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

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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: *Dr 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

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Hepatobiliary Cancers Agenda

MODULE 1: Hepatocellular Carcinoma

MODULE 2: Biliary Tract Cancers

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Hepatobiliary Cancers Agenda

MODULE 1: Hepatocellular Carcinoma

MODULE 2: Biliary Tract Cancers

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Discussion Questions

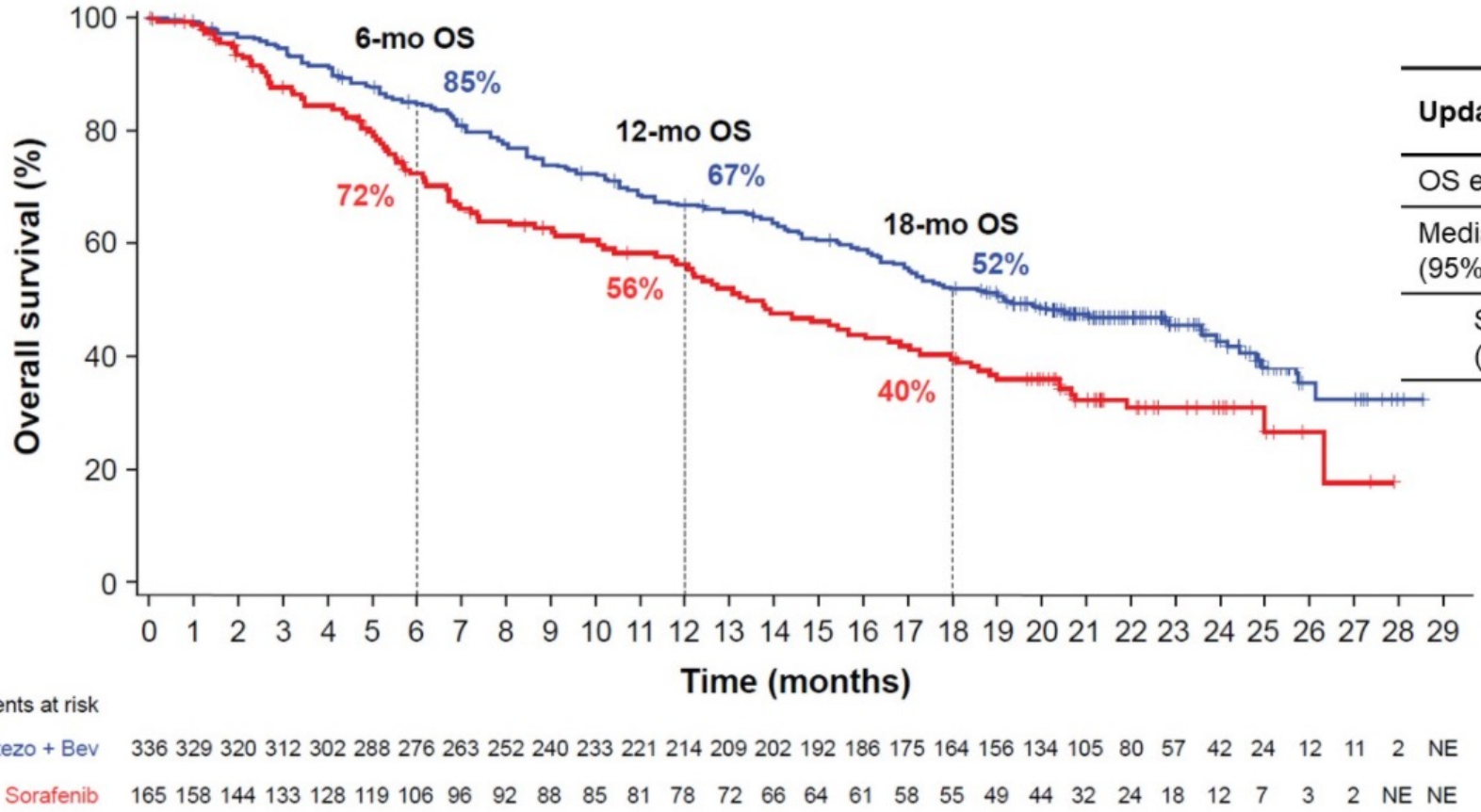
- Generally, in which situations do you not use an immune checkpoint inhibitor as part of up-front treatment for advanced HCC?

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.

