30º CONGRESO SETH
SOCIEDAD ESPAÑOLA DE TRASPLANTE HEPÁTICO
22 - 24 octubre 2025
Adda, Auditorio de la Diputación de Alicante

Riesgos y beneficios de la inmunoterapia y de los ITK pre y postrasplante hepático

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Conflicts of interest

Consultant: AstraZeneca, Guerbert, Boston Scientific, Exact Science, SIRTEX

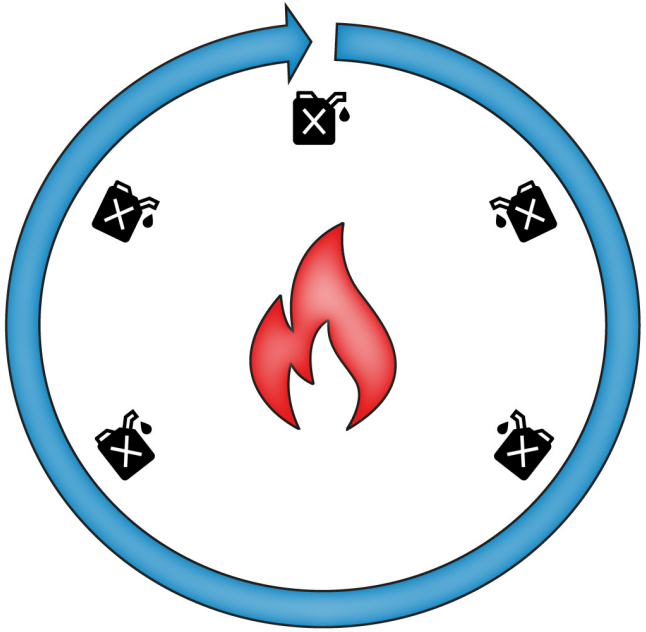
Conferences: Gilead, Roche, Boston Scientific

Transplant Oncology

Factors fueling the renewed interest in the field of transplant oncology

The evolution of LT

LT evolved from a morbid, lethal operation, to an almost routine surgical procedure providing excellent patient- and graft survival



Technical innovations

The advent of surgical and technical innovations, such as liver machine perfusion and normothermic regional perfusion provide the possibility to expand the potential organ pool without compromising outcomes

New systemic treatments

The availability of improved systemic oncologic treatment approaches resulting in synergies between transplantation and oncology

Tumor- and transplant immunology

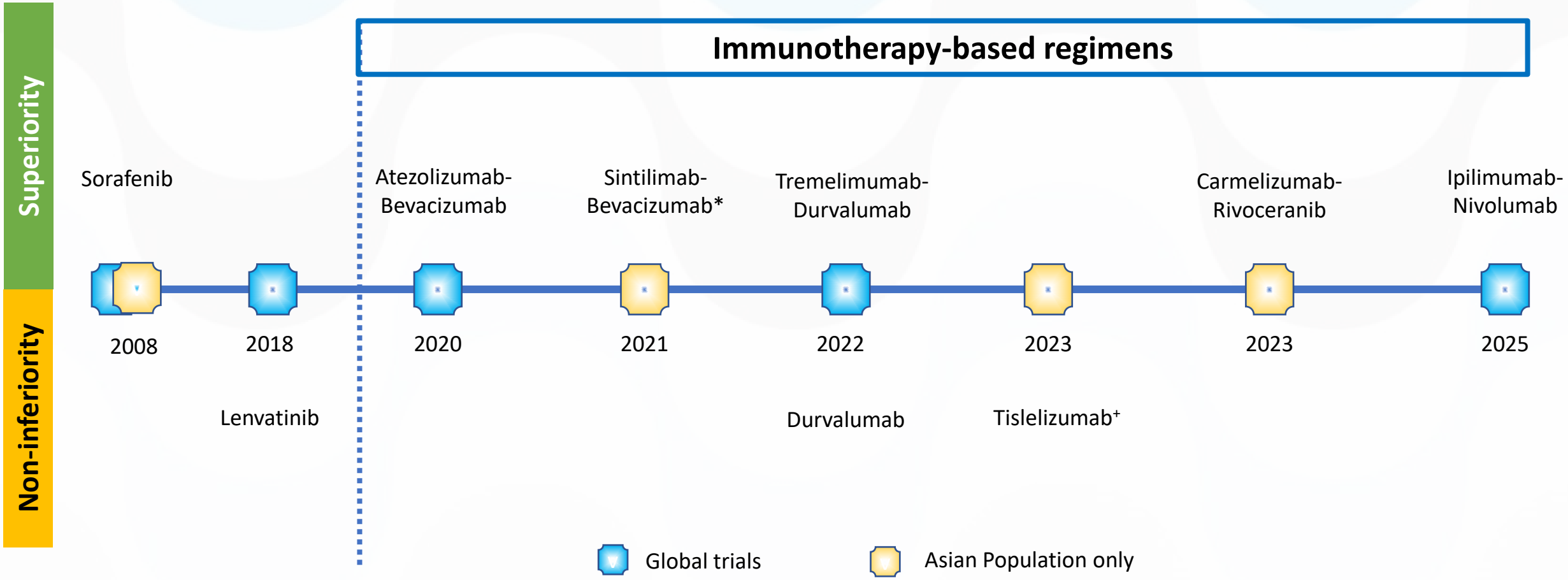
A better understanding of immunosuppression and the interplay between tumor and transplant immunology

Direct-acting antiviral therapy

The approval of the highly efficacious direct-acting antiviral (DAA) treatment for hepatitis C virus (HCV) has led to an increase of LT for other indications

Krendl FJ et al. JHEP Rep. 2023;6(2):100965.

Positive phase 3 trials in first line based on OS

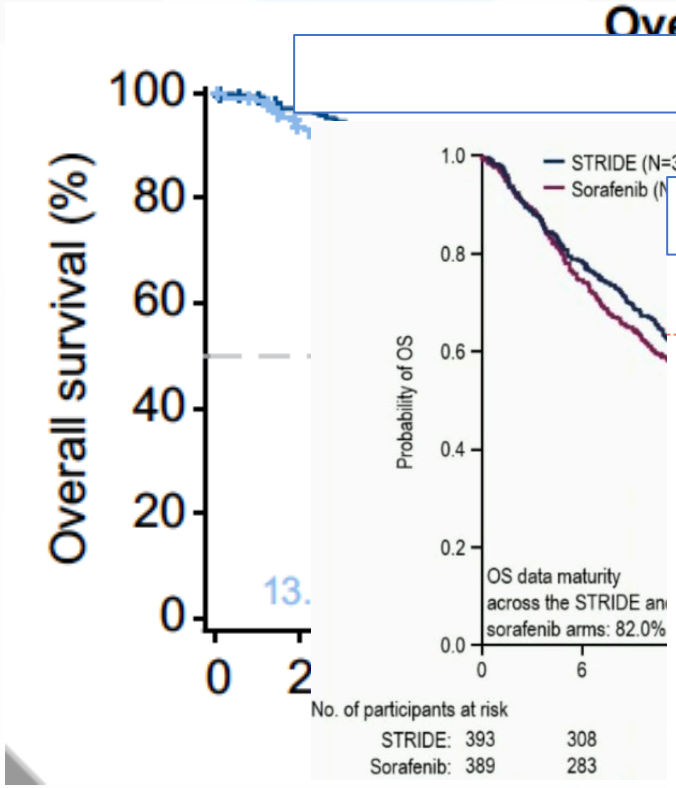


HCC: Hepatocellular Carcinoma; * Biosimilar.

