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MEETING SUMMARY

ASCO GI, FRIDAY JANUARY 16TH 2015

BY DR. MED. THOMAS WINDER, ZURICH, SWITZERLAND

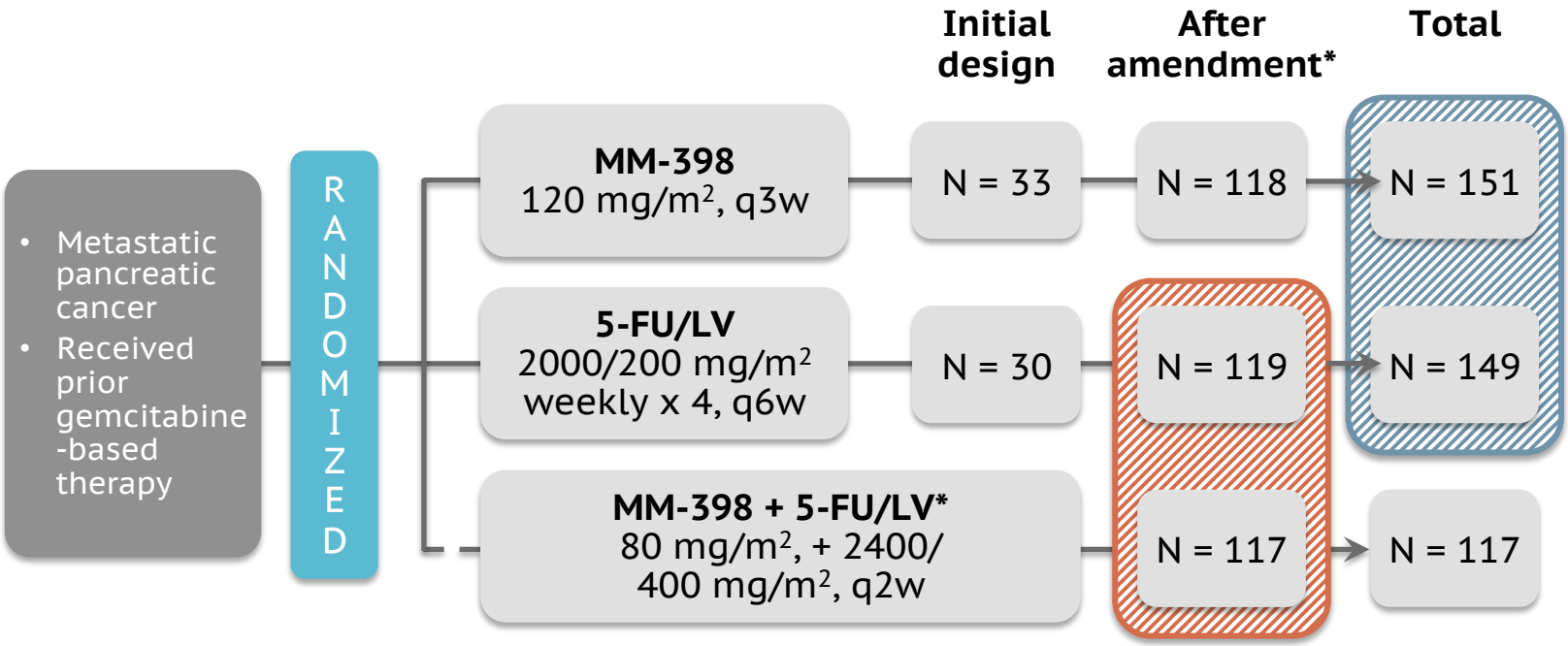
Cancers of the Pancreas, Small Bowel, and Hepatobiliary Tract

EXPANDED ANALYSES OF NAPOLI-1: PHASE 3 STUDY OF MM-398 (NAL-IRI), WITH OR WITHOUT 5-FLUOROURACIL AND LEUCOVORIN, VERSUS 5-FLUOROURACIL AND LEUCOVORIN, IN METASTATIC PANCREATIC CANCER (mPAC) PREVIOUSLY TREATED WITH GEMCITABINE-BASED THERAPY

