The Clinical Implications of Key Recent Data Sets in Oncology: A Daylong Multitumor Educational Symposium in Partnership with Florida Cancer Specialists

A CME/MOC- and NCPD-Accredited Event

Saturday, October 22, 2022
7:30 AM – 5:30 PM ET

RTP
RESEARCH
TO PRACTICE

Agenda

Module 1 — Lung Cancer: *Drs Langer and Lovly*

Module 2 — Chronic Lymphocytic Leukemia and Lymphomas: *Drs LaCasce and Smith*

Module 3 — Prostate and Bladder Cancers: *Drs Morgans and Yu*

Module 4 — Renal Cell Carcinoma: *Prof Powles*

Module 5 — Multiple Myeloma: *Dr Usmani*

Module 6 — Hepatobiliary Cancers: *Prof Abou-Alfa*

Agenda

Module 7 — Breast Cancer: *Drs Goetz and Krop*

Module 8 — Endometrial Cancer: *Dr Westin*

Module 9 — Ovarian Cancer and PARP Inhibitors: *Dr O'Malley*

Module 10 — Gastrointestinal Cancers: *Drs Messersmith and Strickler*

Module 11 — Melanoma: *Prof Long*

Hepatobiliary Cancers Faculty

Ghassan Abou-Alfa, MD, MBA
Attending
Memorial Sloan Kettering Cancer Center
Professor
Weill Cornell Medical College at Cornell University
New York, New York

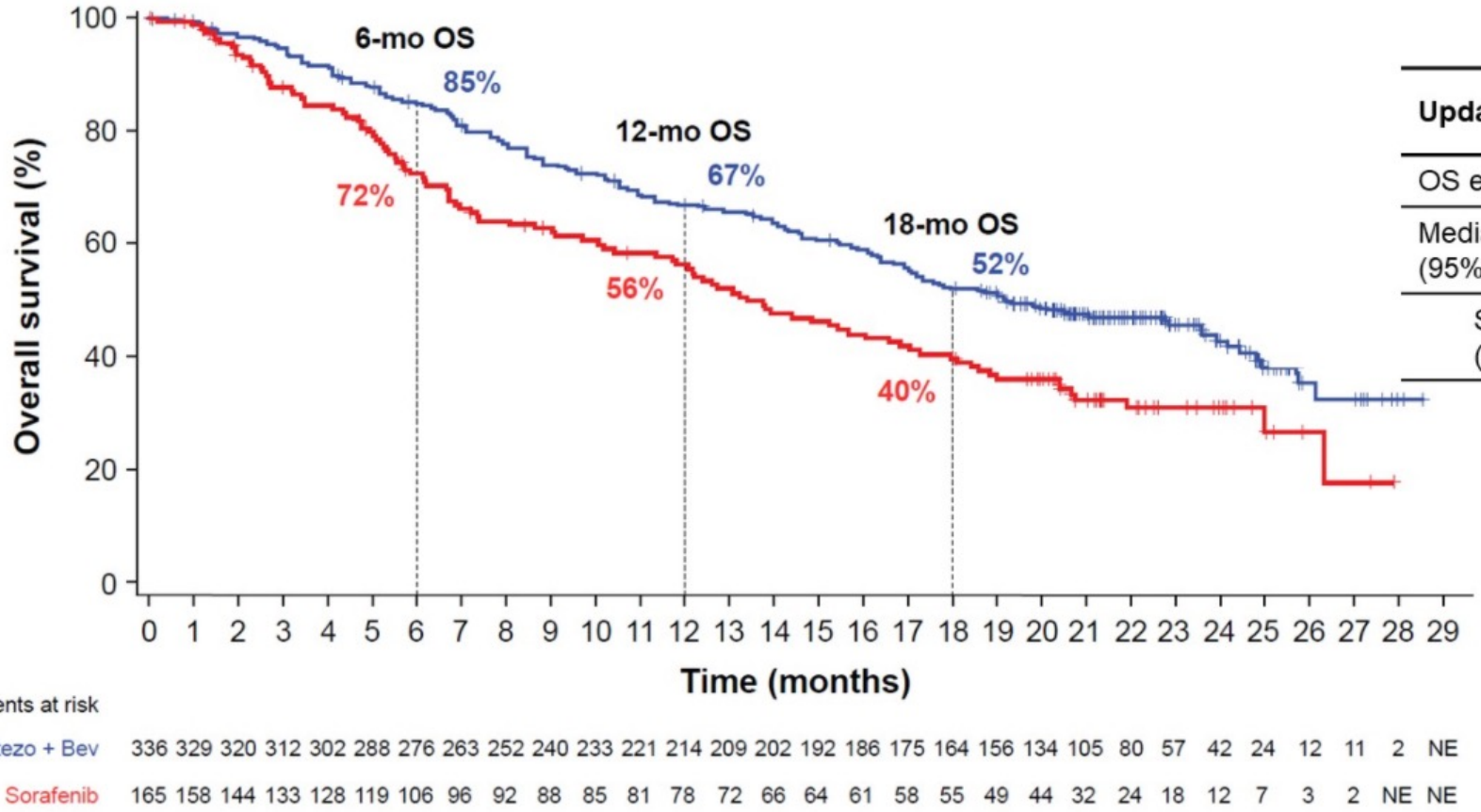
RTP
RESEARCH
TO PRACTICE

Hepatobiliary Cancers

Ghassan Abou-Alfa
Memorial Sloan Kettering Cancer Center

FCS 2022
October 22, 2022

IMbrave150 OS: co-Primary Endpoint



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]	

Clinical cutoff: August 31, 2020; median follow-up: 15.6 mo.

[a] Stratification factors included in the Cox model are geographic region (Asia excluding Japan vs Rest of World), AFP level (< 400 ng/mL vs ≥ 400 ng/mL) at baseline and MVI and/or EHS (Yes vs No) per interactive voice/web response system (IxRS).[b] *P* value for descriptive purposes only.

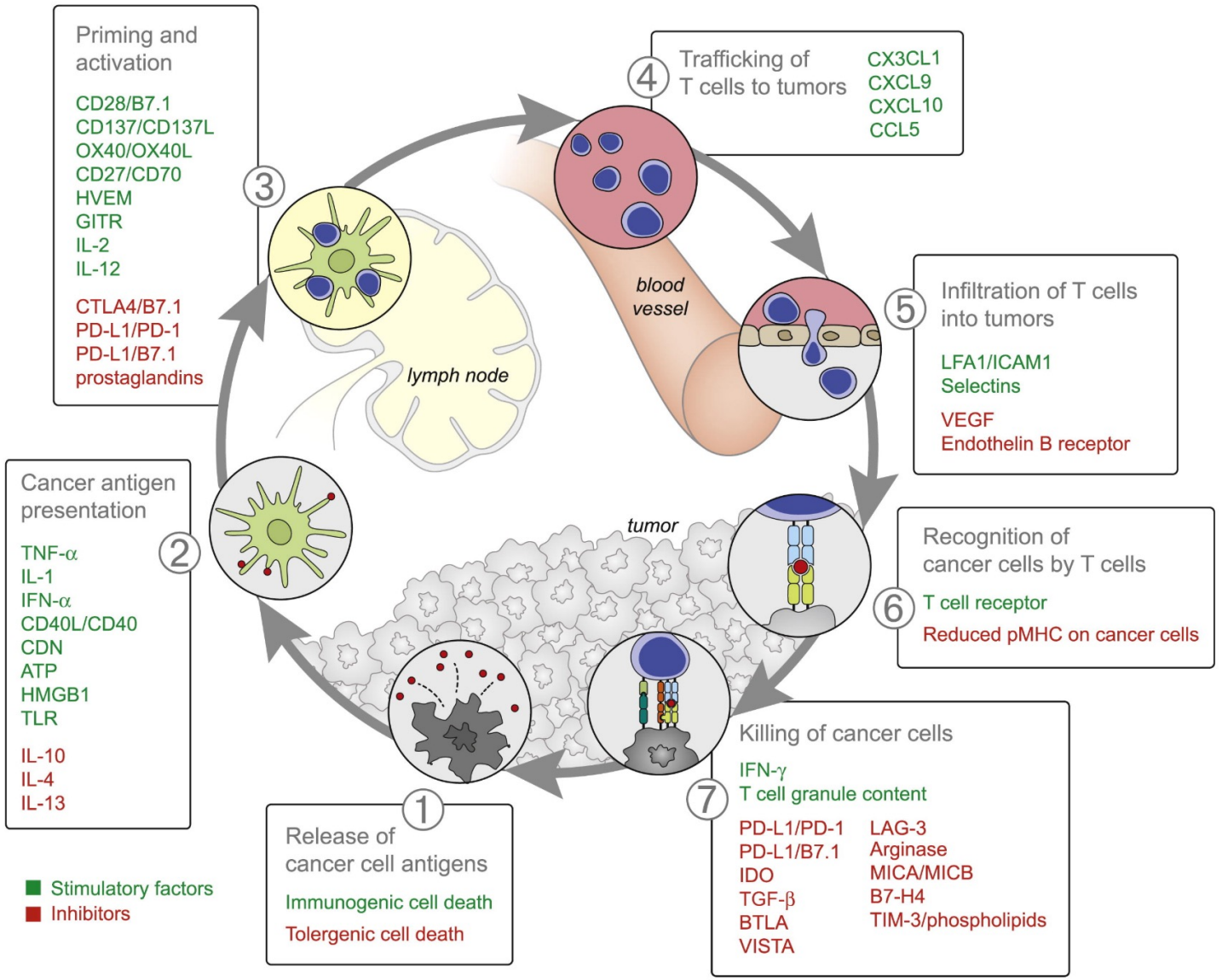
Finn, RS, et al. J Clin Oncol 39, 2021 (suppl 3; abstr 267)

REAL-AB Real World Data Study

O-13 Observational registry of atezolizumab plus bevacizumab use in routine clinical practice: preliminary results of the AB-Real international study. Claudia Angela Maria Fulgenzi (UK)

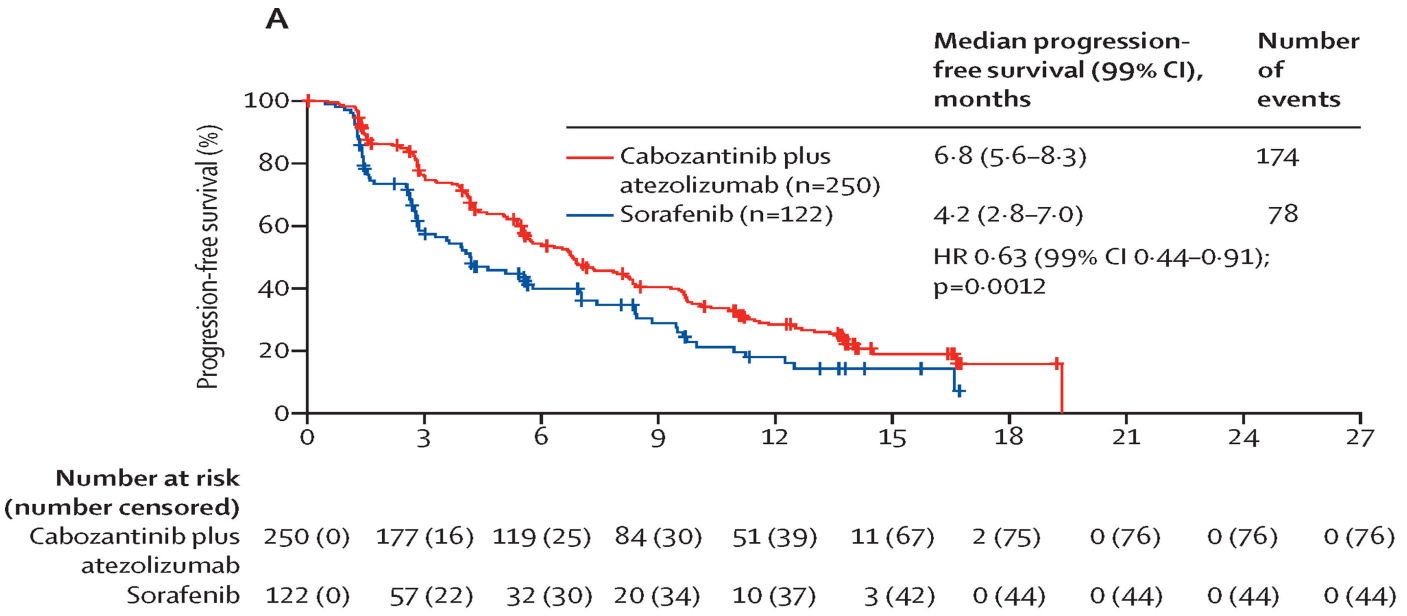
Fulgenzi C, et al. ILCA 2022, Madrid, Spain, September 4, 2022

