COR2ED

THE HEART OF MEDICAL EDUCATION

ADVANCED HCC: TREATMENT STRATEGIES FOR PATIENTS INELIGIBLE FOR IO OR THOSE WITH PROGRESSION ON IO

MICRO LEARNING

Assoc. Prof. Lorenza Rimassa, MD
Humanitas University and IRCCS Humanitas Research Hospital, Italy

Dr Amit Singal, MD, MS
UT Southwestern Medical Center, USA

JUNE 2025

DEVELOPED BY HCC CONNECT

This programme is developed by HCC CONNECT, an international group of experts in the field of hepatocellular carcinoma and brought to you alongside GI CONNECT, an international group of experts in the field of gastrointestinal oncology.

HCC connect® POWERED BY COR2ED

GI connect® POWERED BY COR2ED

Acknowledgement and disclosures

This educational programme is supported through an independent educational grant from Bayer. The programme is therefore independent, the content is not influenced by the supporter and is under the sole responsibility of the experts.

Please note:

- This educational programme is intended for healthcare professionals only
- The views expressed within this programme are the personal opinions of the experts. They do not necessarily represent the views of the experts' academic institutions, organisations, or the rest of the HCC CONNECT and GI CONNECT groups.

Expert disclosures:

- **Assoc. Prof. Lorenza Rimassa** has received financial support/sponsorship for research support, consultation, or speaker fees from the following companies: AbbVie, AstraZeneca, Basilea, Bayer, BeiGene, BMS, Eisai, Elevar Therapeutics, Exelixis, Fibrogen, Genenta, Guerbet, Hengrui, Incyte, Ipsen, Jazz Pharmaceuticals, MSD, Nerviano Medical Sciences, Roche, Servier, Taiho Oncology, TransThera Sciences, Zymeworks
- **Dr Amit Singal** has received financial support/sponsorship for research support, consultation, or speaker fees from the following companies: Abbott, AstraZeneca, Bayer, Boston Scientific, DELFI, Eisai, Elevar, Exact Sciences, Exelixis, FujiFilm Medical Sciences, Genentech, Glycotest, HelioGenomics, HistoSonics, ImCare, Merck, Roche, Sirtex and Universal DX

THIS PROGRAMME HAS BEEN DEVELOPED BY A GROUP OF EXPERTS

Assoc. Prof. Lorenza Rimassa
Humanitas University and IRCCS Humanitas Research Hospital, Italy

Dr Amit Singal
UT Southwestern Medical Center, USA

KEY CLINICAL TAKEAWAYS

ADVANCED HCC: STRATEGIES FOR PATIENTS INELIGIBLE FOR IO OR THOSE WITH PROGRESSION ON IO

- For patients with HCC who are **ineligible for IO**, the tyrosine kinase inhibitors (**TKIs**) sorafenib and lenvatinib remain the **recommended 1st line treatment options**
- After **progression on 1st line IO**, multiple treatment strategies are available. If a **clinical trial** is not available, **switching to a TKI,** or considering **alternative IO-based approaches** may be viable options based on patient eligibility, disease factors, and local availability
- Post-IO progression, two main **approaches** involving TKIs are available: **focusing on 1st line TKIs** (sorafenib or lenvatinib) or **expanding to all available 2nd line options** (sorafenib, lenvatinib, regorafenib, cabozantinib, and ramucirumab[a])
- There are **limited prospective data** available on treatment outcomes following **progression** on 1st line IO therapies. To address this gap, **patients should be referred to clinical trials** whenever possible to help establish evidence-based sequencing strategies
- **Transition** to 2nd line therapy should be considered after **radiologic or clinical progression**, with attention to the **patient's clinical condition** and **liver function**

[a] If serum α-fetoprotein (AFP) levels ≥400 ng/mL

HCC, hepatocellular carcinoma; IO, immuno-oncology (therapy); mRECIST, modified Response Evaluation Criteria in Solid Tumours

1ST LINE SYSTEMIC TREATMENT OPTIONS FOR PATIENTS WITH HCC

INELIGIBLE FOR IO 1ST LINE

HCC, hepatocellular carcinoma; IO, immuno-oncology (therapy)

SYSTEMIC TREATMENT OPTIONS FOR PATIENTS WITH HCC

IMMUNOTHERAPY (IO)[1]

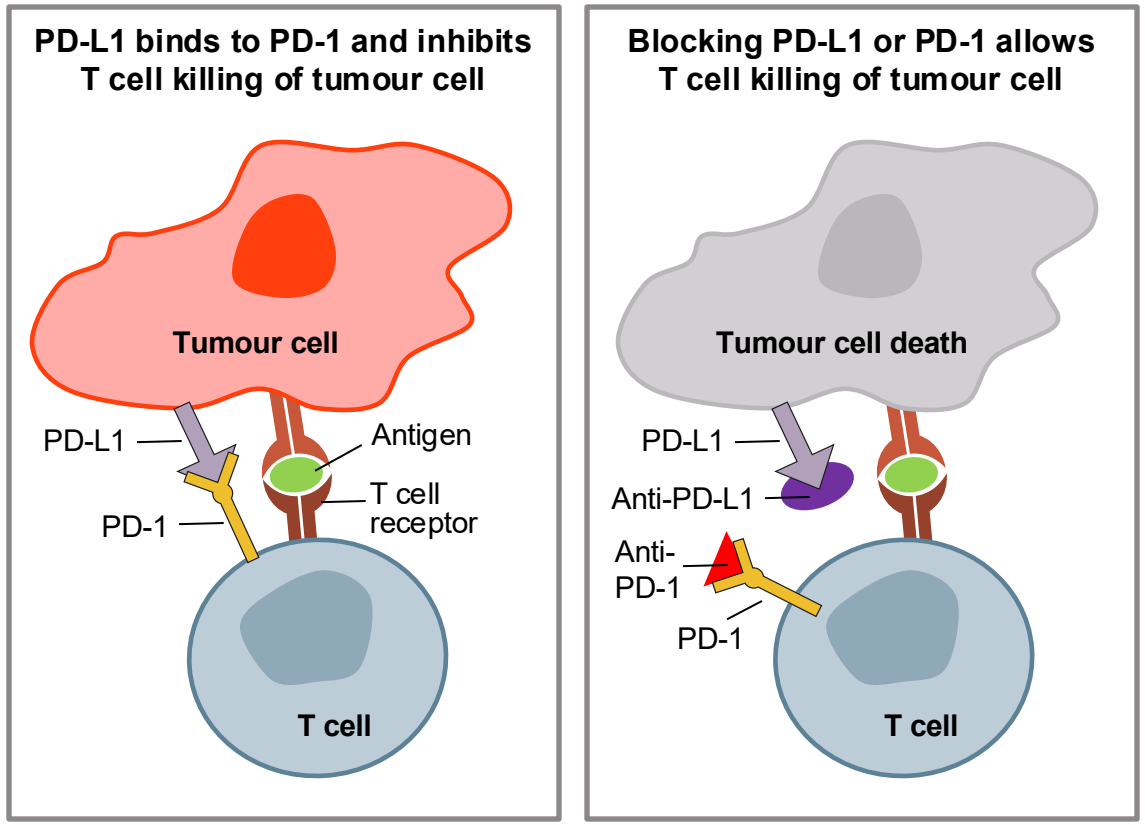


Figure adapted from Terese Winslow LLC

TYROSINE KINASE INHIBITORS (TKIs)[2]

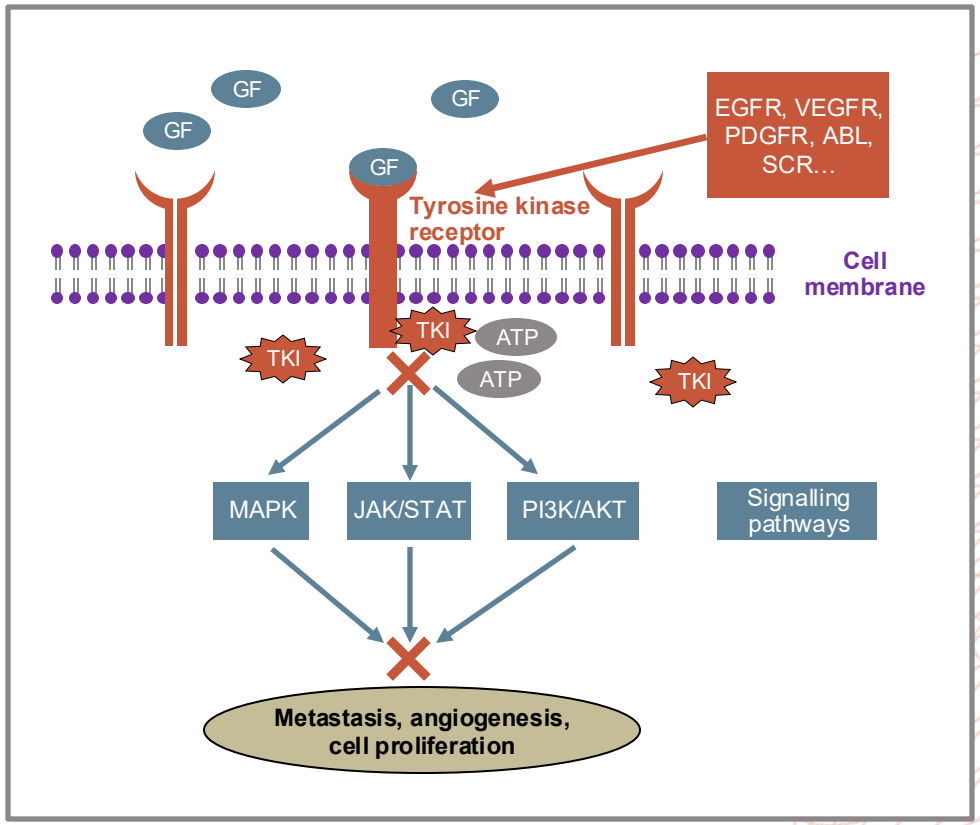


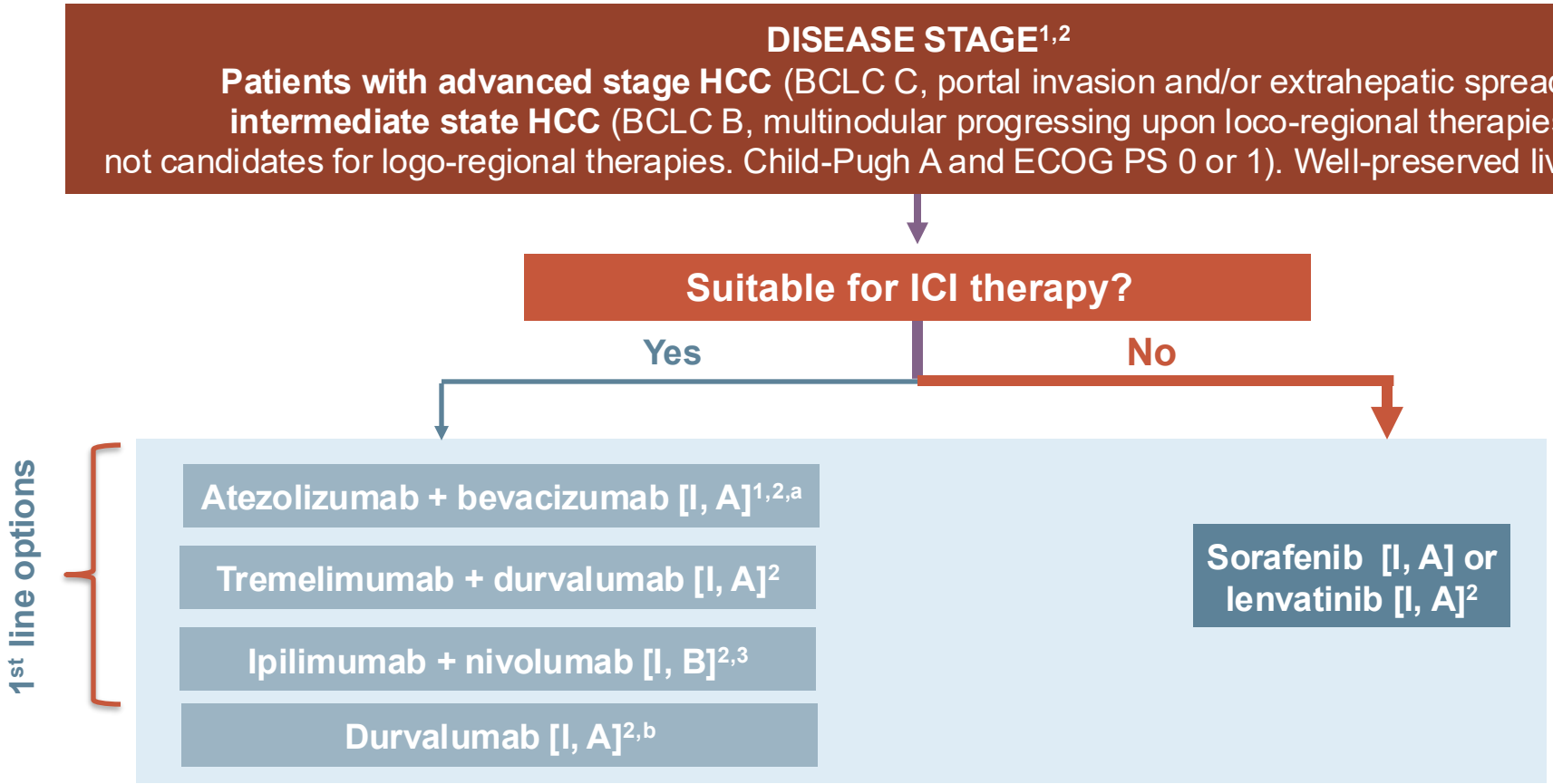
Figure adapted from Gabora K, et al.

ABL, Abelson tyrosine kinase family; AKT, protein kinase B; ATP, adenosine triphosphate; EGFR, endothelial growth factor receptor; GF, growth factor; JAK, Janus kinase protein; MAPK, mitogen-activated protein kinase; PD-1, programmed death 1; PDGFR, platelet-derived growth factor receptor; PD-L1, programmed death ligand 1; PI3K, phosphoinositide-3-kinase; SCR, SCR tyrosine kinase family; STAT, signal transducer and activation of transcription protein; VEGFR, vascular endothelial growth factor receptor

1. Terese Winslow LLC. 2015. Available from: https://www.teresewinslow.com/#/cellular-scientific/ (accessed Jan 2025); 2. Gabora K, et al. Drug Metab Rev. 2019;51:562-569

1ST LINE SYSTEMIC TREATMENT STRATEGY FOR PATIENTS WITH HCC

FOR PATIENTS INELIGIBLE FOR IO THERAPIES, TKIs (SORAFENIB, LENVATINIB) RECOMMENDED AS 1ST LINE TREATMENT



[a] In patients with portal hypertension, screening for varices is strongly recommended before initiation of atezolizumab-bevacizumab[2]

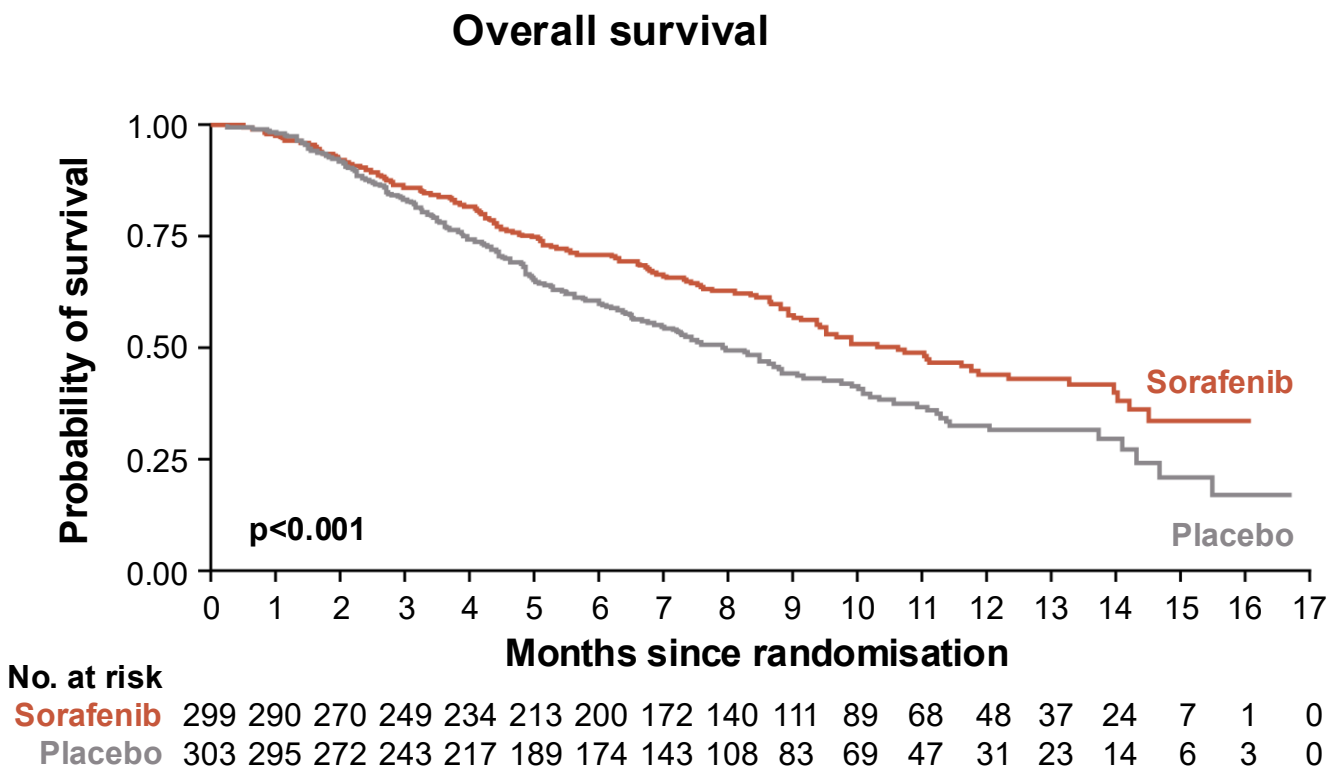
[b] Patients who have contraindications to ICI combination therapies (not FDA-approved)