L.-T. Chen, D.D. Von Hoff, C.-P. Li, A. Wang-Gillam,
G. Bodoky, A. Dean, Y.-S. Shan, G. Jameson, T. Macarulla,
K. Lee, D. Cunningham, J.F. Blanc, R. Hubner, C.-F. Chiu,
G. Schwartsmann, J. Siveke, F. Braiteh, V. Moyo,
B. Belanger, E. Bayever

Presented By Li-Tzong Chen at 2015 Gastrointestinal Cancers Symposium

NAPOLI-1 STUDY DESIGN



Stratification factors: Albumin, KPS and ethnicity

Primary endpoint: Overall survival

Key secondary endpoints: PFS, ORR, CA19-9 response and safety

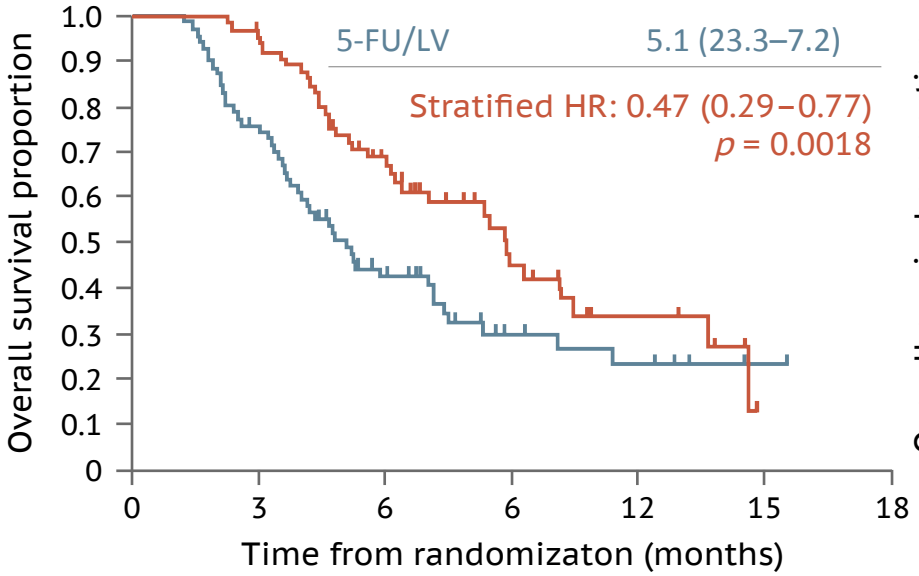
* Study was amended to add the MM-398 + 5-FU/LV arm once safety data on the combination became available. Only those patients enrolled in the 5FU/LV arm after the amendment (N=119), were used as the control for the combination arm.

OVERALL SURVIVAL: PP* VS. NON-PP

Per Protocol Population

	Median OS, Months (95% CI)
MM-398+5-FU/LV	8.9 (6.4–10.5)
5-FU/LV	5.1 (23.3–7.2)

Stratified HR: 0.47 (0.29–0.77)
$p = 0.0018$

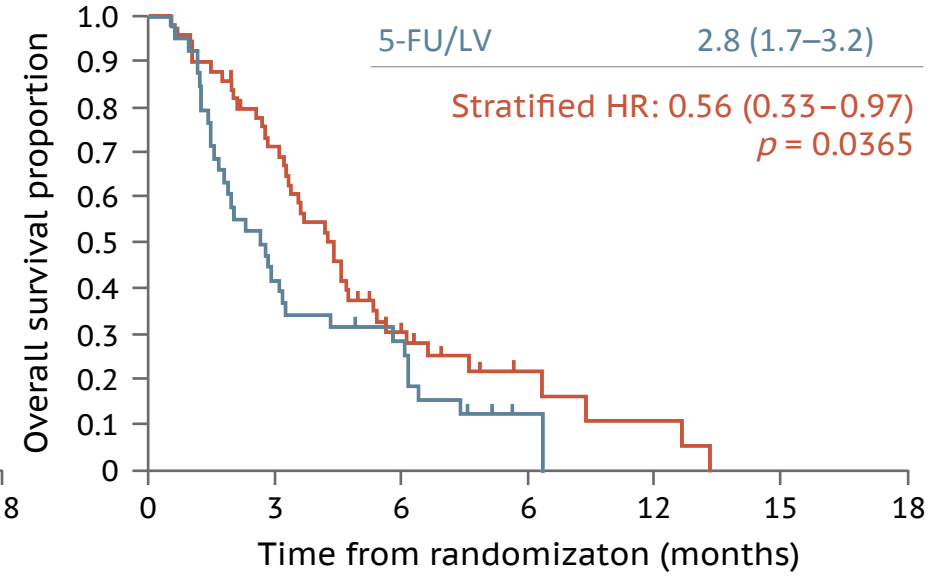


Patients:						
	66	63	38	16	6	0
	71	52	25	10	6	1

Non-Per Protocol Population

	Median OS, Months (95% CI)
MM-398+5-FU/LV	4.4 (3.3–5.3)
5-FU/LV	2.8 (1.7–3.2)