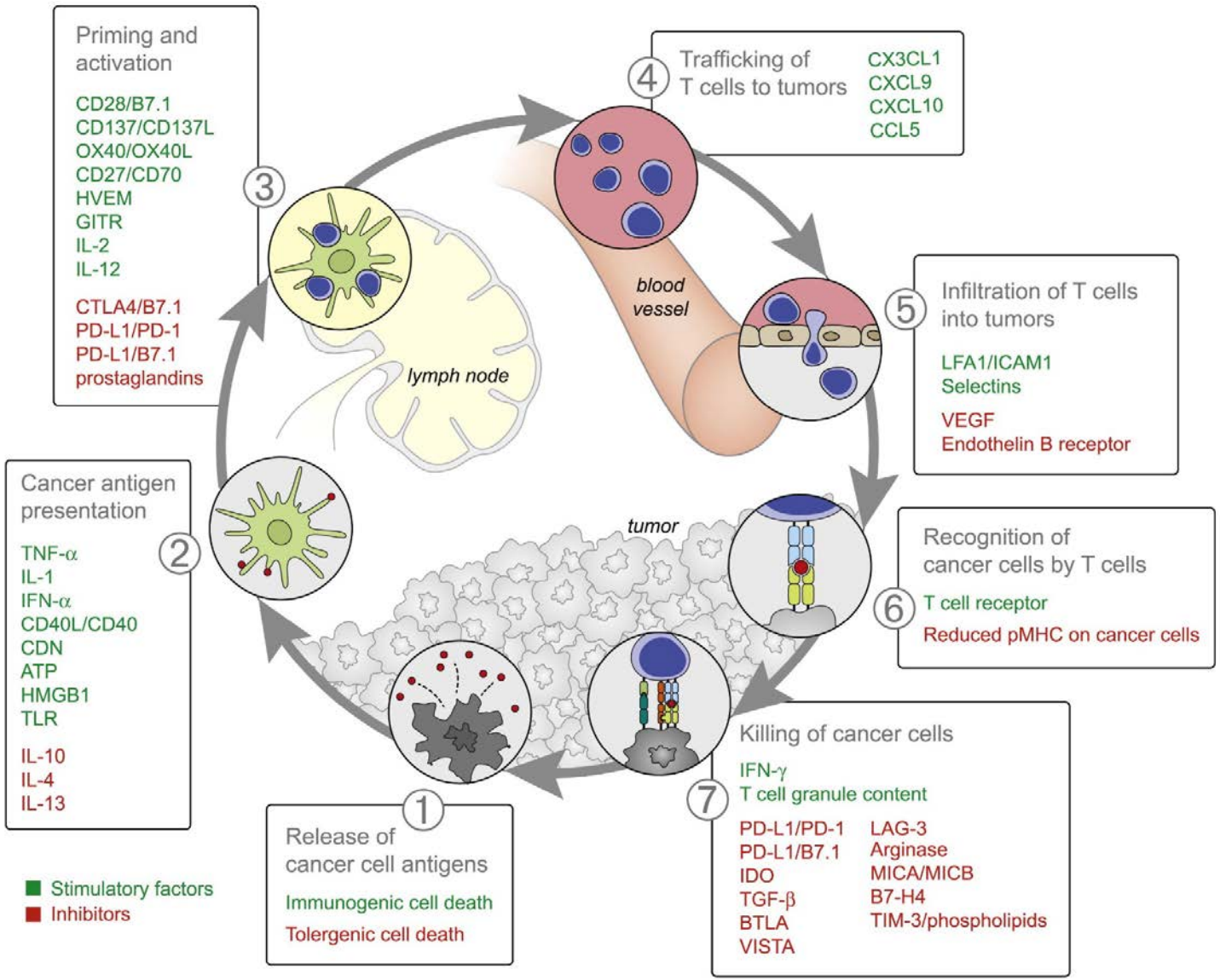
Finn, RS, et al. J Clin Oncol 39, 2021 (suppl 3; abstr 267)

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)