Llovet JM NEJM 2008, Kudo M Lancet 2018; Finn RS NEJM 2020; Ren Z Lancet Oncol 2021; Abou-Alfa NEJM Evid 2022; Qin S JAMA Oncol 2023; Qin S Lancet 2023; Galle P, Lancet 2025

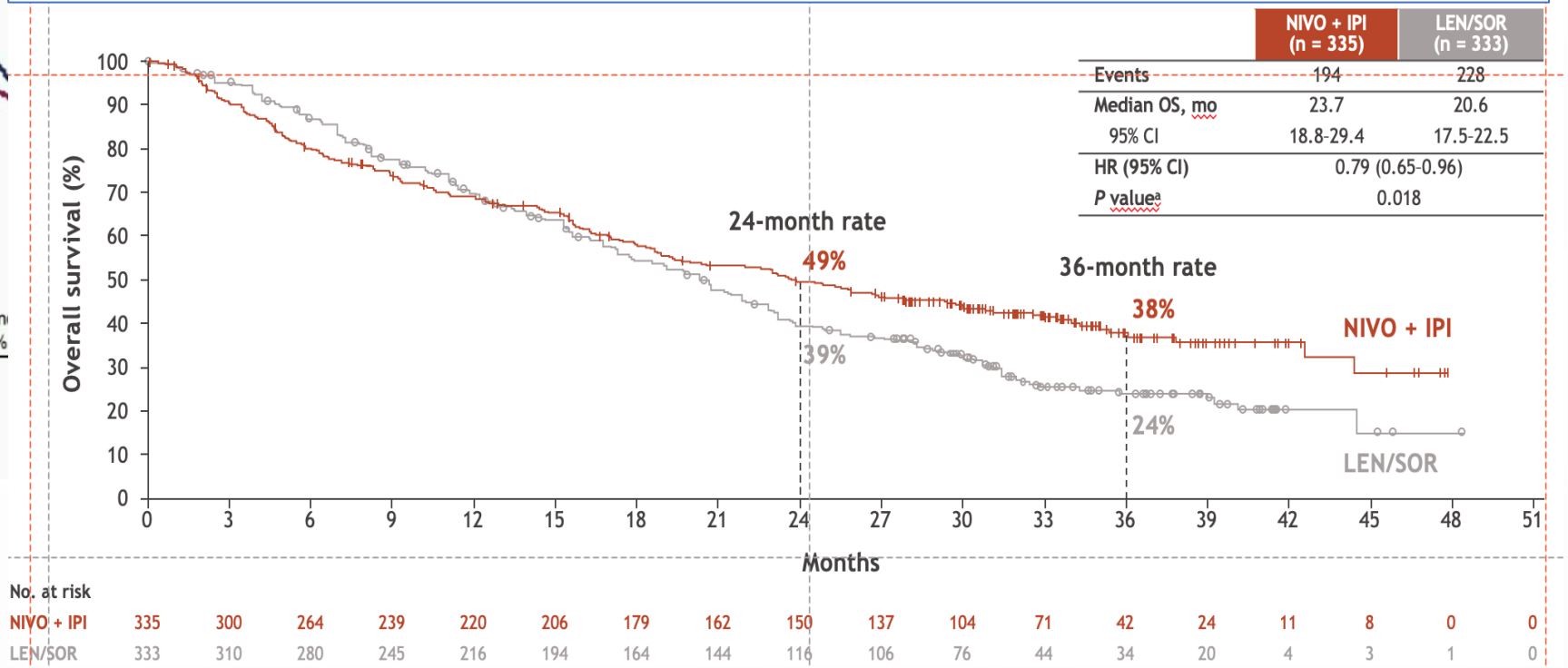
Unprecedent survivals with ICI

Atezolizumab + Bevacizumab



Tremelimumab + Durvalumab

Ipilimumab + Nivolumab



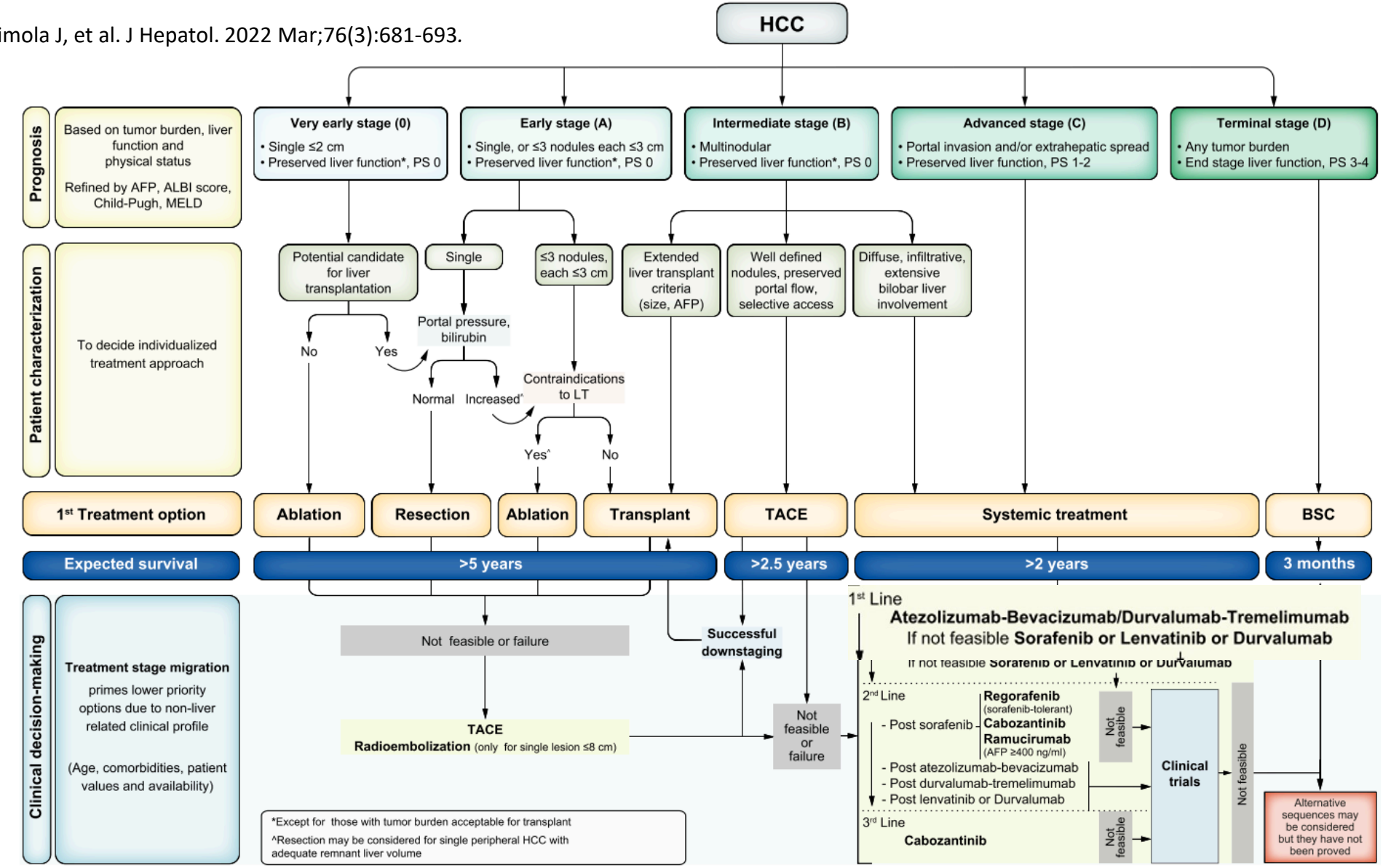
	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Events	194	228
Median OS, mo	23.7	20.6
95% CI	18.8-29.4	17.5-22.5
HR (95% CI)	0.79 (0.65-0.96)	
P value[a]	0.018	

