EL SISTEMA BCLC PARA EL CARCINOMA HEPATOCELULAR EN 2024

María Reig

Head of Liver Oncology Unit - BCLC group

Consultant of Liver Unit

Hospital Clinic, IDIBAPs and CIBEREHD

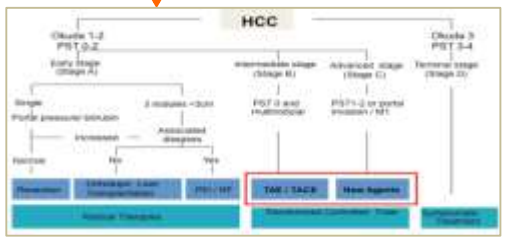
Maria Reig Disclossures

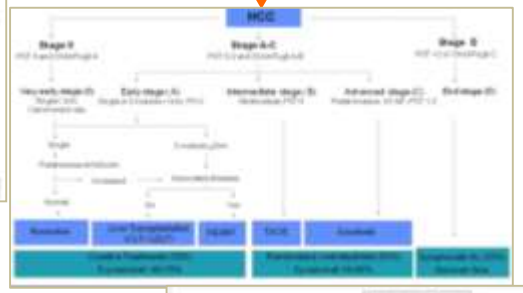
I have an interest in relation to one or more organizations that could be perceived as a possible conflict of interest in the context of the subject of this presentation.

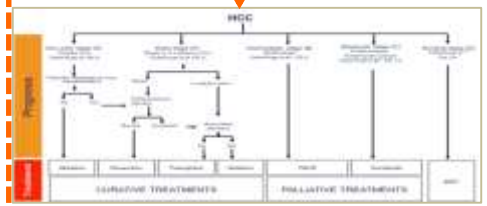
- **Employment:** Head of Liver Oncology Unit. Hospital Clinic Barcelona. Director of BCLC group at IDIBAPS/CIBEREHD.
- **Consultant or Advisory Role:**AstraZeneca, Bayer, BMS, Eli Lilly, Geneos, Ipsen, Merck, Roche, Universal DX, Engitix Therapeutics
- **Research Funding:** Yes (ISCIII, CIBER)
- **Speaking:** AstraZeneca, Bayer, BMS, Eli Lilly, Gilead, Roche, Guerbet, Biotoscana Farma S.A.
- **Travel support:** Astrazeneca, Roche, Bayer, BMS, Lilly, Ipsen
- **Principal or sub-Investigator of drug under development:** Abbvie, BMS, Adaptimmune, Nerviano, Bayer, Ipsen, Astrazeneca, Terumo, Incyte, Roche, Boston Scientific,
- **Grant Research Support (to the institution):** Bayer, Ipsen
- **Educational Support (to the institution):** Bayer, Astrazeneca, BMS, Eisai- Merck MSD, Roche, Ipsen, Lilly, Terumo, Next, Boston Scientific, Ciscar Medical, Eventy 03 LLC (Egypt)

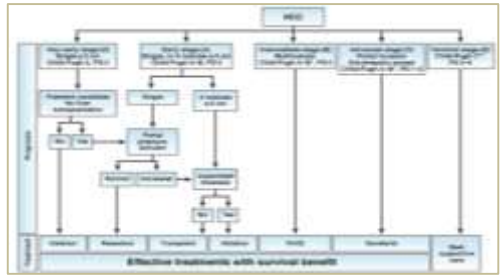
The BCLC staging system

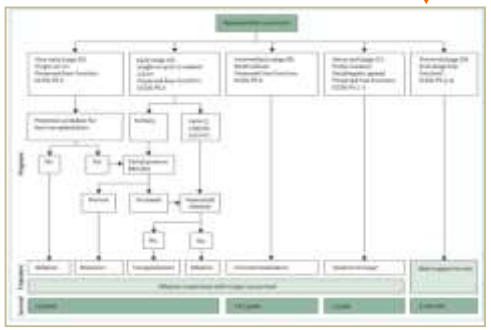
1999 2003 2008 2012 2014 2016 2018 2022 2024-2025

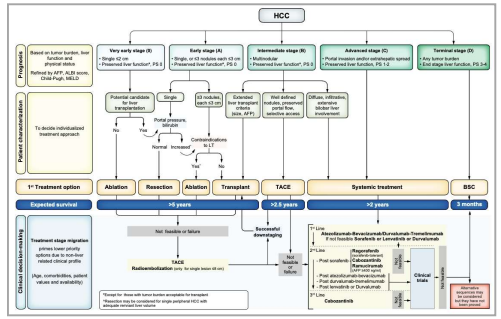












Do we need a new version?

Llovet JM, Bru C, Bruix J. Semin Liver Dis 1999;Llovet JM, Burroughs A, Bruix J. Lancet 2003;Forner A, Reig M, Rodriguez De Lope C, Bruix J. SeminLiver Dis 2010;Forner A, Llovet JM, Bruix J. Lancet 2012;
Reig M, Darnell A, Forner A, Rimola J, Ayuso C, Bruix J. Semin Liver Dis 2014; Bruix J, Reig M, Sherman M. Gastroenterology 2016;Forner A, Reig M, Bruix J. Lancet 2018.

JOURNAL OF HEPATOLOGY
The Home of Liver Research
EASL

M. Reig, A. Forner, J. Rimola, J. Ferrer-Fabrega, M. Burrel, A. Garcia-Criado, R.K. Kelley, P.R. Galle, V. Mazzaferro, R. Salem, B. Sangro, A.G. Singal, A. Vogel, J. Fuster, C. Ayuso, J. Bruix

REVIEW | ARTICLES IN PRESS

BCLC strategy for prognosis prediction and treatment recommendation Barcelona Clinic Liver Cancer (BCLC) staging system. The 2022 update