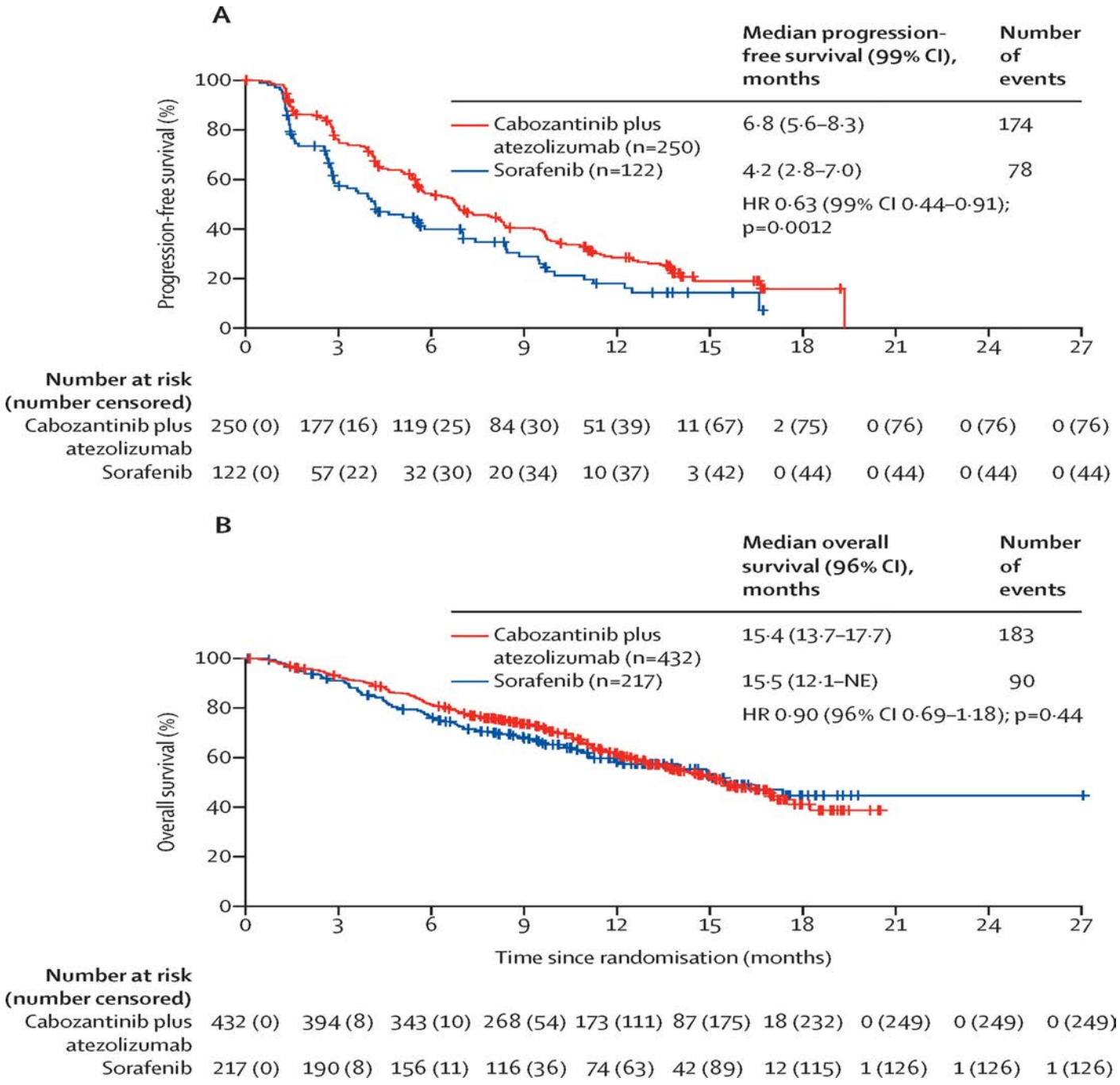
Fulgenzi C, et al. ILCA 2022, Madrid, Spain, September 4, 2022

