Nivolumab in advanced hepatocellular carcinoma: sorafenib-experienced Asian cohort analysis

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Table S1. Patient demographic and baseline disease characteristics of the sorafenib-experienced non-Asian and Asian patients study stratified by response to nivolumab treatment.

	Non-Asian patients (n = 97)			Asian patients (n = 85)		
	All	Responders	Non-responders	All	Responders	Non-responders
Median age (range), years	–	62 (34–77)	64 (19–81)	–	62 (39–78)	62 (22–81)
Male, n (%)	74 (76)	10 (77)	64 (76)	65 (76)	11 (85)	54 (75)
Race, n (%)						
Asian	6 (6)	0	6 (7)	85 (100)	13 (100)	72 (100)
Asian Indian	0	0	0	1 (1)	0	1 (1)
Chinese	4 (4)	0	4 (5)	45 (53)	7 (54)	38 (53)
Japanese	0	0	0	25 (29)	4 (31)	21 (29)
Korean	0	0	0	13 (15)	2 (15)	11 (15)
Other Asian	2 (2)	0	2 (2)	1 (1)	0	1 (1)
White	87 (90)	12 (92)	75 (89)	0	0	0
Black	4 (4)	1 (8)	3 (4)	0	0	0
BCLC stage, n (%)						
B	12 (12)	0	12 (14)	5 (6)	1 (8)	4 (6)
C	82 (85)	12 (92)	70 (83)	80 (94)	12 (92)	68 (94)
Extrahepatic metastases, n (%)	59 (61)	7 (54)	52 (62)	70 (82)	10 (77)	60 (83)
Vascular invasion, n (%)	31 (32)	6 (46)	25 (30)	24 (28)	4 (31)	20 (28)
Child–Pugh score of 5–6, n (%)	96 (99)	12 (92)	84 (100)	84 (99)	13 (100)	71 (99)
AFP ≥400 µg/L, n (%)[*]	30 (31)	4 (31)	26 (31)	37 (44)	9 (69)	28 (39)
Prior therapy, n (%)						
Surgical resection	56 (58)	6 (46)	50 (60)	66 (78)	12 (92)	54 (75)
Radiotherapy	22 (23)	2 (15)	20 (24)	23 (27)	4 (31)	19 (26)
Local treatment for HCC	40 (41)	6 (46)	34 (40)	64 (75)	10 (77)	54 (75)
Sorafenib	97 (100)	13 (100)	84 (100)	85 (100)	13 (100)	72 (100)
Reason for sorafenib discontinuation[†]						
Disease progression	69 (71)	9 (69)	60 (71)	66 (78)	10 (77)	56 (78)
Toxicity	23 (24)	3 (23)	20 (24)	16 (19)	3 (23)	13 (18)
Other	6 (6)	1 (8)	5 (6)	4 (5)	0 (0)	4 (6)
Number of prior therapies, n (%)						
1	86 (89)	13 (100)	73 (87)	55 (65)	11 (85)	44 (61)
2	6 (6)	0	6 (7)	14 (16)	1 (8)	13 (18)
≥3	5 (5)	0	5 (6)	16 (19)	1 (8)	15 (21)

AFP, alpha-fetoprotein; BCLC, Barcelona Clinic Liver Cancer; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ITT, intent-to-treat.

[*]AFP data were not available in 5 patients in the ITT population and in 1 patient in the Asian cohort.

[†]Some patients had more than one reason for sorafenib discontinuation.

Table S2. Antitumor activity of the sorafenib-experienced ITT population, and Asian and non-Asian cohorts.