BCLC, Barcelona Clinic Liver Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; FDA, Food and Drug Administration; HCC, hepatocellular carcinoma; ICI, immune checkpoint inhibitor; IO, immuno-oncology; TKI, tyrosine kinase inhibitor

1. Reig M, et al. J Hepatol. 2022;76:681-693; 2. Vogel A, et al. Ann Oncol. 2025 (article in press; https://doi.org/10.1016/j.annonc.2025.02.006); 3. Nivolumab Plus Ipilimumab Receives EC Approval for First-Line Unresectable HCC. Available here (accessed March 2025)

1ST LINE TKI: SORAFENIB

MEDIAN OVERALL SURVIVAL AND TIME TO PROGRESSION WERE NEARLY 3 MONTHS LONGER FOR PATIENTS TREATED WITH SORAFENIB THAN FOR THOSE GIVEN PLACEBO



- Median OS was 10.7 months in the sorafenib group and 7.9 months in the placebo group (HR in the sorafenib group, 0.69; 95% CI, 0.55 to 0.87; p<0.001)

Incidence of drug-related adverse events (safety population)[a]

Adverse event, %	Sorafenib (N=297)			Placebo (N=302)		
	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4
Overall incidence	80			52		
Constitutional symptoms						
Fatigue	22	3	1	16	3	<1
Weight loss	9	2	0	1	0	0
Dermatologic events						
Alopecia	14	0	0	2	0	0
Dry skin	8	0	0	4	0	0
Hand–foot skin reaction	21	8	0	3	<1	0
Pruritus	8	0	0	7	<1	0
Rash or desquamation	16	1	0	11	0	0
Other	5	1	0	1	0	0
Gastrointestinal events						
Anorexia	14	<1	0	3	1	0
Diarrhoea	39	8	0	11	2	0
Nausea	11	<1	0	8	1	0
Vomiting	5	1	0	3	1	0
Voice changes	6	0	0	1	0	0
Hypertension	5	2	0	2	1	0
Liver dysfunction	<1	<1	0	0	0	0
Abdominal pain not otherwise specified	8	2	0	3	1	0
Bleeding	7	1	0	4	1	<1

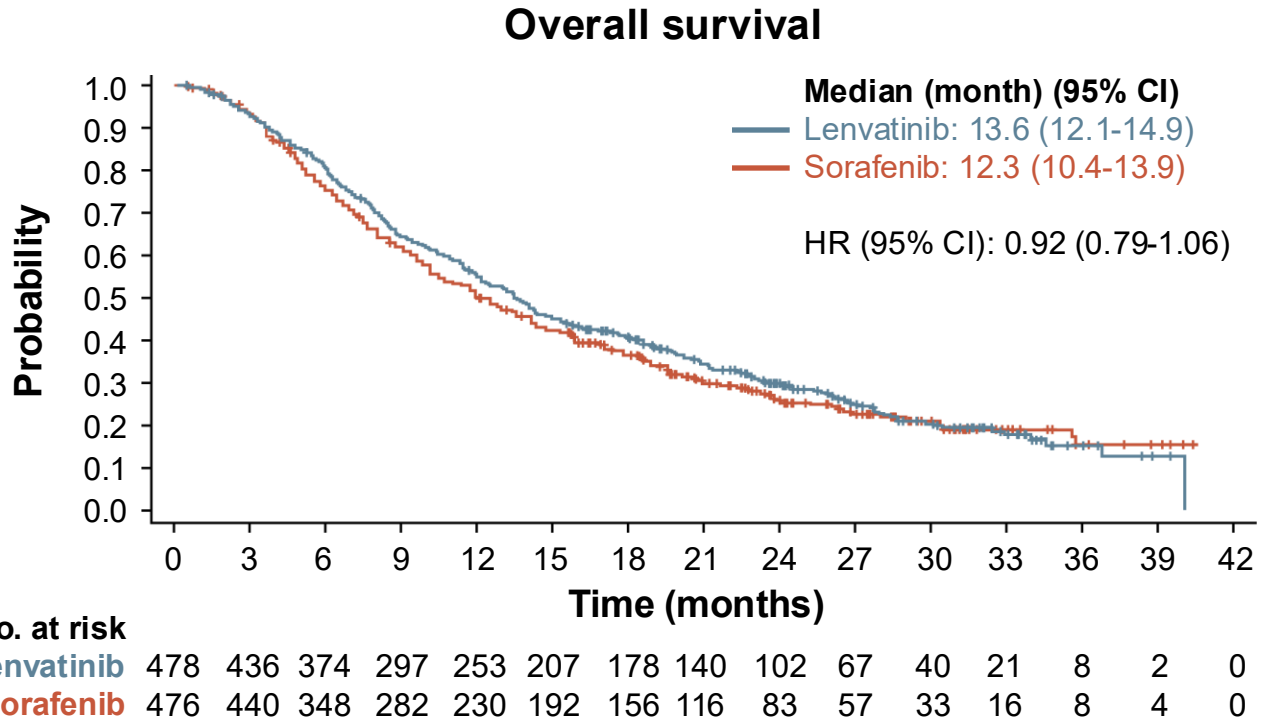
[a] Listed are adverse events, as defined by the National Cancer Institute Common Terminology Criteria (version 3.0), 5% of patients in either study group.

CI, confidence interval; HR, hazard ratio; OS, overall survival; TKI, tyrosine kinase inhibitor

Llovet JM, et al. N Engl J Med. 2008;359;378-390

1ST LINE TKI: LENVATINIB

LENVATINIB WAS NON-INFERIOR TO SORAFENIB IN OVERALL SURVIVAL IN PATIENTS WITH UNTREATED ADVANCED HCC



- Lenvatinib demonstrated a statistically significant improvement to sorafenib in all secondary efficacy endpoints (PFS, TTP, and ORR)

TEAEs occurring in ≥15% of patients in either arm

Adverse event, n (%)	Lenvatinib (N=476)		Sorafenib (N=475)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Palmar-plantar erythrodysaesthesia	128 (26.9)	14 (2.9)	249 (52.4)	54 (11.4)
Diarrhoea	184 (38.7)	20 (4.2)	220 (46.3)	20 (4.2)
Hypertension	201 (42.2)	111 (23.3)	144 (30.3)	68 (14.3)
Decreased appetite	162 (34.0)	22 (4.6)	127 (26.7)	6 (1.3)
Decreased weight	147 (30.9)	36 (7.6)	106 (22.3)	14 (2.9)
Fatigue	141 (29.6)	18 (3.8)	119 (25.1)	17 (3.6)
Alopecia	14 (2.9)	0 (0)	119 (25.1)	0 (0)
Proteinuria	117 (24.6)	27 (5.7)	54 (11.4)	8 (1.7)
Dysphonia	113 (23.7)	1 (0.2)	57 (12.0)	0 (0)
Nausea	93 (19.5)	4 (0.8)	68 (14.3)	4 (0.8)
Abdominal pain	81 (17.0)	8 (1.7)	87 (18.3)	13 (2.7)
Decreased platelet count	87 (18.3)	26 (5.5)	58 (12.2)	16 (3.4)
Elevated aspartate aminotransferase	65 (13.7)	24 (5.0)	80 (16.8)	38 (8.0)
Hypothyroidism	78 (16.4)	0 (0)	8 (1.7)	0 (0)
Vomiting	77 (16.2)	6 (1.3)	36 (7.6)	5 (1.1)
Constipation	76 (16.0)	3 (0.6)	52 (10.9)	0 (0)
Rash	46 (9.7)	0 (0)	76 (16.0)	2 (0.4)

CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; ORR, objective response rate; PFS, progression-free survival; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor; TTP, time to progression

Kudo M, et al. Lancet. 2018;391:1163-1173

SEQUENCING STRATEGIES, TREATMENT OPTIONS, AND AVAILABLE DATA AFTER PROGRESSION ON IO

IO, immuno-oncology (therapy)

SEQUENCING STRATEGIES AFTER PROGRESSION ON 1ST LINE IO

OPTIONS, GUIDELINES AND APPROACHES

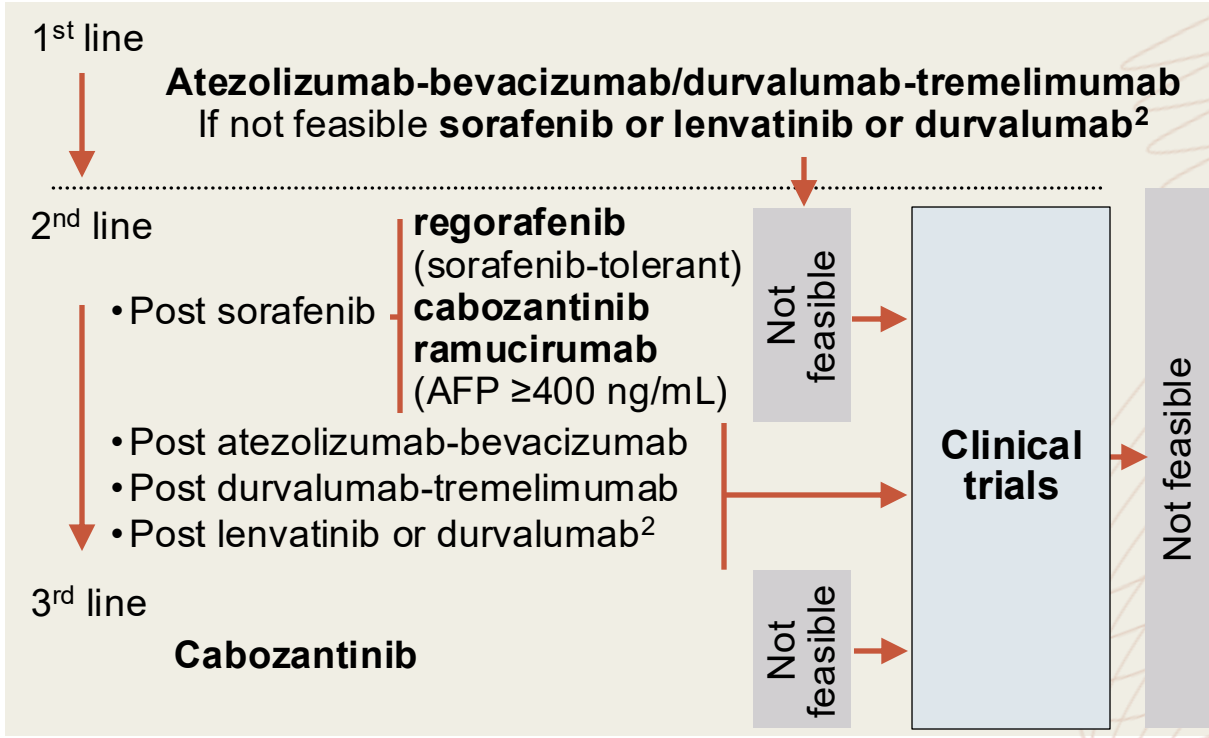
IO, immuno-oncology (therapy)

OPTIONS AFTER PROGRESSION ON 1ST LINE IO IN HCC

OVERVIEW

- Enrolment in a clinical trial
- Switching to a TKI or anti-VEGFR-2
  - T-1 approach
  - Line-agnostic approach
- Considering IO after IO approaches
- Providing best supportive care for patients unsuitable for further systemic therapies

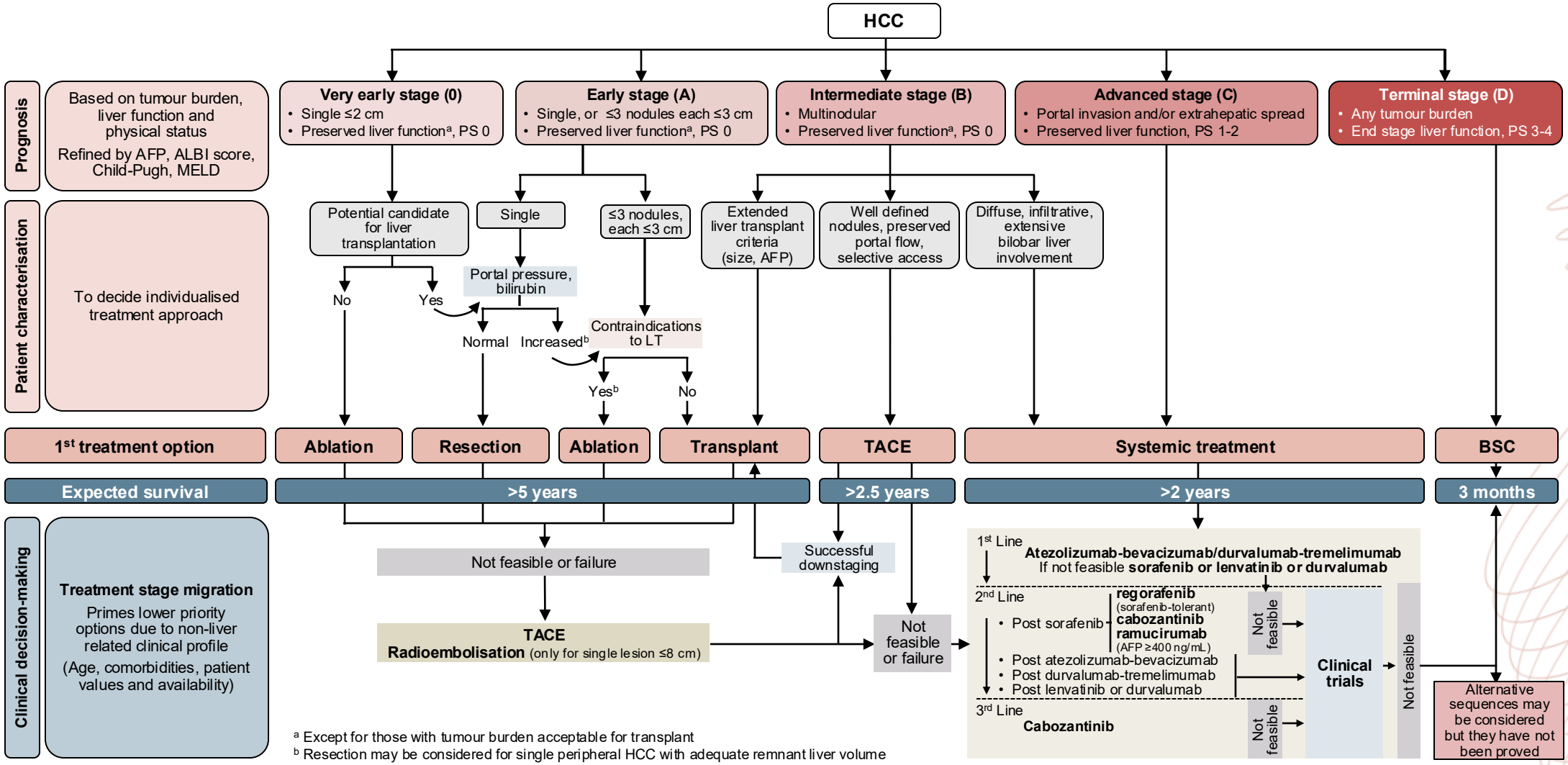
BCLC systemic treatment strategy[1]



AFP, α--fetoprotein; BCLC, Barcelona Clinic Liver Cancer; HCC, hepatocellular carcinoma; IO, immuno-oncology (therapy); TKI, tyrosine kinase inhibitor