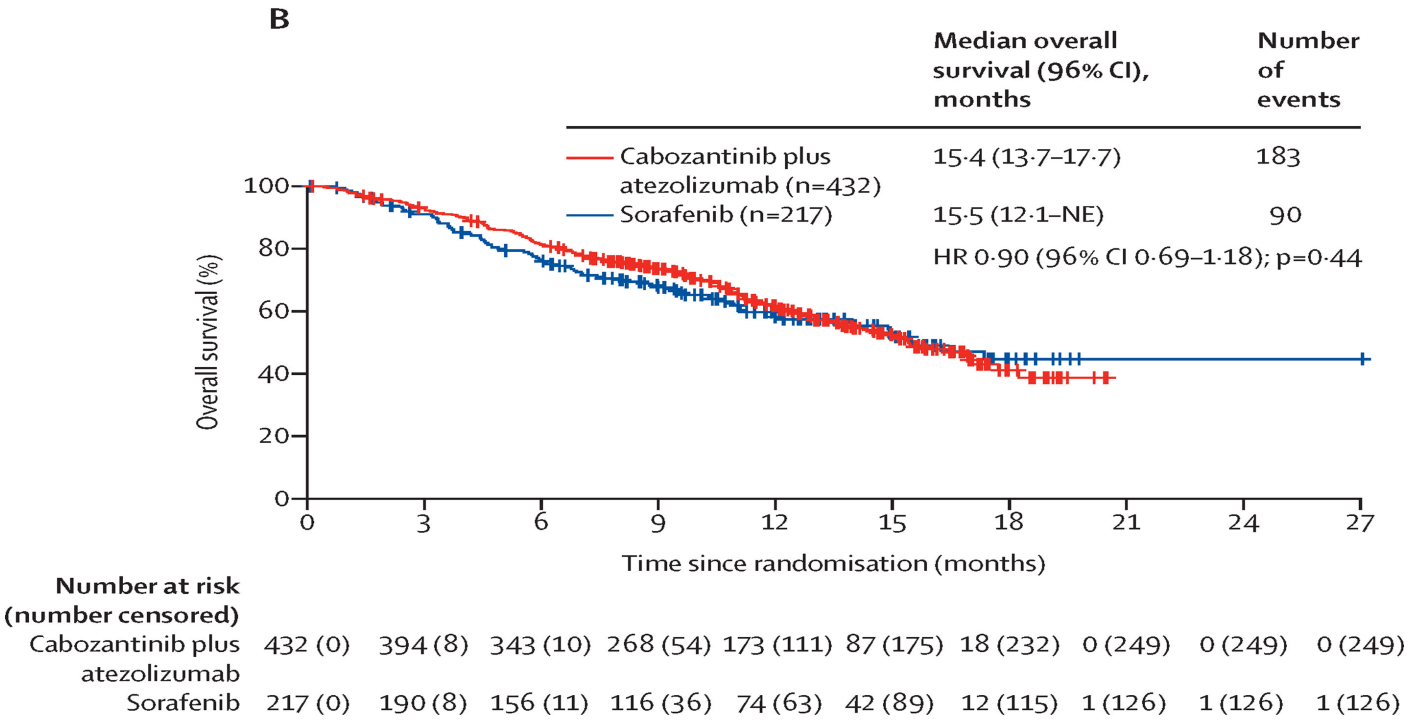
Inhibitory Factors in the Cancer-Immunity Cycle



Chen, DS, Mellman I. Immunity. 2013 Jul 25;39(1):1-10

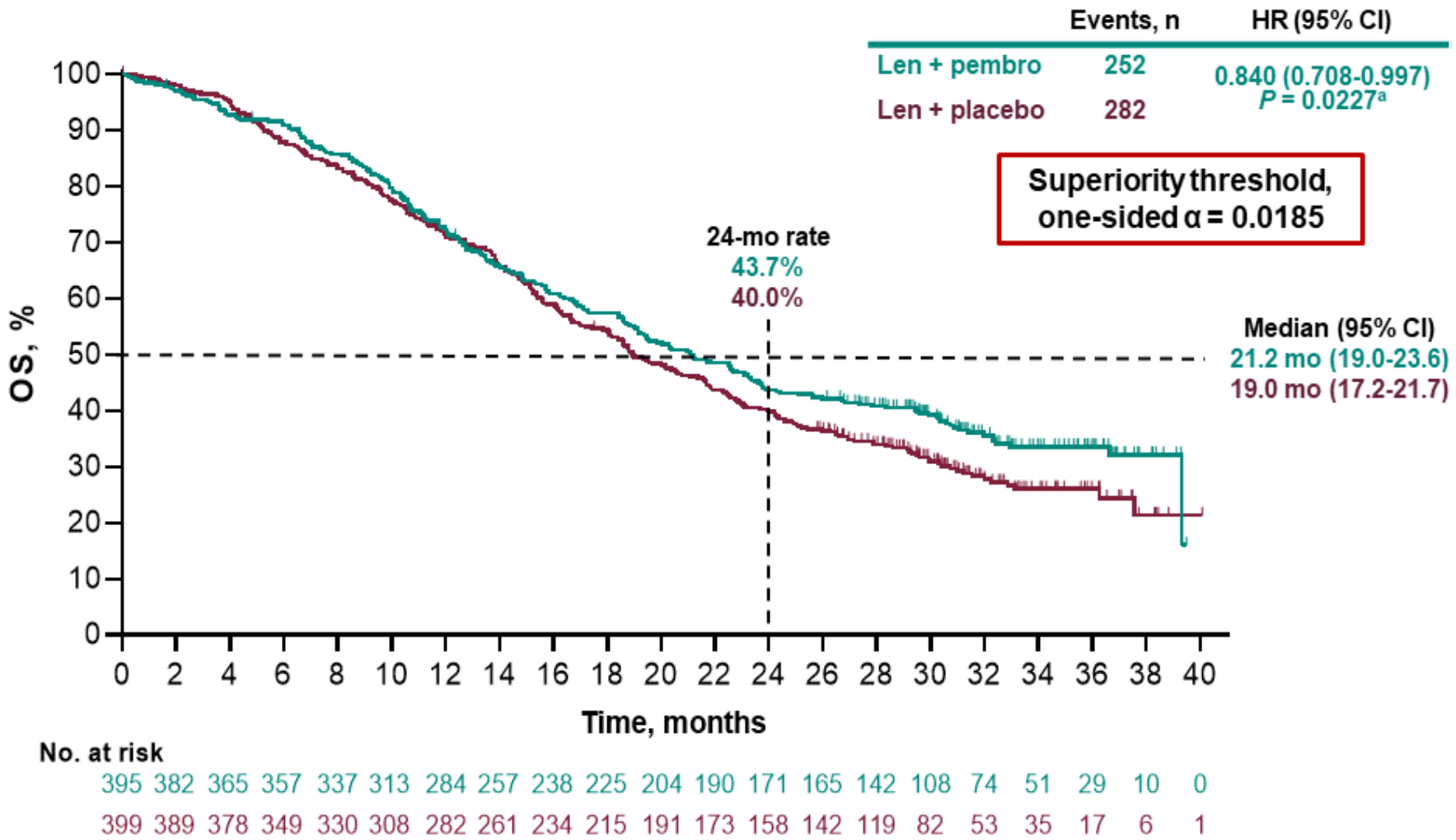
Atezolizumab plus Cabozantinib versus Sorafenib COSMIC-312





Kelley RK et al. Lancet Oncol. 2022 Aug;23(8):995-1008.

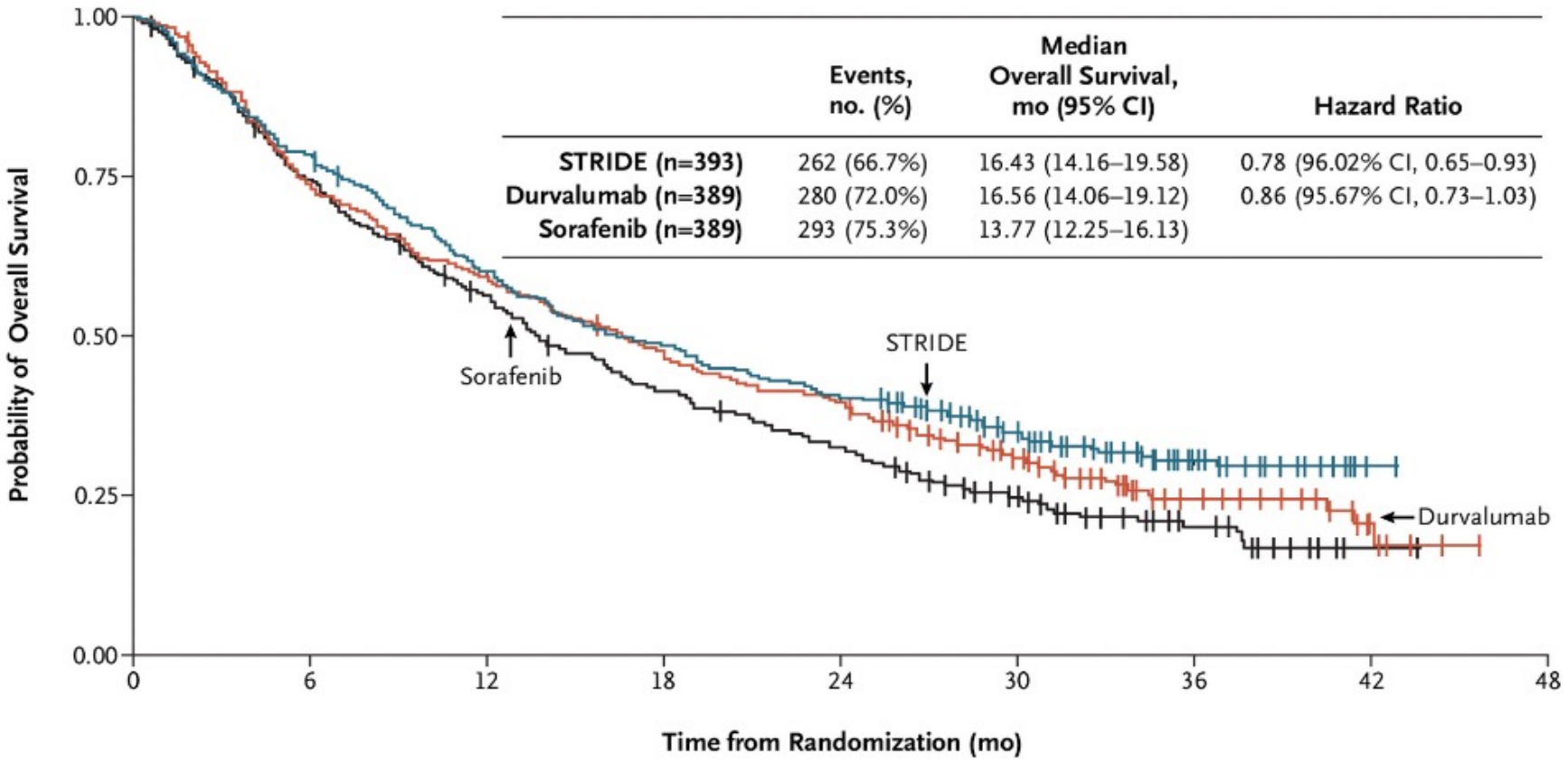
Pembrolizumab plus Lenvatinib LEAP-002



[a]Did not reach superiority threshold, one-sided α=0.0185.
Data cutoff date for FA: 21 June 2022; median follow-up: 32.1 months.