Inhibitory Factors in the Cancer-Immunity Cycle



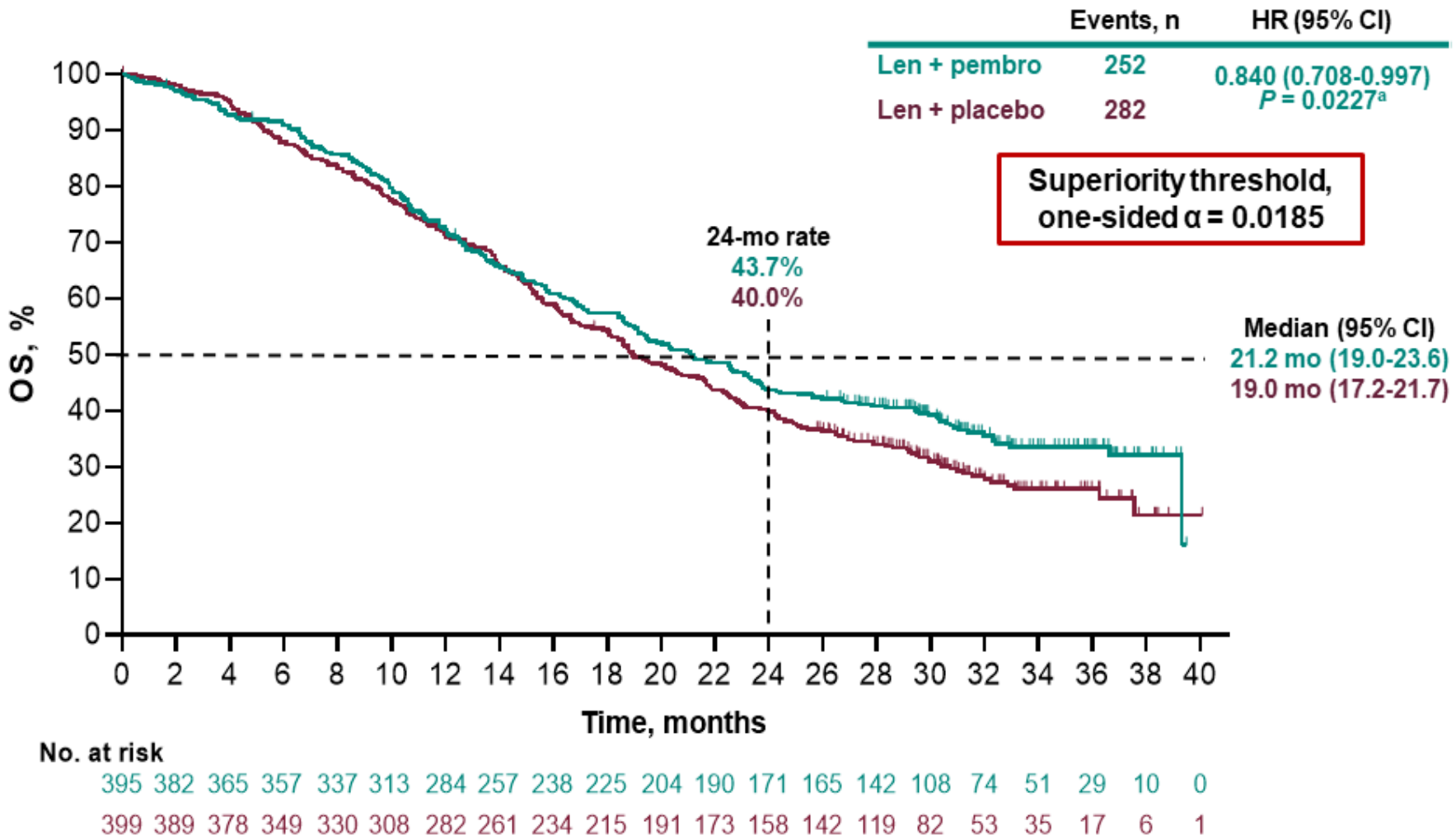
Chen, DS, Mellman I. Immunity. 2013 Jul 25;39(1):1-10

