Supplement

Table S1: Best Overall Tumor Response in Patients Who Received Prior Sorafenib

	Cabozantinib (N=331)	Placebo (N=164)
ORR[*] (95% CI), n (%)	16 (5) (2.8–7.7)	1 (0.6) (0–3.4)
Best overall response, n (%)		
Partial response	16 (5)	1 (0.6)
Stable disease	206 (62)	50 (30)
Progressive disease	62 (19)	91 (55)
Not evaluable/missing	47 (14)	22 (13)

[*]All responses were partial responses.

CI, confidence interval; ORR, overall response rate.

Table S2: Survival From the Start of Prior Sorafenib

	Duration of Prior Sorafenib[*]					
	<3 Months		3 to <6 Months		≥6 Months	
	Cabozantinib (N=89)	Placebo (N=47)	Cabozantinib (N=98)	Placebo (N=43)	Cabozantinib (N=143)	Placebo (N=74)
Median survival, mo (95% CI)	13.3 (11.5–19.0)	10.4 (8.5–14.7)	21.2 (15.6–26.1)	14.1 (10.2–20.0)	29.9 (25.9–32.6)	25.8 (22.3–33.0)

[*]Patients who received prior sorafenib as the only prior systemic therapy for hepatocellular carcinoma.

Table S3: Subsequent Anticancer Therapy

	Duration of Prior Sorafenib*					
	<3 Months		3 to <6 Months		≥6 Months	
	Cabozantinib (N=89)	Placebo (N=47)	Cabozantinib (N=98)	Placebo (N=43)	Cabozantinib (N=143)	Placebo (N=74)
Any systemic therapy, n (%)	28 (31)	17 (36)	23 (23)	13 (30)	30 (21)	17 (23)
Sorafenib	1 (1)	2 (4)	5 (5)	2 (5)	11 (8)	0
Regorafenib	2 (2)	0	2 (2)	1 (2)	4 (3)	1 (1)
Anti–PD-1/PD-L1	5 (6)	4 (9)	5 (5)	3 (7)	3 (2)	3 (4)
Cytotoxic chemotherapy	16 (18)	9 (19)	11 (11)	8 (19)	14 (10)	9 (12)
Investigational agents	4 (4)	3 (6)	6 (6)	3 (7)	6 (4)	4 (5)

*Patients who received prior sorafenib as the only prior systemic therapy for hepatocellular carcinoma.

PD-1, programmed cell death-1; PD-L1, programmed death-ligand 1.

Table S4: Study Treatment Exposure and Discontinuations

	Duration of Prior Sorafenib*					
	<3 Months		3 to <6 Months		≥6 Months	
	Cabozantinib (N=88)	Placebo (N=47)	Cabozantinib (N=97)	Placebo (N=43)	Cabozantinib (N=143)	Placebo (N=74)
Duration of exposure, median (range), months	3.4 (0.1–26.5)	1.9 (0.4–27.2)	3.9 (0.3–37.3)	2.1 (0.0–11.7)	5.1 (0.3–35.3)	2.1 (0.1–22.2)
Average daily dose, median, mg	35.0	59.0	37.2	58.8	34.7	58.9
Dose reductions, n (%)	57 (65)	6 (13)	59 (61)	4 (9)	92 (64)	7 (9)
Discontinuation due to treatment-related adverse event, n (%)	17 (19)	2 (4)	13 (13)	0	25 (17)	2 (3)

*Safety was assessed in all patients who received at least one dose of study treatment.