Stratified HR: 0.56 (0.33–0.97)
$p = 0.0365$



Patients:					
51	34	13	4	2	
48	16	5	1	0	

* Protocol-defined primary analysis data cut (14Feb2014). Per protocol population was defined as patients who received at least 80% of the protocol defined treatment during the first 6 weeks of treatment and did not have protocol deviations related to inclusion/exclusion criteria, receiving prohibited therapies or not receiving treatment as randomized.

Presented By Li-Tzong Chen at 2015 Gastrointestinal Cancers Symposium

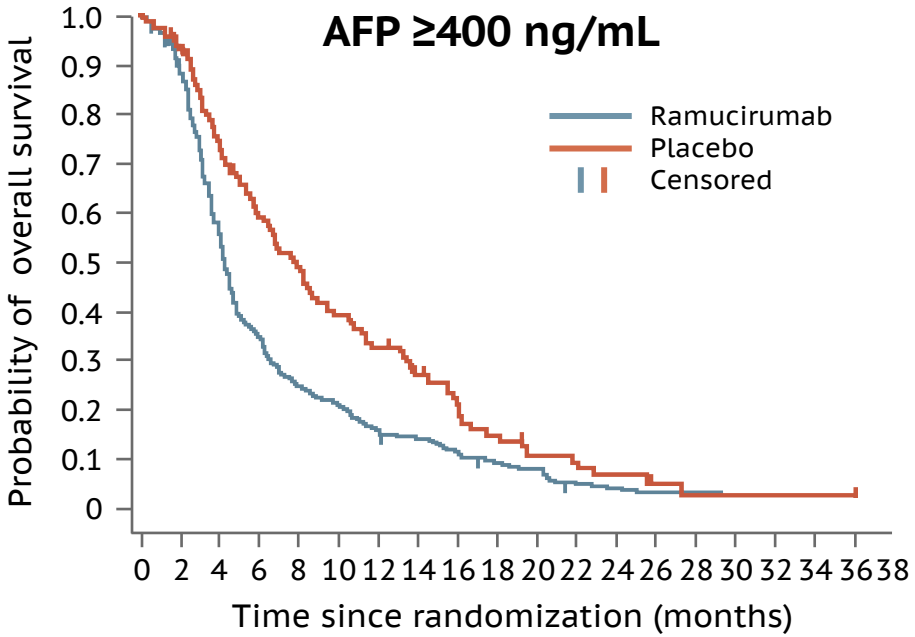
RAMUCIRUMAB AS SECOND-LINE TREATMENT IN PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA: ANALYSIS OF PATIENTS WITH ELEVATED α-FETOPROTEIN FROM THE RANDOMIZED PHASE III REACH STUDY

