (0.55-2.89)	0.6	1.26 (0.55-2.89)	0.6	1.25 (0.55-2.86)	0.6
BCLC2 cohort + Naples cohort + Northern Italy cohort	AA vs AG	0.97 (0.74-1.26)	0.8	0.99 (0.76-1.29)	0.9	0.99 (0.76-1.29)	0.9	0.97 (0.74-1.26)	0.8	0.97 (0.75-1.27)	0.9	0.96 (0.73-1.25)	0.8
	AA vs GG	0.78 (0.56-1.09)	0.15	0.82 (0.59-1.15)	0.3	0.81 (0.58 -1.14)	0.2	0.77 (0.55-1.08)	0.13	0.78 (0.56-1.09)	0.15	0.77 (0.55-1.07)	0.12
	AG vs GG	0.81 (0.6-1.11)	0.2	0.83 (0.61-1.14)	0.2	0.82 (0.6 -1.12)	0.2	0.8 (0.58- 1.09)	0.15	0.8 (0.59- 1.1)	0.17	0.8 (0.59- 1.09)	0.16
BCLC1 cohort + Naples cohort + Northern Italy cohort	AA vs AG	0.86 (0.66-1.1)	0.2	0.88 (0.68-1.14)	0.3	0.87 (0.67 -1.12)	0.3	0.85 (0.66-1.1)	0.2	0.86 (0.67-1.11)	0.3	0.84 (0.65-1.09)	0.18
	AA vs GG	0.88 (0.65-1.21)	0.4	0.88 (0.64-1.2)	0.4	0.84 (0.61 -1.16)	0.3	0.85 (0.62-1.17)	0.3	0.87 (0.64-1.2)	0.4	0.85 (0.62-1.17)	0.3
	AG vs GG	1.03 (0.77-1.38)	0.8	1 (0.74-1.34)	0.9	0.97 (0.72 -1.3)	0.8	1 (0.75 -1.35)	0.9	1.01 (0.76-1.36)	0.9	1.01 (0.75-1.36)	0.9
BCLC1 cohort + BCLC2 cohort + Naples cohort	AA vs AG	0.79 (0.56-1.11)	0.17	0.78 (0.55-1.09)	0.15	0.77 (0.54 -1.08)	0.13	0.78 (0.55-1.09)	0.15	0.79 (0.56-1.11)	0.17	0.78 (0.55-1.1)	0.15
	AA vs GG	0.85 (0.57-1.28)	0.4	0.81 (0.54-1.23)	0.3	0.8 (0.53 -1.22)	0.3	0.84 (0.55-1.26)	0.4	0.85 (0.56-1.28)	0.4	0.84 (0.55-1.26)	0.4
	AG vs GG	1.08 /0.74-1.58)	0.7	1.05 (0.71-1.54)	0.8	1.05 (0.71 -1.55)	0.8	1.08 (0.73-1.58)	0.7	1.08 (0.73-1.59)	0.7	1.07 (0.73-1.58)	0.7

BCLC: Barcelona Clinic Liver Cancer; ECOG-PS: Eastern Cooperative Oncology Group Performance Status; AHT: Arterial Hypertension; DM: Diabetes Mellitus.

Supplementary table 7. Cox regression models for Exitus by AGT2 (rs4762)