1. Reig M, et al. J Hepatol. 2022;76:681-693; 2. Gordan JD, et al. J Clin Oncol. 2024;42:1830-1850

BCLC UPDATED TREATMENT ALGORITHM

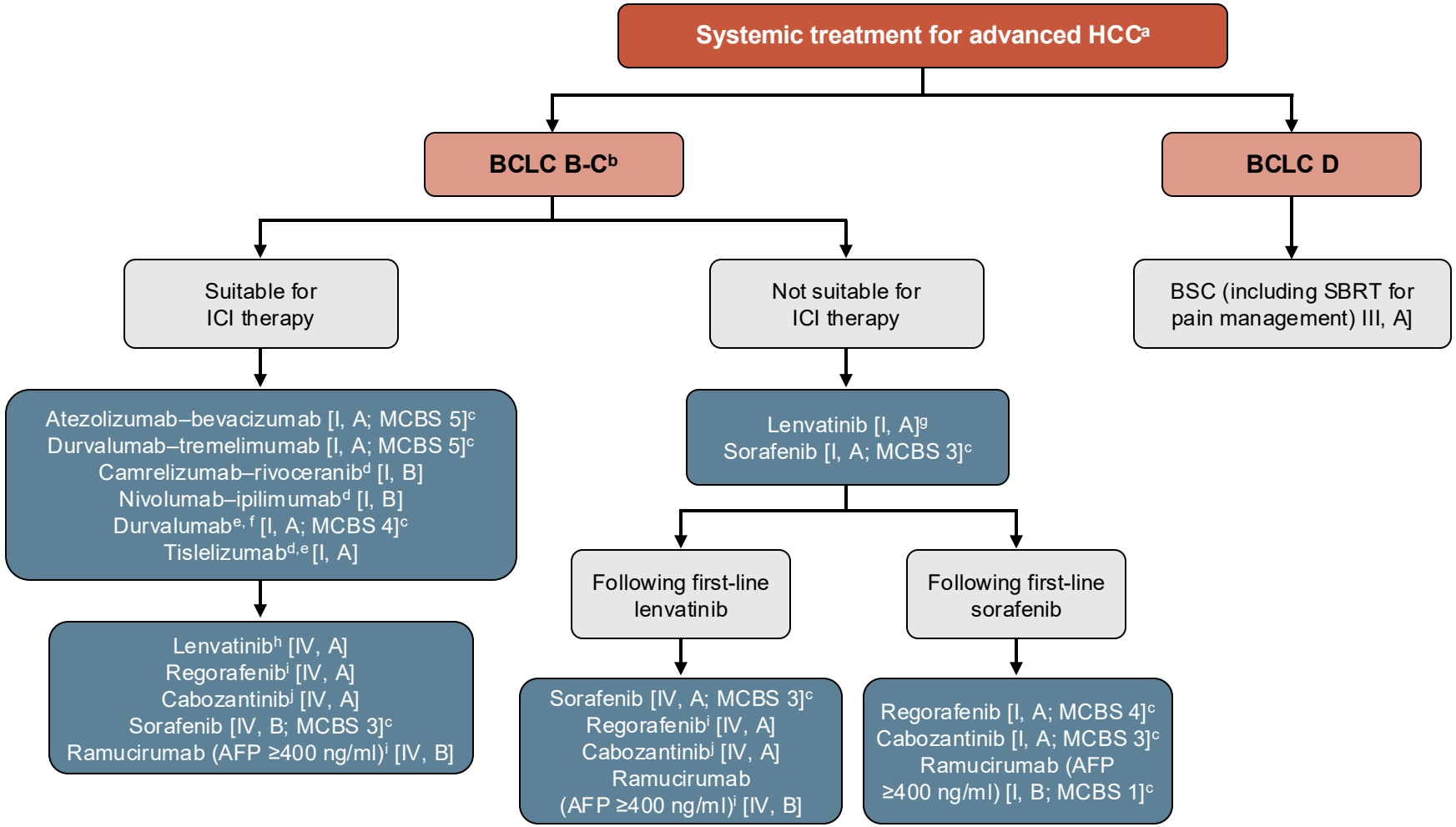


AFP, α-fetoprotein; ALBI, albumin-bilirubin; BCLC, Barcelona Clinic Liver Cancer; BSC, best supportive care; HCC, hepatocellular carcinoma; LT, liver transplantation; MELD, model of end-stage liver disease; PS, performance status; TACE, transarterial chemoembolisation

Reig M, et al. J Hepatol. 2022;76:681-93

HCC ESMO GUIDELINES

MANAGEMENT OF ADVANCED HCC[1]



AFP, α-foetoprotein; BCLC, Barcelona Clinic Liver Cancer; BSC, best supportive care; ECOG PS, Eastern Cooperative Oncology Group performance status; EMA, European Medicines Agency; ESMO, European Society for Medical Oncology; FDA, Food and Drug Administration; HCC, hepatocellular carcinoma; ICI, immune checkpoint inhibitor; MCBS, Magnitude of Clinical Benefit Scale; SBRT, stereotactic body radiotherapy

[a] Locoregional therapies may be appropriate for selected patients [b] Patients with well-preserved liver function and ECOG PS 0-1 [c] ESMO-MCBS v1.1 was used to calculate scores for therapies/indications approved by the EMA or FDA. The scores have been calculated and validated by the ESMO-MCBS Working Group and reviewed by the authors (https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-for-solid-tumours/esmo-mcbs-evaluation-forms [accessed March 2025]). [d] Recently approved in Europe for 1st line unresectable HCC[2]. [e] In patients with contraindications to ICI combinations. [f] EMA approved, not FDA approved. [g] Non-inferiority established versus sorafenib via ESMO-MCBS v1.1. [h] Not EMA or FDA approved for second-line use

1. Vogel A, et al. Ann Oncol. 2025 (artide in press; https://doi.org/10.1016/j.annonc.2025.02.006); 2. Nivolumab Plus Ipilimumab Receives EC Approval for First-Line Unresectable HCC. Available here (accessed March 2025)

NCCN GUIDELINES
PRINCIPLES OF SYSTEMIC THERAPY

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2024
Hepatocellular Carcinoma

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF SYSTEMIC THERAPY[a,b,c]

First-Line Systemic Therapy

Preferred Regimens

- Atezolizumab[d] + bevacizumab (category 1)[e,f,g,1]
- Tremelimumab-actl + durvalumab (category 1)[f,2]

Other Recommended Regimens

- Durvalumab (category 1)[f,2]
- Lenvatinib (category 1)[3,4]
- Sorafenib (category 1)[5,6]
- Tislelizumab-jsgr (category 1)[f,7]
- Pembrolizumab (category 2B)[f,8]

Useful in Certain Circumstances

- For *NTRK* gene-fusion positive tumors:
  - Repotrectinib (category 2B)[9]

Subsequent-Line Systemic Therapy if Disease Progression[h,i,j]

Options

- Cabozantinib (category 1)[12]
- Regorafenib (category 1)[13]
- Lenvatinib
- Sorafenib

Other Recommended Regimens

- Nivolumab + ipilimumab[f,k,l,14-16]
- Pembrolizumab[f,m,n,o,17-19]

Useful in Certain Circumstances

- Ramucirumab (AFP ≥400 ng/mL) (category 1)[20]
- Nivolumab[f,m,n,p,21-24]
- For MSI-H/dMMR tumors
  - Dostarlimab-gxly (category 2B)[f,m,n,q,25]
- For *RET* gene fusion-positive tumors:
  - Selpercatinib (category 2B)[26]

[a] Order does not indicate preference.
[b] See Principles of Liver Functional Assessment (HCC-E) and assess portal hypertension (eg, varices, splenomegaly, thrombocytopenia).

T-1 APPROACH: PROGRESSION ON 1ST LINE IO

PRIOR 1ST LINE THERAPIES (SORAFENIB AND LENVATINIB) ARE USED AS 2ND LINE THERAPIES

Progression on 1st line IO

- Durvalumab + tremelimumab
- Or
- Atezolizumab + bevacizumab

→

2nd line systemic therapy options

Sorafenib Or Lenvatinib

Prior 2nd line systemic therapies are reserved for 3rd line and beyond

Regorafenib Or Cabozantinib Or Ramucirumab[a] Or Nivolumab + ipilimumab[b]

[a] If AFP ≥400 ng/mL

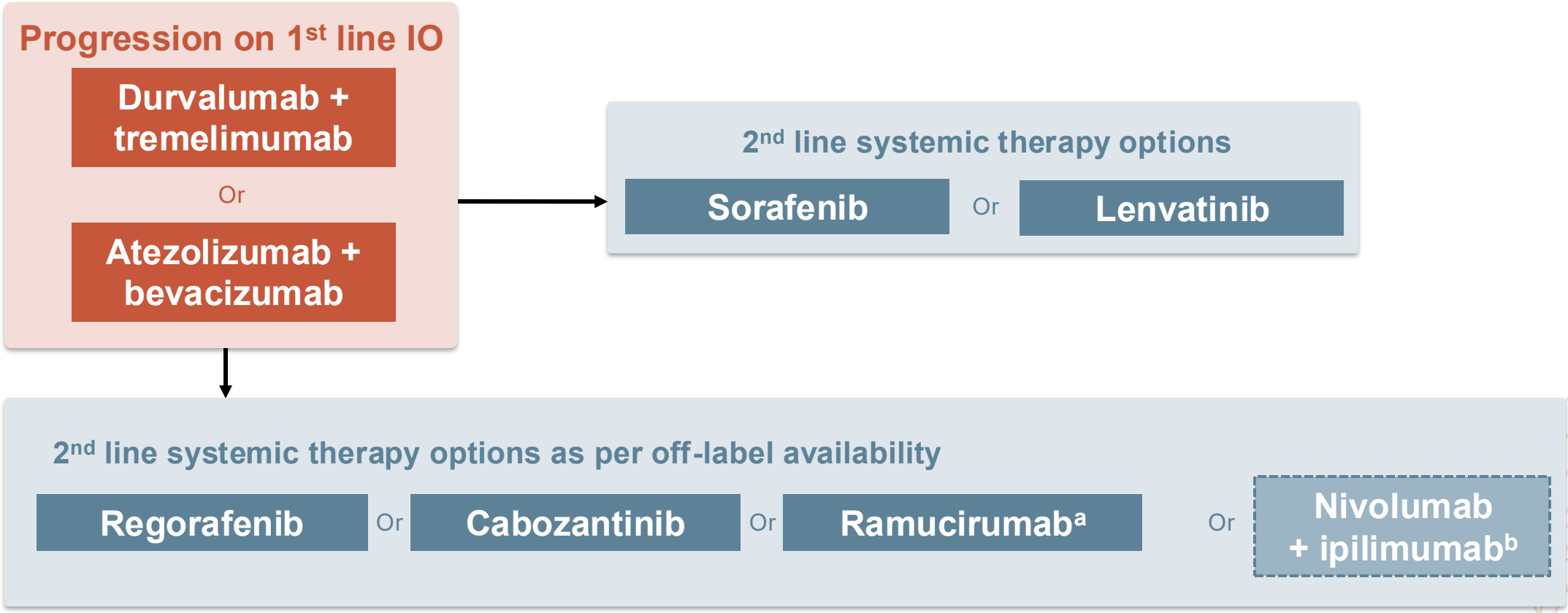
[b] Nivolumab + ipilimumab is approved for 2nd line after progression on sorafenib based on Phase 2 CheckMate 040 data in the US (Saung et al.[1])

AFP, α-fetoprotein; IO, immuno-oncology (therapy); US, United States

1. Saung MT, et al. Oncologist. 2021;26:797-806

LINE-AGNOSTIC APPROACH: PROGRESSION ON 1ST LINE IO

ONE IS AGNOSTIC TO PRIOR LINES OF APPROVAL



In this approach, one is **agnostic to prior lines of approval** and one can choose from **any of the regimens for 2nd line** based on multiple **clinical factors** including patient performance status, tumour burden, liver dysfunction, response to 1st line therapy, patient preference, and local availability

[a] If AFP ≥400 ng/mL

[b] nivolumab + ipilimumab is approved for 2nd line after progression on sorafenib based on Phase 2 CheckMate 040 data in the US (Saung et al.[1])

1L, first-line, 2L, second-line; AFP, α-fetoprotein; IO, immuno-oncology (therapy); US, United States

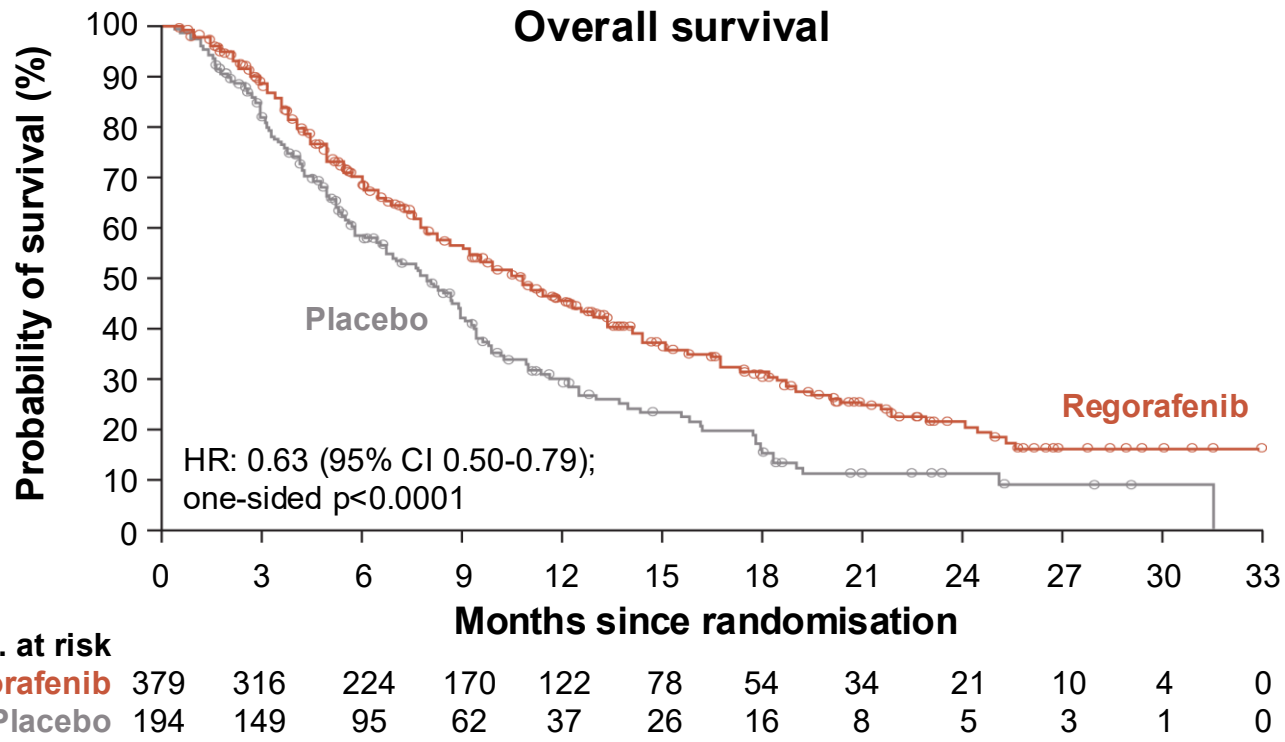
Saung MT, et al. Oncologist. 2021;26:797-806

2ND LINE TREATMENT OPTIONS

REGORAFENIB, CABOZANTINIB AND RAMUCIRUMAB

2ND LINE TKIs: REGORAFENIB (RESORCE)

REGORAFENIB SHOWED SURVIVAL BENEFIT IN PATIENTS WITH HCC PROGRESSING ON SORAFENIB[1]



- REFINE studied the real-world dosing of regorafenib in patients with unresectable hepatocellular carcinoma (uHCC). Safety was consistent with RESORCE[2]
- The safety of regorafenib as second-line therapy for patients who were not included in the RESORCE trial was verified in the Phase 2 REGAIN trial, which included post lenvatinib and post atezolizumab + bevacizumab3

TEAEs occurring in ≥10% of patients in either arm

Adverse event, n (%)	Regorafenib (N=374)			Placebo (N=193)		
	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4
Any adverse event	374 (100)	208 (56)	40 (11)	179 (93)	61 (32)	14 (7)
Hand-foot skin reaction	198 (53)	47 (13)	NA	15 (8)	1 (1)	NA
Diarrhoea	155 (41)	12 (3)	0	29 (15)	0	0
Fatigue	151 (40)	34 (9)	NA	61 (32)	9 (5)	NA
Hypertension	116 (31)	56 (15)	1 (<1)	12 (6)	9 (5)	0
Anorexia	116 (31)	10 (3)	0	28 (15)	4 (2)	0
Increased blood bilirubin	108 (29)	37 (10)	2 (1)	34 (18)	15 (8)	6 (3)
Abdominal pain	105 (28)	13 (3)	NA	43 (22)	8 (4)	NA
Increased AST	92 (25)	37 (10)	4 (1)	38 (20)	19 (10)	3 (2)
Fever	72 (19)	0	0	14 (7)	0	0
Nausea	64 (17)	2 (1%)	NA	26 (13)	0	NA
Constipation	65 (17)	1 (<1)	0	22 (11)	1 (1)	0
Ascites	58 (16)	16 (4)	0	31 (16)	11 (6)	0
Anaemia	58 (16)	16 (4)	2 (1)	22 (11)	10 (5)	1 (1)
Limb oedema	60 (16)	2 (1)	NA	24 (12)	0	NA
Increased ALT	55 (15)	10 (3)	2 (1)	22 (11)	5 (3)	0
Hypoalbuminaemia	57 (15)	6 (2)	0	16 (8)	1 (1)	0
General disorders and administration site conditions, other	53 (14)	16 (4)	2 (1)	29 (15)	6 (3)	3 (2)
Weight loss	51 (14)	7 (2)	NA	9 (5)	0	NA
Oral mucositis	47 (13)	4 (1)	0	6 (3)	1 (1)	0
Vomiting	47 (13)	3 (1)	0	13 (7)	1 (1)	0
Investigations, other	40 (11)	4 (1)	0	11 (6)	1 (1)	0
Back pain	42 (11)	6 (2)	1 (<1)	17 (9)	2 (1)	0
Thrombocytopenia	39 (10)	13 (3)	1 (<1)	5 (3)	0	0
Cough	40 (11)	1 (<1)	NA	14 (7)	0	NA
Hypophosphataemia	37 (10)	30 (8)	2 (1)	4 (2)	3 (2)	0
Hoarseness	39 (10)	0	NA	1 (1)	0	NA

Adverse events were graded using NCI-CTCAE version 4.03.

ALT, alanine transaminase; AST, aspartate transaminase; CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; NA, not applicable; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; OS, overall survival; TEAE, treatment-emergent adverse event; TKI, tyrosine kinase inhibitor (u)HCC, (unresectable) hepatocellular carcinoma

1. Bruix J, et al. Lancet. 2017;389:56-66; 2. Finn RS, et al. J Clin Oncol. 2023;41 (no. 4 suppl):518 (presented at ASCO GI Cancer Symposium); 3. Koroki K, et al. Presented at ILCA 2023. Poster P-97

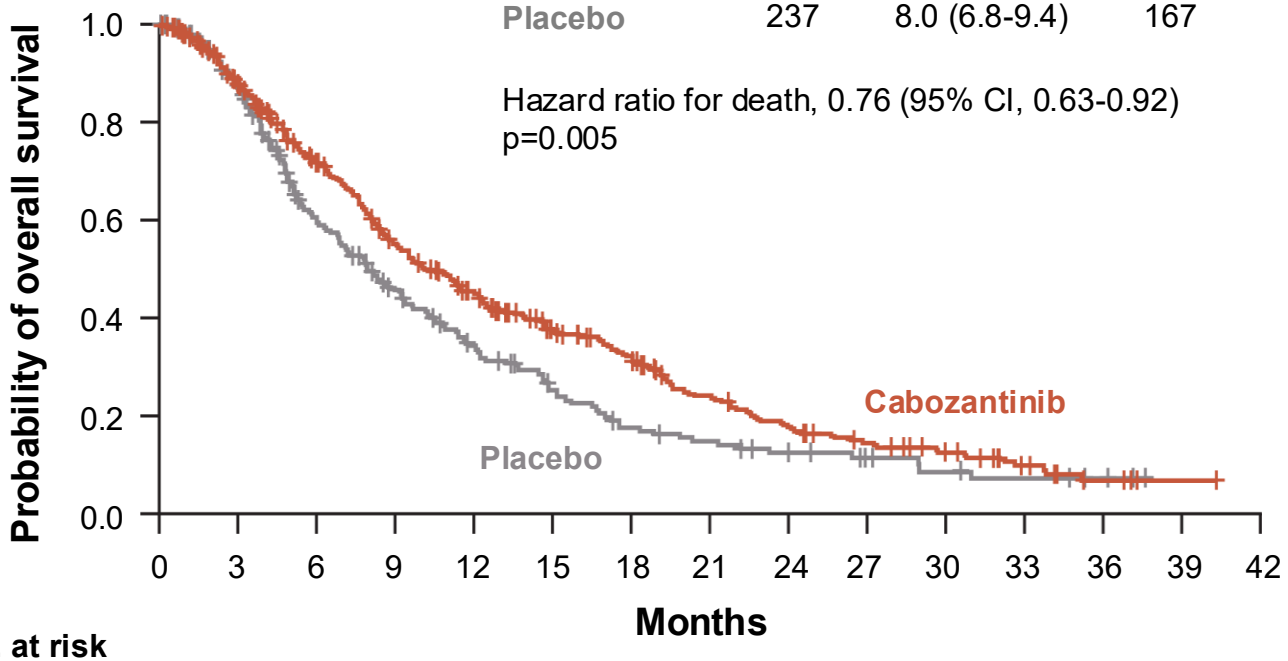
2ND LINE TKIs: CABOZANTINIB (CELESTIAL)

CABOZANTINIB SHOWED SURVIVAL BENEFIT IN PATIENTS WITH HCC PREVIOUSLY TREATED WITH SORAFENIB INCLUDING THOSE WHO HAD RECEIVED UP TO TWO PRIOR SYSTEMIC THERAPIES

Overall survival

	No. of patients	Median OS *mo (95% CI)*	No. of events
Cabozantinib	470	10.2 (9.1-12.0)	317
Placebo	237	8.0 (6.8-9.4)	167

Hazard ratio for death, 0.76 (95% CI, 0.63-0.92)
p=0.005



No. at risk														
Cabozantinib	470	328	281	206	159	116	93	63	44	31	22	12	4	1	0
Placebo	237	190	117	82	57	37	25	20	15	10	7	5	3	0	0

CI, confidence interval; HCC, hepatocellular carcinoma; mo, months; OS, overall survival; TKI, tyrosine kinase inhibitor

Abou-Alfa GK, et al. N Engl J Med. 2018;379:54-63

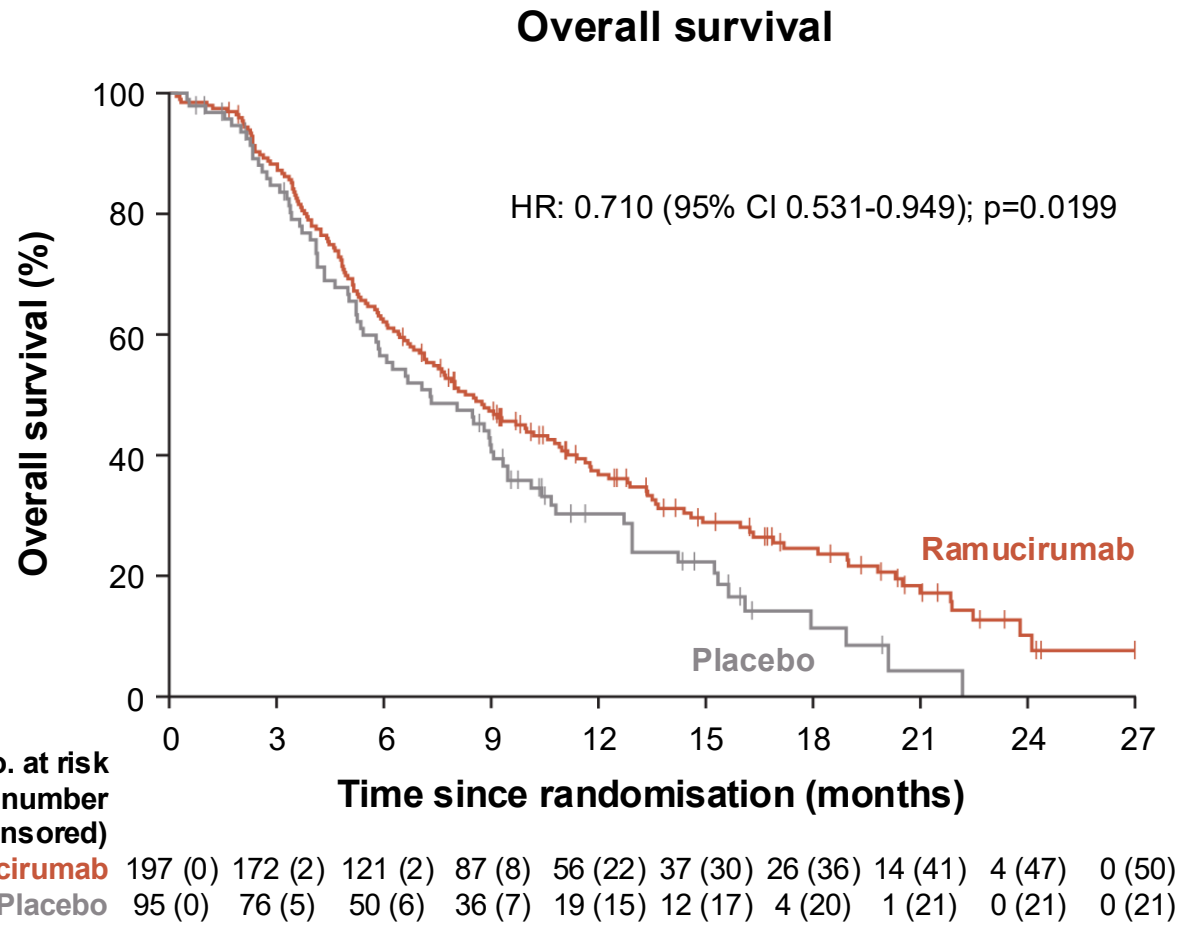
Adverse events occurring in ≥10% of patients in either arm

Event, n (%)	Cabozantinib (N=467)			Placebo (N=237)		
	Any grade	Grade 3	Grade 4	Any grade	Grade 3	Grade 4
Any adverse event	460 (99)	270 (58)	46 (10)	219 (92)	80 (34)	6 (3)
Diarrhoea	251 (54)	45 (10)	1 (<1)	44 (19)	4 (2)	0
Decreased appetite	225 (48)	27 (6)	0	43 (18)	1 (<1)	0
Palmar-plantar erythrodysesthesia	217 (46)	79 (17)	0	12 (5)	0	0
Fatigue	212 (45)	49 (10)	0	70 (30)	10 (4)	0
Nausea	147 (31)	10 (2)	0	42 (18)	4 (2)	0
Hypertension	137 (29)	73 (16)	1 (<1)	14 (6)	4 (2)	0
Vomiting	121 (26)	2 (<1)	0	28 (12)	6 (3)	0
Increased AST	105 (22)	51 (11)	4 (1)	27 (11)	15 (6)	1 (<1)
Asthenia	102 (22)	31 (7)	1 (<1)	18 (8)	4 (2)	0
Dysphonia	90 (19)	3 (1)	0	5 (2)	0	0
Constipation	87 (19)	2 (<1)	0	45 (19)	0	0
Abdominal pain	83 (18)	7 (1)	1 (<1)	60 (25)	10 (4)	0
Weight loss	81 (17)	5 (1)	0	14 (6)	0	0
Increased ALT	80 (17)	23 (5)	0	13 (5)	5 (2)	0
Mucosal inflammation	65 (14)	8 (2)	0	5 (2)	1 (<1)	0
Pyrexia	64 (14)	0	0	24 (10)	1 (<1)	0
Upper abdominal pain	63 (13)	3 (1)	0	31 (13)	0	0
Cough	63 (13)	1 (<1)	0	26 (11)	0	0
Peripheral edema	63 (13)	4 (1)	0	32 (14)	2 (1)	0
Stomatitis	63 (13)	8 (2)	0	5 (2)	0	0
Dyspnea	58 (12)	15 (3)	0	24 (10)	1 (<1)	0
Rash	58 (12)	2 (<1)	0	14 (6)	1 (<1)	0
Ascites	57 (12)	17 (4)	1 (<1)	30 (13)	11 (5)	0
Dysgeusia	56 (12)	0	0	5 (2)	0	0
Hypoalbuminemia	55 (12)	2 (<1)	0	12 (5)	0	0
Headache	52 (11)	1 (<1)	0	16 (7)	1 (<1)	0
Thrombocytopenia	52 (11)	16 (3)	0	1 (<1)	0	0
Insomnia	49 (10)	1 (<1)	0	17 (7)	0	0
Dizziness	48 (10)	2 (<1)	0	15 (6)	0	0
Dyspepsia	47 (10)	0	0	7 (3)	0	0
Anaemia	46 (10)	18 (4)	1 (<1)	19 (8)	12 (5)	0
Back pain	46 (10)	5 (1)	0	24 (10)	1 (<1)	0
Increase in serum bilirubin	45 (10)	10 (2)	4 (1)	17 (7)	2 (1)	2 (1)
Decrease in platelet count	45 (10)	13 (3)	4 (1)	7 (3)	2 (1)	0

* Listed are adverse events, regardless of causality. Severity was graded according to National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.

2ND LINE ANTI-VEGFR-2: RAMUCIRUMAB (REACH-2)

RAMUCIRUMAB SHOWED IMPROVED OVERALL SURVIVAL COMPARED WITH PLACEBO IN PATIENTS WITH HCC AND ELEVATED AFP (≥400 ng/mL) WHO HAD PREVIOUSLY RECEIVED SORAFENIB[1,a]



TEAEs in ≥10% patients (either group)

Adverse event, n (%)	Ramucirumab group (any cause; N=197)				Placebo group (any cause; N=95)			
	Grades 1-2	Grade 3	Grade 4	Grade 5	Grades 1-2	Grade 3	Grade 4	Grade 5
Fatigue	47 (24)	7 (4)	NA	NA	13 (14)	3(3)	NA	NA
Peripheral oedema	47 (24)	3 (2)	0	0	13 (14)	0	0	0
Decreased appetite	43 (22)	3 (2)	0	0	18 (19)	1 (1)	0	0
Abdominal pain	36 (18)	3 (2)	NA	NA	10 (11)	2 (2)	NA	NA
Nausea	37 (19)	0	NA	NA	11 (12)	0	NA	NA
Diarrhoea	32 (16)	0	0	0	13 (14)	1 (1)	0	0
Headache	28 (14)	0	NA	NA	4 (4)	1 (1)	NA	NA
Constipation	26 (13)	1 (1)	0	0	18 (19)	1 (1)	0	0
Insomnia	21 (11)	0	NA	NA	5 (5)	1 (1)	NA	NA
Pyrexia	20 (10)	0	0	0	3 (3)	0	0	0
Vomiting	20 (10)	0	0	0	7 (7)	0	0	0

NA indicated TEAEs for which the Common Terminology Criteria for Adverse Events do not define the grade and no events were reported

[a] Ramucirumab is only recommended for patients with an AFP ≥400 ng/mL and failed to demonstrate a benefit in those with AFP <400 ng/mL

AE, adverse event; AFP, α-fetoprotein; CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; NA, not applicable; TEAE, treatment-emergent adverse event

Zhu AX, et al. Lancet Oncol. 2019;20:282-296

AVAILABLE DATA
AFTER PROGRESSION ON 1ST LINE IO

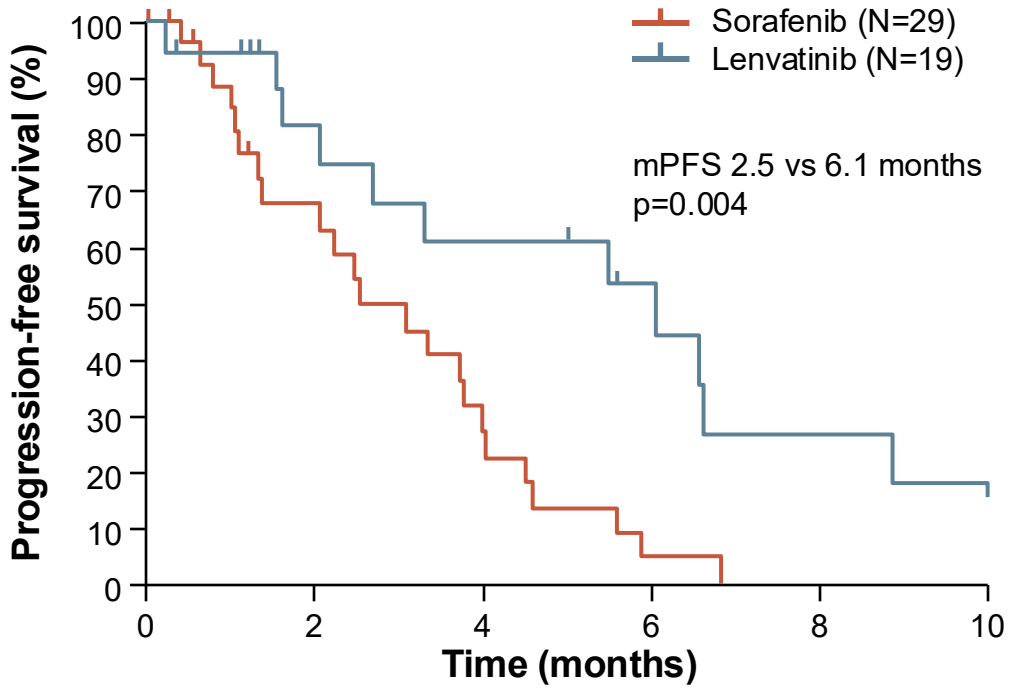
SORAFENIB, LENVATINIB, REGORAFENIB, CABOZANTINIB AND RAMUCIRUMAB

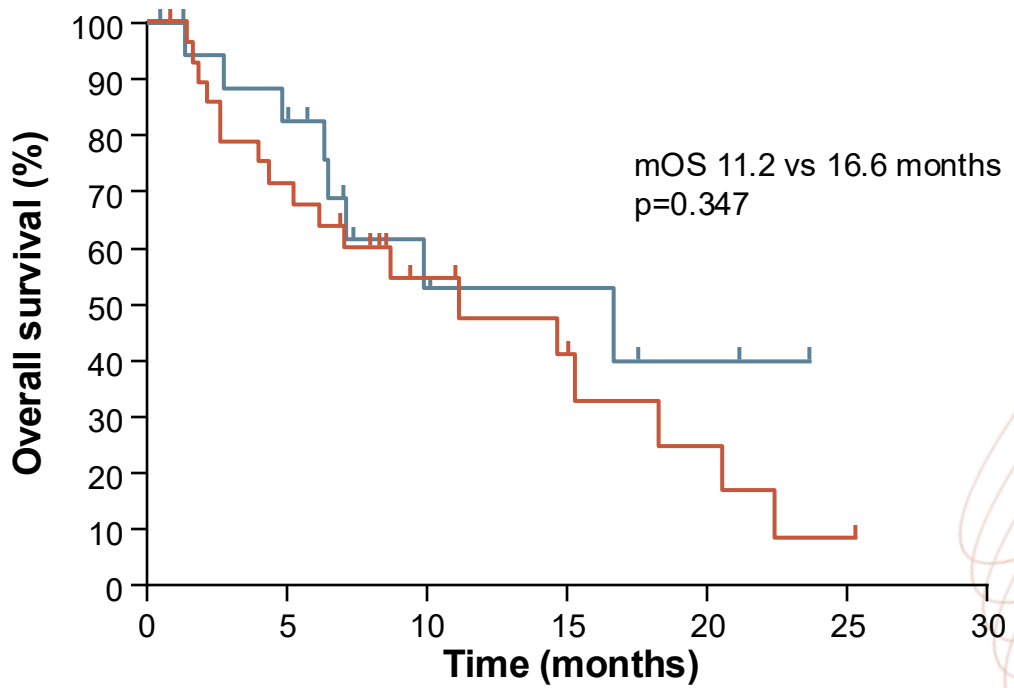
IO, immuno-oncology (therapy)

