Traitement systémique du carcinome hépatocellulaire (CHC) : Nouveautés en 2021

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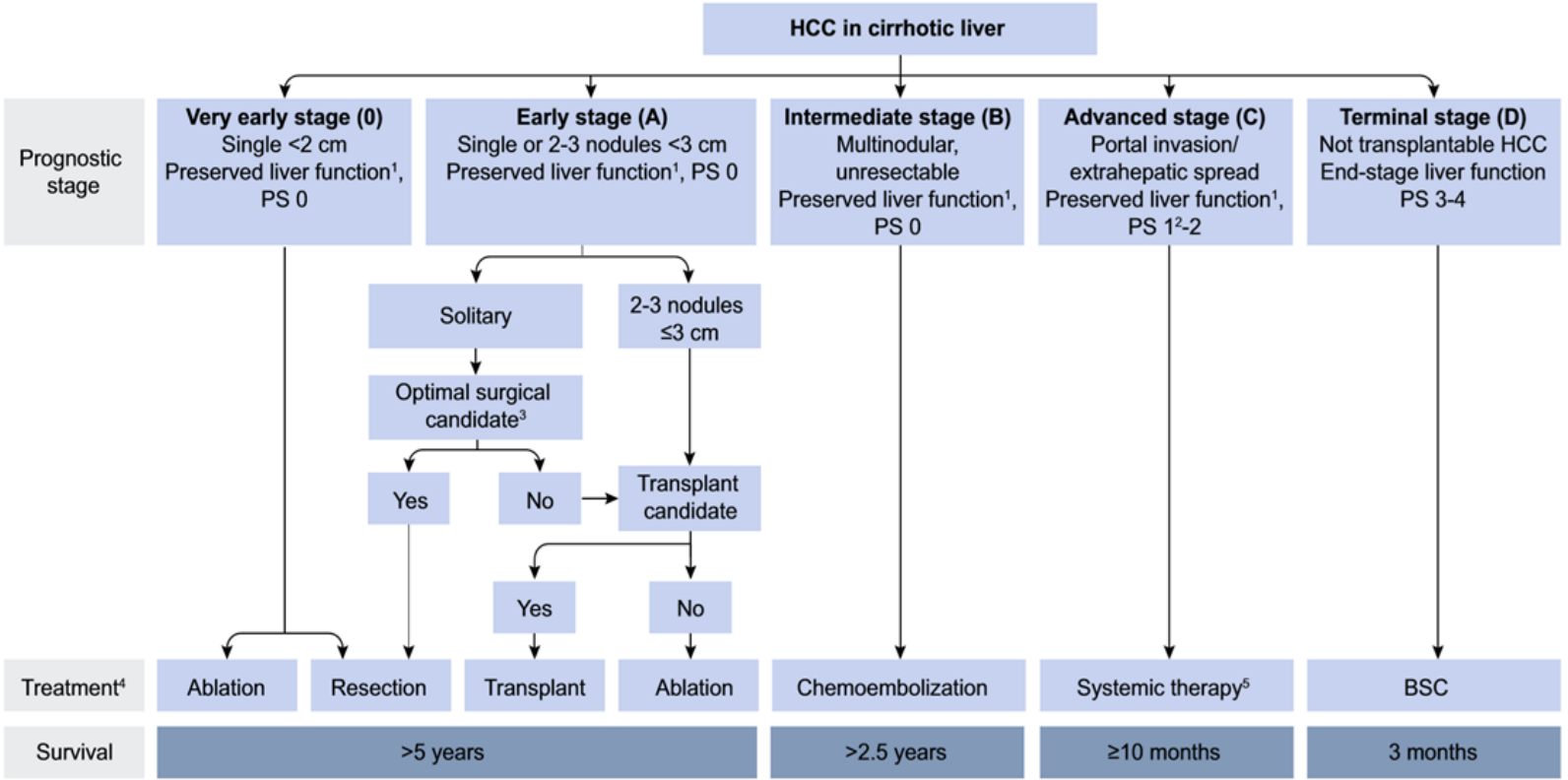
LIENS D’INTÉRÊT

AdBoard et/ou consultance : BAYER, EISAI, IPSEN, EXELIXIS, LILLY, ROCHE, BMS, ASTRA-ZENECA, MSD, ONXEO

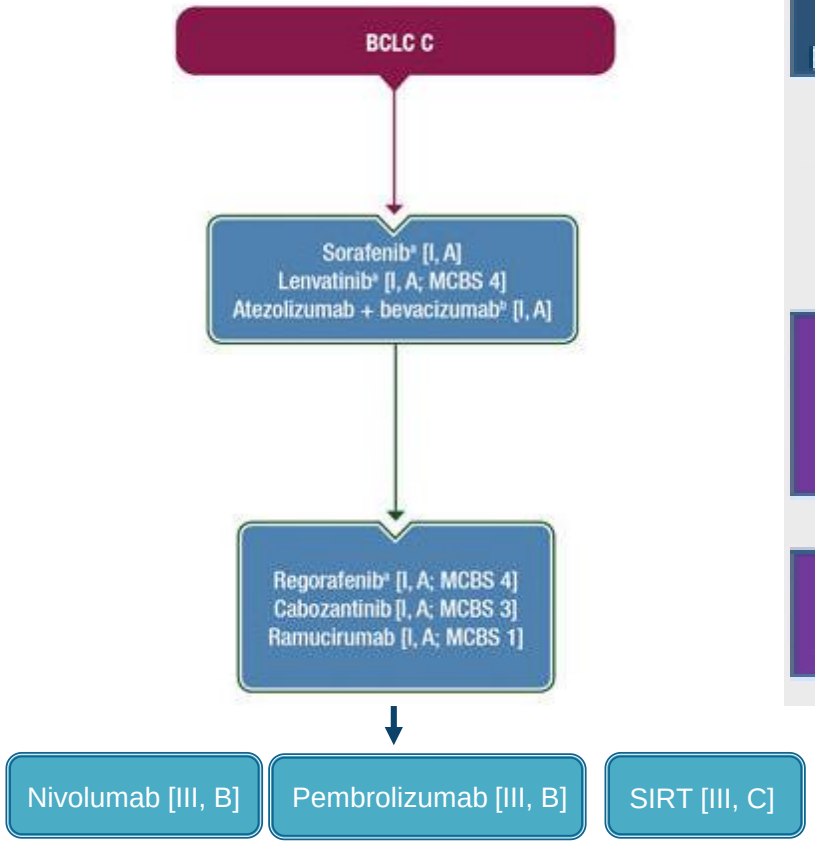
ALGORITHME BCLC : BARCELONA CLINIC LIVER CANCER GROUP



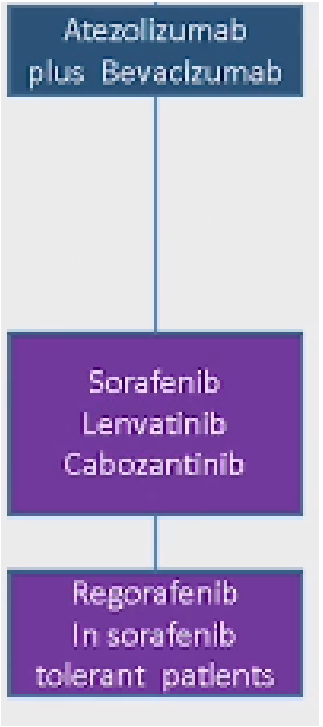
EASL guidelines 2018

Algorithme pour les traitements systémiques du CHC

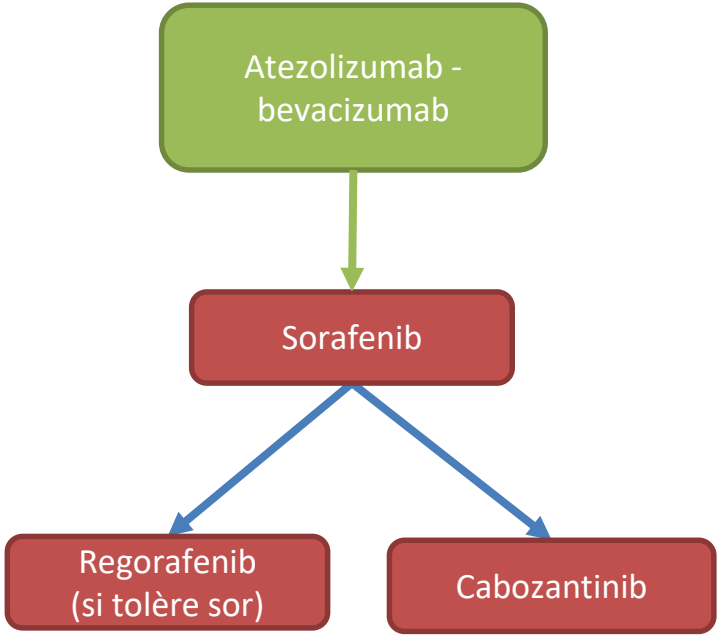
ESMO



ILCA



TNCD



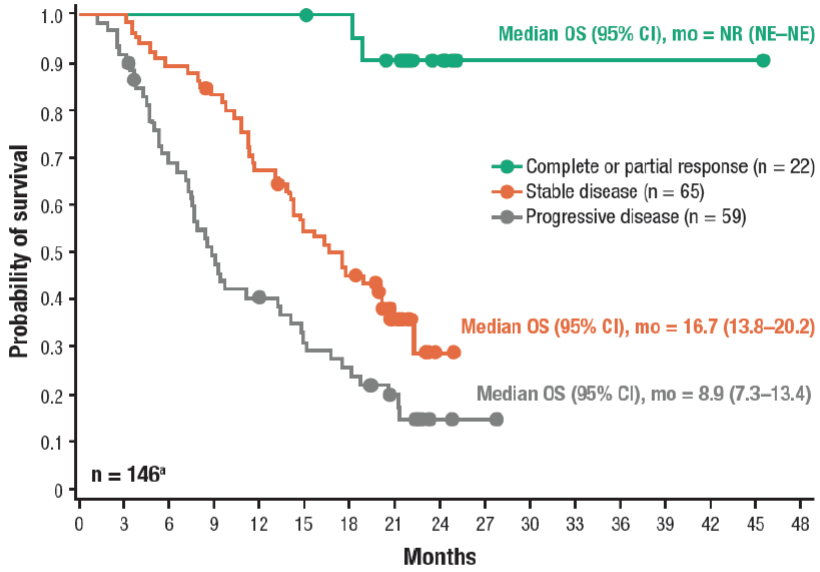
Trop peu de répondeurs en monothérapie d'inhibiteurs de checkpoint immunologiques (ICI) pour impacter sur les médianes de survie

Mais les répondeurs (complets ou partiels) en bénéficient largement

Taux de réponse élevés, DOR prolongées, ORR est un bon marqueur prédictif de survie

Médiane de survie prolongées avec plateau tardif sur courbes de Kaplan-Meier

(A) **Overall Survival by Best Overall Response**



OS rate (95% CI), %	Complete/partial response n = 22	Stable disease n = 65	Progressive disease n = 59
12 month	100 (100–100)	67 (55–77)	41 (28–53)
18 month	100 (100–100)	45 (33–57)	26 (15–38)

[a]Best overall response was unable to be determined in 8 patients

https://www.onclive.com/web-exclusives/fda-approves-nivolumab-for-hepatocellular-carcinoma

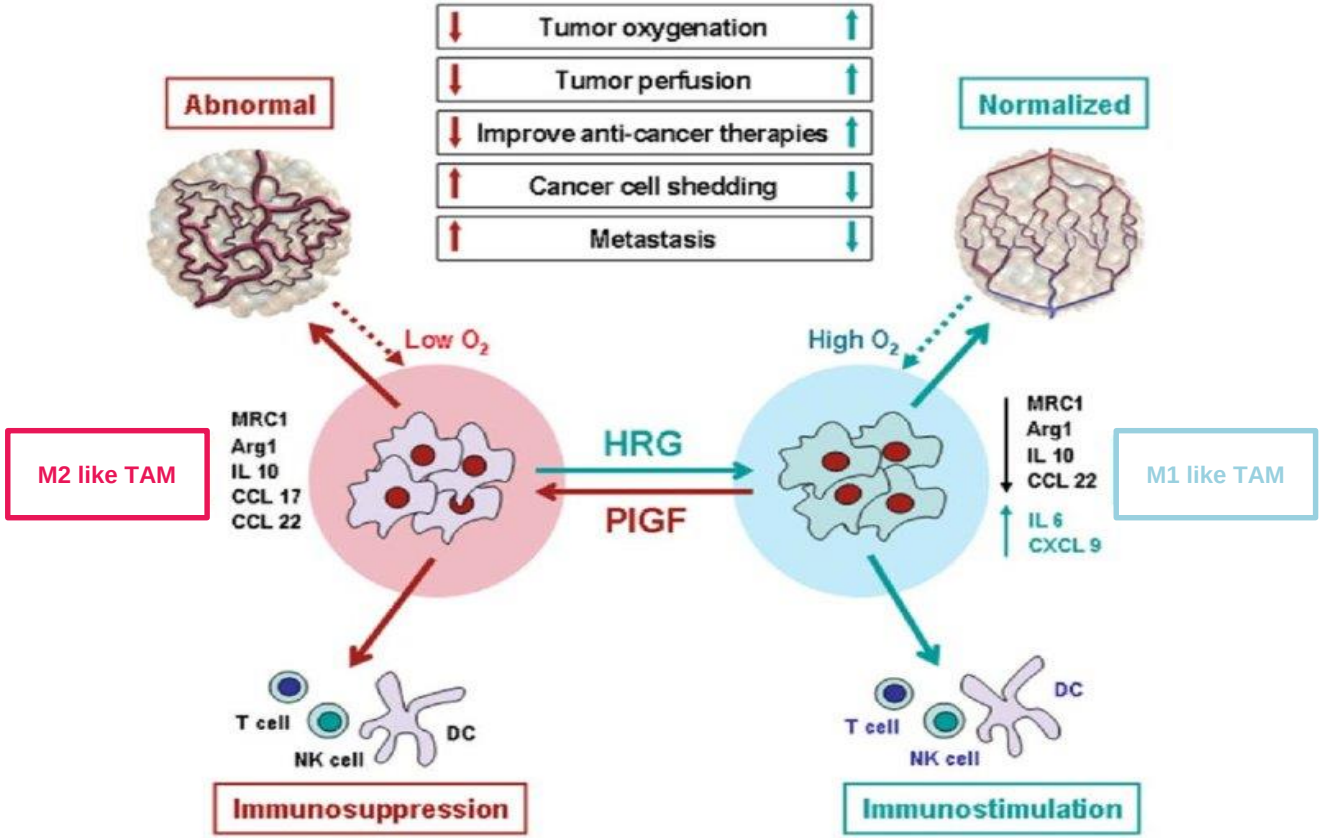
FDA Approves Nivolumab for Hepatocellular Carcinoma

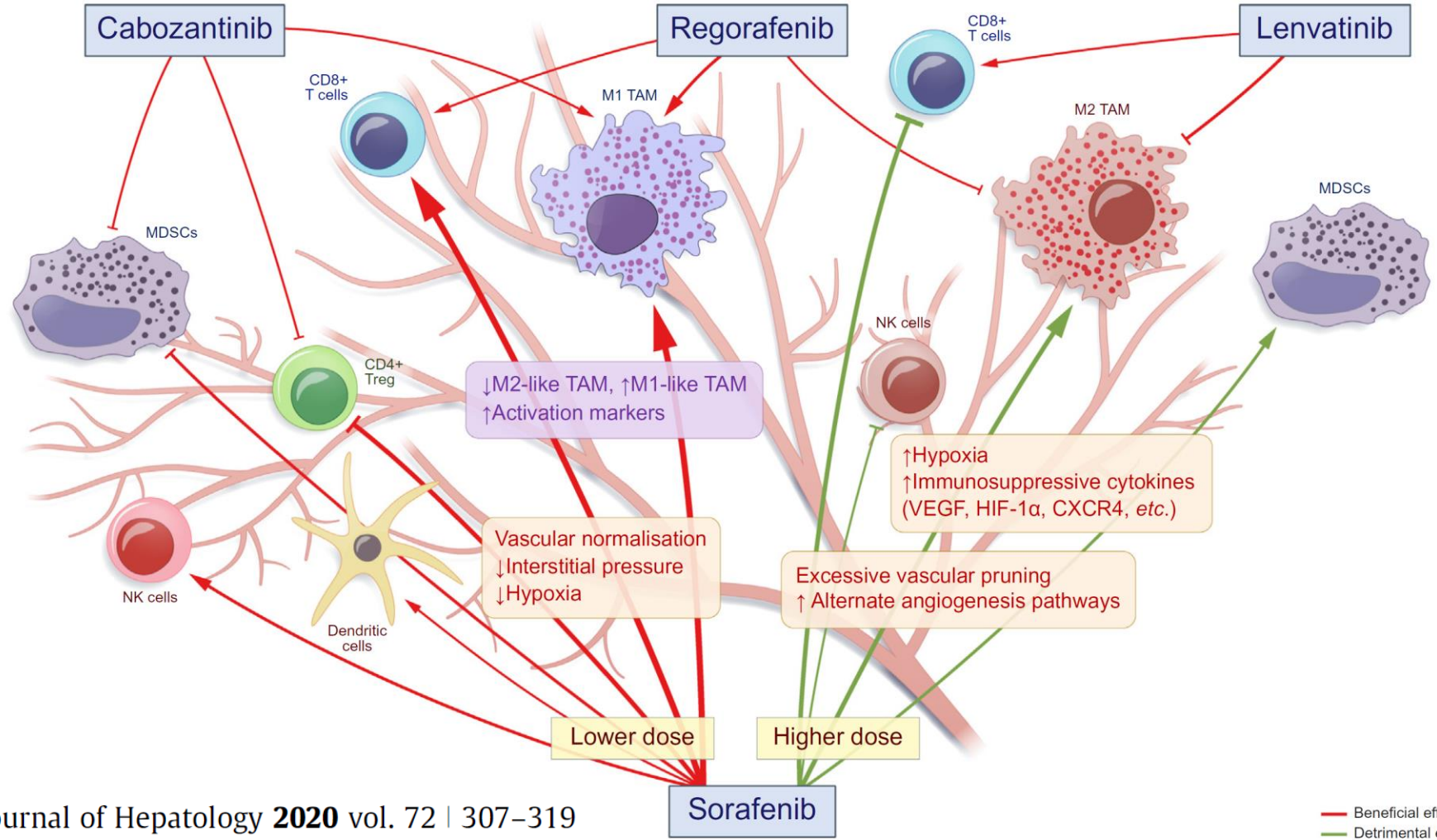
The FDA has granted an accelerated approval to nivolumab (Opdivo) for the treatment of patients with hepatocellular carcinoma (HCC) following prior sorafenib (Nexavar), regardless of PD-L1 status.

Meyer T, EASL 2018

Rationnel des combinaisons (IO + IO) ou (IO + TKI) ou (IO + bevacizumab)

Rationnel des anti-VEGF/VEGFR





Journal of Hepatology **2020** vol. 72 | 307–319

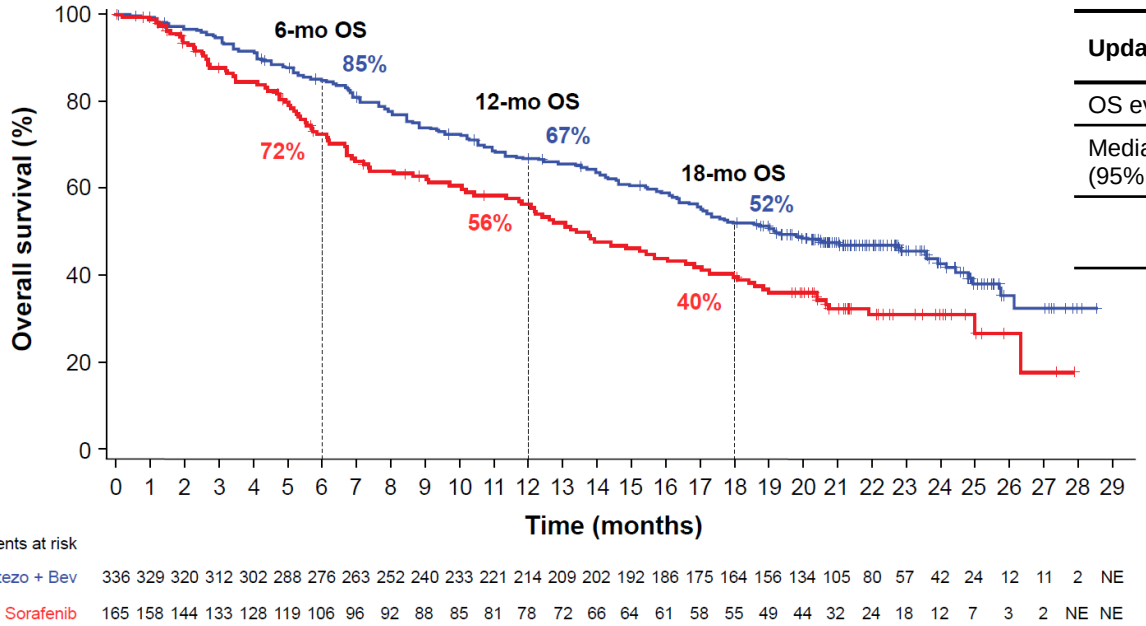
IMbrave150: updated overall survival data from a global, randomized, open-label Phase III study of atezolizumab + bevacizumab vs sorafenib in patients with unresectable hepatocellular carcinoma

Finn RS,[1] Qin S,[2] Ikeda M,[3] Galle PR,[4] Ducreux M,[5] Kim T-Y,[6] Lim HY,[7] Kudo M,[8] Breder V,[9] Merle P,[10] Kaseb A,[11] Li D,[12] Verret W,[13] Shao H,[14] Liu J,[14] Li L,[14] Zhu AX,[15] Cheng AL[16]

[1]Jonsson Comprehensive Cancer Center, Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [2]People's Liberation Army Cancer Center, Nanjing, People's Republic of China; [3]National Cancer Center Hospital East, Kashiwa, Japan; [4]University Medical Center Mainz, Mainz, Germany; [5]Gustave Roussy Cancer Center, Villejuif, France; [6]Seoul National University College of Medicine, Seoul, Korea; [7]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; [8]Kindai University Faculty of Medicine, Osaka, Japan; [9]N.N. Blokhin Russian Cancer Research Center, Moscow, Russia; [10]University Hospital La Croix-Rousse, Lyon, France; [11]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [12]City of Hope Comprehensive Cancer Center and Beckman Research Institute, Duarte, CA, USA; [13]Genentech, Inc., South San Francisco, CA, USA; [14] Roche Product Development, Shanghai, People's Republic of China; [15]Harvard Medical School, Massachusetts General Hospital Cancer Center, Boston, MA, USA; [16]National Taiwan University Cancer Center and National Taiwan University Hospital, Taipei, Taiwan

Finn et al., NEJM 2020; updated in Finn et al., ASCO-GI 2021

Updated OS



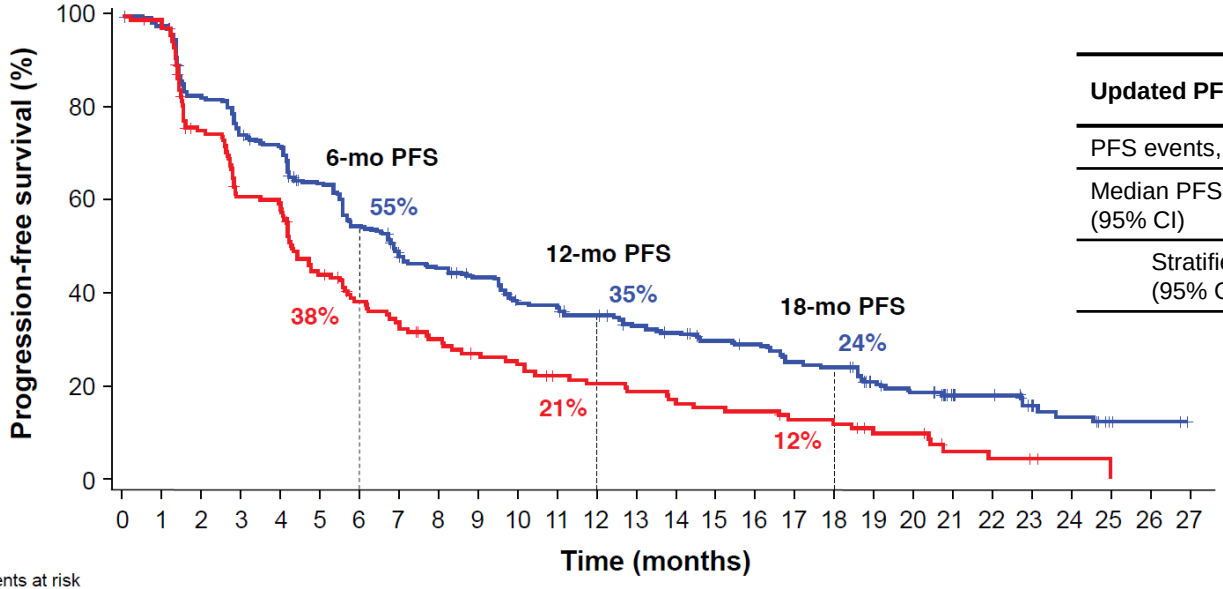
Updated OS	Atezo + Bev (n = 336)	Sorafenib (n = 165)
OS events, n (%)	180 (54)	100 (61)
Median OS, mo (95% CI)	**19.2** (17.0, 23.7)	**13.4** (11.4, 16.9)
Stratified HR (95% CI)[a]	**0.66** (0.52, 0.85) *P* = 0.0009[b]	

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 et al., NEJM 2020; updated in Finn et al., ASCO-GI 2021

Updated PFS by IRF RECIST 1.1



No. of patients at risk

Atezo + Bev	336	323	271	245	234	204	174	149	141	132	113	111	102	93	88	80	77	67	64	47	41	27	25	17	12	4	3	NE
Sorafenib	165	150	110	88	84	63	52	44	39	34	31	26	24	22	19	18	17	14	13	9	9	4	3	2	1	1	NE	NE

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]	

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 et al., NEJM 2020; updated in Finn et al., ASCO-GI 2021

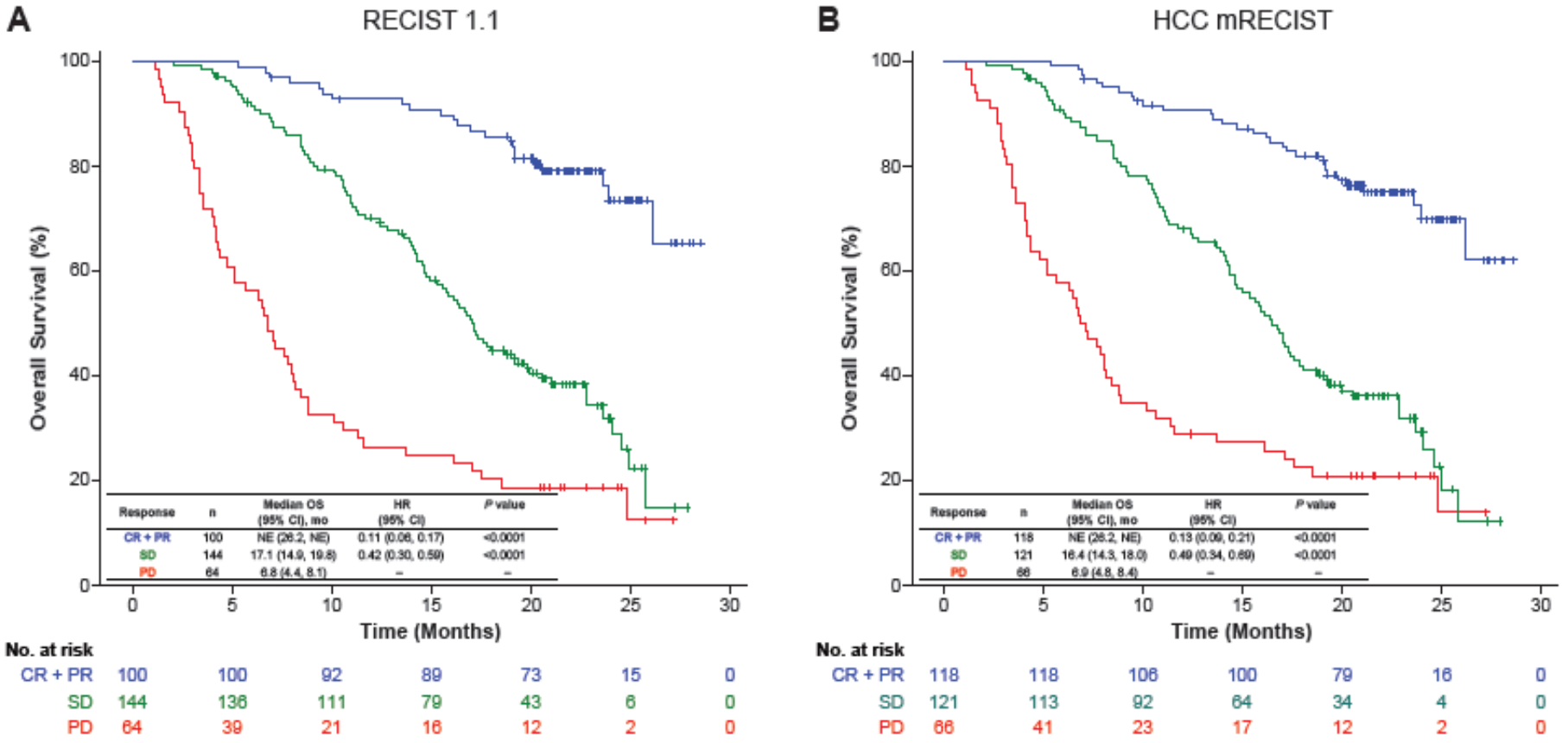
Updated response and duration of response

	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)
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.
[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.

Finn et al., NEJM 2020; updated in Finn et al., ASCO-GI 2021

IMbrave150: Exploratory analysis on association between ORR / OS



Ducreux et al., ASCO 2021

L'AVENIR ?

Pour les CHC avancés

Combination de différents ICI

Durvalumab + Tremelimumab : phase 3 (HIMALAYA)

Nivolumab + Ipilimumab : phase 3 (CheckMate-9DW)

Combination d'un ICI et d'un ITK

Pembrolizumab + Lenvatinib : phase 3 (LEAP-002)

Atezolizumab + Cabozantinib : phase 3 (COSMIC-312)

ESMO VIRTUAL PLENARY

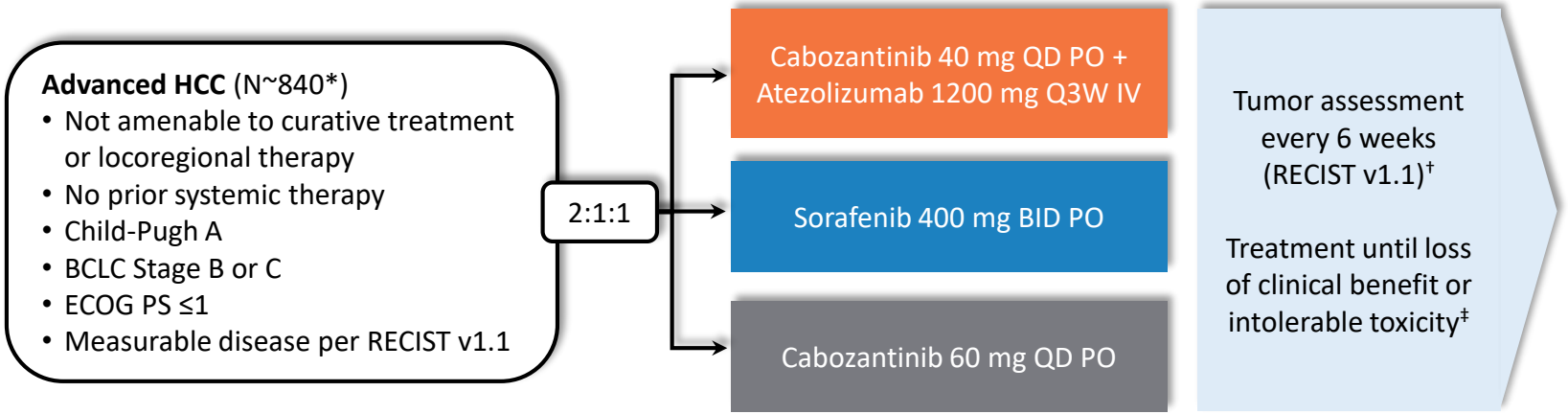
ABSTRACT NUMBER

Cabozantinib plus atezolizumab versus sorafenib as first-line systemic treatment for advanced hepatocellular carcinoma: results from the randomized phase 3 COSMIC-312 trial

Robin Kate Kelley, Thomas Yau, Ann-Lii Cheng, Ahmed Kaseb, Shukui Qin, Andrew Zhu, Stephen Chan, Wattana Sukeepaisarnjaroen, Valery Breder, Gontran Verset, Edward Gane, Ivan Borbath, Jose David Gomez Rangel, Philippe Merle, Fawzi Benzaghou, Kamalika Banerjee, Saswati Hazra, Jonathan Fawcett, Lorenza Rimassa

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

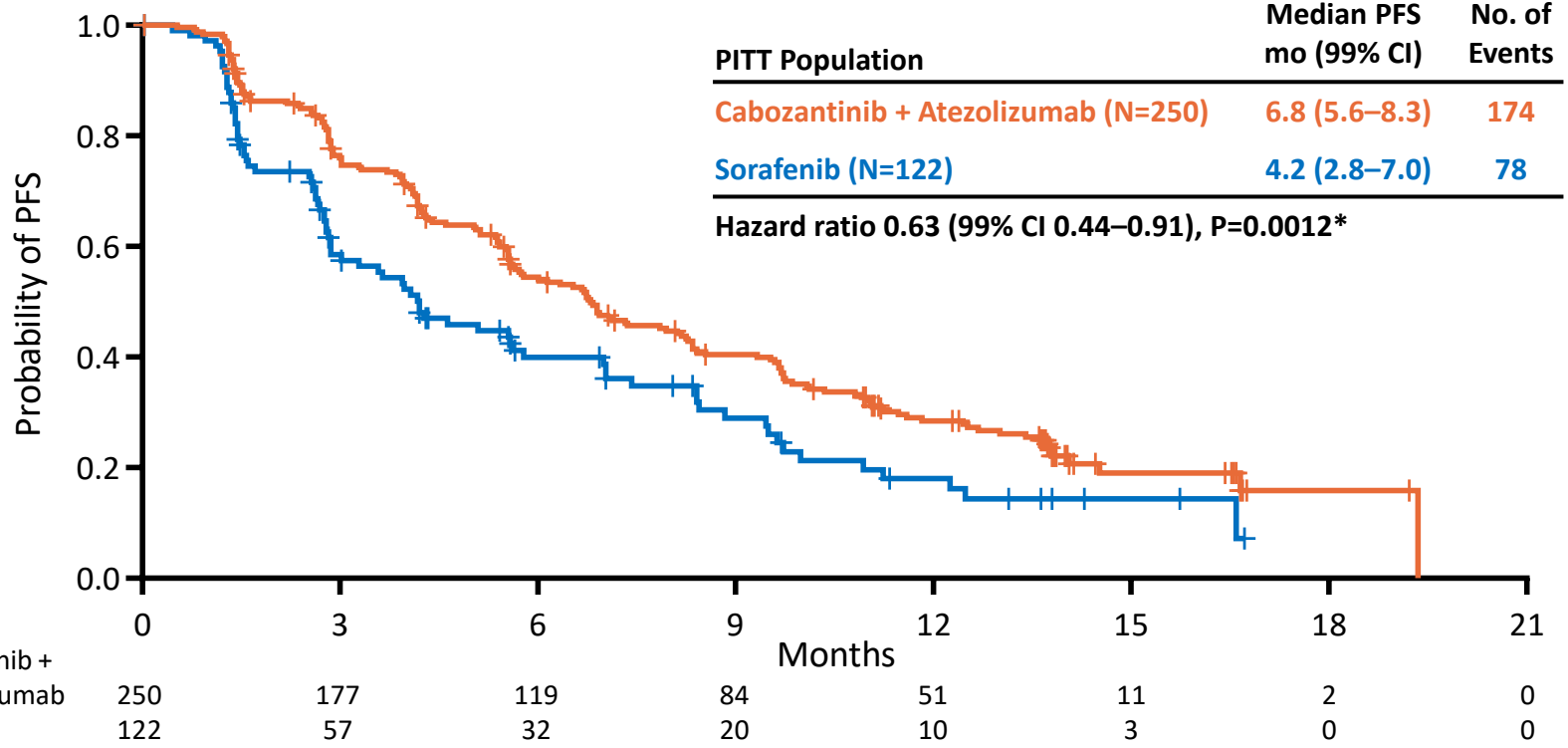
COSMIC-312 Study Design



Stratification
- Disease etiology (HBV, HCV [without HBV], non-viral)
- Region (Asia, other)
- Presence of extrahepatic disease and/or macrovascular invasion (yes, no)

*An Extension Phase in China is ongoing and is not included in the present analyses.
†Every 6 weeks for the first 48 weeks then every 12 weeks thereafter
‡Patients may be treated beyond progression if there is a clinical benefit in the opinion of the investigator.

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



PITT Population	Median PFS mo (99% CI)	No. of Events
Cabozantinib + Atezolizumab (N=250)	6.8 (5.6–8.3)	174
Sorafenib (N=122)	4.2 (2.8–7.0)	78

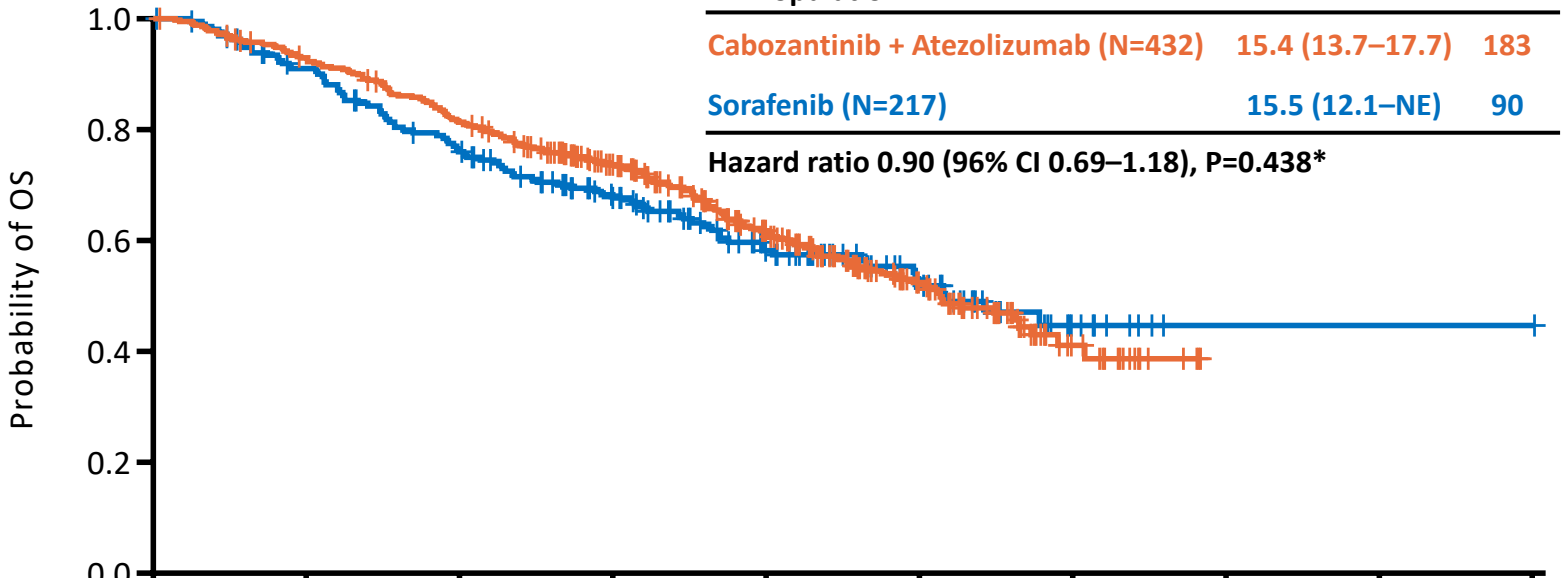
Hazard ratio 0.63 (99% CI 0.44–0.91), P=0.0012*

No. at risk	0	3	6	9	12	15	18	21
Cabozantinib + Atezolizumab	250	177	119	84	51	11	2	0
Sorafenib	122	57	32	20	10	3	0	0

Median follow-up (range): 15.8 (12.8-27.0) months
PFS per RECIST v1.1 by BIRC

*Critical p-value 0.01

Primary Endpoint of Overall Survival: Interim Analysis Cabozantinib + Atezolizumab vs Sorafenib



ITT Population	Median OS mo (96% CI)	No. of Events
Cabozantinib + Atezolizumab (N=432)	15.4 (13.7–17.7)	183
Sorafenib (N=217)	15.5 (12.1–NE)	90

Hazard ratio 0.90 (96% CI 0.69–1.18), P=0.438*

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

Median follow-up (range): 13.6 (6.4-27.0) months

*Critical p-value 0.01362 for the interim analysis

Subsequent Anticancer Therapy

	Cabozantinib + Atezolizumab (N=432)	Sorafenib (N=217)	Cabozantinib (N=188)
Any non-radiation locoregional anticancer therapy, %	0.9	1.4	1.6
Any systemic anticancer therapy, %	20	37	29
Tyrosine kinase inhibitors	14	22	18
VEGF(R)-targeted antibodies	2.1	5.1	7.4
Immune checkpoint inhibitors	3.9	17	13

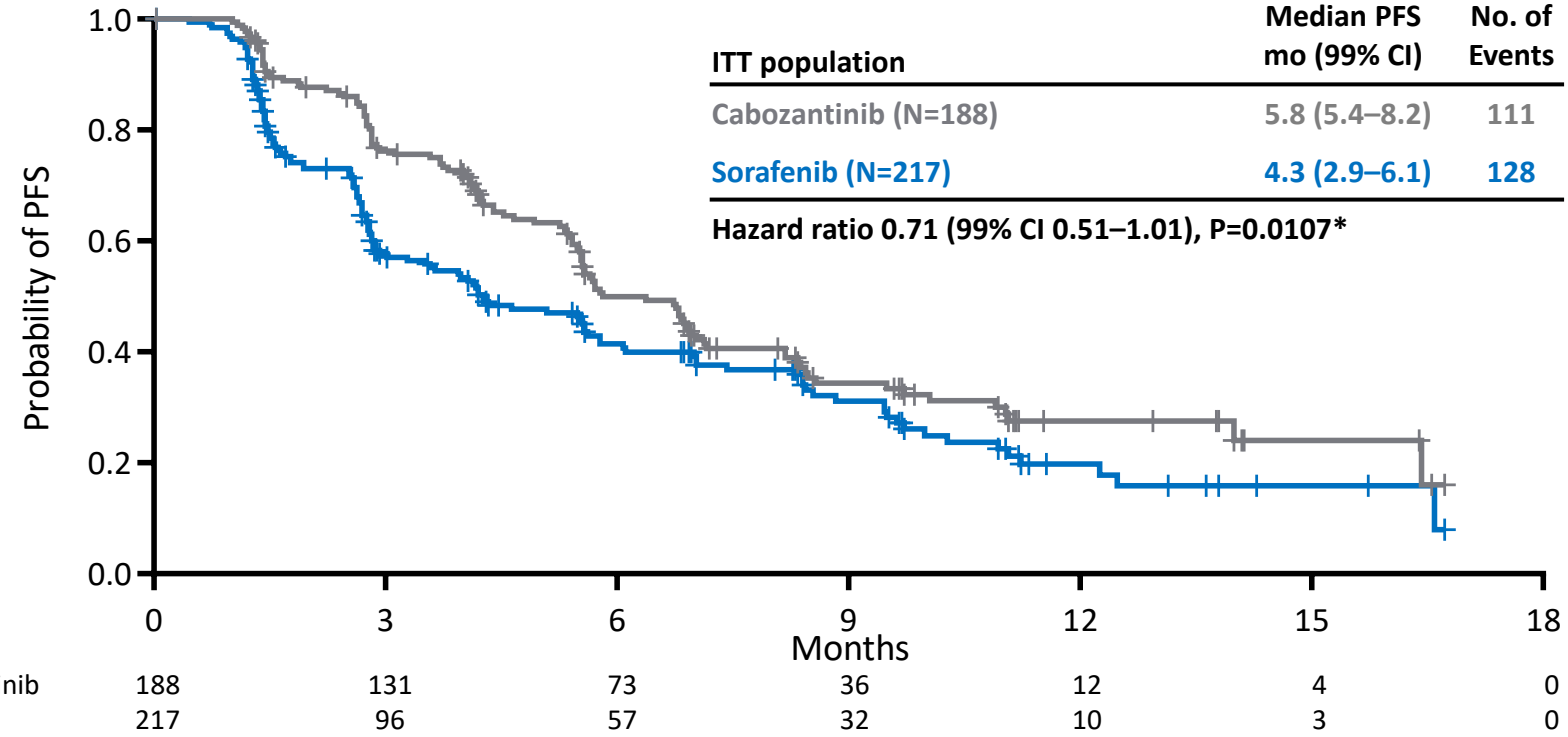
Tumor Response (ITT Population)

	Cabozantinib + Atezolizumab (N=432)	Sorafenib (N=217)	Cabozantinib (N=188)
Objective response rate (95% CI), %	11 (8.1–14)	3.7 (1.6–7.1)	6.4 (3.3–11)
Best overall response, %			
Complete response	0.2	0	0
Partial response	11	3.7	6.4
Stable disease	67	61	77
Progressive disease	14	20	11
No measurable disease, not evaluable, or missing	7.9	15	5.9
Disease control rate, %	78	65	83
Median time to objective response (range), mo	4.0 (1.3–10.0)	3.5 (1.0–5.4)	4.2 (1.4–6.9)
Median duration of response (95% CI), mo	10.6 (7.1–12.7)	8.8 (3.0–NE)	15.1 (4.4–NE)

Tumor response per RECIST 1.1 by BIRC

Disease control rate = complete response + partial response + stable disease

Secondary Endpoint of PFS: Interim Analysis Cabozantinib vs Sorafenib



ITT population	Median PFS mo (99% CI)	No. of Events
Cabozantinib (N=188)	5.8 (5.4–8.2)	111
Sorafenib (N=217)	4.3 (2.9–6.1)	128

Hazard ratio 0.71 (99% CI 0.51–1.01), P=0.0107*

No. at risk							
Cabozantinib	188	131	73	36	12	4	0
Sorafenib	217	96	57	32	10	3	0

Median follow-up (range): 13.6 (6.4-27.0) months
PFS per RECIST v1.1 by BIRC

*Critical p-value 0.00451 for the interim analysis

Abstract 4508

Efficacy, tolerability, and biologic activity of a novel regimen of tremelimumab in combination with durvalumab for patients with advanced hepatocellular carcinoma

R. Katie Kelley,[1] Bruno Sangro,[2] William Harris,[3] Masafumi Ikeda,[4] Takuji Okusaka,[5] Yoon-Koo Kang,[6] Shukui Qin,[7] David Wai Meng Tai,[8] Hoyeong Lim,[9] Thomas Yau,[10] Wei Peng Yong,[11] Ann-Lii Cheng,[12] Antonio Gasbarrini,[13] Silvia Damian,[14] Jordi Bruix,[15] Mitesh Borad,[16] Philip He,[17] Alejandra Negro,[17] Masatoshi Kudo[18] and Ghassan K. Abou-Alfa[19]

[1]University of California, San Francisco, CA; [2]Liver Unit, Clínica Universidad de Navarra, IDISNA and CIBEREHD, Pamplona, Spain; [3]University of Washington, Seattle, WA; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]National Cancer Center Hospital, Tokyo, Japan; [6]Asan Medical Center, Department of Oncology, Seoul, South Korea; [7]PLA Cancer Center & Bayi Clinical Trial Institute, Nanjing, China; [8]National Cancer Centre Singapore, Singapore; [9]Samsung Medical Center Seoul, South Korea; [10]Queen Mary Hospital, Hong Kong; [11]National University Cancer Institute, Singapore; [12]National Taiwan University, Taipei, Taiwan; [13]Catholic University of the Sacred Heart, Milano, Italy; [14] Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy; [15]BCLC, Hospital Clínic, IDIBAPS and CIBEREHD, Barcelona, Spain; [16]Mayo Clinic Cancer Center, Phoenix, AZ; [17]AstraZeneca, Gaithersburg, MD; [18]Kindai University Faculty of Medicine, Osaka, Japan; [19]Memorial Sloan Kettering Cancer Center, New York, NY and Weill Medical College at Cornell University New York, NY.