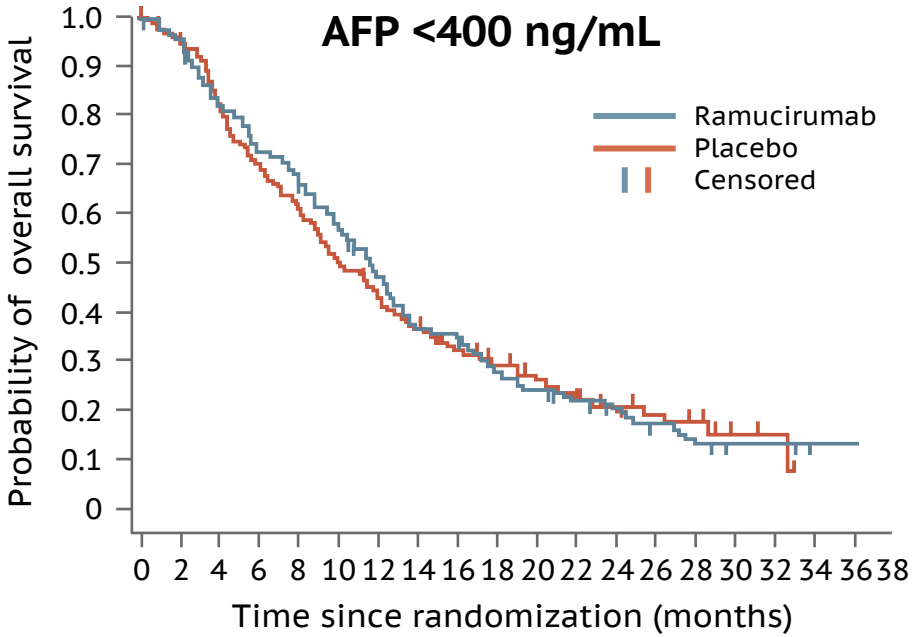
Andrew X. Zhu* Baek-Yeol Ryoo, Chia-Jui Yen, Masatoshi Kudo, Ronnie Poon, Davide Pastorelli, Jean-Frederic Blanc, Hyun Cheol Chung, Ari D. Baron, Tulio Eduardo Flesch Pfiffer, Takuji Okusaka, Katerina Kubackova, Jorg Trojan, Javier Sastre, Ian Chau, Shao-Chun Chang, Paolo B. Abada, Ling Yang, Yanzhi Hsu, Joon Oh Park

*On behalf of the REACH Investigators

Presented By Andrew Zhu at 2015 Gastrointestinal Cancers Symposium

OVERALL SURVIVAL IN PATIENTS WITH BASELINE AFP ≥400 NG/ML OR <400 NG/ML





	Ramucirumab (N=119)	Placebo (N=131)
Median, months	7.8	4.2
(95% CI)	(5.8, 9.3)	(3.7, 4.8)
HR (95% CI)	0.674 (0.508, 0.895)	
P-value (log-rank)	0.0059	

	Ramucirumab (N=160)	Placebo (N=150)
Median, months	10.1	11.8
(95% CI)	(8.7, 12.3)	(9.9, 13.1)
HR (95% CI)	1.093 (0.836, 1.428)	
P-value (log-rank)	0.5059	

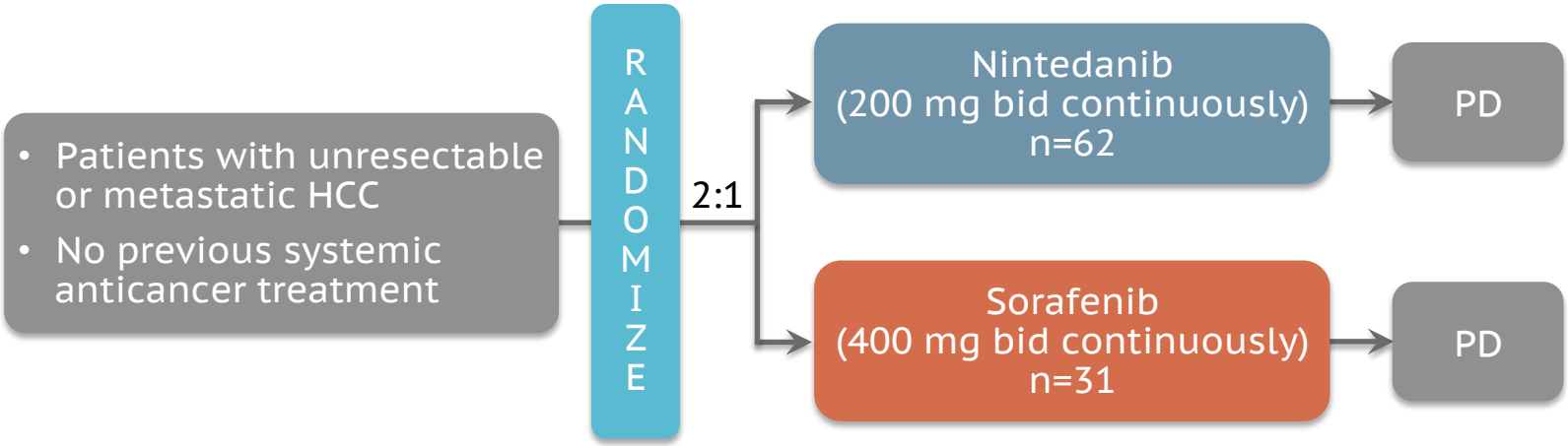
* AFP, a-fetoprotein; CI, confidence interval; HR, hazard ratio; N, number of patients.