AVAILABLE DATA ON TKIs AFTER PROGRESSION ON IO

SORAFENIB VS LENVATINIB AFTER IO IN RETROSPECTIVE STUDY

- 49 pts from Korea, Hong Kong and Singapore who received TKI after progression on 1st line atezolizumab + bevacizumab[a]





[a] One patient received cabozantinib – data not shown

Lenvatinib showed better PFS than sorafenib
No statistical difference in OS between lenvatinib and sorafenib

Limitation: Small sample size

IO, immuno-oncology (therapy); mOS, median OS; mPFS, median PFS; OS, overall survival; PFS, progression-free survival; TKI, tyrosine kinase inhibitor

Yoo C, et al. Liver Cancer. 2021;10:107-114

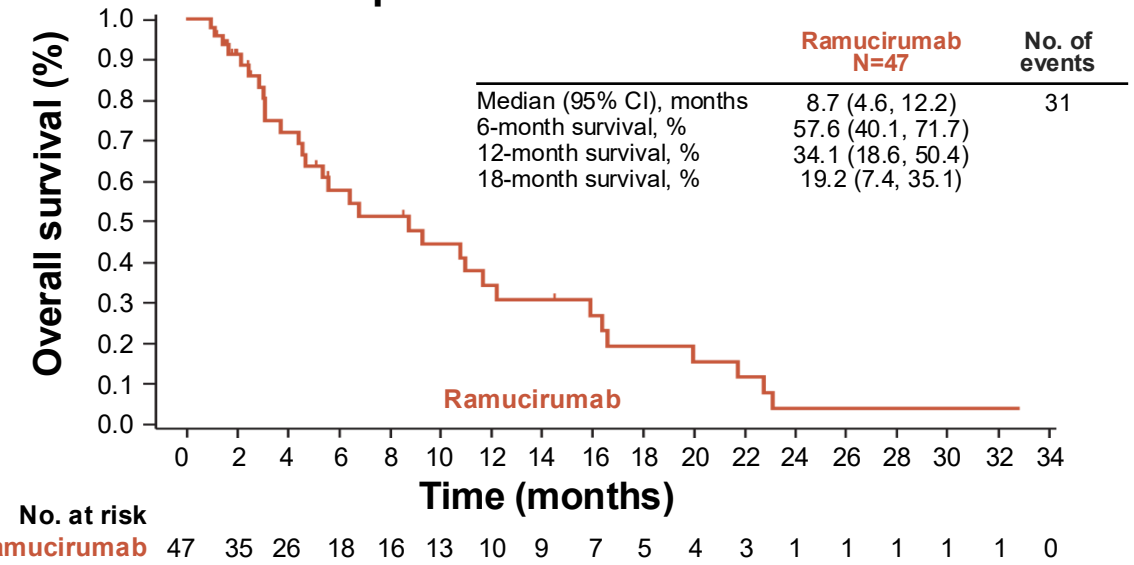
AVAILABLE DATA AFTER PROGRESSION ON IO

REGORAFENIB, CABOZANTINIB AND RAMUCIRUMAB AFTER IO

CELESTIAL study – cabozantinib[1]

Outcomes with cabozantinib	Prior IO (N=14)	Two prior regimens (N=130)
Median OS (95% CI), months	7.9 (5.1-NE)	8.5 (7.4-9.7)
Median PFS (95% CI), months	3.7 (1.9-5.6)	3.7 (3.3-4.1)
Median duration of exposure (range), months	3.7 (1.9-18.7)	3.7 (0.5-23.9)
Grade 3/4 AEs, n (%)	9 (64)	85 (66)
Treatment-related discontinuations, n (%)	1 (7)	19 (15)

REACH-2 expansion cohort – ramucirumab[3]



REFINE study – regorafenib[2]

OS subgroup analyses [N=1008]	Patients, %	Median OS (95% CI), months
Overall population	100	12.9 (11.4-14.6)
CP grade at baseline		
A	62	15.2 (13.3-16.2)
B	12	6.3 (4.9-8.1)
Missing/NE	26	12.2 (9.4-15.3)
ALBI grade at baseline		
1	32	19.8 (16.7-24.6)
2	49	9.9 (8.5-11.1)
Missing	15	12.4 (9.3-15.3)
Prior immunotherapy	9	10.2 (7.4-15.2)
Sorafenib intolerant	9	11.1 (8.6-19.5)
Prior treatment lines		
1 (sorafenib only)	82	13.8 (12.2-15.3)
≥2	14	8.7 (7.4-12.1)

Efficacy and safety comparable to those reported in the Phase 3 trials

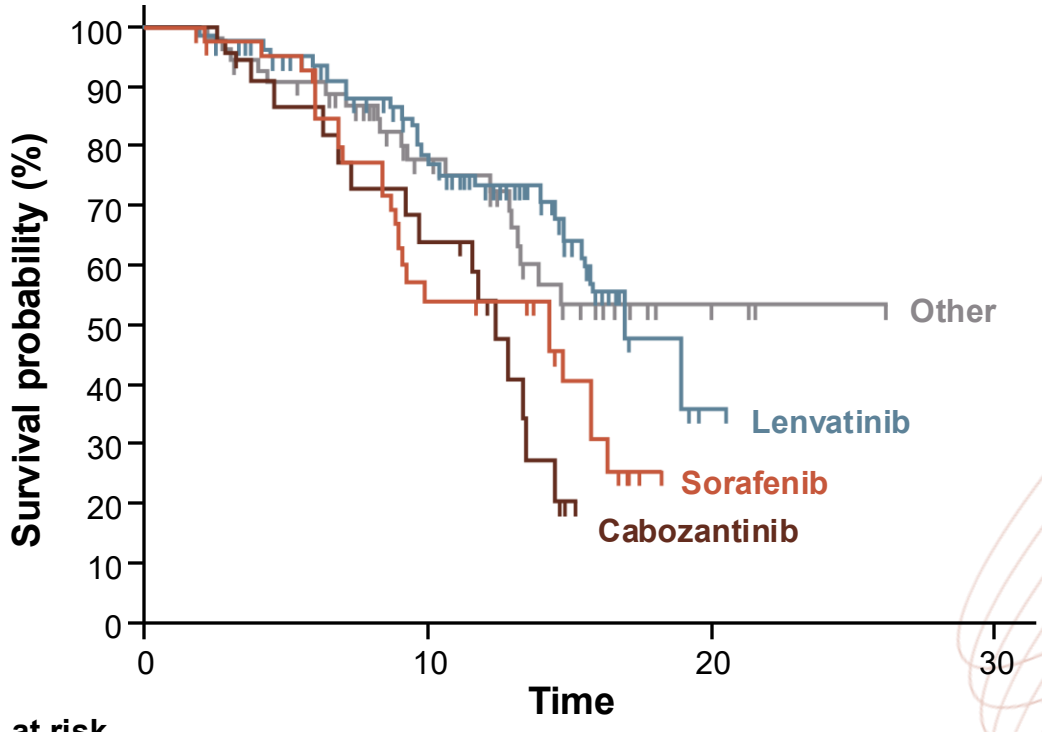
AE, adverse event; CI, confidence interval; CP, Child-Pugh; IO, immuno-oncology (therapy); NE, non-evaluable; OS, overall survival; PFS, progression-free survival;

1, Abou-Alfa GK, et al. Presented at EASL LCS 2020, abstr PB02-04; 2. Finn RS, et al. Presented at EASL LCS 2022, abstr OS-55; 3. Finn RS, et al. Oncologist. 2022;27:e938-e948

AVAILABLE DATA AFTER PROGRESSION ON IO

COMPARISON OF 2ND LINE THERAPIES AFTER ATEZOLIZUMAB + BEVACIZUMAB

- Retrospective analysis of 464 patients previously treated with atezolizumab + bevacizumab from 46 centres in five countries (Italy, Germany, Portugal, Japan, and Korea
- Choice of therapy left to the discretion of the provider
- Median survival was 14.2 months for sorafenib (95% CI: 8.8–15.7), 17.0 months for lenvatinib (95% CI: 14.8–18.9), and 12.4 months for cabozantinib (95% CI: 7.2–13.4)



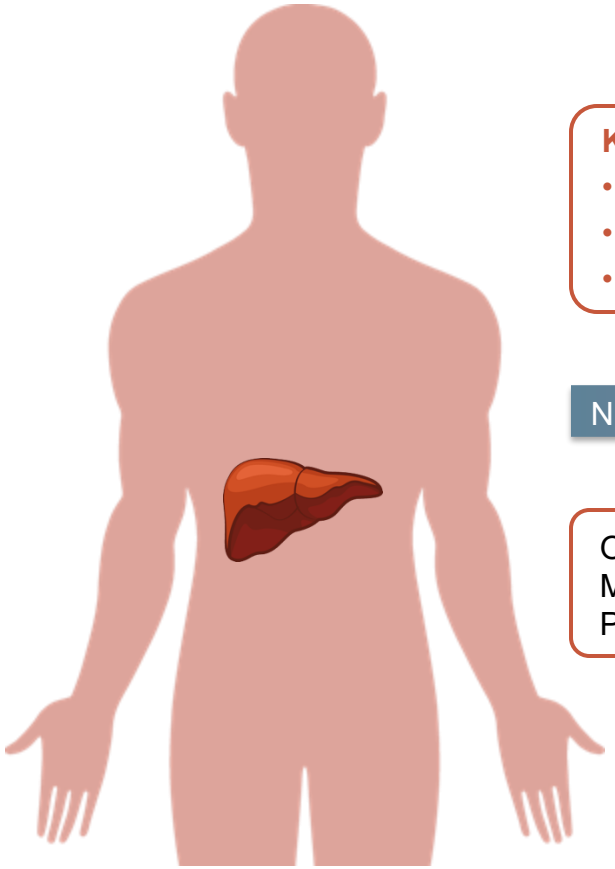
No. at risk				
Other	56	31	4	0
Cabozantinib	23	14	0	0
Lenvatinib	84	48	1	0
Sorafenib	43	17	0	0

CI, confidence interval; IO, immuno-oncology (therapy);

Persano M, et al. Eur J Cancer. 2023;189:112933

2ND LINE TKI: AVAILABLE DATA AFTER PROGRESSION ON IO

CABOZANTINIB AFTER 1ST LINE IO: PHASE 2

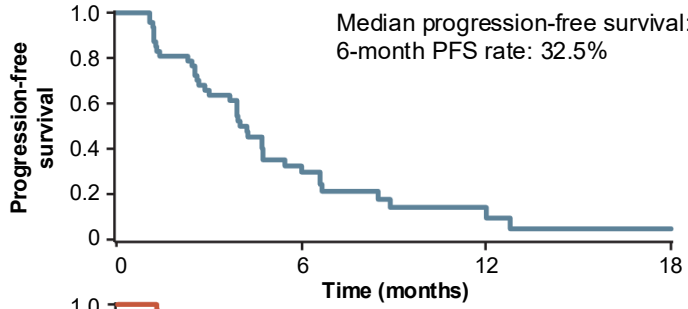


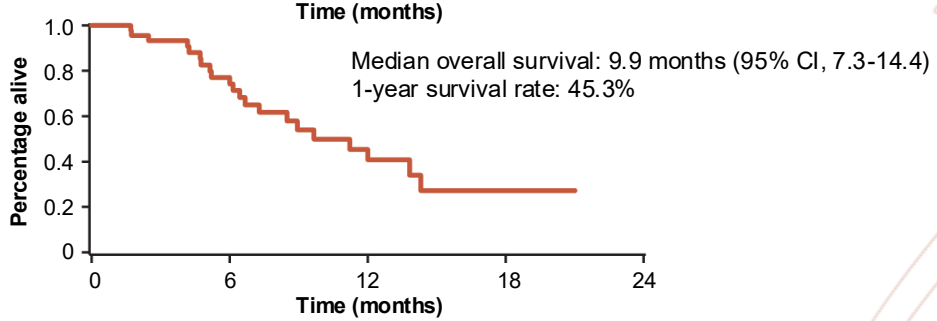
Key eligibility criteria

- Prior immune checkpoint inhibitor
- Child-Pugh class A
- Maximum two prior lines of treatment

N=47 Cabozantinib; 60 mg once daily

Oct 2020 to May 2022
Median follow-up = 11.2 months
Primary endpoint: progression-free survival





2nd line use: OS = 14.3 mo; PFS = 4.3 mo
3rd line use: OS = 6.6 mo; PFS = 4.0 mo

Median dose = 40 mg/day
Median dose intensity = 69.4%

2nd line cabozantinib demonstrated efficacy in patients who progressed on IO

- No new safety signals were observed in the study

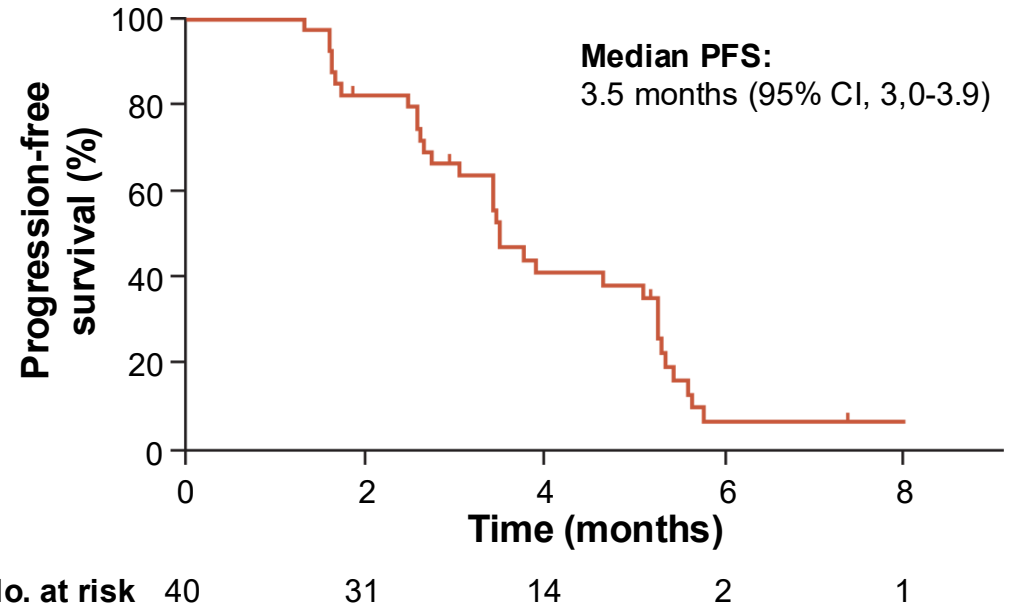
CI, confidence interval; IO, immuno-oncology (therapy); mo, months; OS, overall survival; PFS, progression-free survival; TKI, tyrosine kinase inhibitor

Chan SL, et al. J Hepatol. 2024;81:258-264

2ND LINE TKI: AVAILABLE DATA AFTER PROGRESSION ON IO

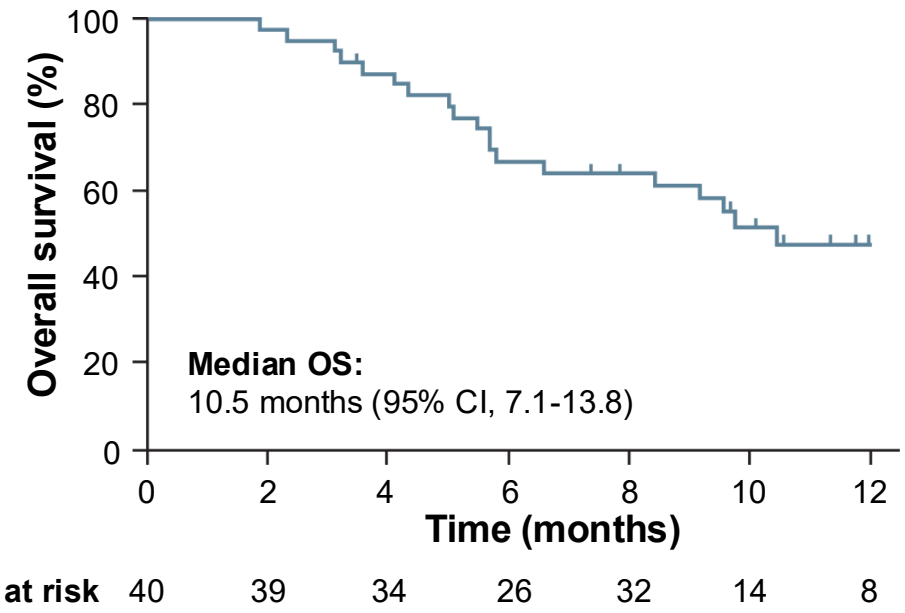
REGORAFENIB AFTER 1ST LINE ATEZOLIZUMAB + BEVACIZUMAB: PHASE 2 REGONEXT

Progression-free survival



No. at risk					
	40	31	14	2	1

Overall survival



No. at risk							
	40	39	34	26	32	14	8

- Regorafenib was effective as 2nd line therapy in unresectable patients with HCC who progressed on 1st line atezolizumab + bevacizumab
- Efficacy and safety of regorafenib were consistent with those observed in the RESORCE trial

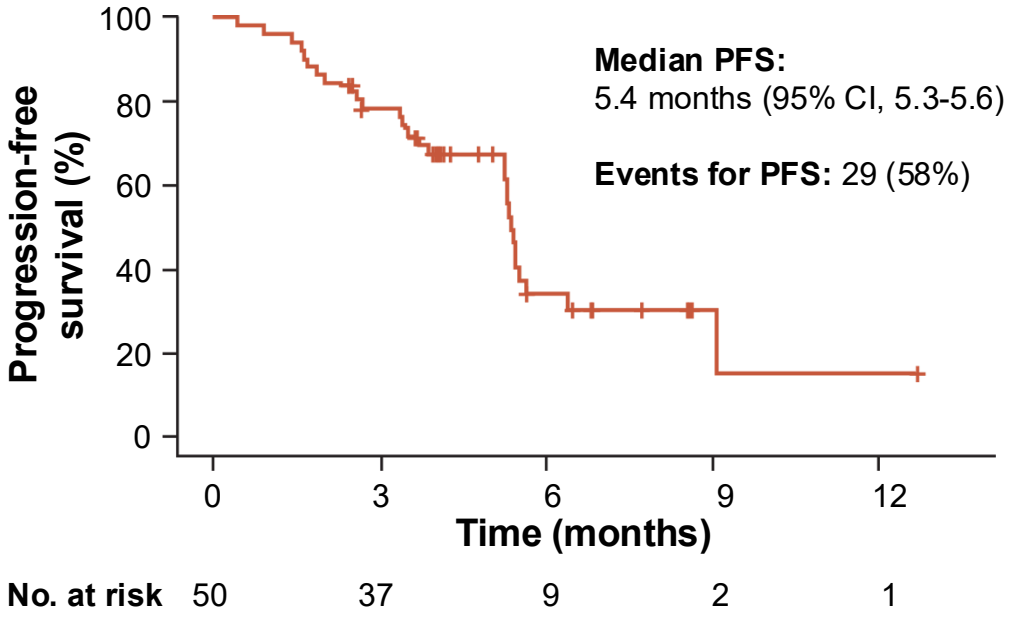
C1, cycle 1; CI, confidence interval; D1, day 1; HCC, hepatocellular carcinoma; IO, immuno-oncology (therapy); OS, overall survival; PFS, progression-free survival; TKI, tyrosine kinase inhibitor

Cheon et al. Liver Cancer 2025;

2ND LINE TKI: AVAILABLE DATA AFTER PROGRESSION ON IO

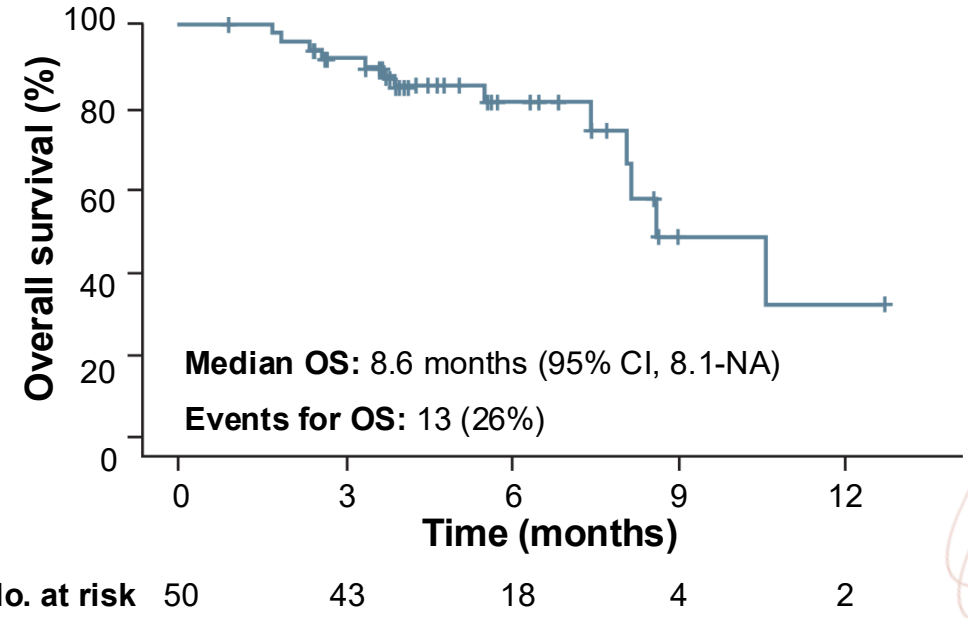
LENVATINIB AFTER 1ST LINE ATEZOLIZUMAB + BEVACIZUMAB: PHASE 2 (KCSG HB23 04)

Progression-free survival



No. at risk	50	37	9	2	1

Overall survival



No. at risk	50	43	18	4	2

- 2nd line lenvatinib in patients who progressed on 1st line atezolizumab + bevacizumab shows a median PFS of 5.4 months and met its primary endpoint in PFS (4.5 months)
- There were no new safety signals of lenvatinib
- OS data are not matured and require follow-up

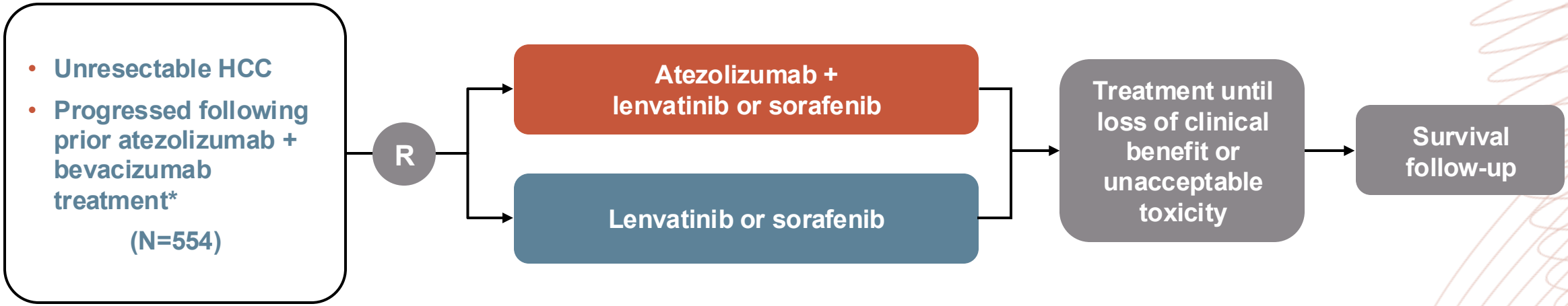
CI, confidence interval; IO, immuno-oncology; PFS, progression-free survival; TKI, tyrosine kinase inhibitor

Yoo C, et al. Ann Oncol. 2024;35 (Supplement 4):S1450. Presented at ESMO Asia, 2024 (LBA1)

ONGOING PHASE 3 STUDY AFTER PROGRESSION ON IO: IMbrave251

2ND LINE ATEZOLIZUMAB + TKI VS TKI ALONE AFTER PROGRESSION ON 1ST LINE ATEZOLIZUMAB + BEVACIZUMAB

Site selects the choice of TKI:
lenvatinib or sorafenib



Efficacy objectives
- **Primary:** OS
- **Secondary:** PFS,* ORR,* DoR,* TTP,* TTD in PROs

Safety objective
- Percentage of patients with AEs

Exploratory
- Number of patients with anti-drug antibodies to atezolizumab
- Serum concentration of atezolizumab

*INV-assessed per RECIST v1.1

AE, adverse event; AFP, α-fetoprotein; ALBI, albumin-bilirubin; DoR, duration of response; HBV/HCV, hepatitis B/C virus; HCC, hepatocellular carcinoma; inv, investigator; IO, immuno-oncology (therapy); OS, overall survival; PFS, progression-free survival; ORR, objective response rate; PRO, patient-reported outcome; RECIST, Response Evaluation Criteria in Solid Tumours; TKI, tyrosine kinase inhibitor; TTD, time to deterioration; TTP, time to progression

ClinicalTrials.gov.Identifier: NCT04770896. Available from: https://clinicaltrials.gov/ct2/show/NCT04770896 (accessed Jan 2025)

PROGRESSION ON 1st LINE IO

THERE IS LIMITED PROSPECTIVE DATA ON TKIs AFTER PROGRESSION ON IO

- IO-based therapies have only **recently become the standard of care** in the 1st line for HCC
- **Prospective clinical trials** focusing on post-progression TKI treatments after progression on IO are still **limited**
  - Enrolment in a **clinical trial** is warmly encouraged
- In the absence of evidence-based interventions, **patients' clinical features, tolerability of the prior therapy, and regulatory approvals** in each country drive the decision-making process
- If a clinical study is not accessible, there exists **initial reassuring evidence** regarding the use of TKIs after IO in routine clinical practice

HCC, hepatocellular carcinoma; IO, immuno-oncology (therapy); TKI, tyrosine kinase inhibitor

Bruix J, et al. J Hepatol. 2021;75:960-974

AVAILABLE DATA
AFTER PROGRESSION ON 1ST LINE IO

IO AFTER IO

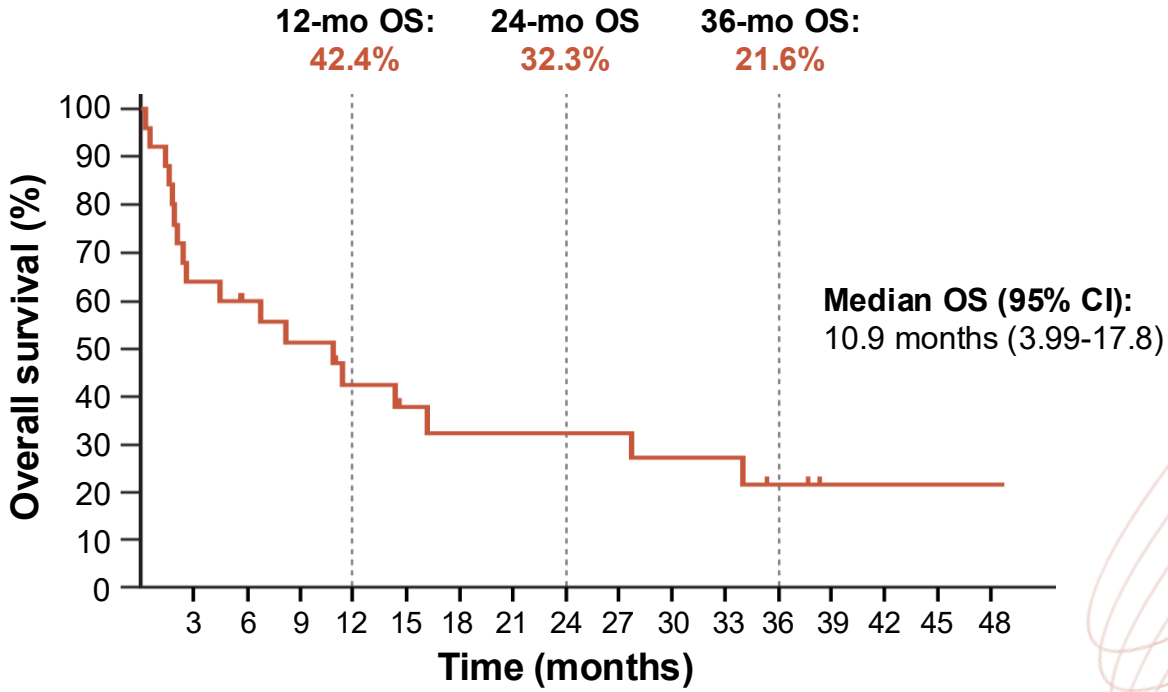
IO, immuno-oncology (therapy)

2ND LINE IO: AVAILABLE DATA AFTER PROGRESSION ON IO

IPILIMUMAB + NIVOLUMAB / PEMBROLIZUMAB AFTER PRIOR IO IN RETROSPECTIVE STUDY

Best objective response

Activity	N (%)
CR	3 (12)
PR	1 (4)
SD	6 (24)
PD	12 (48)
Non-evaluable	3 (12)
ORR	4 (16)



- Ipilimumab combined with nivolumab or pembrolizumab has demonstrated durable anti-tumour activity and promising survival benefits in patients with advanced HCC previously treated with IO
  - Acceptable toxicity

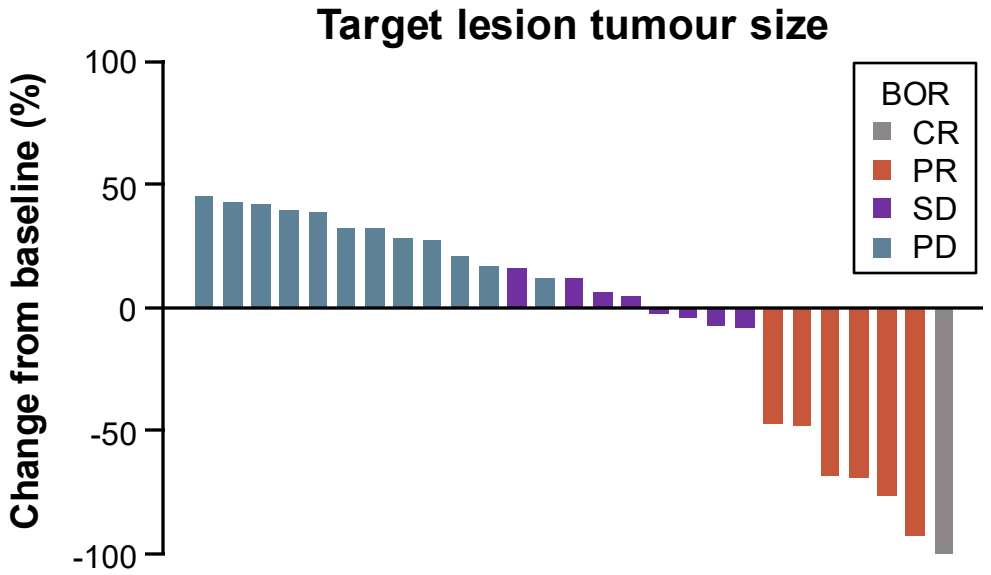
CI, confidence interval; CR, complete response; HCC, hepatocellular carcinoma; IO, immuno-oncology (therapy); ORR, objective response rate; OS, overall survival; PD progressive disease; PR, partial response; SD, stable disease

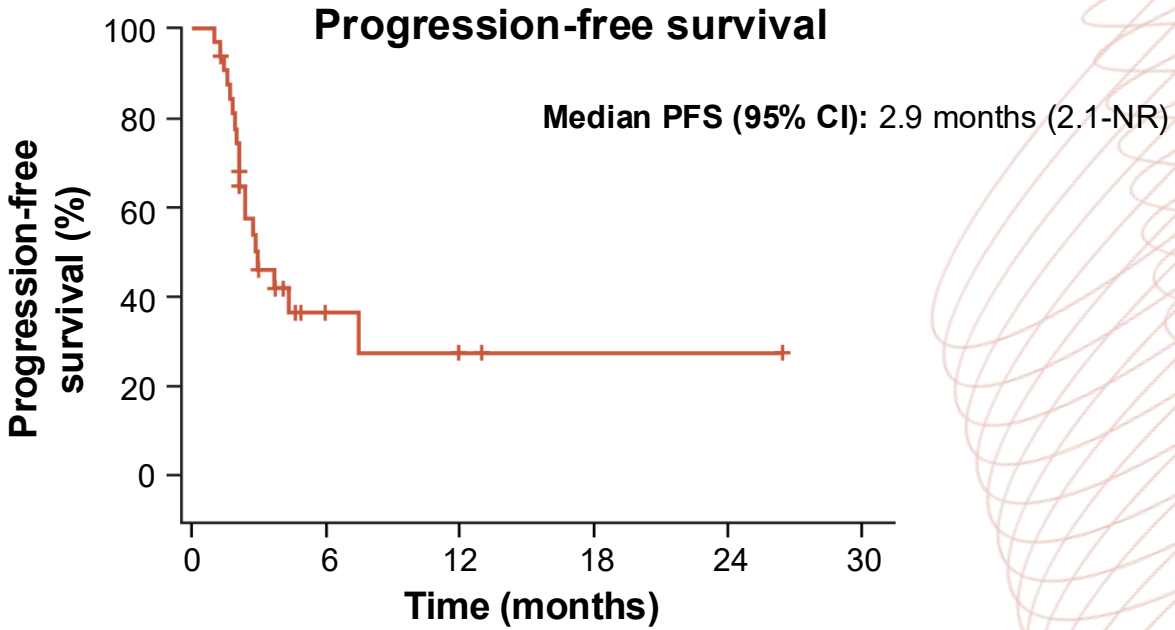
Wong JSL, et al. J Immunother Cancer. 2021;9:e001945

2ND LINE IO: AVAILABLE DATA AFTER PROGRESSION ON IO

IPILIMUMAB + NIVOLUMAB AFTER PRIOR ANTI-PD-(L)1 THERAPY IN RETROSPECTIVE STUDY

- Multicentre retrospective analysis of 32 patients with prior anti-PD-(L)1 therapy, including 16 with prior atezolizumab + bevacizumab, 10 other ICI + VEGF combinations, and 6 ICI monotherapy
- ORR was 22% (1 CR, 6 PR), of whom none had objective response to prior anti-PD(L)1 therapy
- Median PFS was 2.9 months and median OS was 9.2 months
- There were no new safety signals





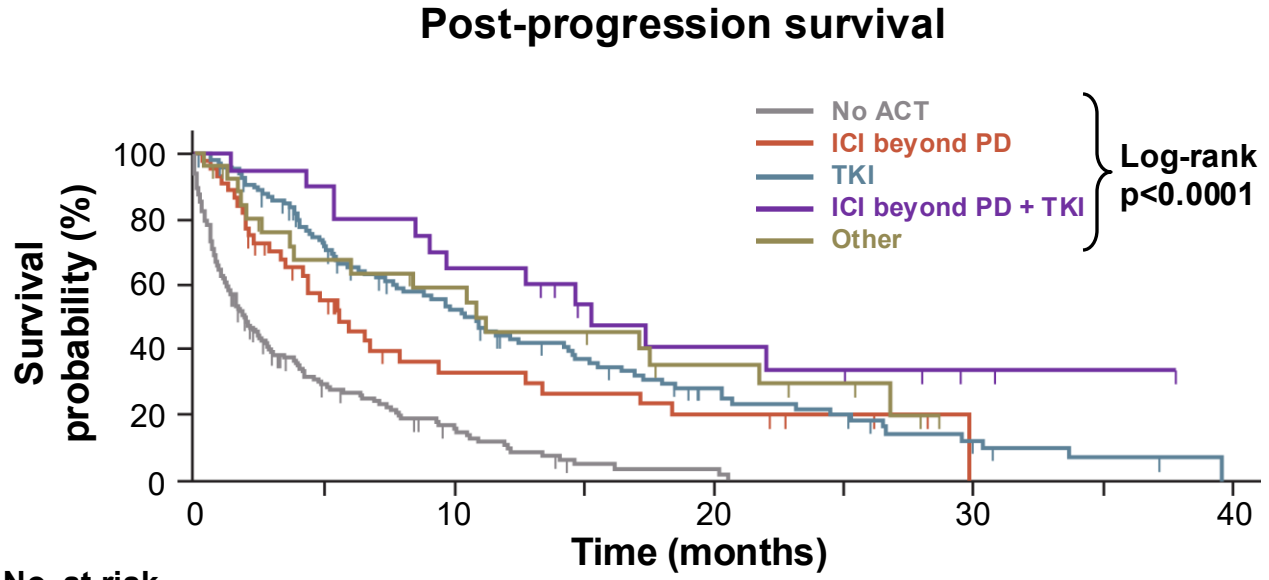
BOR, best overall response; CR, complete response, ICI, immune checkpoint inhibitor; IO, immuno-oncology (therapy); NR, not reached; ORR, objective response rate; OS, overall survival; PD, progressive disease; PD-1, programmed cell death protein; PD-L1, programmed death ligand 1; PFS, progression-free survival; PR, partial response; SD, stable disease; VEGF, vascular endothelial growth factor

Alden S, et al. Cancer Res Commun. 2023;3:1312-1317

2ND LINE IO: AVAILABLE DATA AFTER PROGRESSION ON IO

THERAPEUTIC SEQUENCING FOLLOWING IO IN RETROSPECTIVE STUDY

- IO-TKI sequencing is a consolidated option in advanced HCC
- IO-IO is adopted clinically despite lack of recommendation
  - Future efforts should define which patients benefit from this approach



No. at risk					
No ACT	165	16	2	0	0
ICI beyond PD	44	10	6	0	0
TKI	108	47	19	5	0
ICI beyond PD + TKI	20	13	6	2	0
Other	27	13	6	0	0

Kaplan-Meier curves of post-progression survival (PPS) in hepatocellular carcinoma patients treated with immune checkpoint inhibitor (ICI) according to treatment strategy. Patients who did not receive post-progression anticancer therapy (no ACT): 1.9 months (95% CI: 1.3-2.7, 132 events), patients who received ICIs beyond PD only (ICI beyond PD): 5.6 months (95% CI: 3.5-9.4, 31 events), patients who received post-PD TKIs only (TKI): 10.4 months (95% CI: 7.7-14.4, 79 events), patients who received ICIs beyond PD followed by TKIs (ICI beyond PD + TKI): 15.3 months (95% CI: 8.5-22.0, 12 events), patients who received other post-PD anticancer therapies (other): 10.8 months (95% CI: 3.7-21.7, 17 events).

ACT, anti-cancer therapy; CI, confidence interval; HCC, hepatocellular carcinoma; ICI, immune checkpoint inhibitor; IO, immuno-oncology (therapy); PD, disease progression; TKI, tyrosine kinase inhibitor

Talbot T, et al. Liver Int. 2023;43:695-707

2ND LINE IO: AVAILABLE DATA AFTER PROGRESSION ON IO

EFFICACY AND SAFETY OF IO RECHALLENGE IN RETROSPECTIVE STUDY

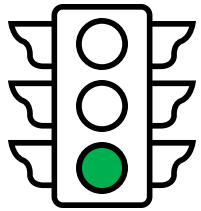
International, retrospective multicentre study:
14 centres
994 patients screened

58 patients with advanced HCC receiving **two lines of ICI-treatment** (ICI-1 and ICI-2)

Efficacy:

	ICI-1	ICI-2
ORR:	22%	26%
DCR:	59%	55%
Median **TTP:**	5.4	5.2 months

Safety:
Grade 3-4 adverse events:
ICI-1: 16%, **ICI-2:** 17%
No treatment-related **deaths**



- IO rechallenge resulted in a treatment benefit in a meaningful proportion of patients with HCC
- IO rechallenge was safe in the study and high-grade treatment-related adverse events were uncommon

DCR, disease control rate; HCC, hepatocellular carcinoma; ICI, immune checkpoint inhibitor; IO, immuno-oncology (therapy); ORR, objective response rate; TTP, time to progression

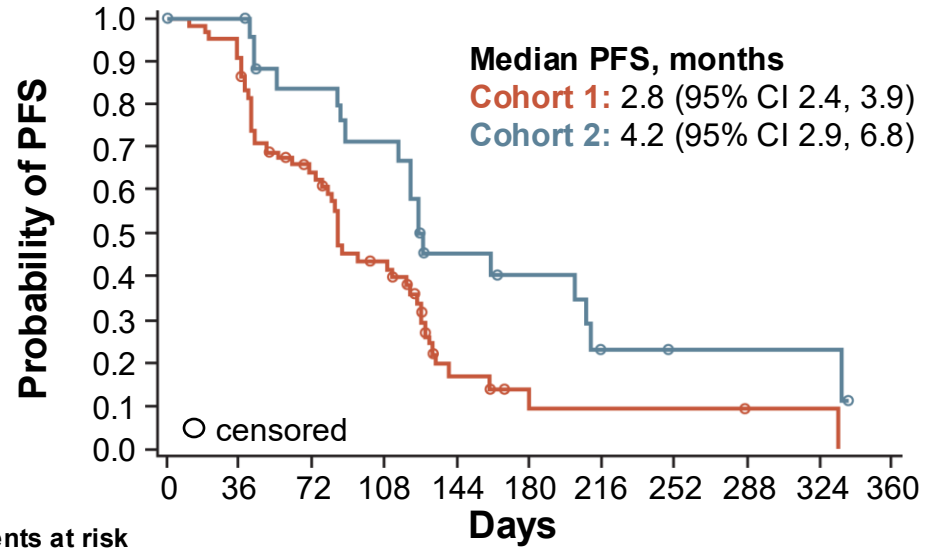
Scheiner B, et al. JHEP Rep. 2022;5:100620

2ND LINE IO: AVAILABLE DATA AFTER PROGRESSION ON IO

REGORAFENIB + PEMBROLIZUMAB AFTER IO – PHASE 2

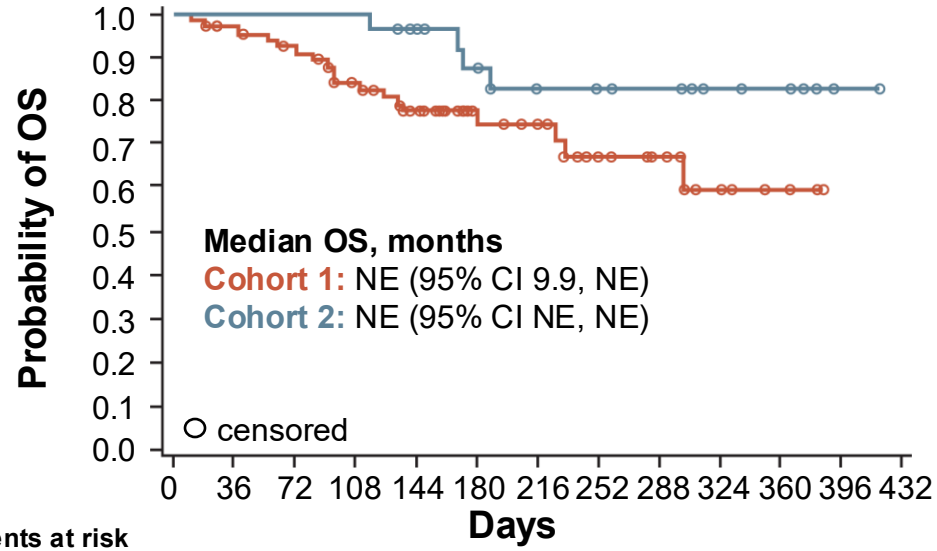
- Open-label, Phase 2 study in 38 centres in eight countries
- Regorafenib + pembrolizumab had modest activity after 1st line IO-based combinations
- The safety profile of the combination was consistent with that observed for each drug individually

PFS by patient subgroup[a]



Patients at risk											
Cohort 1	68	60	39	24	6	3	2	2	1	1	0
Cohort 2	27	26	20	17	9	7	4	2	2	2	0

OS by patient subgroup[a]



Patients at risk													
Cohort 1	68	64	59	50	40	26	23	15	11	6	3	0	0
Cohort 2	27	27	27	27	24	20	17	14	13	7	5	1	0

Kaplan-Meier analyses. PFS was assessed via RECIST version 1.1 by independent central review. At-risk patient counts were calculated at the start of each timepoint.

[a] All patients received regorafenib + pembrolizumab. Cohorts were defined by prior 1st line treatment: Cohort 1 = atezolizumab + bevacizumab; Cohort 2 = any other ICI regimen (alone or combination)

1L, first-line; CI, confidence interval; ICI, immune checkpoint inhibitor; IO, immuno-oncology (therapy), NE, not estimable; OS, overall survival; PFS progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumours

El-Khoueiry AB, et al. J Clin Oncol. 2024;42 (no. 16 suppl):4007 (presented at ASCO Annual Meeting I)

PROGRESSION ON 1st LINE IO

PROSPECTIVE DATA ARE LACKING FOR IO AFTER PROGRESSION ON IO

- IO-based therapies have only **recently become the standard of care** in the 1ST line for HCC
- Data on the use of IO after progression on prior IO therapy are **even more limited** than for TKIs after IO
- If a clinical trial is not available, **switching to an alternative IO regimen** may be considered in clinical practice in select patients, based on individual clinical factors, prior response and toxicity on IO, and local availability

HCC, hepatocellular carcinoma; IO, immuno-oncology (therapy); TKI, tyrosine kinase inhibitor

WHEN TO SWITCH

AFTER PROGRESSION ON 1ST LINE IO

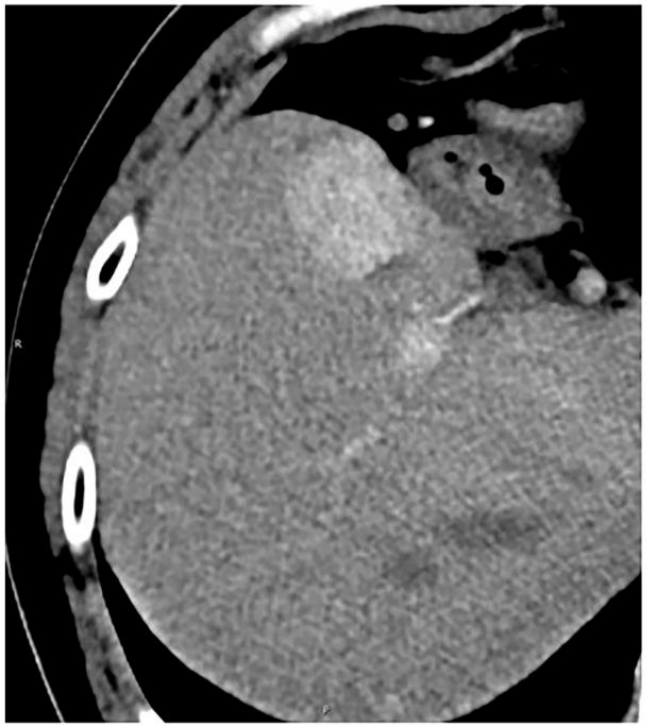
IO, immuno-oncology (therapy)

MEASURING RADIOLOGIC PROGRESSION IN HCC

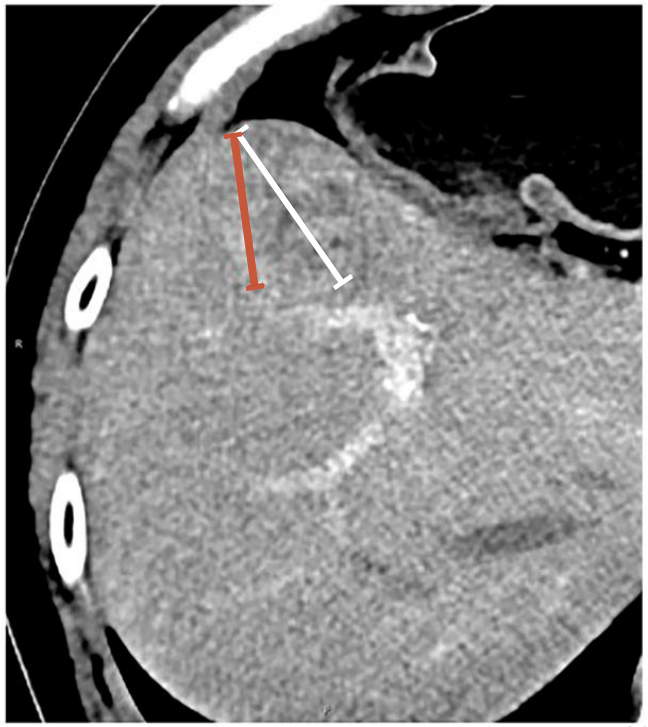
mRECIST CRITERIA HAVE A POWERFUL ABILITY TO DISCRIMINATE BETWEEN RESPONDERS AND NON-RESPONDERS

- Measurement of the longest tumour diameter in a target hepatic lesion: mRECIST vs RECIST
- The response was assessed as progressive disease according to RECIST 1.1 and stable disease based on mRECIST

Before start treatment



After immunotherapy



White line: the overall longest diameter of the tumour according to RECIST 1.1
Red line: the longest diameter of the viable portion of the tumour as per mRECIST and recognized by contrast enhancement

