SEQUENCING OF HCC TREATMENT

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DISCLAIMER

Please note:

The views expressed within this presentation are the personal opinion of the author. They do not necessarily represent the views of the author's academic institution or the rest of the HCC CONNECT group

OPTIMIS STUDY: OBSERVATIONAL STUDY OF TACE

Analysis of **OPTIMIS**:

- An observational study including 977 patients treated with TACE

- Followed or not followed by sorafenib

- Most (n=686, 70%) were BCLC stage B

- 23% (n=227) were BCLC stage C

OPTIMIS STUDY: OBSERVATIONAL STUDY OF TACE

Deterioration	All patients	BCLC B	BCLC C
Any parameter	46%	44%	52%
AST	22%	20%	26%
ALT	15%	14%	15%
Albumin	25%	23%	29%
Bilirubin	14%	12%	19%
INR	11%	10%	15%

In addition to BCLC stage, liver deterioration was also associated with tumor burden (number of lesions and maximum tumor diameter), highlighting the importance of patient selection of TACE versus systemic therapy
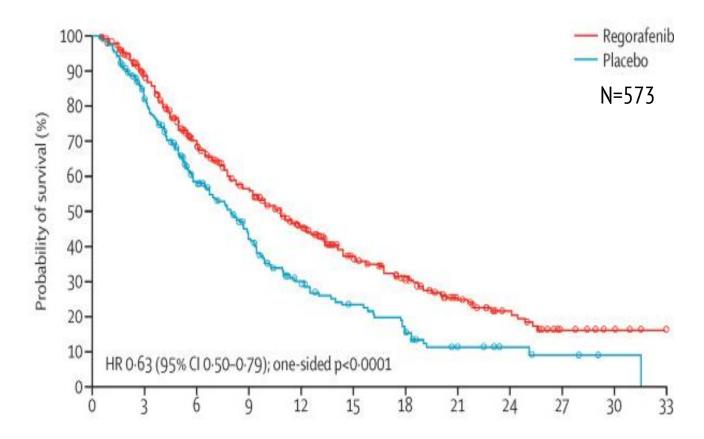
UPDATED ANALYSIS OF RESORCE TRIAL

- RESORCE was a global phase III randomized trial of regorafenib versus placebo in patients who progressed on sorafenib

- Cut-off for primary analysis was February 2016 and cut-off for this updated analysis was January 2017

PREVIOUSLY REPORTED RESULTS OF RESORCE

Median survival: 10.6 months for regorafenib vs. 7.8 months for placebo

Bruix et al. Lancet. 2017 Jan 7;389(10064):56-66

UPDATED OVERALL SURVIVAL ANALYSIS FROM RESORCE TRIAL

	Primary Analysis		Updated Analysis	
	Regorafenib	Placebo	Regorafenib	Placebo
Patients with event, n(%)	233 (61%)	140 (72%)	290 (77%)	169 (87%)
Median overall survival	10.6 (9.1 – 12.1)	7.8 (6.3 – 8.8)	10.7 (9.1 – 12.2)	7.9 (6.4 – 9.0)
HR (95% CI) P-value (1-sided)	0.62 (0.50 – 0.78) <0.0001		0.61 (0.50 – 0.75) <0.0001	

Overall survival at:

- 12 months: regorafenib 47% versus placebo 28%

- 18 months: regorafenib 32% versus placebo 16%

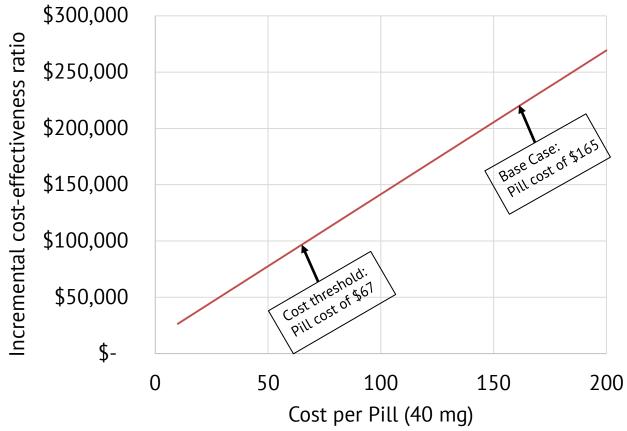- 30 months: regorafenib 16% versus placebo 7%

COST-EFFECTIVENESS OF REGORAFENIB

- Markov model including patients with unresectable HCC and Child A cirrhosis comparing regorafenib versus best supportive care