Finn R, et al. ESMO 2022 Paris, France

HIMALYA OS for Durvalumab + Tremelimumab 300 mg vs Sorafenib and Durvalumab vs Sorafenib



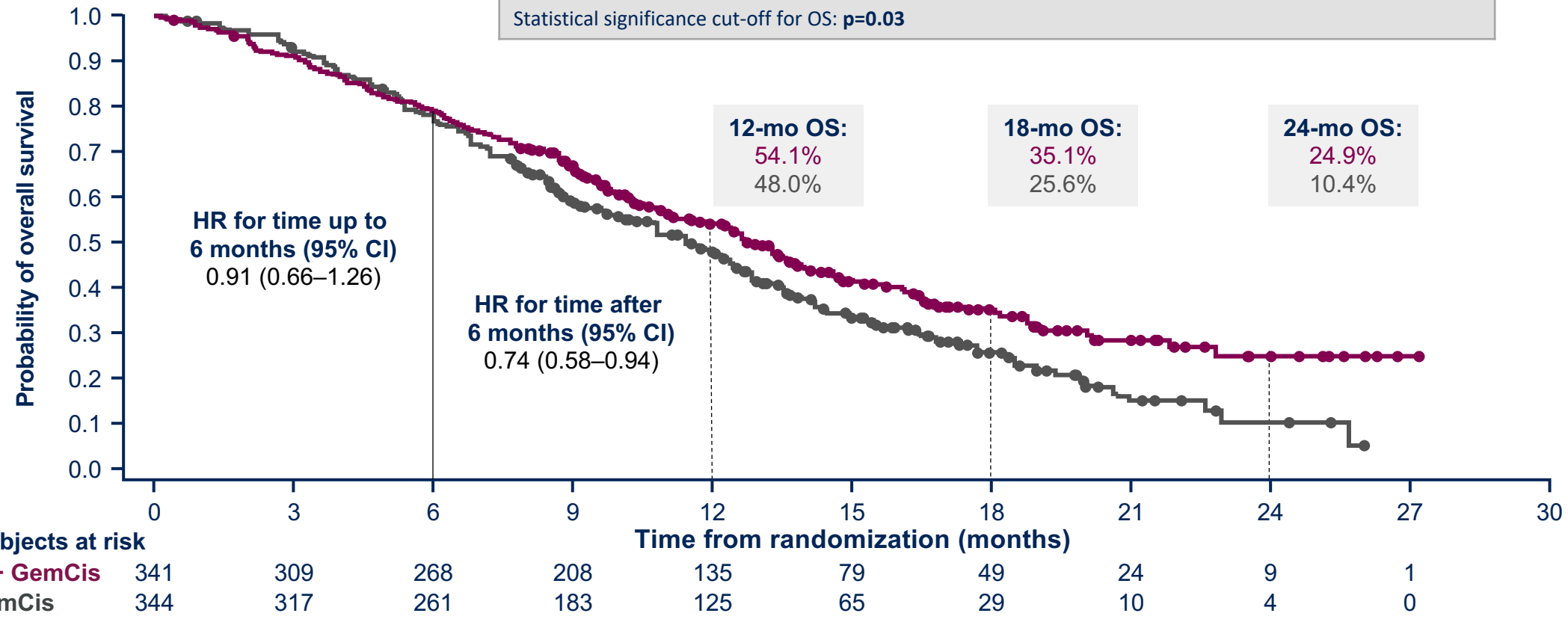
	Events, no. (%)	Median Overall Survival, mo (95% CI)	Hazard Ratio
STRIDE (n=393)	262 (66.7%)	16.43 (14.16–19.58)	0.78 (96.02% CI, 0.65–0.93)
Durvalumab (n=389)	280 (72.0%)	16.56 (14.06–19.12)	0.86 (95.67% CI, 0.73–1.03)
Sorafenib (n=389)	293 (75.3%)	13.77 (12.25–16.13)	

No. at Risk									
STRIDE	393	308	235	190	158	98	32	1	0
Durvalumab	389	286	230	183	153	87	27	6	0
Sorafenib	389	283	211	155	121	62	21	1	0

Abou-Alfa GK et al. NEJM Evidence. Published June 6, 2022. DOI:https://doi.org/10.1056/EVIDoa2100070

TOPAZ-1: Durvalumab + GemCis Improved OS vs. GemCis Alone

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



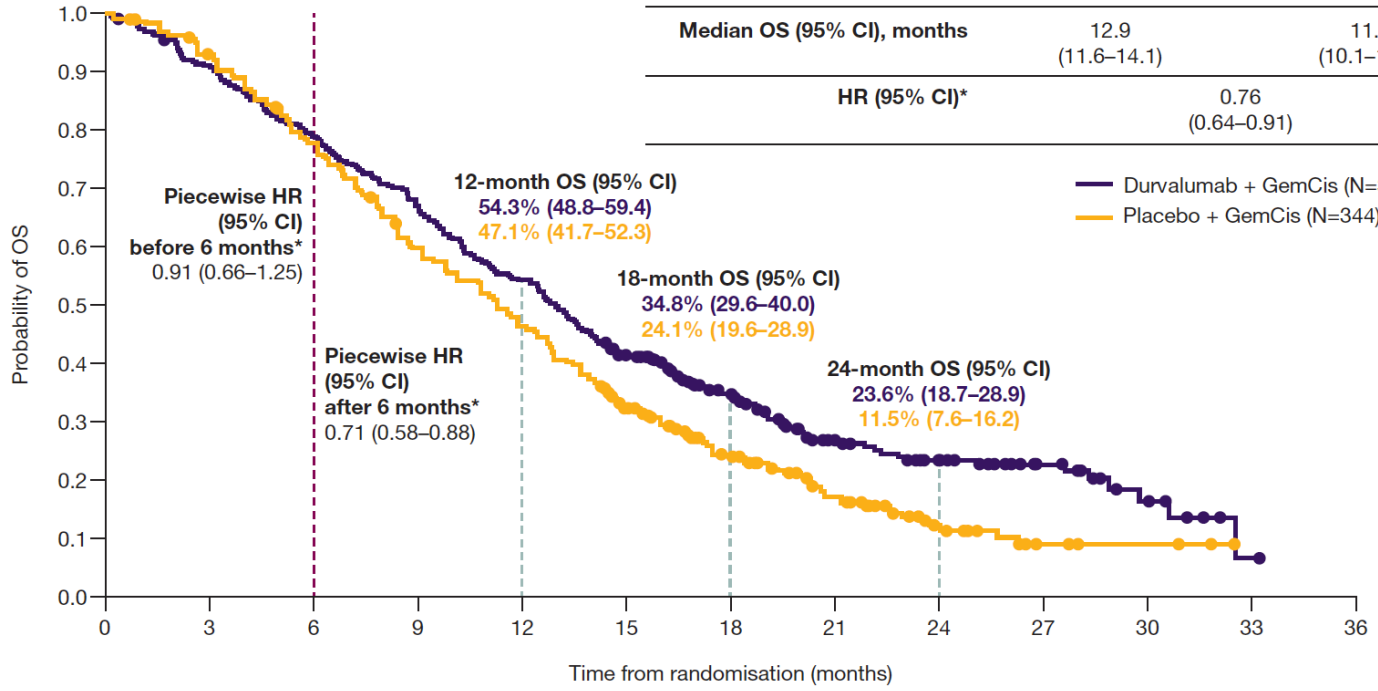
Number of subjects at risk										
Durvalumab + GemCis	341	309	268	208	135	79	49	24	9	1
Placebo + GemCis	344	317	261	183	125	65	29	10	4	0

[a]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 + cisplatin; HR = hazard ratio; mo = month; OS = overall survival.

Oh D-Y, et al. Presented at: ASCO GI Congress; January 20-22, 2022; San Francisco, CA.

TOPAZ-1: Updated Overall Survival and Best Objective Response



	Durvalumab + GemCis (N=341)	Placebo + GemCis (N=344)
Median OS (95% CI), months	12.9 (11.6–14.1)	11.3 (10.1–12.5)
HR (95% CI)*	0.76 (0.64–0.91)	

No. at risk

Durvalumab + GemCis	341	331	324	309	294	278	268	252	240	227	208	194	184	169	152	134	117	96	88	74	61	52	47	44	36	33	27	21	17	10	8	5	3	1	0
Placebo + GemCis	344	337	329	316	298	282	260	241	222	198	187	175	158	138	125	104	92	76	65	53	47	37	29	21	14	11	9	5	3	3	3	2	1	0	0

*Durvalumab + GemCis versus placebo + GemCis. An HR <1 favours durvalumab + GemCis
CI, confidence interval; GemCis, gemcitabine and cisplatin; HR, hazard ratio; OS, overall survival

	Durvalumab + GemCis (N=341)	Placebo + GemCis (N=343)
Responders,[1,*] n (%)	91 (26.7)	64 (18.7)
Complete response,[1] n (%)	7 (2.1)	2 (0.6)
Partial response,[1] n (%)	84 (24.6)	62 (18.1)
Non-responders, n (%)	250 (73.3)	279 (81.3)
Stable disease, n (%)	200 (58.7)	220 (64.1)
Progressive disease,[†] n (%)	47 (13.8)	51 (14.9)
Not evaluable	3 (0.9)	8 (2.3)

*Confirmed response; †Death recorded within 13 weeks after randomisation is considered progression
GemCis, gemcitabine and cisplatin

Oh D-Y et al. ESMO 2022;Abstract 56P.

Research Article
Hepatic and Biliary Cancer

JOURNAL
OF HEPATOLOGY

Updated efficacy and safety data from IMbrave150: Atezolizumab plus bevacizumab *vs.* sorafenib for unresectable hepatocellular carcinoma

Ann-Lii Cheng[1,*], Shukui Qin[2], Masafumi Ikeda[3], Peter R. Galle[4], Michel Ducreux[5], Tae-You Kim[6], Ho Yeong Lim[7], Masatoshi Kudo[8], Valeriy Breder[9], Philippe Merle[10], Ahmed O. Kaseb[11], Daneng Li[12], Wendy Verret[13], Ning Ma[14], Alan Nicholas[15], Yifan Wang[16], Lindong Li[17], Andrew X. Zhu[18,19], Richard S. Finn[20,*]

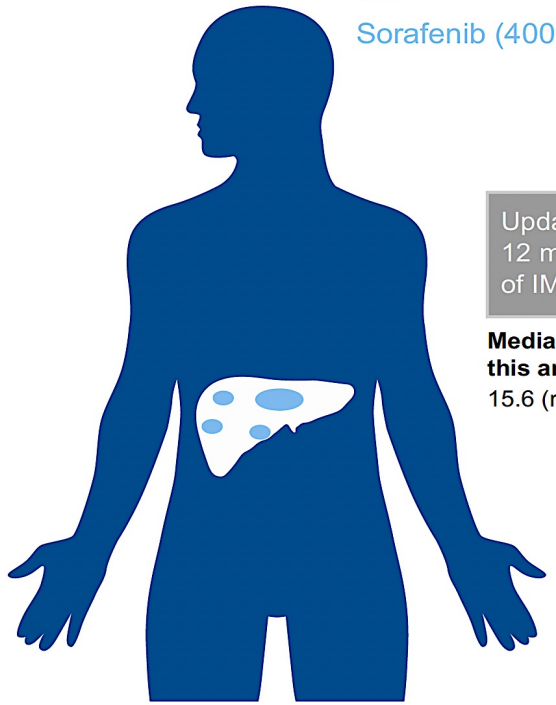
J Hepatol 2022;76(4):862-73.

