Wake Forest®
School of Medicine

Pancreatic, Biliary, and HCC Update

Caio Max S. Rocha Lima, M.D.

M. Robert Cooper Professor in Medical Oncology

Co-leader GI Oncology and Co-leader Phase I Program

Wake Forest School of Medicine

E-mail:crochali@wakehealth.edu

Relevant financial relationships in the past twelve months by presenter or spouse/partner.

Consultant: Celgene, Ipsen, Taiho, Merck

MSI High

MSI in more than CRC

Cancer Type	General population risk	Lynch syndrome (MLH1 and MSH2 heterozygotes)	
		Risk	Mean age of onset
Colon	5.5%	52-82%	44-61 years
Endometrium	2.7%	25-60%	48-62 years
Stomach	< 1%	6-13%	56 years
Ovary	1.6%	4-12%	42.5 years
Hepatobiliary tract	< 1%	1.4-4%%	Not reported
Urinary tract	< 1%	1-4%	~55 years
Small bowel	< 1%	3-6%	49 years
Brain/central nervous system	< 1%	1-3%	~50 years
Sebaceous neoplasms	< 1%	1-9%	Not reported

Pembrolizumab Approved for MSI-H or Mismatch Repair Deficient Tumors

Table 25: Response by Tumor Type

	N	Objective response rate n (%)	95% CI	DOR range (months)
CRC	90	32 (36%)	(26%, 46%)	(1.6+, 22.7+)
Non-CRC	59	27 (46%)	(33%, 59%)	(1.9+, 22.1+)
Endometrial cancer	14	5 (36%)	(13%, 65%)	(4.2+, 17.3+)
Biliary cancer	11	3 (27%)	(6%, 61%)	(11.6+, 19.6+)
Gastric or GE junction cancer	9	5 (56%)	(21%, 86%)	(5.8+, 22.1+)
Pancreatic cancer	6	5 (83%)	(36%, 100%)	(2.6+, 9.2+)
Small intestinal cancer	8	3 (38%)	(9%, 76%)	(1.9+, 9.1+)
Breast cancer	2	PR, PR		(7.6, 15.9)
Prostate cancer	2	PR, SD		9.8+
Bladder cancer	1	NE		
Esophageal cancer	1	PR		18.2+
Sarcoma	1	PD		
Thyroid cancer	1	NE		
Retroperitoneal adenocarcinoma	1	PR		7.5+
Small cell lung cancer	1	CR		8.9+
Renal cell cancer	1	PD		

CR = complete response
PR = partial response
SD = stable disease
PD = progressive disease
NE = not evaluable

Package insert

Presented By Dung Le at 2017 ASCO Annual Meeting

Pancreatic Cancer

We Have Made Progress in the 1st-Line Metastatic Setting

Trial[1]	Date	Patients (n)	Treatment	Median survival (mo)	P value
Burris et al[2]	1997	126 (unresectable, LA or metastatic pancreatic cancer)	5-FU vs. gemcitabine	4.41 5.65*	Log-Rank Test 0.0025
NCIC[3]	2007	569 (unresectable, LA or metastatic pancreatic cancer)	gemcitabine vs. gemcitabine + erlotinib	5.91 6.24	0.038 (HR = 0.82 [95% CI, 0.69–0.99])
PRODIGE[4]	2011	342 (metastatic)	gemcitabine vs. FOLFIRINOX	6.8 11.1	<0.001 (HR = 0.57 [95% CI, 0.45–0.73])
Ueno, et al[5]	2013	834 (LA, or metastatic pancreatic cancer)	gemcitabine vs. S-1 vs. gemcitabine + S-1	8.8 9.7 10.1	gemcitabine vs. S-1: <0.001 (non-inferiority; HR = 0.96 [97.5% CI, 0.78–1.18]) gemcitabine vs. gemcitabine + S-1: 0.15 (superiority; HR = 0.88 [97.5% CI, 0.71–1.08])
MPACT[6]	2013	861 (metastatic)	gemcitabine vs. gemcitabine + nab-paclitaxel	6.7 8.5	<0.001 (HR = 0.72 [95% CI, 0.62–0.83])

1. Ryan DP, et al. N Engl J Med 2014;371:1039;
2. Burris HA, et al. J Clin Oncol 1997;15:2403;
3. Moore MJ, et al. J Clin Oncol 2007;25:1960; 4.Conroy T, et al. N Engl J Med 2011;364:1817;
5. Ueno H, et al. J Clin Oncol 2013;31:1640;
6. Von Hoff DD, et al. N Engl J Med 2013;369:1691.

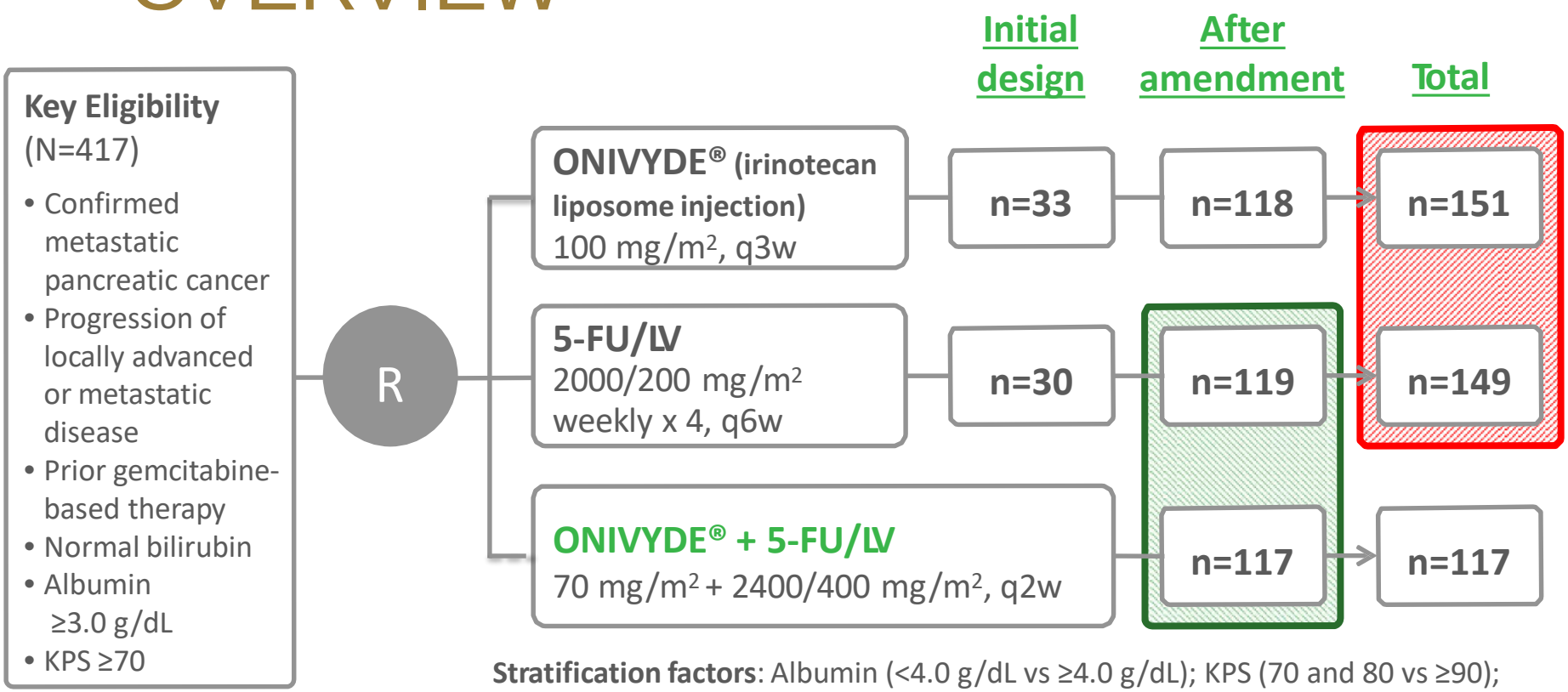
1st-line treatment of MPC – Nab-paclitaxel + gemcitabine or FOLFIRINOX?

	Nab-P/Gem (n=431)	FOLFIRINOX (n=171)
Sites	Global	France
Age >75?	Yes	?
PS	0-2	0-1
Efficacy		
RR,%	29	31.6
PFS, months	5.5	6.4
OS (updated), months	8.7	11.1
1 year, %	35	48
Safety, G≥3 events, %		
Febrile neutropenia	3	5
Growth factors	26	43
Fatigue	17	24
Vomiting	3	15
Diarrhoea	6	13
Neuropathy	17[b]	9

1. Von Hoff et al. N Engl J Med 2013;369:1691-703; 2. Goldstein et al. JNCI 2015; Jan 31;107. pii: dju413. doi: 10.1093/jnci/dju41; 3. Conroy et al. NEJM 2011;364:1817-25

Second-line Therapy Pancreas Cancer

NAPOLI-1: PHASE 3 STUDY OVERVIEW[1,2]



Stratification factors: Albumin (<4.0 g/dL vs ≥4.0 g/dL); KPS (70 and 80 vs ≥90); and ethnicity (Caucasian vs East Asian vs others)