- Model inputs based on RESORCE Trial and literature review

- Calculated quality adjusted life years (QALY) and incremental cost effectiveness ratio (ICER) for regorafenib versus best supportive care
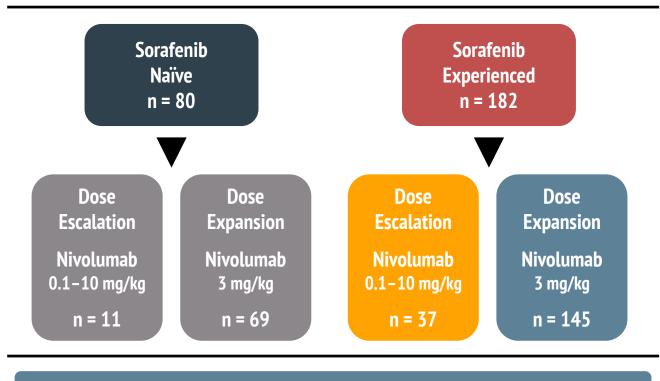
Parikh ND et al. Presented at The International Liver Cancer Association Conference, September 2017; abstract P-003

COST-EFFECTIVENESS OF REGORAFENIB

Regorafenib provided increase of 0.18 QALY at a cost of $47,112
ICER was $224,362 in base case

Parikh ND et al. Presented at The International Liver Cancer Association Conference, September 2017; abstract P-003

CHECKMATE 040 PHASE I/II STUDY

All Patients (N = 262)

Sorafenib Naïve n = 80		Sorafenib Experienced n = 182	
Dose Escalation Nivolumab 0.1–10 mg/kg n = 11	**Dose Expansion** Nivolumab 3 mg/kg n = 69	**Dose Escalation** Nivolumab 0.1–10 mg/kg n = 37	**Dose Expansion** Nivolumab 3 mg/kg n = 145

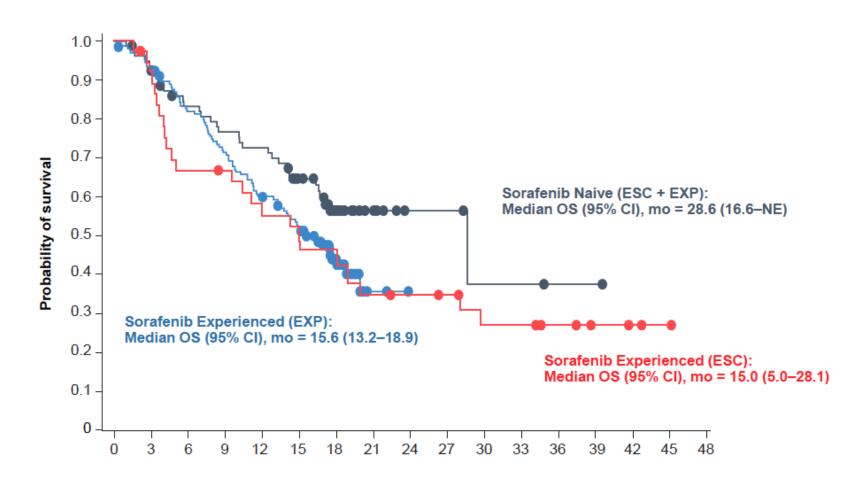**HCV infected, HBV infected, Uninfected**

CHECKMATE 040 PHASE I/II STUDY

Patients, n (%)	Sorafenib Naïve ESC + EXP n = 80*	Sorafenib Experienced ESC n = 37*	Sorafenib Experienced EXP n = 145
Objective response using RECIST v1.1	**16 (20)**	**7 (19)**	**21 (14)**
Complete response	1 (1)	1 (3)	2 (1)
Partial response	15 (19)	6 (16)	19 (13)
Stable disease	25 (31)	12 (32)	60 (41)
Progressive disease	32 (40)	13 (35)	56 (39)
Not evaluable	5 (6)	4 (11)	8 (6)

*Two sorafenib-naïve patients and 1 sorafenib-experienced (ESC) patient had a best overall response reported as non-CR/non-PD by BICR.

15% of sorafenib progressors and 23% of patients who were intolerant of sorafenib achieved an objective response

CHECKMATE 040 PHASE I/II STUDY

Sorafenib Naive (ESC + EXP):
Median OS (95% CI), mo = 28.6 (16.6–NE)

Sorafenib Experienced (EXP):
Median OS (95% CI), mo = 15.6 (13.2–18.9)

Sorafenib Experienced (ESC):
Median OS (95% CI), mo = 15.0 (5.0–28.1)

BENEFITS OF MULTIDISCIPLINARY CARE

- Retrospective cohort study of 694 patients with HCC who received multidisciplinary care at a single center in Korea between 2005 and 2013

- Compared to matched cohort (n=694) who did not receive multidisciplinary care
  - Matched on age, gender, etiology of liver disease, year of diagnosis, BCLC stage, ALBI grade, and AFP

Sinn DH et al. Presented at The International Liver Cancer Association Conference, September 2017; abstract P-066
AFP, alpha-fetoprotein; ALBI, albumin-bilirubin; BCLC, Barcelona Clinic Liver Cancer; HCC, hepatocellular carcinoma
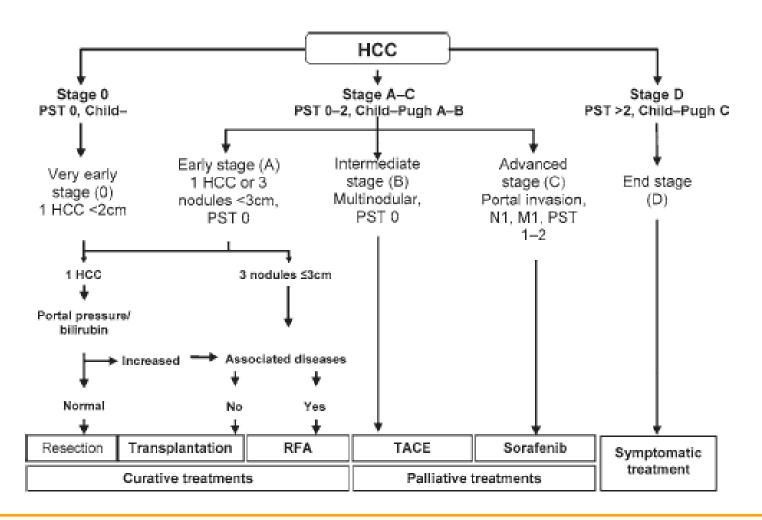
BENEFITS OF MULTIDISCIPLINARY CARE IN HCC

- 5-year survival 73.4% versus 61.9% (HR 0.66, 95% CI 0.56 – 0.78)

- In subgroup analysis, improved survival noted for BCLC stage B (HR 0.44, 95%CI 0.28 – 0.69) and stage C (HR 0.45, 95%CI 0.32 – 0.63) but not for BCLC stage A (HR 0.79, 95%CI 0.61 – 1.04)
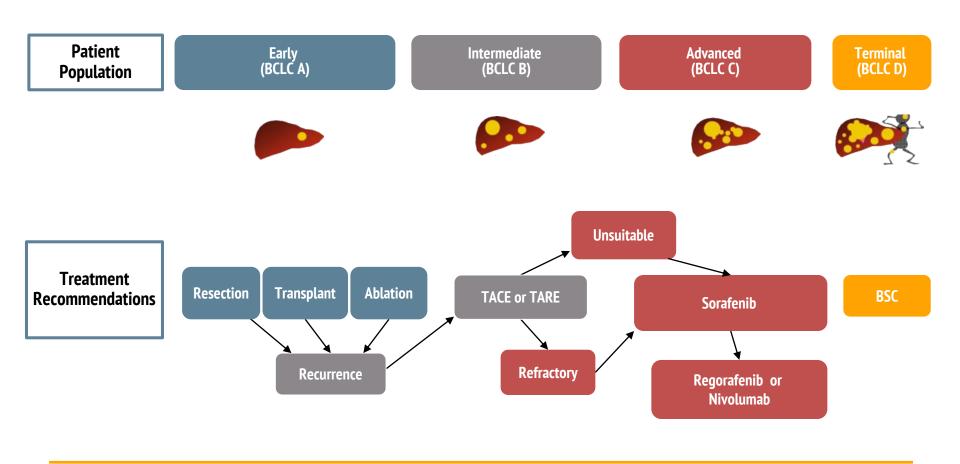
BENEFITS OF MULTIDISCIPLINARY CARE IN HCC

Study	# Patients	Description	Outcomes
Serper 2017[1]	3988	Multidisciplinary conference	Increased curative treatment and reduced mortality
Yopp 2014[2]	355	Single day MDT clinic and conference	Improve early detection, curative treatment, time to treatment, survival
Zhang 2013[3]	343	Single day MDT clinic	Changed imaging/pathology interpretation and therapy plan
Chang 2008[4]	183	Fluid referrals and joint conference	Improve early detection, curative treatment, and survival

1. Serper M et al. Gastroenterology 2017 Jun;152(8):1954-1964; 2. Yopp AC et al. Ann Surg Oncol 2014 Apr;21(4):1287-95; 3. Zhang J et al. Curr Oncol 2013 Apr;20(2):e123-31; 4. Chang TT et al; HPB (Oxford) 2008;10(6):405-11

HCC, HepatoCellular Carcinoma

OLD PERSPECTIVE OF HCC TREATMENT LANDSCAPE

NEW PERSPECTIVE OF HCC TREATMENT LANDSCAPE

BSC, best supportive care; TARE, transarterial radioembolization

NEW PERSPECTIVE OF HCC TREATMENT LANDSCAPE

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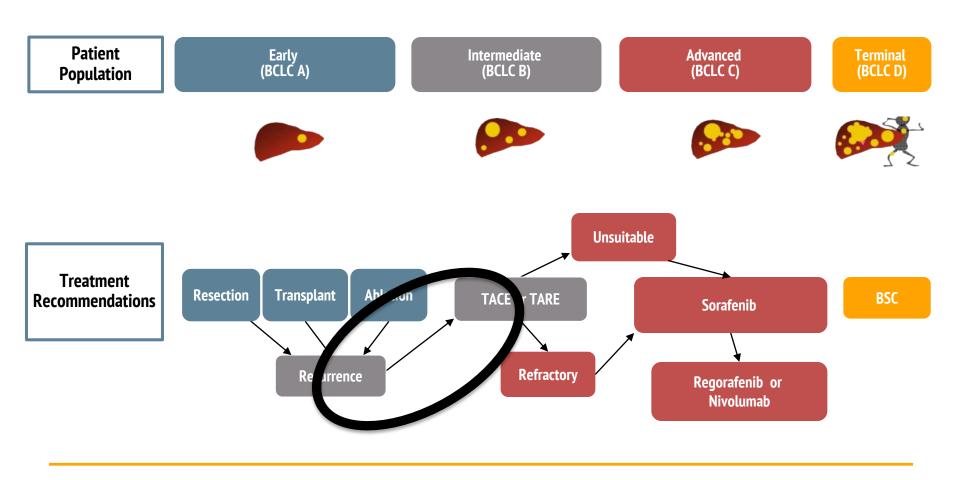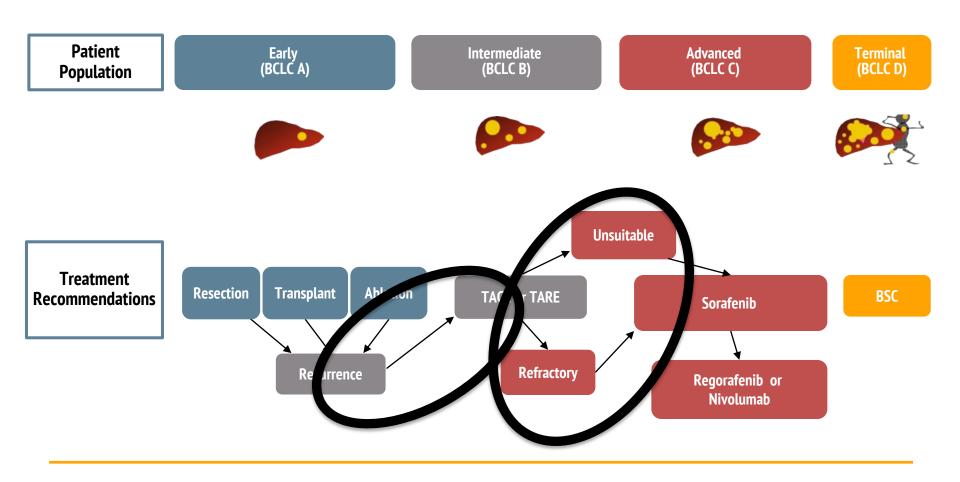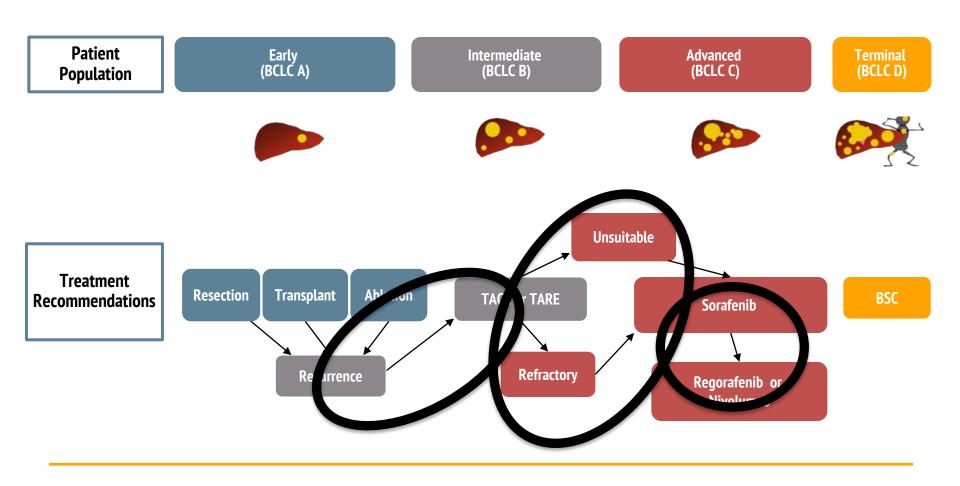
NEW PERSPECTIVE OF HCC TREATMENT LANDSCAPE

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