ICI: Immune Checkpoint Inhibitor

Cheng AI, et al J Hepatol 2021; Rimassa, et al J Hepatol 2025; Yau T, et al Lancet 2025

BCLC staging and treatment strategy, 2022

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



Early and Intermediate HCC: Adjuvant therapies in TKI-era

Sorafenib or placebo plus TACE with doxorubicin-eluting beads for intermediate stage HCC: The SPACE trial

Riccardo Lencioni [1], Josep M Llovet [2], Guohong Han [3], Won Young Tak [4], Jiamei Yang [5], Alfredo Guglielmi [6], Seung Woon Paik [7], Maria Reig [8], Do Young Kim [9], Gar-Yang Chau [10], Angelo Luca [11], Luis Ruiz Del Arbol [12], Marie-Aude Leberre [13], Woody Niu [14], Kate Nicholson [15], Gerold Meinhardt [16], Jordi Bruix [8]

Sorafenib in combination with transarterial chemoembolisation in patients with r…table hepatocellular carcinoma (TACE …lised placebo-controlled, double-b… 3 trial

Tim Meyer [1], Richard Fox [2], Yuk Ting Ma [3], …v James [5], Richard Sturgess [6], Clive Stubbs [2], Deborah D Stocken [7], …atkinson [9], Nigel Hacking [10], T R Jeffry Evans [11], Peter Collins [12], …, David Cunningham [14], John Neil Primrose [10], Philip… Palmer [16]

Brivanib as adjuvant therapy to transarterial chemoembolization in patients with hepatocellular carcinoma: A randomized phase III trial

Masatoshi Kudo [1], Guohong Han, Richard S Finn, Ronnie T P Poon, Jean-Frederic Blanc, Lunan Yan, Jijin Yang, Ligong Lu, Won-Young Tak, Xiaoping Yu, Joon-Hyeok Lee, Shi-Ming Lin, Changping…, Tawesak Tanwandee, Guoliang Shao, Ian B Walters, Christine Dela Cruz, Valerie Poulart, Ji…

Ran… multicentre prospective trial of …ial chemoembolisation (TACE) plus …enib as compared with TACE alone in patients with hepatocellular carcinoma: TACTICS trial

Masatoshi Kudo [# 1], Kazuomi Ueshima [# 2], Masafumi Ikeda [3], Takuji Torimura [4], Nobukazu Tanabe [5], Hiroshi Aikata [6], Namiki Izumi [7], Takahiro Yamasaki [8], Shunsuke Nojiri [9], Keisuke Hino [10], Hidetaka Tsumura [11], Teiji Kuzuya [12], Norio Isoda [13], Kohichiroh Yasui [14], Hajime Aino [15], Akio Ido [16], Naoto Kawabe [17], Kazuhiko Nakao [18], Yoshiyuki Wada [19], Osamu Yokosuka [20], Kenichi Yoshimura [21], Takuji Okusaka [22], Junji Furuse [23], Norihiro Kokudo [24], Kiwamu Okita [25], Philip James Johnson [26], Yasuaki Arai [27]; TACTICS study group

Adjuvant sorafenib for hepatocell… …ma after resection or ablation (STORM); …ase 3, randomised, double-blind, placebo-controlled trial

Jordi Bruix [1], Tadatoshi Takayama [2], Vincenzo Mazzaferro [3], Gar-Yang Chau [4], Jiamei Yang [5], Masatoshi Kudo [6], Jianqiang Cai [7], Ronnie T Poon [8], Kwang-Hyub Han [9], Won Young Tak [10], Han Chu Lee [11], Tianqiang Song [12], Sasan Roayaie [13], Luigi Bolondi [14], Kwan Sik Lee [15], Masatoshi Makuuchi [16], Fabricio Souza [17], Marie-Aude Le Berre [18], Gerold Meinhardt [19], Josep M Llovet [20]; STORM investigators

No adjuvant therapy approved in HCC!!!!

Lencioni R. et al. J Hepatol. 2016 May;64(5):1090-8.
Meyer T, et al. Lancet Gastroenterol Hepatol.; 2017;2:565–575.
Kudo M et al. Hepatology. 2014;60(5):1697-1707.
Kudo M et al. Gut. 2020 Aug;69(8):1492-1501.
Bruix J et al. Lancet Oncol. 2015 Oct;16(13):1344-54.

Rate of objective response with ICI

Combination	Objective Response (RECIST v1.1), %, (95% CI)	Objective Response (mRECIST), %, (95% CI)	Duration of Response months, median (IQR)
Atezolizumab-Bevacizumab (IMbrave150)	30 (25-35)	33.2 (28.1–38.6)	18.1 (4.6-NE).
Tremelimumab-Durvalumab (HIMALAYA)	20 (NA)	NA	22.3 (8.5-NE)
Camrelizumab- Rivoceranib (CARES-310)	26 (20–35)	NA	14.8 (8.4-NE)
Durvalumab (HIMALAYA)	17	NA	16.8 (7.4-NE)
Tislelizumab (RATIONALE-301)	14.3 (10.8-18.5)	NA	36.1 (16.8 to NE)
Ipilimumab-Nivolumab (Checkmate 9DW)	36 (31-42)	NA	30.4 (21.2-NE)

ICI: Immune checkpoint inhibitors**; CI:** Confidential Interval**; NA**: Not Available; LT: Liver transplantation**.**