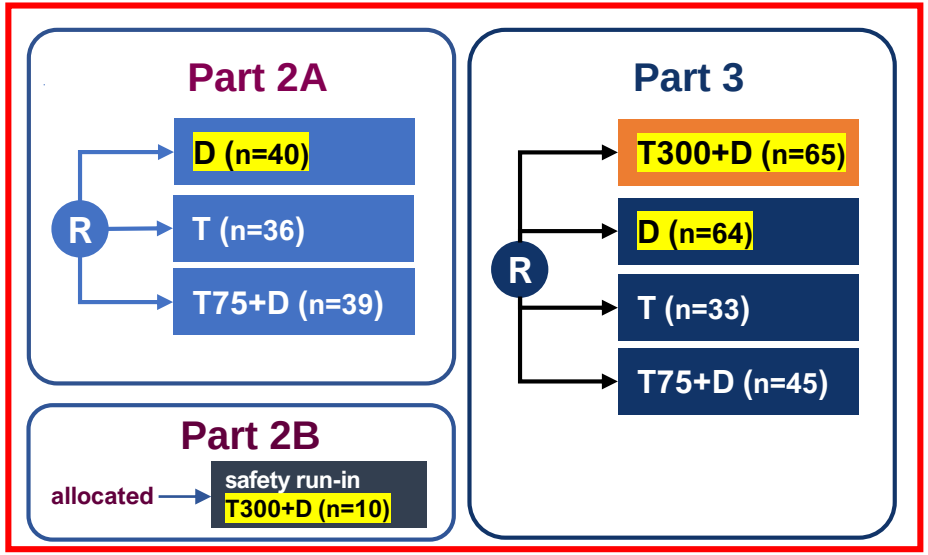
Kelley et al., ASCO 2020

Presented By Robin Kelley at TBD

DURVA/TREME: DESIGN de la phase-1b/2 (résultats de la phase-3 début 2022 – Communiqué de presse positif)

Key Eligibility Criteria:

- Histologically confirmed disease
- Progressed on, intolerant to, or refused sorafenib
  - Predominantly 2L population



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

Objectives and Assessments

Primary Endpoint: Safety

Key Secondary Endpoints
- OS
- Objective response rate
- DOR

Other Secondary Endpoints
- PFS
- DCR
- Time to response

Key Assessments
- Triphasic imaging Q8W
- Circulating immune cells
- PD-L1 status (Ventana SP263)

Kelley et al., ASCO 2020

DURVA/TREME: ORR

	T300+D (n = 75)	D (n = 104)	T (n = 69)	T75+D (n = 84)
Objective Response Rate[a] (95% CI), %	**24.0** (14.9-35.3)	**10.6** (5.4-18.1)	**7.2** (2.4-16.1)	**9.5** (4.2-17.9)
CR, n (%)	1 (1.3)	0	0	2 (2.4)
PR, n (%)	17 (22.7)	11 (10.6)	5 (7.2)	6 (7.1)
SD, n (%)	16 (21.3)	28 (26.9)	29 (42.0)	23 (27.4)
Disease Control Rate, n (%)	34 (45.3)	39 (37.5)	34 (49.3)	31 (36.9)
Median Duration of Response,[b] months	**NR**	**11.17**	**23.95**	**13.21**
Median Time to Response, months	1.86	3.65	1.81	2.86
PFS, months, median (95% CI)	2.17 (1.91-5.42)	2.07 (1.84-2.83)	2.69 (1.87-5.29)	1.87 (1.77-2.43)

[a]By blinded independent central review using RECIST v1.1

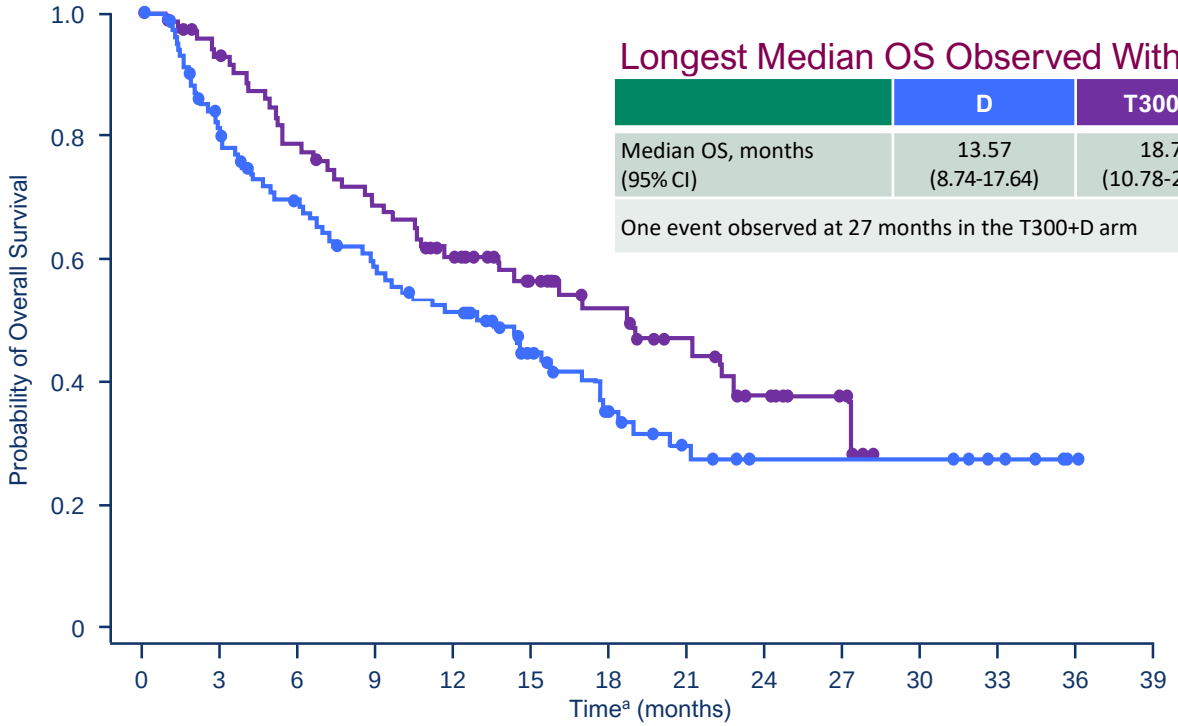
[b]Time from the first documentation of a confirmed CR/PR until the date of progression, death, or the last evaluable RECIST assessment

CI, confidence interval; CR, complete response; D, durvalumab; NR, not reached; PFS, progression-free survival; PR, partial response; SD, stable disease; T, tremelimumab

Kelley et al., ASCO 2020

Presented By Robin Kelley at TBD

DURVA/TREME: OS



Longest Median OS Observed With T300+D

	D	T300+D
Median OS, months (95% CI)	13.57 (8.74-17.64)	18.73 (10.78-27.27)

One event observed at 27 months in the T300+D arm

Kelley et al., ASCO 2020

Nivolumab + Ipilimumab Combination Therapy in Patients With Advanced Hepatocellular Carcinoma: Results From CheckMate 040

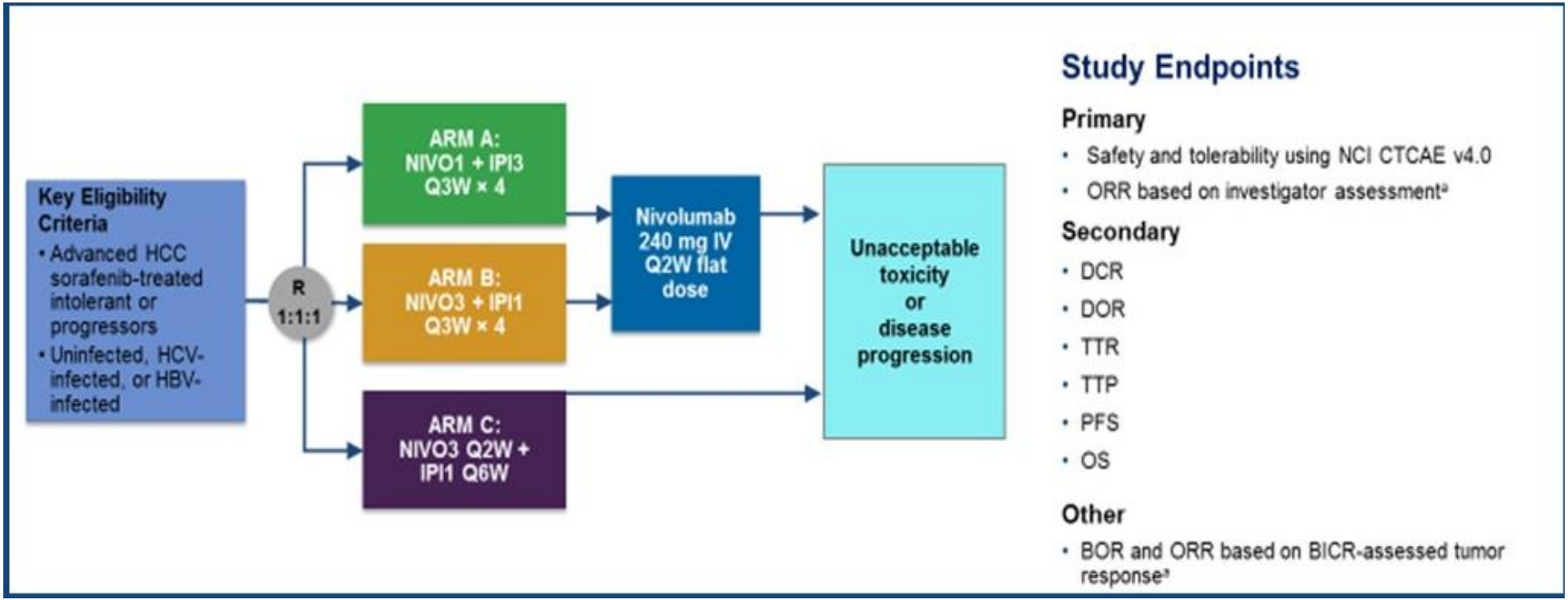
Thomas Yau,[1] Yoon-Koo Kang,[2] Tae-You Kim,[3] Anthony B. El-Khoueiry,[4] Armando Santoro,[5] Bruno Sangro,[6] Ignacio Melero,[7] Masatoshi Kudo,[8] Ming-Mo Hou,[9] Ana Matilla,[10] Francesco Tovoli,[11] Jennifer J. Knox,[12] Aiwu Ruth He,[13] Bassel El-Rayes,[14] Mirelis Acosta-Rivera,[15] Jaclyn Neely,[16] Yun Shen,[16] Carlos Baccan,[16] Chiun Hsu[17]