- Treatment continued until disease progression or unacceptable toxicity

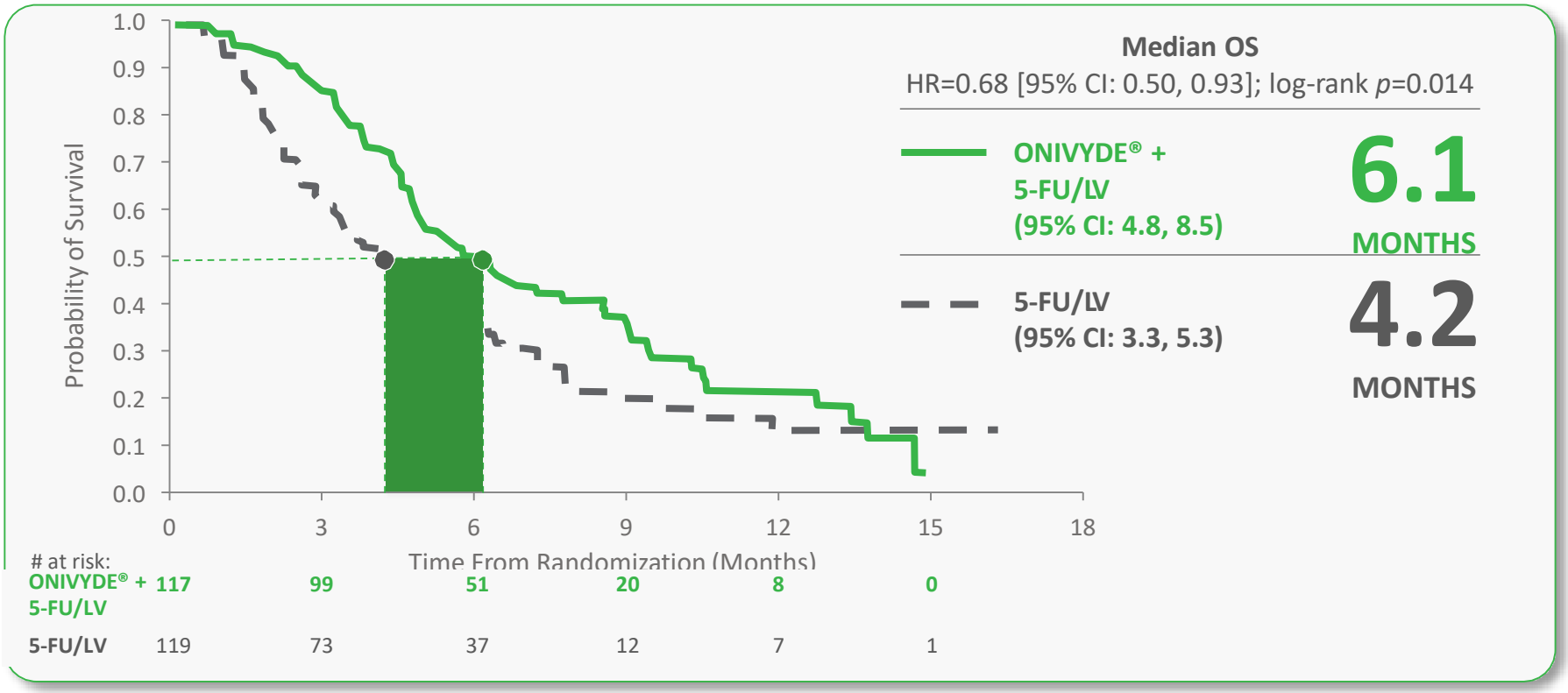
Please see Important Safety Information, including Boxed WARNING, within this presentation and accompanying full Prescribing Information for ONIVYDE®.

KPS=Karnofsky performance status.

References: 1. Wang-Gillam A, et al. *Lancet*. 2016;387:545–557.

EXTENDED OVERALL SURVIVAL[1]

ONIVYDE® (IRINOTECAN LIPOSOME INJECTION) + 5-FU/LV DEMONSTRATED A STATISTICALLY SIGNIFICANT INCREASE IN MEDIAN OS VS 5-FU/LV



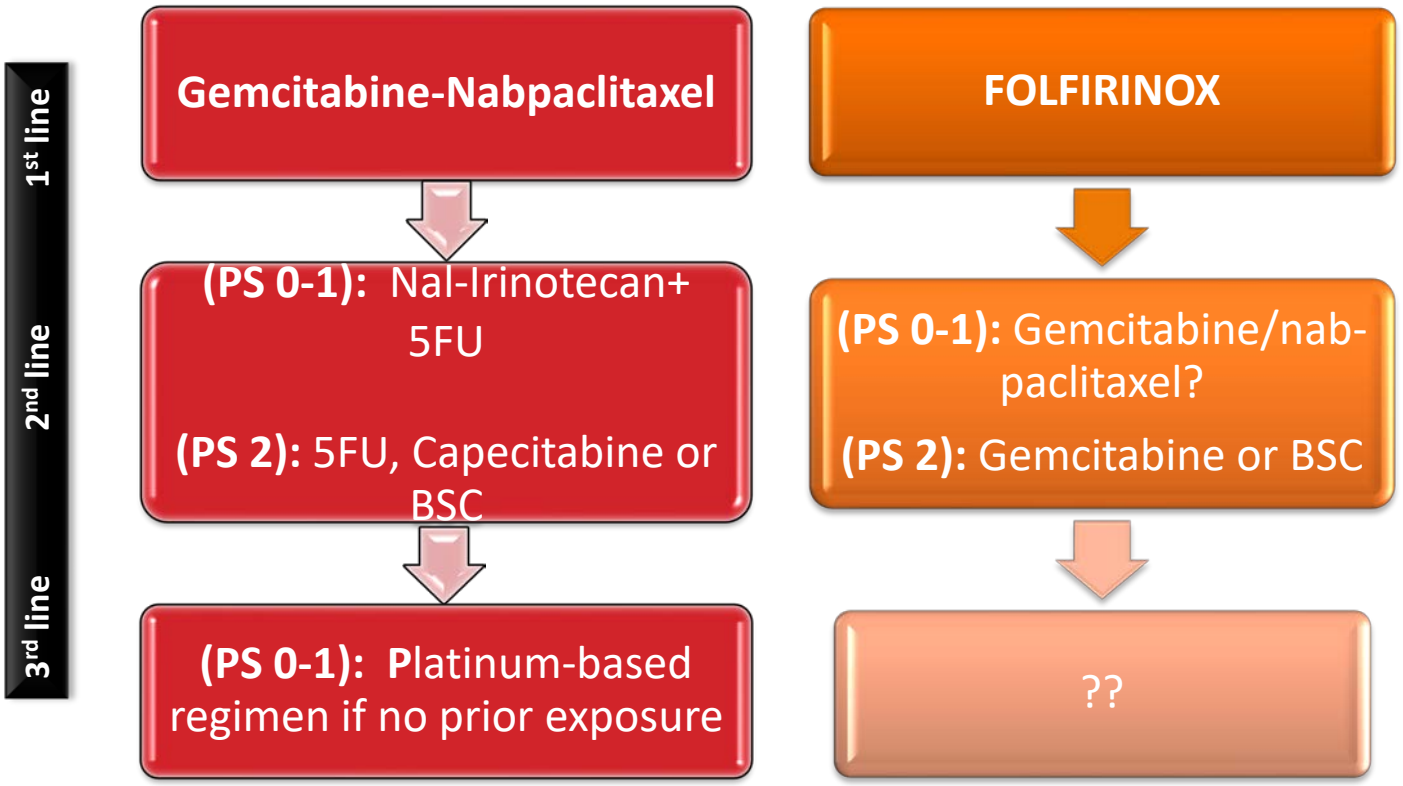
ONIVYDE® is not indicated as a single agent for the treatment of patients with metastatic adenocarcinoma of the pancreas.

- There was no improvement in OS for ONIVYDE® vs 5-FU/LV (HR=1.00; *p*=0.97 [two-sided log-rank])

Please see Important Safety Information, including Boxed WARNING, within this presentation and accompanying full Prescribing Information for ONIVYDE®.

Reference: 1. ONIVYDE® [package insert]. Ipsen Biopharmaceuticals, Inc.; 2017.

Current Approach in Treatment Sequencing for mPCA



HALO-202 Randomized Phase 2 Study of PEGPH20 Plus nab-Paclitaxel/ Gemcitabine (AG) vs. AG in Patients with Untreated, Metastatic Pancreatic Adenocarcinoma

	All Patients (Primary Analysis)		High HA (Exploratory Analysis)	
Combo	PAG	AG	PAG	AG
N pts	166	113	49	35
mPFS (mos)	6	5.3	9.2	5.2
	HR 0.773 p=0.045		HR 0.51 p=0.048	
mOS (mos)			11.5	8.5
	HR p		HR 0.96 p=0.88	
RR (%)	40	33	45	31
Main AEs	PAG: Fatigue, Hematologic and thromboembolic events AG : Fatigue and Hematologic			

Hingorani SL. Abs 4008. ASCO 2017,

Which Subsets of Patients Might Benefit From Specific Therapies?

- MSI-high/mismatch repair-deficient (dMMR)
  - 5 of 6 patients with dMMR pancreatic cancers showed objective response by RECIST to pembrolizumab

- BRCA- or PALB2- mutation carriers
  - Rucaparib: 3/19 (16%) with objective response
  - Olaparib: 5/23 pts (22%) with objective response
    Veliparib: 0/16 pts with objective response

1. Kaufman, et al. J Clin Oncol. 2015;33:244-250.
2. Lowery, et al. ASCO 2015. Abstract 358.
3. Le D, et al. ASCO 2015. Abstract 195.

Biliary Cancers

First-line Therapy

Chemotherapy for advanced BTC
Better than Best Supportive Care (BSC) alone

Study		OS (months)		P value
Glimelius *Ann Oncol* 1996	• Phase III • 5FU/etoposide/LV v BSC • Pancreas (n=53) + BTC (n=37) • Improved QoL • Improved survival	**BSC** FELV	**2.5** 6	<0.01
Sharma *J Clin Oncol* 2010	• Phase III • mGemOx* v 5FU/FA v BSC • Gallbladder cancer only (n=81) • Improved PFS • Improved survival * Gem 900 mg/m^2 + oxali 80 mg/m^2 D1, 8 q21d	**BSC** 5FU mGemOx	**4.5** 4.6 9.5	0.039

Randomized Trials With Combo x Single Agent

Chemotherapy	Phase	N	Categories	Response (%)			Outcome (months)		
				CR	PR	SD	PFS TTP	OS	
Gem/Cis vs. Gem	3	410	Gem	0.7	14.8	56.3	5	8.1	Valle *NEJM* 2010
			Gem/Cis	0.6	25.5	55.3	8	11.7	
	2	83	Gem	0	11.9	38.8	3.7	7.7	Okusaka *BJC* 2010
			Gem/Cis	0	19.5	48.8	5.8	11.2	
Gem+S1 / S1	2	101	S1	NR	17.4	NR	4.2	9	Morizane *Cancer Sci* 2013
			Gem+S1	NR	36.4	NR	7.1	12.5	
5-FU vs.5-FU/FA/Cis	2	58	5-FU	0	7	46	3.3	5	Ducreux *Eur J Cancer* 2005
			5-FU/FA/ Cis	4	15	44	3.3	8	
FELV vs. ECF	3	54	FELV	0	15	45	7.3	12	Rao *BJC* 2005
			ECF	3.8	15.4	46.2	5.2	9	
MMC/Gem vs. MMC/Cape	2	51	MMC/Gem	0	20	36	4.2	6.7	Kornek *Ann Oncol* 2004
			MMC/Cape	0	31	34	5.3	9.25	

Key message:
Combination chemotherapy (doublet) is associated with improved PFS & OS

Table adapted from Geynishman *Disc Medicine* 2012

SIRT | In intra-hepatic cholangiocarcinoma

Systematic review

12 studies (7 prospective, 5 retrospective), 298 patients (prior chemo 54%, surgery 33%)

Endpoint	End-point		Outcome
Overall survival	Co-primary	11 studies	**15.5 months**
Response rate	Co-primary	6 studies	**PR 28%** SD 54%
Conversion to resectability	Secondary	3 studies	**10%** (7/73)

Adverse events

Fatigue
Abdominal pain
Fever
Nausea
Deranged liver function tests
Treatment-related death (n=1)

Others

1 gastroduodenal ulcer
2 pleural effusions
7 ascites
1 duodenal ulcer
1 Pulmonary embolism
4 ascites
2 pleural effusion
2 acute radiation hepatitis
1 chronic radiation hepatitis

Al-Adra *Eur J Surg Oncol* 2015

Second-Line Therapy

Impact of Tumor Location on Genetics of Biliary Cancers

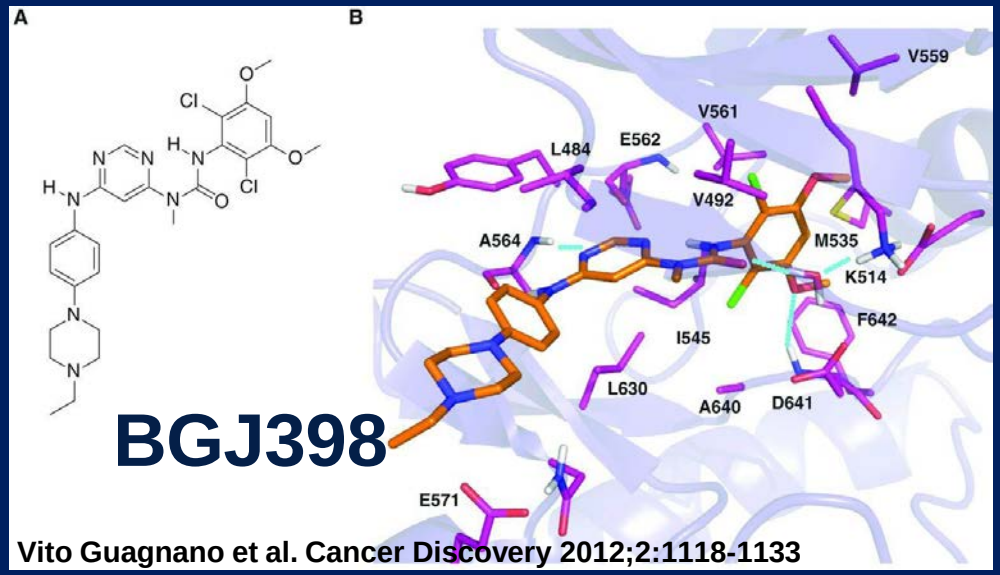
Tumor Genomic Aberrations	IHCC	EHCC	GBC
ERBB2 Amplification **(HER2)**	4%	11%	**16%**
BRAF Substitutions	5%	3%	1%
KRAS Substitutions	22%	**42%**	11%
PI3KCA Substitution	5%	7%	14%
FGFR1-3 Fusions and Amplifications	**11%**	0	3%
CDKN2A/B Loss	27%	17%	19%
IDH1/2 Substitutions	**20%**	0	0
ARID1A Alterations	18%	12%	13%
MET Amplification	2%	0	1%

N=554: IHCC n=412, EHCC n=57, GBC n=85

Javle et al Cancer epub Sep 13, 2016

FGFR2 Inhibitors in IHCC: Approaching the Clinic?

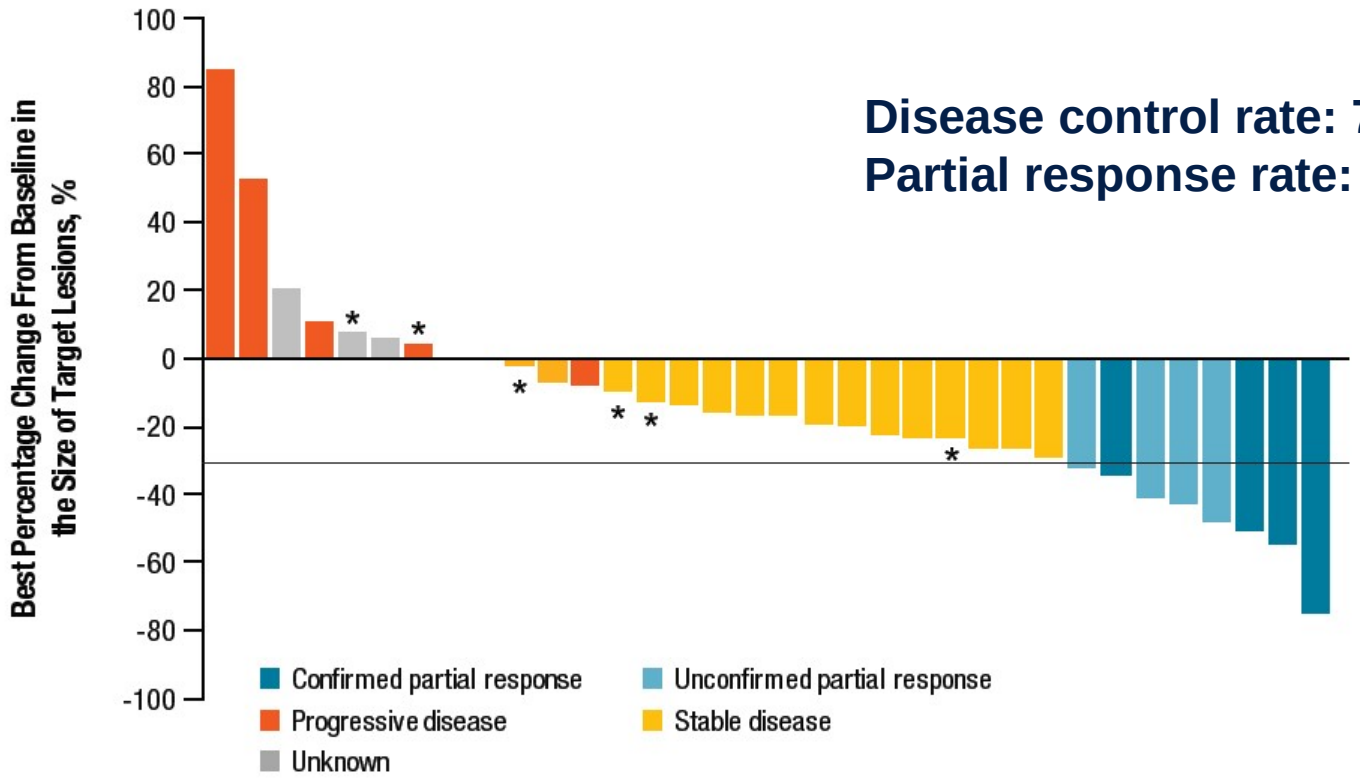
- Activating FGFR2 fusions: ~20% IHCC
- Multiple agents in trials:
  - BGJ398 (Novartis)
  - ARQ 087 (ArQule)
  - INCB054828 (Incyte)
  - Others



Vito Guagnano et al. Cancer Discovery 2012;2:1118-1133

Results: BGJ398 in FGFR2-Mutated IHCC

Figure 3. Best Percentage Change From Baseline in the Size of Target Lesions With BGJ398 Treatment (n = 34)[a,b]



[a] Two patients were not included in the analysis (best percentage change could not be calculated because the scan modality changed [n = 1], patient had no postbaseline scan due to treatment discontinuation [n = 1]).

[b] Patients marked with an asterisk had *FGFR2* mutations (n = 2) or amplification (n = 3), or *FGFR3* amplification (n = 1). All other patients had *FGFR2* fusions (n = 28).

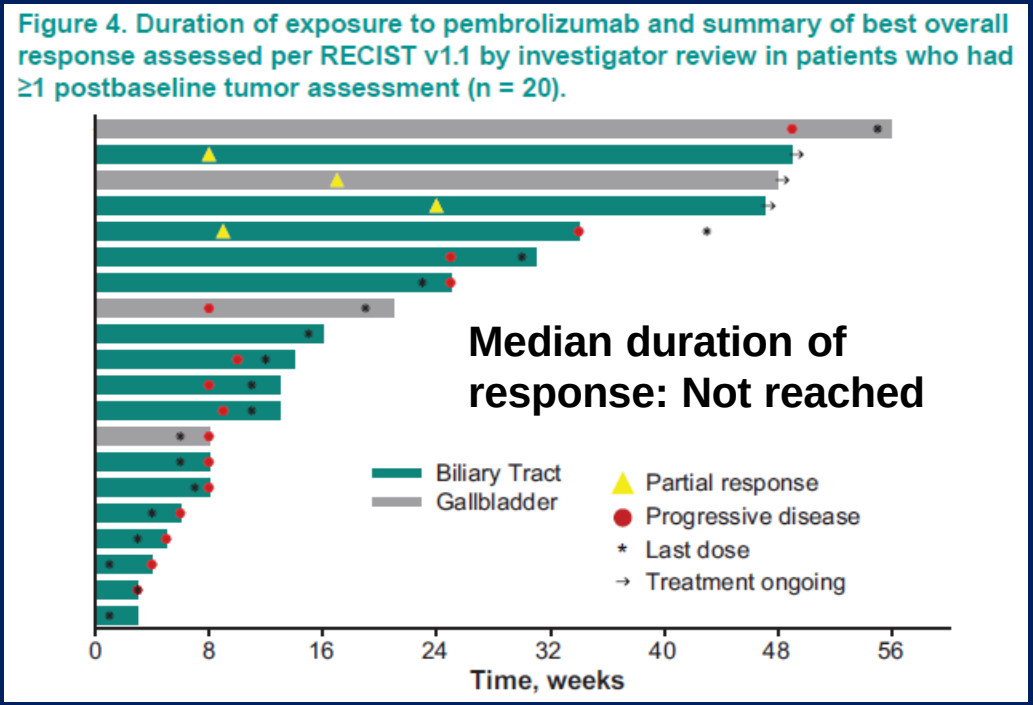
Javle et al GI ASCO 2016

IDH 1/2 Inhibitors for IHCC

- Activating IDH1 or 2 mutations: ~20% of IHCC, lead to dedifferentiation and uncontrolled proliferation
- IDH1/2 inhibitors being tested in cholangiocarcinoma cohorts:
  - AG-120, AG-221, AG-881 (IDH1 and IDH2 inhibitors, Agios)
  - BAY1436032 (IDH1 inhibitor, Bayer)
  - Others

Pembrolizumab (MK-3475, anti-PD-1) in Cholangiocarcinoma: KEYNOTE-028

- Screened 87 patients:
  - 41% tumor PD-L1+
  - Enrolled 24
    - CCA 83%
    - Gall bladder 17%
- Outcomes:
  - Partial response 17%
  - Stable disease 17%
  - Treatment-related grade 3 AE: 17%

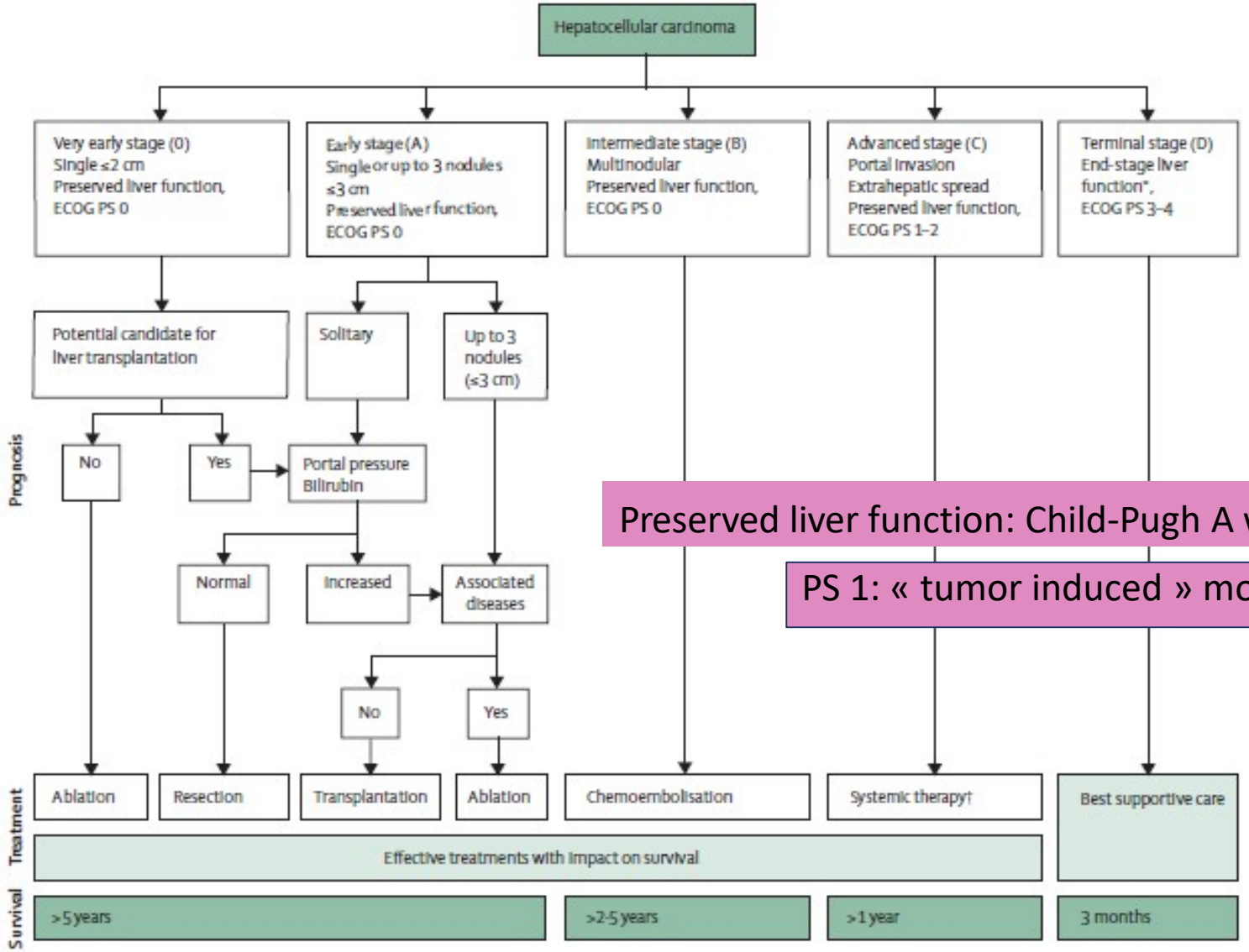


Bang et al ESMO 2015, Abstract 525

HCC

HCC: Treatment

The BCLC staging system is recommended for prognostic selection and treatment assignment



Preserved liver function: Child-Pugh A without ascites

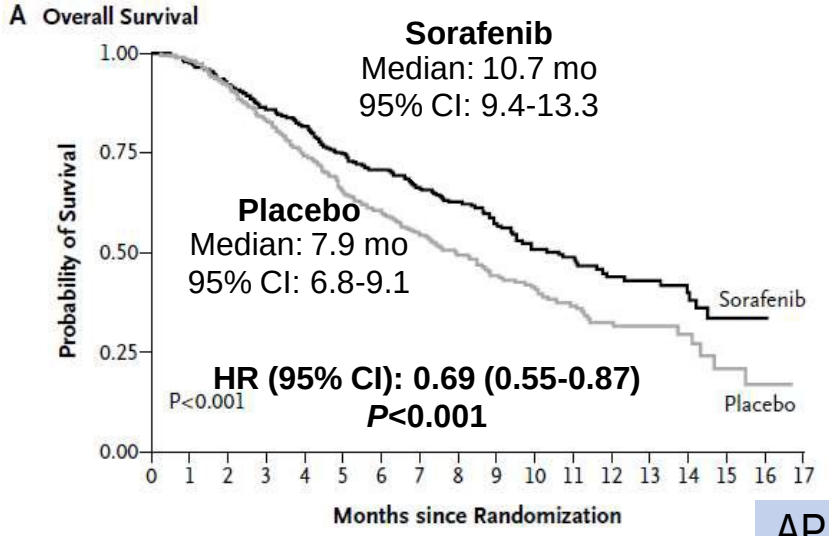
PS 1: « tumor induced » modification in PS

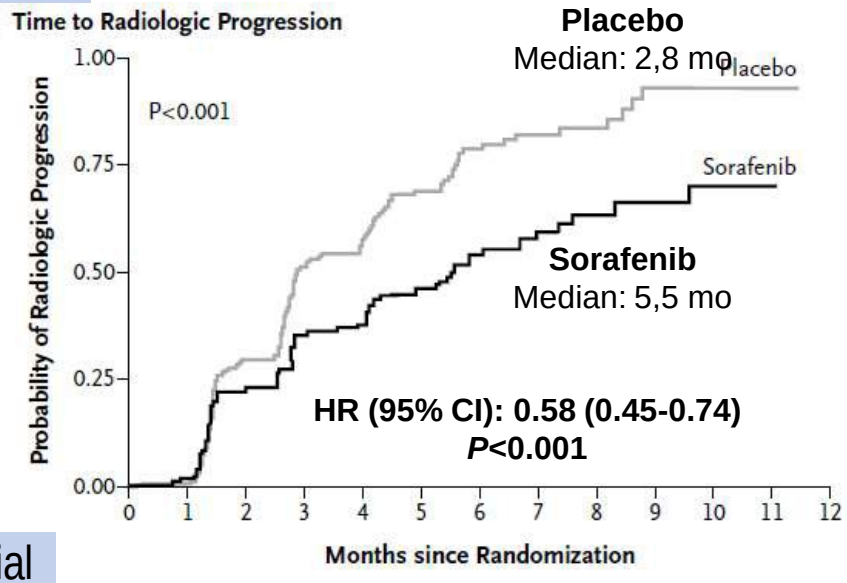
Forner A, et al. Lancet 2018

Advanced stage: Systemic treatments:

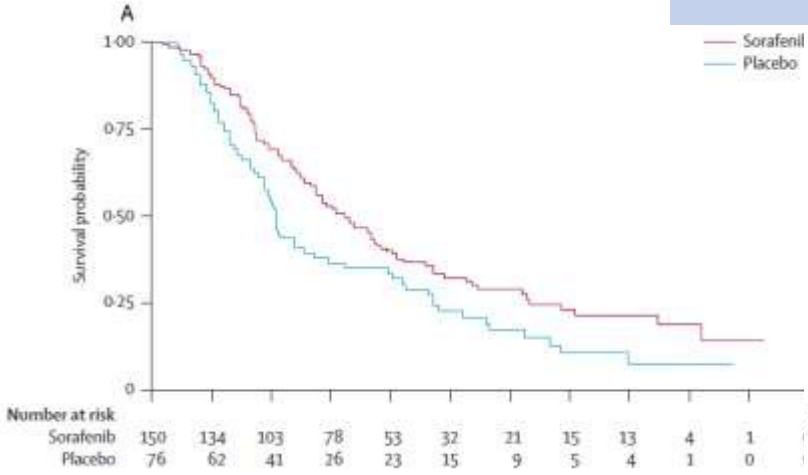
Sorafenib

SHARP trial

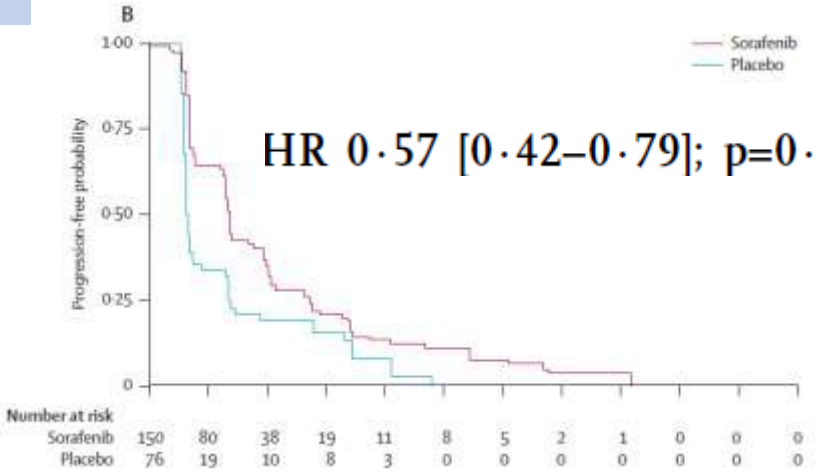




AP trial



[HR] 0·68 [95% CI 0·50–0·93]; p=0·014)



HR 0·57 [0·42–0·79]; p=0·0005)

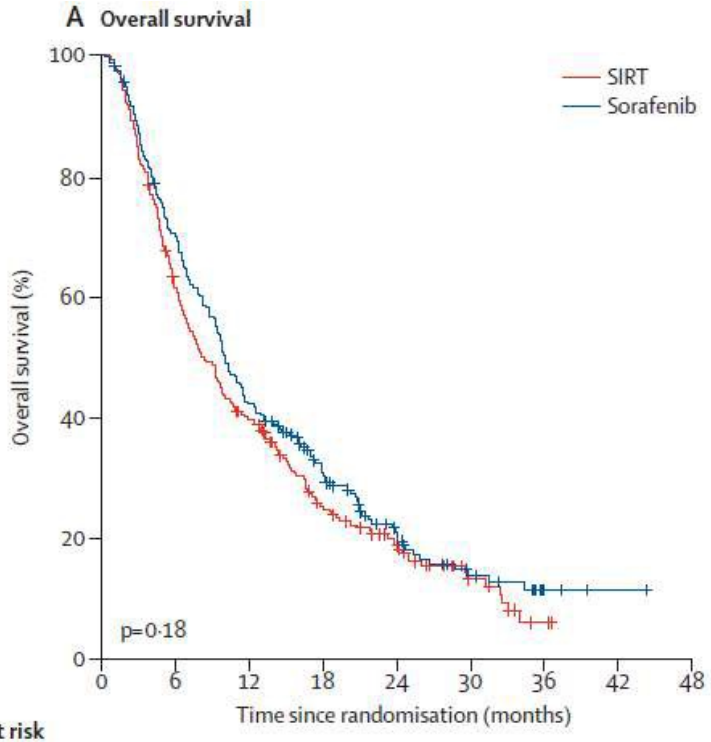
Llovet JM, et al N Engl J Med 2008; Bruix J, et al J Hepatol 2012; Chen AL, et al Lancet Oncol 2009.