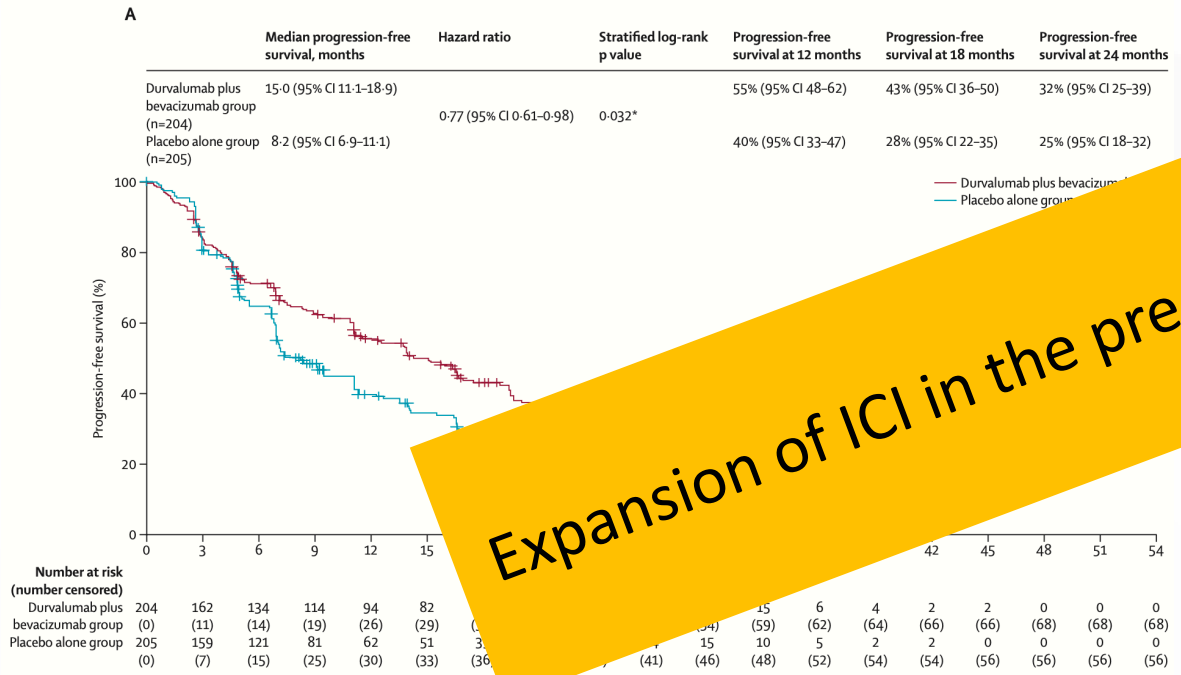
Finn RS, et al. N Engl J Med. 2020;382:1894–1905.

Abou-Alfa et al. NEJM Evidence 2022. DOI:https://doi.org/10.1056/EVIDoa2100070

Adjuvant to TACE

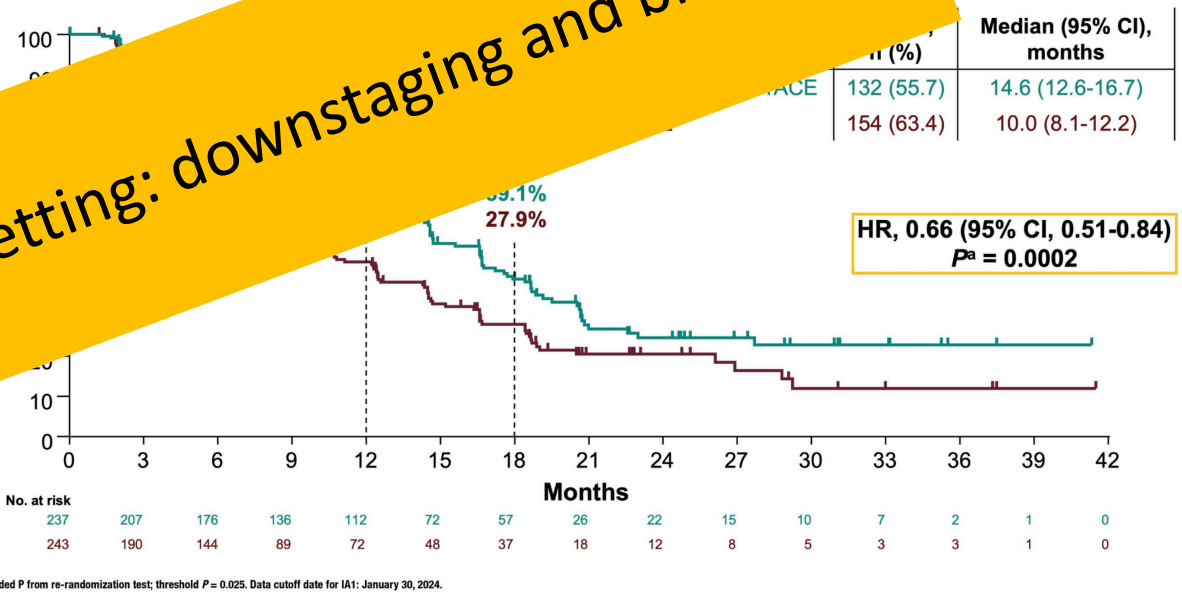
EMERALD-1 and LEAP-012 trials

Expansion of ICI in the pre-LT setting: downstaging and bridging?



A

	Median progression-free survival, months	Hazard ratio	Stratified log-rank p value	Progression-free survival at 12 months	Progression-free survival at 18 months	Progression-free survival at 24 months
Durvalumab plus bevacizumab group (n=204)	15·0 (95% CI 11·1–18·9)	0·77 (95% CI 0·61–0·98)	0·032*	55% (95% CI 48–62)	43% (95% CI 36–50)	32% (95% CI 25–39)
Placebo alone group (n=205)	8·2 (95% CI 6·9–11·1)			40% (95% CI 33–47)	28% (95% CI 22–35)	25% (95% CI 18–32)



	n (%)	Median (95% CI), months
ACE	132 (55.7)	14.6 (12.6-16.7)
	154 (63.4)	10.0 (8.1-12.2)

*One-sided P from re-randomization test; threshold P = 0.025. Data cutoff date for IA1: January 30, 2024.

Sangro B et al. Lancet. 2025 Jan 18;405(10474):216-232.

Kudo M et al. Lancet. 2025 Jan 18;405(10474):203-215.

What to do after objective response?