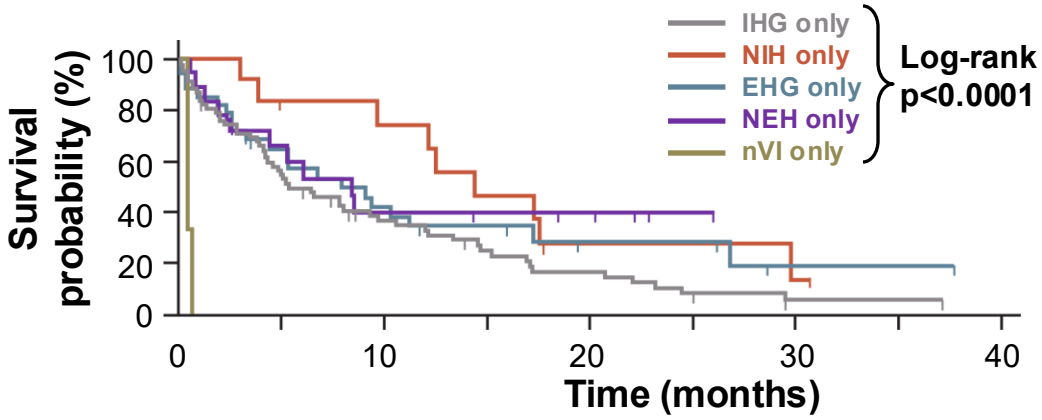
HCC, hepatocellular carcinoma; (m)RECIST, (modified) Response Evaluation Criteria in Solid Tumours

Zhou M, et al. Front Oncol. 2021;11:764189

PATTERNS OF PROGRESSION FOLLOWING 1ST LINE IO

TYPE OF PROGRESSION MAY INFLUENCE RESULTS

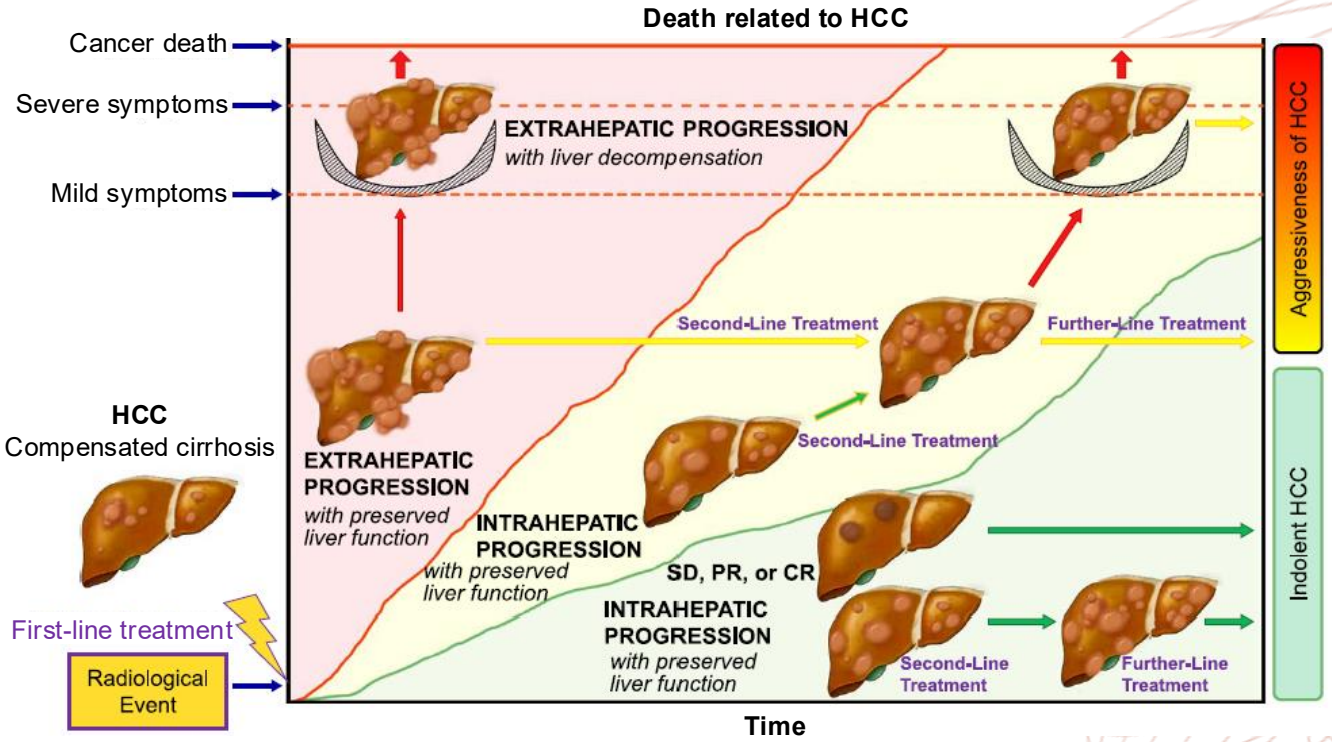
Post-progression survival[1]



No. at risk					
IHG only	67	19	8	1	0
NHI only	12	8	2	1	0
EHG only	34	11	4	1	0
NEH only	19	6	4	0	0
nVI only	3	0	0	0	0

Kaplan-Meier survival estimates for post-progression survival (PPS) according to the radiological pattern of progression. Intrahepatic growth only: 5.3 months (95% CI: 4.2-9.7, 54 events), new intrahepatic lesion only: 14.4 months (95% CI: 3.8-29.8, 9 events), extrahepatic growth only: 7.9 months (95% CI: 3.3-17.3, 21 events), new extrahepatic lesion only: 8.4 months (95% CI: 2.5-8.5, 10 events), new vascular invasion only: 0.4 months (95% CI: 0.4-0.6, 3 events).

Outcome of patients with HCC across the years according to radiologic response[2]

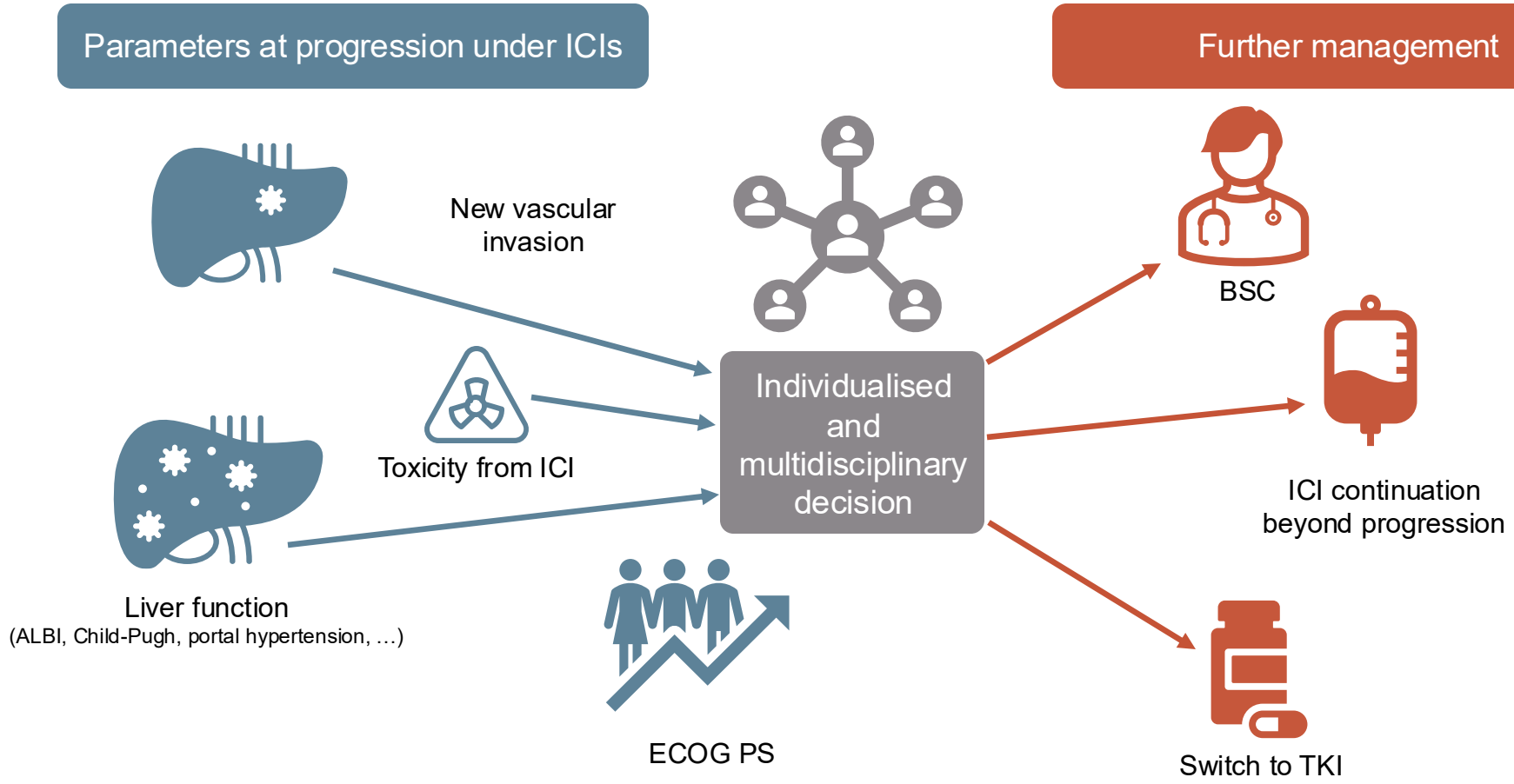


CI, confidence interval; CR, complete response; EHG, extrahepatic growth; HCC, hepatocellular carcinoma; IHG, intrahepatic growth; IO, immuno-oncology (therapy); NEH, new extrahepatic lesions(s); NIH, new intrahepatic lesion(s); nVI, new vascular invasion; PR, partial response; SD, stable disease

1. Talbot T, et al. Liver Int. 2023;43:695-707; 2. Iavarone M, et al. Hepatology. 2024;79:1452-1462

WHEN TO SWITCH AFTER PROGRESSION ON 1ST LINE IO

PARAMETERS INFLUENCING DECISION AT PROGRESSION FOR ADVANCED HCC



Parameters influencing decision at progression on immunotherapy for advanced HCC.

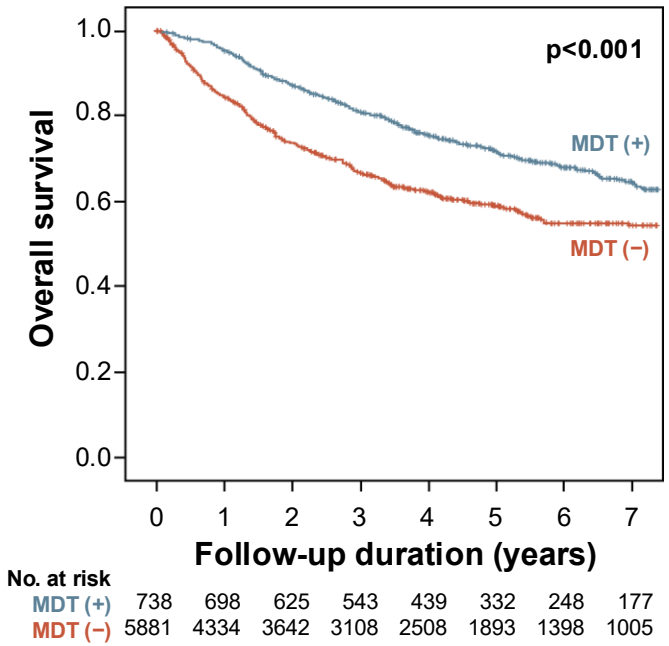
ALBI, albumin-bilirubin score; BSC, best supportive care; ECOG PS, Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; ICI, immune checkpoint inhibitor; IO, immuno-oncology (therapy); TKI, tyrosine kinase inhibitor

Cabibbo G and Edeline J. Liver Int. 2023;43:528-530

MULTIDISCIPLINARY APPROACH FOR HCC

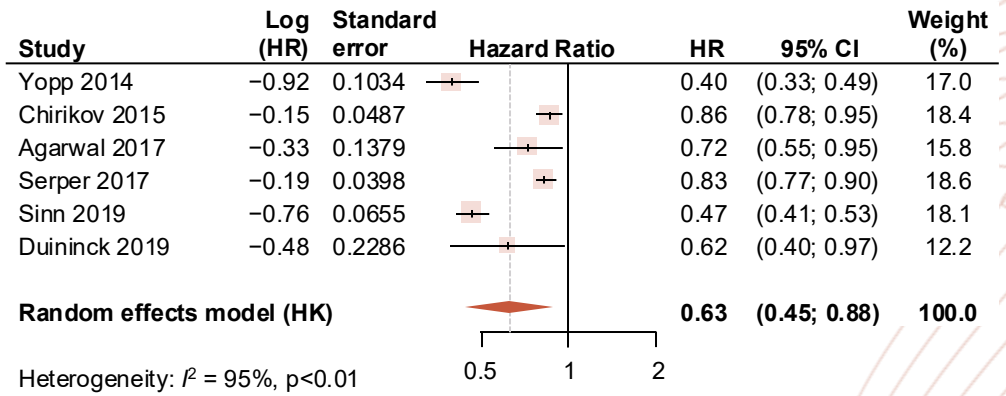
KEY FOR OPTIMISING EACH PATIENT'S TREATMENT

OS entire cohort[1]



5-year survival rate was 71.2% vs. 49.4%, P <0.001
MDT management benefit particularly significant in patients with ALBI 2 and 3, BCLC B and C, AFP > 200 ng/mL

Association between multidisciplinary care and overall survival[2]



Multidisciplinary care was significantly associated with improved survival

AFP, α-fetoprotein; ALBI, albumin-bilirubin score; BCLC, Barcelona Clinic Liver Cancer; CI, confidence interval; HCC, hepatocellular carcinoma; HK, Hartung-Knapp (adjustment); HR, hazard ratio; MDT, multidisciplinary team; OS, overall survival

1. Sinn DH, et al. PLoS One. 2019;14:e0210730; 2. Seif El Dahan K, et al. Hepatol Commun. 2023;26:e0143

WHEN TO SWITCH AFTER PROGRESSION ON 1ST LINE IO

PARAMETERS INFLUENCING DECISION AT PROGRESSION FOR ADVANCED HCC

- Assessing **progression type** and **liver function** is crucial for detailed prognosis evaluation in advanced HCC
  - Highlights the importance of a **multidisciplinary approach** for personalised treatment in advanced HCC
  - **Multidisciplinary care** is associated with **improved overall survival** for patients with HCC
- More **accurate patient stratification** should be enabled by incorporating progression type and liver function decline assessment
- Progression type and liver function decline assessment should be integrated into study designs **to guide treatment decisions** for patients who progress on IO

HCC, hepatocellular carcinoma; IO, immuno-oncology (therapy)

CONCLUSIONS

CONCLUSIONS – WHAT WE KNOW

ADVANCED HCC: STRATEGIES FOR PATIENTS INELIGIBLE FOR IO OR THOSE WITH PROGRESSION ON IO

- For patients with HCC ineligible for IO, TKIs (sorafenib, lenvatinib) are the recommended 1st line treatment options
- After progression on 1st line IO, available strategies include:
  - Enrolment in clinical trials
  - Switching to a TKI or anti-VEGFR-2
  - Considering IO after IO approaches
  - Providing best supportive care for patients unsuitable for further systemic therapies
- Post-IO progression strategies involve two main approaches:
  - **T-1 Approach:** Focusing on sorafenib or lenvatinib as 2nd line options
  - **Line-agnostic Approach:** Expanding to all 2nd line options (sorafenib, lenvatinib, regorafenib, cabozantinib, ramucirumab)
- Transition to 2nd line therapy and decision-making should be guided by:
  - Radiologic progression and the pattern of progression
  - Patient's clinical characteristics, tolerability of prior therapy, and regulatory approvals in each country
- Receiving a 2nd line treatment is key for better outcomes
- Limited prospective data emphasise the need for patient enrolment in clinical trials to optimise sequencing strategies

HCC, hepatocellular carcinoma; IO, immuno-oncology (therapy); TKI, tyrosine kinase inhibitor

CONCLUSIONS – WHAT WE NEED

ADVANCED HCC: STRATEGIES FOR PATIENTS INELIGIBLE FOR IO OR THOSE WITH PROGRESSION ON IO

- Identify and validate **biomarkers** of response and resistance (e.g., anti-drug antibodies?) to guide the selection of optimal treatment sequences for different patient groups
- Increase the collection and analysis of **tumour samples and liquid biopsies** to better understand disease biology and treatment response
- Evaluate the **cost-effectiveness and risk-benefit ratio** of each treatment and sequencing strategy to support evidence-based decision-making
- Conduct **randomised clinical trials** to define the most effective treatment sequences for patients with advanced HCC

HCC, hepatocellular carcinoma; IO, immuno-oncology (therapy)

COR2ED
THE HEART OF MEDICAL EDUCATION

For more information visit

HCC connect®
POWERED BY COR2ED

Connect on
LinkedIn @HCC CONNECT

Watch on
YouTube @COR2ED

Email
info@cor2ed.com

Visit us at
https://cor2ed.com/

Follow us on
X @hccconnectinfo

Heading to the heart of Independent Medical Education since 2012