Center	AGT2 (rs4762)	HR (95%CI)	p-value	HR (95%CI) adjusted by BCLC + ECOG-PS	p-value	HR (95%CI) adjusted by BCLC + ECOG-PS + AHT + DM	p-value	HR (95%CI) adjusted by AHT + DM	p-value	HR (95%CI) adjusted by DM	p-value	HR (95%CI) adjusted by AHT	p-value
BCLC1 cohort	AA vs AG	0.59 (0.21-1.65)	0.3	0.56 (0.2-1.59)	0.3	0.52 (0.18 -1.5)	0.2	0.56 (0.2- 1.58)	0.3	0.57 (0.2- 1.59)	0.3	0.58 (0.21-1.62)	0.3
	AA vs GG	0.84 (0.33-2.11)	0.7	0.77 (0.31-1.96)	0.6	0.77 (0.3 -1.98)	0.6	0.85 (0.34-2.16)	0.8	0.83 (0.33-2.09)	0.7	0.87 (0.35-2.2)	0.8
	AG vs GG	1.41 (0.79-2.51)	0.2	1.38 (0.76-2.51)	0.3	1.48 (0.8 -2.73)	0.2	1.52 (0.84-2.74)	0.17	1.47 (0.82-2.63)	0.2	1.5 (0.83- 2.72)	0.18
BCLC2 cohort	AA vs AG	0.87 (0.1-7.55)	0.9	1.4 (0.15-13.04)	0.8	1.22 (0.13 -11.39)	0.9	0.8 (0.09- 7.01)	0.9	0.82 (0.09-7.12)	0.9	0.88 (0.1- 7.58)	0.9
	AA vs GG	0.48 (0.07-3.47)	0.5	0.51 (0.07-3.77)	0.5	0.49 (0.07 -3.61)	0.5	0.46 (0.06-3.35)	0.5	0.46 (0.06-3.39)	0.4	0.48 (0.07-3.5)	0.5
	AG vs GG	0.55 (0.21-1.4)	0.2	0.37 (0.13-1.06)	0.06	0.4 (0.14 -1.15)	0.09	0.57 (0.22-1.47)	0.2	0.57 (0.22-1.46)	0.2	0.55 (0.21-1.4)	0.2
Northern Italy cohort	AA vs AG	0.59 (0.14-2.44)	0.5	0.45 (0.11-1.9)	0.3	0.48 (0.11 -2.02)	0.3	0.57 (0.14-2.38)	0.5	0.58 (0.14-2.42)	0.5	0.58 (0.14-2.43)	0.5
	AA vs GG	0.66 (0.16-2.67)	0.6	0.46 (0.11-1.9)	0.3	0.5 (0.12 -2.06)	0.3	0.68 (0.17-2.75)	0.6	0.67 (0.17-2.72)	0.6	0.68 (0.17-2.73)	0.6
	AG vs GG	1.13 (0.78-1.62)	0.5	1.02 (0.71-1.49)	0.9	1.04 (0.72 -1.52)	0.8	1.19 (0.82-1.73)	0.4	1.16 (0.8- 1.67)	0.4	1.16 (0.8- 1.68)	0.4
Naples cohort	AG vs GG	0.85 (0.44-1.64)	0.6	0.85 (0.44-1.64)	0.6	0.87 (0.45 -1.69)	0.7	0.87 (0.45-1.7)	0.7	0.85 (0.44-1.64)	0.6	0.87 (0.45-1.7)	0.7
BCLC2 cohort + Naples cohort + Northern Italy cohort	AA vs AG	0.63 (0.26-1.52)	0.3	0.63 (0.26-1.53)	0.3	0.5 (0.15 -1.6)	0.2	0.52 (0.16-1.68)	0.3	0.53 (0.16-1.68)	0.3	0.52 (0.16-1.67)	0.3
	AA vs GG	0.62 (0.27-1.4)	0.2	0.61 (0.27-1.39)	0.2	0.45 (0.14 -1.42)	0.17	0.52 (0.17-1.62)	0.3	0.52 (0.17-1.62)	0.3	0.52 (0.17-1.61)	0.3
	AG vs GG	0.98 (0.66-1.44)	0.9	0.97 (0.65-1.44)	0.9	0.91 (0.67 -1.23)	0.5	0.99 (0.73-1.34)	0.9	0.99 (0.73-1.34)	0.9	0.99 (0.73-1.34)	0.9
BCLC1 cohort + Naples cohort + Northern Italy cohort	AA vs AG	0.63 (0.29-1.38)	0.2	0.61 (0.28-1.34)	0.2	0.6 (0.28 -1.33)	0.2	0.61 (0.28-1.34)	0.2	0.61 (0.28-1.34)	0.2	0.63 (0.29-1.38)	0.3
	AA vs GG	0.71 (0.33-1.5)	0.4	0.67 (0.31-1.42)	0.3	0.68 (0.32 -1.45)	0.3	0.71 (0.34-1.51)	0.4	0.71 (0.33-1.5)	0.4	0.72 (0.34-1.54)	0.4
	AG vs GG	1.13 (0.85-1.49)	0.4	1.09 (0.82-1.45)	0.6	1.12 (0.85 -1.49)	0.4	1.17 (0.88-1.55)	0.3	1.16 (0.87-1.53)	0.3	1.15 (0.87-1.52)	0.3
BCLC1 cohort + BCLC2 cohort + Naples cohort	AA vs AG	0.63 (0.26-1.52)	0.3	0.63 (0.26-1.53)	0.3	0.64 (0.26 -1.54)	0.3	0.64 (0.26-1.53)	0.3	0.63 (0.26-1.52)	0.3	0.63 (0.26-1.53)	0.3
	AA vs GG	0.62 (0.27-1.4)	0.2	0.61 (0.27-1.39)	0.2	0.62 (0.27 -1.4)	0.3	0.62 (0.27-1.41)	0.3	0.62 (0.27-1.4)	0.2	0.62 (0.27-1.41)	0.3
	AG vs GG	0.98 (0.66-1.44)	0.9	0.97 (0.65-1.44)	0.9	0.97 (0.65 -1.44)	0.9	0.98 (0.66-1.45)	0.9	0.98 (0.66-1.44)	0.9	0.98 (0.66-1.45)	0.9