RANDOMIZED PHASE II TRIAL COMPARING THE EFFICACY AND SAFETY OF NINTEDANIB VERSUS SORAFENIB IN CAUCASIAN PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA

Daniel Palmer, Yuk Ting Ma, Markus Peck Radosavljevic, Paul Ross, Janet Graham, Laetitia Fartoux, Andrzej Deptala, Arne Wenz, Julia Hocke, Arsène-Bienvenu Loembé, Tim Meyer

Presented By Daniel Palmer at 2015 Gastrointestinal Cancers Symposium

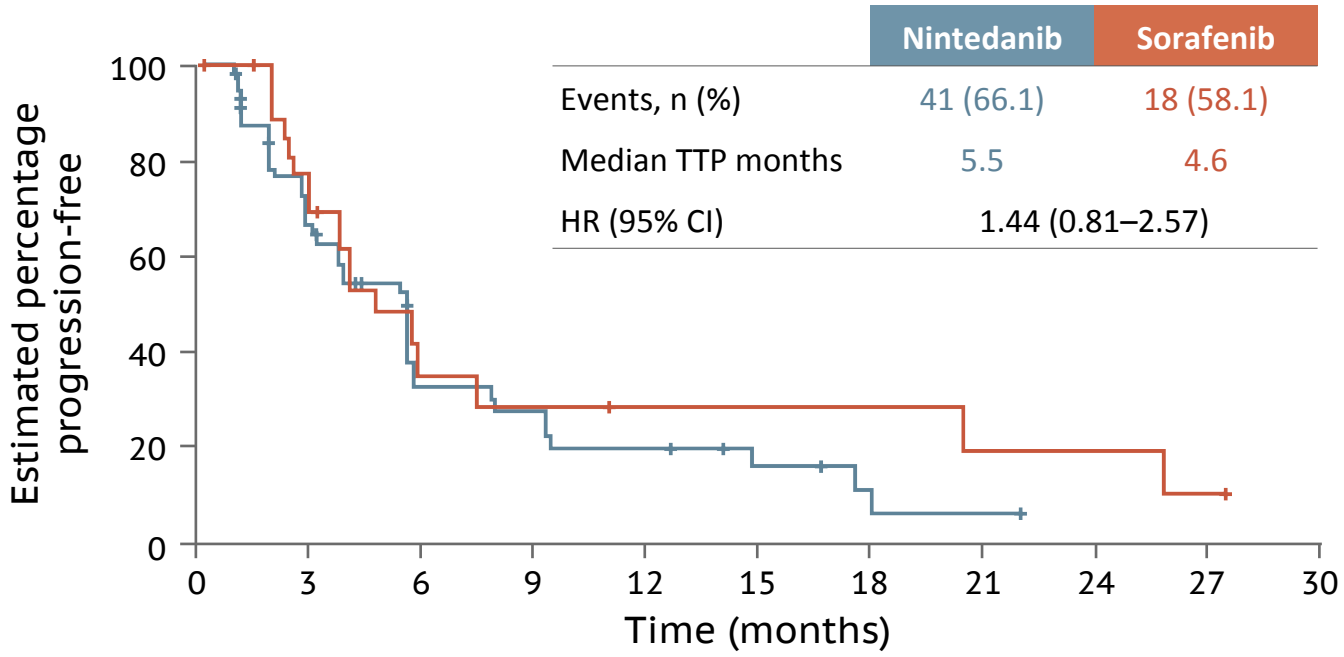
STUDY DESIGN: RANDOMIZED, OPEN-LABEL, PARALLEL-GROUP PHASE II STUDY



- **Primary endpoint:** TTP by central review according to RECIST 1.0
- **Secondary endpoints:** OS and FPS and objective response by central independent review according to RECIST
- **Additional evaluations:** Safety; TTP by investigator assessment (sensitivity analysis)
- **Stratification factors:** macrovascular invasion and/or extrahepatic spread versus no invasion or spread

Bid, twice dail; HCC, hepatocellular carcinoma; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria In Solid Tumors; TTP, time to progression; PD, disease progression.