[1]University of Hong Kong, Hong Kong, China; [2]Asan Medical Center, University of Ulsan, Seoul, South Korea; [3]Seoul National University, Seoul, South Korea; [4]USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [5]Istituto Clinico Humanitas, Rozzano, Italy; [6]Clinica Universidad de Navarra and CIBEREHD, Pamplona, Spain; [7]Universidad de Navarra, Pamplona, Spain; [8]Kindai University Faculty of Medicine, Osaka, Japan; [9]Chang Gung Memorial Hospital, Taipei, Taiwan; [10]Servicio de Digestivo, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [11]Department of Medical & Surgical Sciences, University of Bologna, Bologna, Italy; [12]Princess Margaret Cancer Centre, Toronto, Canada; [13]Georgetown University Hospital, Washington, DC, USA; [14]Emory University Winship Cancer Institute, Atlanta, GA, USA; [15]Fundacion de Investigacion, San Juan, Puerto Rico; [16]Bristol- Myers Squibb, Princeton, NJ, USA; [17]National Taiwan University Hospital, Taipei, Taiwan

Abstract Number 4012

Yau et al., ASCO 2019

NIVO/IPI: DESIGN de la phase-1b/2 (résultats de phase-3 pour 2023)



Yau et al., ASCO 2019

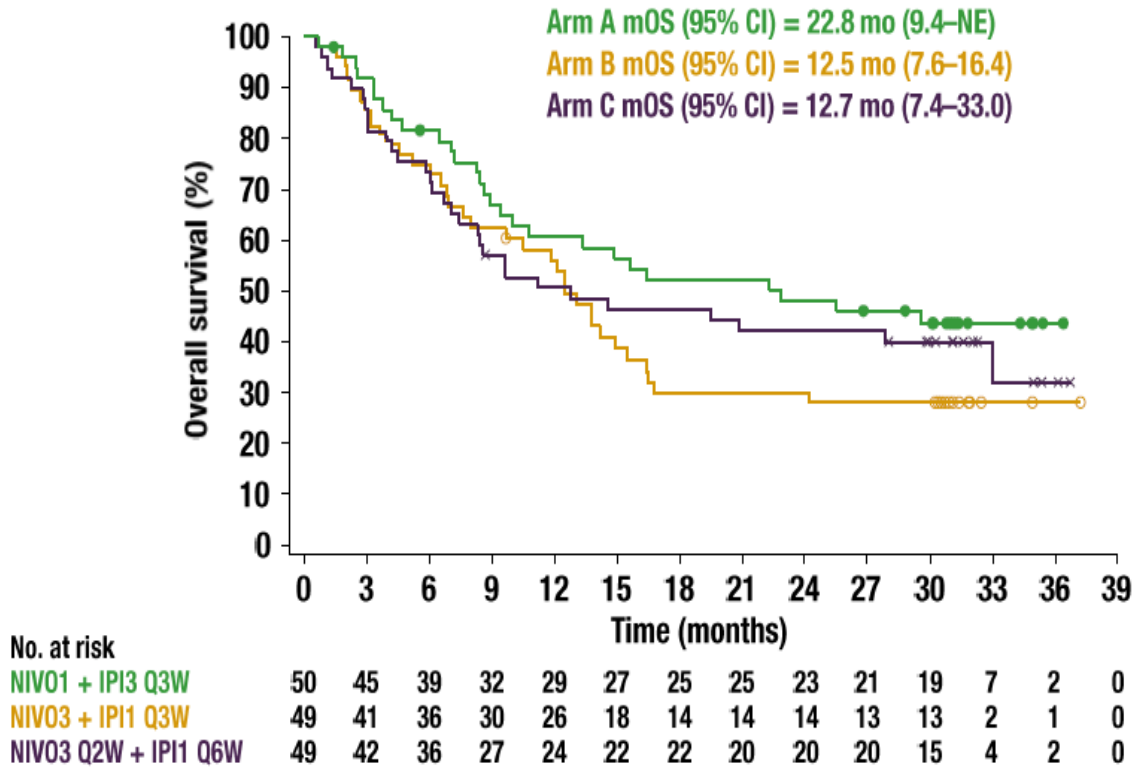
NIVO/IPI: ORR

	Arm A NIVO1/IPI3 Q3W[a] n = 50	Arm B NIVO3/IPI1 Q3W[b] n = 49	Arm C NIVO3 Q2W/IPI1 Q6W n = 49
ORR by BICR using RECIST v1.1,[c] n (%)	16 (32)	15 (31)	15 (31)
BOR, n (%)			
CR	4 (8)	3 (6)	0
PR	12 (24)	12 (24)	15 (31)
SD[d]	9 (18)	5 (10)	9 (18)
PD	20 (40)	24 (49)	21 (43)
Unable to determine	3 (6)	4 (8)	4 (8)
DCR,[e] n (%)	27 (54)	21 (43)	24 (49)
Median TTR (range), months	2.0 (1.1–12.8)	2.6 (1.2–5.5)	2.7 (1.2–8.7)
Median DOR (range), months	17.5 (4.6 to 30.5+)	22.2 (4.2 to 29.9+)	16.6 (4.1+ to 32.0+)
ORR by investigator assessment using RECIST v1.1, n (%)	16 (32)	13 (27)	14 (29)

[a]NIVO1/IPI3 Q3W × 4 followed by nivolumab 240 mg IV Q2W flat dose; [b]NIVO3/IPI1 Q3W × 4 followed by nivolumab 240 mg IV Q2W flat dose; [c]Defined as CR + PR; [d]SD does not include 2 patients in Arm A and 1 patient in Arm B who were reported as non-CR/non-PD; [e]Defined as CR + PR + SD + non-CR/non-PD.
PR, partial response; SD, stable disease.

Yau et al., ASCO 2019

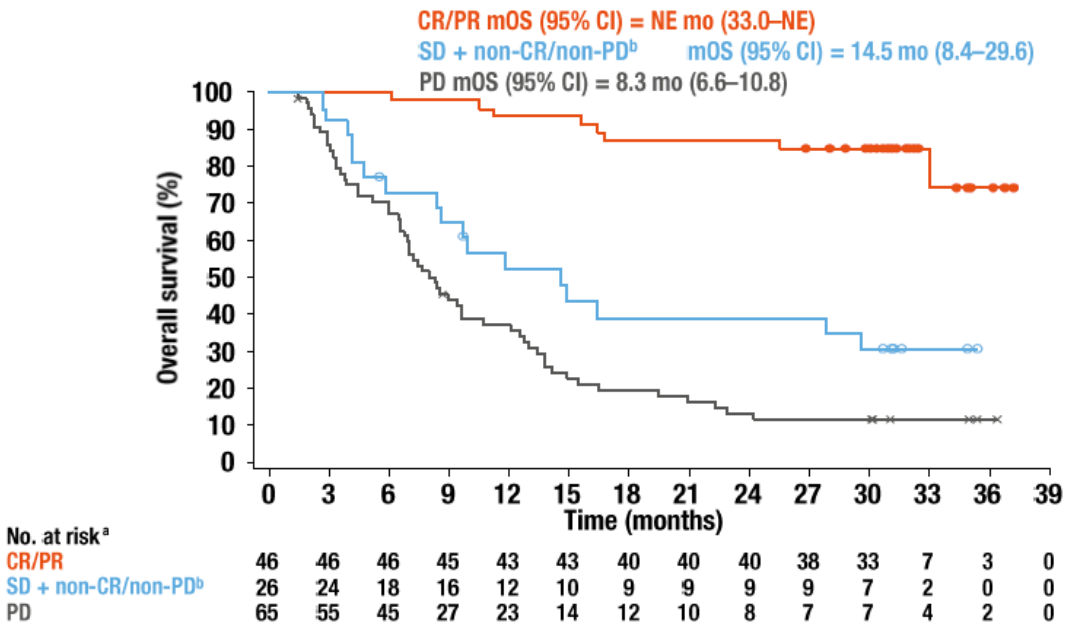
NIVO/IPI: OS



OS parameter	Arm A NIVO1/IPI3 Q3W[a] n = 50	Arm B NIVO3/IPI1 Q3W[b] n = 49	Arm C NIVO3 Q2W/IPI1 Q6W n = 49
12-mo OS rate, % (95% CI)	61 (46–73)	56 (41–69)	51 (36–64)
18-mo OS rate, % (95% CI)	52 (37.5–65)	30 (18–43.5)	47 (32–60)
24-mo OS rate, % (95% CI)	48 (34–61)	30 (18–43.5)	42 (28–56)
30-mo OS rate, % (95% CI)	44 (29.5–57)	28 (16–41)	40 (26.5–54)

Yau et al., ASCO 2019

Figure 4. Overall survival by BOR in overall patient population



	All patients N = 148
ORR by BICR using RECIST v1.1,[c] n (%)	46 (31)
BOR, n (%)	
CR	7 (5)
PR	39 (26)
SD[d]	23 (16)
PD	65 (44)
Unable to determine	11 (7)
DCR,[e] n (%)	72 (49)

[a]Eleven patients did not have a scan; therefore, BOR could not be determined; [b]Non-CR/non-PD are patients who only have non-target lesions at baseline and so do not meet the definition of SD by BICR; [c]Defined as CR + PR; [d]SD does not include 2 patients in Arm A and 1 patient in Arm B who were reported as non-CR/non-PD; [e]Defined as CR + PR + SD + non-CR/non-PD.

Yau et al., ASCO 2019

PEMBRO/LENVA: DESIGN de la phase-1b/2 (Résultats intermédiaires pour début 2022)

Lenvatinib 12 mg or 8 mg daily orally (based on body weight) + **pembrolizumab** 200 mg IV on Day 1 (21-day cycle)

DLT Evaluation (Part 1)
- n=6
- Patients ineligible for other therapies
- Tolerability evaluated by DLTs during cycle 1

Expansion (Part 2)
- n=98
- No prior systemic therapy for uHCC

Key Eligibility Criteria
- uHCC
- BCLC stage B (not applicable for TACE) or C
- Child-Pugh class A
- ECOG PS 0-1
- At least 1 measurable target lesion according to mRECIST

Primary Endpoints
- Safety and tolerability (Part 1)
- ORR and DOR by mRECIST and RECIST version 1.1 based on IIR (Part 2)

Selected Secondary and Exploratory Endpoints
- PFS
- Time to progression
- OS
- Pharmacokinetics
- ADAs for pembrolizumab

Tumor assessments were performed according to mRECIST by IR and IIR, and RECIST version 1.1 per IIR