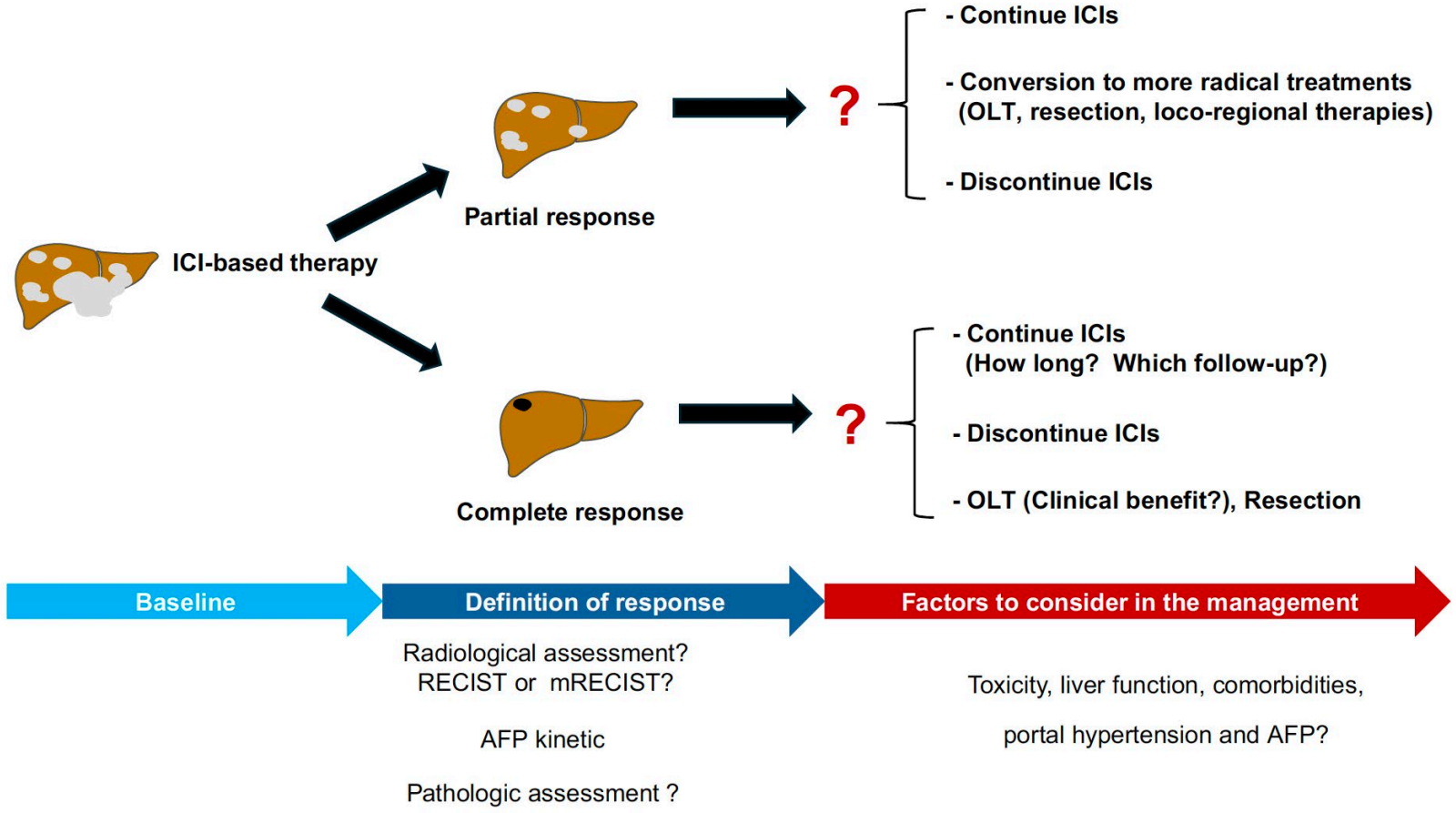
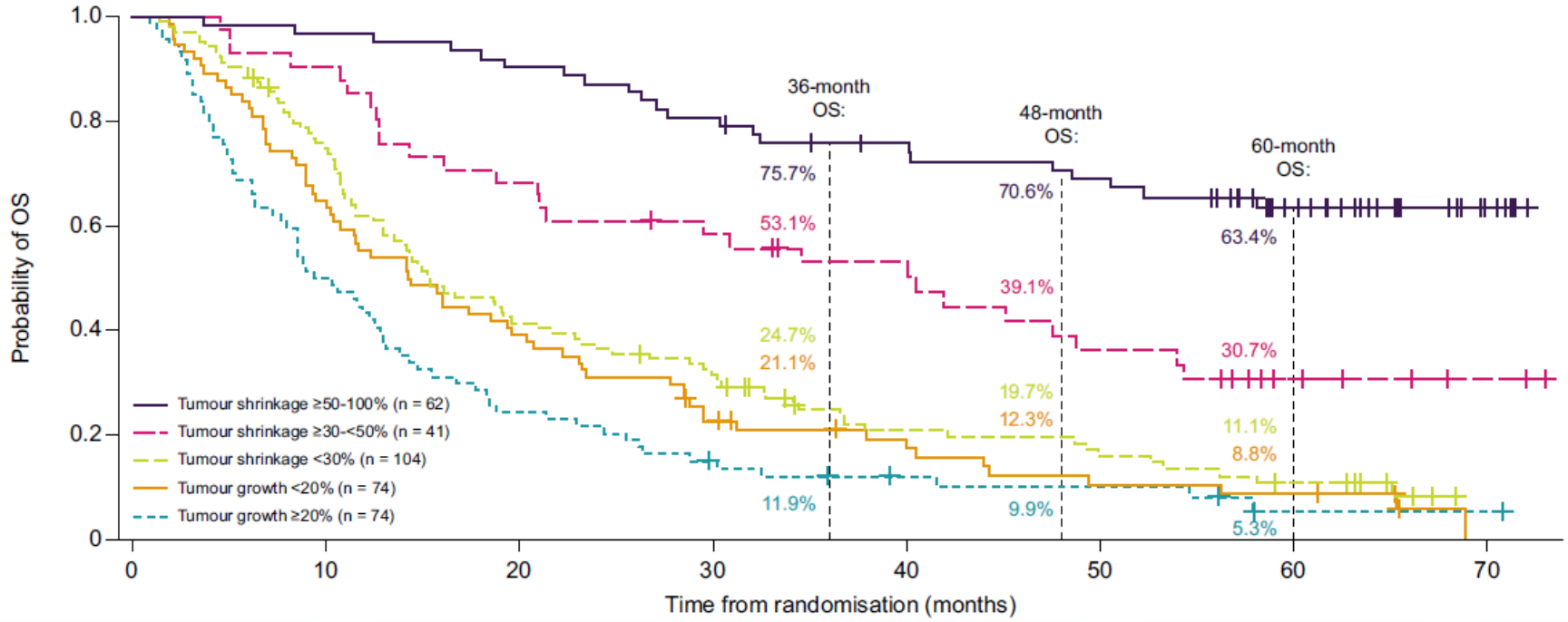


FIGURE 1 Proposed managing algorithm for intermediate/advanced HCC treated with ICI-based therapies according to the objective radiological response. Abbreviations: AFP, alpha-fetoprotein; ICI, immune checkpoint inhibitor; mRECIST, modified Response Evaluation Criteria in Solid Tumors; RECIST, Response Evaluation Criteria in Solid Tumors.

Sanduzzi Zamparelli M and Cabibbo G, Hepatol 2024

Five-year updated results: Himalaya trial

Overall survival by extent of tumour shrinkage



Disease control was defined as CR, PR or SD at the primary analysis data cut-off (27 August 2021). Extent of tumour shrinkage was based on investigator assessment. Updated OS analysis data cut-off: 01 March 2024. CR, complete response; OS, overall survival; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumors; SD, stable disease; STRIDE, Single Tremelimumab Regular Interval Durvalumab.

Rimassa L. et al. J Hepatol 2025;83:899

ILTS / ILCA Consensus 2024

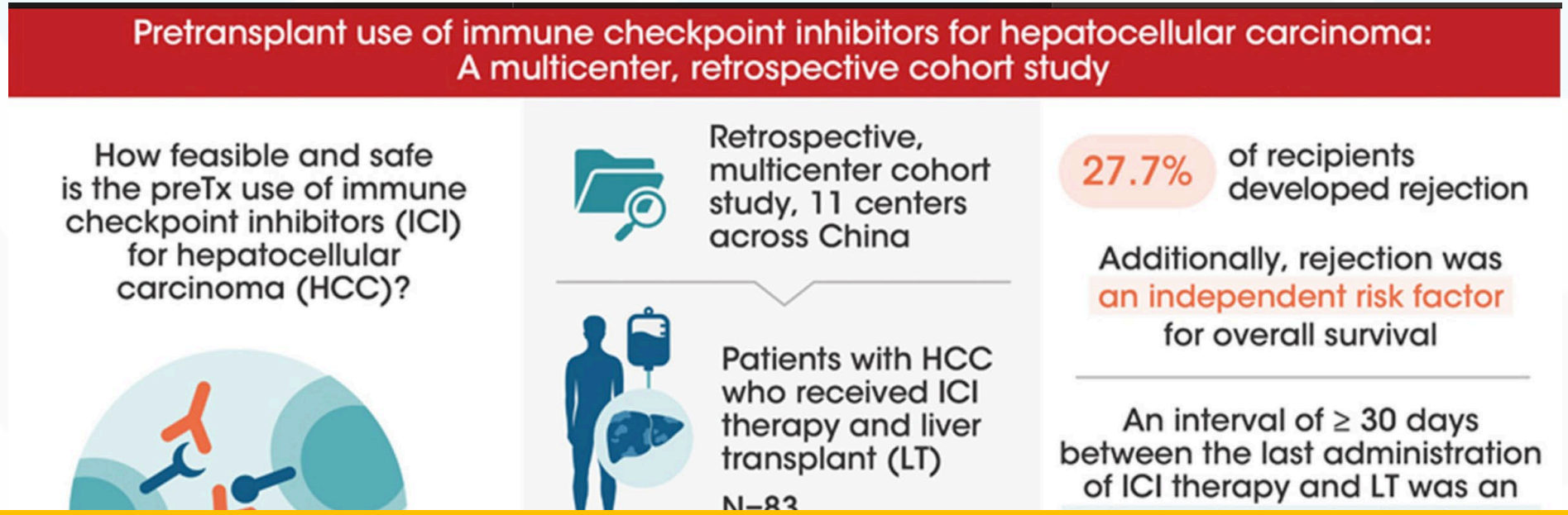
The 2024 ILTS-ILCA consensus re transplantation for HCC and intrah cholangiocarcinoma

Sudha Kodali[1,2] | Laura Kulik[3] | Antonio D'Alle
Abdul Rahman Hakeem[6] | Monica Lewinska[7,8] |
Zorana Maravic[12] | Madhukar S. Patel[13] | David
Ashwin Rammohan[15] | Nicole Rich[16] | Marco S
David W. Victor III[1,2] | Carmen Vinaxia[20,21] | Eli
Augusto Villanueva[23] | Tim Meyer[24,25] | Nazia S
Rafik Mark Ghobrial[1,22] | Mohamed Rela[15] | Gor
ILCA Consensus 2024 Group

Working Group C: Immunotherapy and Liver Transplantation

Who is a good candidate for immunotherapy pretransplant? Should it be considered for downstaging to LT?	In patients beyond transplant criteria, without extrahepatic disease who do not achieve sufficient response to LRT, immunotherapy might be used for downstaging, but clinical trials are needed.	Weak	Moderate
Should patients with macrovascular invasion be considered for transplant after response to immunotherapy?	There is currently no evidence to support the use of immune checkpoint inhibitors (ICIs) before transplant in the context of vascular invasion. Results from the ongoing clinical trials are awaited. On a case-by-case basis, patients may be referred to a transplant program for multidisciplinary tumor board evaluation.	Weak	Strong
Should there be a waiting period after response to ensure no recurrence off immunotherapy?	The panel was unable to make a specific recommendation given lack of scientific evidence available. Prospective clinical studies should evaluate the minimum interval required to consider liver transplantation without risk of recurrence in patients who have been successfully downstaged to transplant criteria.	Weak	Weak
Is there an immunotherapy regimen that is less risky and does this differ according to class of agent (eg, anti-PD-(L)1 +/- anti-CTLA-)?	Despite the differences in ICI mechanisms of action, there is not enough data to support the safety of one ICI over the other.	Weak	Moderate
What should be the washout period for immunotherapy pretransplant?	Although there are no strong data on the safe time interval, the recommendation with respect to a washout period of 2–3 half-lives of the specific ICI regimen, until the results of ongoing clinical trials are available.	Weak	Moderate
Should post-LT immunosuppression be different in those who received immunotherapy prior to LT to avoid rejection?	At this time, there are not enough data available to support the use of a particular immunosuppression regimen when assessing the risk of liver rejection. The decision on which regimen to adopt should be made on a case-by-case basis, according to the clinical judgment of the center's multidisciplinary team.	Weak	Weak
What is the safety and rationale to combine locoregional therapies, immunotherapy, and tyrosine kinase inhibitors in patients on the waiting list?	There is limited evidence in the literature to support the use of combining locoregional therapy, ICIs, and tyrosine kinase inhibitors (TKIs) in patients who are eligible for liver transplantation and are on the waiting list. Until new data are available, we recommend LRT should be preferred alone and not in combination with other therapies as bridging therapy	Weak	Strong

Safety of ICI before LT: retrospective studies



- **Is allograft rejection enough to define it is safe?**
- **Graft loss?**
- **Other post transplant complications? Cardiovascular? De novo tumors?**

Guo et al. Am J Transplant 2024;24(10):1837-1856

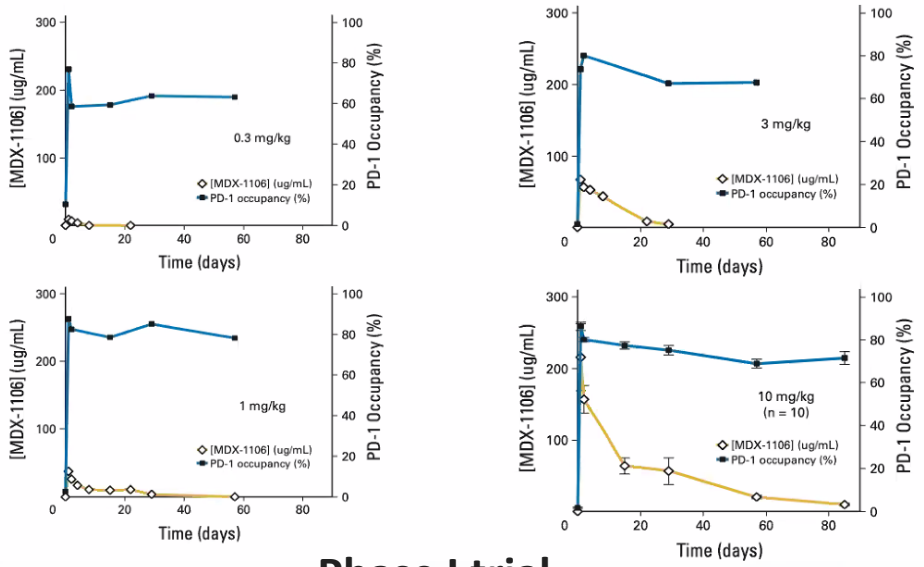
Immunotherapy pre-LT: Measuring the activity

Drug	Mechanism	Half-Life
Nivolumab	PD-1 Inhibitor	26.7 days (FDA 2014)
Pembrolizumab	PD-1 Inhibitor	23 days (FDA 2016)
Atezolizumab	PD-L1 Inhibitor	27 days (FDA 2018)
Durvalumab	PD-L1 Inhibitor	18 days (FDA 2018)
Ipilimumab	CTLA-4 Inhibitor	15.4 days (FDA 2015)

- Liver transplant within one half-life (27 days) of the drug experienced acute rejection in 3/4 (75%) of cases.
- 6 /19 patients (32%) within 3 half-lives of nivolumab treatment.
- 2 /14 patients (14%) who were transplanted beyond 3 half-lives of nivolumab treatment.