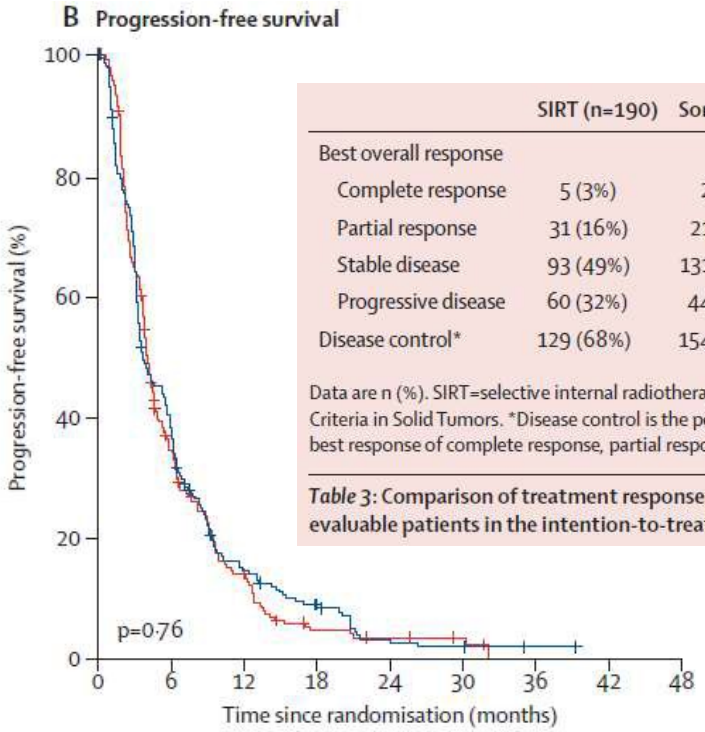
Systemic treatments:
Sorafenib: indications

- Advanced stage:
  - Portal vein invasion,
  - Extra-hepatic metastases,
  - Child-Pugh A, B
  - PS: 0 – 2
- SHARP and AP trials: inclusions limited to
  - Advanced stages BCLC or progression after TACE
  - PS 0, 1, 2
  - Child-Pugh A
  - Biology « correct »
- No molecular biomarker available.

Llovet JM, et al N Engl J Med 2008

SORAFENIB VS. SIRT





	SIRT (n=190)	Sorafenib (n=198)	p value
Best overall response			
Complete response	5 (3%)	2 (1%)	0·0077
Partial response	31 (16%)	21 (11%)	..
Stable disease	93 (49%)	131 (66%)	..
Progressive disease	60 (32%)	44 (22%)	..
Disease control*	129 (68%)	154 (78%)	0·0346

Data are n (%). SIRT=selective internal radiotherapy. RECIST=Response Evaluation Criteria in Solid Tumors. *Disease control is the percentage of patients who had a best response of complete response, partial response, or stable disease.

Table 3: Comparison of treatment responses (RECIST 1.1) among evaluable patients in the intention-to-treat population

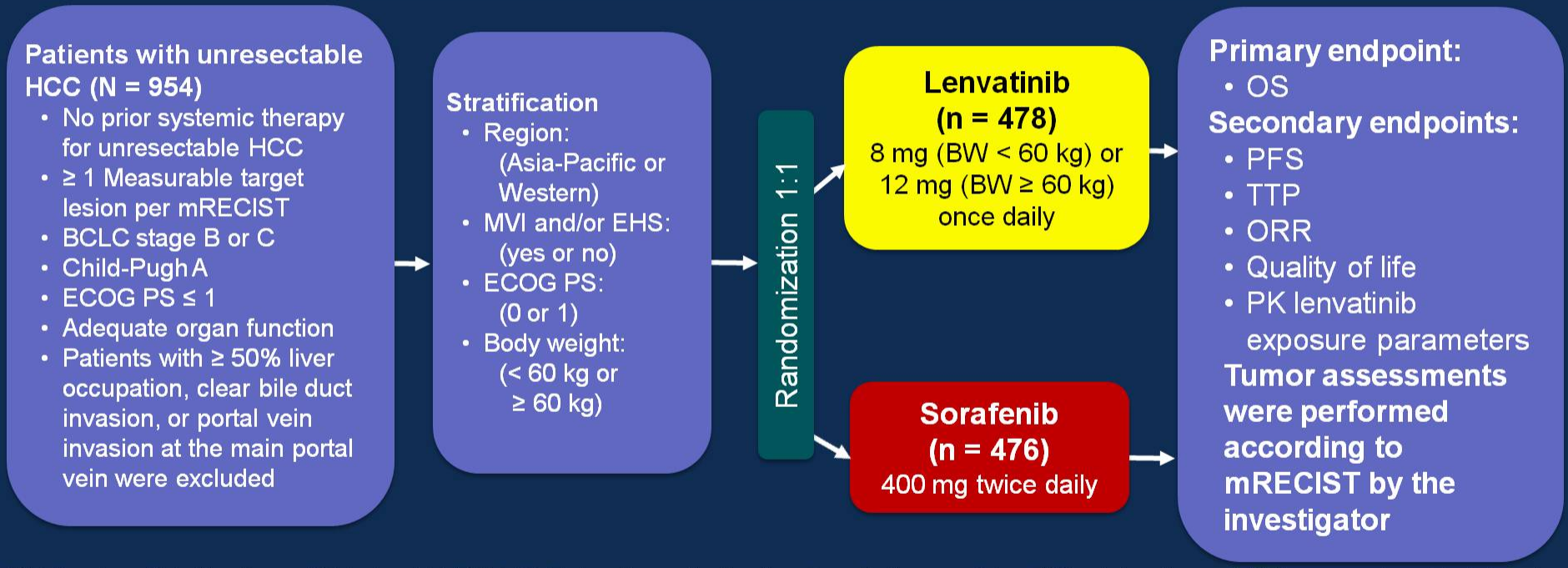
Number at risk (number censored)									
SIRT	237 (0)	143 (3)	90 (5)	49 (15)	30 (23)	11 (35)	2 (39)	0 (41)	0 (41)
Sorafenib	222 (0)	153 (3)	92 (3)	57 (15)	28 (27)	14 (33)	3 (42)	1 (44)	0 (45)

SIRT	237 (0)	76 (10)	29 (13)	8 (15)	5 (16)	3 (18)	0 (19)	0 (19)	0 (19)
Sorafenib	222 (0)	82 (6)	29 (10)	15 (13)	5 (14)	3 (14)	1 (16)	0 (17)	0 (17)

Vilgrain V, et al. Lancet Oncol 2017

Study Schema

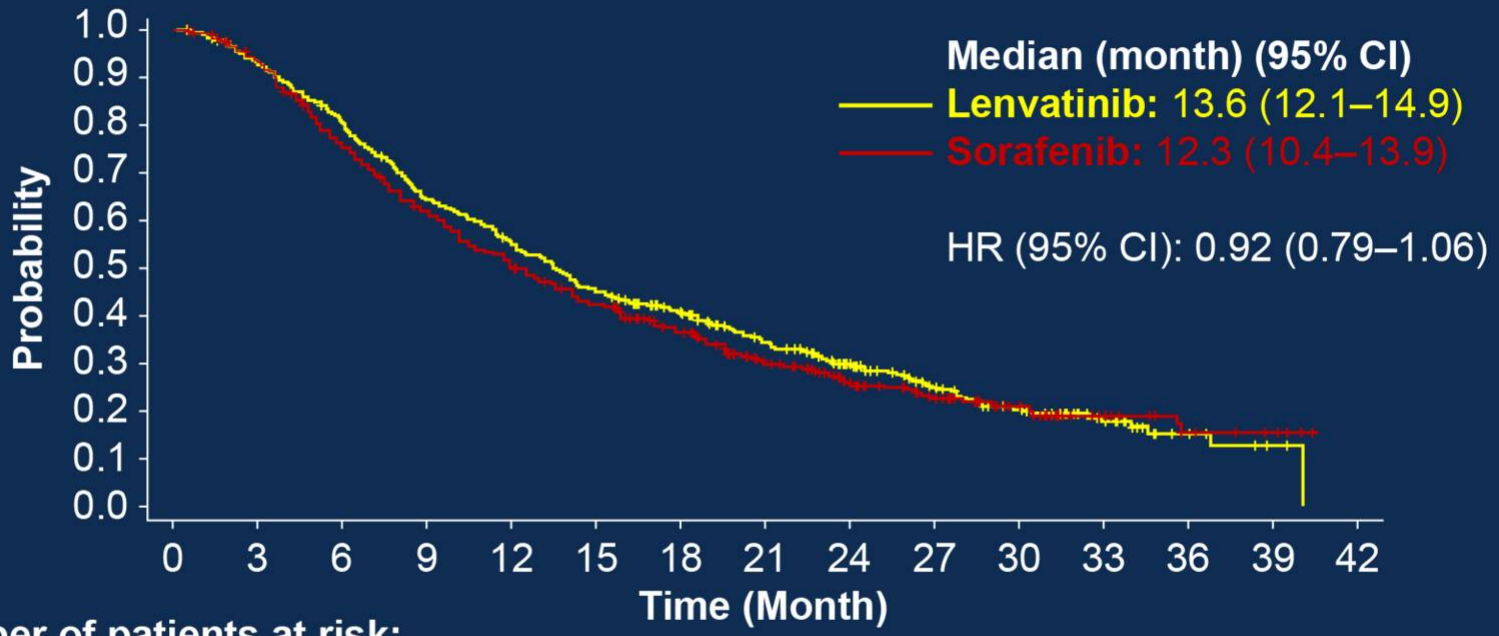
Global, randomized, open-label, phase 3 noninferiority study



BCLC, Barcelona Clinic Liver Cancer; BW; body weight; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EHS, extrahepatic spread; MVI, macroscopic portal vein invasion; mRECIST, modified Response Evaluation Criteria In Solid Tumors; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; RECIST, Response Evaluation Criteria in Solid Tumors; TTP, time to progression.