IMbrave150: Updated Overall Survival and Progression-Free Survival with Atezolizumab with Bevacizumab (Median Follow-Up 15.6 Mo)

Atezolizumab (1,200 mg) plus bevacizumab (15 mg/kg) every 3 weeks

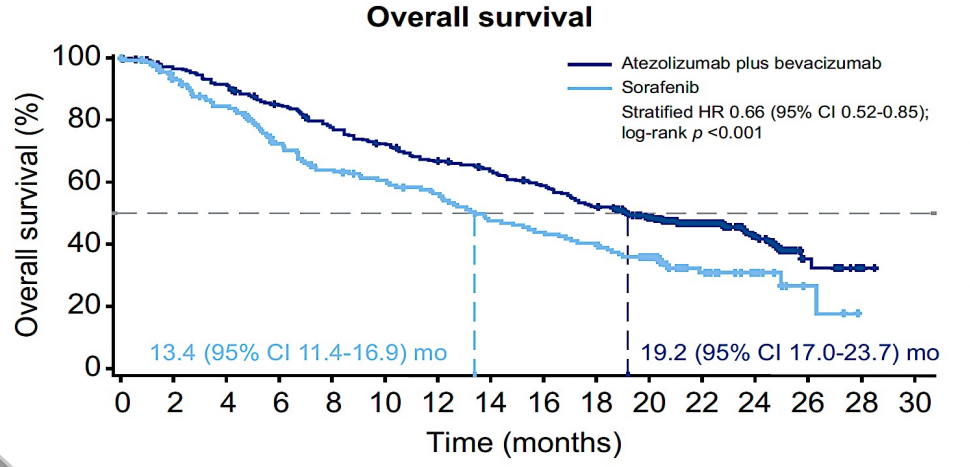
OR

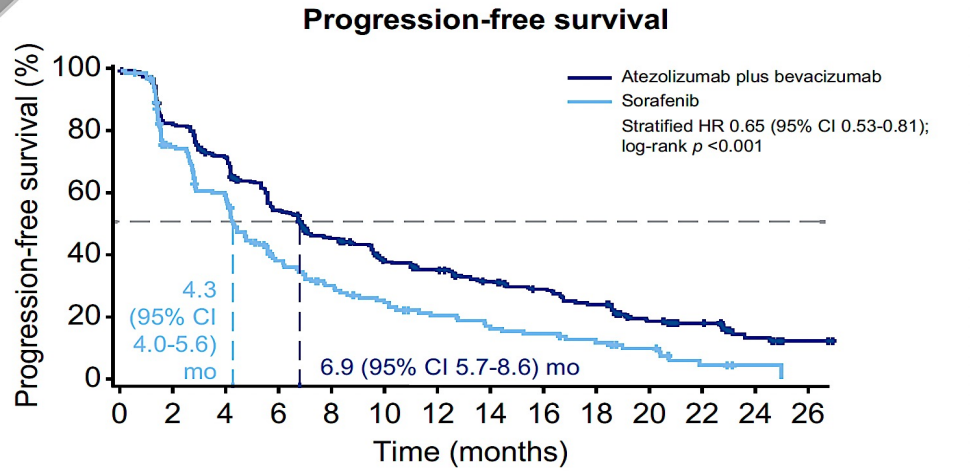
Sorafenib (400 mg twice daily)



Updated analysis
12 months after primary analysis of IMbrave150 study

Median follow-up for this analysis:
15.6 (range, 0-28.6) mo





Confirmed objective response rate: 30% with atezolizumab plus bevacizumab, 11% with sorafenib

Cheng A-L et al. *J Hepatol* 2022;76(4):862-73.

FDA Grants Priority Review to Tremelimumab for Unresectable HCC

Press Release — April 26, 2022

Tremelimumab's biologics license application was accepted by the FDA and was given priority review, further supporting the use of a single priming dose of anti-CTLA4 with durvalumab in unresectable hepatocellular carcinoma.

"A biologics license application (BLA) for tremelimumab for the treatment of patients with unresectable hepatocellular carcinoma (HCC) was accepted and granted priority review from the FDA was based on results from the phase 3 HIMALAYA trial (NCT03298451)… additionally, a supplemental BLA for durvalumab in the same indication was submitted.

The combination utilizes a novel dose and schedule known as the Single Tremelimumab Regular Interval Durvalumab (STRIDE) regimen."

https://www.cancernetwork.com/view/fda-grants-priority-review-to-tremelimumab-for-unresectable-hcc

RTP RESEARCH TO PRACTICE

NEJM Evidence

Published June 6, 2022

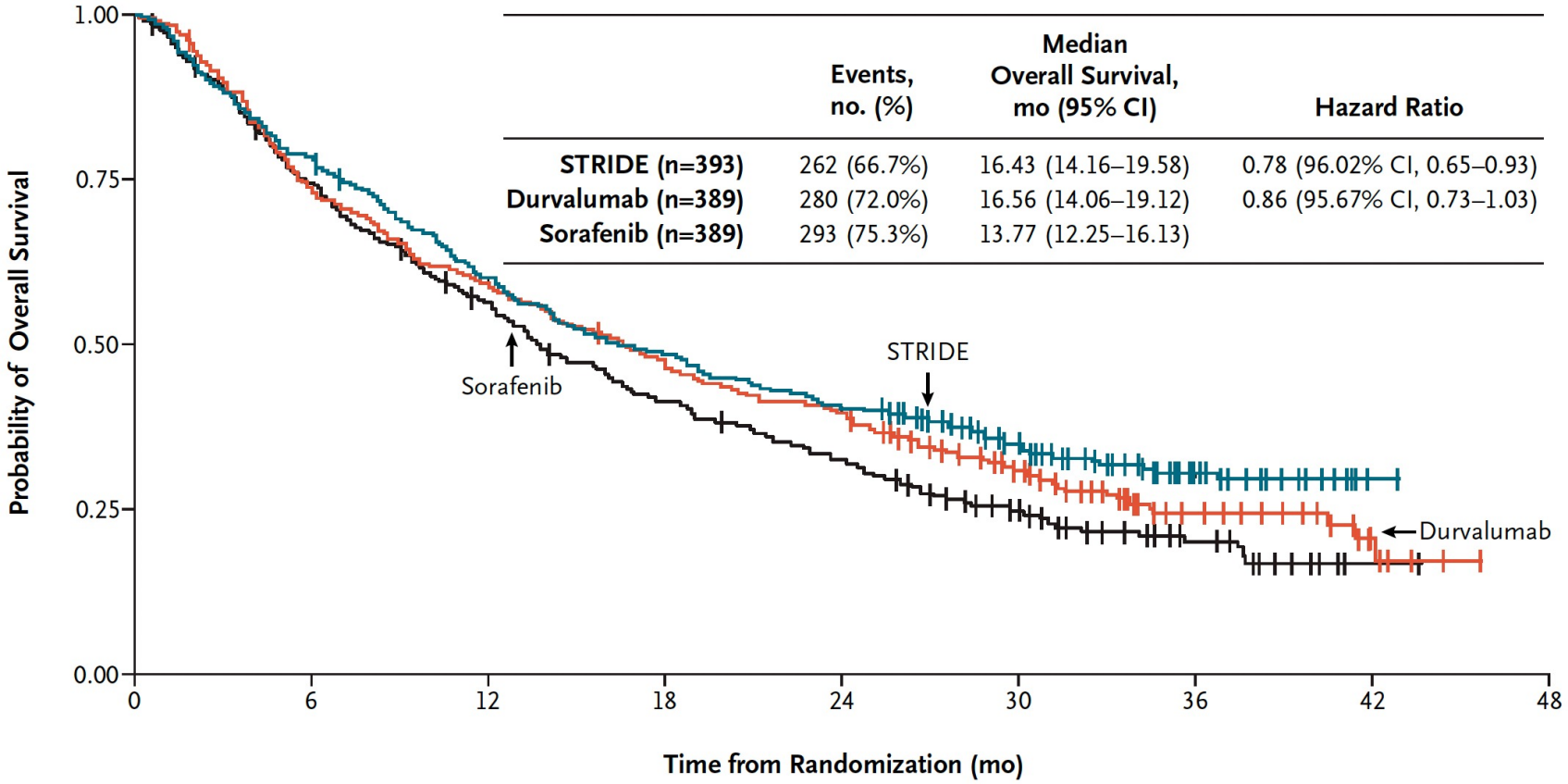
DOI: 10.1056/EVIDoa2100070

ORIGINAL ARTICLE

Tremelimumab Plus Durvalumab in Unresectable Hepatocellular Carcinoma

Ghassan K. Abou-Alfa, M.D., M.B.A.,[1,2] George Lau, M.D., F.R.C.P.,[3] Masatoshi Kudo, M.D., Ph.D.,[4] Stephen L. Chan, M.D.,[5] Robin Kate Kelley, M.D.,[6] Junji Furuse, M.D., Ph.D.,[7] Wattana Sukeepaisarnjaroen, M.D.,[8] Yoon-Koo Kang, M.D., Ph.D.,[9] Tu Van Dao, M.D., Ph.D.,[10] Enrico N. De Toni, M.D., Ph.D.,[11] Lorenza Rimassa, M.D.,[12,13] Valeriy Breder, M.D., Ph.D.,[14] Alexander Vasilyev, M.D.,[15] Alexandra Heurgué, M.D.,[16] Vincent C. Tam, M.D.,[17] Kabir Mody, M.D.,[18] Satheesh Chiradoni Thungappa, M.D.,[19] Yuriy Ostapenko, M.D.,[20] Thomas Yau, M.D.,[21] Sergio Azevedo, M.D.,[22] María Varela, M.D., Ph.D.,[23] Ann-Lii Cheng, M.D., Ph.D.,[24] Shukui Qin, M.D., Ph.D.,[25] Peter R. Galle, M.D., Ph.D.,[26] Sajid Ali, M.D.,[27] Michelle Marcovitz, Ph.D.,[27] Mallory Makowsky, Pharm.D.,[27] Philip He, Ph.D.,[27] John F. Kurland, Ph.D.,[27] Alejandra Negro, Ph.D.,[27] and Bruno Sangro, M.D., Ph.D.[28]

HIMALAYA: Overall Survival



	Events, no. (%)	Median Overall Survival, mo (95% CI)	Hazard Ratio
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Sorafenib (n=389)	293 (75.3%)	13.77 (12.25–16.13)	

No. at Risk									
STRIDE	393	308	235	190	158	98	32	1	0
Durvalumab	389	286	230	183	153	87	27	6	0
Sorafenib	389	283	211	155	121	62	21	1	0

Abou-Alfa G et al. *NEJM Evid* June 6, 2022;1(8).

Update on Phase III LEAP-002 Trial Evaluating Pembrolizumab with Lenvatinib versus Lenvatinib Monotherapy for Patients with Unresectable Hepatocellular Carcinoma

Press Release — August 3, 2022

"Today [it was] announced that the Phase 3 LEAP-002 trial investigating pembrolizumab plus lenvatinib, the orally available multiple receptor tyrosine kinase inhibitor, versus lenvatinib monotherapy did not meet its dual primary endpoints of overall survival (OS) and progression-free survival (PFS) as a first-line treatment for patients with unresectable hepatocellular carcinoma (uHCC). There were trends toward improvement in OS and PFS for patients who received pembrolizumab plus lenvatinib versus lenvatinib monotherapy; however, these results did not meet statistical significance per the pre-specified statistical plan.

The median OS of the lenvatinib monotherapy arm in LEAP-002 was longer than that observed in previously reported clinical trials evaluating lenvatinib monotherapy in uHCC. The safety profile of pembrolizumab plus lenvatinib was consistent with previously reported data on the combination. [The companies] plan to present these data at an upcoming medical conference."

https://finance.yahoo.com/news/merck-eisai-phase-3-leap-104500062.html

RTP RESEARCH TO PRACTICE

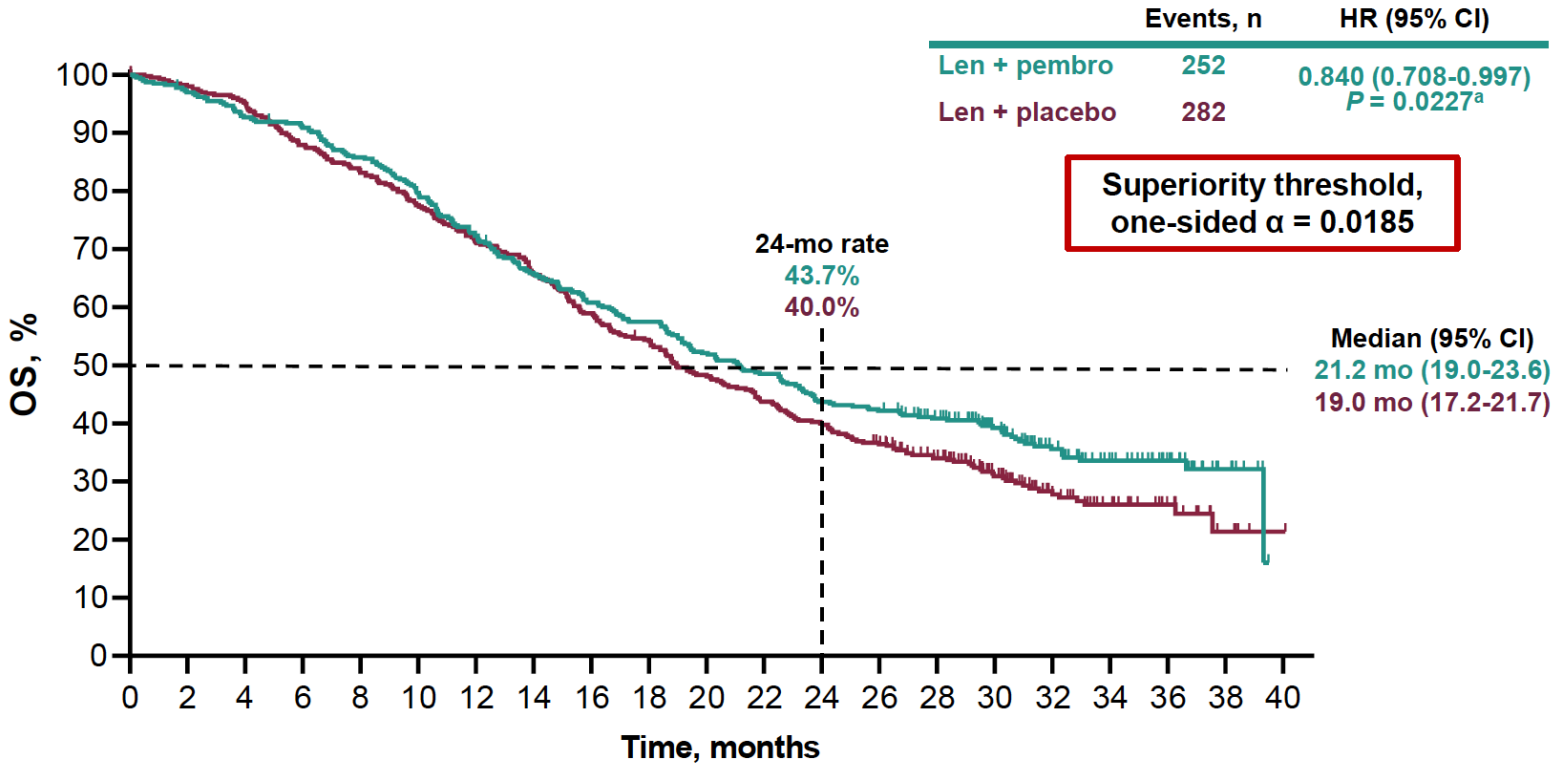
ESMO 2022;Abstract LBA34.