Pharmacodynamics of anti–programmed death-1 (PD-1) monoclonal antibody (MDX-1106)

PD-1 occupancy on circulating CD3⁺ T cells



Phase I trial

n= 39 pts solid tumors

Sustained mean occupancy of > 70% of PD-1 on circulating T cells ≥ 2 months following infusion, regardless of dose.

Woo SM et al Curr Oncol. 2022 13;29(12)

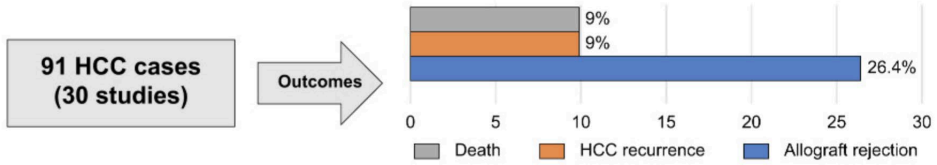
Brahmer JR. J Clin Oncol. 2010;28(19):3167-3175.

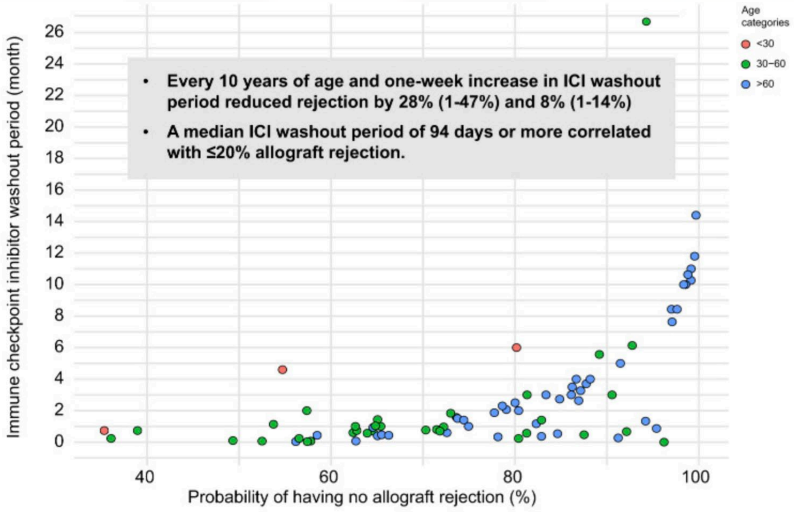
Immunotherapy and liver transplantation

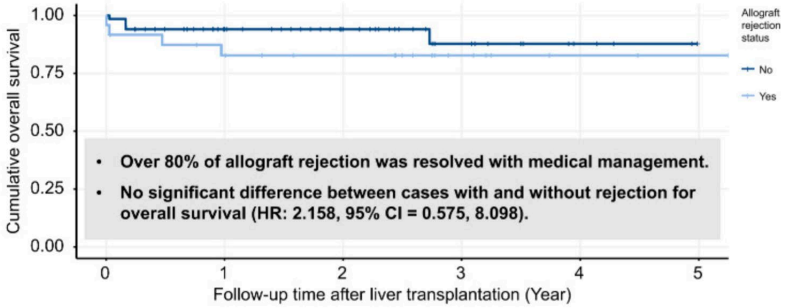
Risk of rejection

Methodology

Study type	• Systematic review and individual patients data meta-analysis
Eligibility criteria	• All study types in which ICIs had been used in patients with HCC prior to LT
Outcomes	• Allograft rejection, HCC recurrence, and overall survival
Search in	• Electronic databases and meeting abstracts







- Age and ICI washout length relate to the allograft rejection risk, and a 3-month washout may reduce it to that of patients without ICI exposure
- The data underscore the need for large-scale multicenter studies to provide robust evidence supporting the efficacy and safety of ICI for HCC in LT candidates

Rezaee-Zavareh, MS et al. J Hepatol. 2024;82(1): 107-119

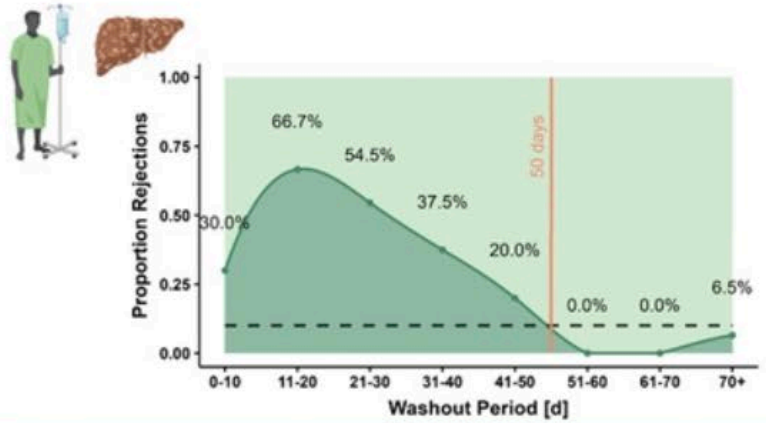
Immunotherapy and liver transplantation

Risk of rejection

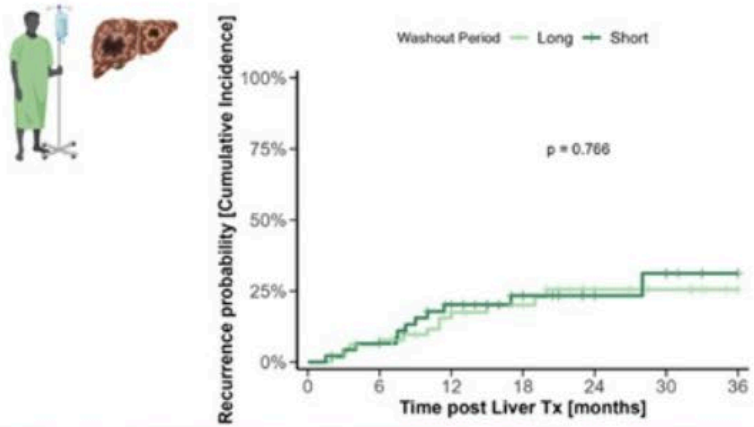
Determining safe washout period for immune checkpoint inhibitors prior to liver transplantation: An international retrospective cohort study