Kudo M et al: The Lancet. Feb 2018

Primary Endpoint: Kaplan-Meier Estimate of OS

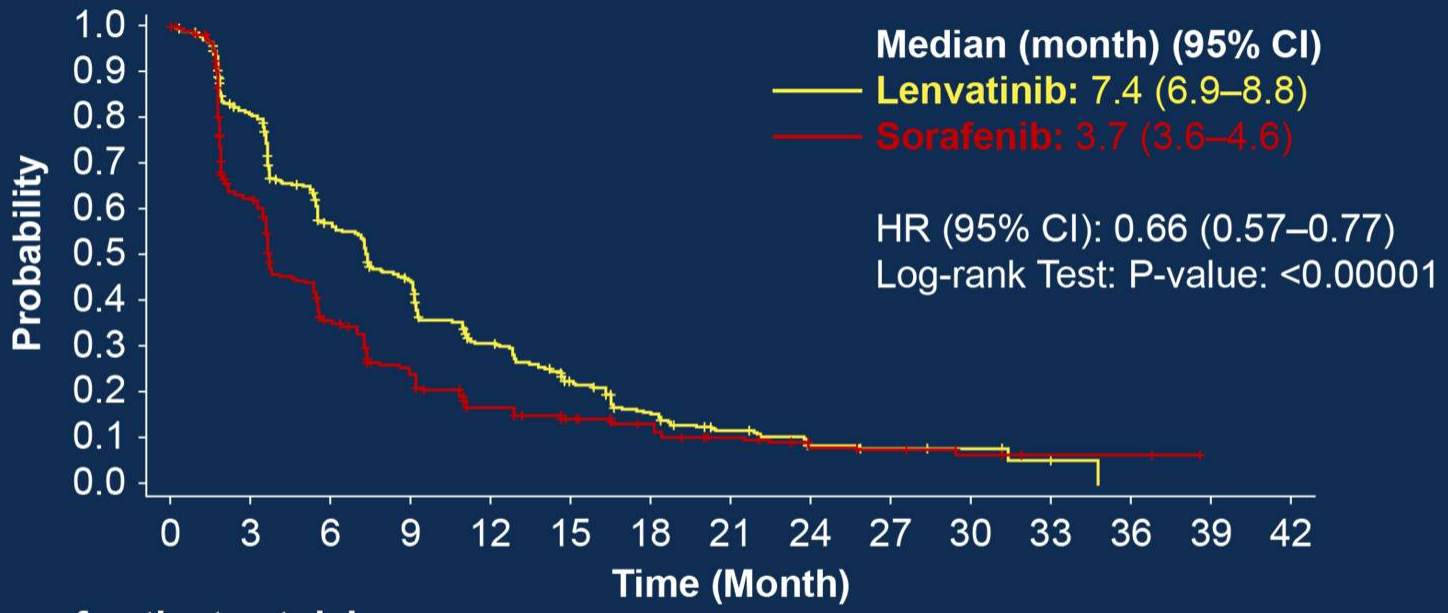


Number of patients at risk:

Lenvatinib	478	436	374	297	253	207	178	140	102	67	40	21	8	2	0
Sorafenib	476	440	348	282	230	192	156	116	83	57	33	16	8	4	0

Kudo M et al: The Lancet. Feb 2018

Secondary Endpoint: Kaplan-Meier Estimate of PFS by mRECIST



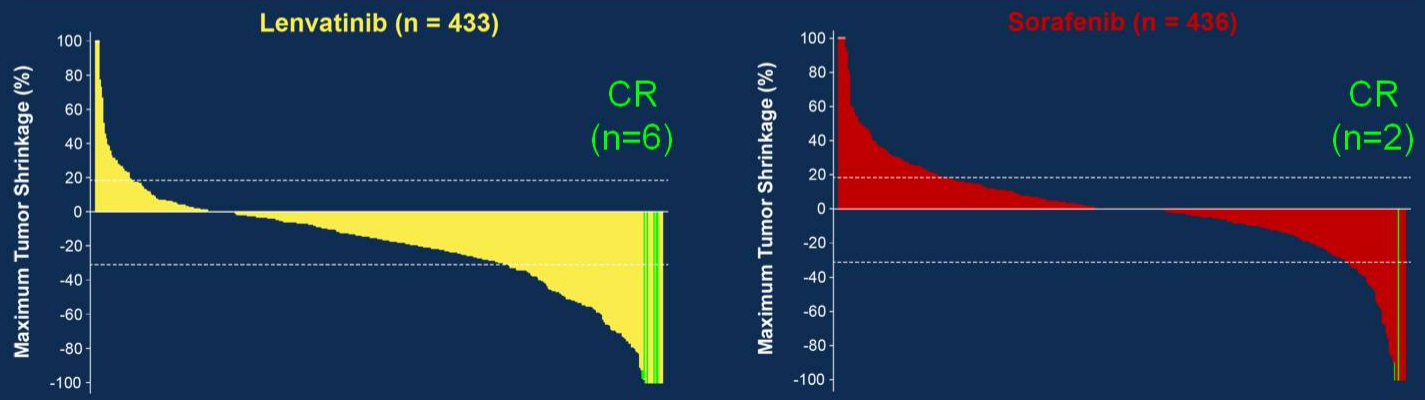
Number of patients at risk:

Lenvatinib	478	345	223	172	106	69	44	28	14	9	4	2	0	0
Sorafenib	476	262	140	94	56	41	33	22	14	9	4	2	2	0

Kudo M et al: The Lancet. Feb 2018

Maximum Change in Tumor Size by mRECIST

n, (%)	Lenvatinib (n = 478)	Sorafenib (n = 476)	Odds Ratio (95% CI)
ORR	115 (24.1)	44 (9.2)	3.13 (2.15–4.56)
95% CI	20.2–27.9	6.6–11.8	*P* < 0.00001
CR	6 (1.3)	2 (0.4)	
PR	109 (22.8)	42 (8.8)	
SD	246 (51.5)	244 (51.3)	
Durable SD	167 (34.9)	139 (29.2)	
PD	71 (14.9)	147 (30.9)	
Unknown/NE	46 (9.6)	41 (8.6)	
DCR	361 (75.5)	288 (60.5)	
95% CI	71.7–79.4	56.1–64.9	



Percentage change in tumor size is truncated at 100% (rectangles). ORR is defined as CR+PR, according to mRECIST; durable SD is defined as SD lasting ≥ 23 weeks.
CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

Kudo M et al: The Lancet. Feb 2018

Most Frequent TEAEs (≥ 15%)

Adverse event, n (%)	Lenvatinib (n = 476)		Sorafenib (n = 475)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Hypertension	201 (42)	111 (23)	144 (30)	68 (14)
Diarrhea	184 (39)	20 (4)	220 (46)	20 (4)
Decreased appetite	162 (34)	22 (5)	127 (27)	6 (1)
Decreased weight	147 (31)	36 (8)	106 (22)	14 (3)
Fatigue	141 (30)	18 (4)	119 (25)	17 (4)
Palmar-plantar erythrodysesthesia	128 (27)	14 (3)	249 (52)	54 (11)
Proteinuria	117 (25)	27 (6)	54 (11)	8 (2)
Dysphonia	113 (24)	1 (0)	57 (12)	0 (0)
Nausea	93 (20)	4 (1)	68 (14)	4 (1)
Decreased platelet count	87 (18)	26 (6)	58 (12)	16 (3)
Abdominal pain	81 (17)	8 (2)	87 (18)	13 (3)
Hypothyroidism	78 (16)	0 (0)	8 (2)	0 (0)
Vomiting	77 (16)	6 (1)	36 (8)	5 (1)
Constipation	76 (16)	3 (1)	52 (11)	0 (0)
Elevated aspartate aminotransferase	65 (14)	24 (5)	80 (17)	38 (8)
Rash	46 (10)	0 (0)	76 (16)	2 (0)
Alopecia	14 (3)	0 (N/A)	119 (25)	0 (N/A)

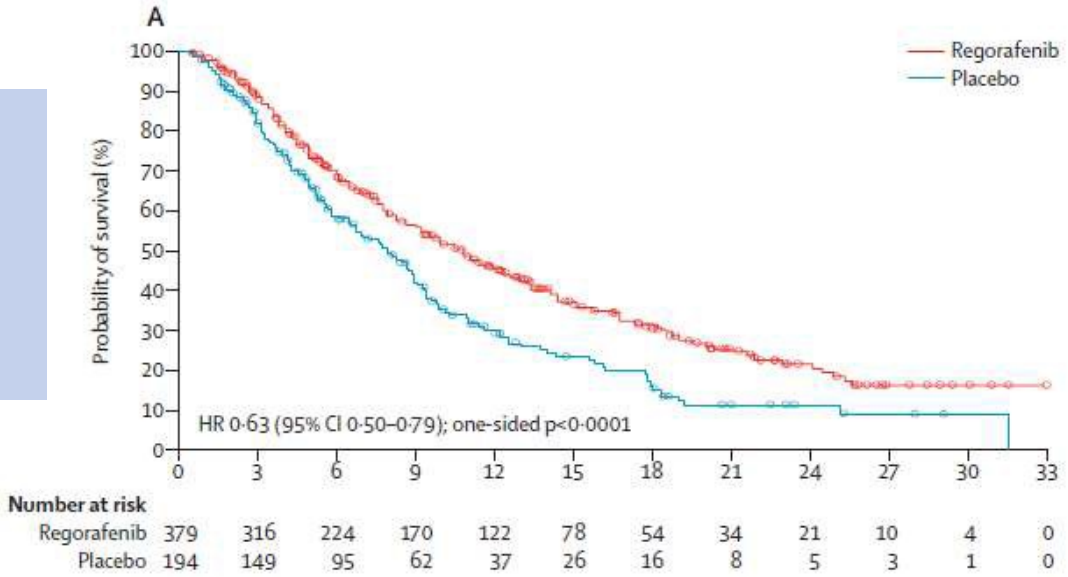
Kudo M et al: The Lancet. Feb 2018

Second-Line

Second line after sorafenib: regorafenib: RESORCE trial

- RESORCE trial:
  - Progression during sorafenib
  - In patients who tolerated well sorafenib (> 400 mg/d , 20 d / month)
  - 160 mg/OD 3 weeks on 1 week off