PRIMARY ENDPOINT: TIME TO PROGRESSION (CENTRAL REVIEW)



Patients at risk

Nintedanib	62	32	12	10	7	4	1	1	0	0	0
Sorafenib	31	18	5	4	3	3	3	2	2	1	0

According to RECIST 1.0
CI, confidence interval, HR, hazard ratio; RECIST, Response Evaluation Criteria In Solid Tumors; TTP, time to progression.

RANDOMIZED PHASE 2 STUDY OF FRONTLINE DOVITINIB (TKI258) VS SORAFENIB IN PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA

Ann-Lii Cheng, Sumitra Thongprasert, Ho Yeong Lim, Wattana Sukeepaisarnjaroen, Tsai-Shen Yang, Cheng-Chung Wu, Yee Chao, Stephen L. Chan, Masatoshi Kudo, Masafumi Ikeda, Yoon-Koo Kang, Hongming Pan, Kazushi Numata, Guohong Han, Binaifer Balsara, Yong Zhang, Ana-Marie Rodgriguez, Yi Zhang, Yongyu Wang, Ronnie T.P. Poon

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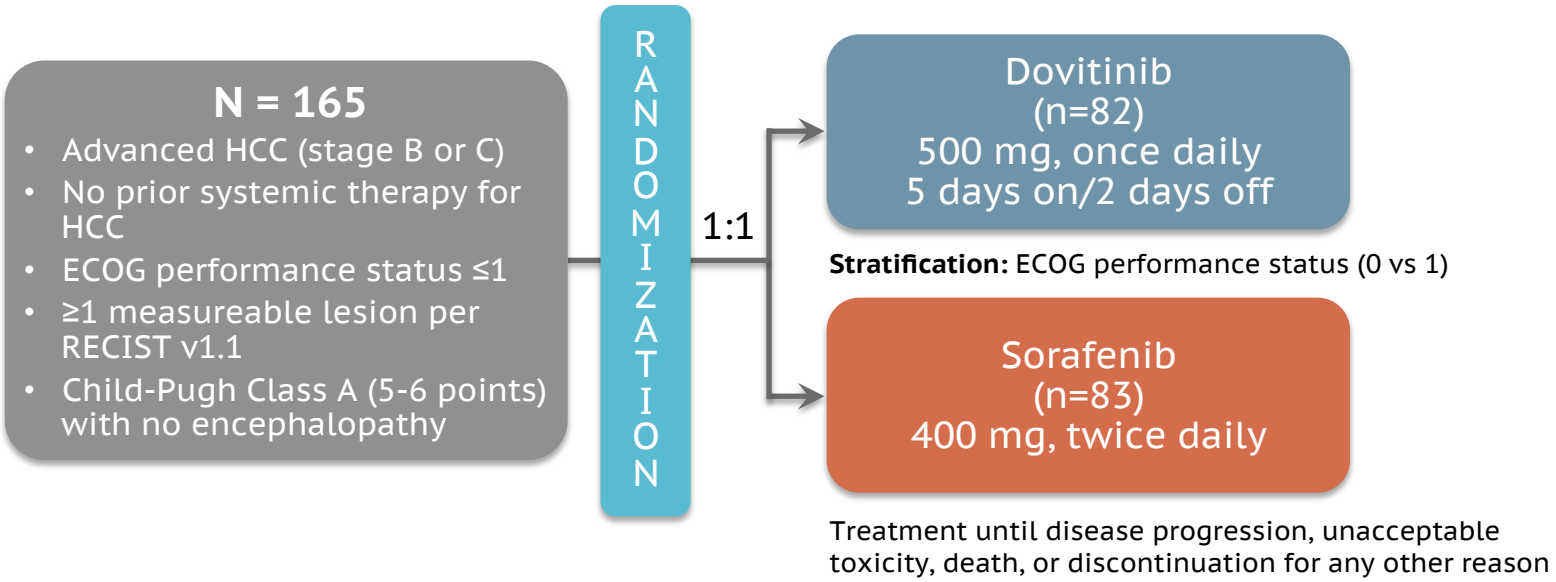
Presented By Ann-Lii Cheng at 2015 Gastrointestinal Cancers Symposium

