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SEQUENTIAL SORAFENIB AND REGORAFENIB YIELDS IMPRESSIVE RESULTS IN PATIENTS WITH ADVANCED HCC

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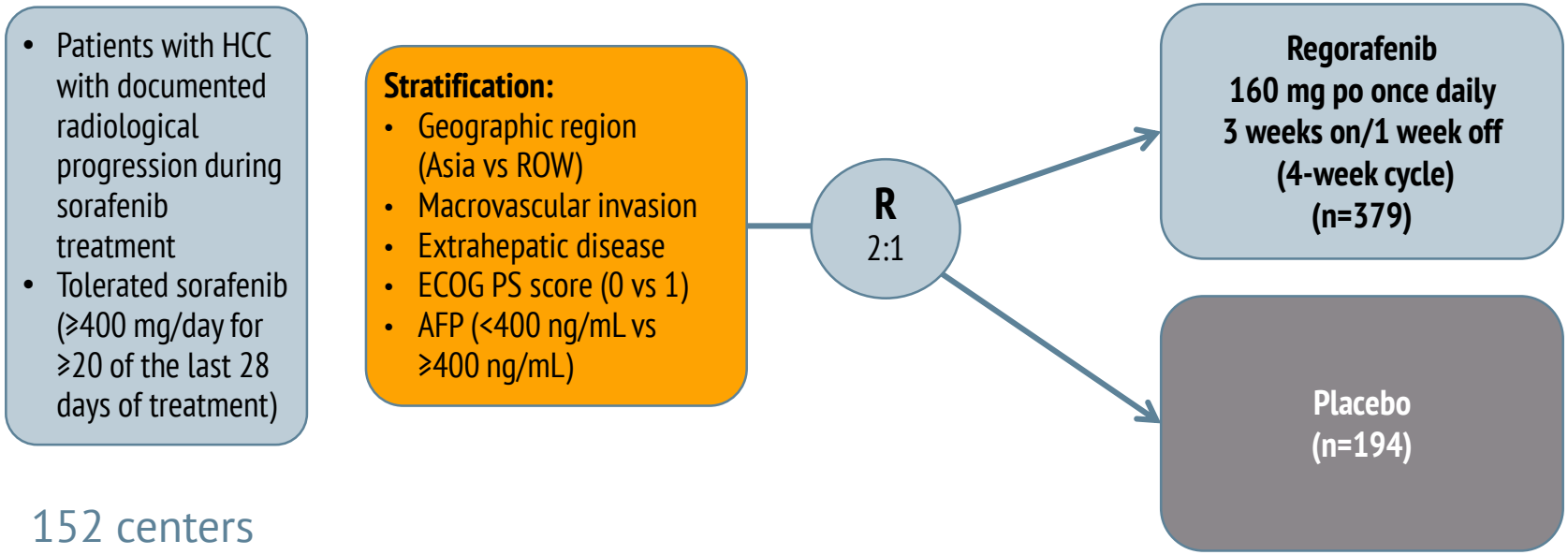
RESORCE TRIAL DESIGN



- 152 centers
- Treat until progression, unacceptable toxicity, withdrawal, investigator decision or death

Endpoints:

Primary: OS in ITT population

Secondary: PFS, TTP, RR, DCR

AFP, alpha-fetoprotein; BSC, best supportive care; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; ITT, intention-to-treat; OS, overall survival; PFS, progression free survival; ROW, rest of the world; RR, response rate; TTP, time to progression

Bruix J, et al. Lancet 2017;389:56-66.

REGORAFENIB SIGNIFICANTLY IMPROVES OS AND REDUCES RISK OF DEATH BY 37% FOR PATIENTS WITH HCC IN 2ND-LINE SETTING

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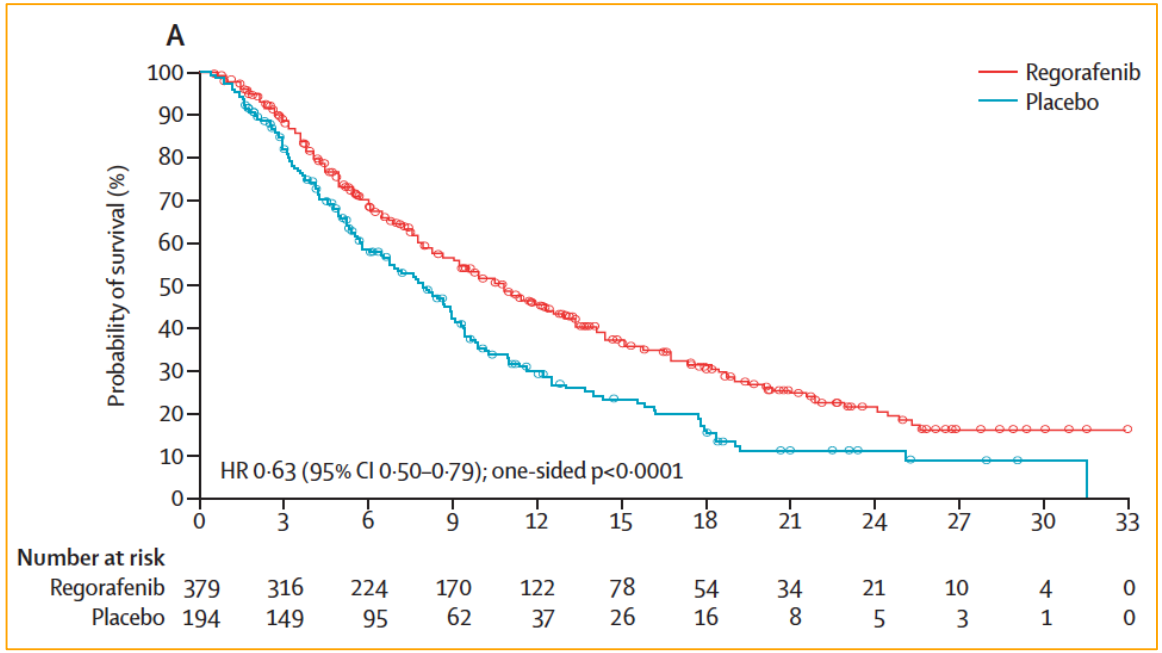

	Regorafenib (n=379)	Placebo (n=194)
Median OS (95% CI)	10.6 months (9.1–12.1)	7.8 months (6.3–8.8)
HR: 0.63 (95% CI, 0.50–0.79); *P*<0.0001		

CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; OS, overall survival

Bruix J, et al. Lancet 2017;389:56-66.

ADDITIONAL ANALYSES FROM THE PHASE 3 RESORCE TRIAL

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Outcomes of sequential treatment with sorafenib followed by regorafenib for HCC: Additional analyses from the phase III RESORCE trial

Richard S. Finn[1,*,†], Philippe Merle[2], Alessandro Granito[3], Yi-Hsiang Huang[4], György Bodoky[5], Marc Pracht[6], Osamu Yokosuka[7], Olivier Rosmorduc[8], René Gerolami[9], Chiara Caparello[10], Roniel Cabrera[11], Charissa Chang[12], Weijing Sun[13,‡], Marie-Aude LeBerre[14], Annette Baumhauer[15], Gerold Meinhardt[16], Jordi Bruix[17,*,†]

- Exploratory analysis of the RESORCE trial
- Outcomes of patients with advanced HCC treated with the sequence of sorafenib followed by regorafenib

HCC, hepatocellular carcinoma

Finn RS, et al. J Hepatol 2018; doi: https://doi.org/10.1016/j.jhep.2018.04.010.

SEQUENTIAL SORAFENIB AND REGORAFENIB EXTENDED THE MEDIAN OS TO 26 MONTHS; AFTER 2 YEARS, 47% OF PATIENTS WERE ALIVE

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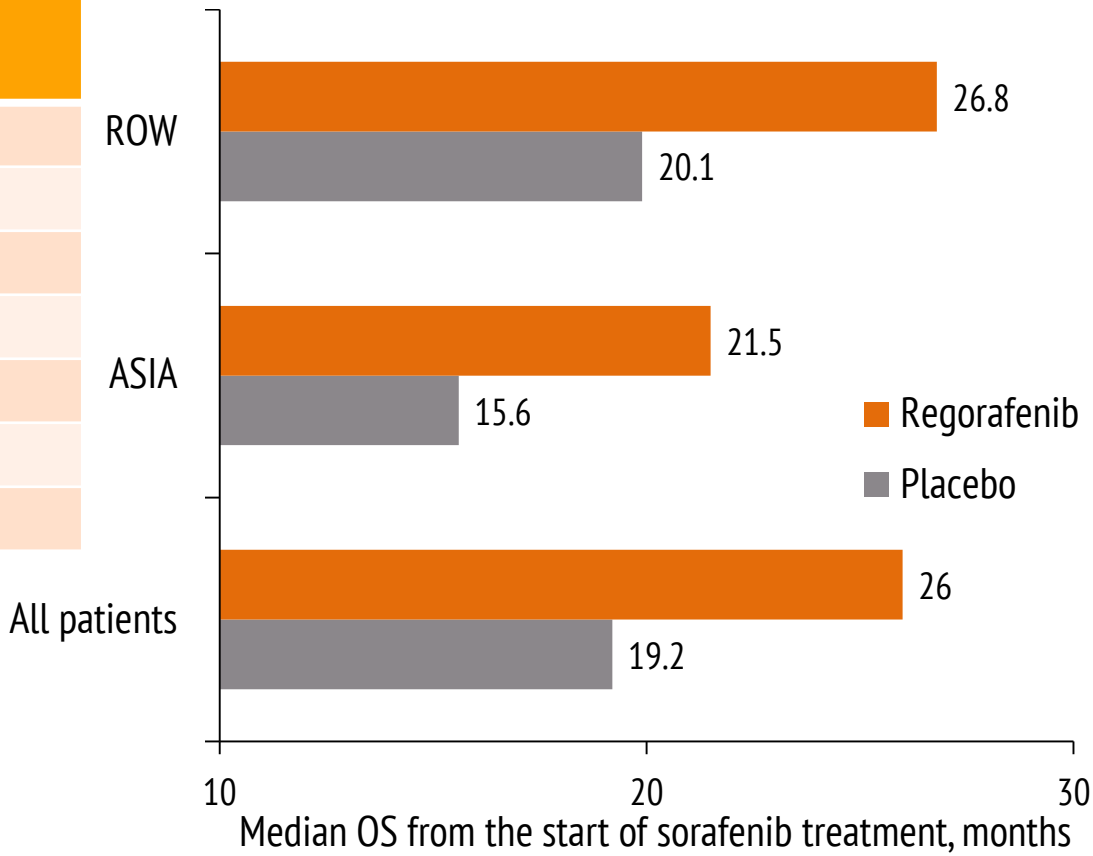
Survival rate	Sorafenib-Regorafenib N=379	Sorafenib-Placebo N=194
6 months	97%	97%
12 months	82%	76%
24 months	53%	42%
36 months	31%	20%
48 months	19%	12%
60 months	16%	3%
72 months	10%	3%



CI, confidence interval; OS, overall survival; ROW, rest of world.

Finn RS, et al. J Hepatol 2018; doi: https://doi.org/10.1016/j.jhep.2018.04.010.

REGORAFENIB WAS EFFECTIVE REGARDLESS OF THE TIME OF PROGRESSION ON SORAFENIB

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Time (months)	Regorafenib (n=374)	Placebo (n=193)
From start of prior sorafenib treatment to start of RESORCE study drug		
Median (IQR)	8.7 (5.1–15.7)	9.2 (5.3–15.5)
Mean (SD)	12.7 (11.4)	12.5 (10.7)
From start of prior sorafenib treatment to progression on sorafenib		
Median (IQR)*	7.2 (3.3–14.3)	7.1 (3.7–14.2)
From progression on prior sorafenib treatment to start of RESORCE study drug		
Median (IQR)	1.4 (0.9–2.3)	1.4 (0.9–2.2)
Mean (SD)	1.8 (1.4)	1.8 (1.7)
From permanent discontinuation of sorafenib to start of RESORCE study drug		
Median (IQR)	0.9 (0.7–1.3)	0.9 (0.7–1.3)
Mean (SD)	1.0 (0.5)	1.0 (0.5)

Generated using a Kaplan–Meier model.
IQR, interquartile range; SD, standard deviation.
Finn RS, et al. J Hepatol 2018; doi: https://doi.org/10.1016/j.jhep.2018.04.010.

LAST DOSE OF SORAFENIB HAS NO SIGNIFICANT IMPACT ON TOLERABILITY OF REGORAFENIB

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Treatment-emergent adverse events (TEAEs)* by last sorafenib dose during prior treatment

TEAEs, n (%)	Last sorafenib dose 800 mg/day		Last sorafenib dose <800 mg/day	
	Regorafenib (n=225)	Placebo (n=115)	Regorafenib (n=139)	Placebo (n=74)
Any	225 (100)	106 (92)	139 (100)	69 (93)
Grade 3	118 (52)	35 (30)	84 (60)	24 (32)
Grade 4	25 (11)	9 (8)	14 (10)	5 (7)
Grade 5	33 (15)	28 (24)	17 (12)	10 (14)
Most common†				
HFSR‡				
Any grade	113 (50)	10 (9)	80 (58)	5 (7)
Grade 3	22 (10)	0	24 (17)	1 (1)
Diarrhea				
Any grade	95 (42)	14 (12)	56 (40)	15 (20)
Grade 3	7 (3)	0	5 (4)	0
Grade 4	0	0	0	0
Fatigue‡				
Any grade	81 (36)	40 (35)	69 (50)	22 (30)
Grade 3	19 (8)	7 (6)	15 (11)	2 (3)
Hypertension				
Any grade	70 (31)	6 (5)	41 (29)	5 (7)
Grade 3	33 (15)	6 (5)	21 (15)	2 (3)
Grade 4	1 (<1)	0	0	0
Anorexia				
Any grade	57 (25)	19 (17)	55 (40)	9 (12)
Grade 3	4 (2)	2 (2)	6 (4)	2 (3)
Grade 4	0	0	0	0

Last sorafenib dose is defined as the dose received during the last 24 h period before discontinuation.
*Regardless of relationship to study drug.
†Occuring in ≥30% of either treatment group in the whole cohort.
‡Grade 3 is worst severity.