Atezolizumab plus Cabozantinib versus Sorafenib COSMIC-312



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

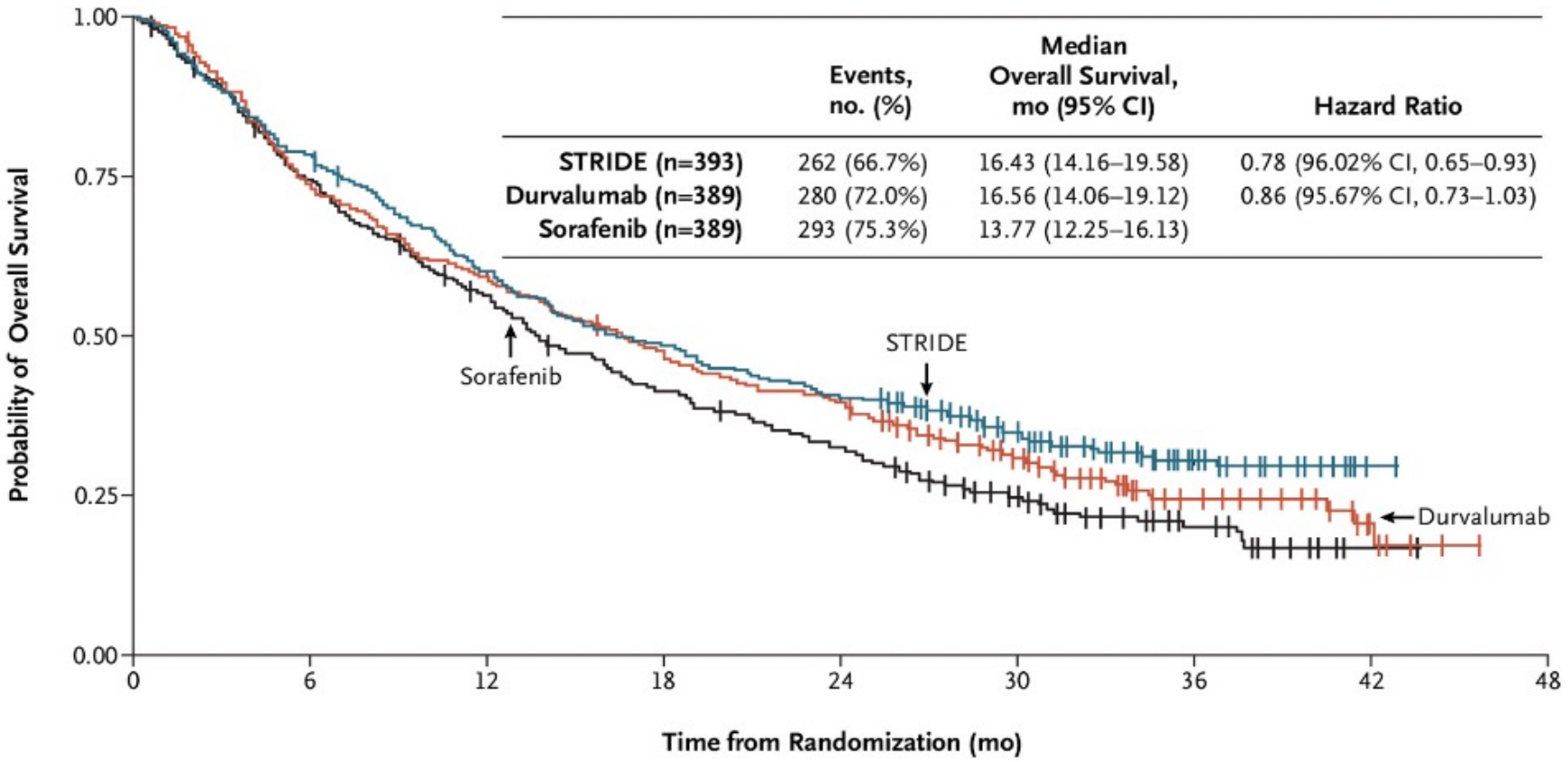
Pembrolizumab plus Lenvatinib LEAP-002



[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



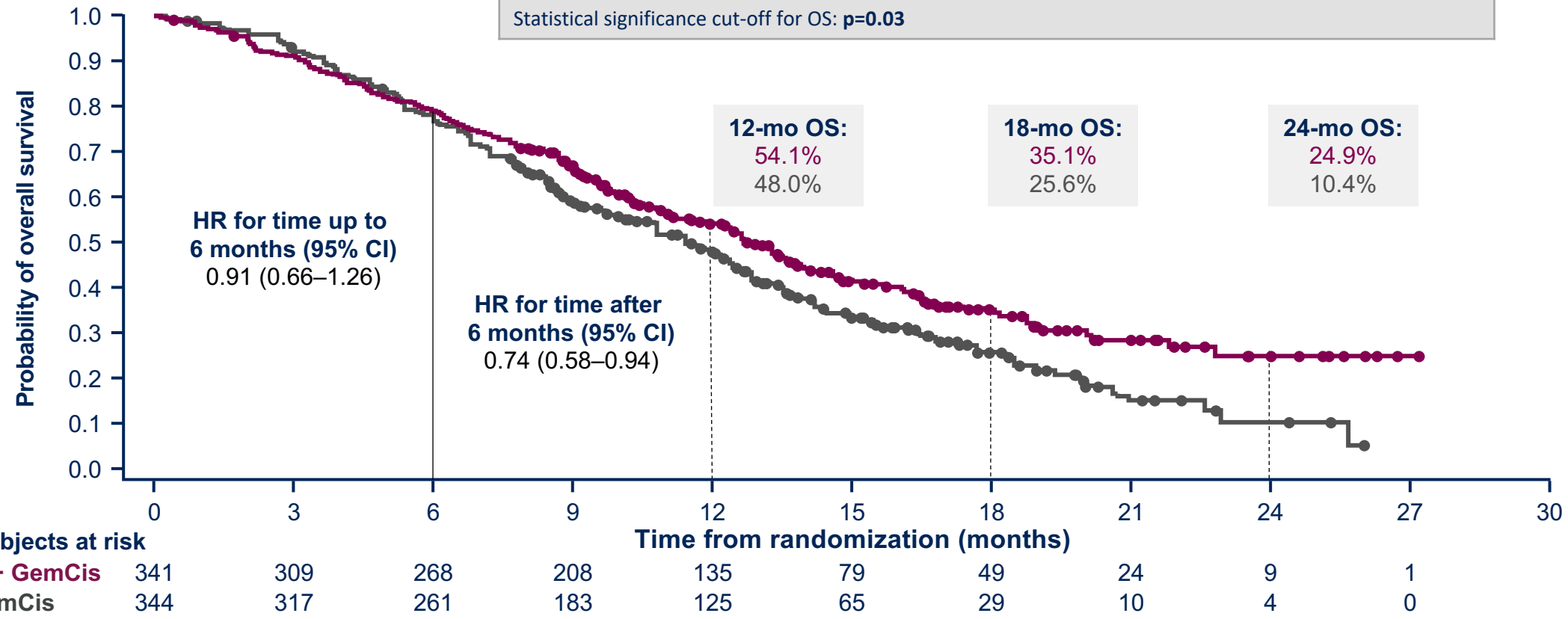
	Events, no. (%)	Median Overall Survival, mo (95% CI)	Hazard Ratio
STRIDE (n=393)	262 (66.7%)	16.43 (14.16–19.58)	0.78 (96.02% CI, 0.65–0.93)
Durvalumab (n=389)	280 (72.0%)	16.56 (14.06–19.12)	0.86 (95.67% CI, 0.73–1.03)
Sorafenib (n=389)	293 (75.3%)	13.77 (12.25–16.13)	

