UPDATES IN Non-Colorectal GI ONCOLOGY

SUMA SATTI, MD

OCHSNER HEALTH

Disclosures

- Speaker for Merck, BMS, Elitek, Janssen, Astra Zeneca
- Advisory Board for Deciphera

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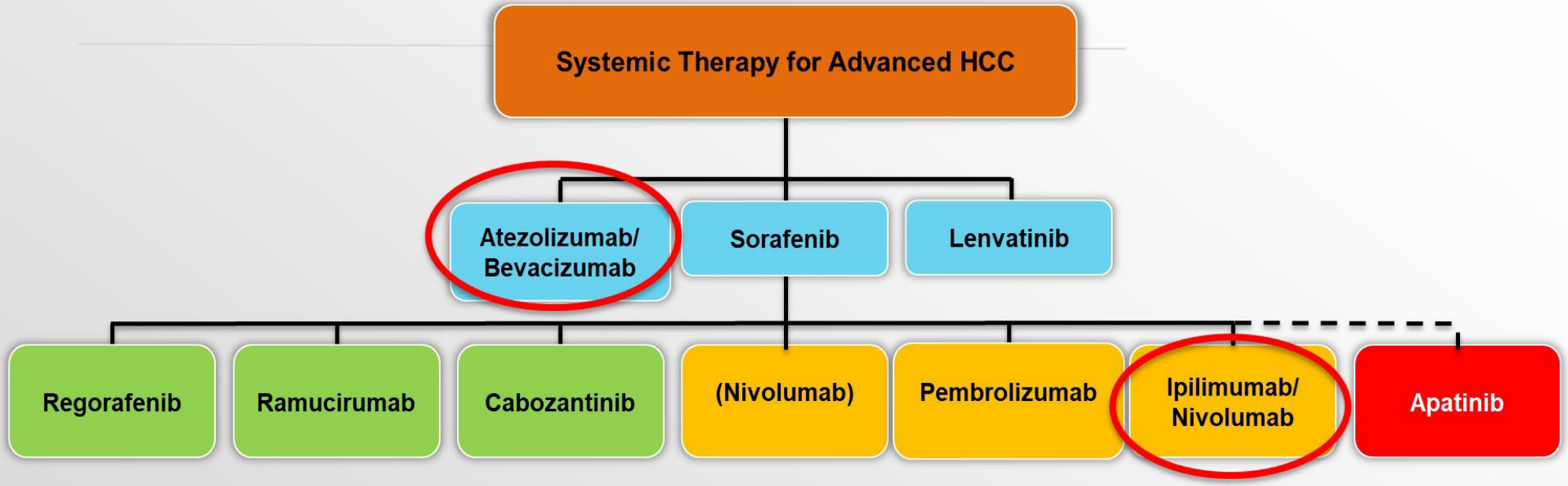
ADVANCED HCC



Combination Treatments on the Horizon

The NEW ENGLAND JOURNAL of MEDICINE

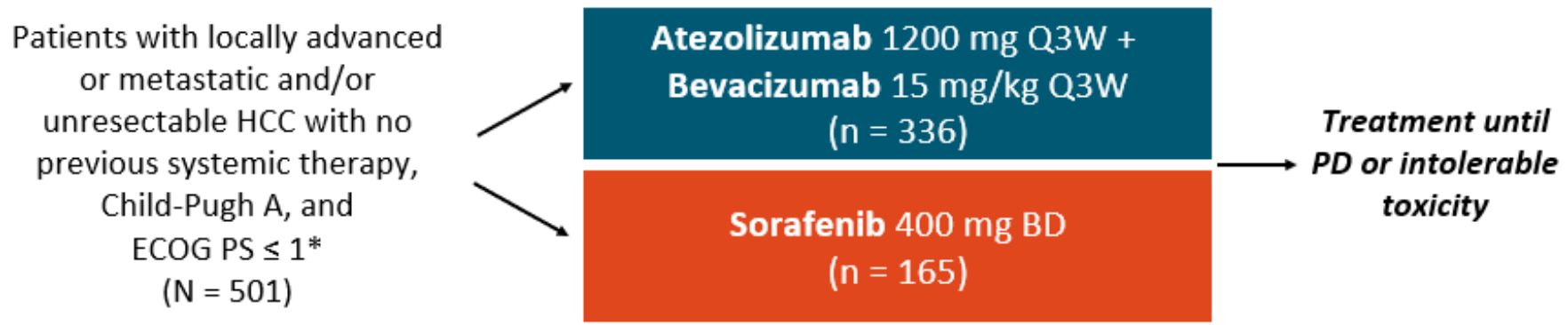
ORIGINAL ARTICLE

Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma

Richard S. Finn, M.D., Shukui Qin, M.D., Masafumi Ikeda, M.D., Peter R. Galle, M.D., Michel Ducreux, M.D., Tae-You Kim, M.D., Masatoshi Kudo, M.D., Valeriy Breder, M.D., Philippe Merle, M.D., Ahmed O. Kaseb, M.D., Daneng Li, M.D., Wendy Verret, Ph.D., Derek-Zhen Xu, M.D., Sairy Hernandez, Ph.D., Juan Liu, Ph.D., Chen Huang, M.D., Sohail Mulla, Ph.D., Yulei Wang, Ph.D., Ho Yeong Lim, M.D., Andrew X. Zhu, M.D., Ph.D., and Ann-Lii Cheng, M.D., for the IMbrave150 Investigators*

IMbrave150: Atezolizumab + Bevacizumab vs Sorafenib for First-Line Treatment of Advanced HCC

- Multicenter, randomized, open-label phase III trial[1]
  - GO30140: randomized phase Ib study showed potential benefit of atezolizumab + bevacizumab for patients with advanced HCC (ORR 36%)[2]



- Coprimary endpoints: OS and PFS

*Trial included subgroups of high-risk patients excluded from other contemporary phase III trials: ≈ 40% had macrovascular invasion; specifically included patients with 50% hepatic involvement or main portal vein invasion or invasion of the portal vein branch contralateral to the primarily involved lobe.

1. Finn. NEJM. 2020;382:1894. 2. Lee. Lancet Oncol. 2020;21:808.

Slide credit: clinicaloptions.com

IMbrave150: Baseline Characteristics

Characteristic	Atezo + Bev (n = 336)	Sorafenib (n = 165)
Median age, yrs (range)	64 (26-88)	66 (33-87)
Male, n (%)	277 (82)	137 (83)
Asia excluding Japan| rest of world, n (%)	133 (40) | 203 (60)	68 (41) | 97 (59)
ECOG PS 0 | 1, n (%)	209 (62) | 127 (38)	103 (62) | 62 (38)
Child-Pugh score A5 | A6, n (%)	239 (72) | 94 (28)	121 (73) | 44 (27)
Barcelona Clinic Liver Cancer stage B | C, n (%)	52 (15) | 276 (82)	26 (16) | 133 (81)
AFP at baseline ≥ 400 ng/mL, n (%)	126 (38)	61 (37)
MVI | EHS present, n (%)	129 (38) | 212 (63)	71 (43) | 93 (56)
MVI and/or EHS present, n (%)	258 (77)	120 (73)
Varices at baseline | treated at baseline, n (%)	88 (26) | 36 (11)	43 (26) | 23 (14)
HCC etiology: hepatitis B | C | nonviral, n (%)	164 (49) | 72 (21) | 100 (30)	76 (46) | 36 (22) | 53 (32)

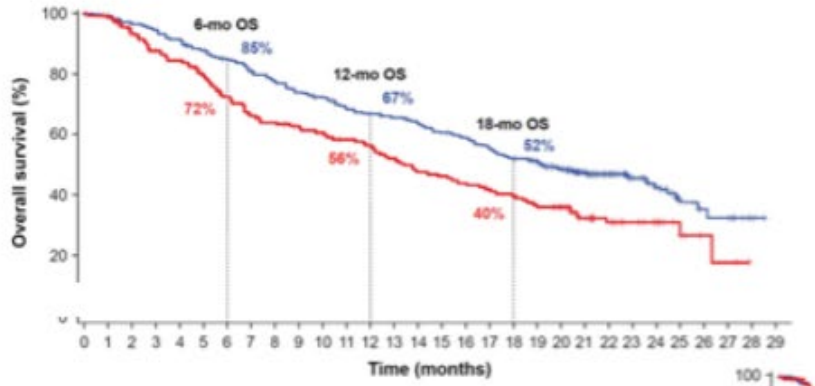
Finn. NEJM. 2020;382:1894.

Slide credit: clinicaloptions.com

IMbrave150 Trial

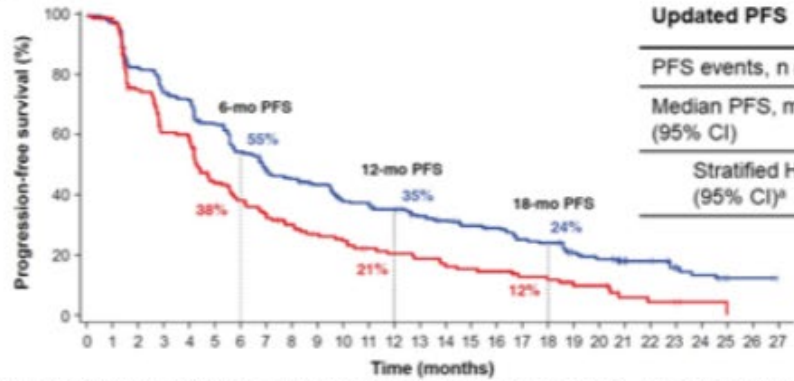
Key Efficacy Data: Updated OS and PFS

– Primary analysis OS/PFS HR: 0.58/0.59 (median follow-up: 8.6 mo)



Updated OS	Atezo + Bev (n = 336)	Sorafenib (n = 165)
OS events, n (%)	180 (54)	100 (61)
Median OS, mo (95% CI)	**19.2** (17.0, 23.7)	**13.4** (11.4, 16.9)
Stratified HR (95% CI)[a]	**0.66** (0.52, 0.85) *P* = 0.0009[b]	

– Median follow-up: 15.6 mo



Updated PFS	Atezo + Bev (n = 336)	Sorafenib (n = 165)
PFS events, n (%)	257 (76)	130 (79)
Median PFS, mo (95% CI)	**6.9** (5.7, 8.6)	**4.3** (4.0, 5.6)
Stratified HR (95% CI)[a]	**0.65** (0.53, 0.81) *P* = 0.0001[b]	

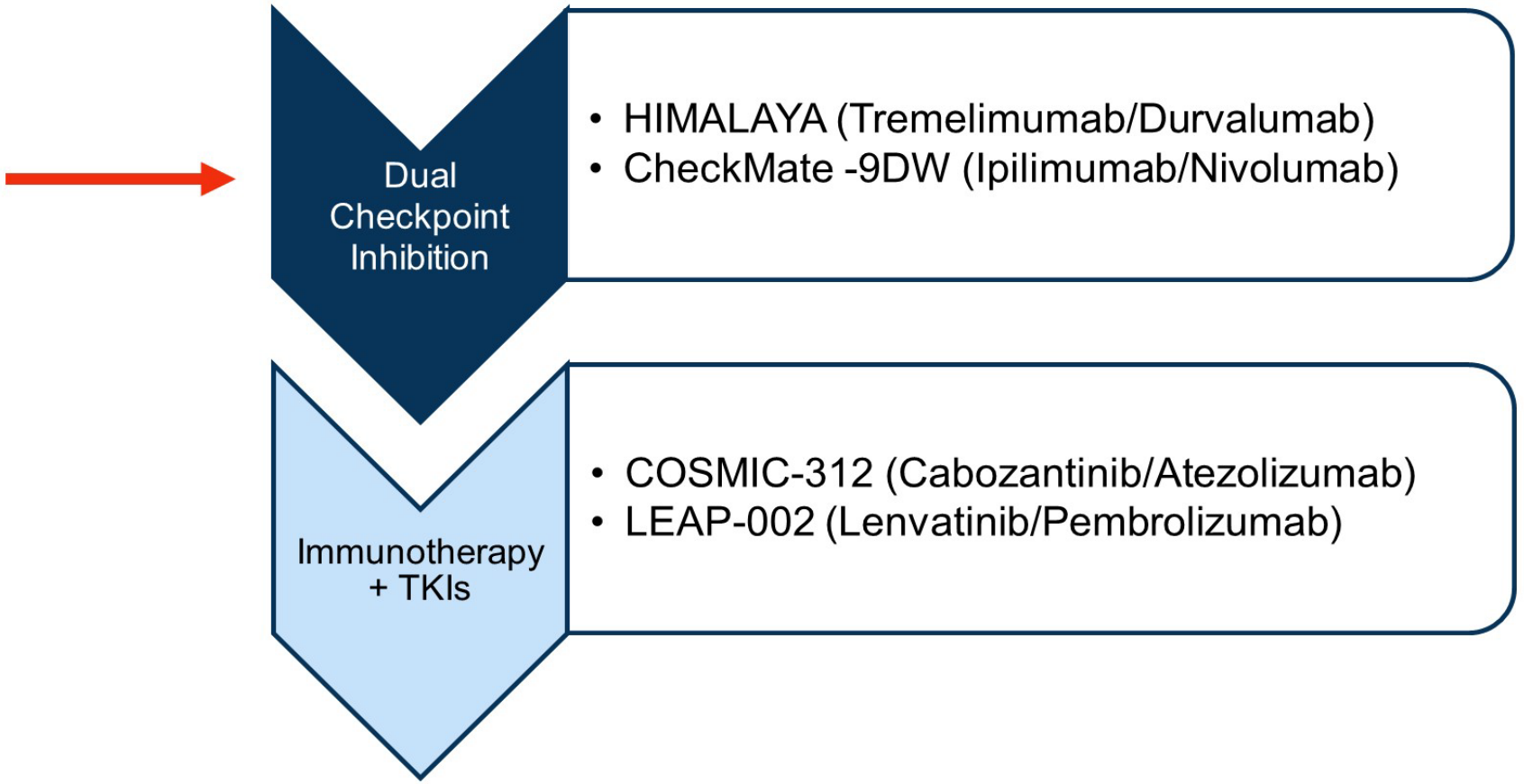
- Finn RS et al NEJM 2020, Finn RS, et al. Presented at: Gastrointestinal Cancers Symposium Virtual; 2021. Abstract 267.

Updated response and duration of response

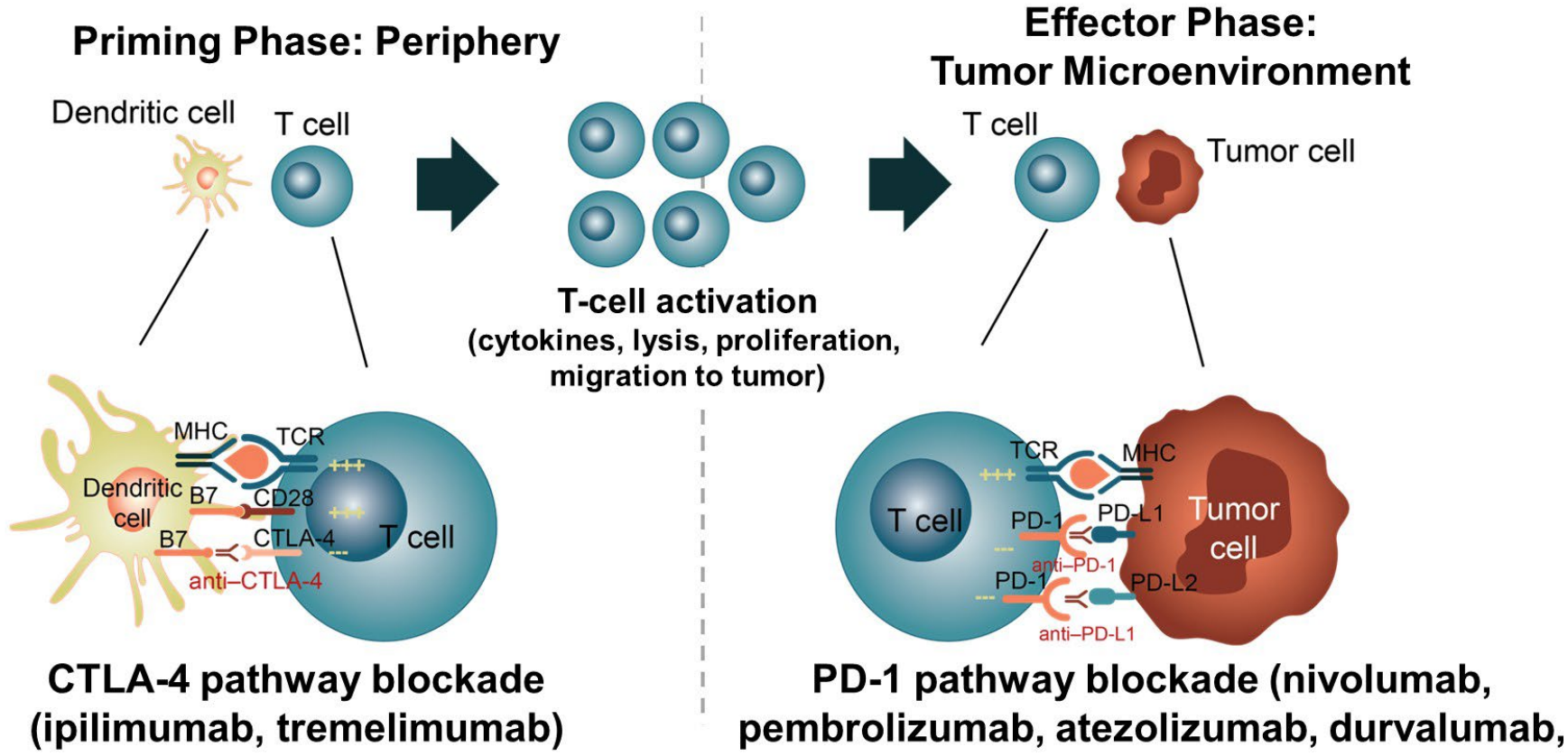
	Updated analysis[a]			
	RECIST 1.1		HCC mRECIST	
	Atezo + Bev (n = 326)	Sorafenib (n = 159)	Atezo + Bev (n = 325)	Sorafenib (n = 158)
Confirmed ORR (95% CI), %	**30 (25, 35)**	**11 (7, 17)**	**35 (30, 41)**	**14 (9, 20)**
CR, n (%)	25 (8)	1 (< 1)	39 (12)	4 (3)
PR, n (%)	72 (22)	17 (11)	76 (23)	18 (11)
SD, n (%)	144 (44)	69 (43)	121 (37)	65 (41)
DCR, n (%)	241 (74)	87 (55)	236 (73)	87 (55)
PD, n (%)	63 (19)	40 (25)	65 (20)	40 (25)
Ongoing response, n (%)	54 (56)	5 (28)	58 (50)	6 (27)
Median DOR (95% CI), mo[b]	**18.1 (14.6, NE)**	**14.9 (4.9, 17.0)**	**16.3 (13.1, 21.4)**	**12.6 (6.1, 17.7)**

Clinical cutoff: August 31, 2020; median follow-up: 15.6 mo. DCR, disease control rate.
[a] Only patients with measurable disease at baseline were included in the analysis of ORR.
[b] Only confirmed responders were included in the analysis of ORR and DOR.

New Frontline Systemic Therapy Combinations in Advanced HCC



Immuno-Oncology: Blocking CTLA-4 and PD-1 Pathways With Monoclonal Antibodies[1]

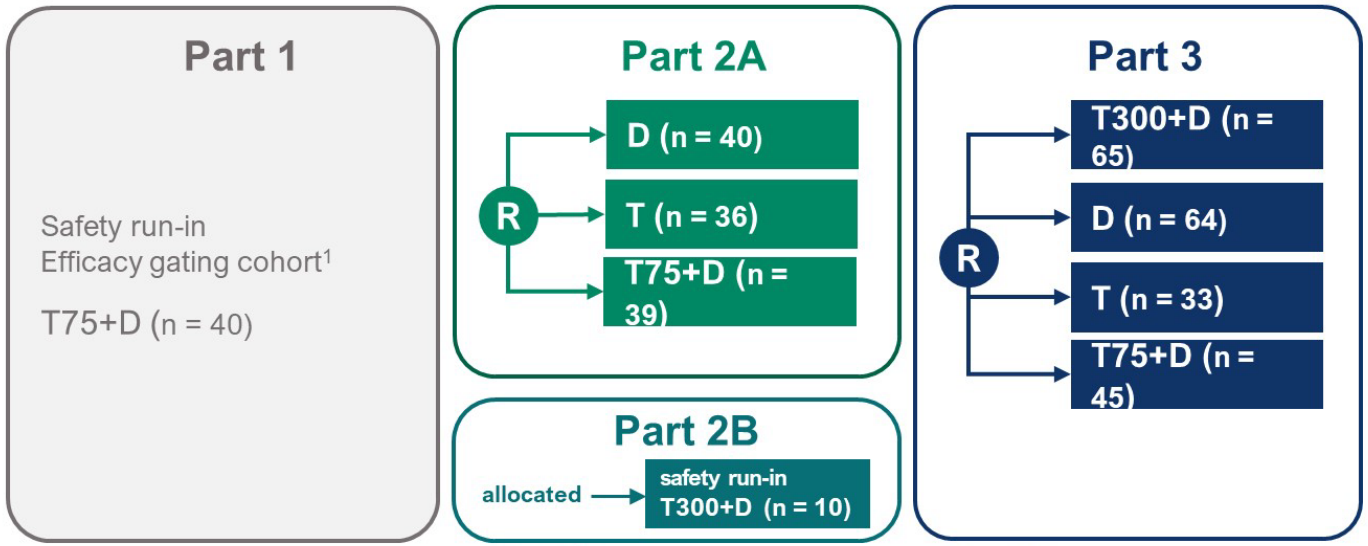


CTLA-4 pathway blockade (ipilimumab, tremelimumab)

PD-1 pathway blockade (nivolumab, pembrolizumab, atezolizumab, durvalumab, tislelizumab)

1. Wolchock J et al. 2013 American Society of Clinical Oncology Annual Meeting (ASCO 2013). Abstract 9012.

Study 22: Phase II of Tremelimumab and Durvalumab



Key Milestones

FSI Part 2A	February 2017
FSI Part 2B	October 2017

Key Milestones

FSI Part 3	February 2018
LSI Part 3	April 2019

Treatments and Regimens

T300+D	tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W
D	durvalumab 1500 mg Q4W
T	tremelimumab monotherapy 750 mg Q4W × 7 doses, Q12W thereafter
T75+D	tremelimumab 75 mg × 4 doses + durvalumab 1500 mg Q4W

Key Eligibility

- Unresectable HCC with fresh or archival tumor biopsy sample available
- Progressed on, intolerant to, or refused prior sorafenib
- Child Pugh A liver function