Primary Results From the Phase 3 LEAP-002 Study: Lenvatinib Plus Pembrolizumab Versus Lenvatinib as First-line Therapy for Advanced Hepatocellular Carcinoma

Richard S. Finn[1], Masatoshi Kudo[2], Philippe Merle[3], Tim Meyer[4], Shukui Qin[5], Masafumi Ikeda[6], Ruocai Xu[7], Julien Edeline[8], Baek-Yeol Ryoo[9], Zhenggang Ren[10], Ann-Lii Cheng[11], Peter R. Galle[12], Shuichi Kaneko[13], Hiromitsu Kumada[14], Anran Wang[15], Kalgi Mody[16], Leonid Dubrovsky[15], Abby B. Siegel[15], Josep Llovet[17,18]

[1]Department of Medicine, University of California, Los Angeles, Los Angeles, CA, USA; [2]Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan; [3]Hopital de la Croix Rousse, Lyon, France; [4]Royal Free London NHS Foundation Trust, London, the United Kingdom; [5]Cancer Centre of Jinling Hospital, Nanjing University of Chinese Medicine, Nanjing, China; [6]National Cancer Center Hospital East, Kashiwa, Chiba, Japan; [7]Hunan Cancer Hospital, Changsha, Hunan, China; [8]Department of Medical Oncology, Centre Eugene Marquis, Rennes, France; [9]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; [10]Zhongshan Hospital, Fudan University, Shanghai, China; [11]National Taiwan University Hospital, Taipei, Taiwan; [12]Mainz University Medical Center, Mainz, Germany; [13]Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, Kanazawa, Japan; [14]Department of Hepatology, Toranomon Hospital, Tokyo, Japan; [15]Merck & Co., Inc., Rahway, NJ, USA; [16]Eisai Inc., Nutley, NJ, USA; [17]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA, [18]August Pi i Sunyer Biomedical Research Institute-Hospital Clinic, University of Barcelona, Catalonia, Spain.

Overall Survival, ITT, FA



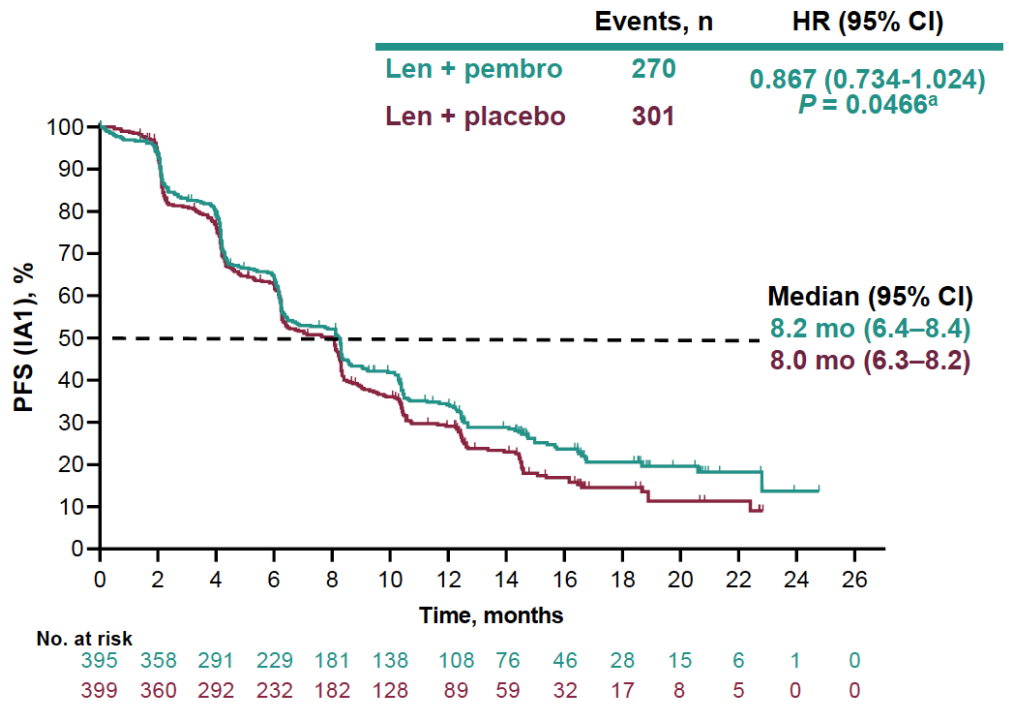
[a]Did not reach superiority threshold, one-sided α=0.0185.
Data cutoff date for FA: 21 June 2022; median follow-up: 32.1 months.

ITT = intent-to-treat; FA = final analysis; len = lenvatinib; pembro = pembrolizumab; OS = overall survival

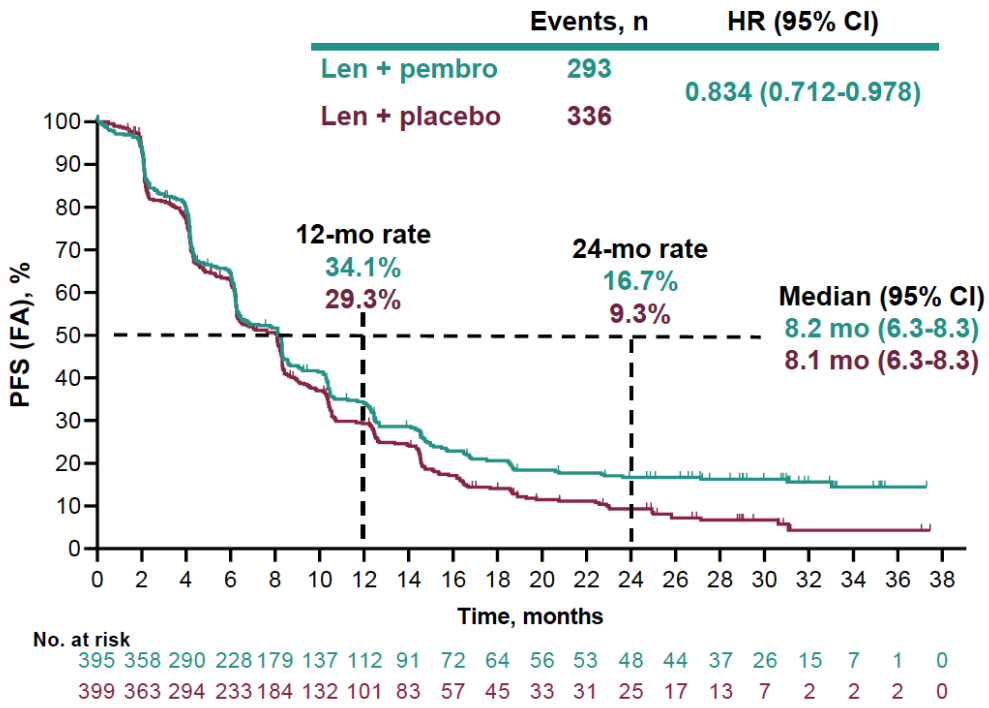
Finn RS et al. ESMO 2022;Abstract LBA34.

Progression-Free Survival, per RECIST 1.1 by BICR, ITT

IA1 (Final PFS Analysis)



FA



[a]Did not reach superiority threshold (one-sided α= 0.002) at IA1 (there was no statistical testing of PFS at FA).
Data cutoff date for IA1: 5 April 2021; Data cutoff date for FA: 21 June 2022.

BICR = blinded independent central review; ITT = intent-to-treat; IA1 = first interim analysis; PFS = progression-free survival; FA = final analysis; len = lenvatinib; pembro = pembrolizumab

Finn RS et al. ESMO 2022;Abstract LBA34.

Ongoing Phase III Studies of Immune Checkpoint Inhibitors for Localized Hepatocellular Carcinoma

Study	N	Eligibility	Randomization arms	Estimated primary completion
CheckMate 9DX	545	• High-risk of recurrence after curative hepatic resection or ablation	• Nivolumab • Placebo	December 2024
KEYNOTE-937	950	• Complete radiologic response after surgical resection or ablation	• Pembrolizumab • Placebo	June 2025
EMERALD-2	908	• High-risk of recurrence after curative hepatic resection or ablation	• Durvalumab + bevacizumab • Durvalumab + placebo • Placebo + placebo	May 2023
IMbrave050	668	• High-risk of recurrence after curative hepatic resection or ablation	• Atezolizumab + bevacizumab • Active surveillance	September 2023

www.clinicaltrials.gov. Accessed September 2022.

FDA Approves Durvalumab in Combination with Gemcitabine/Cisplatin for Locally Advanced or Metastatic Biliary Tract Cancers

Press Release – September 2, 2022

"On September 2, 2022, the Food and Drug Administration approved durvalumab in combination with gemcitabine and cisplatin for adult patients with locally advanced or metastatic biliary tract cancer (BTC). Efficacy was evaluated in TOPAZ-1 (NCT03875235), a randomized, double-blind, placebo-controlled, multiregional trial that enrolled 685 patients with histologically confirmed locally advanced unresectable or metastatic BTC who had not previously received systemic therapy for advanced disease… Patients were randomized 1:1 to receive:

- Durvalumab 1,500 mg on Day 1+ gemcitabine 1,000 mg/m2 and cisplatin 25 mg/m2 on Days 1 and 8 of each 21-day cycle up to 8 cycles, followed by durvalumab 1,500 mg every 4 weeks, or
- Placebo on Day 1+ gemcitabine 1,000 mg/m2 and cisplatin 25 mg/m2 on Days 1 and 8 of each 21-day cycle up to 8 cycles, followed by placebo every 4 weeks.

The recommended durvalumab dose is 1,500 mg every 3 weeks for patients with a body weight ≥30 kg when given with gemcitabine and cisplatin, followed by 1,500 mg every 4 weeks as a single agent until disease progression or unacceptable toxicity. For patients with a body weight <30 kg, the recommended dose is 20 mg/kg every 3 weeks with gemcitabine and cisplatin followed by 20 mg/kg every 4 weeks until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-durvalumab-locally-advanced-or-metastatic-biliary-tract-cancer

RTP RESEARCH TO PRACTICE

NEJM Evidence

Published June 1, 2022

DOI: 10.1056/EVIDoa2200015

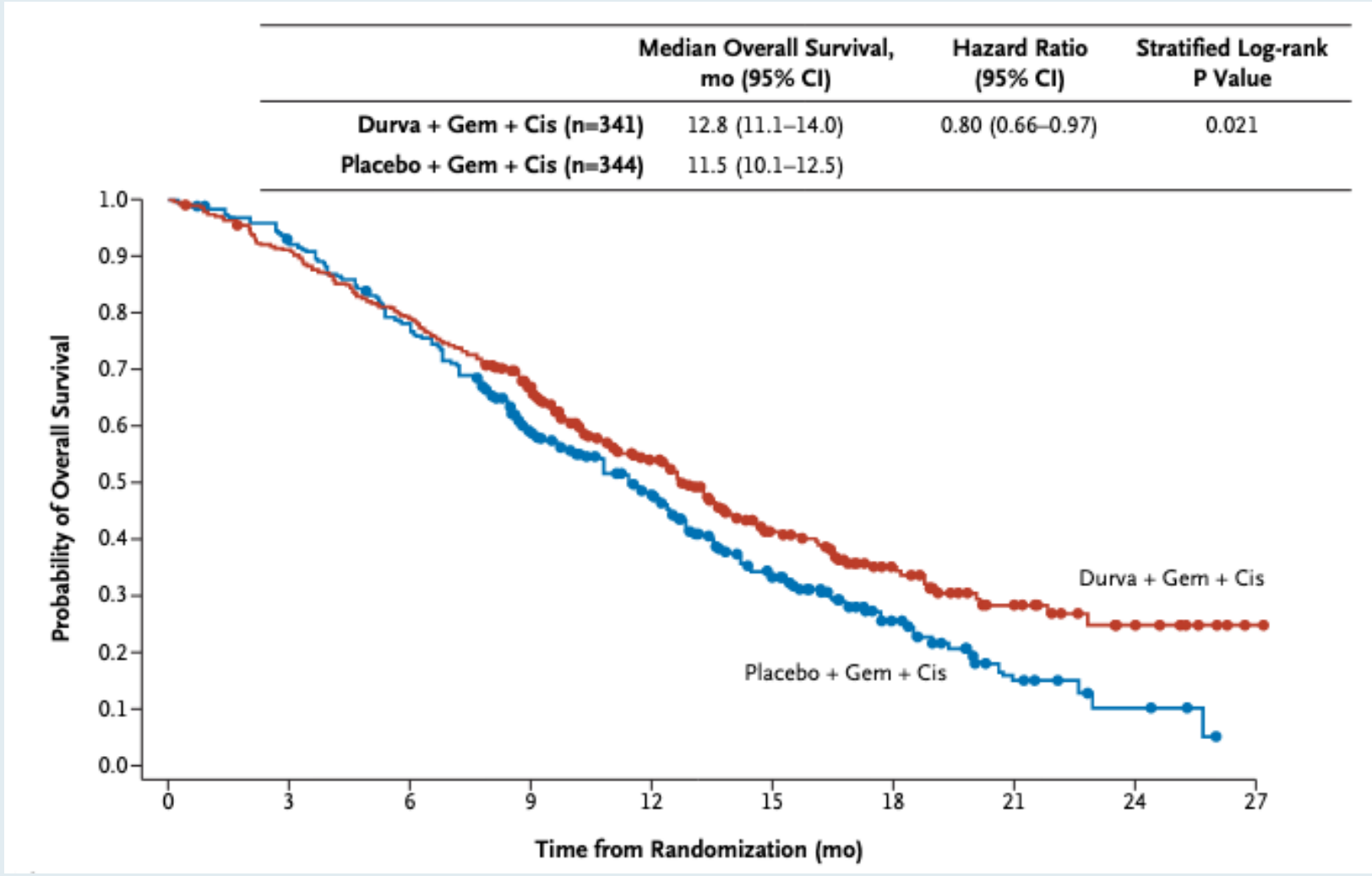
ORIGINAL ARTICLE

Durvalumab plus Gemcitabine and Cisplatin in Advanced Biliary Tract Cancer

Do-Youn Oh, M.D., Ph.D.,[1] Aiwu Ruth He, M.D., Ph.D.,[2] Shukui Qin, M.D.,[3] Li-Tzong Chen, M.D., Ph.D.,[4,5,6] Takuji Okusaka, M.D., Ph.D.,[7] Arndt Vogel, M.D.,[8] Jin Won Kim, M.D., Ph.D.,[9] Thatthan Suksomboon charoen, M.D.,[10] Myung Ah Lee, M.D., Ph.D.,[11] Masayuki Kitano, M.D., Ph.D.,[12] Howard Burris, M.D.,[13] Mohamed Bouattour, M.D.,[14] Suebpong Tanasanvimon, M.D.,[15] Mairéad G. McNamara, M.B., Ph.D.,[16] Renata Zaucha, M.D., Ph.D.,[17] Antonio Avallone, M.D.,[18] Benjamin Tan, M.D.,[19] Juan Cundom, M.D.,[20] Choong-kun Lee, M.D., Ph.D.,[21] Hidenori Takahashi, M.D., Ph.D.,[22] Masafumi Ikeda, M.D., Ph.D.,[23] Jen-Shi Chen, M.D.,[24] Julie Wang, Ph.D.,[25] Mallory Makowsky, Pharm.D.,[25] Nana Rokutanda, M.D., Ph.D.,[25] Philip He, Ph.D.,[25,26] John F. Kurland, Ph.D.,[25] Gordon Cohen, M.D., M.P.H.,[25] and Juan W. Valle, M.D.[16]

TOPAZ-1: Primary OS Endpoint with Durvalumab with Gemcitabine/Cisplatin for Advanced Biliary Tract Cancer

	Median Overall Survival, mo (95% CI)	Hazard Ratio (95% CI)	Stratified Log-rank P Value
Durva + Gem + Cis (n=341)	12.8 (11.1–14.0)	0.80 (0.66–0.97)	0.021
Placebo + Gem + Cis (n=344)	11.5 (10.1–12.5)		



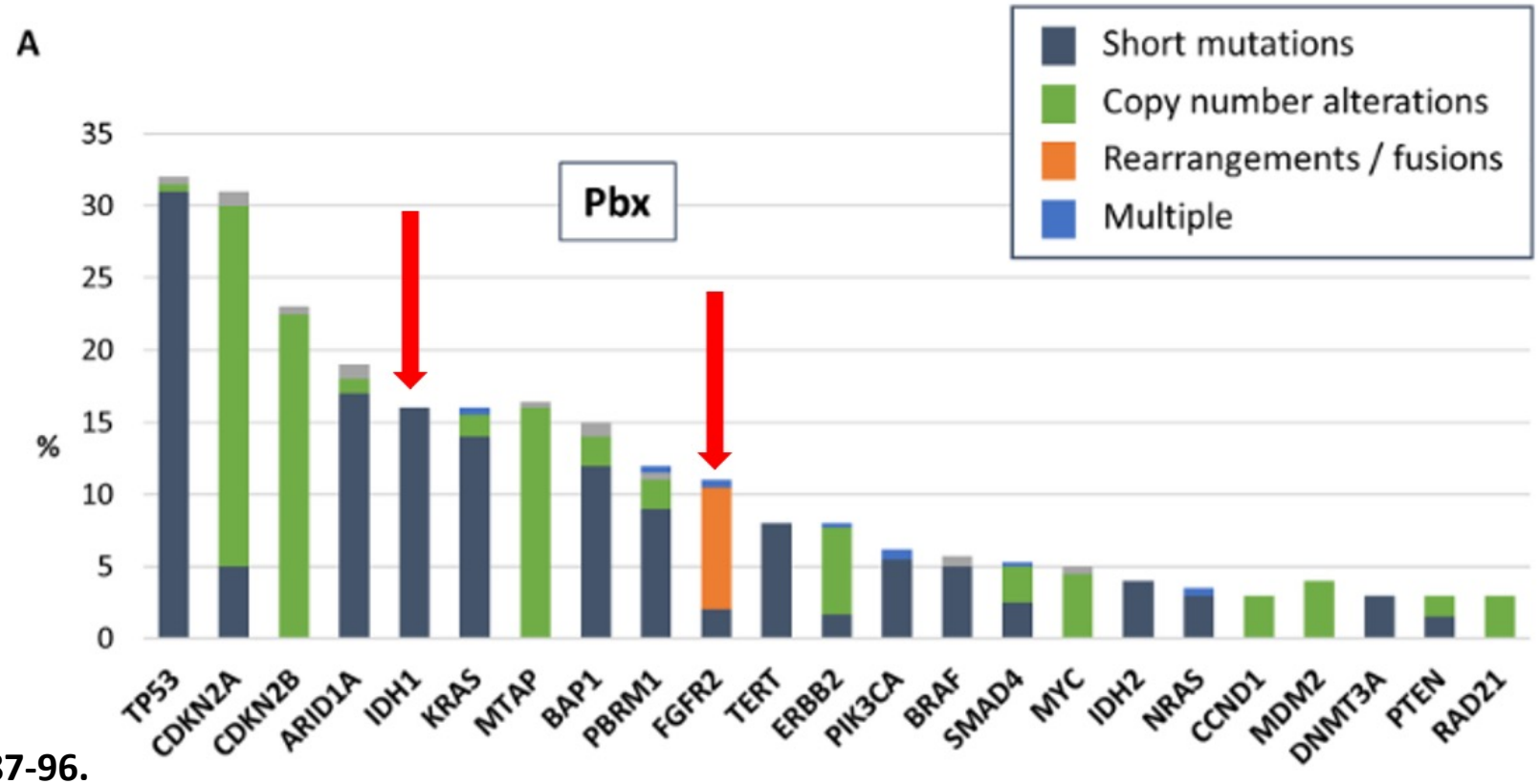
Durva = durvalumab; gem = gemcitabine; cis = cisplatin

Oh D-Y et al. *NEJM Evid* June 1, 2022;1(8).

RTP RESEARCH TO PRACTICE

Emerging Targets in Cholangiocarcinoma: Focus on FGFR2 and IDH1

- Mutation profiling of N=1632 iCCA using Foundation Medicine panel
  - n=1048 with primary tumor biopsy (Pbx)
  - *FGFR2* fusion or rearrangement: 9%
  - *IDH1* mutation: 16%



Israel MA et al. *Oncologist* 2021;26(9):787-96.

iCCA = intrahepatic cholangiocarcinoma

Content courtesy of Katie Kelley, MD.

RTP RESEARCH TO PRACTICE

Therapeutic Targets and Approach to Molecular Profiling for Biliary Tract Cancers

Target	Frequency	Targeted agents	Molecular test
IDH1	**13%** of intrahepatic cholangiocarcinomas	Ivosidenib	Tumor next-generation DNA sequencing or targeted sequencing for hotspot mutations in coding region of IDH1
FGFR pathway	**20%** of intrahepatic cholangiocarcinomas	Erdafitinib; futibatinib; infigratinib; pemigatinib	Tumor next-generation DNA sequencing including FGFR2 intronic region, targeted RNAseq or FISH testing for FGFR2 translocation
BRAF	**5%** of intrahepatic cholangiocarcinomas	Dabrafenib with trametinib; vemurafenib	Tumor next-generation DNA sequencing or targeted sequencing for hotspot mutations in coding region of BRAF
MSI-high or MMR deficiency	**2%** of biliary tract cancers	Pembrolizumab	Multiple testing modalities available: PCR, immunohistochemistry or tumor next-generation DNA sequencing
ERBB2 (HER2)	**15%-20%** gallbladder cancer; extrahepatic cholangiocarcinomas	—	Multiple testing modalities available including immunohistochemistry and FISH for expression and amplification, tumor next-generation DNA sequencing for mutations

FISH = fluorescence in situ hybridization

Valle JW et al. *Lancet* 2021;397(10272):428-44.

FGFR Inhibitor Efficacy for FGFR2 Fusion-Positive Cholangiocarcinoma

	Pemigatinib* (N = 107)	Infigratinib* (N = 108)	Futibatinib (N = 67)	Derazantinib (N = 29)
ORR	35.5%	23.1%	37.3%	20.7%
Disease control rate	82.2%	84.3%	82.1%	82.8%
Median progression-free survival	6.9 mo	7.3 mo	7.2 mo	5.7 mo
Median overall survival	21.1 mo	12.2 mo	NR	NR
Toxicities	Hyperphosphatemia, Alopecia, Diarrhea	Hyperphosphatemia, Stomatitis, Fatigue	Hyperphosphatemia, Diarrhea, Dry mouth	Hyperphosphatemia, Fatigue, Ocular

*FDA approved

Content courtesy of Tanios Bekaii-Saab, ASCO 2022

Abou-Alfa GK et al. *Lancet Oncol* 2020;21(5):671-84; Javle M et al. GI Cancers Symposium 2021; Goyal L et al. ASCO 2020; Mazzaferro V et al. *Br J Cancer* 2019;120(2):165-71.

FDA Grants Accelerated Approval for Infigratinib for Metastatic Cholangiocarcinoma

Press Release – May 28, 2021

"The Food and Drug Administration granted accelerated approval to infigratinib, a kinase inhibitor for adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test.

The FDA also approved FoundationOne® CDx for selection of patients with FGFR2 fusion or other rearrangement as a companion diagnostic device for treatment with infigratinib.

Efficacy was demonstrated in CBGJ398X2204 (NCT02150967), a multicenter open-label single-arm trial, that enrolled 108 patients with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with an FGFR2 fusion or rearrangement as determined by local or central testing. Patients received infigratinib 125 mg orally once daily for 21 consecutive days followed by 7 days off therapy, in 28-day cycles until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-infigratinib-metastatic-cholangiocarcinoma

Lancet Gasteroenterol Hepatol 2021;6(10):803-15.

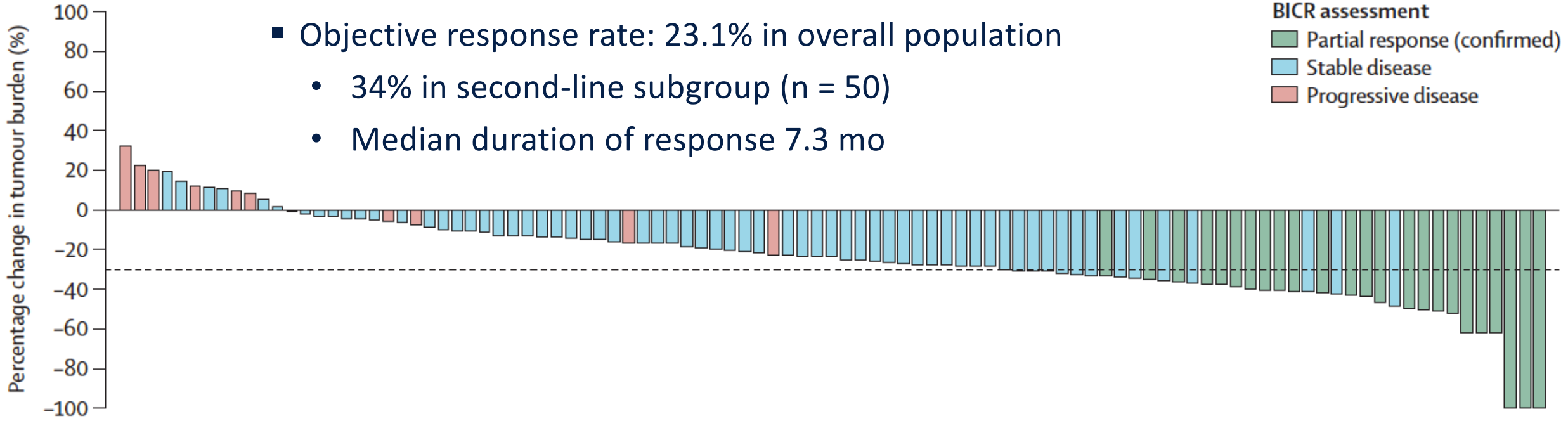
Articles

Infigratinib (BGJ398) in previously treated patients with advanced or metastatic cholangiocarcinoma with *FGFR2* fusions or rearrangements: mature results from a multicentre, open-label, single-arm, phase 2 study

Milind Javle, Sameek Roychowdhury, Robin Kate Kelley, Saeed Sadeghi, Teresa Macarulla, Karl Heinz Weiss, Dirk-Thomas Waldschmidt, Lipika Goyal, Ivan Borbath, Anthony El-Khoueiry, Mitesh J Borad, Wei Peng Yong, Philip A Philip, Michael Bitzer, Surbpong Tanasanvimon, Ai Li, Amit Pande, Harris S Soifer, Stacie Peacock Shepherd, Susan Moran, Andrew X Zhu, Tanios S Bekaii-Saab, Ghassan K Abou-Alfa

Phase II Study of Infigratinib for Advanced or Metastatic Cholangiocarcinoma Harboring FGFR2 Fusions or Rearrangements

- Objective response rate: 23.1% in overall population
  - 34% in second-line subgroup (n = 50)
  - Median duration of response 7.3 mo



BICR = blinded independent central review

Javle M et al. *Lancet Gasteroenterol Hepatol* 2021;6(10):803-15.

WORLD CONGRESS ON Gastrointestinal Cancer

2022 | Abstract O-2

O-2

#575

Presented at the 2022 ESMO World Congress on Gastrointestinal Cancer; 29 June–2 July, 2022; Barcelona, Spain

Pemigatinib for Previously Treated Locally Advanced or Metastatic Cholangiocarcinoma: Final Results From FIGHT-202

Arndt Vogel, MD

Arndt Vogel, MD,[1] Vaibhav Sahai, MBBS, MS,[2] Antoine Hollebecque, MD,[3] Gina M. Vaccaro, MD,[4] Davide Melisi, MD, PhD,[5] Raed M. Al Rajabi, MD,[6] Andrew S. Paulson, MD,[7] Mitesh J. Borad, MD,[8] David Gallinson, DO,[9] Adrian G. Murphy, MD,[10] Do-Youn Oh, MD, PhD,[11] Efrat Dotan, MD,[12] Daniel V. Catenacci, MD,[13] Eric Van Cutsem, MD, PhD,[14] Christine F. Lihou, BS,[15] Huiling Zhen, PhD,[15] Luisa Veronese, MD,[16] Ghassan K. Abou-Alfa, MD[17]

RTP RESEARCH TO PRACTICE

FIGHT-202 Final Results: Response to Pemigatinib

	FGFR2 fusions or rearrangements	Other FGF/FGFR genetic alterations	No FGF/FGFR genetic alterations
Parameter	**Cohort A (n=108)**	**Cohort B (n=20)**	**Cohort C (n=17)**
Duration of follow-up, median (range), mo	42.9 (19.9–52.2)	47.5 (43.7–51.1)	51.9 (49.5–53.7)
ORR,* % (95% CI)	37 (28, 47)	0 (0, 17)	0 (0, 20)
DCR,† % (95% CI)	82 (74, 89)	40 (19, 64)	18 (4, 43)
Best overall response, %			
Complete response	3	0	0
Partial response	34	0	0
Stable disease	45	40	18
Progressive disease	15	35	65
Not evaluable	3	25	18
DOR, median (95% CI), mo	9.1 (6.0, 14.5)	—	—

DCR, disease control rate; DOR, duration of response; ORR, objective response rate.

*ORR is complete response + partial response; †DCR is complete response + partial response + stable disease.

Vogel A et al. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract O-2.

FDA Grants Accelerated Approval for Futibatinib for Cholangiocarcinoma

Press Release – September 30, 2022

"The Food and Drug Administration granted accelerated approval to futibatinib for adult patients with previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements.

Efficacy was evaluated in TAS-120-101 (NCT02052778), a multicenter, open-label, single-arm trial that enrolled 103 patients with previously treated, unresectable, locally advanced, or metastatic intrahepatic cholangiocarcinoma harboring a FGFR2 gene fusion or other rearrangement. The presence of FGFR2 fusions or other rearrangements was determined using next generation sequencing testing. Patients received 20 mg of futibatinib orally once daily until disease progression or unacceptable toxicity.

The major efficacy outcome measures were overall response rate (ORR) and duration of response (DoR) as determined by an independent review committee according to RECIST v1.1. ORR was 42%; all 43 responders achieved partial responses. The median DoR was 9.7 months."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-futibatinib-cholangiocarcinoma

RTP RESEARCH TO PRACTICE

Updated Results of the FOENIX-CCA2 Trial: Efficacy and Safety of Futibatinib in Intrahepatic Cholangiocarcinoma Harboring *FGFR2* Fusions/Rearrangements

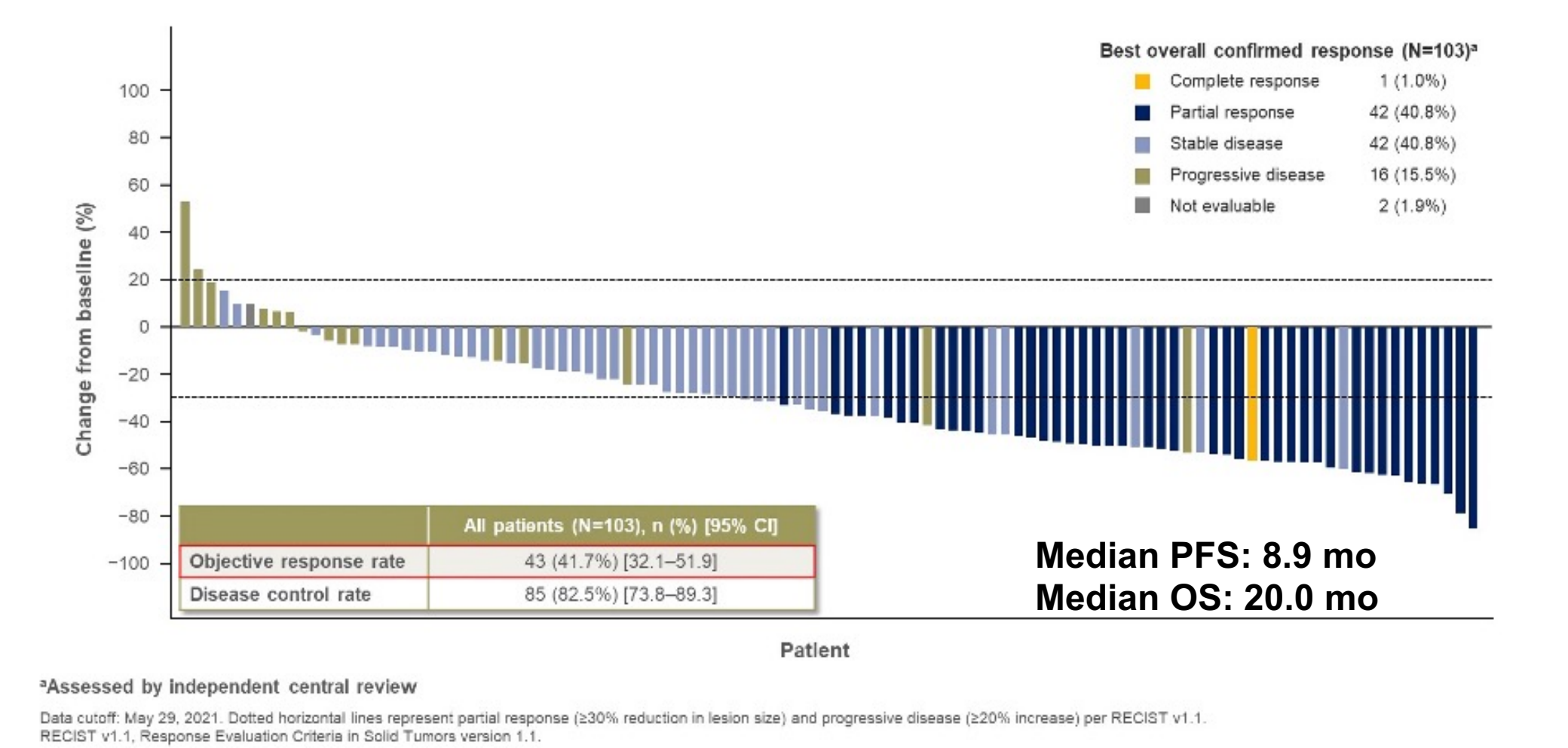
Lipika Goyal,[1] Funda Meric-Bernstam,[2] Antoine Hollebecque,[3] Chigusa Morizane,[4] Juan W. Valle,[5] Thomas B. Karasic,[6] Thomas A. Abrams,[7] Robin Kate Kelley,[8] Philippe Cassier,[9] Junji Furuse,[10] Heinz-Josef Klümpen,[11] Heung-Moon Chang,[12] Li-Tzong Chen,[13] Yoshito Komatsu,[14] Kunihiro Masuda,[15] Daniel Ahn,[16] Kate Li,[17] Karim A. Benhadji,[17] Volker Wacheck,[17] John A. Bridgewater[18]

[1]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [2]University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Gustave Roussy, Drug Development Department (DITEP), F-94805, Villejuif, France; [4]National Cancer Center Hospital, Tokyo, Japan; [5]University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; [6]Hospital of the University of Pennsylvania, Philadelphia, PA, USA; [7]Dana-Farber Cancer Institute, Boston, MA, USA; [8]University of California, San Francisco, CA, USA; [9]Centre Léon-Bérard, Lyon, France; [10]Kyorin University, Faculty of Medicine, Tokyo, Japan; [11]Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, The Netherlands; [12]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; [13]National Institute of Cancer Research, National Health Research Institutes, Tainan, Taiwan; [14]Hokkaido University Hospital Cancer Center, Hokkaido, Japan; [15]Tohoku University Graduate School of Medicine, Miyagi, Japan; [16]Mayo Clinic, Phoenix, AZ, USA; [17]Taiho Oncology, Inc., Princeton, NJ, USA; [18]UCL Cancer Institute, London, UK

ASCO 2022;Abstract 4009.