M. Reig * • A. Forner • J. Rimola • ... J. Fuster • C. Ayuso • J. Bruix * • Show all authors •

BARCELONA CLINIC LIVER CANCER

ICMDM DIGESTIVES I METABÒLIQUES
Unitat d'Oncologia Hepàtica - BCLC

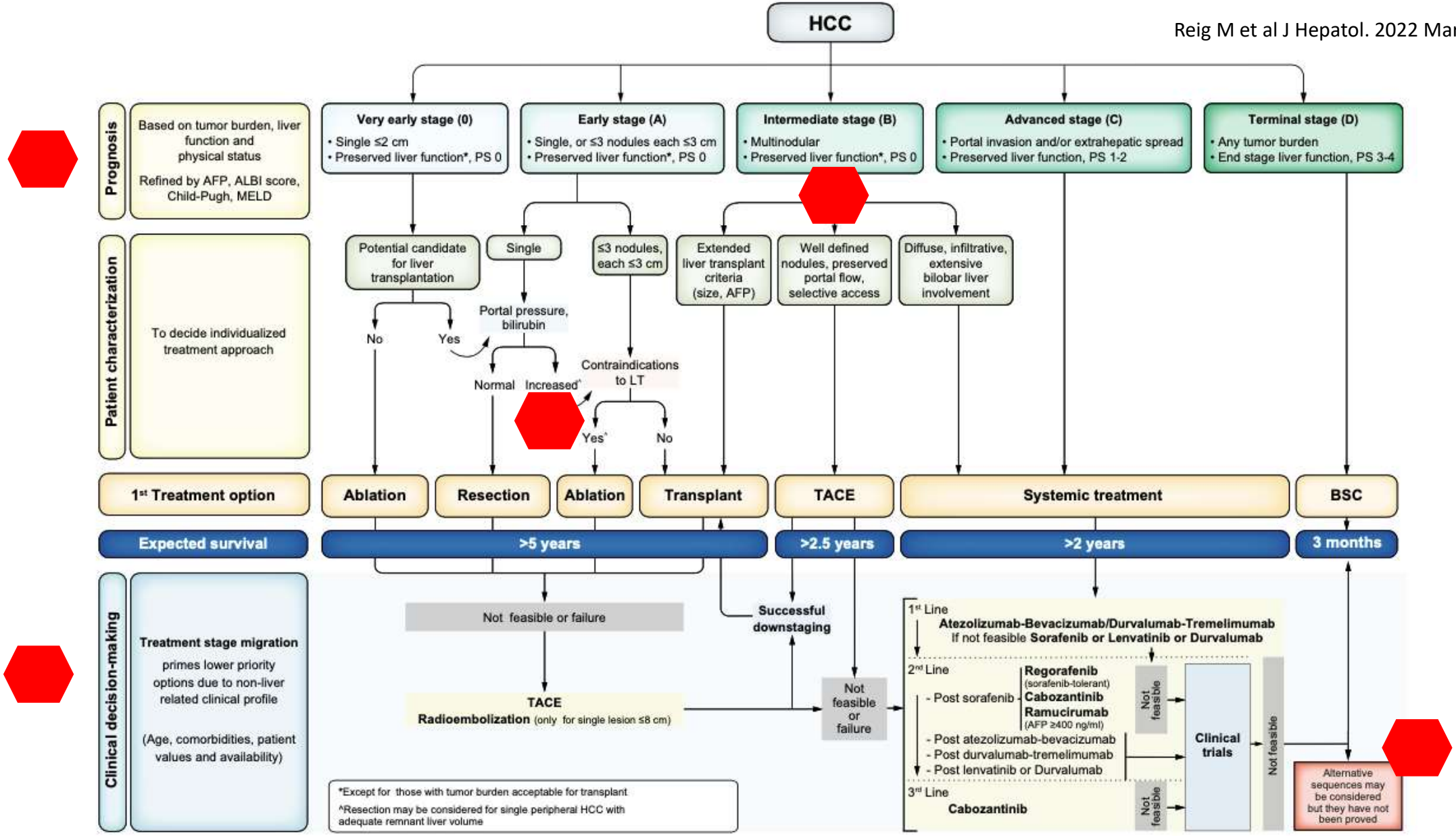
ciberehd isciii

IDIBAPS

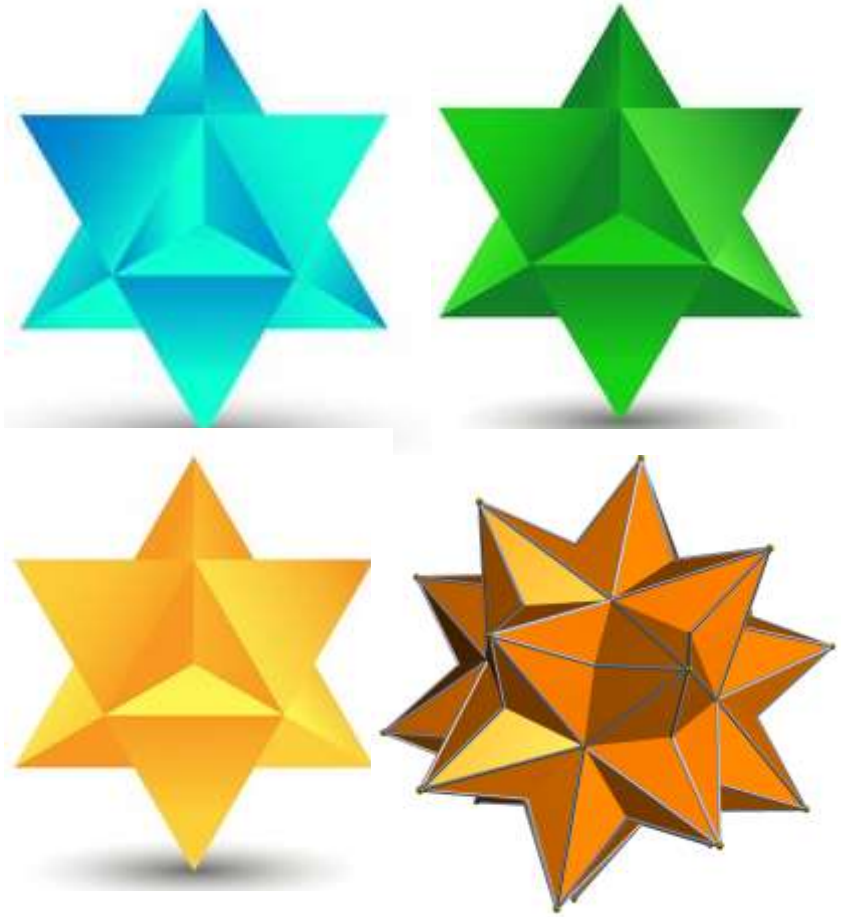
UNIVERSITAT DE BARCELONA

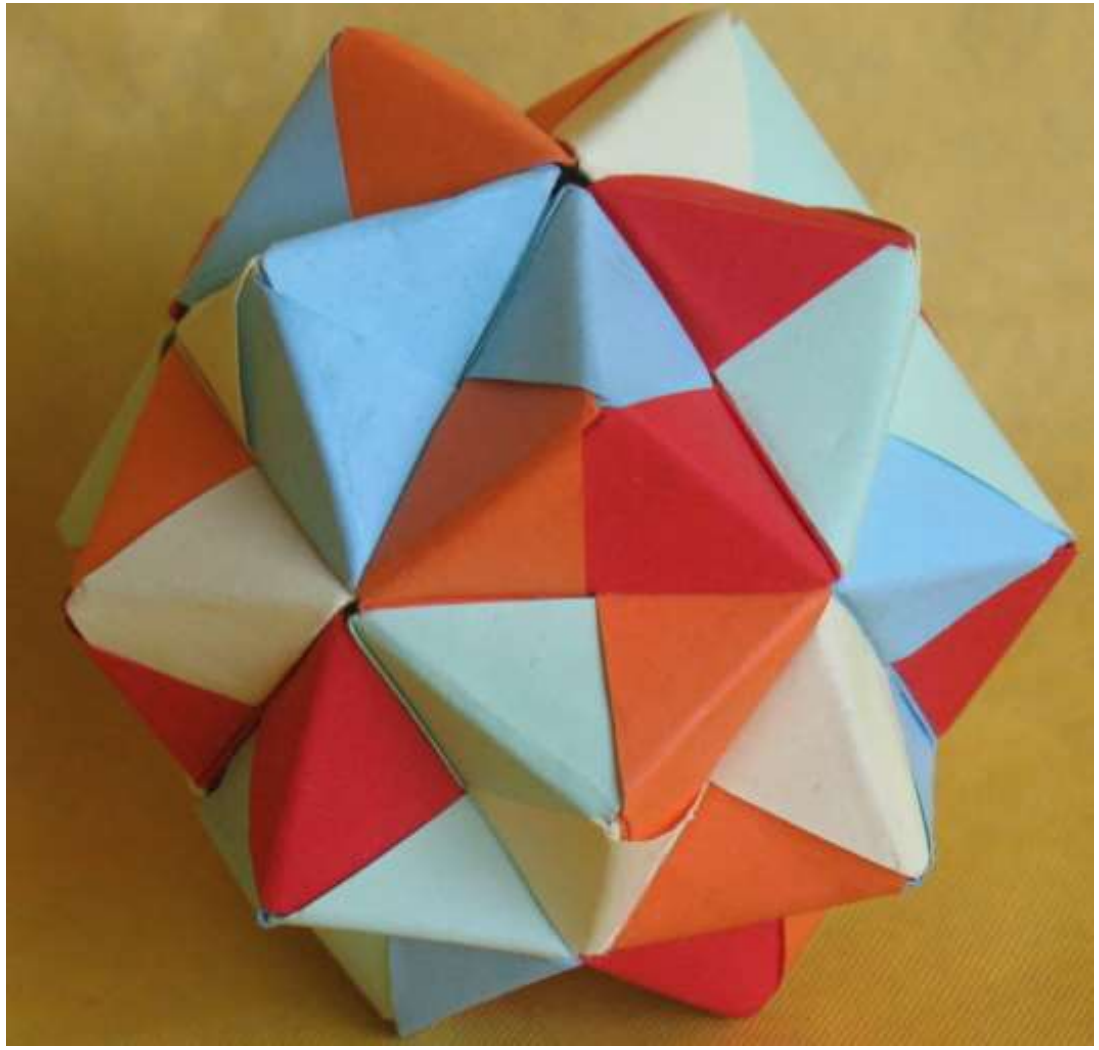
BCLC 2024

Reig M et al J Hepatol. 2022 Mar;76(3):681-693.