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**			

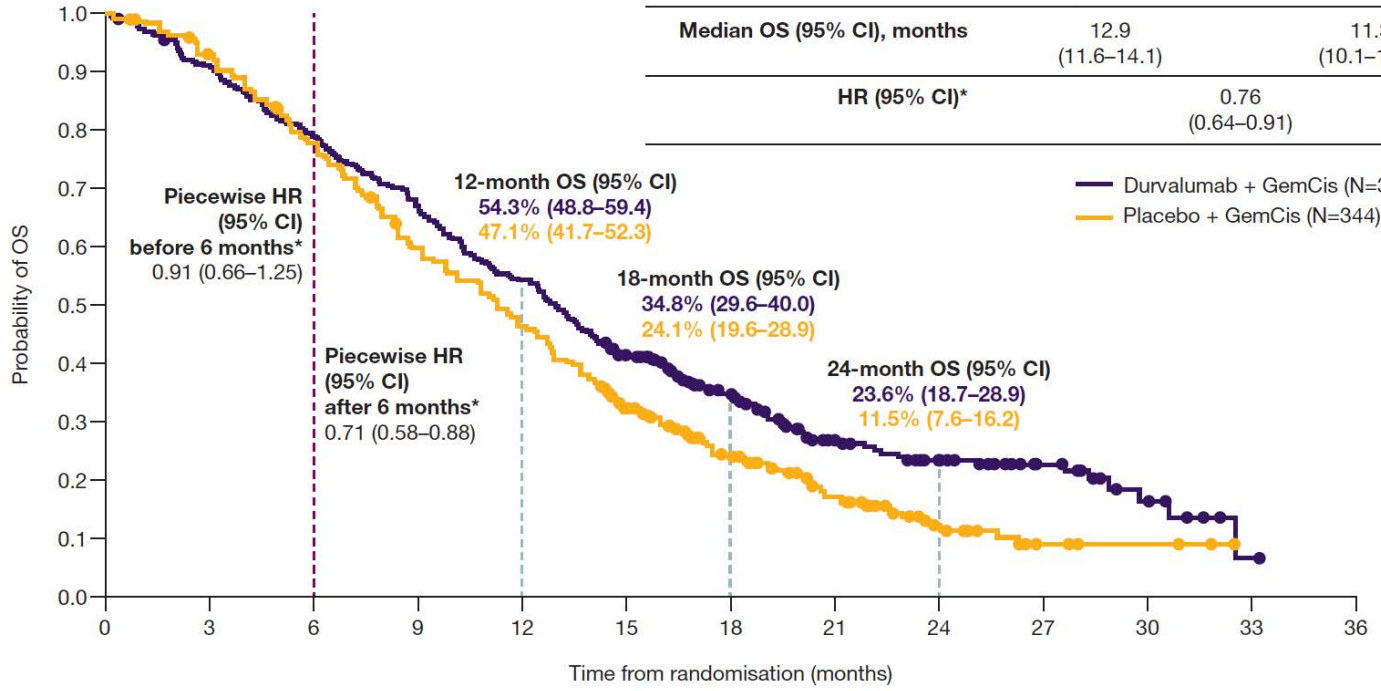


[a]Median duration of follow-up (95% CI) was 16.8 (14.8–17.7) months with durvalumab + GemCis and 15.9 (14.9–16.9) months with placebo + GemCis.