BCLC: Barcelona Clinic Liver Cancer; ECOG-PS: Eastern Cooperative Oncology Group Performance Status; AHT: Arterial Hypertension; DM: Diabetes Mellitus.

Supplementary Table 8. Impact of IEACA medication on training and BCLC validation cohorts.

Event	Cohort	Adjusting factor	HR for IECAS medication (95%CI)	p-value
Death	BCLC1 cohort	none	0.96 (0.58 - 1.6)	0.9
		BCLC + ECOG-PS + DM	0.96 (0.57 - 1.63)	0.9
		BCLC + ECOG-PS + DM + AHT	1.04 (0.58 - 1.86)	0.9
	BCLC2 cohort	none	1.02 (0.47 - 2.22)	0.95
		BCLC + ECOG-PS + DM	1.02 (0.46 - 2.26)	0.95
		BCLC + ECOG-PS + DM + AHT	1.06 (0.44 - 2.54)	0.9
	BCLC1 & BCLC2 cohorts	none	0.98 (0.65 - 1.49)	0.9
		BCLC + ECOG-PS + DM	1 (0.66 - 1.53)	0.98
		BCLC + ECOG-PS + DM + AHT	1.07 (0.67 - 1.70)	0.8
eDAE	BCLC1 cohort	none	0.61 (0.3 - 1.26)	0.18
		BCLC + ECOG-PS + DM	0.54 (0.256 - 1.12)	0.1
		BCLC + ECOG-PS + DM + AHT	0.63 (0.27 - 1.47)	0.3
	BCLC2 cohort	none	0.71 (0.26 - 1.93)	0.5
		BCLC + ECOG-PS + DM	0.72 (0.26 - 2.04)	0.5
		BCLC + ECOG-PS + DM + AHT	0.70 (0.22 - 2.27)	0.6
	BCLC1 & BCLC2 cohorts	none	0.62 (0.35 - 1.11)	0.11
		BCLC + ECOG-PS + DM	0.6 (0.33 - 1.07)	0.08
		BCLC + ECOG-PS + DM + AHT	0.64 (0.33 - 1.25)	0.2
DAE	BCLC1 cohort	none	0.64 (0.34 - 1.22)	0.18
		BCLC + ECOG-PS + DM	0.59 (0.31 - 1.14)	0.11
		BCLC + ECOG-PS + DM + AHT	0.88 (0.42 - 1.82)	0.7
	BCLC2 cohort	none	0.76 (0.31 - 1.87)	0.6
		BCLC + ECOG-PS + DM	0.79 (0.31 - 1.99)	0.6
		BCLC + ECOG-PS + DM + AHT	0.92 (0.33 - 2.55)	0.9
	BCLC1 & BCLC2 cohorts	none	0.65 (0.38 - 1.09)	0.1
		BCLC + ECOG-PS + DM	0.63 (0.37 - 1.06)	0.08
		BCLC + ECOG-PS + DM + AHT	0.82 (0.46 - 1.49)	0.5

DAE: Dermatologic Adverse Events; eDAE: early Dermatologic Adverse Events; BCLC: Barcelona Clinic Liver Cancer; ECOG-PS: Eastern Cooperative Oncology Group Performance Status; AHT: Arterial Hypertension; DM: Diabetes Mellitus.

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