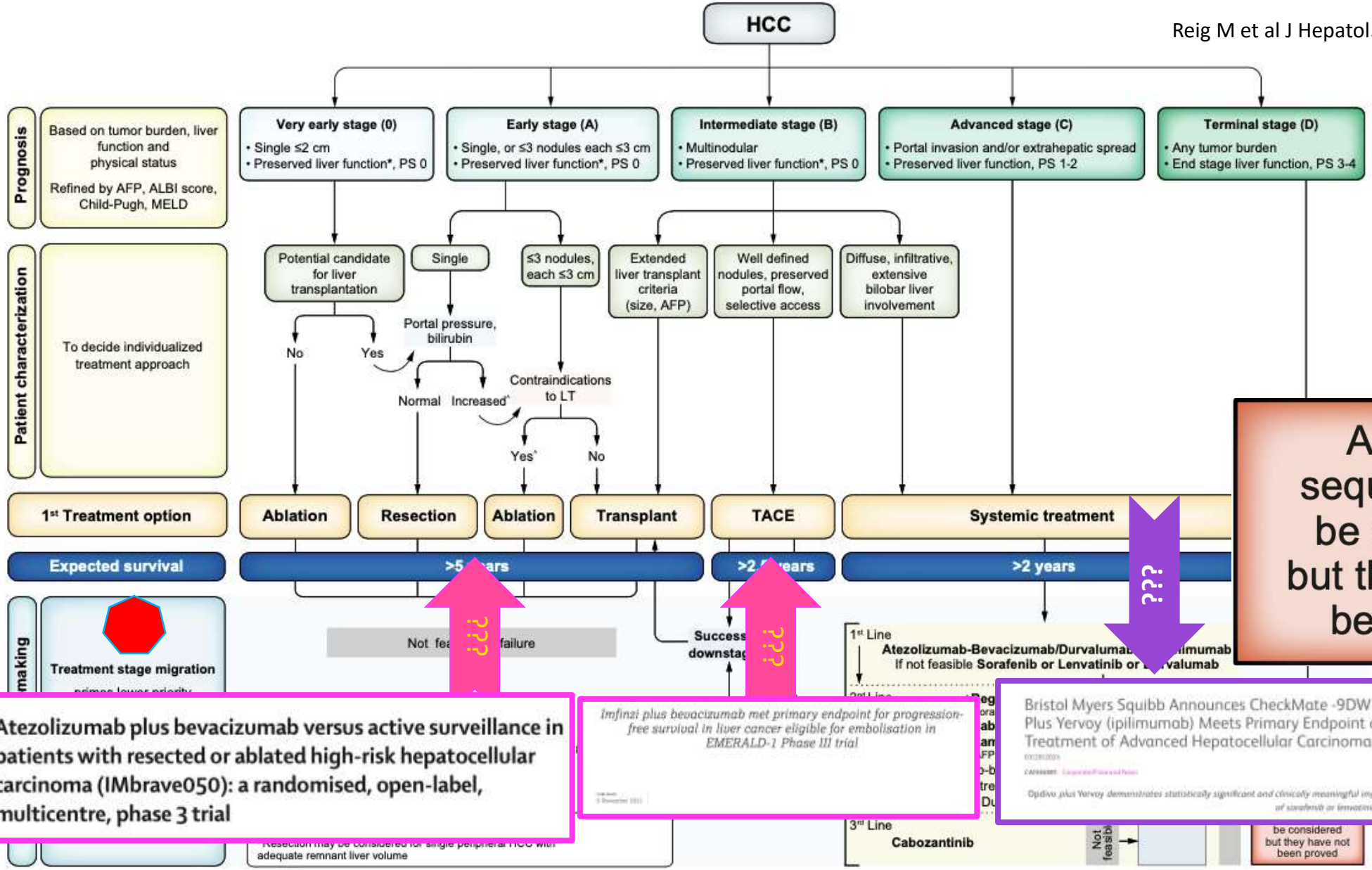
Management of the Complexity



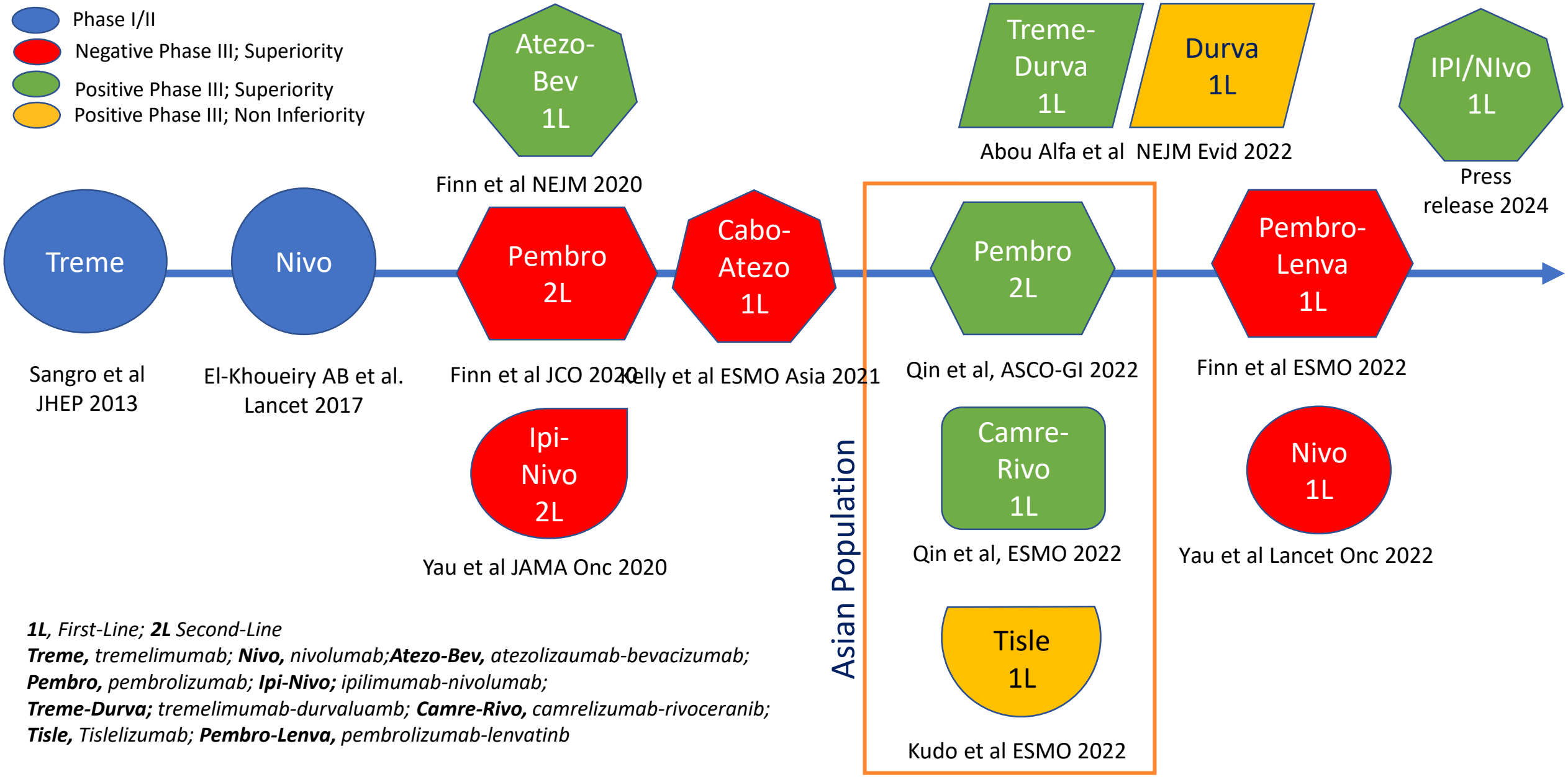


BCLC 2024

Reig M et al J Hepatol. 2022 Mar;76(3):681-693.



Immunotherapy in Hepatocelullar Carcinoma



***1L**, First-Line; **2L** Second-Line*
***Treme,** tremelimumab; **Nivo,** nivolumab;**Atezo-Bev,** atezolizaumab-bevacizumab;*
***Pembro,** pembrolizumab; **Ipi-Nivo;** ipilimumab-nivolumab;*
***Treme-Durva;** tremelimumab-durvaluamb; **Camre-Rivo,** camrelizumab-rivoceranib;*
***Tisle,** Tislelizumab; **Pembro-Lenva,** pembrolizumab-lenvatinb*

Prognosis

Based on tumor burden, liver function and physical status

Refined by AFP, ALBI score, Child-Pugh, MELD

Patient characterization

To decide individualized treatment approach

1st Treatment option

Expected survival

Clinical decision-making

Treatment stage migration

primes lower priority options due to non-liver related clinical profile

(Age, comorbidities, patient values and availability)

Evidence-based

Expected survival

Regulatory approvals?

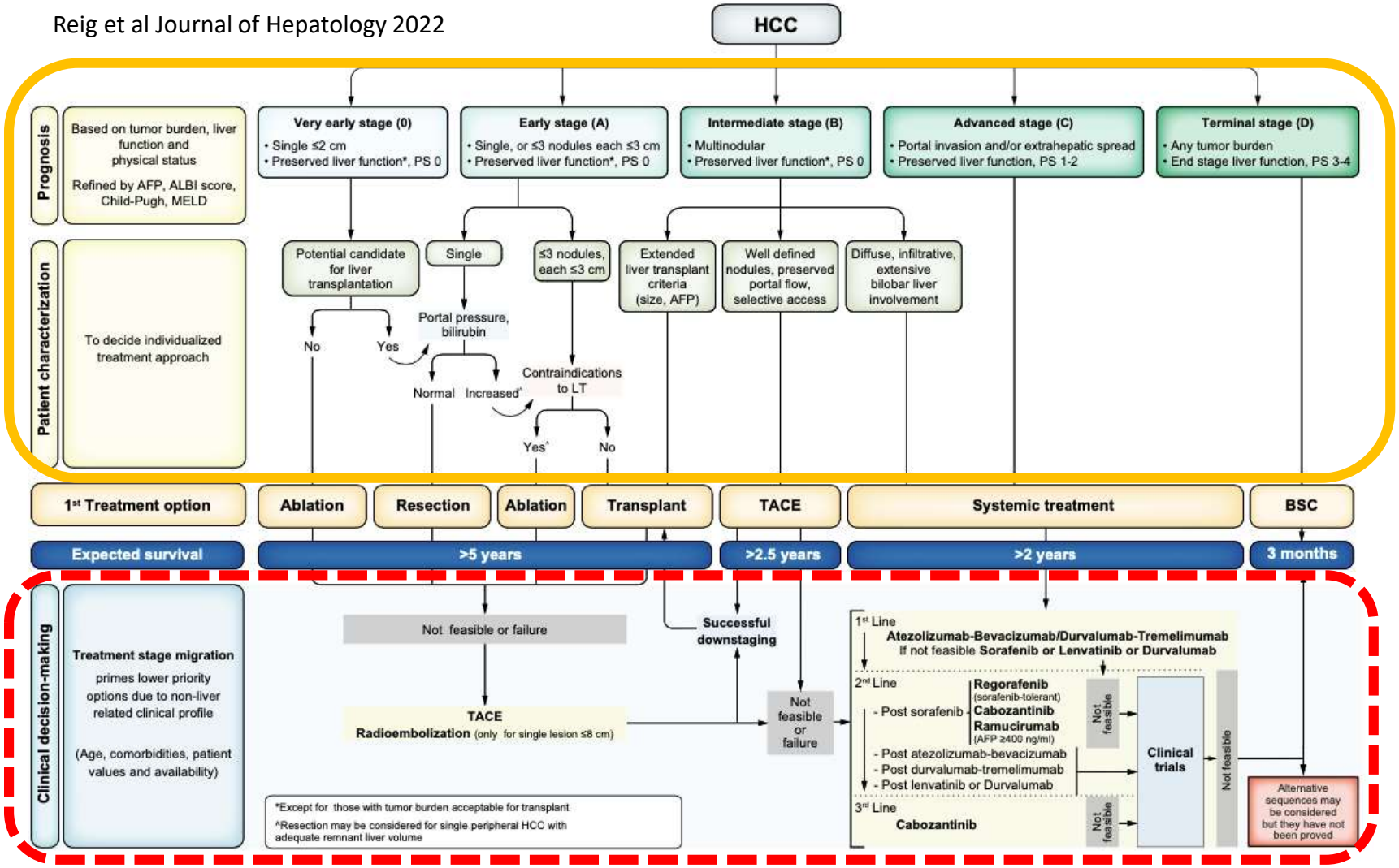
Clinical-Practice

Physicians – Multidisciplinary Teams --> RESPONSABILITY

'Shared-Decision Making' and 'Value-Based Healthcare'

Manage 'subjectivity,' 'complexity,' or 'uncertainty' in the clinical decision-making process in Liver Cancer

Reig et al Journal of Hepatology 2022



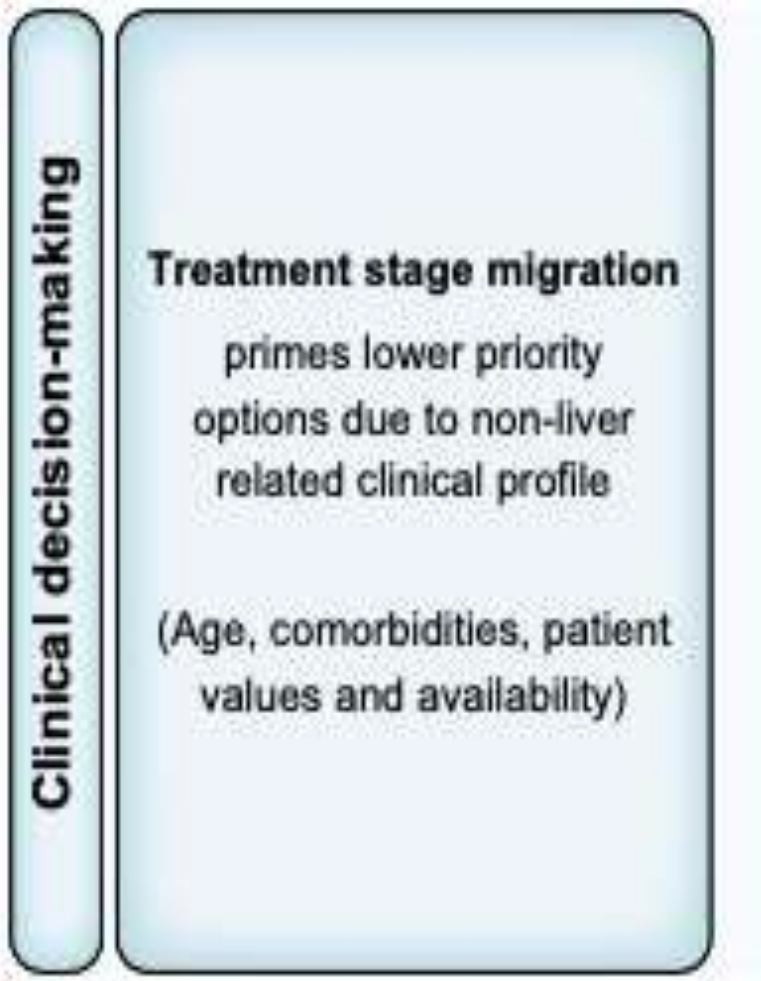
These are objective data derived from tomography, laboratory tests, and other assessments that have a defined value

They are subjective, complex, or unknown data in ~50 % of clinical decisions

Clinical Decision-making – BCLC 2024

Physician – Multidisciplinary Team --> RESPONSABILITY

'Shared-Decision Making' and 'Value-Based Healthcare'



- Age
- Comorbidities
- Patient values
- Treatment availability
- HCC location
- Techniques (type of ablation, surgery or material for loco-regional treatments)
- Type of systemic treatments
- Etc.

HCC, hepatocelular carcinoma; .

Reig et al. J Hepatol. 2022.

Risk factors for death by change of treatment strategy post ablation

Event	Parameter	Contrasts	HR (95%CI)	p-value (contrast)	pvalue (parameter)
Death	Change of treatment strategy (td)	**BSC for UTP-comorbidities vs. TACE or systemic treatment.**	**2 (1.04 - 3.82)**	**0.0369**	**<.0001**
		BSC for UTP-HCC vs. BSC for UTP-liver dysfunction.	**3.23 (1.36 - 7.65)**	**0.0079**	
		BSC for UTP-HCC vs. BSC for UTP-comorbidities.	**3.65 (1.53 - 8.26)**	**0.0035**	
		BSC for UTP-liver dysfunction vs. BSC for UTP-comorbidities.	1.13 (0.53 - 2.42)	0.7470	

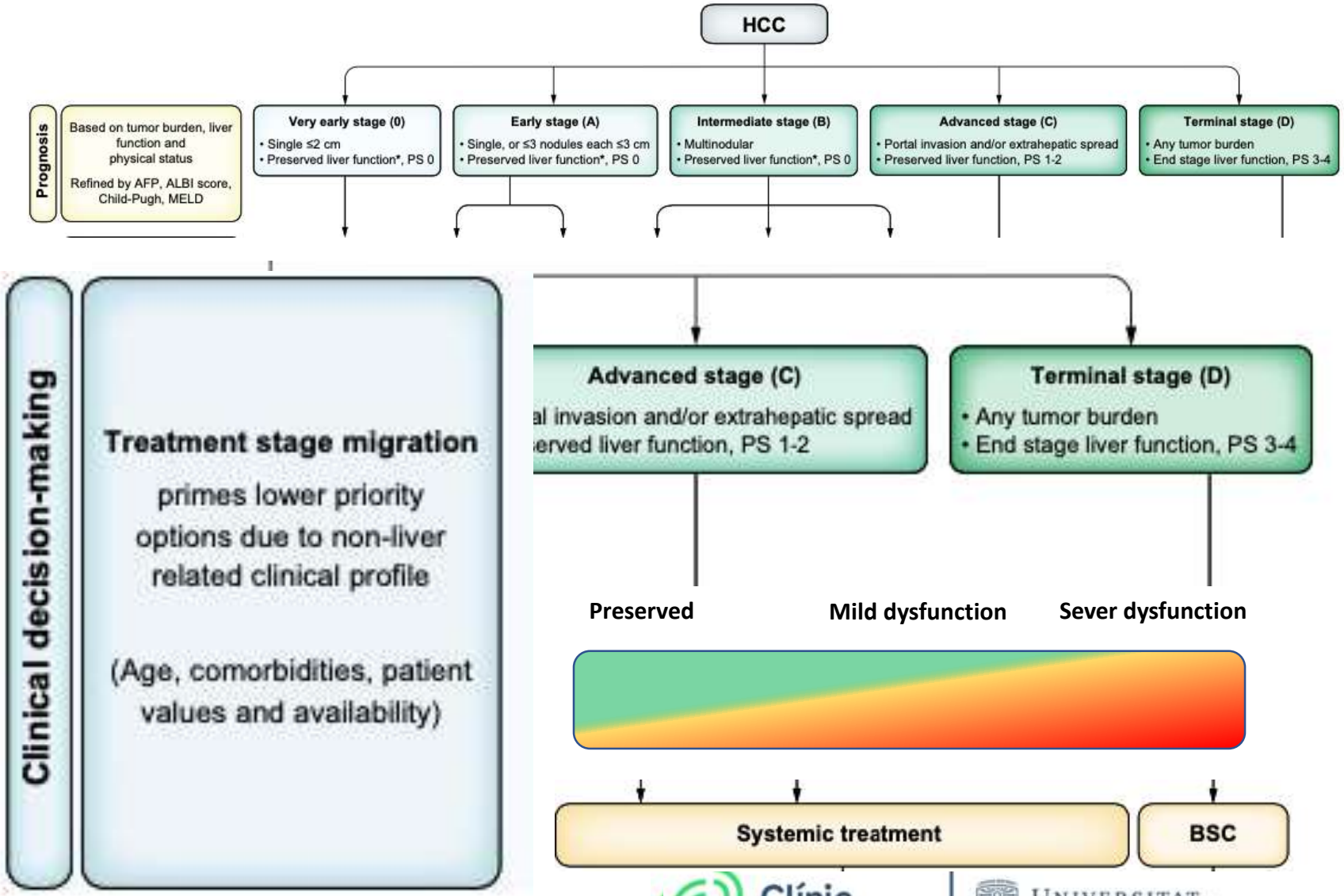
td: time-dependent; HCC: Hepatocellular carcinoma; BSC: Best support care; UTP-liver dysfunction: Untreatable progression due liver dysfunction; UTP-comorbidities: Untreatable progression due comorbidities; UTP-HCC: Untreatable progression due symptomatic progression; TACE: Transarterial chemoembolization.

Muñoz et al 2023

Liver Function Paves the Way, But It's Not the Only Factor!

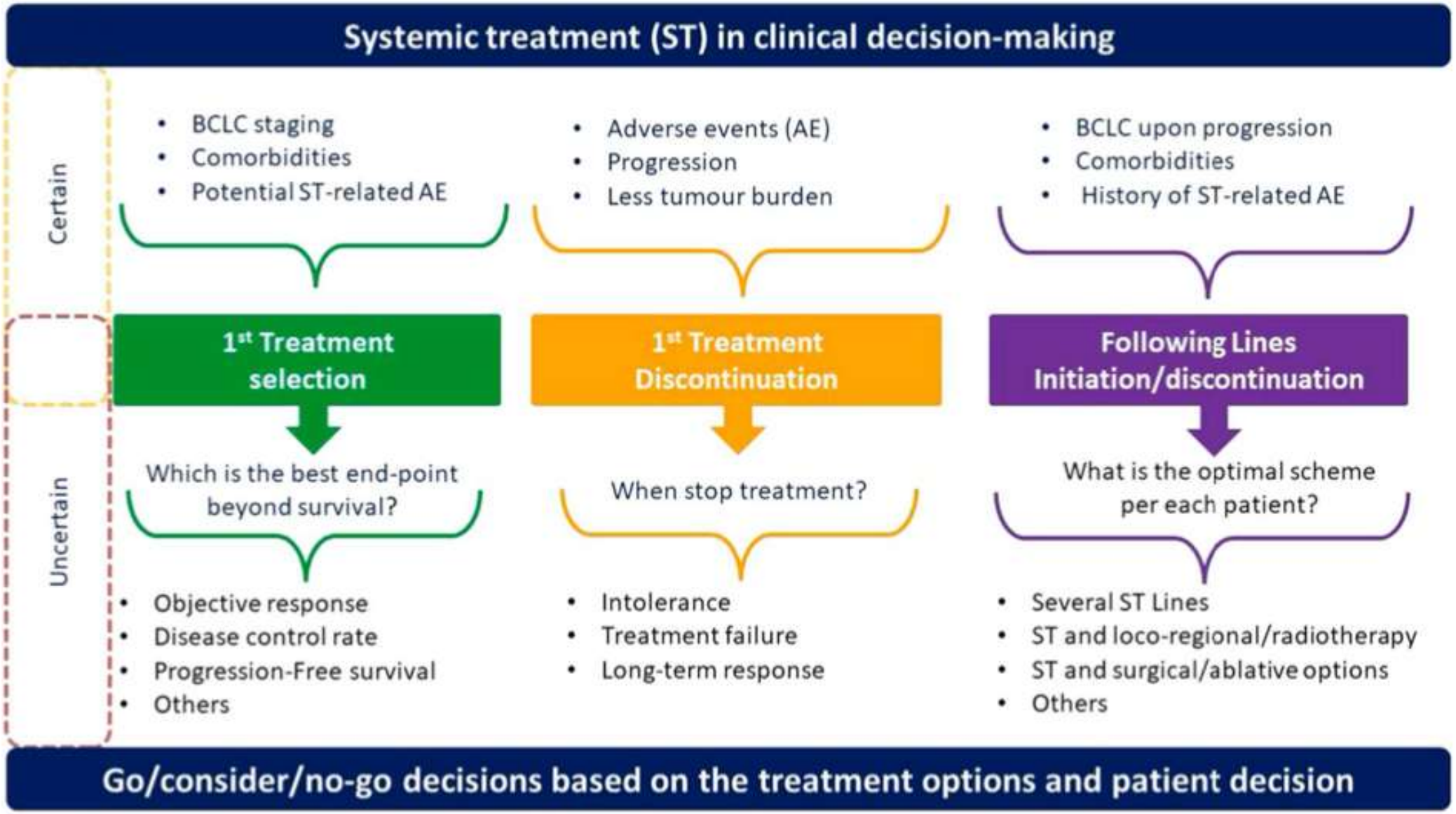
- Tumor Burden
- Symptoms
- Comorbidities
- Treatment options
- Line of treatment

Impaired liver function and systemic treatment



Reig et al. Jorunal of Hepatology 2022

Certain and uncertain factors that influence the decision-making process



Fortuny et al. United european gastroenterology journal 2023

Systemic treatment (ST) in clinical decision-making

Fortuny et UEG Journal2024

Certain

Uncertain

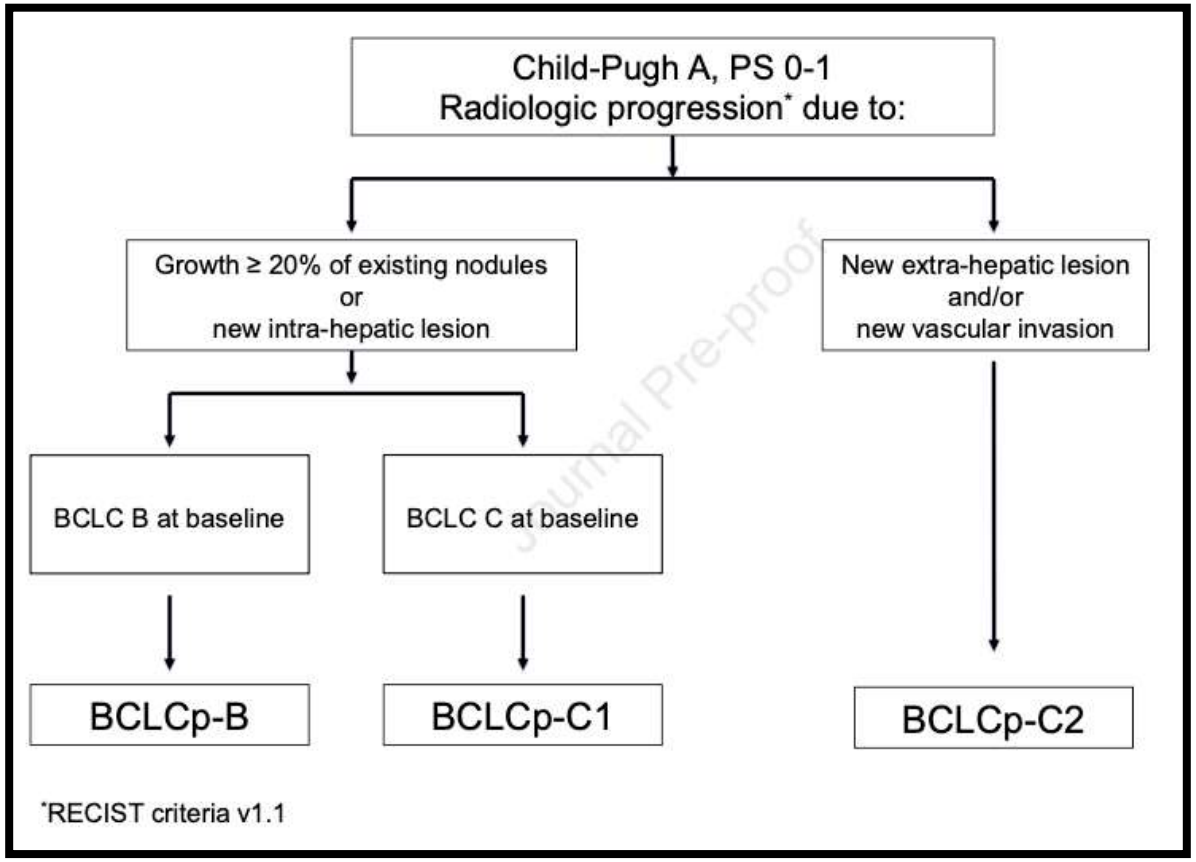
- Severe Adverse events (AE)
- Symptomatic progression
- Patient decision

1st Treatment Discontinuation

When is the right time for discontinuing?

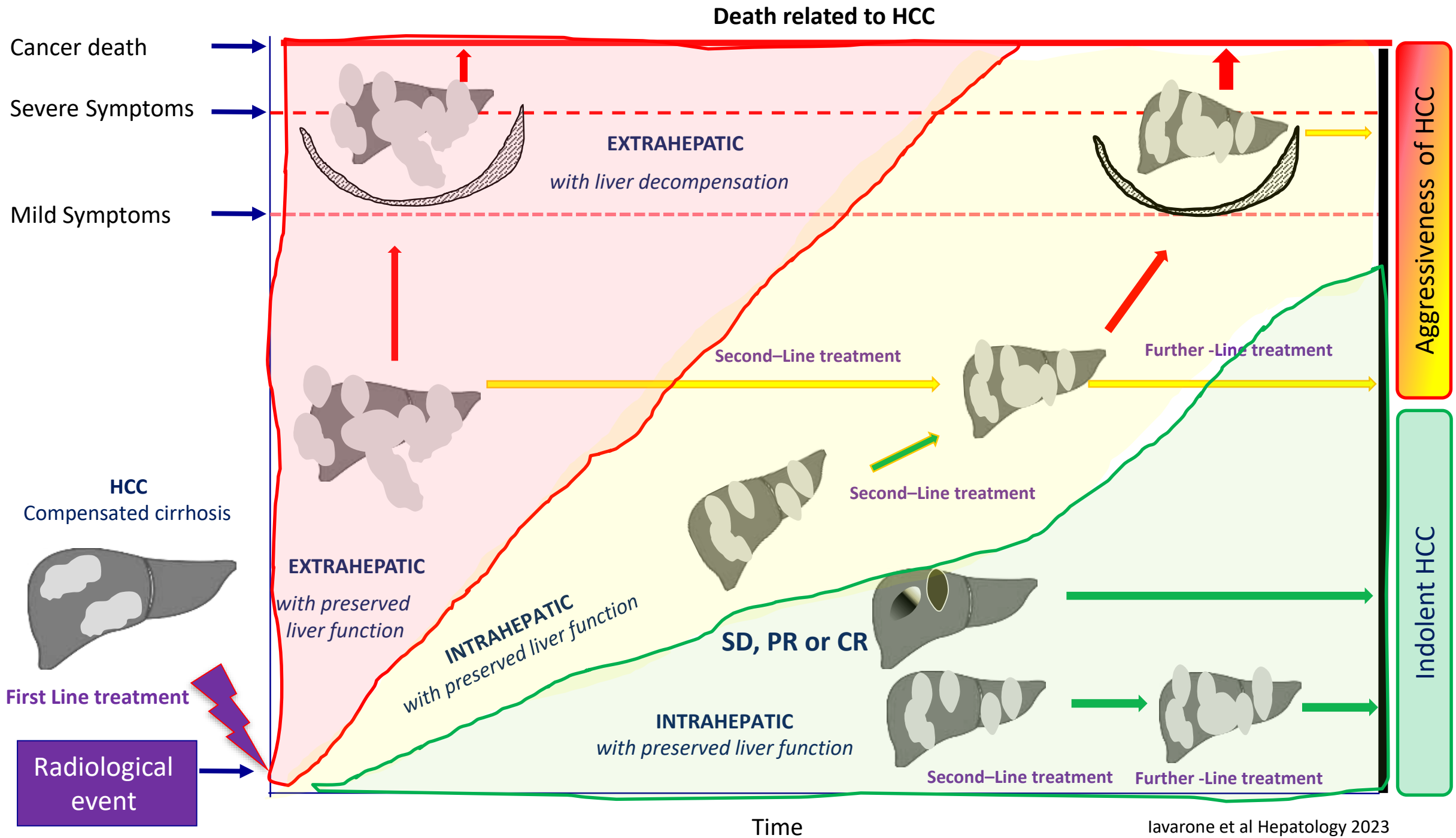
- Treatment failure
  - **Pattern of progression**
  - **Intolerance**
- Substantial response
  - **Less tumour burden (Downsizing)**
  - **Downstaging**

BCLC upon progression



Reig M et al. Hepatology 2013;58:2023–31

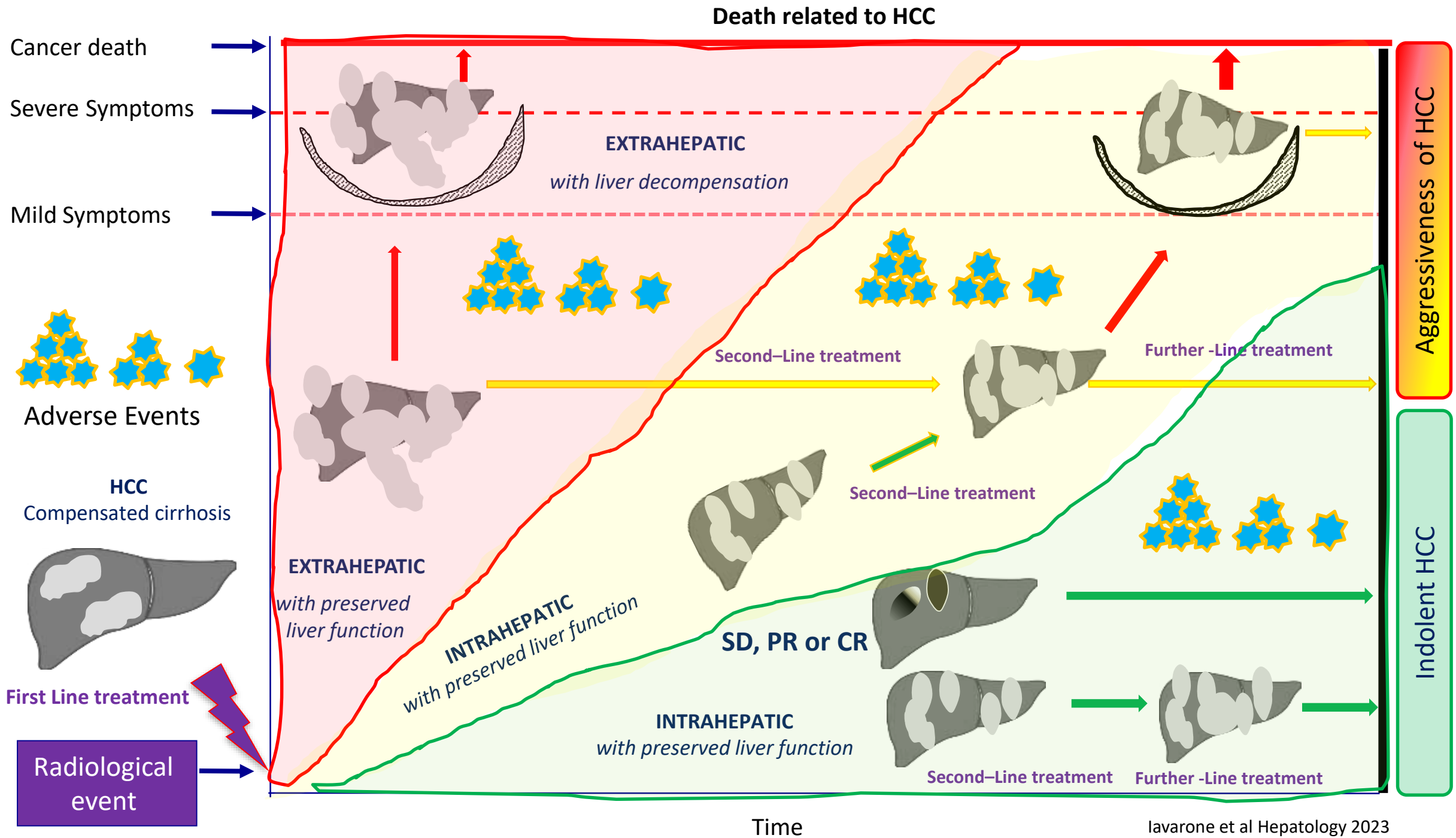
Go/consider/no-go decisions based on the treatment options and patient decision



Iavarone et al Hepatology 2023

Impact of Pattern of progression on Post-Progression Survival

Sorafenib	Iavarone et al. Hepatology 2015; Ogasawara et al Invest New Drugs. 2016;
Regorafenib	Bruix et al. Lancet. 2016
Tivantinib	Rimassa et al. Lancet Oncol. 2018
Ramucirumab	Reig at al Liver Interantional 2021
Radioembolization	de la Torre-Aláez et al.Cardiovasc Intervent Radiol 2020
Atezolizumab-Bevacizumab	Talbot et al. Liver Internatiuonal 2022;Campani et al Hepatology 2023



Iavarone et al Hepatology 2023

Systemic treatment (ST) in clinical decision-making

Fortuny et al UEG Journal 2023 (accepted)

Certain

Uncertain

- BCLC upon progression
- Comorbidities and the history of AE with previous ST

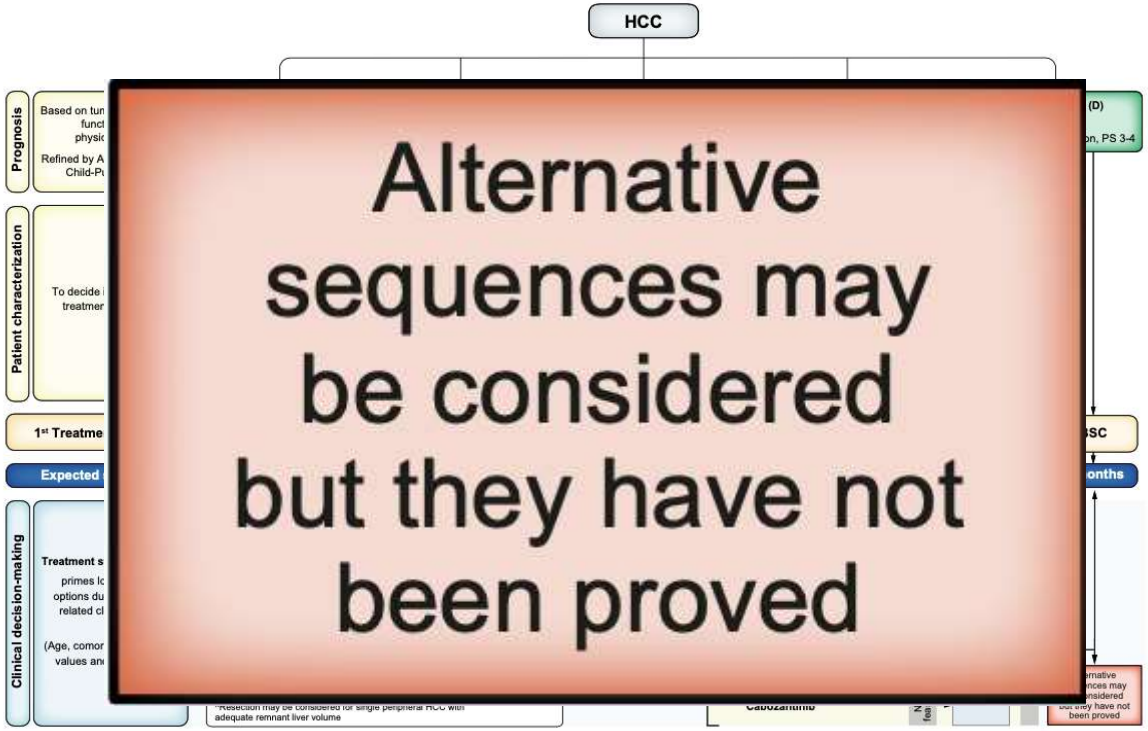
Following Lines Initiation

What is the optimal scheme per each patient?

- Several ST Lines
- ST and loco-regional/radiotherapy
- ST and surgical/ablative options
- Others

What is the alternative?

What is the evidence to deciding the discontinuation?



Go/consider/no-go decisions based on the treatment options and patient decision

Systemic treatment (ST) in clinical decision-making

Fortuny et al UEG Journal 2023 (accepted)

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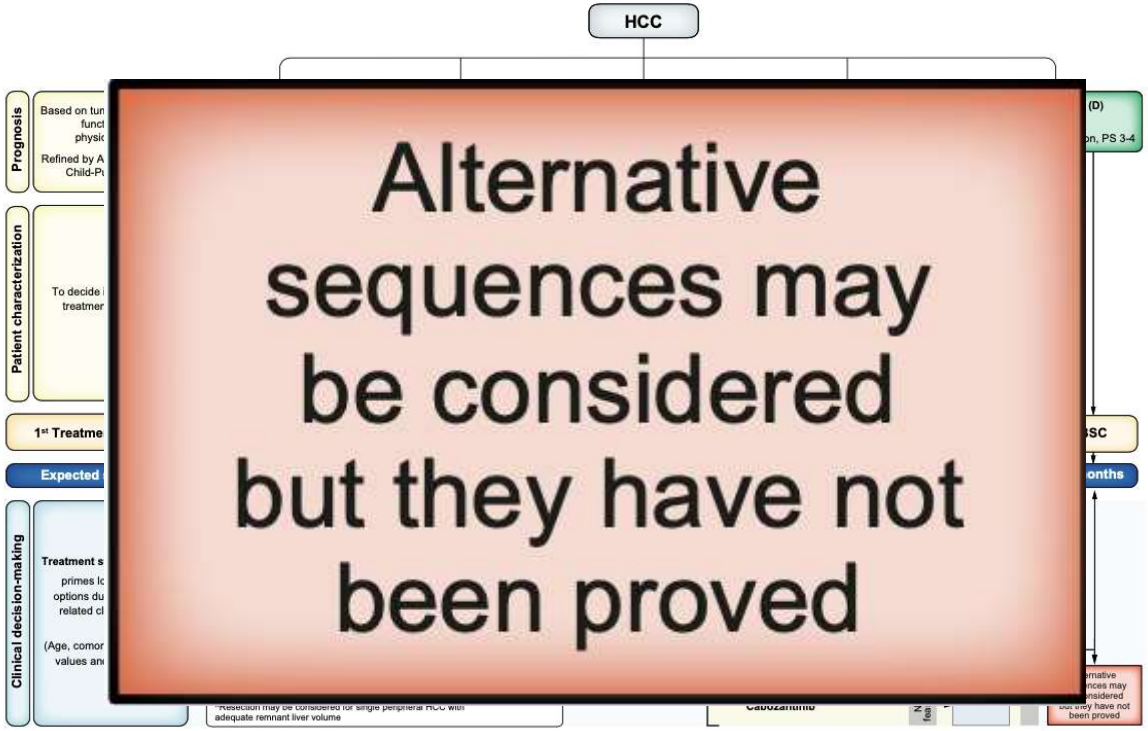
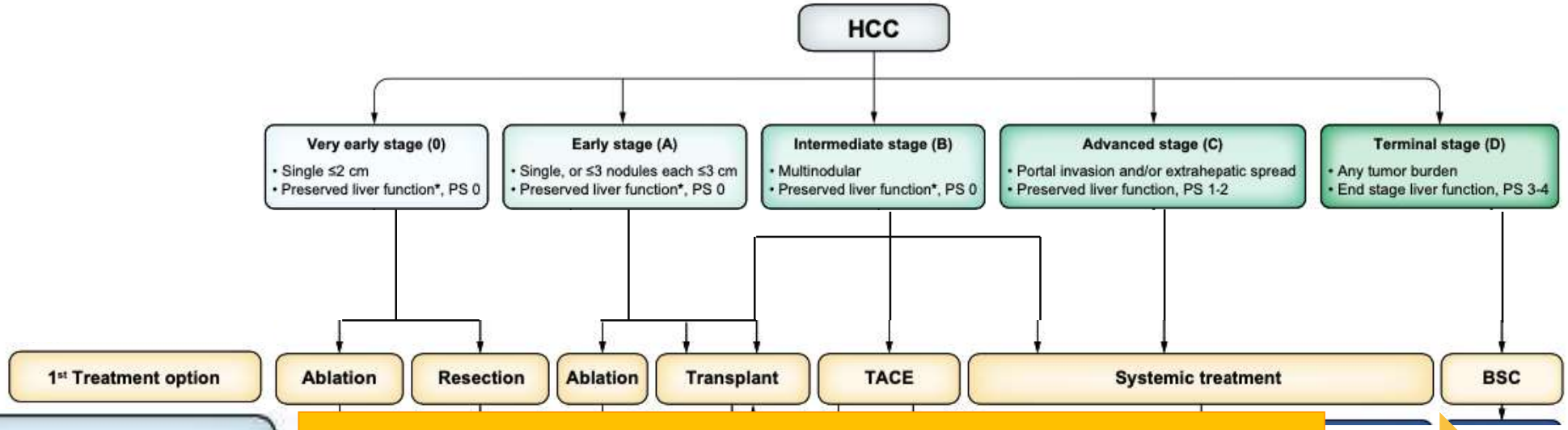


Go/consider/no-go decisions based on the treatment options and patient decision

Treatment Stage Migration –Indication



Treatment Stage Migration

Clinical decision-making

Treatment stage migration

primes lower priority options due to non-liver related clinical profile

(Age, comorbidities, patient values and availability)

Radioembolisation with Y90-resin microspheres followed by nivolumab for advanced hepatocellular carcinoma (CA 209-678): a single arm, single centre, phase 2 trial

Tai et al Lancet gastroenterology and Hepatology 2021

Nivolumab after selective internal radiation therapy for the treatment of hepatocellular carcinoma: a phase 2, single-arm study *Nivollumab, No esta aprobado*

De la Torre at aJ Immunother Cancer 2022l

Alternative sequences may be considered but they have not been proved

Reig M et al J Hepatol. 2022 Mar;76(3):681-693.