	ITT population (n = 182)	Non-Asian cohort (n = 97)	Asian cohort (n = 85)
ORR by RECIST v1.1, n (%)[*,†,‡]	26 (14)	13 (13)	13 (15)
CR	5 (3)	2 (2)	3 (4)
PR	21 (12)	11 (11)	10 (12)
SD, n (%)[†,δ]	72 (40)	43 (44)	29 (34)
PD, n (%)[†]	70 (38)	30 (31)	40 (47)
DCR, n (%)[†,]	100 (55)	58 (60)	42 (49)
KM Median DOR (95% CI), months[†]	19.4 (9.7–NE)	NE (16.6–NE)	9.7 (5.6–NE)
ORR by mRECIST, n (%)[¶,‡,**]	33 (18)	13 (13)	20 (24)
CR	7 (4)	2 (2)	5 (6)
PR	26 (14)	11 (11)	15 (18)
SD[**,δ]	65 (36)	43 (44)	22 (26)
PD[**]	71 (39)	31 (32)	40 (47)

BICR, blinded independent central review; CI, confidence interval; CR, complete response; DCR, disease control rate; DOR, duration of response; ITT, intent-to-treat; mRECIST, modified RECIST; NE, not estimable; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

[*]Tumor responses were not evaluable in 12 patients in the ITT population, 3 patients in the Asian cohort and 9 patients in the non-Asian cohort.

[†]Reported by BICR using RECIST v1.1.

[‡]Defined as CR + PR.

[δ]Stable disease was reported as non-CR/non-PD in 2 patients in the ITT population and non-Asian cohort. DCR defined as CR + PR + SD.

[¶]Tumor responses were not evaluable in 11 patients in the ITT population, 3 patients in the Asian cohort, and 8 patients in the non-Asian cohort.

[**]Reported by BICR using mRECIST.

Table S3. Tumor response to nivolumab stratified by age in the sorafenib-experienced ITT population and Asian cohort.

	ITT population		Asian cohort	
	Age <65 (n = 104)	Age ≥65 (n = 78)	Age <65 (n = 54)	Age ≥65 (n = 31)
ORR, n (%)	15 (14)	11 (14)	8 (15)	5 (16)
DCR, n (%)	53 (51)	47 (60)	25 (46)	17 (55)
DOR, KM median (95% CI), months	19.4 (8.3–NE)	16.6 (8.3–NE)	11.2 (2.8–NE)	9.4 (3.2–NE)

CI, confidence interval; DCR, disease control rate; DOR, duration of response; ITT, intent-to-treat; NE, not estimable; ORR, objective response rate.

Table S4. Select adverse events in the sorafenib-experienced Asian cohort.

	Asian cohort							
	Uninfected (n = 24)		HBV (n = 47)		HCV (n = 14)		All (n = 85)	
	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
TRAEs, n (%)								
Skin[*]	11 (46)	0	17 (36)	1 (2)	4 (29)	0	32 (38)	1 (1)
Gastrointestinal[†]	2 (8)	0	5 (11)	1 (2)	2 (14)	0	9 (11)	1 (1)
Hypothyroidism	1 (4)	0	4 (8)	0	1 (7)	0	6 (7)	0
Hepatic	1 (4)	0	3 (6)	0	1 (7)	1 (7)	5 (6)	1 (1)
Adrenal insufficiency	0	0	2 (4)	1 (2)	0	0	2 (2)	1 (1)
Hyperthyroidism	1 (4)	0	0	0	0	0	1 (1)	0
Thyroiditis	0	0	1 (2)	0	0	0	1 (1)	0
Pneumonitis	1 (4)	0	0	0	0	0	1 (1)	0
Renal	0	0	1 (2)	0	0	0	1 (1)	0
Hypersensitivity/infusion-related reaction	0	0	1 (2)	0	0	0	1 (1)	0
Requiring immune-modulating therapy, n (%)								
Skin[‡]	7 (29)	0	7 (15)	1 (2)	4 (29)	0	18 (21)	1 (1)
Gastrointestinal[δ]	0	0	2 (4)	1 (2)	0	0	2 (2)	1 (1)
Adrenal insufficiency	0	0	2 (4)	0	0	0	2 (2)	0
Pneumonitis	1 (4)	0	0	0	0	0	1 (1)	0
Thyroiditis	0	0	1 (2)	0	0	0	1 (1)	0
Hypersensitivity/infusion-related reaction	0	0	1 (2)	0	0	0	1 (1)	0

Includes events reported between first dose and 30 days after last dose of study therapy. Event terms were reported by investigators and were not predefined.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; TRAE, treatment-related adverse event.

[*]Includes pruritus; rash; rash maculopapular; pruritus generalized; pemphigoid; rash pruritic.

