

# Sorafenib in extended patient populations in real-world clinical practice: Baseline characteristics from OPTIMIS and GIDEON

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## INTRODUCTION

- Sorafenib, lenvatinib, and the recently approved atezolizumab plus bevacizumab are first-line systemic treatments for advanced hepatocellular carcinoma (HCC)<sup>1-4</sup>
- Clinical characteristics of patients will inform selection of first-line systemic therapy
- In the randomized, phase 3 IMbrave150 clinical study of atezolizumab plus bevacizumab in patients with unresectable HCC (NCT03434379), patients were excluded if they had Eastern Cooperative Oncology Group performance status (ECOG PS)  $\geq 2$ , Child-Pugh B/C liver function, moderate or severe ascites, a history of or active autoimmune disease or immune deficiency, history of hepatic encephalopathy, or were at high risk of bleeding events<sup>5</sup>
- In a real-world clinical setting, certain patient populations may not be suitable for treatment with atezolizumab plus bevacizumab

## OBJECTIVE

- Here, we compare some of the key eligibility criteria from IMbrave150 with baseline characteristics of patients with unresectable HCC enrolled in two large international, real-world, prospective, non-interventional studies of sorafenib

## METHODS

- GIDEON (NCT00812175) was conducted between 2009 and 2012, and patients were enrolled when a decision to treat with sorafenib was made by their physician
- OPTIMIS (NCT01933945) enrolled patients between 2013 and 2017 at the time of their first transarterial chemoembolization (TACE) who subsequently received sorafenib (or not) after becoming TACE ineligible
- Patients who had received systemic anti-cancer therapy prior to their first TACE and who did not subsequently receive sorafenib were excluded from the analysis
- Baseline characteristics were collected prior to initiation of sorafenib treatment, either at study start (GIDEON) or at last observation before start of sorafenib (OPTIMIS), including for patient subgroups that were excluded from IMbrave150

## RESULTS

### Baseline characteristics

- For this analysis, 3202 patients from GIDEON and 373 from OPTIMIS (of 1676 patients enrolled) were eligible (Table 1)
- Baseline characteristics of patients were generally similar in these real-world studies
  - A higher proportion of patients had non-alcoholic steatohepatitis as an etiology for HCC in OPTIMIS, which was the more recent study, compared with GIDEON
- A proportion of patients with unresectable HCC who received treatment with sorafenib in the real-world GIDEON and OPTIMIS studies would not have met some of the eligibility criteria for IMbrave150
  - Child-Pugh B/C liver function (23%), risk of bleeding (bleeding history [15%]; concomitant aspirin use [6%]), ECOG PS  $\geq 2$  (11%), moderate ascites (5%), history of or active autoimmune disease or immune deficiency (3%), and encephalopathy (2%)

Table 1. Baseline characteristics of patients enrolled in the real-world GIDEON and OPTIMIS studies

Characteristic	GIDEON (n=3202)	OPTIMIS (n=373)	Overall population (N=3575)
Male sex, n (%)	2631 (82)	304 (82)	2935 (82)
Age, years Median (range)	62 (15, 98)	62 (18, 88)	62 (15, 98)
Non-viral etiology, n (%)*	1025 (32)	132 (35)	1157 (32)
Alcohol use	834 (26)	100 (27)	934 (26)
NASH	90 (3)	34 (9)	124 (3)
Unknown	392 (12)	48 (13)	440 (12)
History of liver transplantation, n (%)	83 (3)	0	83 (2)
ECOG PS, n (%)			
0/1	2636 (82)	333 (89)	2969 (83)
$\geq 2$	372 (12)	25 (7)	397 (11)
Missing	194 (6)	15 (7)	209 (6)
Child-Pugh classification, n (%)			
A	1968 (61)	273 (73)	2241 (63)
B	666 (21)	83 (22)	749 (21)
C	74 (2)	7 (2)	81 (2)
Not evaluable	493 (15)	0	493 (14)
Missing	1 (<1)	10 (3)	11 (<1)
BCLC stage, n (%)			
0	0	3 (1)	3 (<1)
A	226 (7)	9 (2)	235 (7)
B	634 (20)	94 (25)	728 (20)
C	1664 (52)	246 (66)	1910 (53)
D	173 (5)	14 (4)	187 (5)
Unknown/missing	505 (16)	7 (2)	512 (14)
History of autoimmune disease or immune deficiency, n (%)	114 (4)	10 (3)	124 (3)
History of bleeding, n (%)	472 (15)	58 (16)	530 (15)
Concomitant use of aspirin, n (%)	187 (6)	16 (4)	203 (6)
Ascites, n (%)			
Slight	479 (15)	50 (13)	529 (15)
Moderate	183 (6)	12 (3)	195 (5)
Unknown/missing	113 (4)	10 (3)	123 (3)
Encephalopathy at baseline, n (%)			
Stage 0	3005 (94)	353 (95)	3358 (94)
Stage 1-2	62 (2)	7 (2)	69 (2)
Stage 3-4	3 (<1)	1 (<1)	4 (<1)
Unknown/missing	132 (4)	12 (3)	144 (4)

\*Patients may have more than one etiology of HCC. BCLC, Barcelona Clinic Liver Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; NASH, non-alcoholic steatohepatitis.

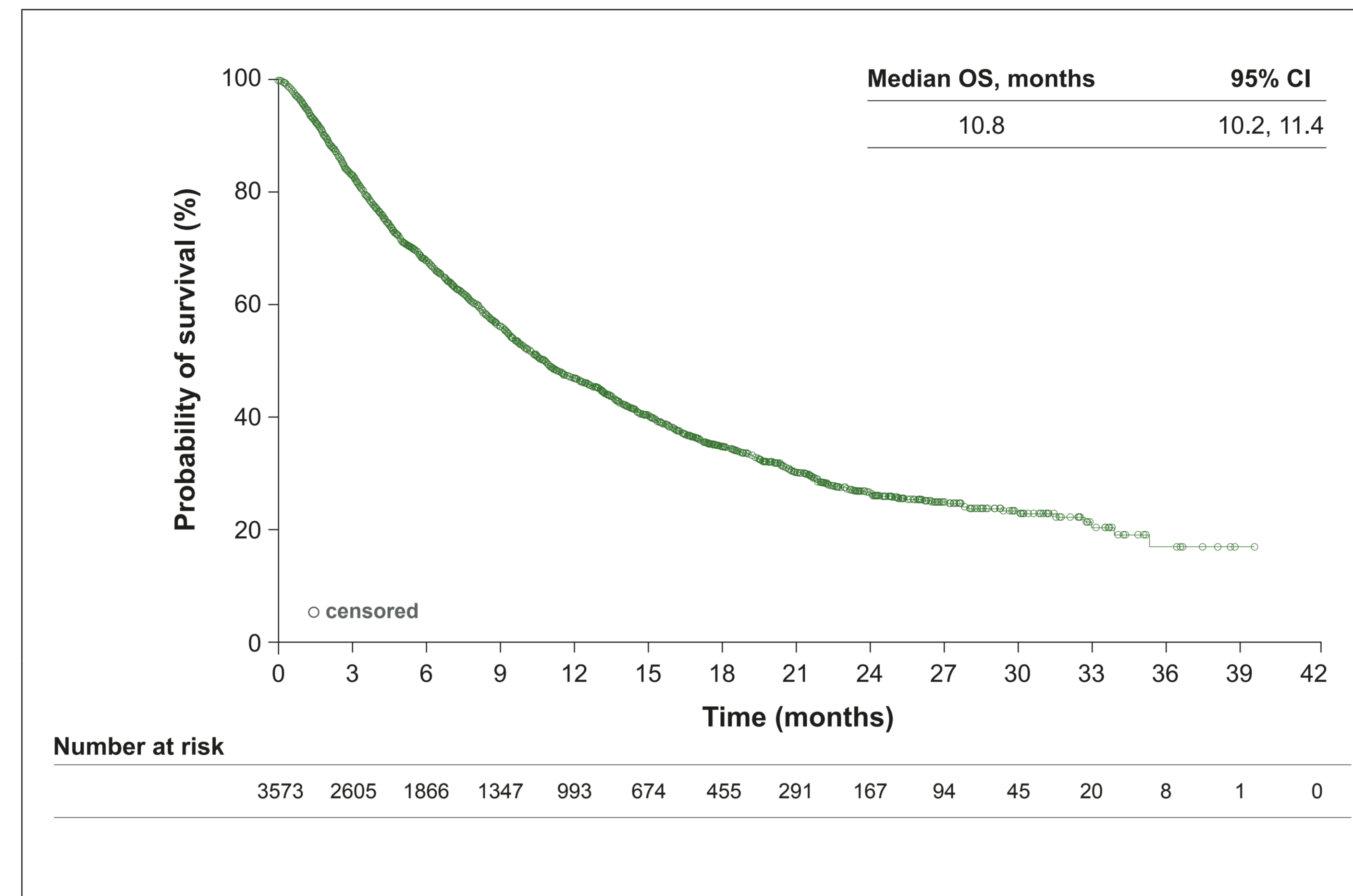
## Efficacy

- Median overall survival (OS), which included patients who had been excluded from clinical trials, was consistent with data from randomized clinical trials of sorafenib<sup>5,6</sup> (Figure 1)
- Median OS in patients with Child-Pugh A liver function was longer than in patients with Child-Pugh B and B7 liver function (Figure 2)
- Median OS in patients with Barcelona Clinic Liver Cancer (BCLC) stage B at baseline was longer than in patients with BCLC stage C at baseline (Figure 3)

## Safety

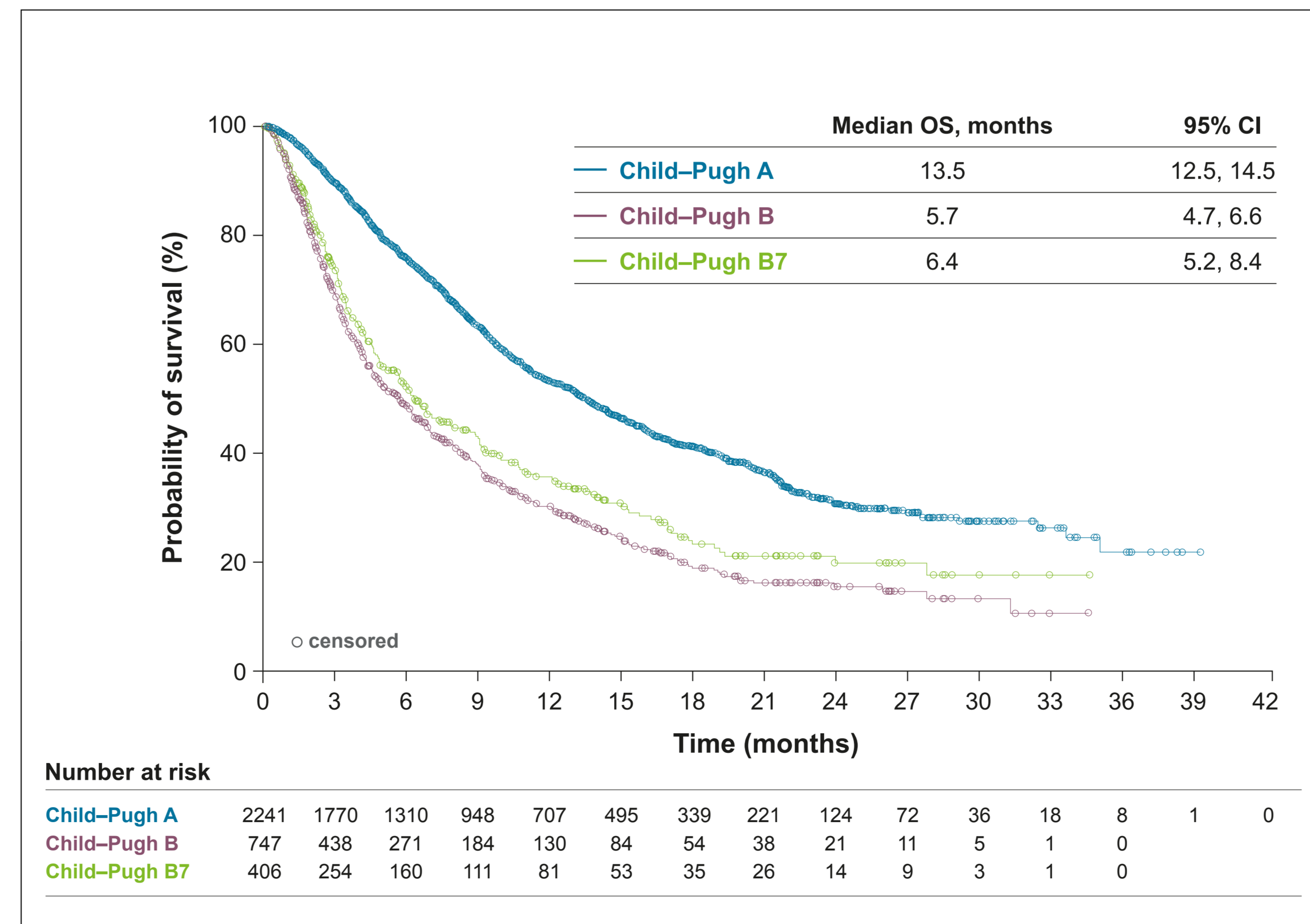
- Incidences of treatment-emergent adverse events (TEAEs) and drug-related TEAEs were similar in patients with Child-Pugh A, B, and B7 liver function and consistent with the overall population (Table 2)
- In the overall population, the most common TEAEs/drug-related TEAEs were diarrhea (29%/26%), hand-foot skin reaction (24%/24%), fatigue (16%/11%), and decreased appetite (14%/9%)

Figure 1. Overall survival



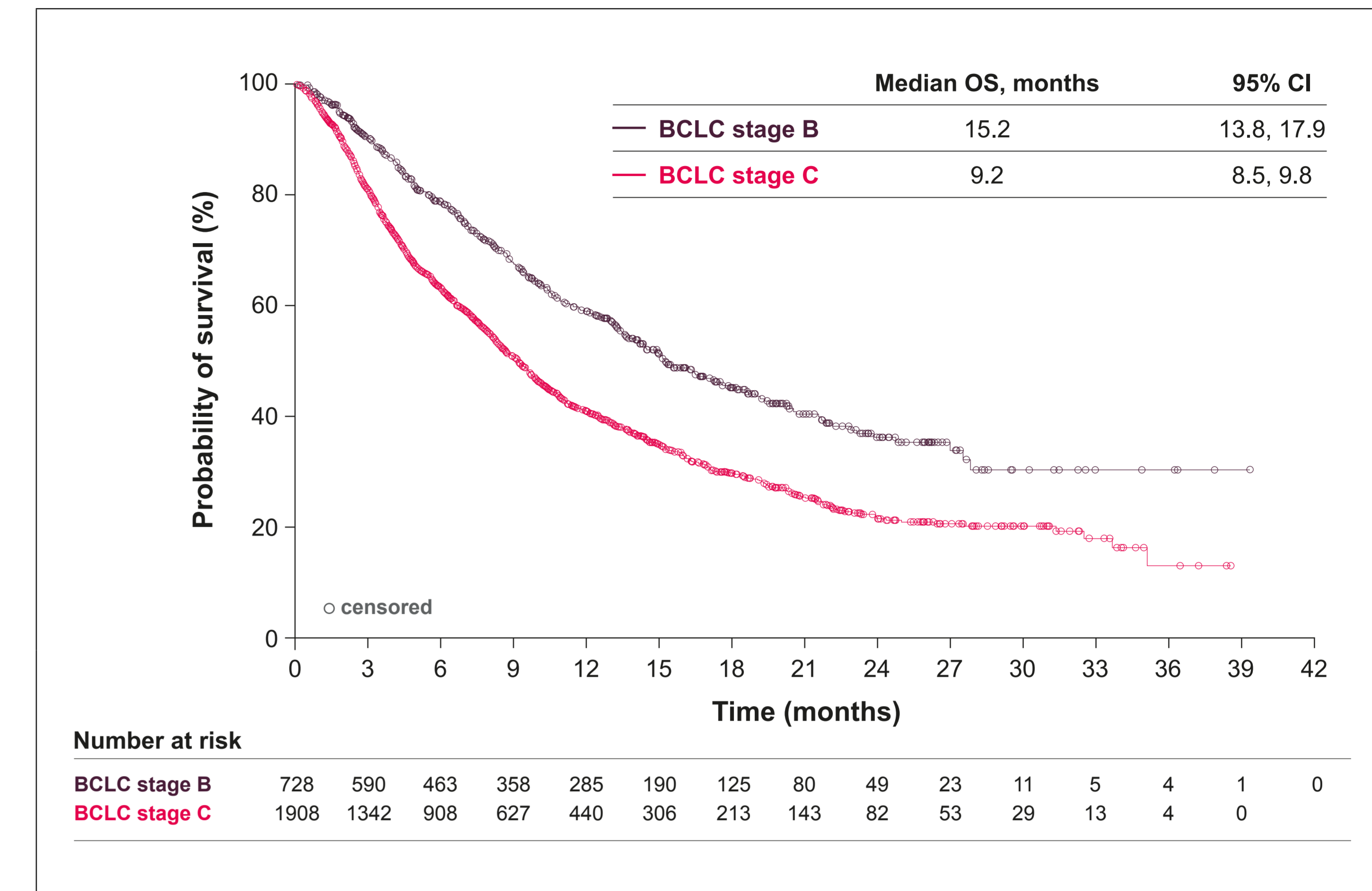
CI, confidence interval; OS, overall survival.

Figure 2. Overall survival in patients with Child-Pugh A, B, and B7 liver function



CI, confidence interval; OS, overall survival.

Figure 3. Overall survival in patients with BCLC stage B/C at baseline\*



\*Of the patients with BCLC stage B/C at baseline, 20%/23% had Child-Pugh B liver function. BCLC, Barcelona Clinic Liver Cancer; CI, confidence interval; OS, overall survival.

Table 2. Treatment-emergent and drug-related treatment-emergent adverse events

TEAE, n (%)	Patients with Child-Pugh A liver function (n=2241)	Patients with Child-Pugh B liver function (n=749)	Patients with Child-Pugh B7 liver function (n=408)	Pooled (N=3575)
Any grade	1871 (83)	656 (88)	353 (87)	3029 (85)
Grade 3 or 4	701 (31)	223 (30)	119 (29)	1094 (31)
Grade 5	443 (20)	285 (38)	136 (33)	913 (26)
Serious	816 (36)	449 (60)	220 (54)	1553 (43)
Drug-related	1498 (67)	465 (62)	265 (65)	2306 (65)
Grade 3 or 4	548 (24)	156 (21)	86 (21)	813 (23)
Grade 5	29 (1)	22 (3)	11 (3)	53 (1)
Serious	195 (9)	103 (14)	53 (13)	329 (9)

TEAE, treatment-emergent adverse event.

## CONCLUSIONS

- Sorafenib has been evaluated in broad patient populations in large, international, real-world, non-interventional studies such as GIDEON (enrollment 2009–2012) and OPTIMIS (enrollment 2013–2017)
  - Despite differing timelines and study designs, baseline characteristics were similar for patients enrolled in both studies
- Median OS for this extended patient population (10.8 months), including patient subgroups that were excluded from IMbrave150, was similar to the median OS in the phase 3 SHARP study (10.7 months)<sup>5,6</sup>
- The median OS of 13.5 months in real-world patients with Child-Pugh A liver function was similar to the median OS of the sorafenib group in IMbrave150 (13.2 months)<sup>5</sup>
- Safety in this broad patient population enrolled in the real-world GIDEON and OPTIMIS studies was in line with the known safety profile of sorafenib<sup>6</sup>
- These data demonstrate the importance of patient characteristics to inform selection of first-line systemic therapy for unresectable HCC

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