RTP RESEARCH TO PRACTICE

FOENIX-CCA2: Phase II Study of Futibatinib for Intrahepatic Cholangiocarcinoma with FGFR2 Fusions/Rearrangements



PFS = progression-free survival; OS = overall survival

Goyal L et al. ASCO 2022;Abstract 4009.

RTP RESEARCH TO PRACTICE

FDA Approves Ivosidenib for Advanced or Metastatic Cholangiocarcinoma

Press Release – August 25, 2021

"The Food and Drug Administration approved ivosidenib for adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with an isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.

Today, the FDA also approved the Oncomine Dx Target Test as a companion diagnostic device to aid in selecting patients with cholangiocarcinoma for treatment with ivosidenib.

Ivosidenib was investigated in a randomized (2:1), multicenter, double-blind, placebo-controlled clinical trial (Study AG120-C-005, NCT02989857) of 185 adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 mutation. The patient's disease must have progressed following at least one, but not more than two prior regimens, including at least one gemcitabine- or 5-flurouracil-containing regimen. Patients were randomized to receive either ivosidenib 500 mg orally once daily or matched placebo until disease progression or unacceptable toxicity."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-ivosidenib-advanced-or-metastatic-cholangiocarcinoma

RTP RESEARCH TO PRACTICE

Research

JAMA Oncol 2021;7(11):1669-77.

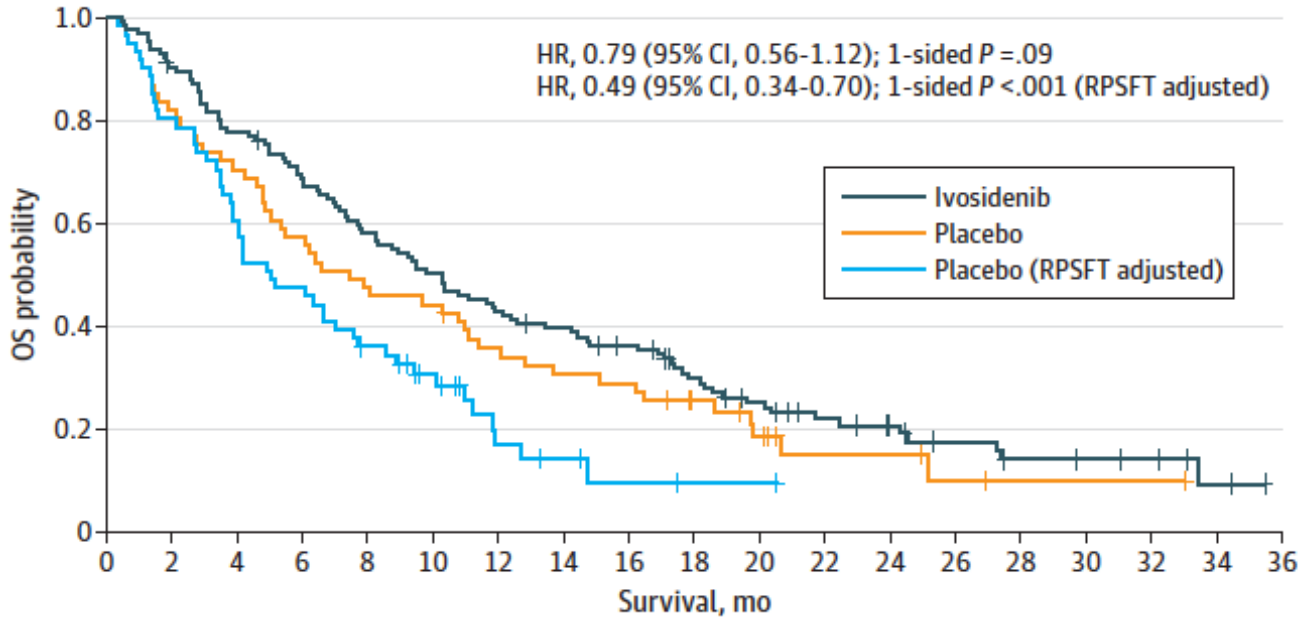
JAMA Oncology | Original Investigation

Final Overall Survival Efficacy Results of Ivosidenib for Patients With Advanced Cholangiocarcinoma With *IDH1* Mutation

The Phase 3 Randomized Clinical ClarIDHy Trial

Andrew X. Zhu, MD, PhD; Teresa Macarulla, MD; Milind M. Javle, MD; R. Kate Kelley, MD; Sam J. Lubner, MD; Jorge Adeva, MD; James M. Cleary, MD; Daniel V. T. Catenacci, MD; Mitesh J. Borad, MD; John A. Bridgewater, PhD; William P. Harris, MD; Adrian G. Murphy, MD; Do-Youn Oh, MD; Jonathan R. Whisenant, MD; Maeve A. Lowery, MD; Lipika Goyal, MD; Rachna T. Shroff, MD; Anthony B. El-Khoueiry, MD; Christina X. Chamberlain, PhD; Elia Aguado-Fraile, PhD; Sung Choe, PhD; Bin Wu, PhD; Hua Liu, PhD; Camelia Gliser, BS; Shuchi S. Pandya, MD; Juan W. Valle, MD; Ghassan K. Abou-Alfa, MD

ClarIDHy: Final OS with Ivosidenib for Patients with Advanced Cholangiocarcinoma with IDH1 Mutation



No. at risk																		
Ivosidenib	126	113	97	85	72	62	53	48	42	32	25	18	14	10	7	6	5	2
Placebo	61	50	43	35	29	27	21	18	17	12	8	4	4	2	1	1	1	
Placebo (RPSFT adjusted)	61	49	37	29	21	14	6	4	2	1	1							

Treatment group	Events/patients, No.	OS, median (95% CI), mo
Ivosidenib	100/126	10.3 (7.8-12.4)
Placebo	50/61	7.5 (4.8-11.1)
Placebo adjusted by RPSFT	49/61	5.1 (3.8-7.6)

RPSFT = rank-preserving structural failure time

Zhu AX et al. *JAMA Oncol* 2021;7(1):1669-77.

RTP RESEARCH TO PRACTICE

2022 ASCO ANNUAL MEETING

Abstract 4006

Trastuzumab deruxtecan (T-DXd; DS-8201) in patients (pts) with HER2-expressing unresectable or recurrent biliary tract cancer (BTC): An investigator-initiated multicenter phase 2 study (HERB trial)

Akihiro Ohba[1], Chigusa Morizane[1], Yasuyuki Kawamoto[2], Yoshito Komatsu[2], Makoto Ueno[3], Satoshi Kobayashi[3], Masafumi Ikeda[4], Mitsuhito Sasaki[4], Junji Furuse[5], Naohiro Okano[5], Nobuyoshi Hiraoka[1], Hiroshi Yoshida[1], Aya Kuchiba[1], Ryo Sadachi[1], Kenichi Nakamura[1], Naoko Matsui[1], Yoshiaki Nakamura[4], Wataru Okamoto[6], Takayuki Yoshino[4], Takuji Okusaka[1]

[1]National Cancer Center Hospital, [2]Hokkaido University Hospital, [3]Kanagawa Cancer Center, [4]National Cancer Center Hospital East, [5]Kyorin University Faculty of Medicine, [6]Hiroshima University Hospital

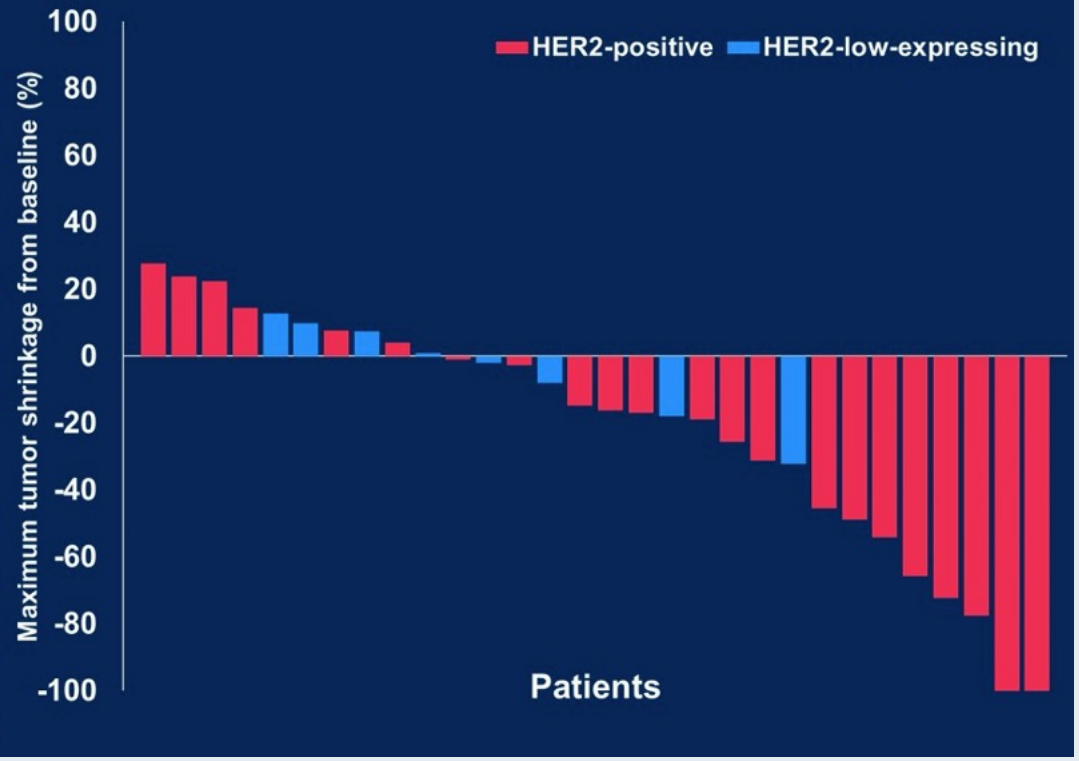
HERB Primary Endpoint: Confirmed ORR by BICR with T-DXd for Biliary Tract Cancer

- Tumor response

*: P =0.01

	HER2-positive (n=22)	HER2-low-expressing (n=8)	All pts (n=30)
Confirmed ORR	**36.4%**	12.5%	30.0%
(90% CI)	**(19.6-56.1)***	–	–
(95% CI)	(17.2–59.3)	(0.3–52.7)	(14.7–49.4)
Confirmed DCR	81.8%	75.0%	80.0%
(95% CI)	(59.7–94.8)	(34.9–96.8)	(61.4–92.3)
Confirmed best response, n (%)			
CR	2 (9.1)	0 (0)	2 (6.7)
PR	6 (27.3)	1 (12.5)	7 (23.3)
SD	10 (45.5)	5 (62.5)	15 (50.0)
PD	3 (13.6)	1 (12.5)	4 (13.3)
NE	1 (4.5)	1 (12.5)	2 (6.7)

- Best percentage change



ORR = objective response rate; BICR = blinded independent central review

Ohba A et al. ASCO 2022;Abstract 4006.

Ongoing Phase III Studies of FGFR Inhibitors for Advanced Cholangiocarcinoma

Study	N	Eligibility	Randomization arms	Estimated primary completion
FIGHT-302	434	• Previously untreated • Unresectable and/or metastatic • FGFR2 rearrangement	• Pemigatinib • Gemcitabine + cisplatin	March 2027
PROOF	300	• Previously untreated • Unresectable and/or metastatic • FGFR2 fusion/translocation	• Infigratinib • Gemcitabine + cisplatin	January 2026
FOENIX-CCA3	216	• Previously untreated • Unresectable and/or metastatic • FGFR2 rearrangement	• Futibatinib • Gemcitabine + cisplatin	April 2025

www.clinicaltrials.gov. Accessed June 2022.

Thank you for joining us!

CME, MOC and NCPD credit information will be emailed to each participant within 5 business days.

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