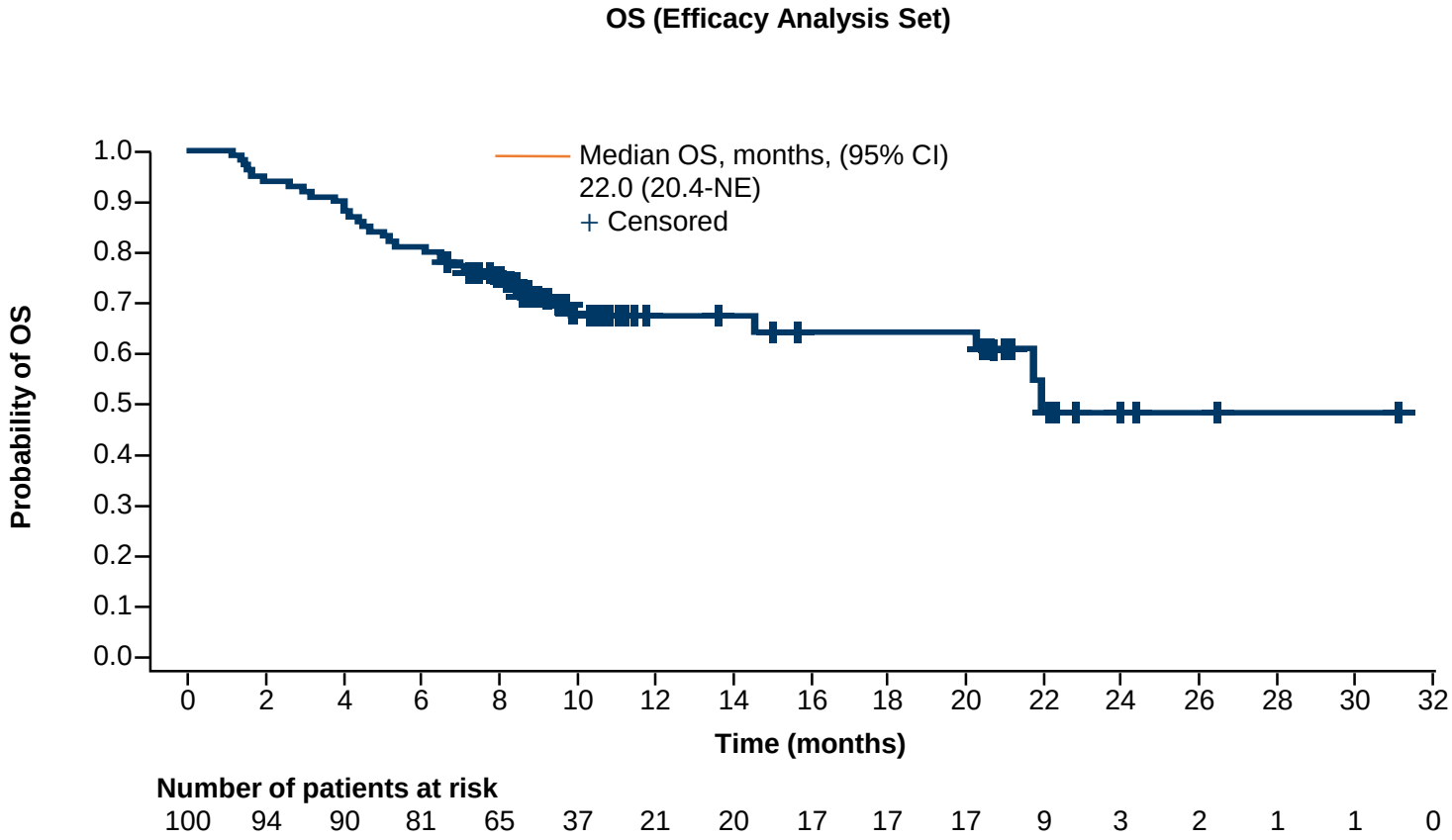
Zhu et al., ASCO 2020

PEMBRO/LENVA: ORR

Summary of Efficacy Outcomes			
	Lenvatinib + pembrolizumab (N=100)		
Parameter	**mRECIST per IIR**	**RECIST version 1.1 per IIR**	**mRECIST per IR**
ORR (confirmed response), n (%) (95% CI)[a]	45 (46) (36.0–56.3)	36 (36) (26.6–46.2)	41 (41) (31.3–51.3)
Best overall response, n (%)			
Complete response	11 (11)	1 (1)	5 (5)
Partial response	35 (35)	35 (35)	36 (36)
Stable disease[b]	42 (42)	52 (52)	45 (45)
Progressive disease	7 (7)	7 (7)	7 (7)
Unknown/not evaluable	5 (5)	5 (5)	7 (7)
Median DOR[c] for confirmed responders, months (95% CI)[d]	8.6 (6.9–NE)	12.6 (6.9–NE)	12.6 (6.2–18.7)
Median TTR for confirmed responders, months (range)	1.9 (1.2–5.5)	2.8 (1.2–7.7)	2.7 (1.2–11.8)
DCR, n (%) (95% CI)[a]	88 (88) (80.0–93.6)	88 (88) (80.0–93.6)	86 (86) (77.6–92.1)

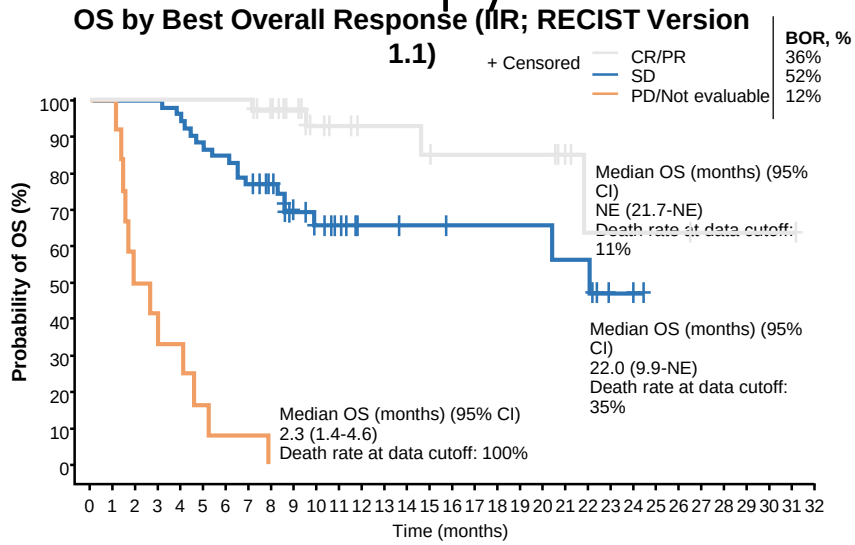
Zhu et al., ASCO 2020

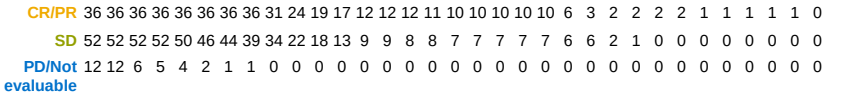
PEMBRO/LENVA: ORR

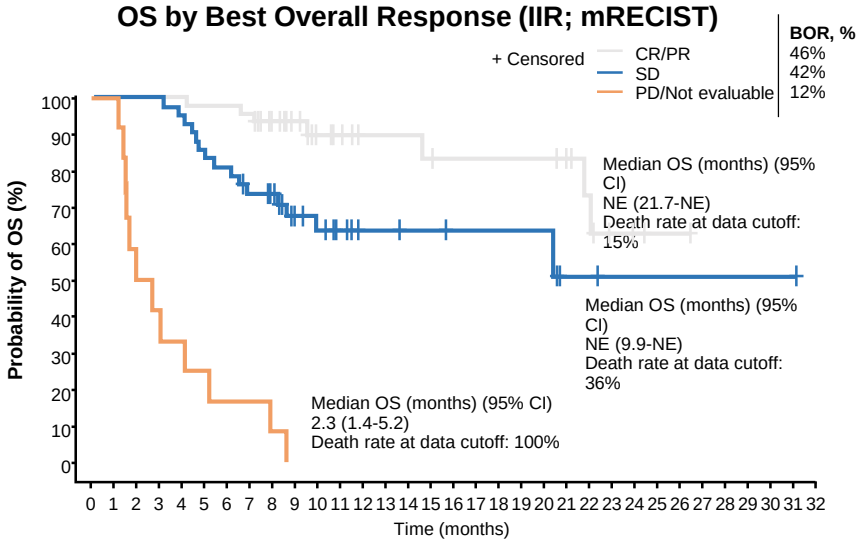


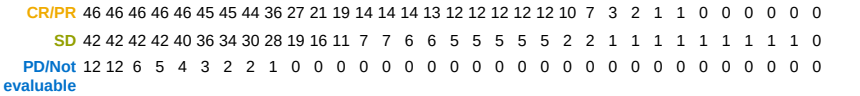
Zhu et al., ASCO 2020

KEYNOTE-524: ORR as a Potential Surrogate Marker for the Outcome of Patients Under IO Monotherapy









Zhu et al., ASCO 2020

Et après-demain ?

Pour les CHC avancés

Combinaison de différents ICI en 2L

Anti-PD1 + anti-LAG3 : phase 2 (après échec de TKI)

Anti-PD1 + anti-TIM3 : phase 2

Combinaision d'un ICI et d'un ITK en 2L après échec d'IO en 1L

Anti-PD-L1 + Lenvatinib (après échec Atezo/Bev en 1L)

Anti-PD-1 + Régorafenib (après échec de combinaison d'IO en 1L)