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.

Discussion Questions

- What do you consider the optimal up-front treatment for advanced HCC?
- What do you consider to be relative and absolute contraindications to the use of bevacizumab as part of up-front treatment for advanced HCC?

Hepatobiliary Cancers Agenda

MODULE 1: Hepatocellular Carcinoma

MODULE 2: Biliary Tract Cancers

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Discussion Questions

- When do you order multiplex genomic testing for biliary tract cancer, and which type of assay?
- What is your preferred time to use an FGFR inhibitor in biliary tract cancer, and which agent is optimal? Is there a role for the use of a second FGFR inhibitor for a patient with response and progression on prior FGFR inhibition?
- Regulatory and reimbursement issues aside, is there a role for HER2-targeted treatment in biliary tract cancer, and if so, which agent?

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

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NEJM Evidence

Published June 1, 2022

DOI: 10.1056/EVIDoa2200015

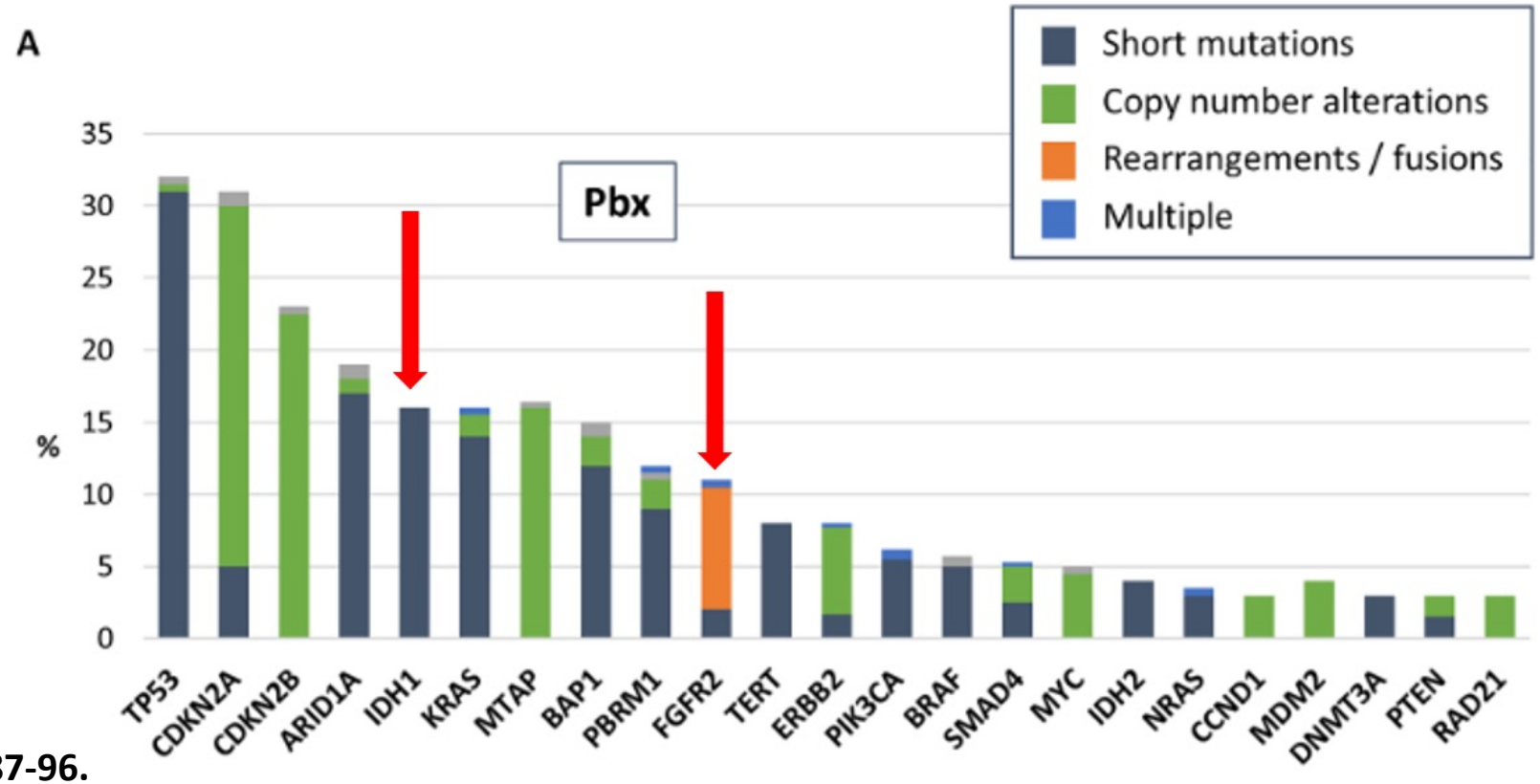
ORIGINAL ARTICLE

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]