HFSR, hand-foot skin reaction; TEAE, treatment-emergent adverse event

Finn RS, et al. J Hepatol 2018; doi: https://doi.org/10.1016/j.jhep.2018.04.010.

THE BENEFIT OF REGORAFENIB WAS OBSERVED IRRESPECTIVE OF THE LAST DOSE OF SORAFENIB

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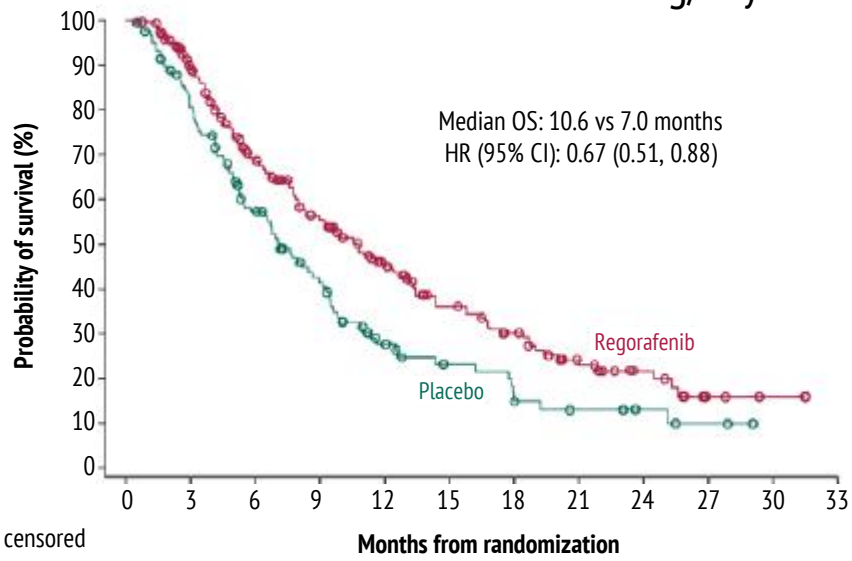
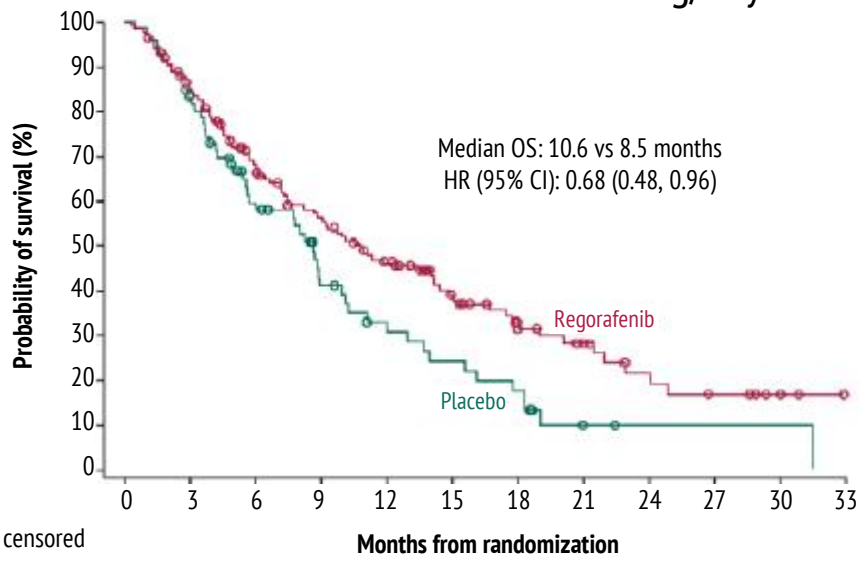
Last dose of sorafenib 800 mg/day



Number at risk

Regorafenib	227	189	130	97	67	44	33	19	12	4	2	0
Placebo	116	89	58	38	21	14	8	6	4	2	0	0

Last dose of sorafenib <800 mg/day



Number at risk

Regorafenib	142	119	86	68	52	35	20	14	9	6	2	0
Placebo	74	56	35	21	14	11	8	2	1	1	1	0

CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; OS, overall survival

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KEY LEARNING POINTS

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- Sequential treatment with sorafenib and regorafenib improves the OS of patients with HCC by 26 months
- TTP on sorafenib does not impact the clinical benefit of regorafenib
- The last dose of sorafenib has no impact on the clinical benefit and tolerability of regorafenib

HCC, hepatocellular carcinoma; OS, overall survival; TTP, time to progression.

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