Systemic treatment (ST) in clinical decision-making

Fortuny et al UEG Journal 2023 (accepted)

Certain

Uncertain

- BCLC upon progression
- Comorbidities and the history of AE with previous ST

Following Lines Initiation

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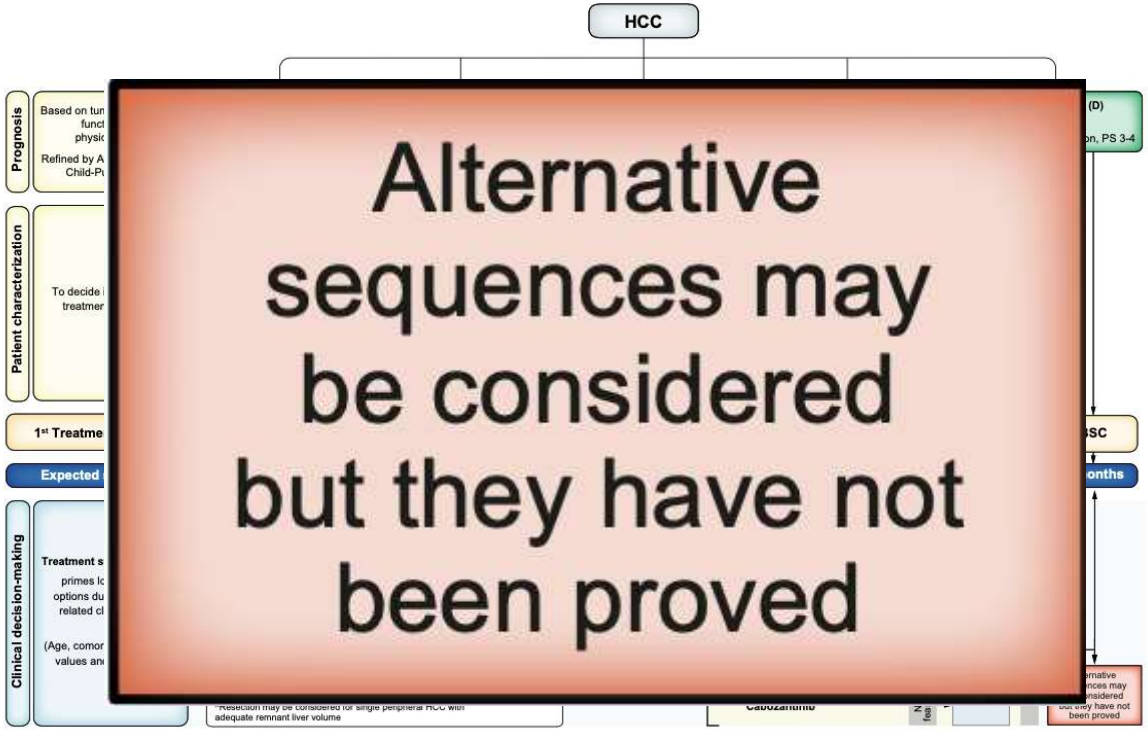
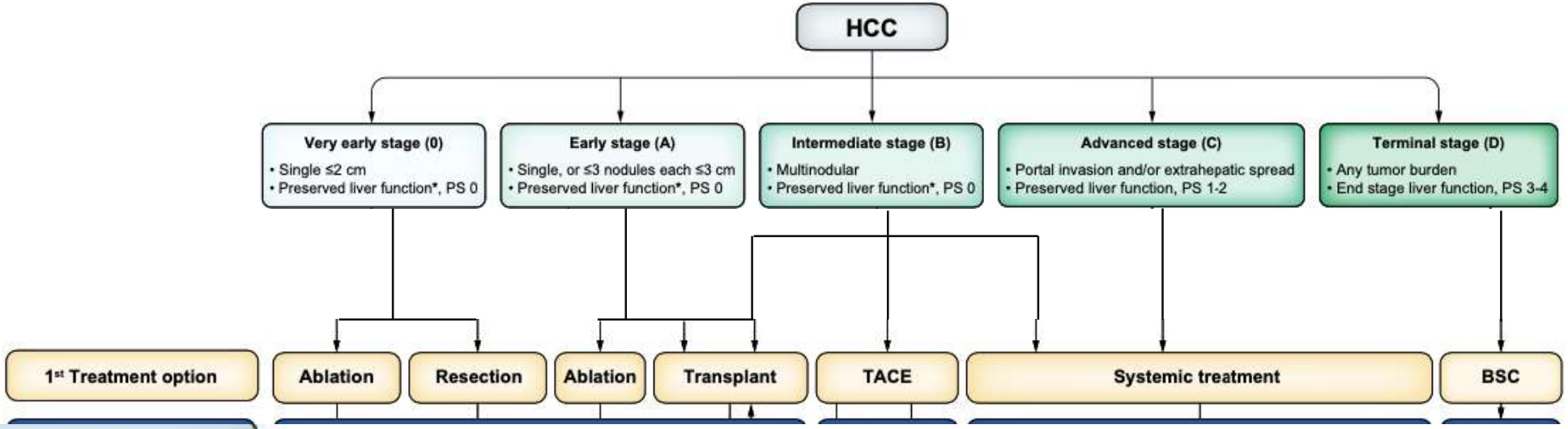


Go/consider/no-go decisions based on the treatment options and patient decision

Treatment Stage Migration –Indication



Clinical decision-making

Treatment stage migration

primes lower priority options due to non-liver related clinical profile

(Age, comorbidities, patient values and availability)

Treatment Stage Migration → Downsizing

Sequential transarterial chemoembolisation and stereotactic body radiotherapy followed by immunotherapy as conversion therapy for patients with locally advanced, unresectable hepatocellular carcinoma (START-FIT): a single-arm, phase 2 trial

Chiang et al Lancet Gastroenterol Hepatol 2023; 8: 169–78

Alternative sequences may be considered but they have not been proved

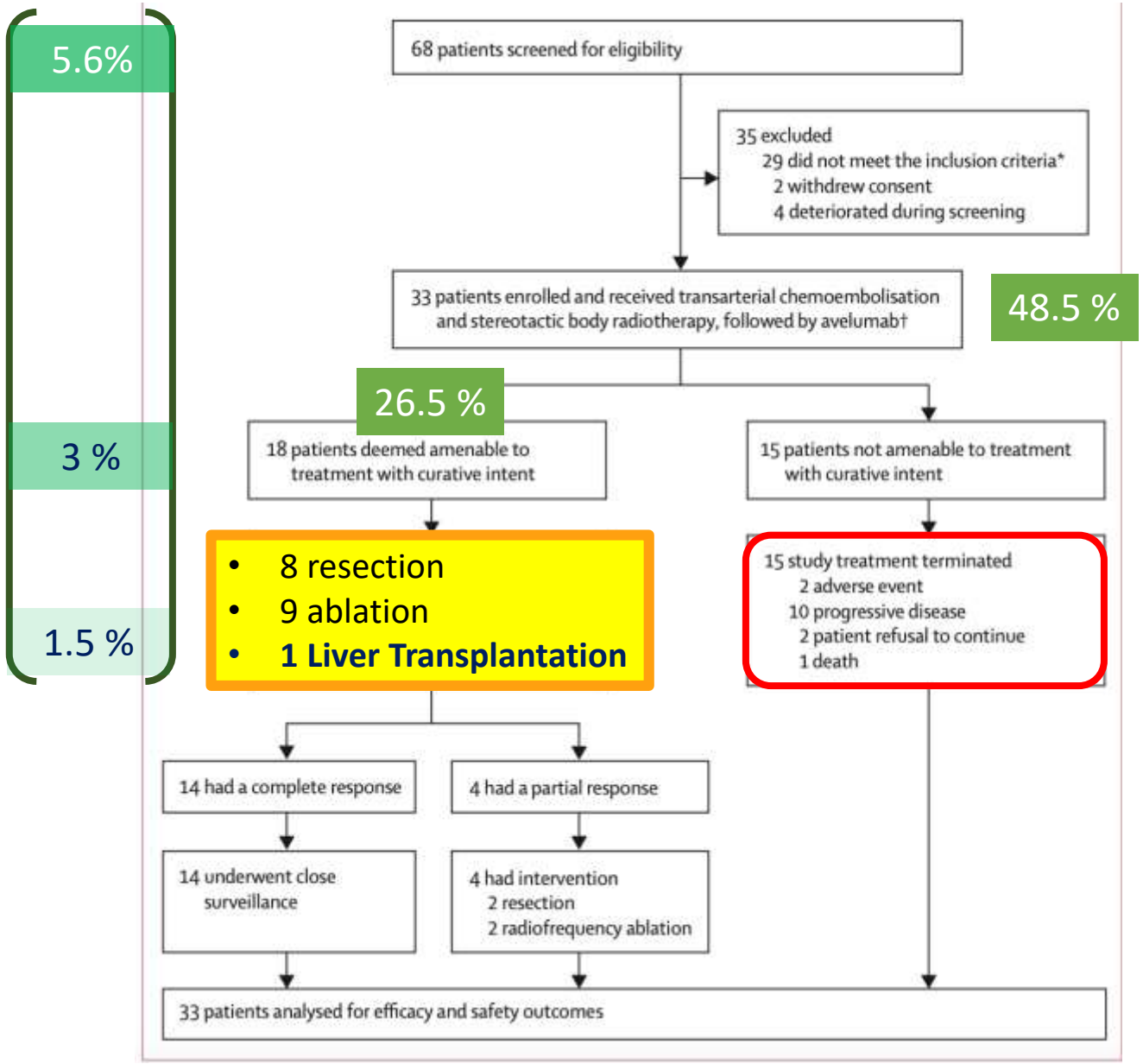
Reig M et al J Hepatol. 2022 Mar;76(3):681-693.

Exploring HCC Conversion Therapy: Early Steps on a New Path

Potential Candidate

Candidate for Conversion

Candidate for LT



Chiang et al Lancet Gastroenterol Hepatol 2023; 8: 169–78

Exploring HCC Conversion Therapy: Early Steps on a New Path

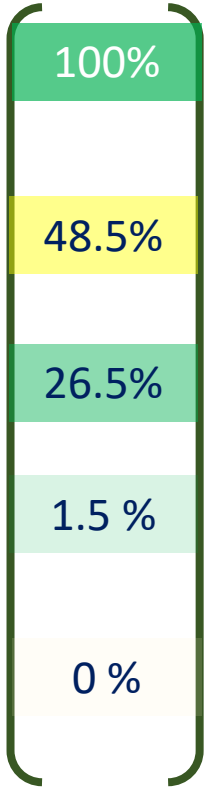
Potential Candidate For conversion

Treated with Immunotherapy

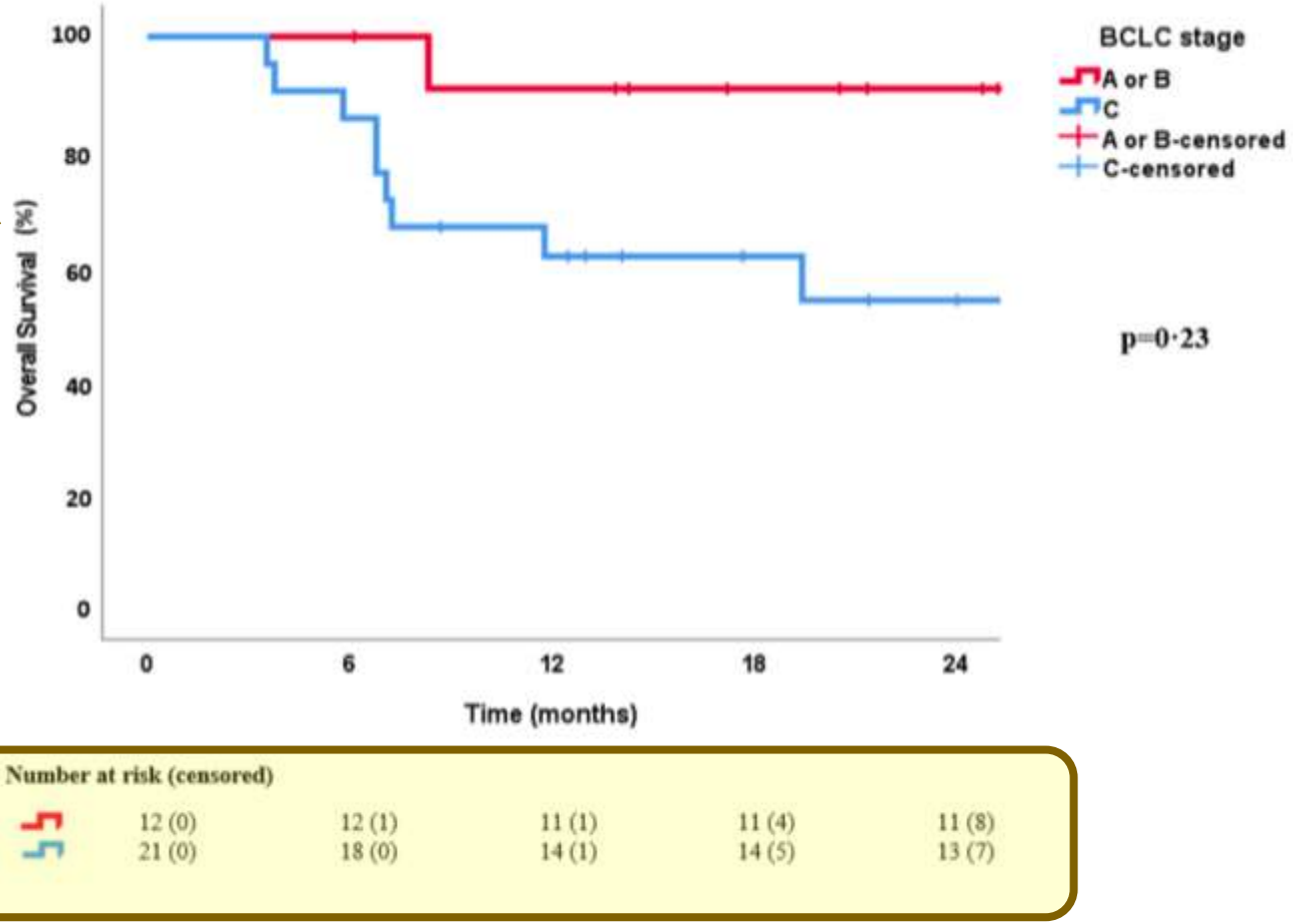
Candidate for Conversion

Candidate for LT

Transplanted



Overall Survival (n=33)



Chiang et al Lancet Gastroenterol Hepatol 2023; 8: 169–78

Combination of IO based combinations

Evidence

Overall Survival

Response

Phase III trials

Phase II/III trials

Propose & Population

Adjuvant Therapy

Combination Treatment

Phase III trials:
Progression Free Survival
Recurrence Free Survival

Phase III trials:
Survival

Bridge Liver Transplantation

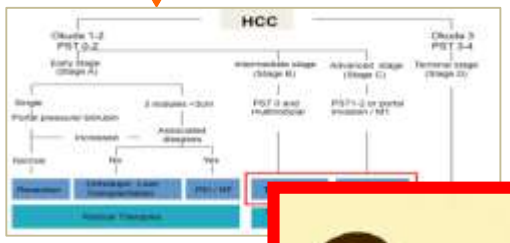
Downstaging

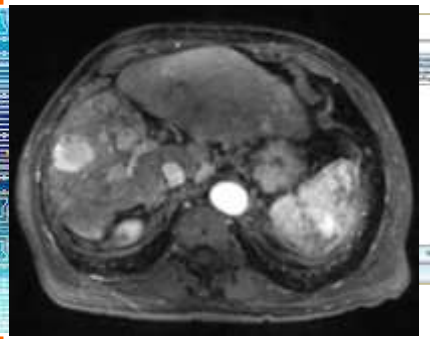
Downsizing

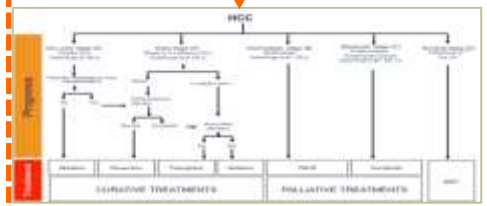
Preliminar data and controversia

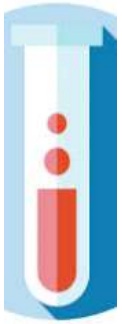
The BCLC staging system

1999 2003 2008 2012 2014 2016 2018 2022 2024-2025



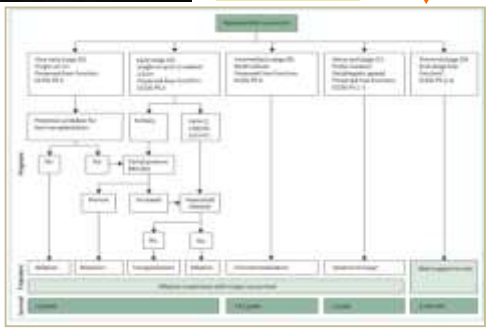


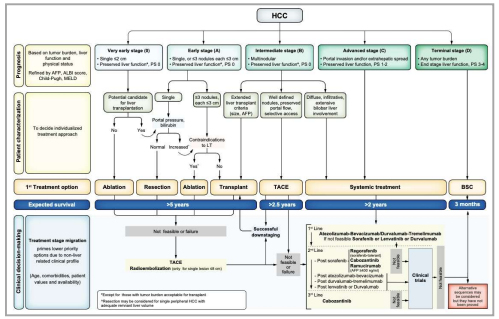




Precision medicine?
Tailoring medicine?

need a
version





IDIBAPS Institut d'Investigacions Biomèdiques August Pi i Sunyer

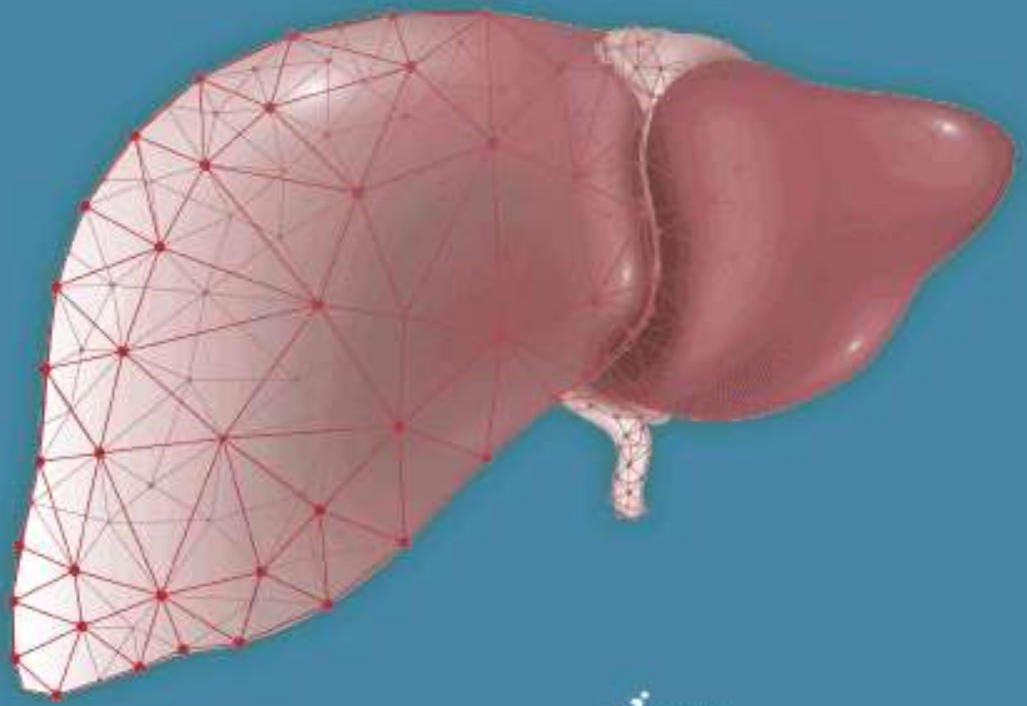
Universitat de Barcelona

ciber EHD

Llovet JM, Bru C, Bruix J. Semin Liver Dis 1999;Llovet JM, Burroughs A, Bruix J. Lancet 2003;Forner A, Reig M, Rodriguez De Lope C, Bruix J. SeminLiver Dis 2010;Forner A, Llovet JM, Bruix J. Lancet 2012;
Reig M, Darnell A, Forner A, Rimola J, Ayuso C, Bruix J. Semin Liver Dis 2014; Bruix J, Reig M, Sherman M. Gastroenterology 2016;Forner A, Reig M, Bruix J. Lancet 2018.

BCLC 2024 update

Forging a Multidisciplinary Ecosystem to Revolutionize Liver Cancer Management



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November 25th - 26th 2024

BCLC group 2024