PHASE 2 OPEN-LABEL STUDY IN FRONTLINE HCC



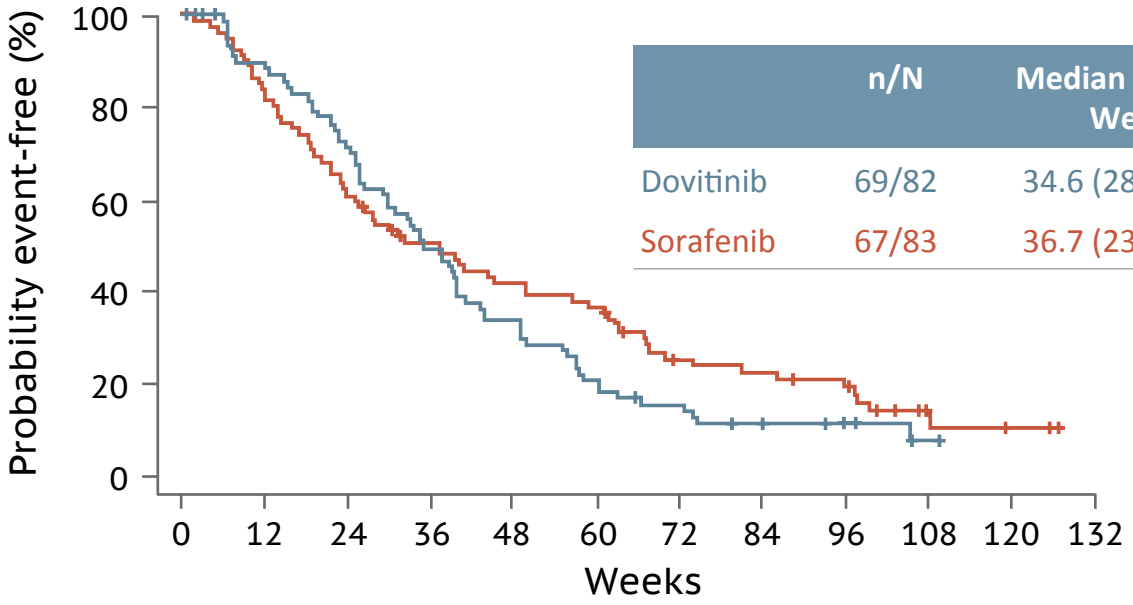
Endpoints

Primary: OS

Secondary: Time to tumor progression (per investigator assessment), disease control rate (per investigator assessment), time to definitive deterioration in ECOG performance status, safety, and pharmacokinetics

ECOG, Eastern Cooperative Oncology Group; RECIST, Response Evaluation Criteria In Solid Tumors.

OS WAS SIMILAR BETWEEN THE ARMS



	n/N	Median (95% CI), Weeks	Hazard Ratio (95% CI)
Dovitinib	69/82	34.6 (28.6–39.4)	1.27 (0.90–1.79)
Sorafenib	67/83	36.7 (23.3–49.3)	

Dovitinib	82	68	54	38	26	16	11	6	4	1	0	0
Sorafenib	83	67	50	39	32	28	17	15	12	3	2	0

- The observed OS drop in the KM plot ini the dovitinib arm between weeks 24 and 42 was not due to toxicity
  - Patients whose OS was within 24 to 42 weeks and who had already discontinued dovitinib due to AEs lived between 6.9 and 37.1 weeks after they discontinued dovitinib

KM, Kaplan-Meier; n, number of events included in the analysis; N, number of patients included in the analysis.

CONCLUSIONS

- Liposomal Irinotecan (nal-Iri, MM-398) in combination with 5-FU/Leucovorin (LV) demonstrates significant OS benefit over 5-FU/LV (median OS per-protocol 3.8 months, and intention-to-treat 4.4 months) in metastatic pancreatic cancer patients pre-treated with Gemcitabine based regimens in the NAPOLI-1 study
- Post-hoc analysis of the REACH study shows that poor prognostic patients with elevated AFP > 400 ng/mL have a significant OS benefit of 3.6 months (median OS 7.8 vs 4.2 months) in advanced HCC patients treated with Ramucirumab versus placebo after Sorafenib progression
- Two randomized phase II studies with either Nintendanib or Dovitinib did not show PFS or OS benefit compared to Sorafenib in frontline treatment of advanced hepatocellular carcinoma patients