[†]Includes diarrhea; colitis; enteritis.

[‡]Includes pruritus; rash; rash maculopapular; pemphigoid; rash pruritic.

[δ]Includes diarrhea.

Fig. S1. Patient disposition for CheckMate 040 Study. Patients included in the current analysis are indicated in bold. HBV, hepatitis B virus; HCV, hepatitis C virus.

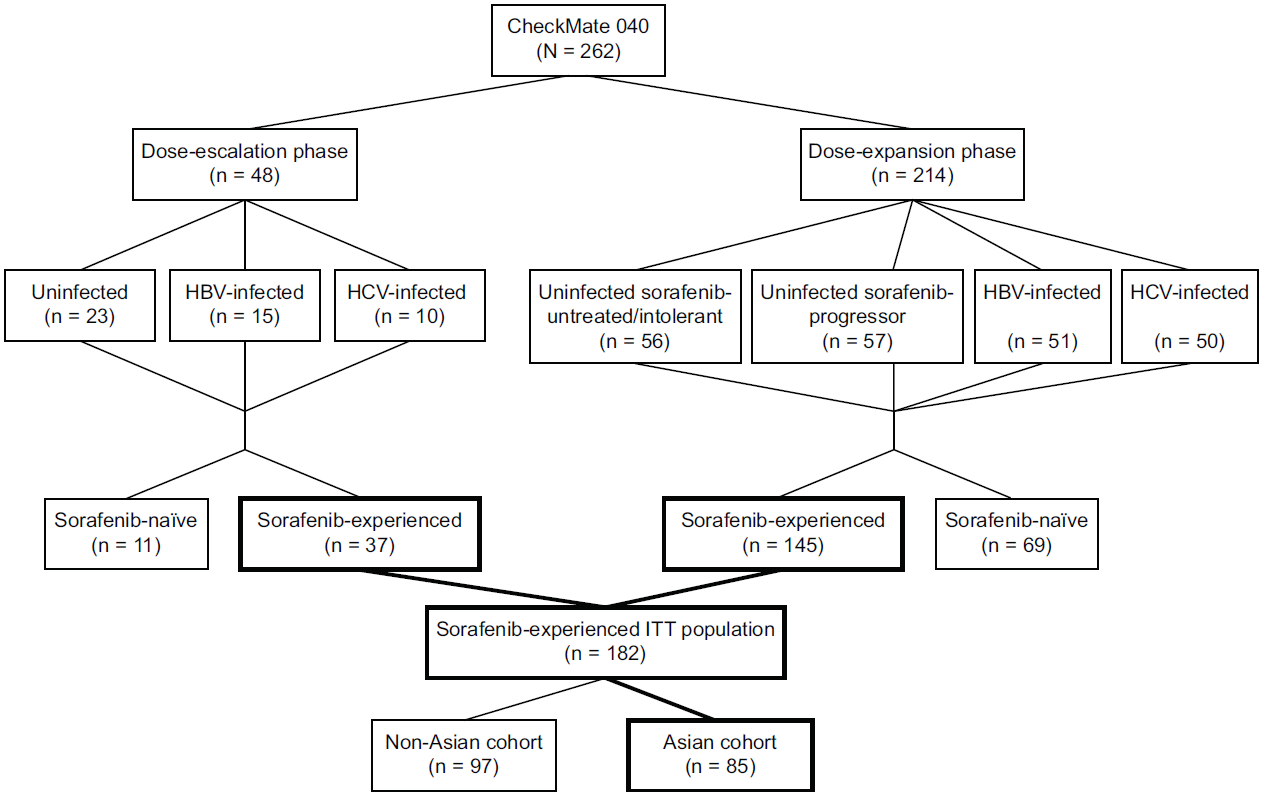

Fig. S2. Kaplan–Meier analysis of overall survival stratified by age. (A) Sorafenib-experienced ITT population. (B) Sorafenib-experienced Asian cohort. CI, confidence interval; ITT, intent-to-treat; OS, overall survival.