Objectives and Assessments

Primary Endpoint: Safety

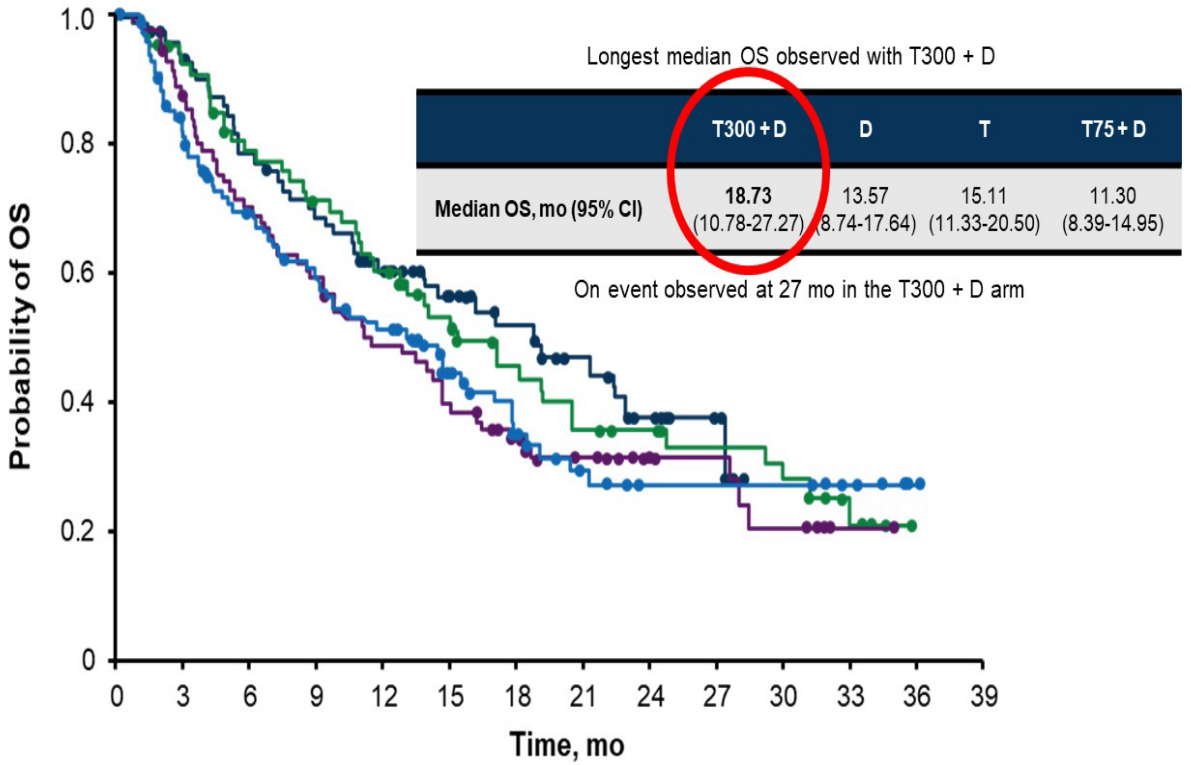
Key Secondary Endpoints
- Overall survival
- Objective response rate
- Duration of response

Key Assessments
- Multiphase imaging Q8 weeks
- Circulating immune cells
- PD-L1 status (Ventana SP263)

1. Kelley RK, et al. JCO, 2017.35:4073-4073.
2. Kelley, RK, etal., ASCO 2020

PRESENTED BY: Lipika Goyal

Phase 2 Trial: Tremelimumab and Durvalumab[1]



No. at Risk														
T300 + D	75	67	56	48	39	30	22	16	10	5	0	0	0	0
D	104	78	65	54	46	31	20	14	8	8	8	5	1	0
T	69	62	51	45	38	29	23	18	16	13	11	5	0	0
T75 + D	84	69	56	48	38	30	23	17	10	9	6	2	0	0

1. Kelley RK et al. *J Clin Oncol*. 2021;39:2991-3001.

Phase 2 Trial: Tremelimumab and Durvalumab[1]

	T300 + D (n = 75)	T75 + D (n = 84)	D (n = 104)	T (n = 69)
Grade 3/4 TRAEs, %	**35.1**	24.4	17.8	42
Serious TRAEs, %	**13.5**	11.0	10.9	21.7
TRAEs requiring systemic steroids,[2] %	**24.3**	24.4	9.9	26.1
Discontinuation due to TRAEs, %	**10.8**	6.1	7.9	11.6
ORR (95% CI), %	**24 (14.9-35.3)**	9.5 (4.2-17.9)	10.6 (5.4-18.1)	7.2 (2.4-16.1)
Median DOR, mo	**NR**	13.2	11.2	24.0

[a] Hepatic failure. [b] Abnormal hepatic function, hepatic failure, and/or pneumonitis.

1. Kelley RK et al. *J Clin Oncol*. 2021;39:2991-3001. 2. Kelley, RK et al ASCO 2020.

RESPONSES OCCURRED IRRESPECTIVE OF PDL1 OR VIRAL STATUS

Phase 3 randomized, open-label, multicenter study of tremelimumab and durvalumab as first-line therapy in patients with unresectable hepatocellular carcinoma: HIMALAYA

Ghassan K Abou-Alfa,[1,2*] Stephen L Chan,[3*] Masatoshi Kudo,[4*] George Lau,[5*] Robin Kate Kelley,[6] Junji Furuse,[7] Wattana Sukeepaisarnjaroen,[8] Yoon-Koo Kang,[9] Tu V Dao,[10] Enrico N De Toni,[11] Lorenza Rimassa,[12,13] Valery Breder,[14] Alexander Vasilyev,[15] Alexandra Heurgué,[16] Vincent C Tam,[17] Kabir Mody,[18] Satheesh Chiradoni Thungappa,[19] Philip He,[20] Alejandra Negro,[20] and Bruno Sangro[21]

[1]Department of Medicine, Memorial Sloan Kettering Center, New York, NY, USA; [2]Weill Medical College, Cornell University, New York, NY, USA; [3]State Key Laboratory of Translational Oncology, Department of Clinical Oncology, Sir Yue-Kong Pao Center for Cancer, The Chinese University of Hong Kong, Hong Kong, China; [4]Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan; [5]Humanity and Health Clinical Trial Center, Humanity and Health Medical Group, Hong Kong, China; [6]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, CA, USA; [7]Department of Medical Oncology, Kyorin University Faculty of Medicine, Mitaka, Japan; [8]Department of Medicine, Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand; [9]Department of Oncology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea; [10]Cancer Research and Clinical Trial Center, National Cancer Hospital, Hanoi, Vietnam; [11]Department of Medicine II, University Hospital, LMU Munich, Munich, Germany; [12]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy; [13]Humanitas Cancer Center, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy; [14]Chemotherapy Department No17, N.N. Blokhin Russian Cancer Research Center, Moscow, Russia; [15]Railway Clinical Hospital, St. Petersburg, Russia; [16]Service d'Hépato-Gastro-entérologie, Hôpital Robert-Debré, Reims, France; [17]Tom Baker Cancer Centre, University of Calgary, Calgary, AB, Canada; [18]Division of Hematology/Oncology, Department of Medicine, Mayo Clinic, Jacksonville, FL, USA; [19] Sri Venkateshwara Hospital, Bangalore, India; [20]AstraZeneca, Gaithersburg, MD, USA; [21]Liver Unit and HPB Oncology Area, Clinica Universidad de Navarra and CIBEREHD, Pamplona, Spain

*Drs Ghassan K Abou-Alfa, Stephen L Chan, Masatoshi Kudo, and George Lau contributed equally to this work.

ASCO Gastrointestinal Cancers Symposium

#GI22

PRESENTED BY: Ghassan K Abou-Alfa, MD, MBA

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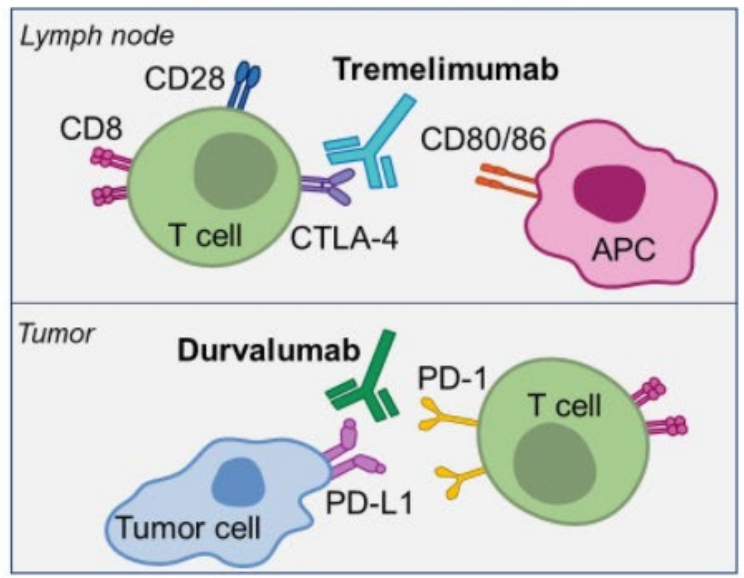
BACKGROUND

Atezolizumab (anti-PD-L1) plus bevacizumab (anti-VEGF) showed significant survival benefit vs sorafenib in IMbrave150[3] and has become a standard of care following approval in 2020[4,5]

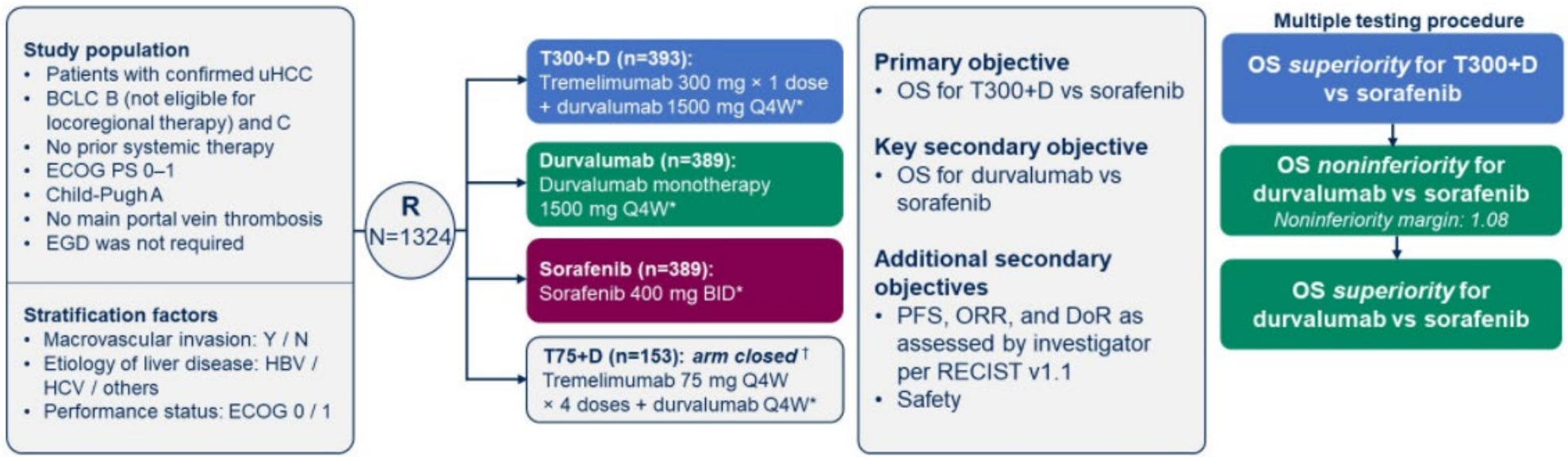
The STRIDE (Single Tremelimumab Regular Interval Durvalumab; T300+D) regimen, a novel combination featuring a single high-priming dose of tremelimumab (anti-CTLA-4) and regular interval durvalumab (anti-PD-L1), showed encouraging clinical activity and was well tolerated in a Phase 2 trial in uHCC[6]

Mechanism of action of T300+D[7]



HIMALAYA study design

HIMALAYA was an open-label, multicenter, global, Phase 3 trial



*Treatment continued until disease progression. Patients with progressive disease who, in the investigator's opinion, continued to benefit from treatment and met the criteria for treatment in the setting of progressive disease could continue treatment. †The T75+D arm was closed following a preplanned analysis of a Phase 2 study. Patients randomized to this arm (n=153) could continue treatment following arm closure. Results from this arm are not reported in this presentation.

BID, twice a day; EGD, esophagogastroduodenoscopy; Q4W, every 4 weeks.

PRESENTED BY: Ghassan K Abou-Alfa, MD, MBA

Baseline characteristics

Characteristic	T300+D (n=393)	Durvalumab (n=389)	Sorafenib (n=389)
Male sex, n (%)	327 (83.2)	323 (83.0)	337 (86.6)
Median age (range), years	65.0 (22–86)	64.0 (20–86)	64.0 (18–88)
Region, n (%)			
Asia (excluding Japan)	156 (39.7)	167 (42.9)	156 (40.1)
Rest of world (including Japan)	237 (60.3)	222 (57.1)	233 (59.9)
Viral etiology,*,† n (%)			
HBV	122 (31.0)	119 (30.6)	119 (30.6)
HCV	110 (28.0)	107 (27.5)	104 (26.7)
Nonviral	161 (41.0)	163 (41.9)	166 (42.7)
ECOG PS, n (%)			
0	244 (62.1)	237 (60.9)	241 (62.0)
1	148 (37.7)	150 (38.6)	147 (37.8)
BCLC,† n (%)			
B	77 (19.6)	80 (20.6)	66 (17.0)
C	316 (80.4)	309 (79.4)	323 (83.0)

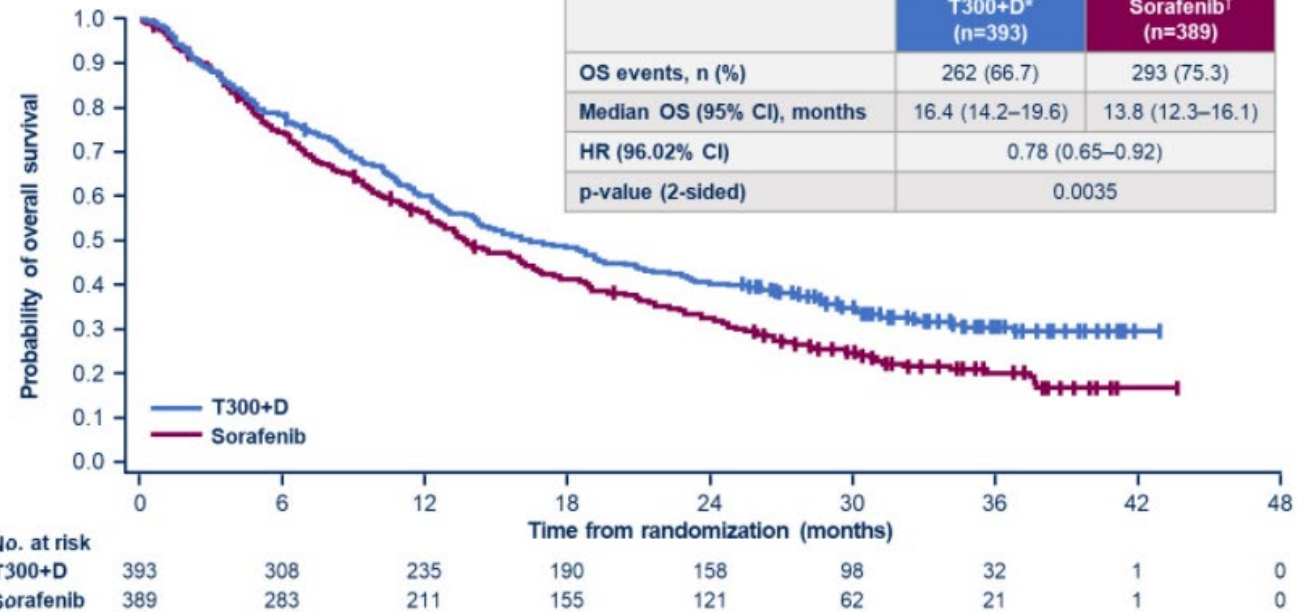
Characteristic	T300+D (n=393)	Durvalumab (n=389)	Sorafenib (n=389)
Child-Pugh classification,† n (%)			
A	392 (99.7)	388 (99.7)	386 (99.2)
B	0	1 (0.3)	3 (0.8)
Missing	1 (0.3)	0	0
ALBI grade, n (%)			
1	217 (55.2)	198 (50.9)	203 (52.2)
2	174 (44.3)	189 (48.6)	185 (47.6)
3	1 (0.3)	2 (0.5)	1 (0.3)
MVI,† n (%)	103 (26.2)	94 (24.2)	100 (25.7)
EHS,† n (%)	209 (53.2)	212 (54.5)	203 (52.2)
PD-L1 positive,‡ n (%)	148 (37.7)	154 (39.6)	148 (38.0)
AFP ≥400 ng/ml,† n (%)	145 (36.9)	137 (35.2)	124 (31.9)

*HBV: patients who tested positive for HBsAg or anti-HBc with detectable HBV DNA; HCV: patients who tested positive for HCV or had history of HCV infection; Nonviral: no active viral hepatitis identified. †Determined at screening. ‡Defined as tumor area positivity score ≥1%.

T300+D, tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W.

Primary objective: overall survival for T300+D vs sorafenib

	T300+D* (n=393)	Sorafenib† (n=389)
OS events, n (%)	262 (66.7)	293 (75.3)
Median OS (95% CI), months	16.4 (14.2–19.6)	13.8 (12.3–16.1)
HR (96.02% CI)	0.78 (0.65–0.92)	
p-value (2-sided)	0.0035	



No. at risk									
T300+D	393	308	235	190	158	98	32	1	0
Sorafenib	389	283	211	155	121	62	21	1	0

- HIMALAYA met its primary endpoint: T300+D was superior to sorafenib for OS
- T300+D appeared to have a long-term survival benefit in this mature dataset with substantial follow-up time

Data cut-off: August 27, 2021. Median duration of follow-up was 33.18 (95% CI, 31.74–34.53) months for T300+D and 32.23 (95% CI, 30.42–33.71) months for sorafenib. *Tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W. †Sorafenib 400 mg BID.

CI, confidence interval; HR, hazard ratio; OS, overall survival.

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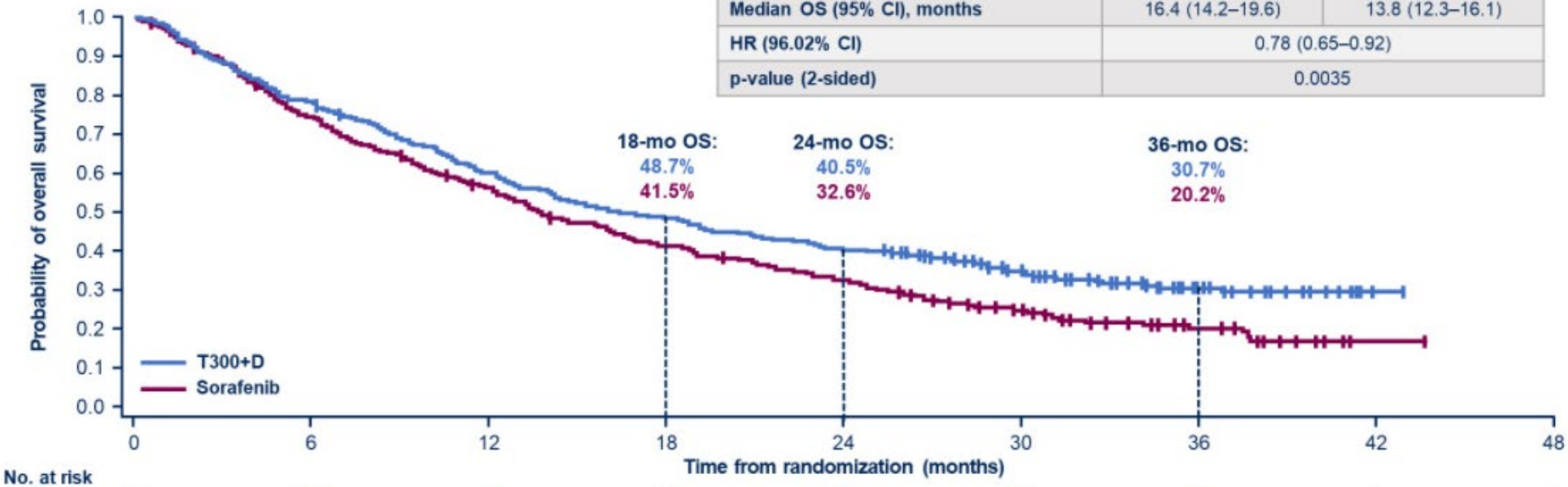

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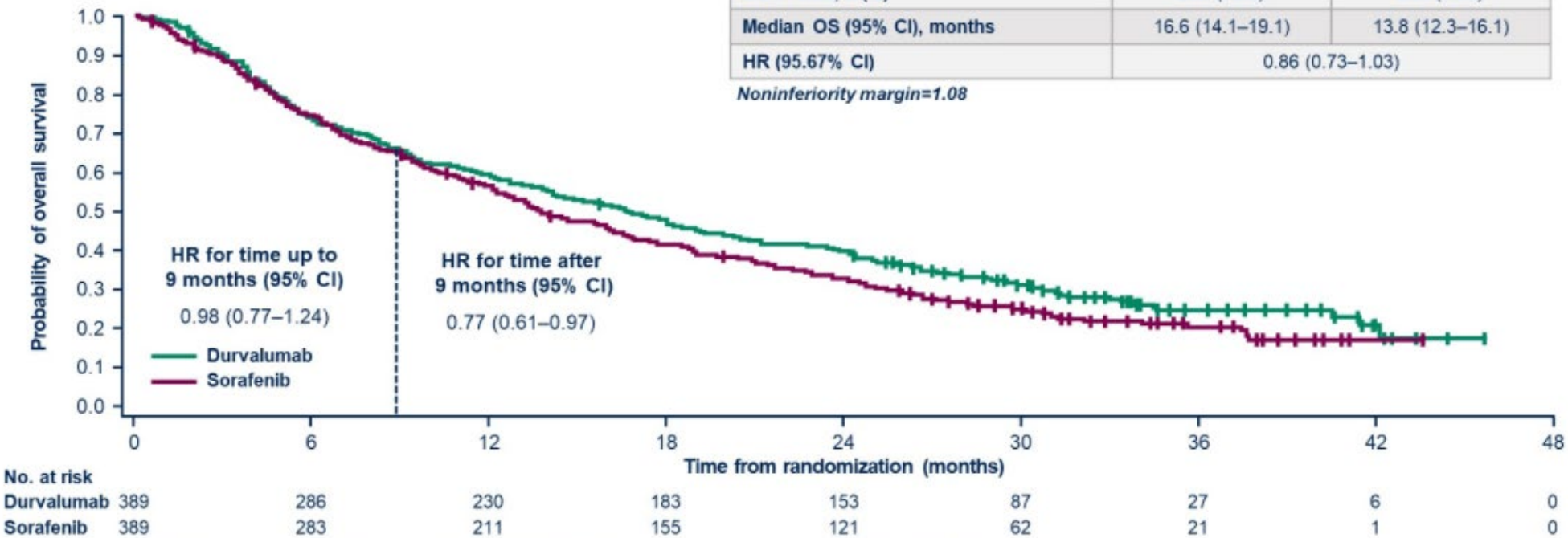
PRESENTED BY: Ghassan K Abou-Alfa, MD, MBA

Secondary objective: overall survival for durvalumab vs sorafenib

	Durvalumab (n=389)	Sorafenib (n=389)
OS events, n (%)	280 (72.0)	293 (75.3)
Median OS (95% CI), months	16.6 (14.1–19.1)	13.8 (12.3–16.1)
HR (95.67% CI)	0.86 (0.73–1.03)	

Noninferiority margin=1.08



No. at risk									
Durvalumab	389	286	230	183	153	87	27	6	0
Sorafenib	389	283	211	155	121	62	21	1	0

Data cut-off: August 27, 2021. Median duration of follow-up was 32.56 (95% CI, 31.57–33.71) months for durvalumab and 32.23 (95% CI, 30.42–33.71) months for sorafenib.

CI, confidence interval; HR, hazard ratio; NI, noninferiority; OS, overall survival.

PRESENTED BY: Ghassan K Abou-Alfa, MD, MBA

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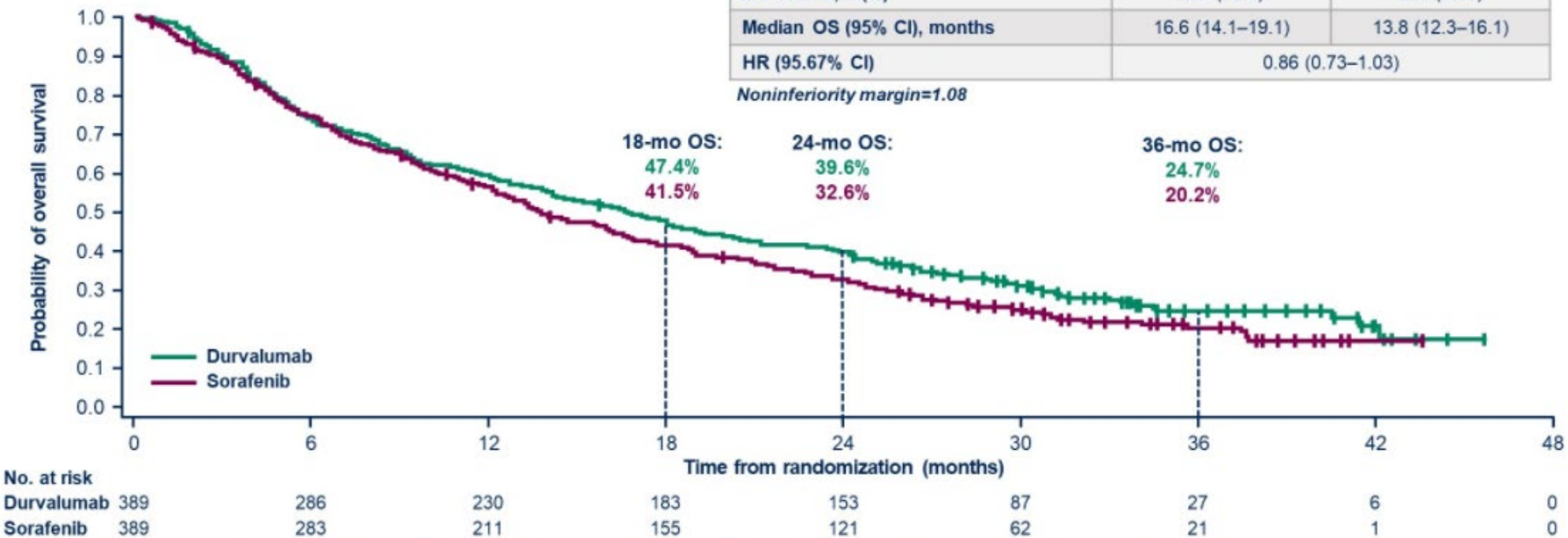

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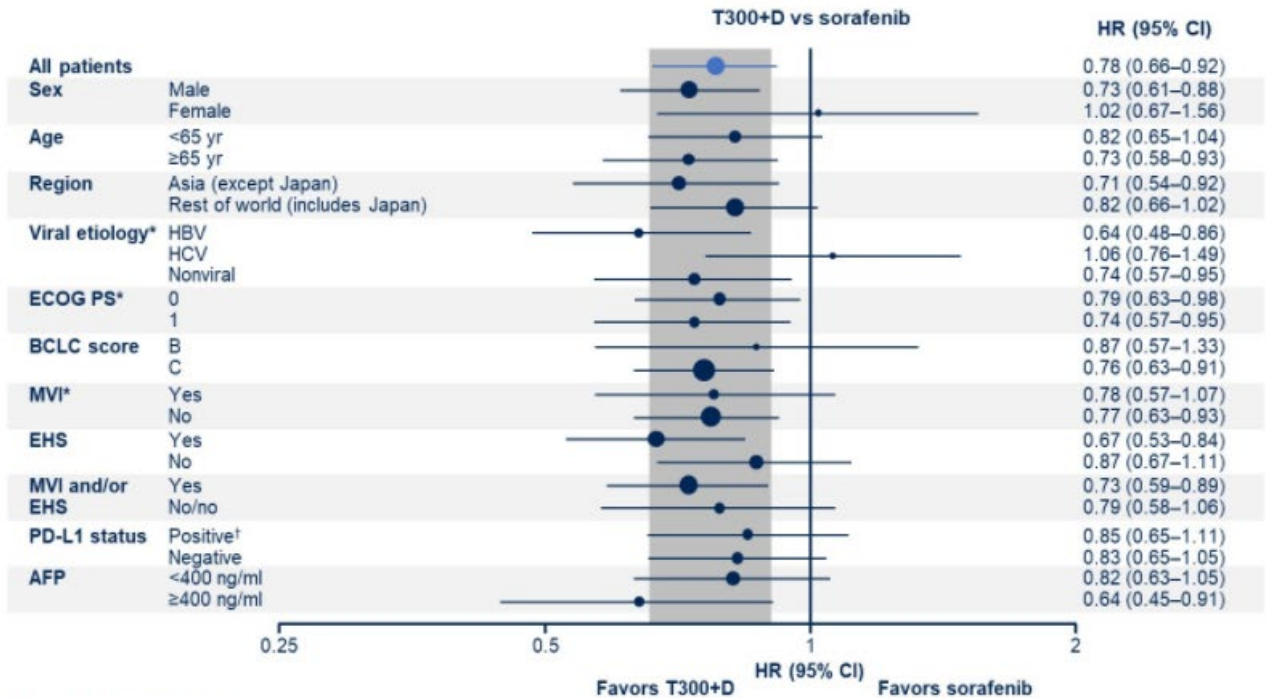
CI, confidence interval; HR, hazard ratio; NI, noninferiority; OS, overall survival.

PRESENTED BY: Ghassan K Abou-Alfa, MD, MBA

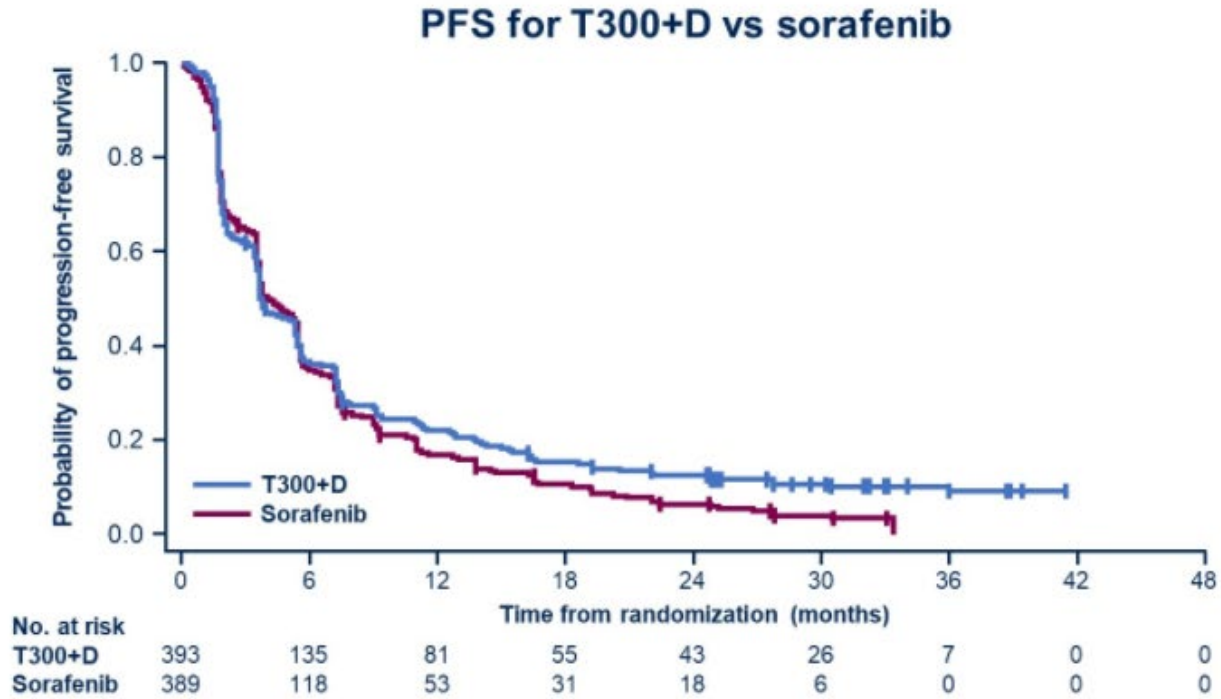
Forest plot of OS for T300+D vs sorafenib in patient subgroups



*Stratification factor. †Defined as tumor area positivity score ≥1%.
T300+D, tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W.

PRESENTED BY: Ghassan K Abou-Alfa, MD, MBA

Progression-free survival



	T300+D (n=393)	Durvalumab (n=389)	Sorafenib (n=389)
PFS events, n (%)	335 (85.2)	345 (88.7)	327 (84.1)
Median PFS (95% CI), months	3.78 (3.68–5.32)	3.65 (3.19–3.75)	4.07 (3.75–5.49)
PFS HR* (95% CI)	0.90 (0.77–1.05)	1.02 (0.88–1.19)	–
Progression-free at DCO, n (%)	49 (12.5)	32 (8.2)	19 (4.9)
Median TTP (95% CI), months	5.42 (3.81–5.62)	3.75 (3.68–5.42)	5.55 (5.13–5.75)
Treated ≥1 cycle beyond progression, n (%)†	182 (46.9)	188 (48.5)	134 (34.4)

*Versus sorafenib. †Percent calculated from total patients in the safety analysis set: T300+D, N=388; durvalumab, N=388, sorafenib, n=374.
CI, confidence interval; DCO, data cutoff; HR, hazard ratio; PFS, progression-free survival; T300+D, tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W; TTP, time to progression.

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Tumor response

	T300+D (n=393)	Durvalumab (n=389)	Sorafenib (n=389)
ORR,* n (%)	**79 (20.1)**	**66 (17.0)**	**20 (5.1)**
CR, n (%)	12 (3.1)	6 (1.5)	0
PR, n (%)	67 (17.0)	60 (15.4)	20 (5.1)
SD,† n (%)	157 (39.9)	147 (37.8)	216 (55.5)
PD, n (%)	157 (39.9)	176 (45.2)	153 (39.3)
DCR, %	60.1	54.8	60.7
Median DoR,‡ months 25th percentile 75th percentile	22.34 8.54 NR	16.82 7.43 NR	18.43 6.51 25.99
Median TTR (95% CI), months	2.17 (1.84–3.98)	2.09 (1.87–3.98)	3.78 (1.89–8.44)
Remaining in response,‡ % 6 months 12 months	 82.3 65.8	 81.8 57.8	 78.9 63.2

*By investigator assessment according to RECIST v1.1. Responses are confirmed. †Defined as neither sufficient decrease in sum of diameters to qualify for PR nor sufficient increase to qualify for PD. ‡Calculated using Kaplan-Meier technique.

CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease; T300+D, tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W; TTR, time to response.

PRESENTED BY: Ghassan K Abou-Alfa, MD, MBA

Treatment-related hepatic or hemorrhage SMQ events

Event, n (%)	T300+D (n=388)		Durvalumab (n=388)		Sorafenib (n=374)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Patients with hepatic SMQ TRAE	66 (17.0)	27 (7.0)	55 (14.2)	20 (5.2)	46 (12.3)	18 (4.8)
Patients with hemorrhage SMQ TRAE	7 (1.8)	2 (0.5)	3 (0.8)	0	18 (4.8)	6 (1.6)
Alanine aminotransferase increased	18 (4.6)	4 (1.0)	22 (5.7)	5 (1.3)	8 (2.1)	3 (0.8)
Aspartate aminotransferase increased	22 (5.7)	9 (2.3)	25 (6.4)	9 (2.3)	10 (2.7)	6 (1.6)
Blood bilirubin increased	6 (1.5)	1 (0.3)	6 (1.5)	0	10 (2.7)	2 (0.5)
Ascites	1 (0.3)	0	0	0	2 (0.5)	0
Hepatic encephalopathy	0	0	0	0	2 (0.5)	1 (0.3)
International normalized ratio increased	4 (1.0)	1 (0.3)	0	0	0	0
Esophageal varices hemorrhage	0	0	0	0	0	0

Includes adverse events with onset or increase in severity on or after the date of the first dose through 90 days following the date of the last dose or the date of initiation of the first subsequent therapy. Treatment-related was as assessed by investigator.

SMQ, Standardized MedDRA Query; T300+D, tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W; TRAE, treatment-related adverse event.

Immune-mediated adverse events

Event, n (%)	T300+D (n=388)				Durvalumab (n=388)			
	All grades	Grade 3 or 4	Received high-dose steroids	Leading to discontinuation	All grades	Grade 3 or 4	Received high-dose steroids	Leading to discontinuation
Patients with immune-mediated event	139 (35.8)	49 (12.6)	78 (20.1)	22 (5.7)	64 (16.5)	25 (6.4)	37 (9.5)	10 (2.6)
Hepatic events	29 (7.5)	16 (4.1)	29 (7.5)	9 (2.3)	26 (6.7)	17 (4.4)	25 (6.4)	5 (1.3)
Diarrhea/colitis	23 (5.9)	14 (3.6)	20 (5.2)	5 (1.3)	3 (0.8)	1 (0.3)	2 (0.5)	1 (0.3)
Dermatitis/rash	19 (4.9)	7 (1.8)	12 (3.1)	2 (0.5)	3 (0.8)	1 (0.3)	3 (0.8)	1 (0.3)
Pancreatic events	9 (2.3)	7 (1.8)	7 (1.8)	0	2 (0.5)	1 (0.3)	2 (0.5)	0
Adrenal insufficiency	6 (1.5)	1 (0.3)	1 (0.3)	0	6 (1.5)	3 (0.8)	3 (0.8)	0
Hyperthyroid events	18 (4.6)	1 (0.3)	2 (0.5)	0	4 (1.0)	0	0	0
Hypothyroid events	42 (10.8)	0	1 (0.3)	0	19 (4.9)	0	0	0
Pneumonitis	5 (1.3)	0	4 (1.0)	1 (0.3)	3 (0.8)	1 (0.3)	3 (0.8)	2 (0.5)
Renal events	4 (1.0)	2 (0.5)	3 (0.8)	2 (0.5)	0	0	0	0

Includes adverse events with onset or increase in severity on or after the date of the first dose through 90 days following the date of the last dose or the date of initiation of the first subsequent therapy. Patients may have had >1 event. Events include those that occurred in ≥1% of patients in either treatment arm.

T300+D, tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W.

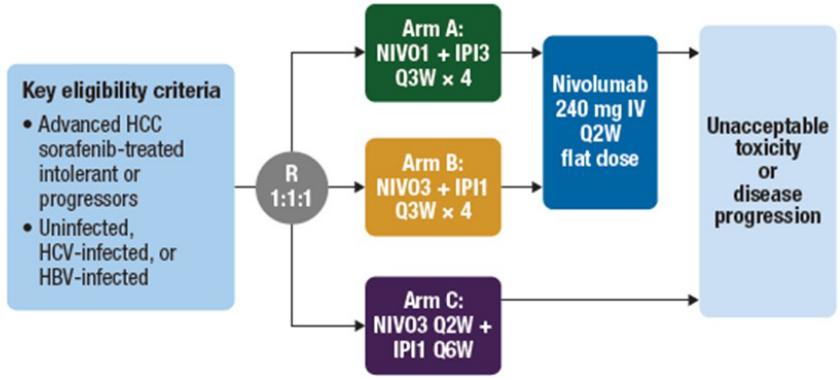
Conclusions

- The HIMALAYA study was a large, Phase 3 study that included a global, heterogeneous population, representative of patients with uHCC
- A single priming dose of tremelimumab plus regular interval durvalumab with the STRIDE (T300+D) regimen statistically significantly improved overall survival versus sorafenib
  - Median overall survival was 16.4 months for STRIDE (T300+D) and 13.8 months for sorafenib
  - STRIDE (T300+D) appeared to provide a long-term survival benefit, with a landmark 36-month overall survival of 30.7%
- Overall survival for durvalumab monotherapy was noninferior to sorafenib, with a favorable benefit-risk profile
- Both STRIDE (T300+D) and durvalumab monotherapy had manageable safety profiles, with lower rates of grade 3/4 TRAEs and TRAEs leading to discontinuation than sorafenib and no increase in liver toxicity or bleeding risk
- The STRIDE (T300+D) regimen and durvalumab monotherapy may represent new treatment options for patients with uHCC

T300+D, tremelimumab 300 mg × 1 dose + durvalumab 1500 mg Q4W; TRAE, treatment-related adverse event; uHCC, unresectable hepatocellular carcinoma.

PRESENTED BY: Ghassan K Abou-Alfa, MD, MBA

CheckMate-040 Cohort: Phase 1/2 Nivolumab Plus Ipilimumab



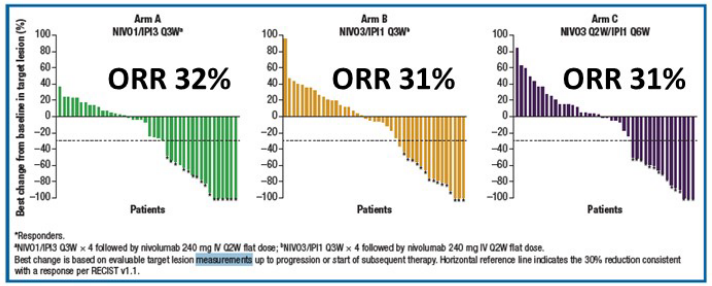
Study endpoints

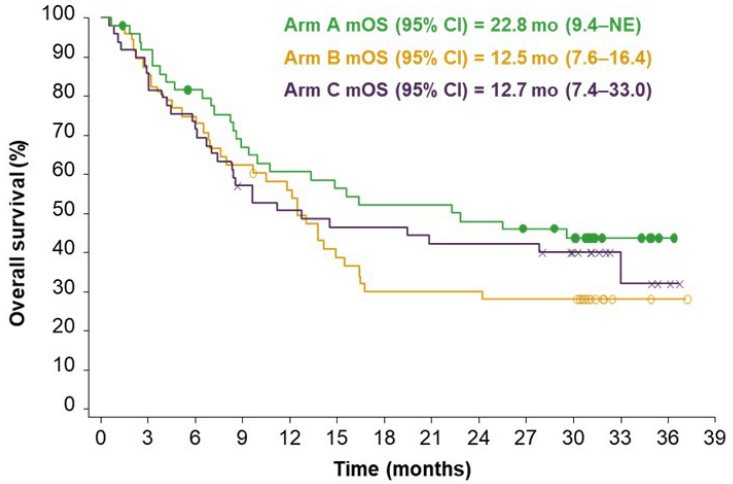
Primary
- Safety and tolerability using NCI CTCAE v4.0
- ORR and DOR based on investigator assessment[a]

Secondary
- DCR
- PFS
- OS
- TTP
- TTR

Other
- BOR and ORR based on BICR-assessed tumor response[a]

[a]Using RECIST v1.1.

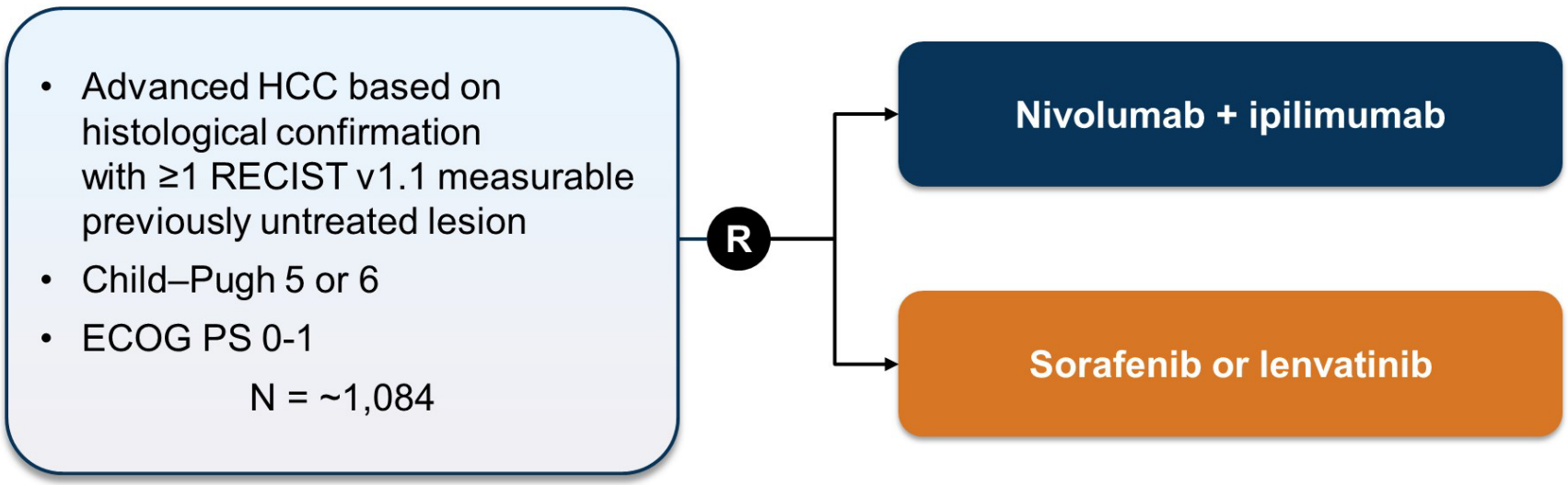




Treatment-related AE grade 3-4: **53%**, 29%, 31% for Arms A-C
Systemic steroid requirement: **51%**, 24%, 23% for Arms A-C
Received accelerated FDA approval Spring 2020

Yau. JAMA Oncol. 2020;6:e204564. El-Khoueiry. ASCO GI 2021. Abstr 269.