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.

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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.

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]

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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.

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.

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

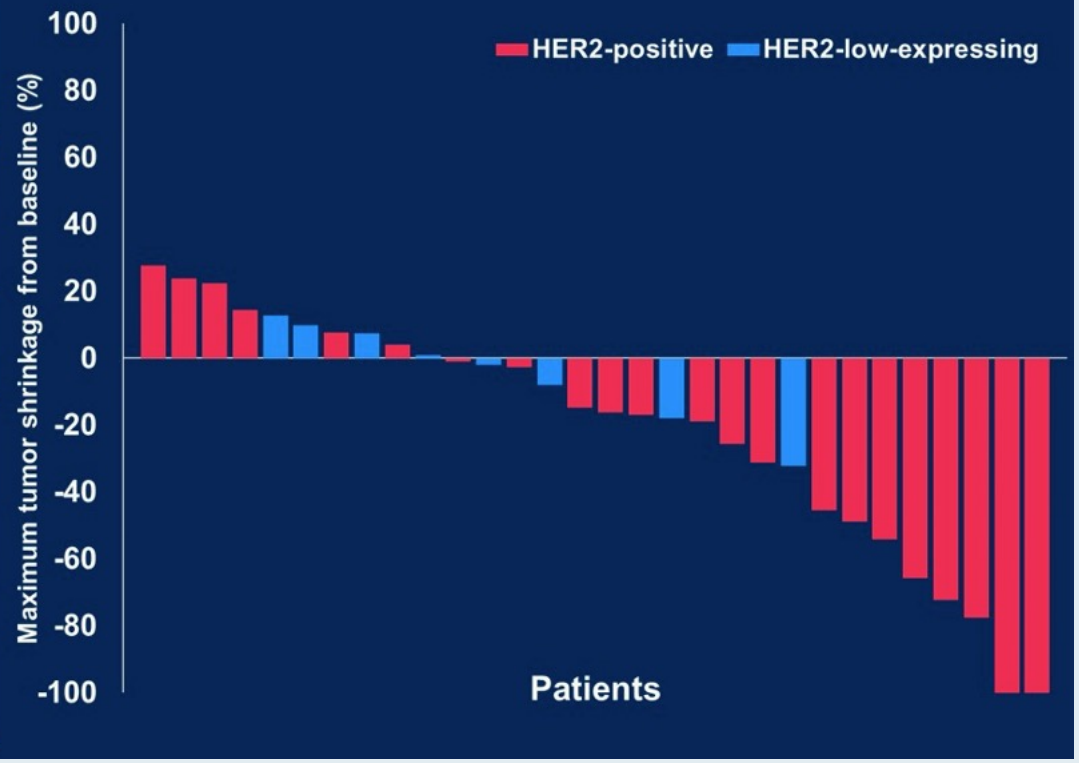
HERB Primary Endpoint: Confirmed ORR by BICR with T-DXd for Biliary Tract Cancer

- Tumor response

*: P =0.01

	HER2-positive (n=22)	HER2-low-expressing (n=8)	All pts (n=30)
Confirmed ORR (90% CI) (95% CI)	**36.4%** **(19.6-56.1)*** (17.2–59.3)	12.5% – (0.3–52.7)	30.0% – (14.7–49.4)
Confirmed DCR (95% CI)	81.8% (59.7–94.8)	75.0% (34.9–96.8)	80.0% (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.

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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We are taking a lunch break!

The program will resume at 2:00 PM ET

Up Next…

Drs Matthew Goetz and Ian Krop
discuss the management of breast cancer

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