Pour les CHC intermédiaires

CEL +/- Atezo/Beva

CEL +/- Pembro/Lenva

CEL *vs.* combinaison d'IO

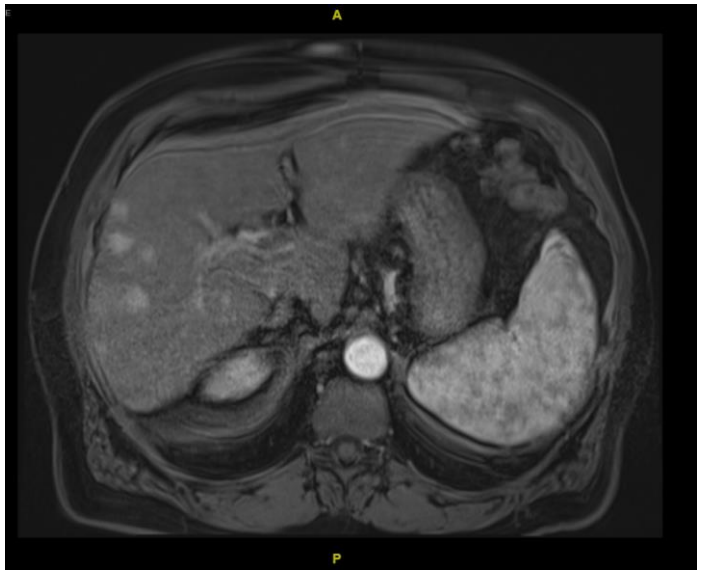
Pour les CHC précoces

Chirurgie ou RFA +/- combinaison d'IO

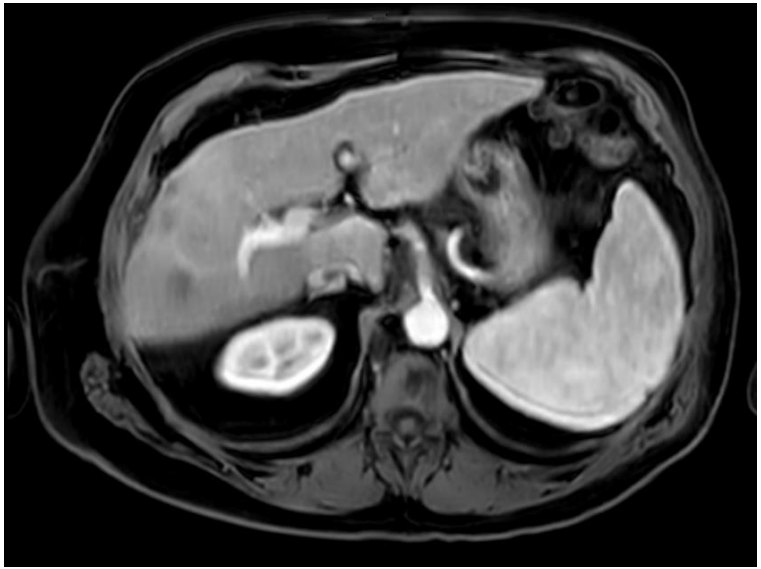
Homme de 70 ans

IO + TACE

JAN 2021 AFP = 68

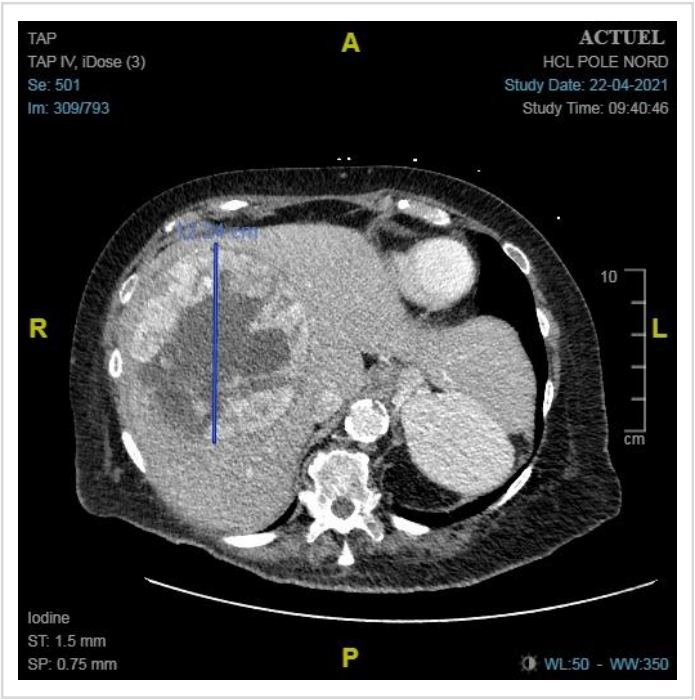


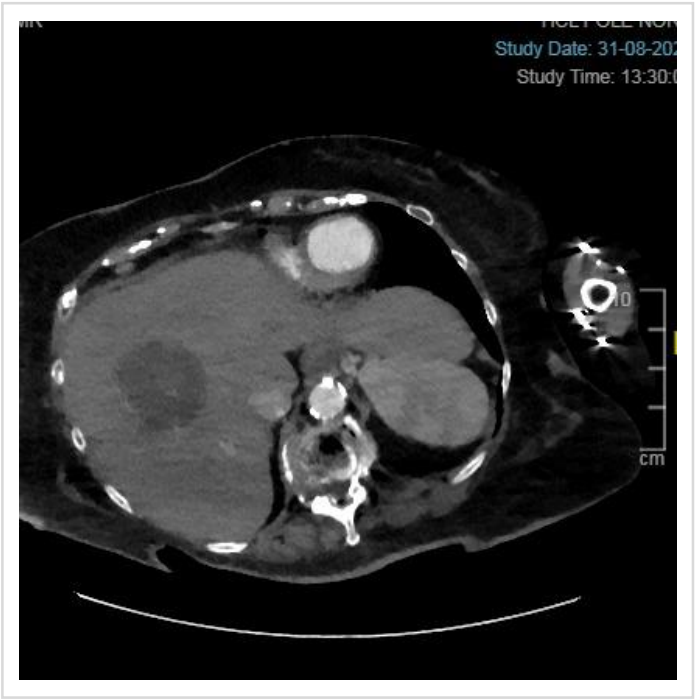
JUIN 2021 AFP = 5,6



Femme de 80 ans

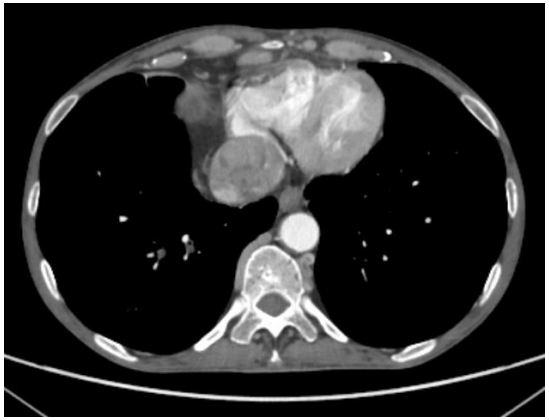
IO chez patients fragiles

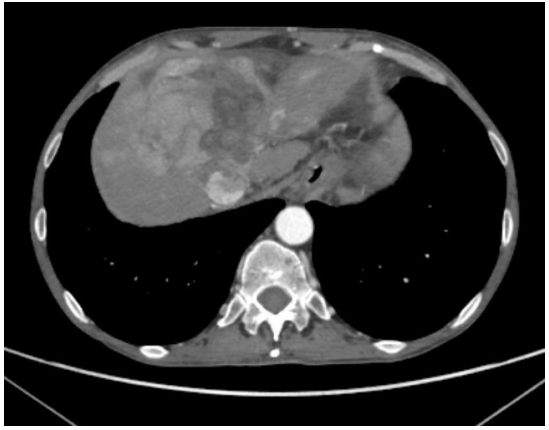




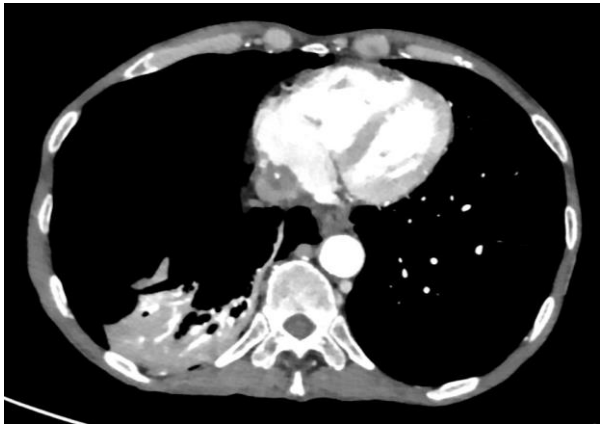
IO + SBRT

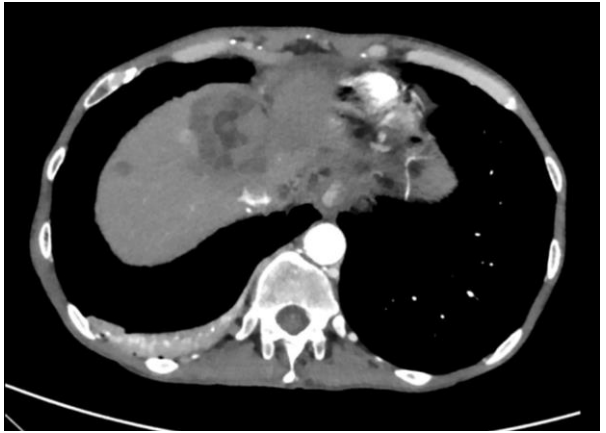
JUIL 2020 AFP = Nale





NOV 2021 AFP = Nale

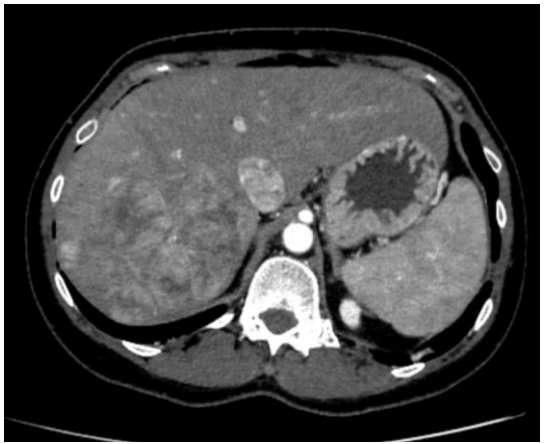




Femme de 40 ans

IO en association avec chirurgie

OCT 2020 AFP = Nale



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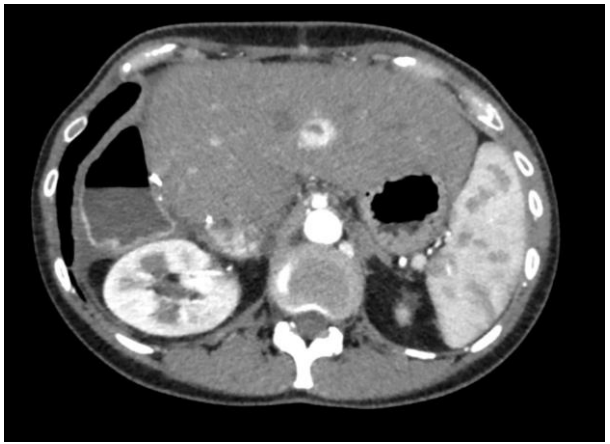

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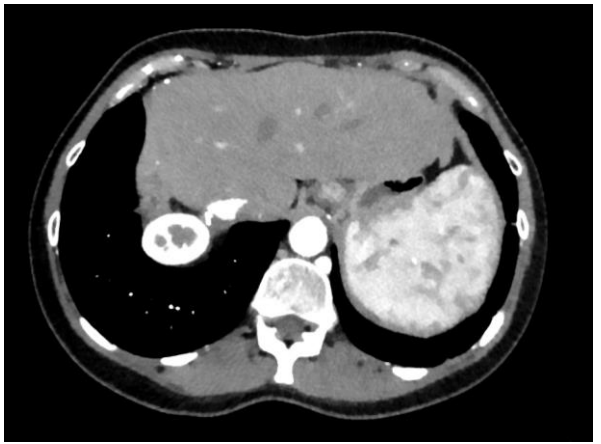
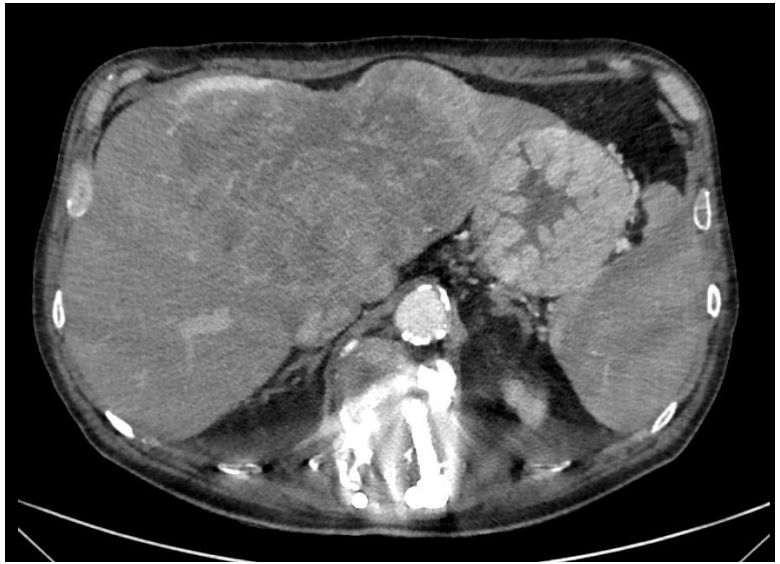


Carcinome hépatocellulaire -de 29 cm de grand axe, non encapsulé, multifocal, - moyennement différencié avec un contingent minoritaire macrotrabéculaire - grade d'Edmondson : 3 - d'exérèse incomplète : - au niveau de la capsule de Glisson (effractions capsulaires) - au niveau de la limite de résection intra-parenchymateuse - nombreux emboles veineux tumoraux Curage ganglionnaire lymphatique à part : 2N-. Pas d'infiltration tumorale de la vésicule biliaire. Classification TNM UICC 8ème édition : pT3 N0 R1.

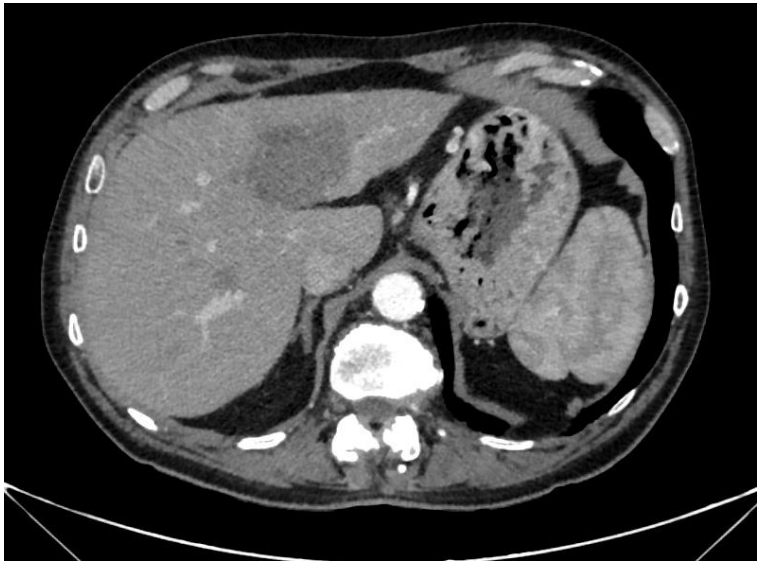
Homme de 62 ans

IO en association avec chirurgie

MARS 2021 AFP = 217000



OCT 2021 AFP = 7,9



JOURNÉE D'HÉPATOLOGIE ET DE TRANSPLANTATION HÉPATIQUE DE LYON

Institut d' Hépatologie de Lyon

AVEC LE SOUTIEN DE :