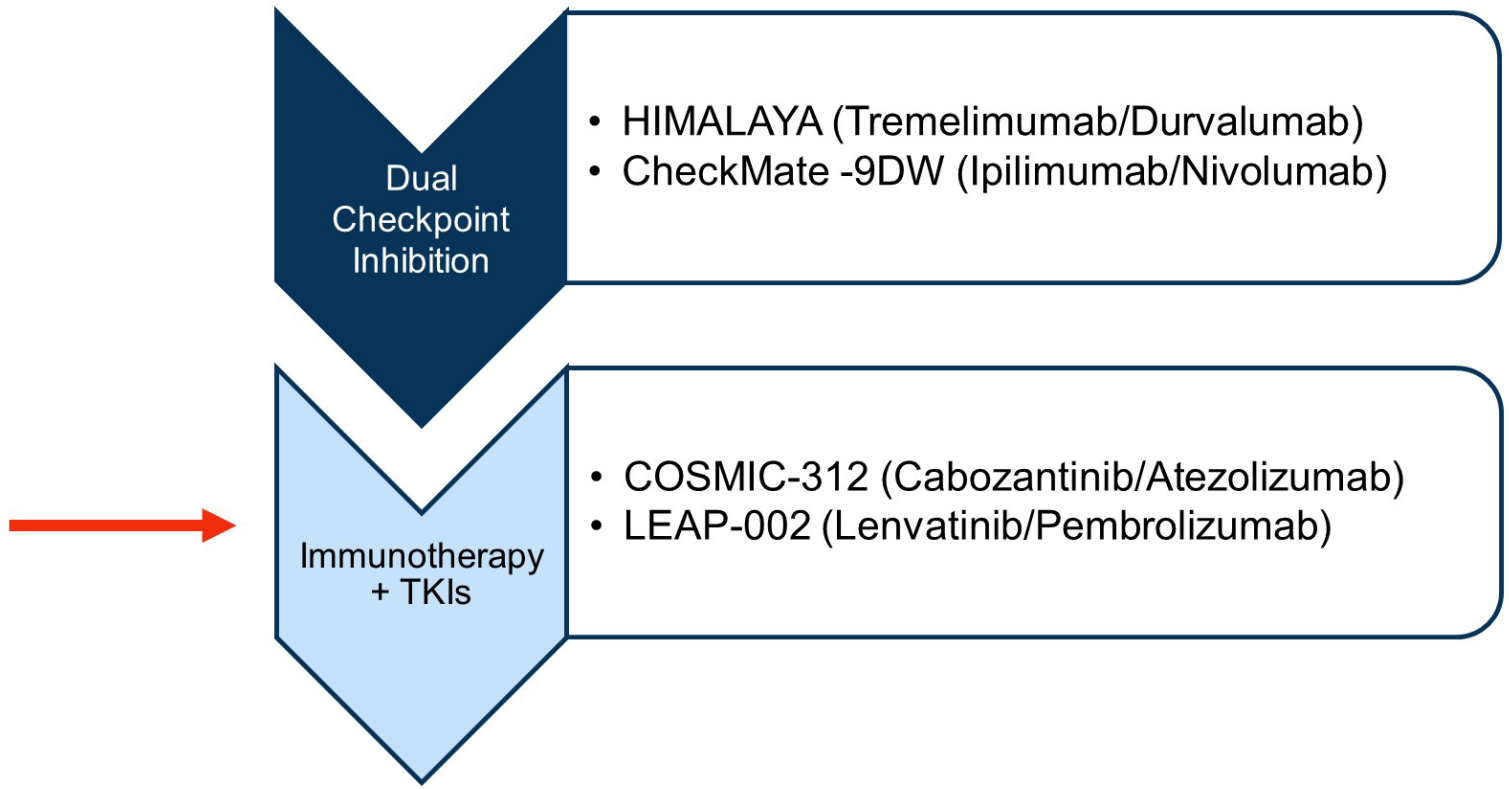
Phase 3 CheckMate-9DW Trial: First-Line Nivolumab Plus Ipilimumab[1]



- **Primary endpoint:** OS
- **Secondary endpoints:** ORR, DOR, and time to symptom deterioration

1. https://clinicaltrials.gov/ct2/show/NCT04039607.

New Frontline Systemic Therapy Combinations in Advanced HCC



IMMUNOTHERAPY +TKI

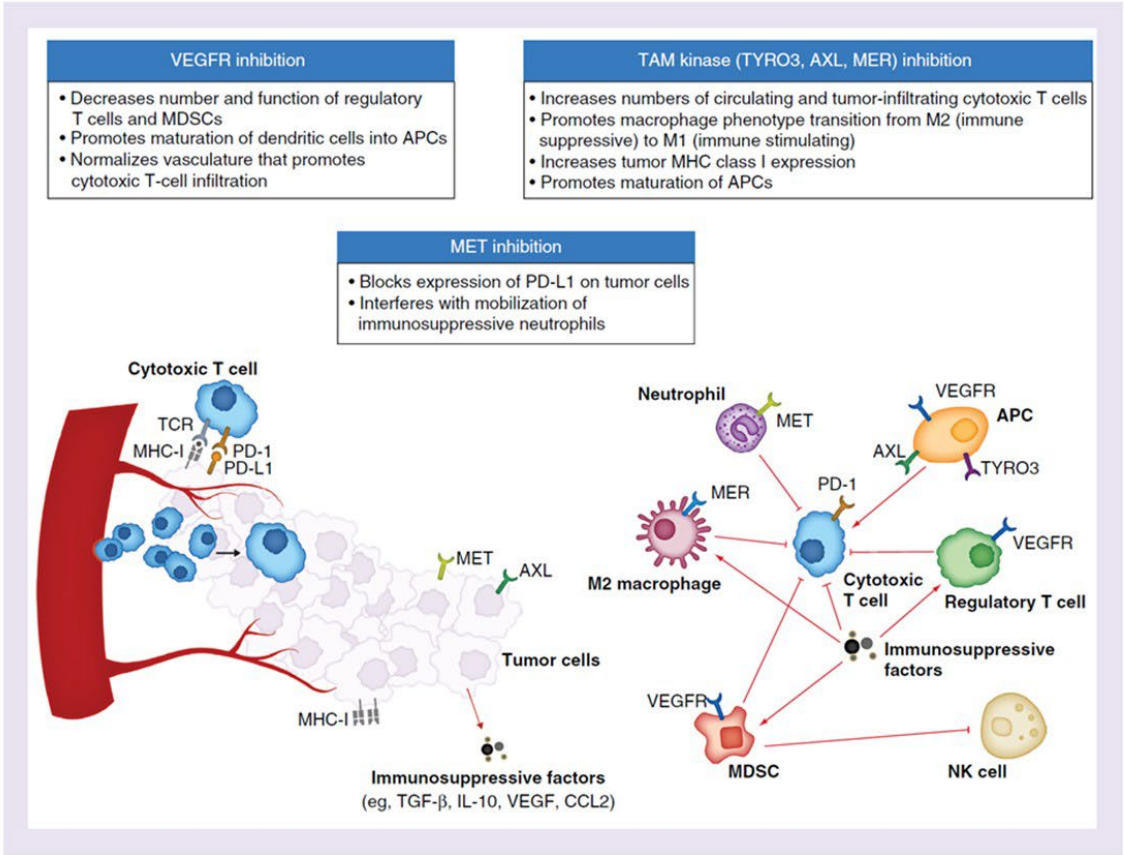
COSMIC 312

Rationale for Immunotherapy/TKI combinations
Overcoming Resistance Mechanisms

- Response rates in this setting remains modest with single agent PD-1 inhibitors

Lenvatinib targets:
VEGFR1-3, FGFR1-4, PDGFRα, KIT, RET

Cabozantinib targets:
VEGFR1-3, MET, TYRO3, AXL, MER



Kelley RK, et al, *Future Oncol*. 2020;16:1525-1536.

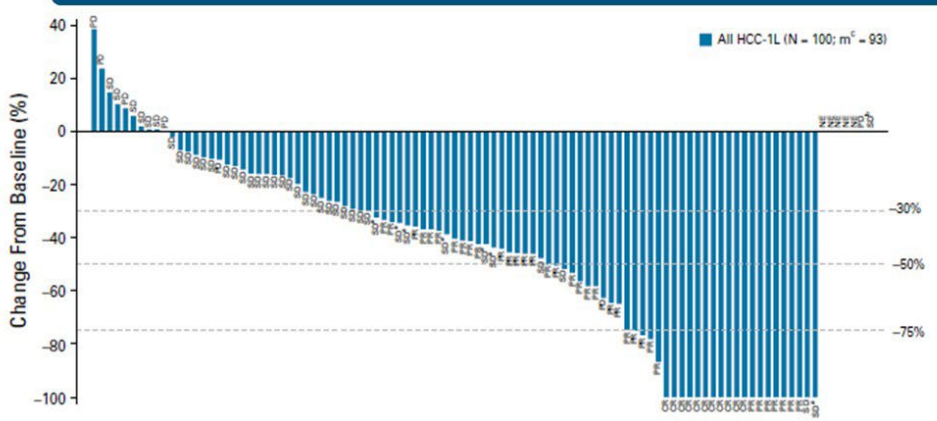
Phase 1b Study of Lenvatinib + Pembrolizumab in Patients With Unresectable Hepatocellular Carcinoma

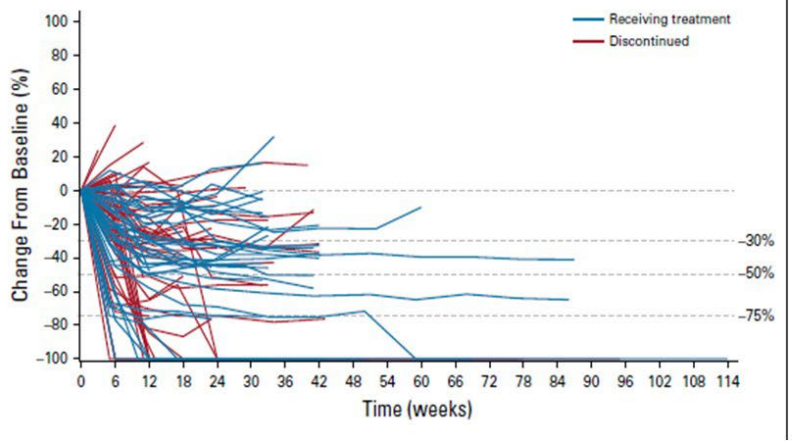
N = 104 patients
No DLTs in DLT phase
Expansion phase in 1L unresectable HCC
BCLC B (n = 29), BCLC C (n = 71)
Median follow-up: 10.6 mo

Efficacy Parameter	RECIST v1.1	modified RECIST
ORR	36.0%	46.0%
Median DOR	12.6 mo	8.6 mo
Median PFS	8.6 mo	9.3 mo

Median OS: 22 mo (95% CI, 20.4-NE)

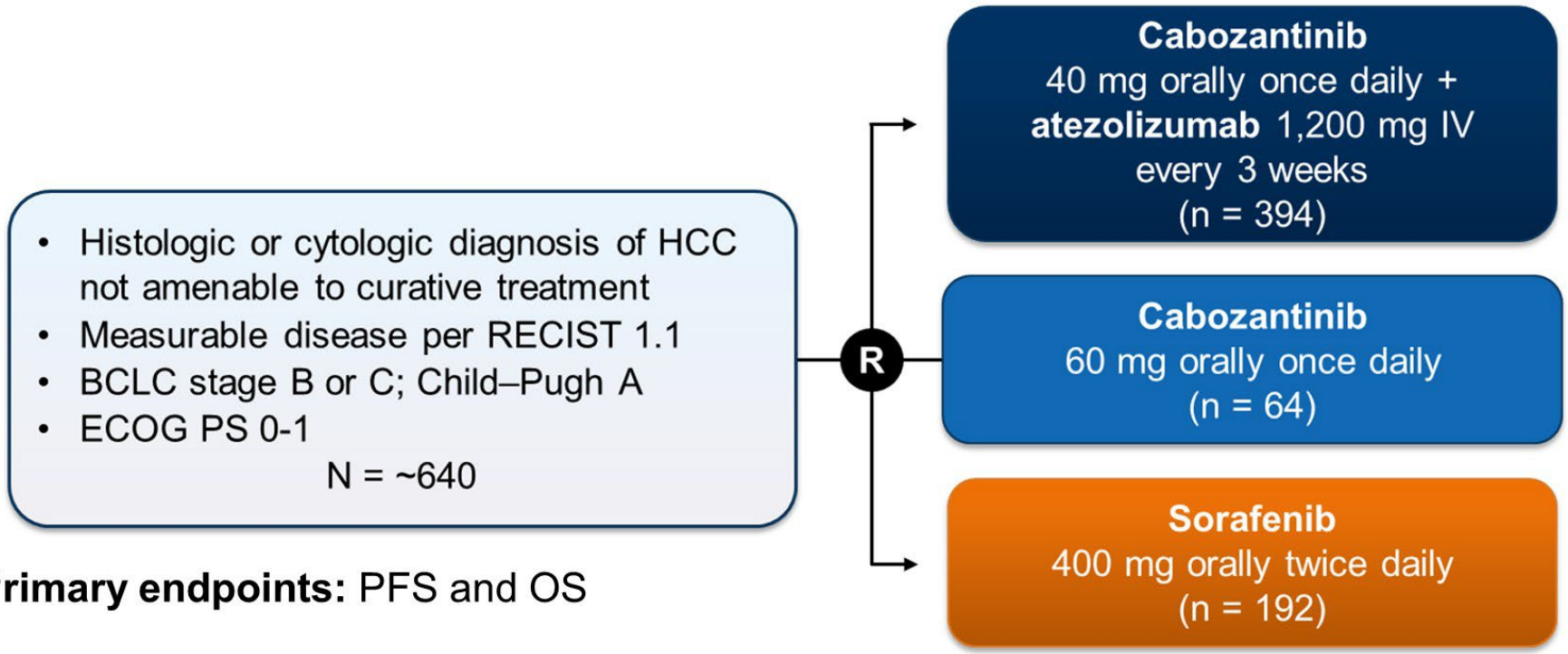
% change from Baseline in Sum of Target Lesions by **modified RECIST** (mRECIST) per independent imaging review





Finn RS, et al. *J Clin Oncol.* 2020;38:2960-2970.

Phase 3 COSMIC-312 Trial: First-Line Cabozantinib With or Without Atezolizumab Versus Sorafenib[1]

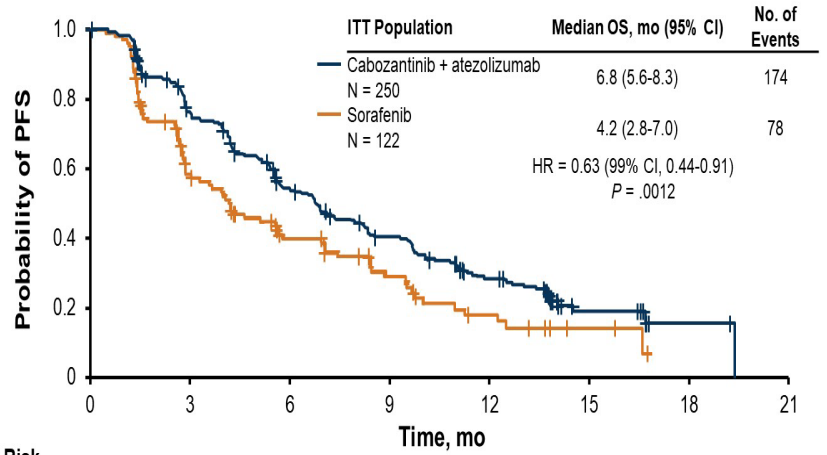


- **Primary endpoints:** PFS and OS

1. https://clinicaltrials.gov/ct2/show/NCT03755791.

Phase 3 COSMIC-312 Trial: PFS[1]

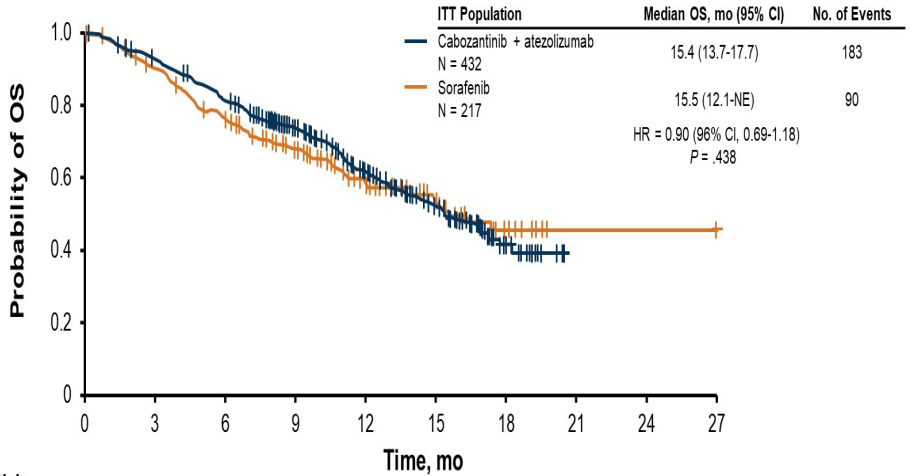
Primary Endpoint of PFS: Final Analysis
Cabozantinib + Atezolizumab vs Sorafenib



No. at Risk								
Cabozantinib + atezolizumab	250	177	119	84	51	11	2	0
Sorafenib	122	57	32	20	10	3	0	0

1. Kelley RK et al. ESMO Asia 2021. Abstract VP10-2021.

Phase 3 COSMIC-312 Trial: OS[1]



No. at Risk										
Cabozantinib + atezolizumab	432	394	343	268	173	87	18	0	0	0
Sorafenib	217	190	156	116	74	42	12	1	1	1

1. Kelley RK et al. ESMO Asia 2021. Abstract VP10-2021.

Phase 3 COSMIC-312 Trial: Tumor Response[1]

	Cabozantinib + Atezolizumab (n = 432)	Sorafenib (n = 217)	Cabozantinib (n = 188)
ORR (95% CI),%	**11 (8.1-14)**	3.7 (1.6-7.1)	6.4 (3.3-11)
Best OR, %			
CR	0.2	0	0
PR	11	3.7	6.4
SD	67	61	77
PD	14	20	11
NE	7.9	15	5.9
Median time to OR (range), mo	4.0 (1.3-10)	3.5 (1.0-5.4)	4.2 (1.4-6.9)
Median DOR (95% CI), mo	10.6 (7.1-12.7)	8.8 (3.0-NE)	15.1 (4.4-NE)
DCR, %	78	65	84

1. Kelley RK et al. ESMO Asia 2021. Abstract VP10-2021.

Phase 3 COSMIC-312 Trial: Adverse Events[1]

	Cabozantinib + Atezolizumab (n = 432)		Sorafenib (n = 217)		Cabozantinib (n = 188)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
TRAE[a]						
Any AEs, %	93	55	90	33	95	55
Diarrhea	42	3.5	42	1	48	5.3
Palmar-plantar erythrodysesthesia	42	7.9	44	8.2	44	8.5
ALT increased	22	6.3	5.8	1.9	22	5.9
AST increased	21	6.5	8.2	2.4	22	5.3
Decreased appetite	21	0.9	16	1.9	30	3.2
Fatigue	20	2.6	14	3.4	27	3.2
Hypertension	19	7	15	6.3	26	11
AEs of interest (all-cause)						
Any hemorrhage,%	17	2.8	14	4.8	15	3.2
Any immune-mediated AEs leading to systemic steroid use,[b] %	**7.2**	4.4	1	0.5	0	0

[a] TRAEs occuring in ≥20% of patients in any treatment arm. [b] TEAEs of special interest leading to initiation of systemic immune-modulating medication.
1. Kelley RK et al. ESMO Asia 2021. Abstract VP10-2021.

Reported Phase 3 First Line Combination Trials in HCC

	IMBRAVE 150		HIMALAYA		COSMIC 312	
	Atezo/Bev	Sorafenib	STRIDE	Sorafenib	Cabozantinib/Atezo	Sorafenib
mOS (mo)	19.2 HR 0.66 (0.52,0.85)	13.4	16.4 HR 0.78 (0.65-0.92)	13.8	15.4* HR 0.9 (96% CI 0.69–1.18)	15.5
mPFS (mo)	6.9 HR 0.65(0.53, 0.81)	4.3	3.78 HR 0.9 (0.77-1.05)	4.07	6.8 0.63 (99% CI 0.44–0.91)	4.2
ORR (RECIST 1.1)	30%	11%	20.1%	5.1%	11%	3.7%
CR	8%		3.1%		0.2%	
PD	19%		39.9%		14%	
Median DoR (months)	18.1	14.9	22.3	18.4	10.6	8.8
DCR	74%	55%	60.1%	60.7%	78%	65%

Kelley RK. ESMO ASIA 2021

ASCO Gastrointestinal Cancers Symposium

Lenvatinib plus TransArterial Chemoembolization versUs Lenvatinib alone as first-line treatmeNt for Primary AdvanCed Hepatocellular Carcinoma: A Phase 3, Multicenter, Randomized Controlled Trial (LAUNCH)

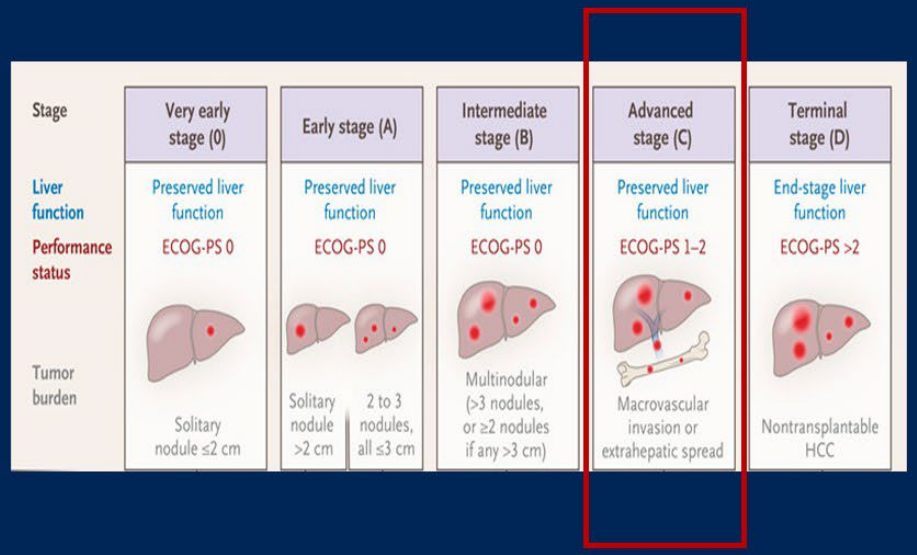
Zhenwei PENG[1], Wenzhe FAN[1], Bowen ZHU[1], Jiping WANG[2], Jiaping LI[1], Ming KUANG[1]

1 ,Cancer center, First Affiliated Hospital, Sun Yat-sen University, China

2, Brigham and Women's Hospital, Harvard Medical School, USA

Introduction

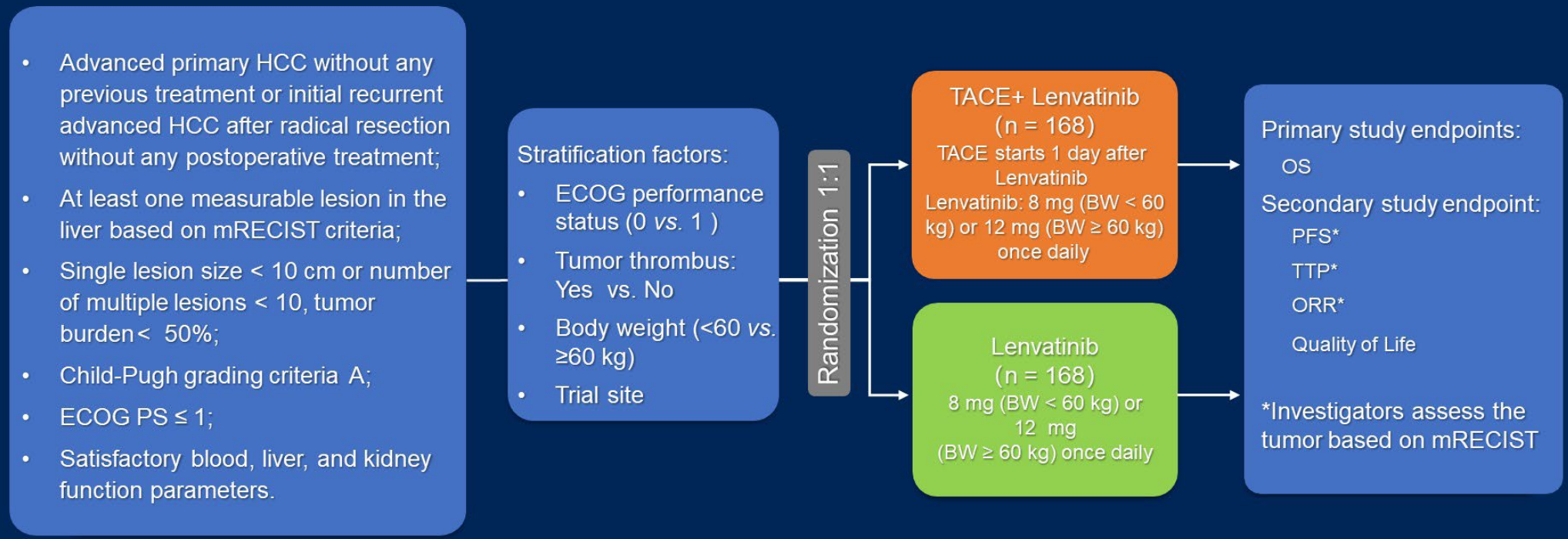
>50% HCC patients are advanced stage at the time of diagnosis



BCLC, n(%)	North America (N=1588)	Europe (N=2261)	China (N=6501)
0	107 (7)	84 (4)	192 (3)
A	474 (30)	582 (26)	1973 (30)
B	157 (10)	253 (11)	519 (9)
C	**673 (42)**	**1158 (51)**	**3606 (55)**
D	177 (11)	184 (8)	139 (2)

Villanueva A, et al. N Engl J Med 2019 Mar; 380:1450-1462; Park JW, et al. Liver Int. 2015 Sep;35(9):2155-66.

Schematic Diagram



HCC, Hepatocellular carcinoma; BCLC, Barcelona Clinic Liver Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; TACE, transarterial chemoembolization; BW, body weight; OS, overall survival; PFS, progression-free survival; TTP, time to progression; ORR, objective response rate; mRECIST, modified response evaluation criteria in solid tumors.

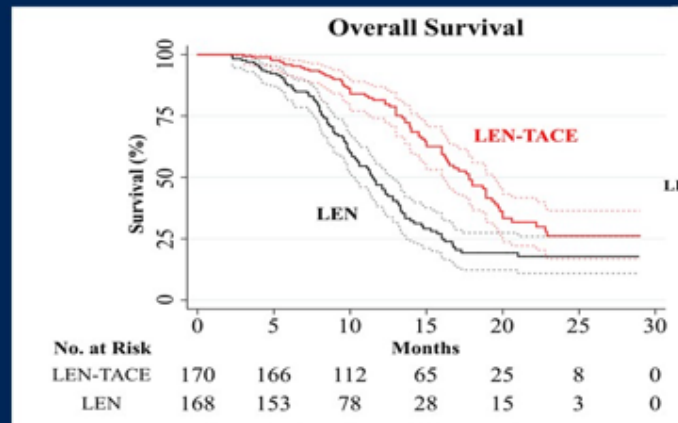
Tumor Response

The ORR and DCR were both higher in LEN-TACE group than in the LEN group.

Variable	RECIST 1.1			mRECIST		
	Group, No (%)		*P* value	Group, No (%)		*P* value
	LEN-TACE group (n=170)	LEN group (n=168)		LEN-TACE group (n=170)	LEN group (n=168)	
Complete response	1 (0.6)	1 (0.6)	0.993	5 (2.9)	1 (0.6)	0.102
Partial response	77 (45.3)	34 (20.2)	<0.001	87 (51.2)	41 (24.4)	<0.001
Stable disease	79 (46.5)	87 (51.8)	0.328	68 (40.0)	81 (48.2)	0.128
Progressive disease	13 (7.6)	46 (27.4)	<0.001	10 (5.9)	45 (26.8)	<0.001
Objective response rate	78 (45.9)	35 (20.8)	<0.001	92 (54.1)	42 (25.0)	<0.001
Disease control rate	157 (92.4)	122 (72.6)	<0.001	160 (94.1)	123 (73.2)	<0.001

LEN, Lenvatinib; TACE, transarterial chemoembolization; ORR, objective response rate; DCR, disease control rate; RECIST, response evaluation criteria in solid tumors. mRECIST, modified RECIST.

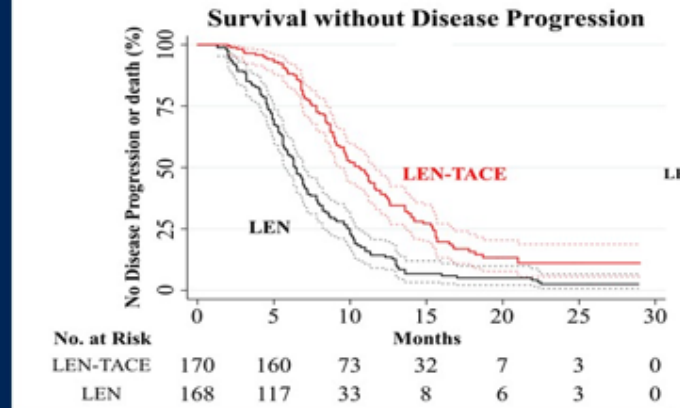
Survival Outcome



	No. of Events/ No. of Patients (%)	Median Overall Survival (95% CI) mo	Overall Survival at 6 Mo %	Overall Survival at 12 Mo %	Overall Survival at 24 Mo %
LEN-TACE	75/170 (44.1)	17.8 (16.1-19.5)	95.9 (91.5-98.0)	81.5 (74.0-87.0)	26.1 (16.8-36.4)
LEN	104/168 (61.9)	11.5 (10.3-12.7)	87.4 (81.3-91.6)	46.9 (38.2-55.0)	17.8 (11.0-26.0)

Hazard ratio for death, 0.45
(95% CI, 0.33-0.61)
Log-rank P<0.001

- **The median OS was 17.8 vs 11.5**
- **HR = 0.45**



	No. of Events/ No. of Patients (%)	Median Progression-free Survival (95% CI) mo	Progression-free Survival at 6 Mo %	Progression-free Survival at 12 Mo %
LEN-TACE	122/170 (71.8)	10.6 (9.5-11.7)	88.2 (82.3-92.2)	39.2 (31.2-47.0)
LEN	149/168 (88.7)	6.4 (5.8-7.0)	54.8 (46.9-61.9)	14.3 (9.1-20.6)

Hazard ratio for progression or death, 0.43
(95% CI, 0.34-0.55)
Log-rank P<0.001

- **The median PFS was 10.6 vs 6.4**
- **HR = 0.43**

LEN, Lenvatinib; TACE, transarterial chemoembolization; OS, overall survival; PFS, progression-free survival; HR, harzard ratio; CI, confidence interval

Conclusion

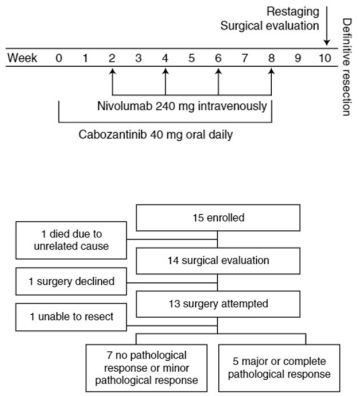
- Lenvatinib plus TACE was safe and effective for patients with advanced HCC, demonstrating remarkable improvements in OS, PFS and ORR, as well as acceptable toxicity.
- Lenvatinib plus TACE may represent a potential new first-line treatment option for patients with advanced HCC.

EARLY HCC

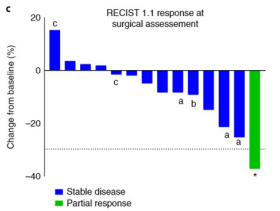
Neoadjuvant therapy (downstaging)

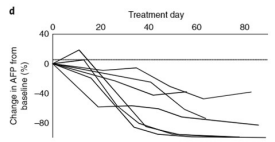
Nivolumab plus Cabozantinib

Study design

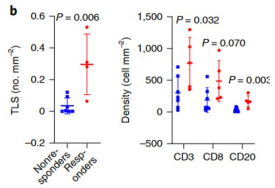


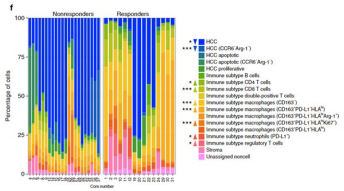
Response





Mechanism



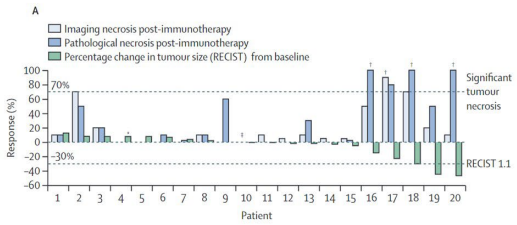


Ho WJ et al. *Nat Cancer* 2021

Neoadjuvant therapy (decrease recurrence)

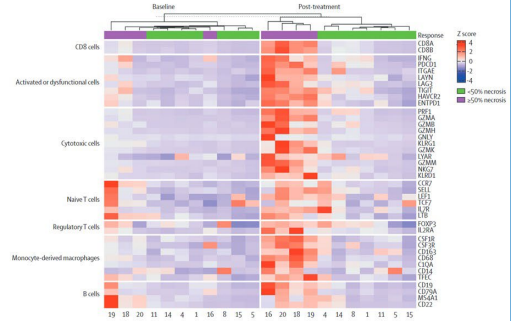
Cemiplimab (phase 2, n=21)

Tumor response after immunotherapy



4/20 (20% significant tumor necrosis >70%)
7/20 (35%, necrosis > 50%)

Impact on immune landscape

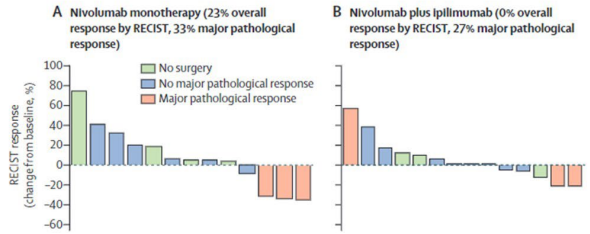


Marron T et al. *Lancet Gastroenterol Hepatol* 2022 (in press)

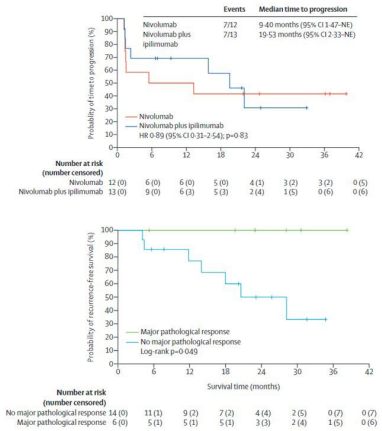
Neoadjuvant therapy (decrease recurrence)

Nivolumab vs Nivolumab + Ipilimumab (phase 2, n=30)

Tumor response after immunotherapy



Outcomes after immunotherapy



Kaseb AO T et al. *Lancet Gastroenterol Hepatol* 2022 (in press)

Immune check-point inhibitors in LT

Risk of graft rejection **post-LT** (de novo malignancy)

Patient	Reference	Malignancy	Compound	Transplant to immunotherapy in years	Response	OS (months)	Graft rejection	PD-L1 status	status	Immunosuppression
1	[17]	Melanoma	Ipilimumab	8	No	>5[a]	No	N/A	N/A	Low dose tacrolimus
2	[10]	Melanoma	Ipilimumab	8	Yes	>4[a]	No	N/A	N/A	Low dose sirolimus
3	[7]	HCC	Nivolumab	1	Yes	10	No	0%	N/A	Low dose tacrolimus
4	[14]	Fibrolamellar HCC	Nivolumab	4	N/A	1	Yes, lethal	Positive	Positive	Sirolimus
5	[14]	Fibrolamellar HCC	Nivolumab	3	N/A	1	Yes, lethal	Positive	Positive	Tacrolimus
6	[9]	Melanoma	Pembrolizumab	N/A	N/A	N/A	Yes, lethal	N/A	N/A	Ciclosporine
7	[19]	HCC	Pembrolizumab	8	No	3	No	N/A	N/A	Low dose tacrolimus
8	[15]	HCC	Nivolumab	2.7	No	1.2	No	N/A	10%	Tacrolimus
9	[15]	Melanoma	Pembrolizumab	5.5	Yes	9.5	No	0%	5%	Everolimus, MMF
10	[15]	HCC	Nivolumab	7.8	No	1.1	No	0%	N/A	Sirolimus, MMF
11	[15]	HCC	Nivolumab	3.7	No	1.3	No	0%	0%	Tacrolimus
12	[15]	HCC	Nivolumab	1.2	N/A	0.3	No	N/A	0%	Tacrolimus
13	[15]	HCC	Nivolumab	1.1	N/A	0.9	Yes	30%	0%	N/A
14	[11]	Melanoma	Ipilimumab/ pembrolizumab	6	Yes/yes	18[a]	No	N/A	N/A	Sirolimus

Munker S et al. *United European Gastroenterol J* 2018

Immune check-point inhibitors in LT

Risk of graft rejection **pre-LT** (bridge therapy)

No.	Age	Gender	ULD	Max tumor diameter (cm)	Max pre-LT AFP	No. of LRT	Salvage/type transplantation	Pathology Milan in/ out	Cycles	Nivolumab (days pre-LT)	PRBC (U)	Duration of follow-up post LT (months)	Complication	Rejection	Recurrence
1	69	M	None	10	3	2	Yes/LDLT	Milan out within UCSF	21	18	0	23	None	None	None
2	56	F	HCV	5.4	4.4	2	No/DDLT	Milan out within UCSF	8	22	14	22	None	None	None
3	58	M	HBV	21	9.4	6	Yes/DDLT	Milan in	32	1	30	22	None	None	None
4	63	M	HCV, HIV	4.4	507	7	No/DDLT	Milan in	4	2	15	21	None	None	None
5	30	M	HBV	3.2	1493	2	Yes/DDLT	Milan in	25	22	0	16	None	Mild (low tacrolimus level)	None
6	63	M	HBV, HIV	2	158	0	No/DDLT	Milan in	4	13	1	14	Bile leak	None	None
7	66	M	HBV	2.5	479	2	Yes/DDLT	Milan in	9	253	7	14	None	None	None
8	55	F	HBV	2.8	820	3	No/DDLT	Milan in	12	7	0	8	None	None	None
9	53	F	NASH	8.7	124	1	Yes/DDLT	Milan out within UCSF	2	30	17	8	None	None	None

Tabrizian P et al. *AJT* 2020

BILIARY TRACT CANCER

TIMELINE FOR NEW AGENTS IN CCA

Pre-2010	No SOC
2010	Gemcitabine and cisplatin improves survival compared with single agent gemcitabine
2010-2018	No drug or drug combination is better than Gemcitabine and cisplatin 1L
2018	Gem/cis + S1 superior to Gem/cis in Asian patients
2019	FOLFOX superior to ASC
2020	**Pemigatinib FDA approved**
2021	**Infigratinib FDA approved** **Ivosidenib FDA approved**
2021	NalIRI superior to 5FU (phase 2) Dabrafenib + Trametinib (BRAF V600E) Trastuzumab + Pertuzumab (Her2/neu)
2021-2	Futibatinib, Derazantinib pivotal, Gem/cis + nab paclitaxel studies competed.
2022	TOPAZ-1 study presented GI ASCO

TOPAZ-1

Background

- BTC comprises a group of heterogenous malignancies that represents the second most common group of primary liver cancers, and incidence is rising worldwide[1,2]
- Advanced, unresectable BTC is an area of high unmet need due to its aggressive nature, limited treatment options, and poor prognosis[1,2]
- First-line standard of care for advanced BTC, GemCis chemotherapy, has remained unchanged for over a decade[3,4]
- Reports on immunogenic features of BTC indicate it is a good candidate for immunotherapy,[5,6] although only limited clinical activity has been reported for immune checkpoint inhibitor monotherapies in the second-line setting[7,8]
- Durvalumab, a PD-L1 inhibitor, plus GemCis demonstrated promising antitumor activity as first-line treatment for patients with advanced BTC in a Phase 2 study[9]

TOPAZ-1 (NCT03875235) is the first global Phase 3 study evaluating immunotherapy plus chemotherapy as first-line treatment for advanced BTC to report results

BTC, biliary tract cancer; GemCis, gemcitabine and cisplatin; ICI, immune checkpoint inhibition; PD-L1, programmed cell death ligand-1.

1. Ahn DH and Bekaii-Saab T. *J Gastrointest Oncol* 2017;8:293–301. 2. Boilève A, et al. *Cancers (Basel)* 2021;13:1569. 3. Valle J, et al. *N Engl J Med* 2010;362:1273–1281. 4. Okusaka T, et al. *Br J Cancer* 2010;103:469–474. 5. Fluxá P, et al. *BMC Cancer* 2018;18:243. 6. Kim R, et al. *Oncotarget* 2018;9:23366–23372. 7. Bang Y-J, et al. *J Clin Oncol* 2019;37(suppl 15). Abs 4079. 8. Kim RD, et al. *JAMA Oncol* 2020;6:888–894. 9. Oh D-Y, et al. Poster presented at: ASCO Annual Meeting 2020; 29–31 May 2020; Virtual Meeting.

PRESENTED BY: Do-Youn Oh, MD, PhD

TOPAZ-1 study design

TOPAZ-1 is a double-blind, multicenter, global, Phase 3 study

Key eligibility
- Locally advanced or metastatic BTC (ICC, ECC, GBC)
- Previously untreated if unresectable or metastatic at initial diagnosis
- Recurrent disease >6 months after curative surgery or adjuvant therapy
- ECOG PS 0 or 1

Stratification factors
- Disease status
  - (initially unresectable versus recurrent)
- Primary tumor location
  - (ICC versus ECC versus GBC)

R (1:1)
N=685

Durvalumab 1500 mg Q3W + GemCis (up to 8 cycles) → Durvalumab 1500 mg Q4W until PD

Placebo Q3W + GemCis (up to 8 cycles) → Placebo Q4W until PD

Primary objective
- Overall survival

Secondary objectives
- Progression-free survival
- Objective response rate
- Duration of response
- Efficacy by PD-L1 status
- Safety

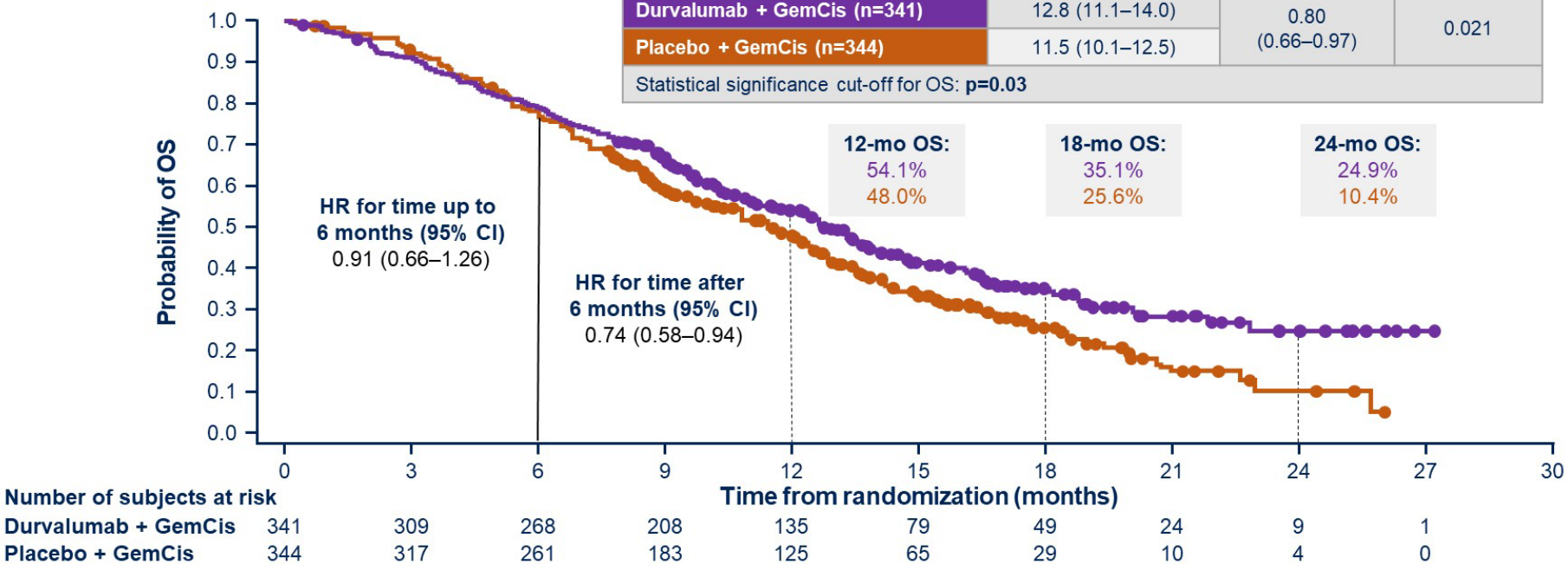
GemCis treatment: gemcitabine 1000 mg/m2 and cisplatin 25 mg/m2 on Days 1 and 8 Q3W administered for up to 8 cycles.