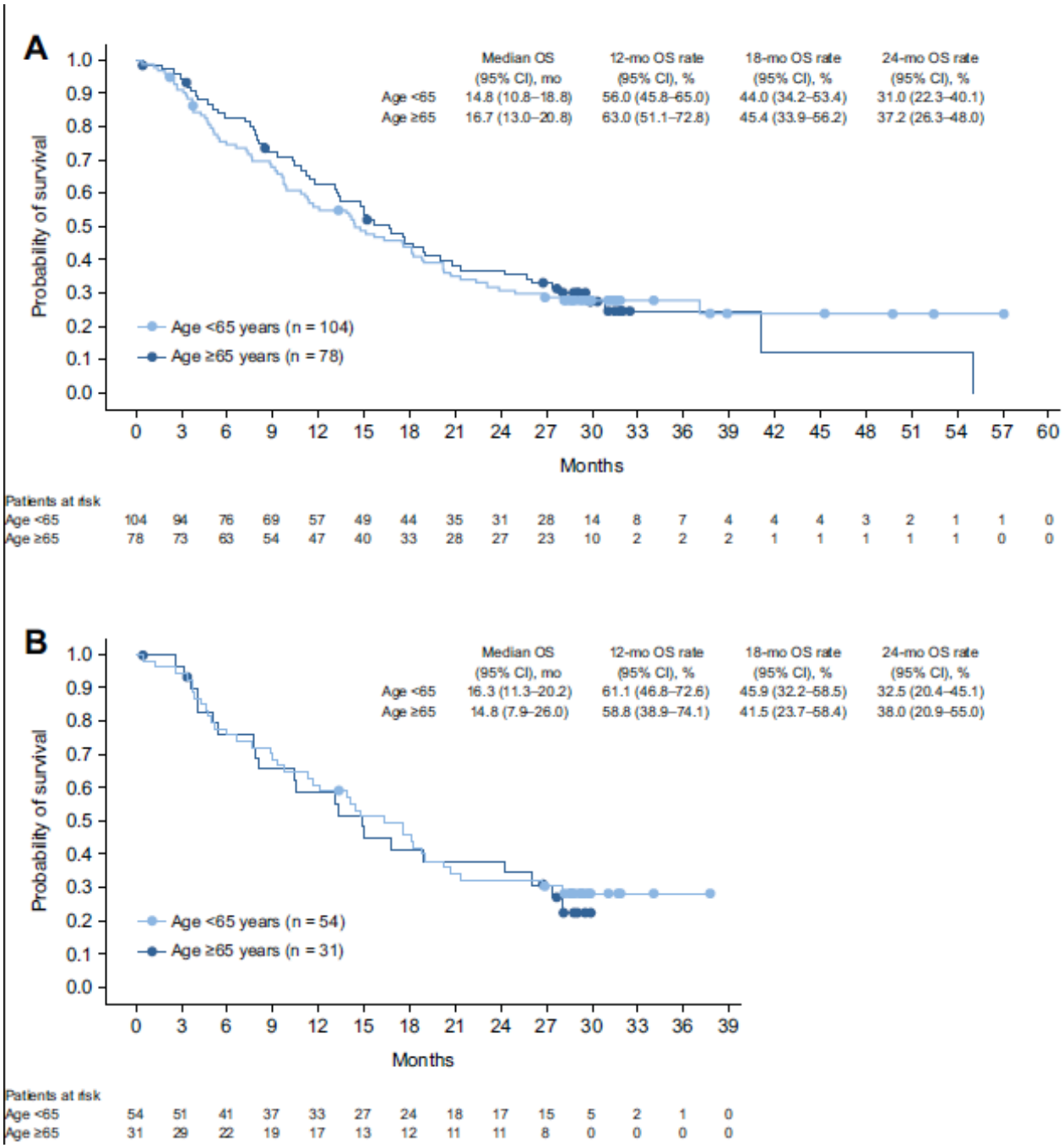

Fig. S3. Kaplan–Meier analysis of overall survival stratified by response to nivolumab treatment. (A) Sorafenib-experienced ITT population. (B) Sorafenib-experienced Asian cohort. Tumor response assessed by BICR using RECIST v1.1. BICR, blinded independent central review; CI, confidence interval; CR, complete response; ITT, intent-to-treat; NE, not estimable; OS, overall survival; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease