
HCC
connect
POWERED BY COR2ED

MEETING SUMMARY

ILCA 2018, London, UK

DR. AIWU RUTH HE, MD, PHD

Associate Professor of Medicine
Georgetown University, Washington DC

UPDATE ON HCC TREATMENT

DISCLAIMER

HCC connect
POWERED BY COR2ED

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

REACH-2: RAMUCIRUMAB VS PLACEBO AS 2ND LINE TREATMENT IN PATIENTS WITH ADVANCED HCC AND ELEVATED BASELINE AFP FOLLOWING 1ST LINE SORAFENIB,

A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

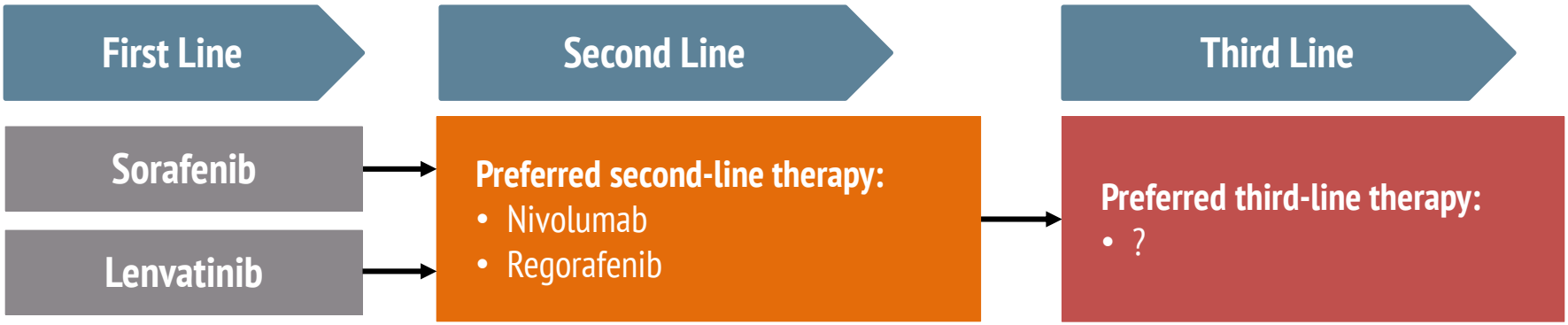
Abstract O-001

Peter Galle et al.

CURRENT SYSTEMIC THERAPY SEQUENCES IN ADVANCED HCC

HCC connect
POWERED BY COR2ED

FDA approved in the US



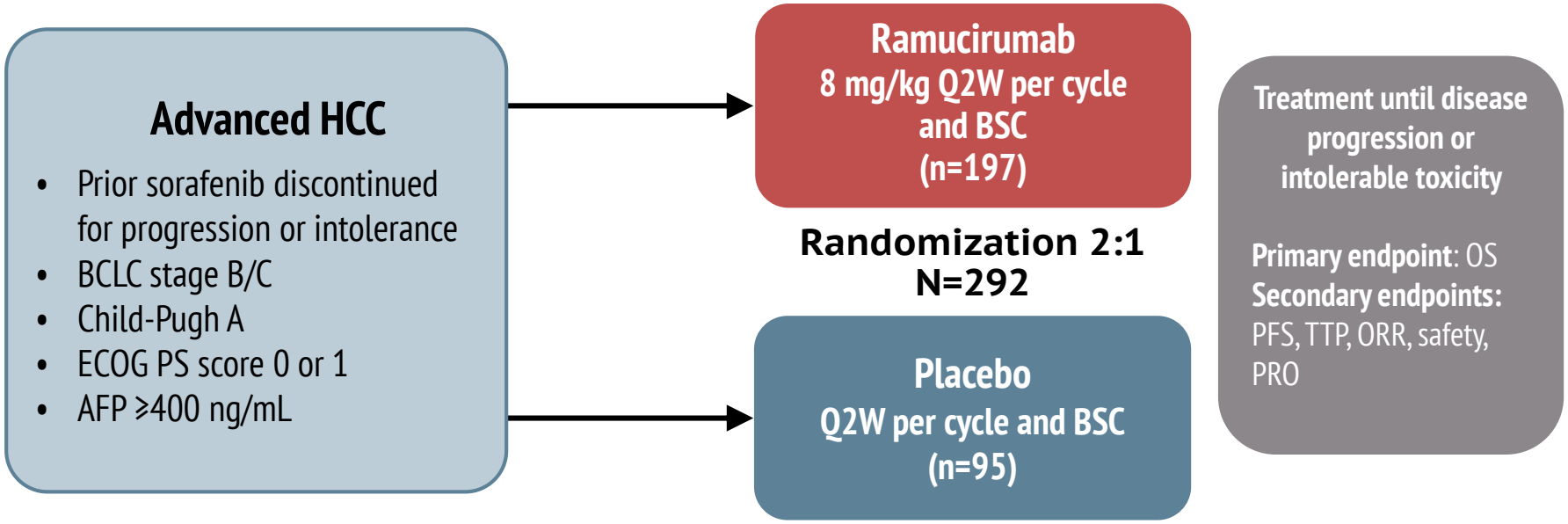
Positive data from randomized phase III studies, under FDA review in the US, pending approval

HCC, hepatocellular carcinoma; FDA, Food and Drug Administration; US United States

REACH-2 STUDY DESIGN

HCC connect
POWERED BY COR2ED

Main Cohort*

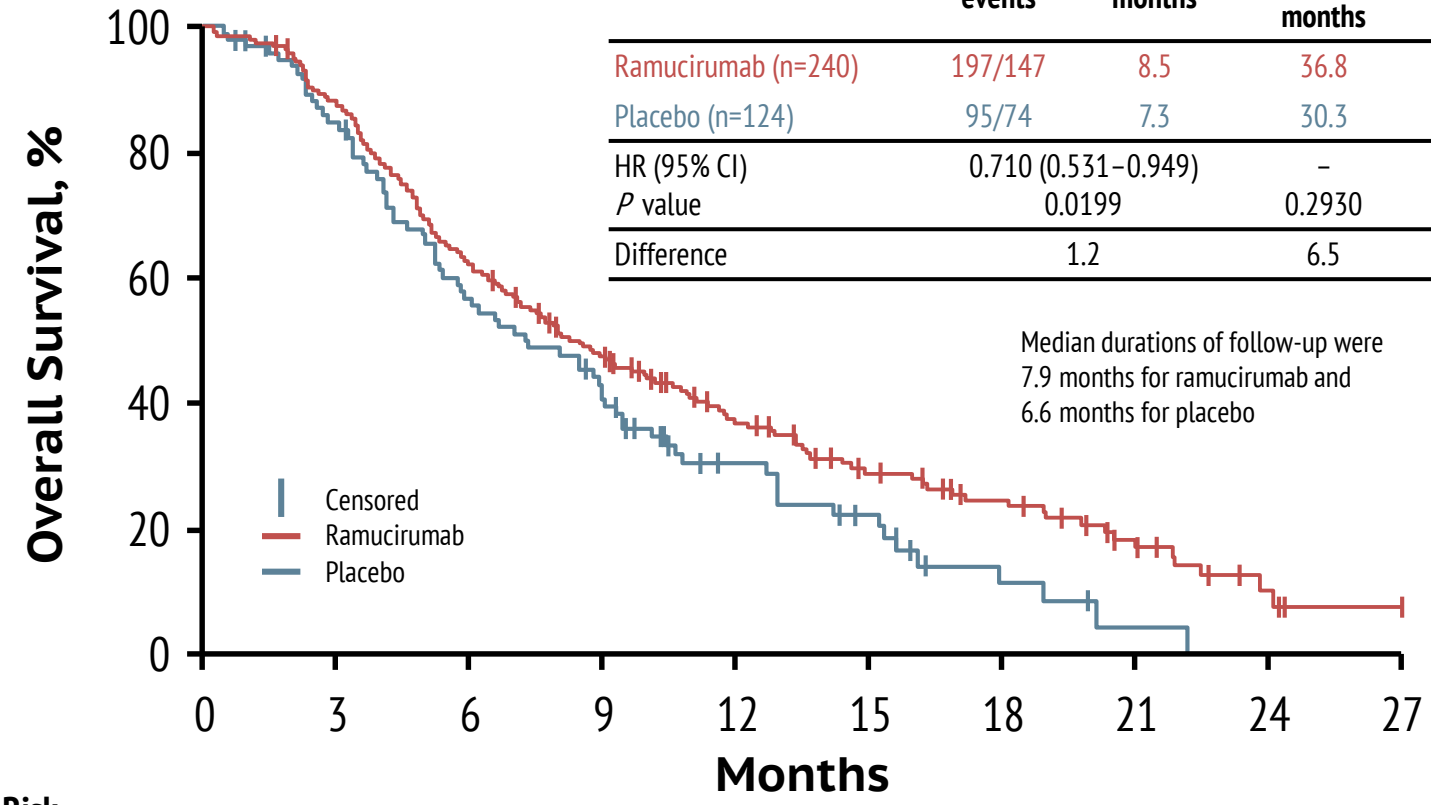


*A second, single arm, open-label cohort of ~44 patients will be enrolled with the same eligibility and treatment as the main cohort except a requirement for prior treatment other than sorafenib and some exclusions of checkpoint inhibitor-related adverse events. The primary objective is safety; secondary objectives include OS, PFS, and PRO. A third randomized cohort of ~65 Chinese patients will be enrolled with the same objectives, eligibility, treatment, and evaluations as the main cohort. Analysis of Open-Label and Chinese cohorts will be independent of the main REACH-2 cohort.

AFP, alpha-fetoprotein; BCLC, Barcelona Clinic Liver Cancer; BSC, best supportive care; ECOG PS, Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; OS, overall survival; ORR, overall response rate; PFS, progression-free survival; PRO, patient-reported outcome; Q2W, once every two weeks; TTP, time to progression. Zhu AX, et al. Presented at: ASCO. 2018 (abstr 4003). Galle P, et al. Presented at: ILCA 2018 (abstr 0-001). https://clinicaltrials.gov/ct2/show/NCT02435433

REACH-2: OVERALL SURVIVAL

	Patients/ events	Median OS, months	Survival rate (%) at 12 months	Survival rate (%) at 18 months
Ramucirumab (n=240)	197/147	8.5	36.8	24.5
Placebo (n=124)	95/74	7.3	30.3	11.3
HR (95% CI)	0.710 (0.531–0.949)		–	–
P value	0.0199		0.2930	0.0187
Difference	1.2		6.5	13.2



No. at Risk										
Ramucirumab	197	172	121	87	56	37	26	14	4	0
Placebo	95	76	50	36	19	12	4	1	0	0

CI, confidence interval; HR, hazard ratio; OS, overall survival. Zhu AX, et al. Presented at: ASCO. 2018 (abstr 4003)
Galle P, et al. Presented at: ILCA 2018 (abstr 0-001)

REACH-2: PFS AND ORR

HCC connect
POWERED BY COR2ED

n (%) except where indicated	Ramucirumab (n=197)	Placebo (n=95)	*P* Value
Median PFS, months	2.8	1.6	<0.0001
HR, 95% CI	0.452 (0.339–0.603)		
ORR (CR+PR)	9 (4.6)	1 (1.1)	0.1697
95% CI	1.7-7.5	0.0-3.1	
DCR (CR+PR+SD)	118 (59.9)	37 (38.9)	0.0006
95% CI	53.1–66.7	29.1–48.8	
Best overall response			
CR	0 (0.0)	0 (0.0)	–
PR	9 (4.6)	1 (1.1)	–
SD	109 (55.3)	36 (37.9)	–
PD	66 (33.5)	48 (50.5)	–
Not evaluable	13 (6.6)	10 (10.5)	–

CI, confidence interval; CR, complete response; DCR, disease control rate; HR, hazard ratio; ORR, overall response rate; PD, progressive disease; PFS, progression free survival; PR, partial response; SD, stable disease. Zhu AX, et al. Presented at: ASCO. 2018 (abstr 4003).
Galle P, et al. Presented at: ILCA 2018 (abstr 0-001)

REACH-2: ADVERSE EVENTS

n (%)	Ramucirumab (n=197)		Placebo (n=95)	
Discontinuation due to treatment-related AE*	21 (10.7)		3 (3.2)	
Dose adjustment† due to AE	68 (34.5)		13 (13.7)	
Deaths due to treatment-related AE*	3 (1.5)		0	
TEAEs in ≥15% patients in ramucirumab arm	**Any Grade**	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Patients with ≥1 TEAE	191 (97.0)	116 (58.9)	82 (86.3)	42 (44.3)
Fatigue	54 (27.4)	7 (3.6)	16 (16.8)	3 (3.2)
Peripheral edema	50 (25.4)	3 (1.5)	13 (13.7)	0
Hypertension	48 (24.4)	24 (12.2)	12 (12.6)	5 (5.3)
Decreased appetite	46 (23.4)	3 (1.5)	19 (20.0)	1 (1.1)
Proteinuria	40 (20.3)	4 (2.0)	4 (4.2)	0
Abdominal pain	39 (19.8)	3 (1.5)	12 (12.6)	2 (2.1)
Nausea	37 (18.8)	0	11 (11.6)	0
Ascites	35 (17.8)	8 (4.1)	7 (7.4)	2 (2.1)
Diarrhea	32 (16.2)	0	14 (14.7)	1 (1.1)

*Related per investigator judgment; †Dose adjustment = dose delay, dose reduction, and dose omission.

AE, adverse event; TEAE, treatment emergent adverse event. Zhu AX, et al. Presented at: ASCO. 2018 (abstr 4003).
Galle P, et al. Presented at: ILCA 2018 (abstr 0-001)

PRELIMINARY SAFETY AND CLINICAL ACTIVITY RESULTS FROM A PHASE 1B STUDY OF ATEZOLIZUMAB + BEVACIZUMAB IN HCC

Abstract O-011

Aiwu Ruth He et al.

PHASE IB GO30140 STUDY (NCT02715531)

HCC connect
POWERED BY COR2ED

Eligibility Criteria:

- Measurable disease per RECIST v1.1
- ECOG PS score 0/1
- Adequate hematologic and end-organ function
- No prior treatment with anti–CTLA-4, anti–PD-1, or anti–PD-L1 therapeutic antibodies

(N=130-310)

Arm A: unresectable or metastatic HCC
- No prior systemic therapy
- Up to Child-Pugh score B7

Atezolizumab 1200 mg IV q3w + bevacizumab 15 mg/kg IV q3w

Arm B: HER2-gastric cancer
Arm C: Pancreatic cancer
Arm D: HCC (atezolizumab+vanucizumab vs atezolizumab+bevacizumab)
Arm E: Esophageal cancer (squamous and adenocarcinoma)

Until disease progression, unacceptable toxicity or loss of clinical benefit

- **Primary endpoints:** Safety and tolerability
- **Key secondary endpoints:** ORR, DOR and PFS per RECIST v1.1 and HCC mRECIST per IRF, and OS

At clinical data cut-off (January 11, 2018), 43 patients were evaluable for safety and 23 patients were evaluable for efficacy with a minimum follow-up of 16 weeks

CTLA-4, cytotoxic T-lymphocyte associated protein; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; HER2, human epidermal growth factor receptor 2; IRF, independent review facility; mRECIST, modified Response Evaluation Criteria in Solid Tumours; ORR, objective response rate; OS, overall survival; PD-1, programmed-death protein 1; PD-L1, programmed-death ligand 1; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours. He R, et al. Presented at: ILCA 2018 (abstr 0-011)

EFFICACY RESULTS BY INV- AND IRF-ASSESSED RECIST v1.1

HCC connect
POWERED BY COR2ED

	INV-Assessed (n=23)	IRF-Assessed (n=23)
ORR, n (%)	**14 (61)**	**15 (65)**
CR	0	1 (4)
PR	14 (61)	14 (61)
SD, n (%)	5 (22)	7 (30)
PD, n (%)	4 (17)	1 (4)
DCR, n (%)		
CR + PR + SD	19 (83)	22 (96)
CR + PR + SD ⩾6 months	15 (65)	16 (70)
Median DOR, months	Not reached (1.7+ to 14.0+)	Not reached (1.9+ to 14.0+)
Median PFS (range), months	Not reached (1.7 to 17.0+)	Not reached (1.9 to 17.0+)
6-month PFS	65%	65%
Median OS (range), months	Not reached (3.5+ to 17.3+)	
6-month OS	86%	

Clinical cut-off date: January 11, 2018

+, censored; CR, complete response; DCR, disease control rate; DOR, duration of response; INV, investigator; IRF, independent review facility; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease

He R, et al. Presented at: ILCA 2018 (abstr 0-011)

CONCLUSIONS

- The combination of atezolizumab + bevacizumab was safe and well tolerated
  - No new safety signals were identified beyond the established safety profile for each single agent
- The combination of atezolizumab + bevacizumab showed promising early efficacy
  - The confirmed ORR was 61% by INV assessment and 65% by IRF assessment (both per RECIST v1.1)
  - Responses were observed in all clinically relevant patient subgroups, including etiology, geographic region and AFP level at baseline
- Responses were durable, with 10 responses ongoing for ≥6 months and 3 of these ongoing for ≥1 year per INV assessment (median follow-up: 10.3 months)
  - Median OS, PFS and DOR had not been reached at the clinical cut-off date
- The promising clinical activity of atezolizumab + bevacizumab supports further investigation as first-line treatment option for patients with advanced HCC
  - The US FDA has granted Breakthrough Therapy Designation for atezolizumab in combination with bevacizumab as a first-line treatment for patients with advanced or metastatic HCC

AFP, alpha-fetoprotein; DOR, duration of response; FDA, Food and Drug Administration; HCC, hepatocellular carcinoma; INV, investigator; IRF, independent review facility; ORR, overall response rate; RECIST, Response Evaluation Criteria in Solid Tumours; US, United States

He R, et al. Presented at: ILCA 2018 (abstr 0-011)

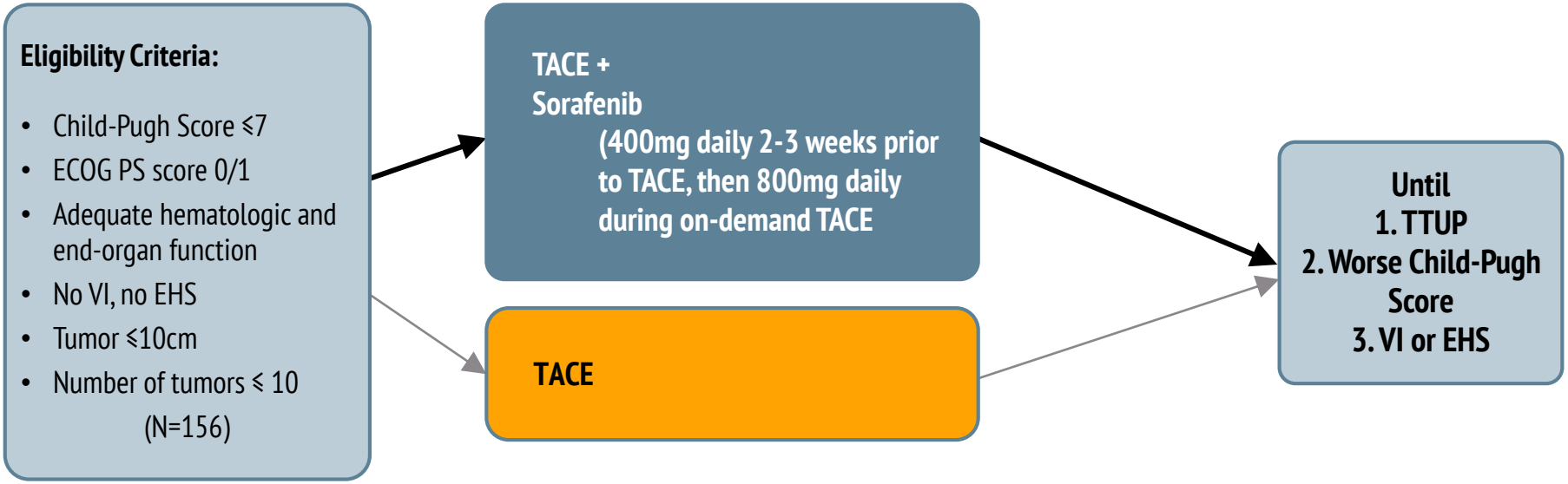
TACTICS: TACE THERAPY IN COMBINATION WITH SORAFENIB AS COMPARED WITH TACE ALONE IN PATIENTS WITH HCC,

A RANDOMIZED, OPEN LABEL, MULTICENTER, PHASE 2 TRIAL (NCT01217034)

Abstract O-004

Kazuomi Ueshima et al. and TACTICS Study Group

TACTICS: STUDY DESIGN



- **Primary endpoints:** PFS and OS

  (PFS is expected to 40% extension from 18 months (control arm) to 25 months, target HR was 0.71, with a power of 0.80)

- **Key secondary endpoints:** time to progression and safety

Stratification by institution, Milan criteria (in or out), and number of previous TACE (0 or 1-2)

ECOG, Eastern Cooperative Oncology Group performance status; EHS, extrahepatic spread; TACE, transcatheter arterial chemoembolisation; TTUP, time to untreatable progression; VI, vascular invasion

Ueshima K, et al. Presented at: ILCA 2018 (abstr 0-004)

TACTICS: RESULTS

Median survival and time to progression (months)	TACE	TACE + Sorafenib	HR (95% CI)	*P* value
PFS	13.5	25.2	0.59 (0.41–0.87)	0.006
OS	Not reached	Not reached		
TTUP	20.6	26.7	0.57 (0.35–0.92)	0.02

CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; TACE, transcatheter arterial chemoembolisation; TTUP, time to untreatable progression

Ueshima K, et al. Presented at: ILCA 2018 (abstr 0-004)

TACTICS: CONCLUSION

- Sorafenib in combination with TACE significantly improved PFS over TACE alone in patients with unresectable HCC

- Adverse events were consistent with the known safety profile with previous TACE combination trials

HCC, hepatocellular carcinoma; PFS, progression-free survival; TACE, transcatheter arterial chemoembolization

Ueshima K, et al. Presented at: ILCA 2018 (abstr 0-004)

HCC CONNECT
Bodenackerstrasse 17
4103 Bottmingen
SWITZERLAND

Dr. Antoine Lacombe
Pharm D, MBA
Phone: +41 79 529 42 79
antoine.lacombe@cor2ed.com

Dr. Froukje Sosef
MD
Phone: +31 6 2324 3636
froukje.sosef@cor2ed.com