BTC, biliary tract cancer; ECC, extrahepatic cholangiocarcinoma; ECOG, Eastern Cooperative Oncology Group; GBC, gallbladder cancer; GemCis, gemcitabine and cisplatin; ICC; intrahepatic cholangiocarcinoma; PD, progressive disease; PD-L1, programmed cell death ligand-1; PS, performance status; QnW, every n weeks; R, randomization.

PRESENTED BY: Do-Youn Oh, MD, PhD

Primary endpoint: OS

	Median OS (95% CI), months	Hazard ratio (95% CI)	p-value
Durvalumab + GemCis (n=341)	12.8 (11.1–14.0)	0.80 (0.66–0.97)	0.021
Placebo + GemCis (n=344)	11.5 (10.1–12.5)		
Statistical significance cut-off for OS: **p=0.03**			

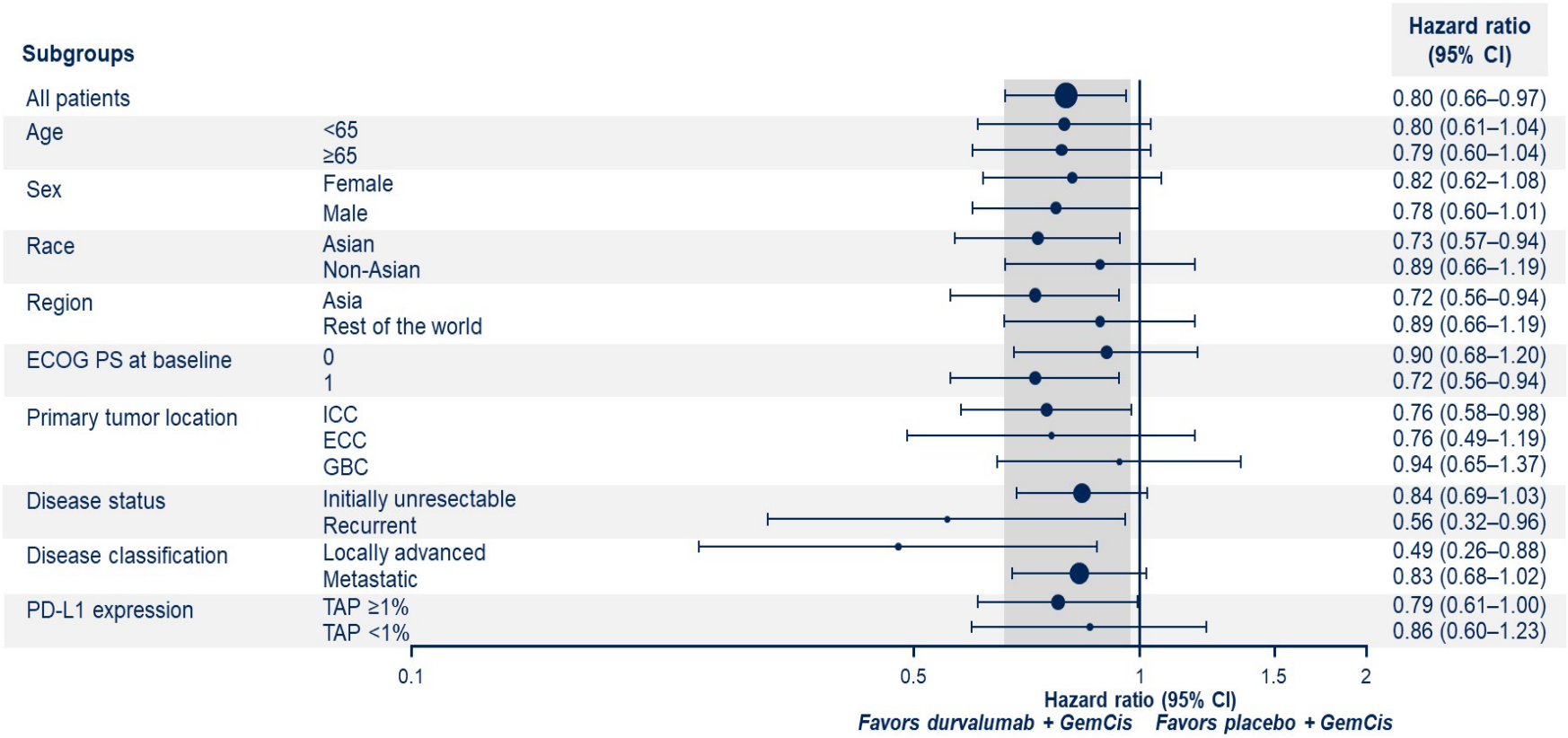


Number of subjects at risk										
Durvalumab + GemCis	341	309	268	208	135	79	49	24	9	1
Placebo + GemCis	344	317	261	183	125	65	29	10	4	0

Median duration of follow-up (95% CI) was 16.8 (14.8–17.7) months with durvalumab + GemCis and 15.9 (14.9–16.9) months with placebo + GemCis.
CI, confidence interval; GemCis, gemcitabine and cisplatin; HR, hazard ratio; mo, month; OS, overall survival.

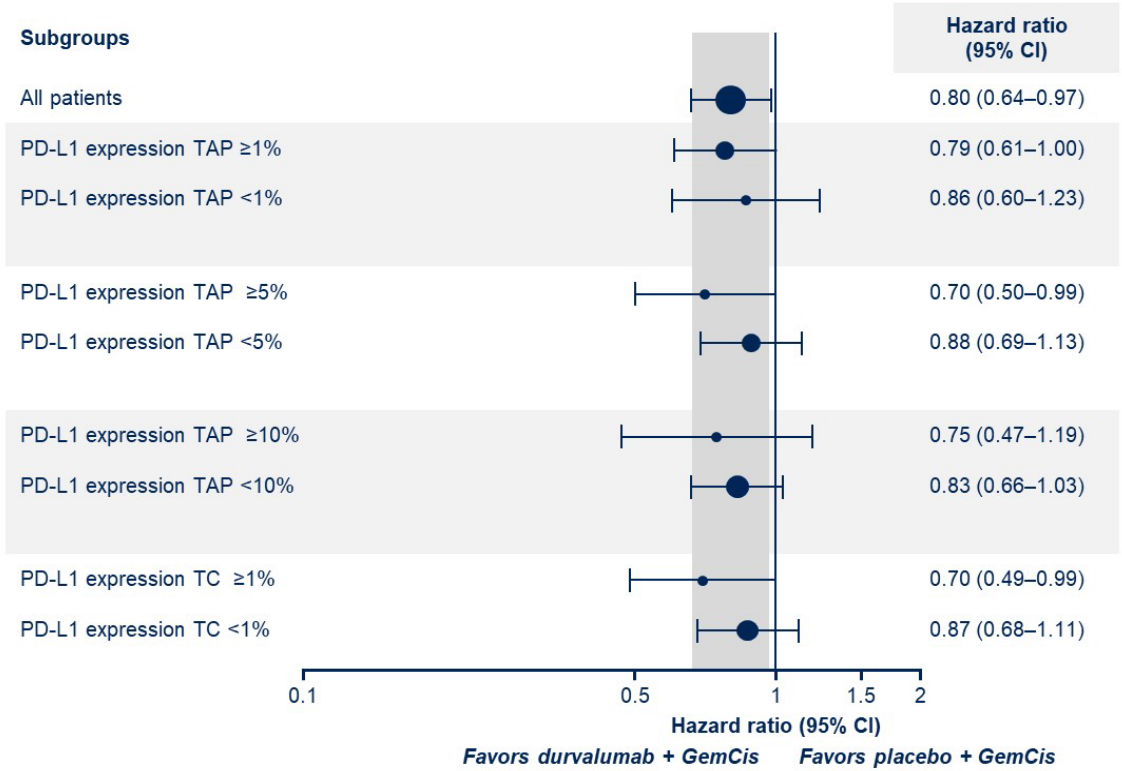
PRESENTED BY: Do-Youn Oh, MD, PhD

Subgroup analysis of OS

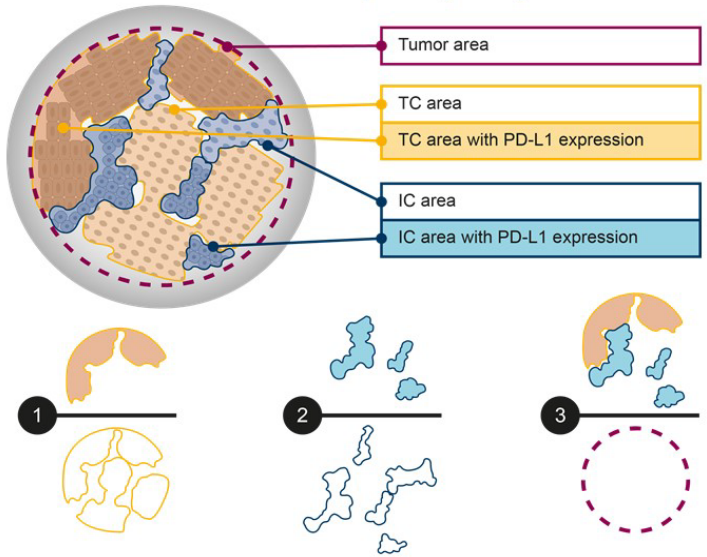


CI, confidence interval; ECC, extrahepatic cholangiocarcinoma; ECOG, Eastern Cooperative Oncology Group; GBC, gallbladder cancer; GemCis, gemcitabine and cisplatin; ICC, intrahepatic cholangiocarcinoma; OS, overall survival; PD-L1, programmed cell death ligand-1; PS, performance status; TAP, tumor area positivity.

OS in subgroups by PD-L1 expression



Tumor Area Positivity (TAP) score using the Ventana PD-L1 (SP263) Assay

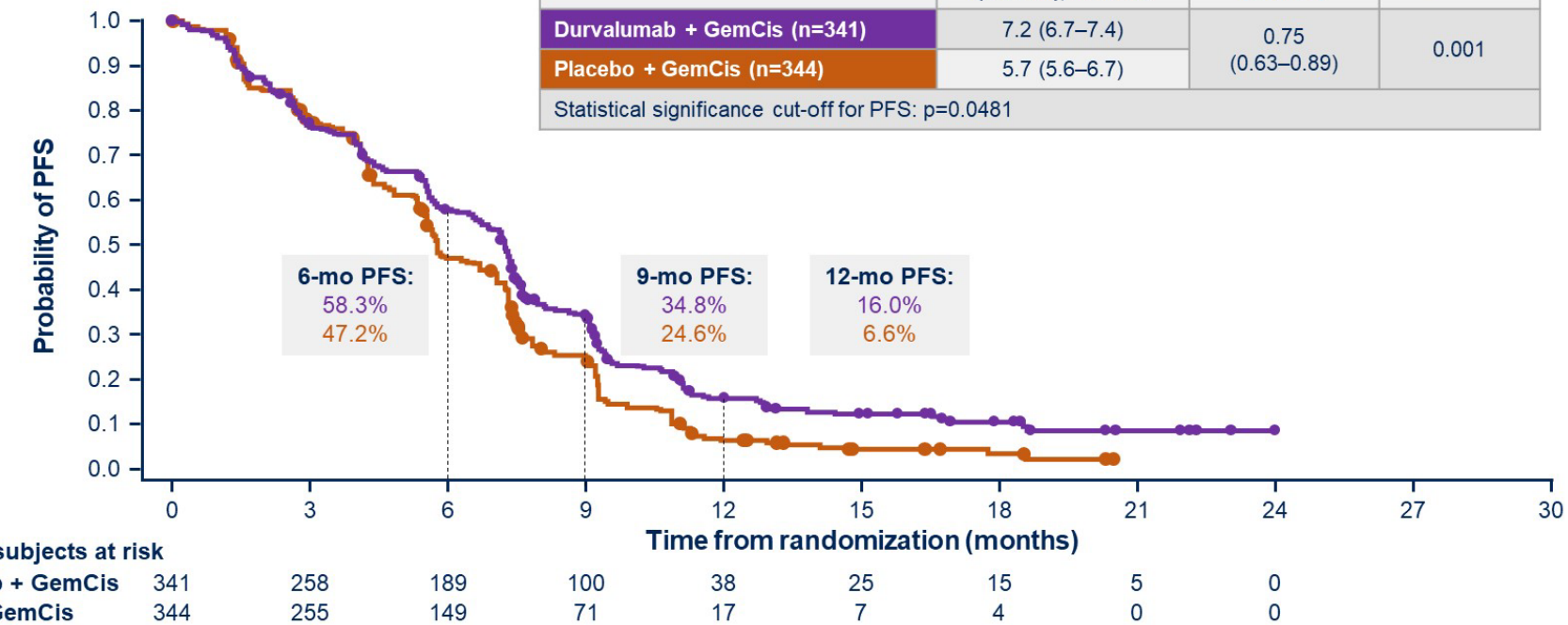


1. TC: proportion of TCs with PD-L1 membrane staining at any intensity
2. IC: proportion of tumor-associated ICs with PD-L1 cytoplasmic/membrane staining at any intensity
3. **Combined TCs and ICs:** Proportion of tumour area occupied by TCs with membrane and ICs with cytoplasmic/membrane PD-L1 staining at any intensity (TAP score)

CI, confidence interval; IC, immune cell; OS, overall survival; PD-L1, programmed cell death ligand-1; TC, tumor cell; TAP, tumor area positivity

Secondary endpoint: PFS

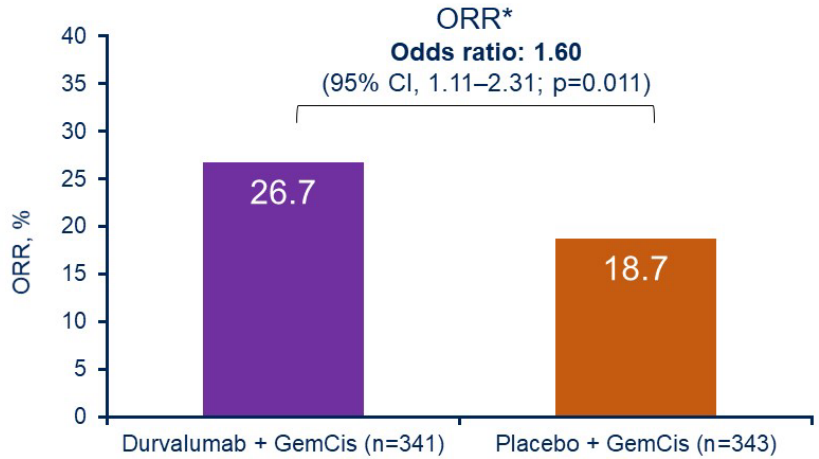
	Median PFS (95% CI), months	Hazard ratio (95% CI)	p-value
Durvalumab + GemCis (n=341)	7.2 (6.7–7.4)	0.75 (0.63–0.89)	0.001
Placebo + GemCis (n=344)	5.7 (5.6–6.7)		
Statistical significance cut-off for PFS: p=0.0481			



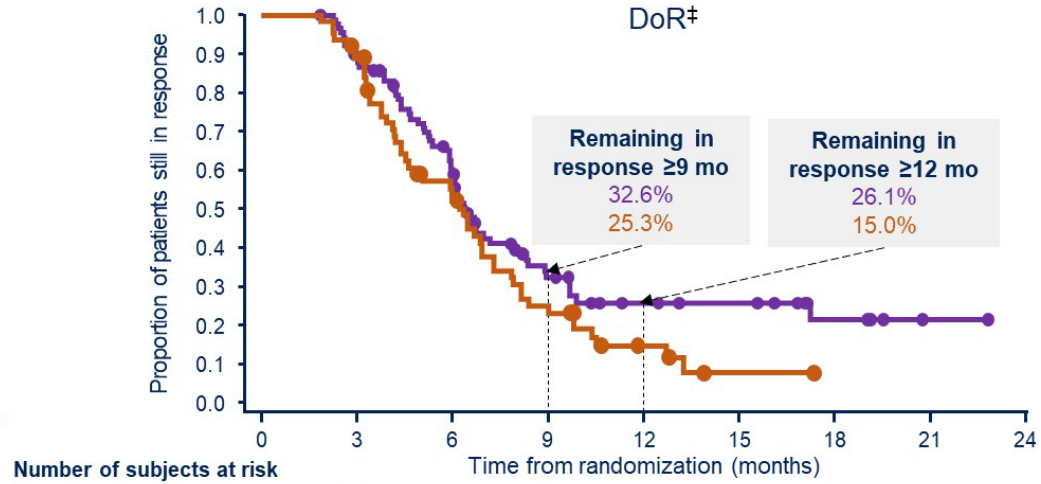
Median duration of follow-up (95% CI) was 9.2 (0.0–24.0) months with durvalumab + GemCis and 6.9 (0.0–20.4) months with placebo + GemCis.
CI, confidence interval; GemCis, gemcitabine and cisplatin; PFS, progression-free survival.

PRESENTED BY: Do-Youn Oh, MD, PhD

Secondary endpoint: Tumor response



	Durvalumab + GemCis (n=341)	Placebo + GemCis (n=343)
ORR, n (%)	91 (26.7)	64 (18.7)
CR, n (%)	7 (2.1)	2 (0.6)
PR, n (%)	84 (24.6)	62 (18.1)
DCR, n (%)†	291 (85.3)	284 (82.6)



	Durvalumab + GemCis (n=91)	Placebo + GemCis (n=64)
Median DoR (quartile 1–3), months	6.4 (4.6–17.2)	6.2 (3.8–9.0)
Median time to response (quartile 1–3), months	1.6 (1.3–3.0)	2.7 (1.4–4.1)

*By investigator assessments using RECIST v1.1 based on patients in the final analysis set who had measurable disease at baseline. †Analysis of DCR was based on all patients in the full analysis set. ‡Analysis of DoR was based on patients in the full analysis set who had an objective response and measurable disease at baseline.

CI, confidence interval; CR, complete response; DCR, disease control rate; DoR, duration of response; GemCis, gemcitabine and cisplatin; mo, month; ORR, objective response rate; PR, partial response.

PRESENTED BY: Do-Youn Oh, MD, PhD

Conclusions

- TOPAZ-1 is the first global Phase 3 study to report positive results testing immunotherapy plus chemotherapy as first-line treatment for advanced BTC
- TOPAZ-1 met its primary endpoint at the prespecified interim analysis: durvalumab plus GemCis demonstrated statistically significant and clinically meaningful prolonged overall survival compared with placebo plus GemCis
- Durvalumab did not add additional toxicity to that observed with GemCis, and no new safety signals were identified from the known safety profiles of each individual treatment
- Durvalumab plus GemCis is an effective first-line therapy, and could become a new standard of care, for patients with advanced BTC

BTC, biliary tract cancer; GemCis, gemcitabine and cisplatin.

ESOPHAGEAL AND GASTRIC CANCER

Trastuzumab Deruxtecan (T-DXd; DS-8201) in Patients With HER2–Positive Advanced Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma: Final Overall Survival (OS) Results From a Randomized, Multicenter, Open-Label, Phase 2 Study (DESTINY-Gastric01)

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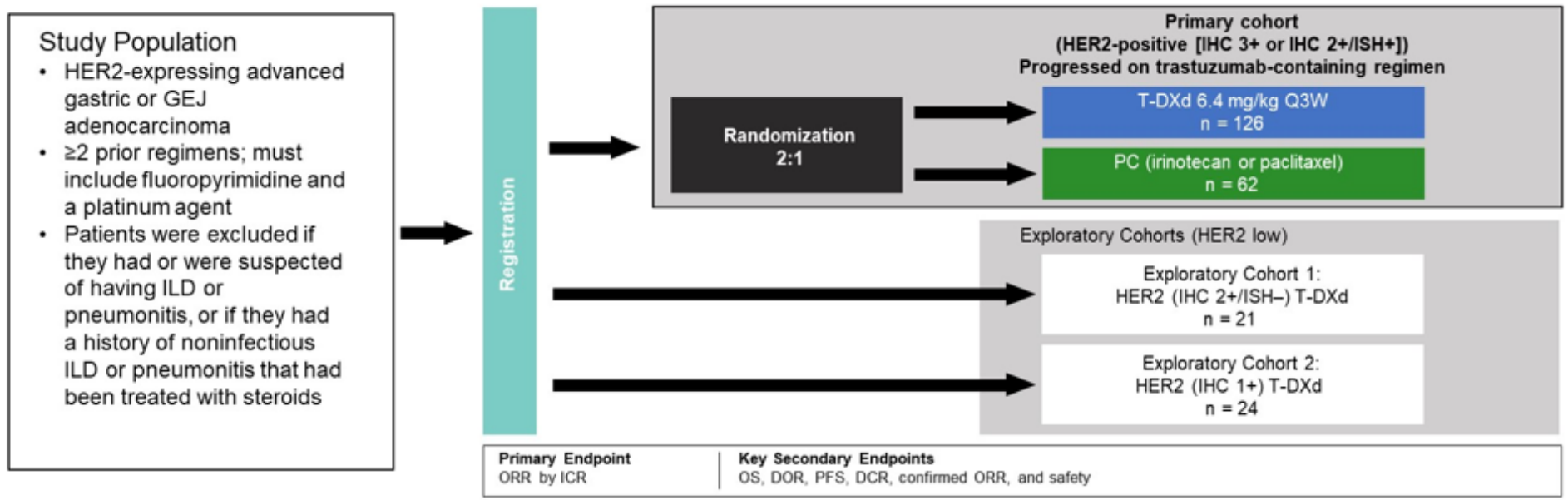
DESTINY-Gastric01 Study Design

An open-label, multicenter phase 2 study (NCT03329690)



- Patients were stratified by country, ECOG PS score, and HER2 status
- In the primary analysis (data cutoff: Nov 8, 2019; 101 OS events; median survival follow-up, 12.3 months), T-DXd showed statistically significant benefit vs standard chemotherapy in ORR and OS
- Key secondary endpoint of OS was to be statistically evaluated hierarchically if the primary endpoint was statistically significant
- Data cutoff: June 3, 2020 (133 OS events; median survival follow-up: 18.5 months)

DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; ICR, independent central review; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; ORR, objective response rate; OS, overall survival; PC, physician's choice; PFS, progression-free survival; Q3W, every 3 weeks; T-DXd, trastuzumab deruxtecan.

Shitara K et al. Trastuzumab deruxtecan in previously treated HER2-positive gastric cancer. *N Engl J Med*. 2020;382:2419-2430.

Prior Treatment

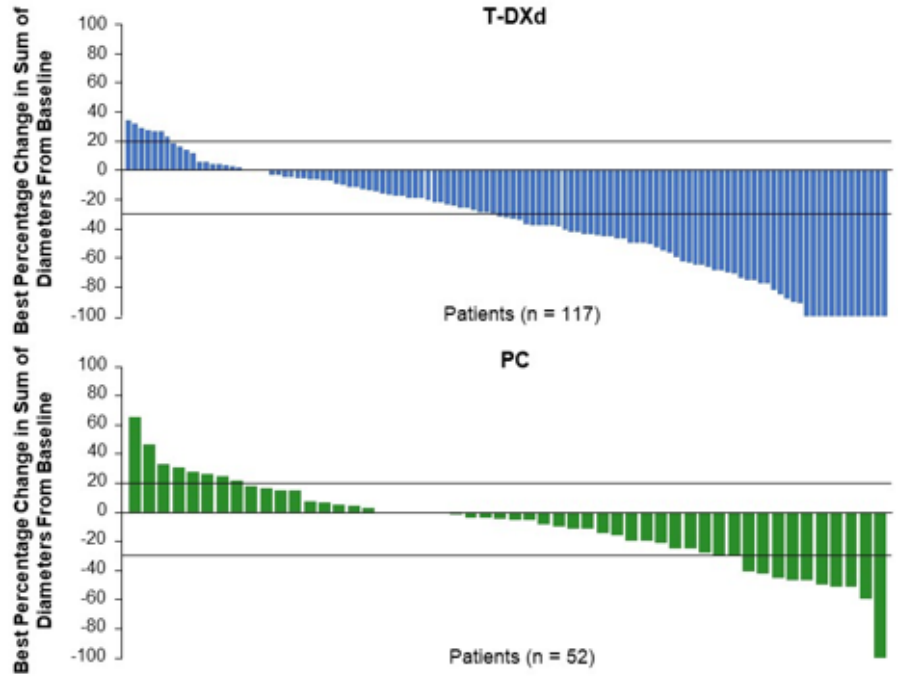
	T-DXd n = 125	PC Overall n = 62
Prior systemic therapies for advanced/metastatic disease,[a] %		
2	52.8	61.3
3	27.2	29.0
≥4	20.0	9.7
Prior treatment, %		
Containing trastuzumab	100	100
Containing ramucirumab	75.2	66.1
Containing taxane	84.0	88.7
Irinotecan or other topoisomerase I inhibitor	6.4	8.1
Immune checkpoint inhibitors	35.2	27.4

PC, physician's choice; PD, progressive disease; T-DXd, trastuzumab deruxtecan.
[a]Therapies intended for "locally advanced/metastatic" or as "neoadjuvant" or "adjuvant" if PD occurred within 6 months of the treatment ending.

ORR and Other Efficacy Endpoints

	T-DXd n = 119	PC Overall n = 56
ORR (CR + PR) by ICR, n (%)[a]	**61 (51.3) 95% CI, 41.9-60.5**	**8 (14.3) 95% CI, 6.4-26.2**
	P < 0.0001[b]	
CR	11 (9.2)	0
PR	50 (42.0)	8 (14.3)
SD	42 (35.3)	27 (48.2)
PD	14 (11.8)	17 (30.4)
Not evaluable	2 (1.7)	4 (7.1)
Confirmed ORR (CR + PR) by ICR, n (%)[a]	50 (42.0) 95% CI, 33.0-51.4	7 (12.5) 95% CI, 5.2-24.1
CR	10 (8.4)	0
PR	40[c] (33.6)	7 (12.5)
SD	52 (43.7)	28 (50.0)
PD	14 (11.8)	17 (30.4)
Not evaluable	3 (2.5)	4 (7.1)
Confirmed DCR (CR + PR + SD), n (%)[a]	102 (85.7) 95% CI, 78.1-91.5	35 (62.5) 95% CI, 48.5-75.1
Confirmed DOR, median, months	12.5 95% CI, 5.6-NE	3.9 95% CI, 3.0-4.9
TTR, median, months	1.5 95% CI, 1.4-1.7	1.6 95% CI, 1.3-1.7

Best Percentage Change from Baseline in Tumor Size for Individual Patients[d]



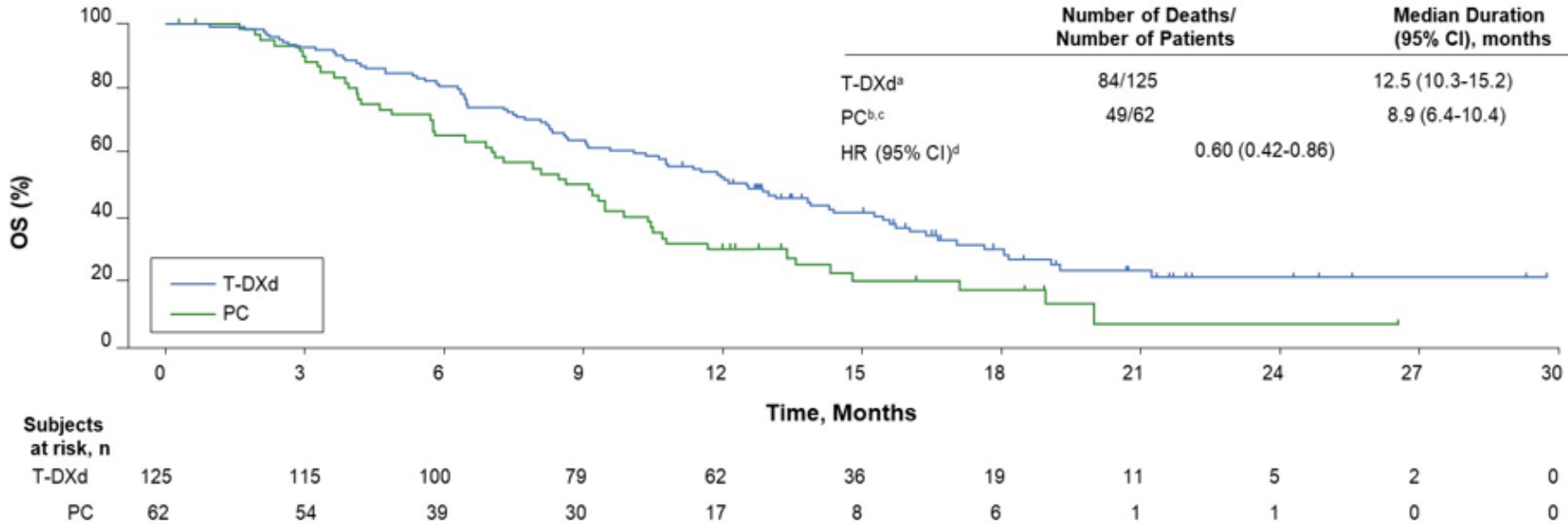
CR, complete response; DCR, disease control rate; DOR, duration of response; ICR, independent central review; NE, not estimable; ORR, objective response rate; PC, physician's choice; PD, progressive disease; PR, partial response; SD, stable disease; T-DXd, trastuzumab deruxtecan; TTR, time to response.

Confirmed ORR: responses were confirmed by a follow-up scan ≥4 weeks after initial CR/PR. [a]Includes data for the response-evaluable set: all randomized patients who received ≥1 dose of study drug and had measurable tumors based on ICR at baseline (T-DXd, n = 119; PC overall, n = 56; irinotecan, n = 51; paclitaxel, n = 5). [b]Comparison between T-DXd and PC overall using Cochran-Mantel-Haenszel test stratified by region. [c]According to the procedure of the ICR, the adjudicator assessment was changed from PR to SD in 1 patient at data cutoff of the final OS analysis. [d]Includes patients who had both baseline and postbaseline target lesion assessments by ICR in both treatment arms. 6 patients were excluded from this analysis because they had no postbaseline tumor assessment (T-DXd, n = 2; PC, n = 4).

Line at 20% indicates progressive disease; line at –30% indicates partial response.

Overall Survival

Kaplan-Meier Analysis of OS



	Number of Deaths/ Number of Patients	Median Duration (95% CI), months
T-DXd[a]	84/125	12.5 (10.3-15.2)
PC[b,c]	49/62	8.9 (6.4-10.4)
HR (95% CI)[d]	0.60 (0.42-0.86)	

Subjects at risk, n											
T-DXd	125	115	100	79	62	36	19	11	5	2	0
PC	62	54	39	30	17	8	6	1	1	0	0

As in the primary analysis (101 OS events; 54.0% maturity), in this updated analysis (133 OS events; 71.1% maturity), T-DXd showed superior antitumor activity compared to PC

HR, hazard ratio; OS, overall survival; PC, physician's choice; T-DXd, trastuzumab deruxtecan.
[a]In the T-DXd arm, 41 patients (32.8%) were censored.
[b]In the PC arm, 13 patients (21.0%) were censored.
[c]1 patient in the PC arm received crossover treatment of T-DXd.
[d]HR and corresponding 95% CI were estimated using Cox proportional hazards model stratified by region.

Conclusions

- With continued follow-up after the primary analysis, T-DXd demonstrated clinically meaningful OS benefit (~40% reduced risk of death) and clinically relevant improvement in ORR compared with PC standard chemotherapy in HER2-positive advanced gastric or GEJ cancer
- The overall safety profile of T-DXd was manageable and consistent with that of the primary analysis
  - The most common AEs were gastrointestinal or hematologic in nature
  - 16 patients (12.8%) had T-DXd-related ILD as determined by an independent adjudication committee. Most were grade 1 or 2
- Additional follow-up provides further evidence that T-DXd is an effective treatment option for patients with HER2+ advanced gastric or GEJ adenocarcinoma who have progressed after ≥2 previous lines of therapy, including trastuzumab, fluoropyrimidine, and a platinum agent

AE, adverse event; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; ILD, interstitial lung disease; ORR, objective response rate; OS, overall survival; PC, physician's choice; T-DXd, trastuzumab deruxtecan.
Shitara K et al. *J Clin Oncol*. 2020;38:4513.

ASCO Gastrointestinal Cancers Symposium

Nivolumab plus chemotherapy versus chemotherapy as first-line treatment for advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma: expanded analyses from 24-month follow-up of CheckMate 649

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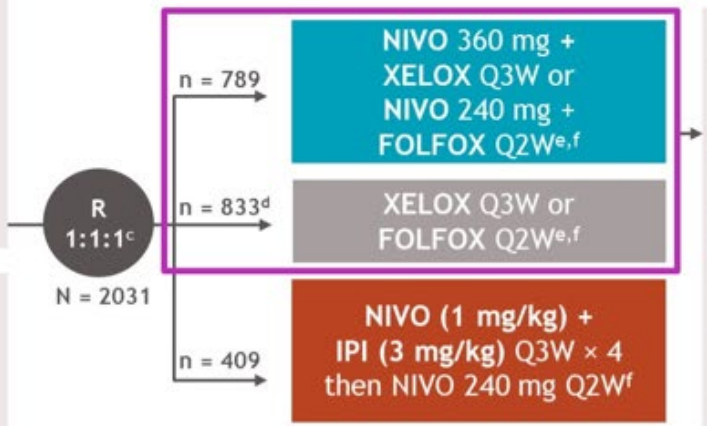
Abstract number 240

CheckMate 649 study design

- CheckMate 649 is a randomized, open-label, global phase 3 study[a]

Key eligibility criteria
- Previously untreated, unresectable, advanced or metastatic gastric/GEJ/esophageal adenocarcinoma
- No known HER2-positive status
- ECOG PS 0-1

Stratification factors
- Tumor cell PD-L1 expression (≥ 1% vs < 1%[b])
- Region (Asia vs United States/Canada vs ROW)
- ECOG PS (0 vs 1)
- Chemo (XELOX vs FOLFOX)



Dual primary endpoints:
- OS and PFS[g] (PD-L1 CPS ≥ 5)

Secondary endpoints:
- OS (PD-L1 CPS ≥ 1, all randomized)
- OS (PD-L1 CPS ≥ 10)
- PFS[g] (PD-L1 CPS ≥ 10, ≥ 1, all randomized)
- ORR[g]

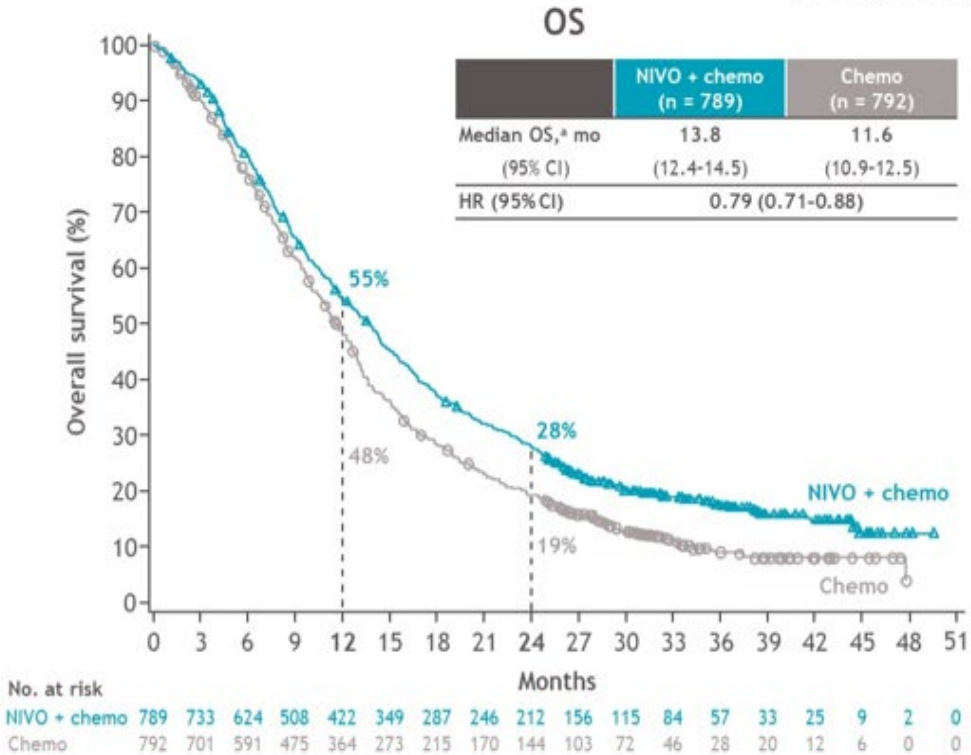
Exploratory endpoints:
- Safety
- QoL

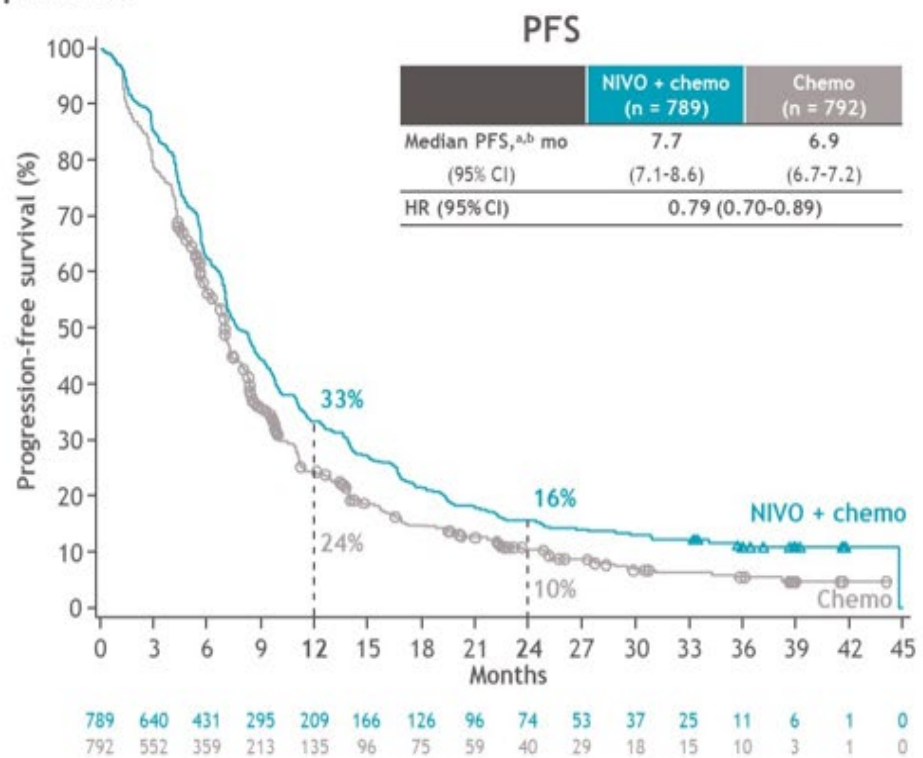
- At data cutoff (May 27, 2021), the minimum follow-up[h] was 24.0 months in the NIVO + chemo arm

[a]ClinicalTrials.gov. NCT02872116; [b]Less than 1% includes indeterminate tumor cell PD-L1 expression; [c]After NIVO + chemo arm was added and before new patient enrollment in the NIVO + IPI arm was stopped early (June 5, 2018) based on DMC recommendation; patients already enrolled in the NIVO + IPI arm were allowed to remain on study; [d]Includes patients concurrently randomized to chemo vs NIVO + IPI (October 2016-June 2018) and to NIVO + chemo (April 2017-April 2019); [e]XELOX: oxaliplatin 130 mg/m^2 IV (day 1) and capecitabine 1000 mg/m^2 orally twice daily (days 1-14); FOLFOX: oxaliplatin 85 mg/m^2, leucovorin 400 mg/m^2, and FU 400 mg/m^2 IV (day 1) and FU 1200 mg/m^2 IV daily (days 1-2); [f]Until documented disease progression (unless consented to treatment beyond progression for NIVO + chemo or NIVO + IPI), discontinuation due to toxicity, withdrawal of consent, or study end. NIVO is given for a maximum of 2 years; [g]BICR assessed; [h]Time from concurrent randomization of the last patient to clinical data cutoff.
Janjigian YY, et al. *Lancet* 2021;398:27-40.

Overall survival and progression-free survival

All randomized patients



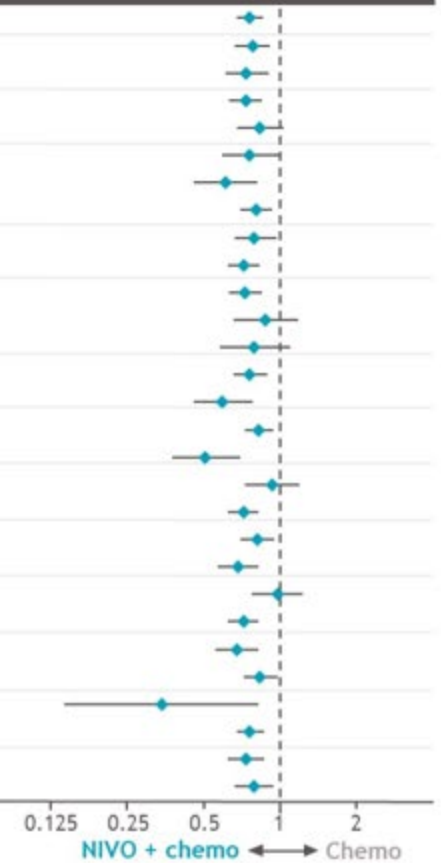


- Clinically meaningful improvement in OS and PFS with NIVO + chemo vs chemo was maintained with longer follow-up

[a]Minimum follow-up, 24.0 months. [b]Per BICR assessment. Janjigian YY et al. Oral presentation at ESMO; September 16-21, 2021; Virtual. Abstract LBA7.

Overall survival subgroup analysis

Category (all randomized)	Subgroup	Median OS, months		Unstratified HR for death	Unstratified HR (95% CI)
		NIVO + chemo	Chemo		
Overall (N = 1581)		13.8	11.6	0.78	
Age	< 65 (n = 961)	12.9	11.8	0.80	
	≥ 65 (n = 620)	14.4	11.3	0.76	
Sex	Male (n = 1100)	14.0	11.3	0.76	
	Female (n = 481)	12.8	12.1	0.85	
Region	Asia (n = 356)	16.3	12.8	0.78	
	United States (n = 263)	15.3	12.1	0.64	
	ROW (n = 962)	12.1	10.9	0.82	
ECOG PS	0 (n = 664)	16.8	14.2	0.81	
	1 (n = 913)	11.5	9.8	0.74	
Primary tumor location	GC (n = 1110)	14.2	11.3	0.75	
	GEJC (n = 260)	12.6	12.8	0.89	
	EAC (n = 211)	12.3	11.6	0.81	
Baseline tumor burden[a]	< Q3 (n = 904)	14.0	11.6	0.78	
	≥ Q3 (n = 308)	11.4	9.2	0.62	
Tumor cell PD-L1 expression[b]	< 1% (n = 1324)	13.4	12.0	0.84	
	≥ 1% (n = 253)	16.1	9.8	0.54	
Baseline albumin[c]	< LLN (n = 357)	9.2	8.8	0.94	
	≥ LLN (n = 1159)	14.7	12.5	0.74	
Baseline NLR[d]	< 4 (n = 929)	15.5	13.5	0.83	
	≥ 4 (n = 612)	9.8	8.2	0.71	
Peritoneal metastases[e]	Yes (n = 377)	9.3	10.0	0.98	
	No (n = 1155)	14.5	11.8	0.74	
Liver metastases[e]	Yes (n = 614)	12.5	10.6	0.70	
	No (n = 918)	14.2	12.3	0.85	
MSI status[f]	MSI-H (n = 44)	38.7	12.3	0.38	
	MSS (n = 1378)	13.8	11.5	0.78	
Chemotherapy regimen	FOLFOX (n = 828)	13.8	11.8	0.76	
	XELOX (n = 721)	13.8	11.7	0.81	

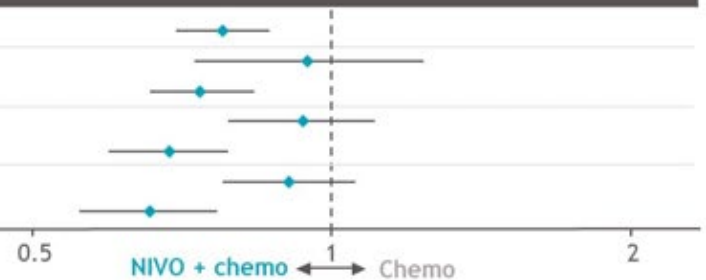


- OS favored NIVO + chemo vs chemo across key subgroups in all randomized patients

Efficacy subgroup analysis by PD-L1 CPS

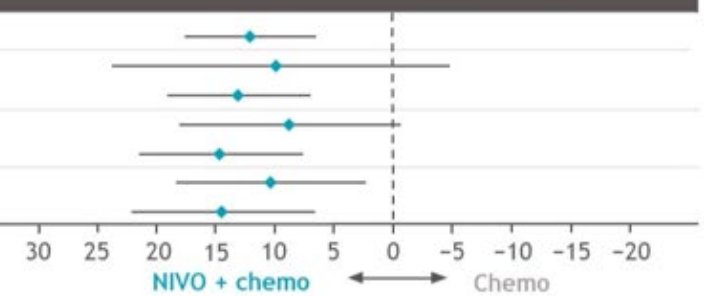
Overall survival

PD-L1 CPS[a]	Number of patients	Median, months		Unstratified HR[b]	Unstratified HR (95% CI)
		NIVO + chemo	Chemo		
Overall (N = 1581)		13.8	11.6	0.78	
< 1	265	13.1	12.5	0.95	
≥ 1	1297	13.8	11.3	0.74	
< 5	607	12.4	12.3	0.94	
≥ 5	955	14.4	11.1	0.69	
< 10	795	12.4	12.5	0.91	
≥ 10	767	15.0	10.9	0.66	



Objective response rate

PD-L1 CPS[c]	Number of patients	Objective response rate, %		Unweighted ORR difference,[d] %	Unweighted ORR difference,[d] % (95% CI)
		NIVO + chemo	Chemo		
Overall (N = 1210)		58	46	12	
< 1	179	51	41	10	
≥ 1	1017	59	46	13	
< 5	428	55	46	9	
≥ 5	768	60	45	15	
< 10	579	58	47	10	
≥ 10	617	59	44	15	



- OS benefit with NIVO + chemo was enriched at higher PD-L1 CPS cutoffs
- ORR was higher across all PD-L1 CPS subgroups vs chemo

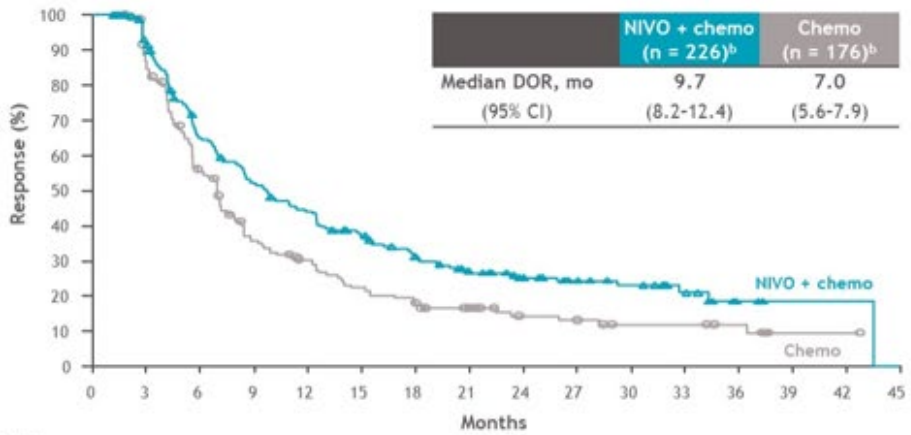
[a]PD-L1 CPS expression indeterminate/not evaluable/not reported, n = 19; [b]Unstratified HR for death (OS); [c]Randomized patients who had target lesion measurements at baseline, per BICR. PD-L1 CPS expression indeterminate/not evaluable/not reported, n = 14; [d]Percentages may not reflect an exact difference due to rounding.

Response and duration of response

PD-L1 CPS ≥ 5[1]

Response per BICR	NIVO + chemo (n = 378)[a]	Chemo (n = 390)[a]
ORR, % (95% CI)	60 (55-65)	45 (40-50)
CR	13	7
PR	47	38
SD	28	34
PD	7	11

	NIVO + chemo (n = 226)[b]	Chemo (n = 176)[b]
Median DOR, mo	9.7	7.0
(95% CI)	(8.2-12.4)	(5.6-7.9)



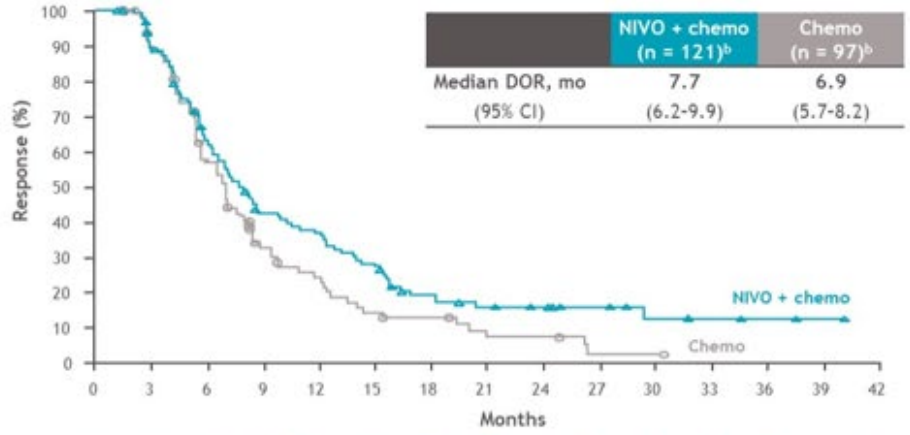
No. at risk

NIVO + chemo	226	196	135	107	90	73	58	45	34	25	20	10	3	1	1	0
Chemo	176	142	87	53	42	31	24	19	12	11	7	7	5	1	1	0

PD-L1 CPS < 5

Response per BICR	NIVO + chemo (n = 219)[a]	Chemo (n = 209)[a]
ORR, % (95% CI)	55 (48-62)	46 (40-53)
CR	7	4
PR	48	42
SD	30	32
PD	7	10

	NIVO + chemo (n = 121)[b]	Chemo (n = 97)[b]
Median DOR, mo	7.7	6.9
(95% CI)	(6.2-9.9)	(5.7-8.2)



NIVO + chemo	121	104	70	45	39	29	17	13	10	7	4	3	2	1	0
Chemo	97	84	49	24	17	10	8	4	4	1	1	0	0	0	0

- ORR was higher and responses were more durable with NIVO + chemo vs chemo regardless of PD-L1 CPS ≥ 5 or < 5

[a]Randomized patients who had target lesion measurements at baseline per BICR assessment; [b]Number of responders. 1. Janjigian YY et al. Oral presentation at ESMO; September 16-21, 2021; Virtual. Abstract LBA7.

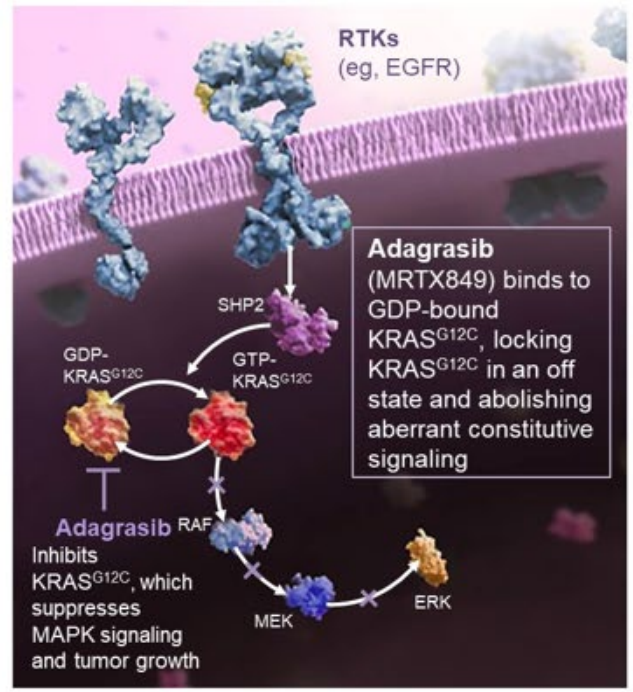
Summary

- NIVO + chemo continued to demonstrate clinically meaningful improvement in efficacy vs chemo with an acceptable safety profile with longer follow-up in previously untreated patients with advanced GC/GEJC/EAC
  - Favorable PFS2
  - OS benefit across key subgroups and enriched at higher PD-L1 CPS cutoffs
  - Higher ORR across all evaluated PD-L1 CPS subgroups
  - More deep and more durable responses regardless of PD-L1 CPS ≥ 5 or < 5
  - OS and ORR benefit across PD-L1 CPS subgroups consistent with the all randomized population when excluding patients with MSI-H tumors
  - No new safety signals; TRAEs with potential immunologic etiology resolved in most patients with the use of established management algorithms
- These data further support the use of NIVO + chemo as standard 1L treatment in patients with advanced GC/GEJC/EAC

PANCREATIC CANCER

Adagrasib (MRTX849) is a Differentiated, Selective Inhibitor of KRAS^{G12C}

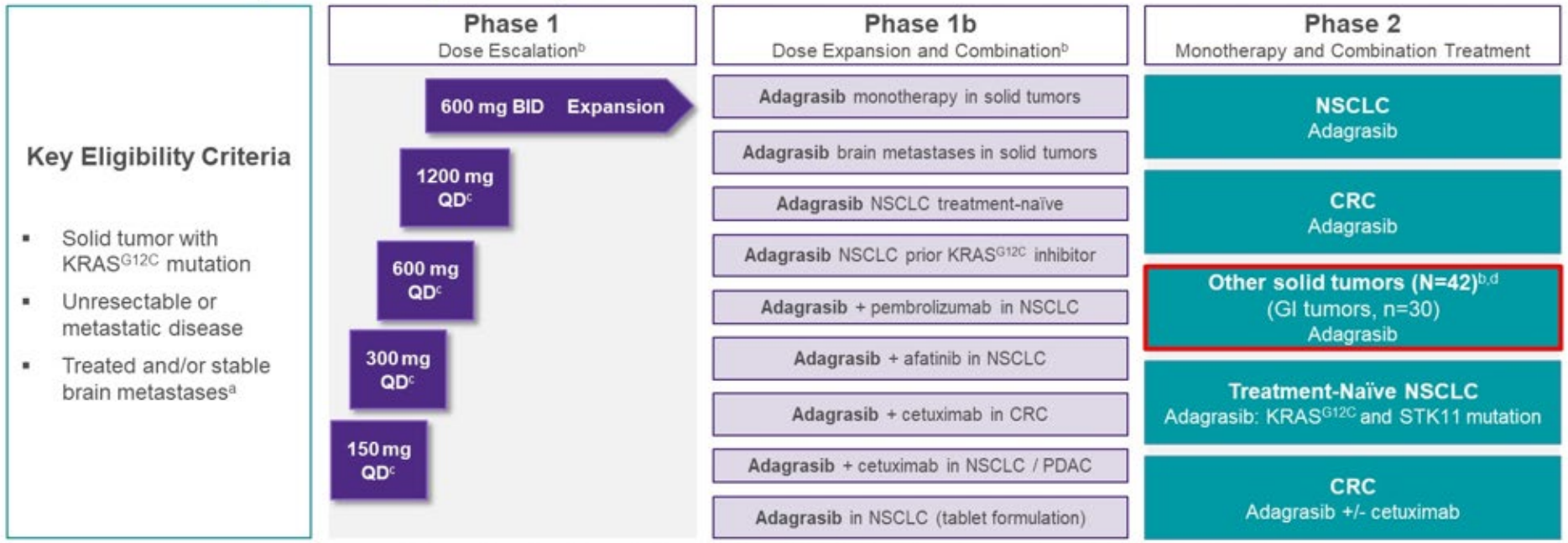
- KRAS mutations occur in approximately 90% of pancreatic cancer[1]; ~2% of these are KRAS^{G12C} mutations[2]
- The KRAS protein cycles between GTP-on and GDP-off states and has a protein resynthesis half-life of ~24 hours[3,4]
- Adagrasib, a covalent inhibitor of KRAS^{G12C}, irreversibly and selectively binds KRAS^{G12C} in its inactive, GDP-bound state
- Adagrasib was optimized for desired properties of a KRAS^{G12C} inhibitor[5]:
  - Long half-life of ~24 hours
  - Dose-dependent PK
  - CNS penetration
- Maintaining continuous exposure of adagrasib above a target threshold enables inhibition of KRAS-dependent signaling for the complete dose interval and maximizes depth and duration of antitumor activity



CNS, central nervous system; EGFR, epidermal growth factor receptor; PK, pharmacokinetics; RTK, receptor tyrosine kinase.

1. Prior IA, et al. *Cancer Res*. 2012;72(10):2457–2467. 2. Nollmann FI & Alexander Ruess D. *Biomedicines*. 2020;8(8):281. 3. Bos JL, et al. *Cell*. 2007;129:865–877. 4. Shukla S, et al. *Neoplasia*. 2014;16(2):115–128. 5. Hallin J, et al. *Cancer Discov*. 2020;10(1):54–71.

KRYSTAL-1 (849-001) Study Design



Phase 2 Endpoints **Primary:** ORR (RECIST 1.1) **Secondary:** DOR, PFS, OS, safety

- Previously reported data demonstrated clinical activity with adagrasib in patients with various $KRAS^{G12C}$-mutated solid tumors, including NSCLC, CRC and other tumors such as PDAC, ovarian and endometrial cancers, and cholangiocarcinoma[1–3]
- Here we report preliminary data from a Phase 2 cohort evaluating adagrasib 600 mg BID in patients with previously-treated GI tumors (n=30), excluding CRC, with a focus on PDAC (n=12) and other GI cancers (n=18), with a $KRAS^{G12C}$ mutation

CRC, colorectal cancer; ctDNA, circulating tumor deoxyribonucleic acid; GI, gastrointestinal; NSCLC, non–small-cell lung cancer; PDAC, pancreatic ductal adenocarcinoma.
1. Jänne PA et al. Presented at: 2020 EORTC-NCI-AACR Symposium; Oct 25, 2020. 2. Weiss J et al. Presented at: 2021 ESMO Congress; Sept 19, 2021. 3. Johnson ML et al. Presented at: 2020 EORTC-NCI-AACR Symposium; Oct 25, 2020.
[a]Most cohorts allow patients with brain metastases if adequately treated and stable; additional phase 1/1b cohort allows limited brain metastases; [b]$KRAS^{G12C}$ mutation detected in tumor tissue and/or ctDNA; [c]Patients subsequently dose escalated up to 600 mg BID; [d]Solid tumors included GI tumors (n=30) and non-GI tumors (n=12).
Data as of 10 September 2021. ClinicalTrials.gov. NCT03785249.

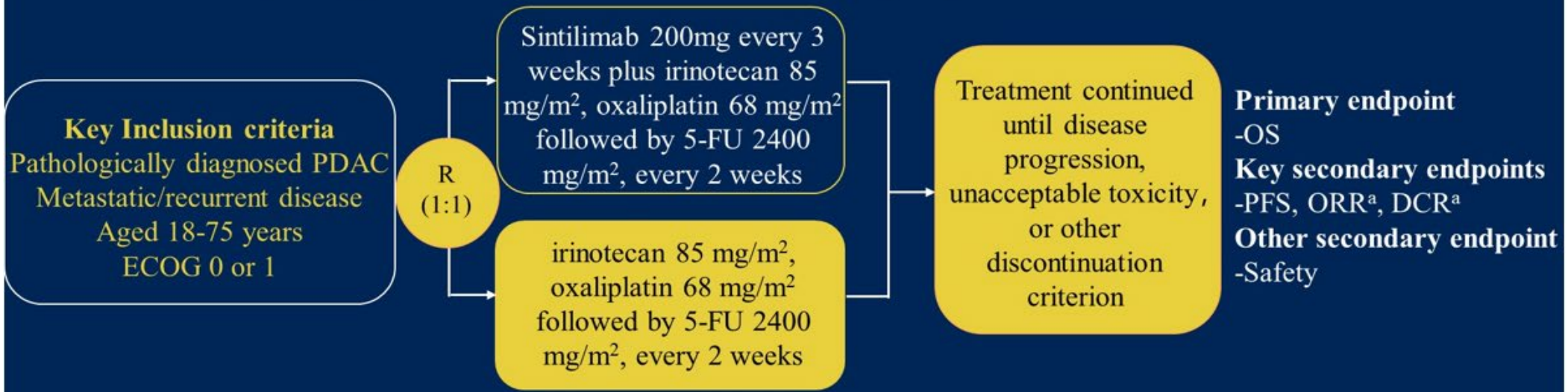
Adagrasib in Patients With PDAC and Other GI Tumors:[a] Objective Response Rate

Efficacy outcome[b], n (%)	PDAC (n=10)[c]	Other GI cancers (n=17)[d]	Overall GI cancers[a] (n=27)[c,d]
Objective response rate	5 **(50)**[e]	6 **(35)**[f]	11 **(41)**[g]
Best overall response			
Complete response (CR)	0 (0)	0 (0)	0 (0)
Partial response (PR)	5 (50)[e]	6 (35)[f]	11 (41)[g]
Stable disease (SD)	5 (50)	11 (65)	16 (59)
Disease control rate	10 **(100)**	17 **(100)**	27 **(100)**

A total of 30 patients were enrolled: 12 PDAC, 18 Other GI.
[a]Excluding CRC; [b]Based on investigator assessment of the clinically evaluable patients (measurable disease with ≥ 1 on-study scan); [c]Evaluable population (n=10) excludes 2 patients who had discontinued treatment prior to first scan due to unrelated adverse events and were not evaluable for clinical activity; [d]Evaluable population (n=17) excludes 1 patient who withdrew consent prior to the first scan; [e]Includes 1 unconfirmed PR as of data cut-off; [f]Includes 2 unconfirmed PR as of data cut-off; [g]Includes 3 unconfirmed PR as of data cut-off.
Data as of 10 Sept 2021 (median follow-up: overall, 6.3 months; PDAC, 8.1 months; other GI cancers: 6.3 months).

Study design

Phase III, Single Center, Randomized, Open Label



[a]Per Response Evaluation Criteria in Solid Tumors version 1.1
DCR, disease control rate; ORR, objective response rate; OS, overall survival; PFS, progression free survival; R, randomization

PRESENTED BY: Tingbo Liang, the First Affiliated Hospital, Zhejiang University School of Medicine

Tumor response

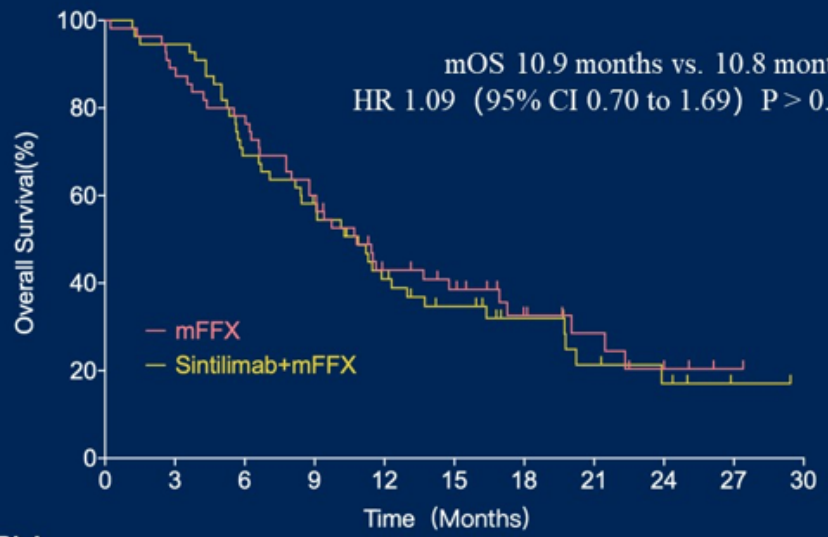
	Sintilimab + mFFX (n = 55)	mFFX (n = 55)	p value
Best overall response*			
Complete response	1	0	
Partial response	21	11	
Stable disease	15	22	
Progressive disease	7	13	
Not evaluable	11	9	
Objective response rate, %	50	23.9	**P < 0.05**
Disease Control rate, %	84.0	71.7	P > 0.05
Response duration, months	7.85	4.63	P > 0.05

*Per Response Evaluation Criteria in Solid Tumors version 1.1

PRESENTED BY: Tingbo Liang, the First Affiliated Hospital, Zhejiang University School of Medicine

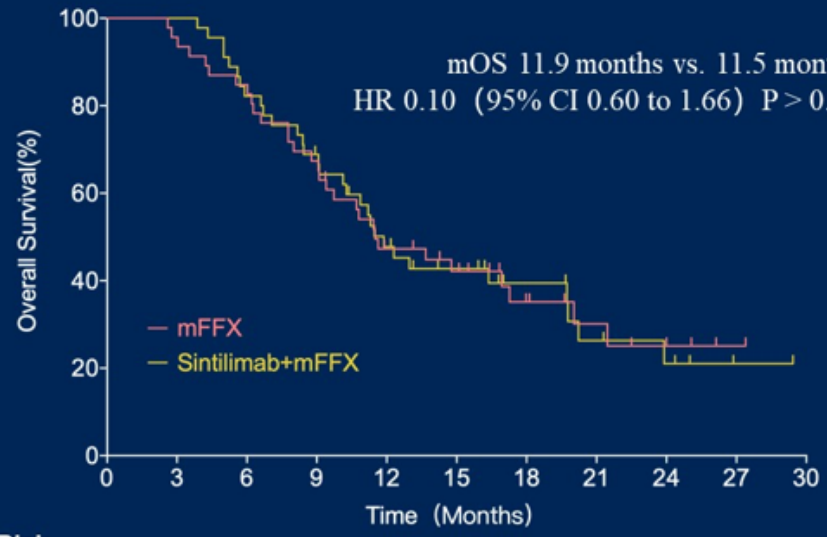
Overall Survival

Intention to treatment



No. at Risk											
mFFX	55	50	44	35	22	18	11	8	4	2	0
Sintilimab+mFFX	55	53	39	32	22	16	11	7	5	2	0

Per Protocol



No. at Risk											
mFFX	46	45	40	32	21	17	10	7	4	2	0
Sintilimab+mFFX	45	45	38	31	21	16	11	7	5	2	0

PRESENTED BY: Tingbo Liang, the First Affiliated Hospital, Zhejiang University School of Medicine

Conclusions
HCC

- IMBRAVE 150 (Atezolizumab + Bevacizumab versus Sorafenib: Increased OS, PFS, ORR and Disease control Rate
- HIMALAYA (Durvalumab+Tremelimumab versus Durvalumab versus Sorafenib): Increased OS, ORR, PFS; No disease control rate benefit
- COSMIC 312: Cabozantinib + Atezolizumab Versus Cabozantinb versus Sorafenib): Increased PFS, ORR and disease control rate; no increase in OS
- LAUNCH: Lenvatinib+TACE versus Lenvatinib: Increased OS, PFS and ORR

Conclusions
Biliary Tract Cancer

- TOPAZ 1: Durvalumab +Cisplatin +Gemcitabine versus Cisplatin + Gemcitabine: Increased OS

Conclusions
Esophageal/Gastric Cancer

- Her 2 Destiny, Gastric 01: Enhertu increased OS, ORR
- Checkmate 649 (24 month follow-up) Nivolumab +chemo versus chemo: increased PFS2, OS (irrespective of PDL1), ORR, depth of response and duration of response

Conclusions
Pancreatic Cancer

- Adagrasib in KRAS G12C: Increased ORR, disease control rate

- Sintilumab +FOLFIRINOX versus FOLFIRINOX: Increased ORR, disease Control rate, no OS

Questions?