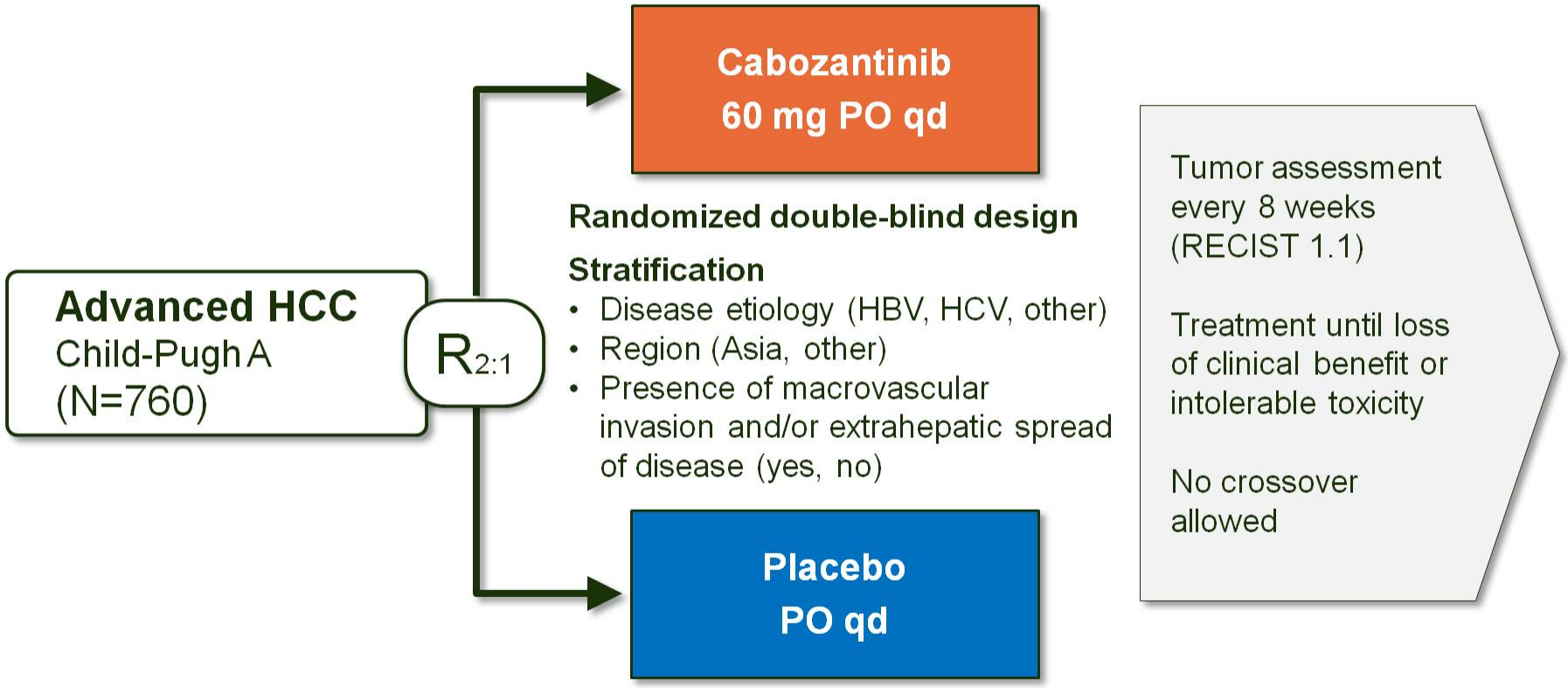
	Regorafenib	HR:	Placebo
mOS	10.6 m	0.63	7.8 m
mTTP	3.2 m	0.44	1.5 m
ORR	10.6%		4.1%
DCR	65.2%		36.1%



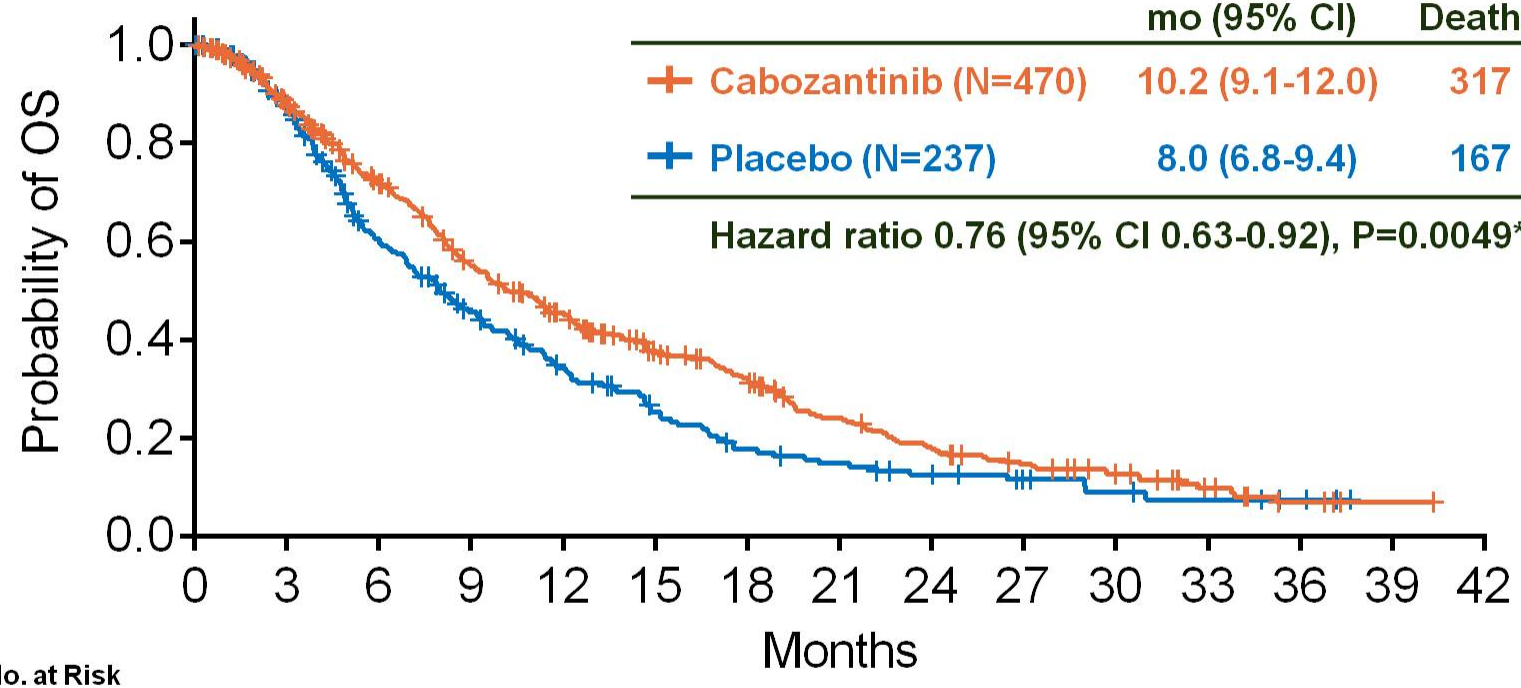
Cabozantinib: positive results !
CELESTIAL trial
mOS: 8.0 => 10.2 m

Bruix J, et al. Lancet 2016

CELESTIAL Study Design



Overall Survival



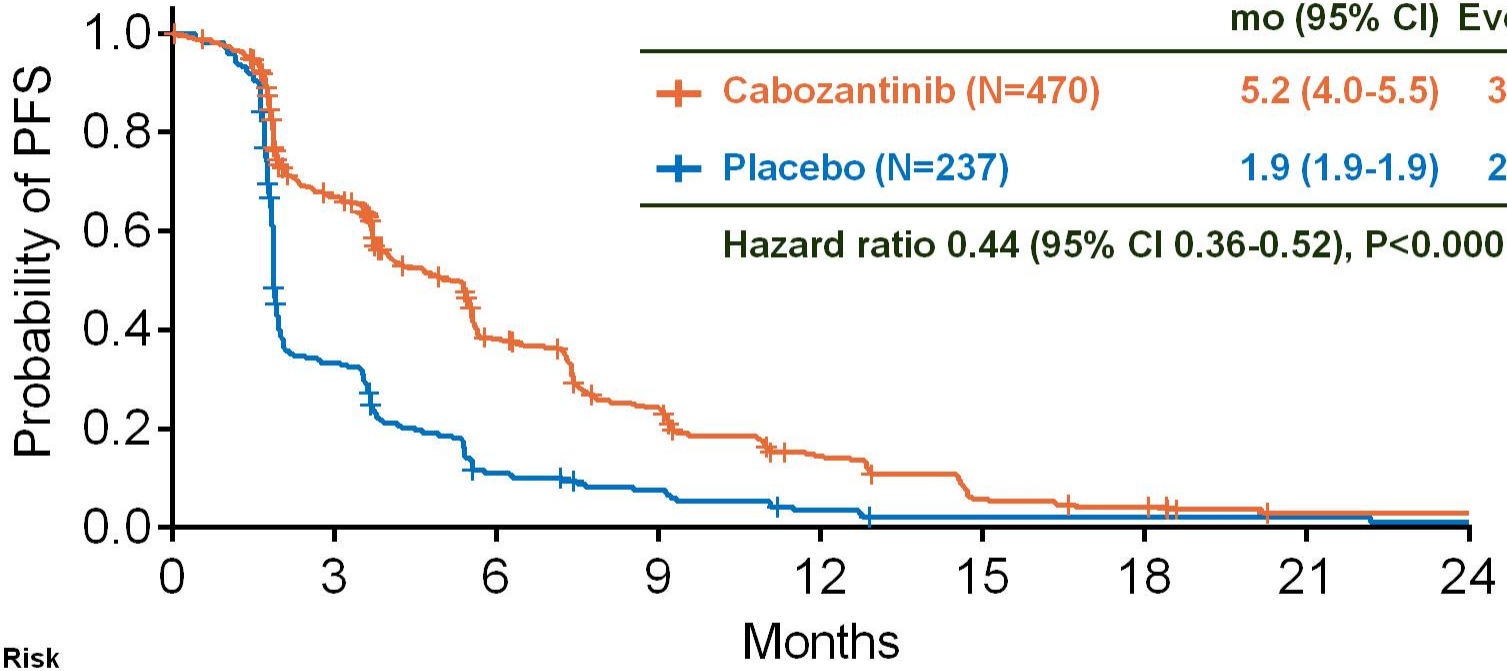
	Median OS mo (95% CI)	No. of Deaths
Cabozantinib (N=470)	10.2 (9.1-12.0)	317
Placebo (N=237)	8.0 (6.8-9.4)	167

Hazard ratio 0.76 (95% CI 0.63-0.92), P=0.0049*

No. at Risk															
Cabozantinib	470	382	281	206	159	116	93	63	44	31	22	12	4	1	0
Placebo	237	190	117	82	57	37	25	20	15	10	7	5	3	0	0

*Critical p-value ≤ 0.021 for second interim analysis

Progression-free Survival



	Median PFS mo (95% CI)	No. of Events
Cabozantinib (N=470)	5.2 (4.0-5.5)	349
Placebo (N=237)	1.9 (1.9-1.9)	205

Hazard ratio 0.44 (95% CI 0.36-0.52), P<0.0001

No. at Risk									
Cabozantinib	470	266	131	80	39	15	10	3	3
Placebo	237	70	21	13	5	2	2	2	1

Progression-free survival assessed per RECIST 1.1

Lancet. 2017 Apr 20.

Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): an open-label, non-comparative, phase 1/2 dose escalation and expansion trial

Anthony B El-Khoueiry,*Bruno Sangro,* Thomas Yau, Todd S Crocenzi, Masatoshi Kudo, Chiun Hsu, Tae-You Kim, Su-Pin Choo, Jörg Trojan, Theodore H Welling 3rd, Tim Meyer, Yoon-Koo Kang, Winnie Yeo, Akhil Chopra, Jeffrey Anderson, Christine dela Cruz, Lixin Lang, Jaclyn Neely, Hao Tang, Homa B Dastani, Ignacio Melero

FDA grants accelerated approval to nivolumab for HCC previously treated with sorafenib

Biomarkers for immunotherapy in HCC

	Escalation phase (n=44)*	Expansion phase (n=174)*
PD-L1 ≥1%†	11 (25%)	34 (20%)
Objective response	3/11 (27%; 6–61)	9/34 (26%; 13–44)
Complete response	1 (9%)	1 (3%)
Partial response	2 (18%)	8 (24%)
Stable disease	0	16 (47%)
Progressive disease	7 (64%)	9 (26%)
Not determined	1 (9%)	0
PD-L1 <1%†	33 (75%)	140 (80%)
Objective response	4/33 (12%; 3–28)	26/140 (19%; 13–26)
Complete response	2 (6%)	2 (1%)
Partial response	2 (6%)	24 (17%)
Stable disease	19 (58%)	62 (44%)
Progressive disease	8 (24%)	46 (33%)
Not determined	2 (6%)	6 (4%)

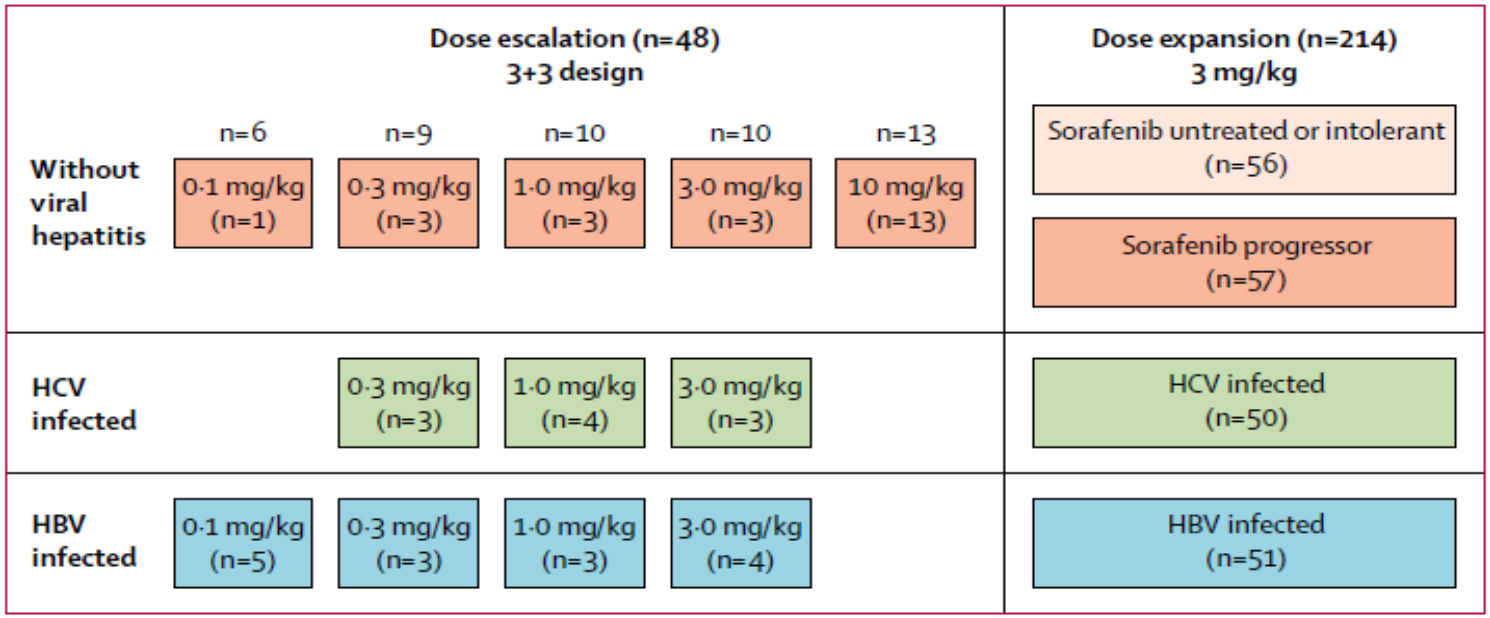
Data are n (%); n/N (%; 95% CI). PD-L1=programmed death-ligand 1.
*Four patients in the dose-escalation phase and 40 patients in the dose-expansion phase did not have tumour PD-L1 expression data available.
†PD-L1 membrane expression on tumour cells.

El-Khoueiry A et al, Lancet, online April 2017

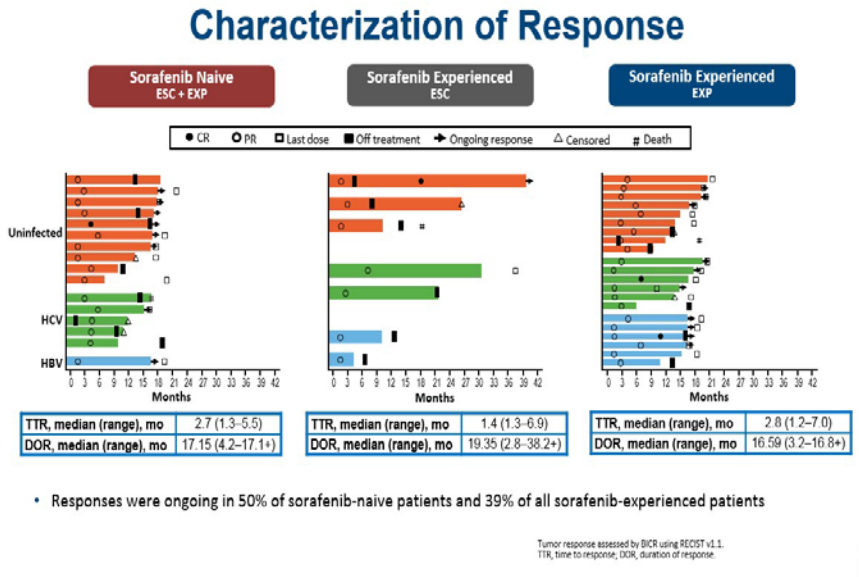
- About 20% were PDL-1 positive
- Objective responses were observed in 26% of patients with PD-L1 expression on at least 1% of tumor cells (95% CI 13–44) and in 19% of patients with PD-L1 on less than 1% of tumour cells (95% CI 13–26).

Nivolumab HCC

Nivolumab:

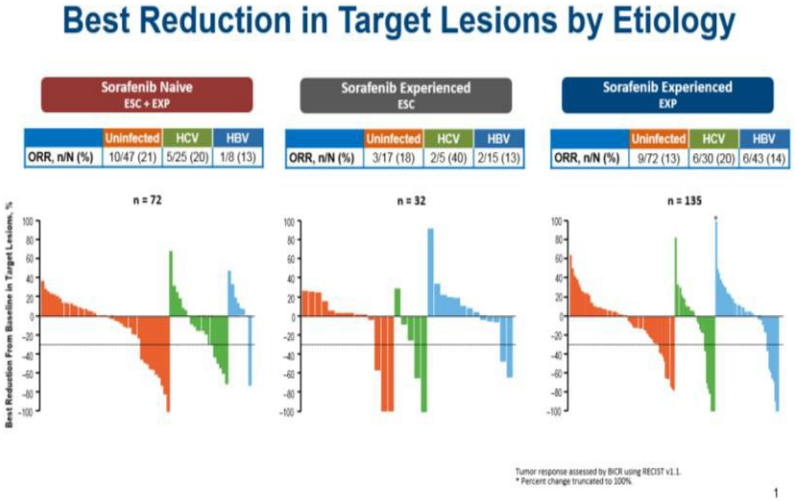


El-Khoueiry A, et al. Lancet 2017



- Responses were ongoing in 50% of sorafenib-naive patients and 39% of all sorafenib-experienced patients

Tumor response assessed by BICR using RECIST v1.1.
TTR, time to response; DOR, duration of response.



Tumor response assessed by BICR using RECIST v1.1.
* Percent change truncated to 100%.

Responses were durable

No reactivation of hepatitis B was observed

Nivolumab had little anti-viral effect (36% of HCV patients had >1 log decrease in HCV RNA load and 3 HBV patients had > 1 log decrease in HBsAg)

Majority of responders had >1 log decline in AFP

Sangro ILCA 2017

Conclusions Systemic treatment of HCC

1st line
sorafenib
lenvatinib

2nd line
Regorafenib
Nivolumab
Cabozantinib

Conclusion Biliary Cancers: Advanced Metastatic Disease

First-Line therapy: Level one evidence for the gemcitabine and DDP

Second-Line:

Chemotherapy of limited benefit in selected patients.

Tumor sequencing is suggested (in our service we obtain at Dx and if possible post progression)

MSI-high/MMR deficient: checkpoint inhibitor or refer to immunotherapy trials

Heptatic Embolization may be an option for liver predominant disease.

Conclusions Pancreatic Cancer

- Participation in clinical trials is paramount and should be the first line of choice.
- Folfirinox is an option in good organ function and PS 0-1.
- Gem/Nab is an option for patients with PS 0-2.
- Liposomal Irinotecan + 5- FU is the second-line option based on phase III data and it is level 1 by NCCN guidelines.
- The selection of treatment is dictated by patients' characteristics and physician's choice rather than efficacy.

Conclusions

- Activity in MSI-High tumors is stablished
- Targeted Therapy and immunotherapy combo are emerging.
- Biomarkers to predict benefit from immuno are desperately needed.
- Solid tumor CAR-T is coming soon

Thanks For The Attention !!!