Study Design

Outcomes



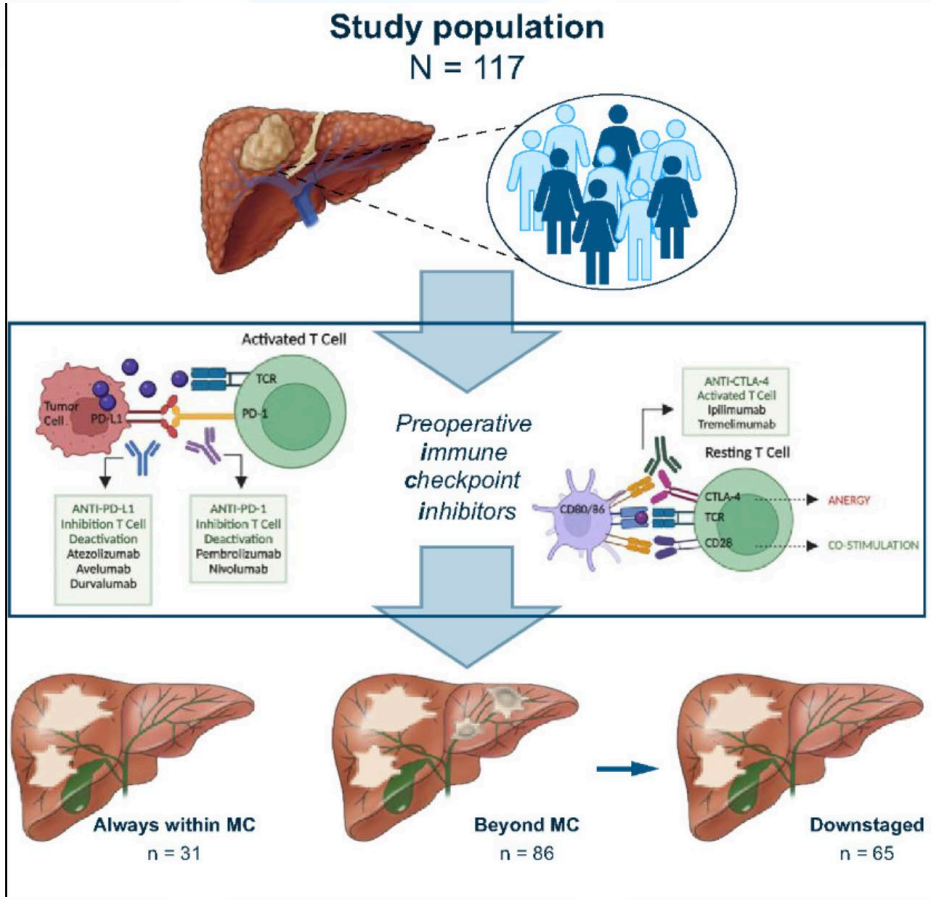
After 50 days of washout, the rejection rate dropped below 10%, matching rates in ICI-naïve recipients, defining 50 days as a safe washout period

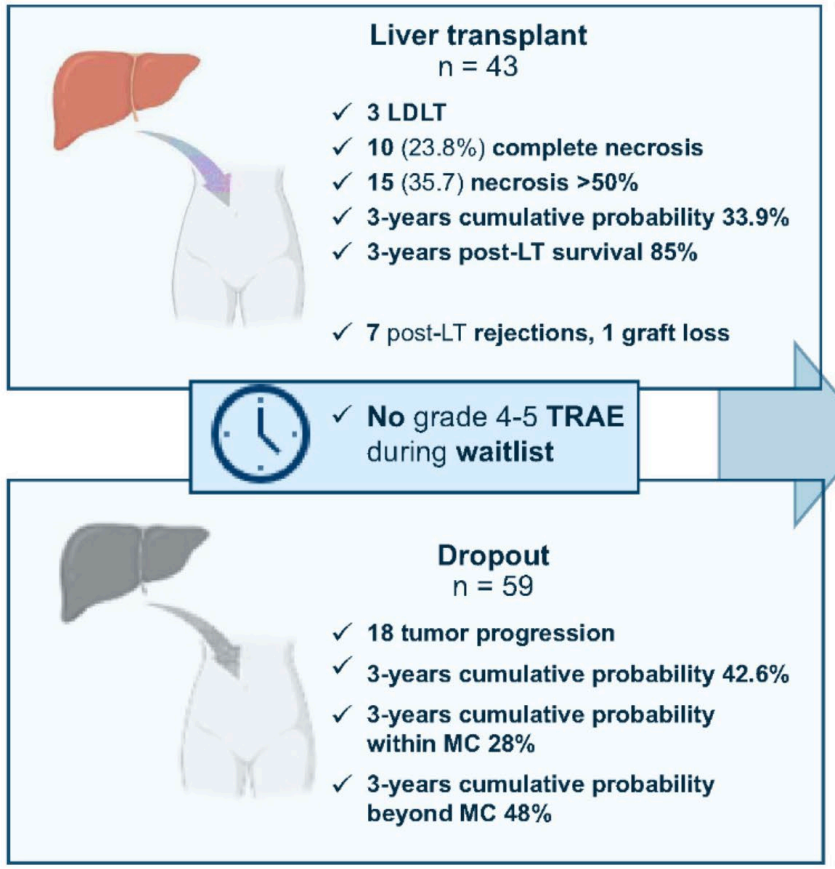


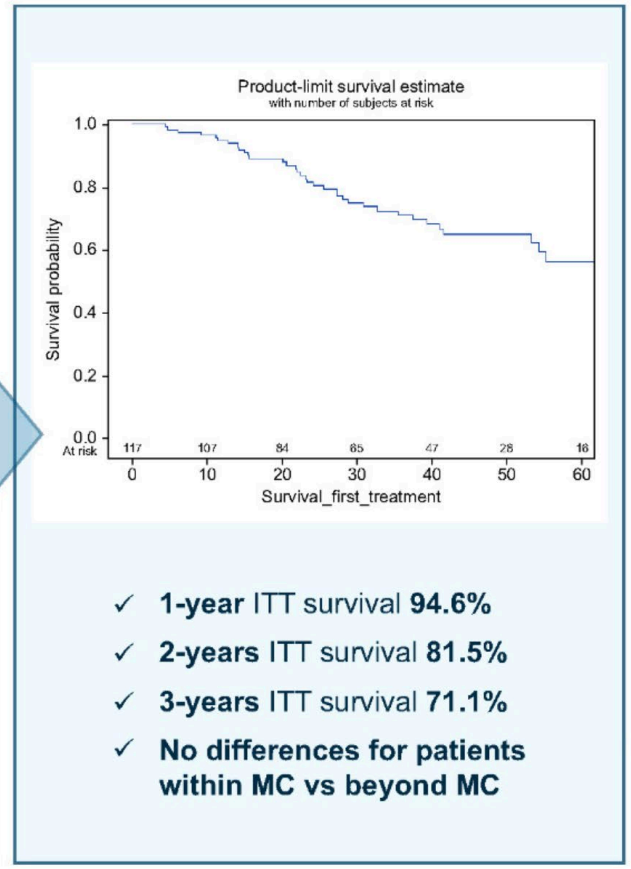
Longer washout periods (>50 days) did not compromise recurrence-free survival (71% vs. 67% at 36 months, p = 0.77

Moeckli et al. Hepatology. 2025 Mar 5. doi: 10.1097/HEP.0000000000001289.

VITALIty study

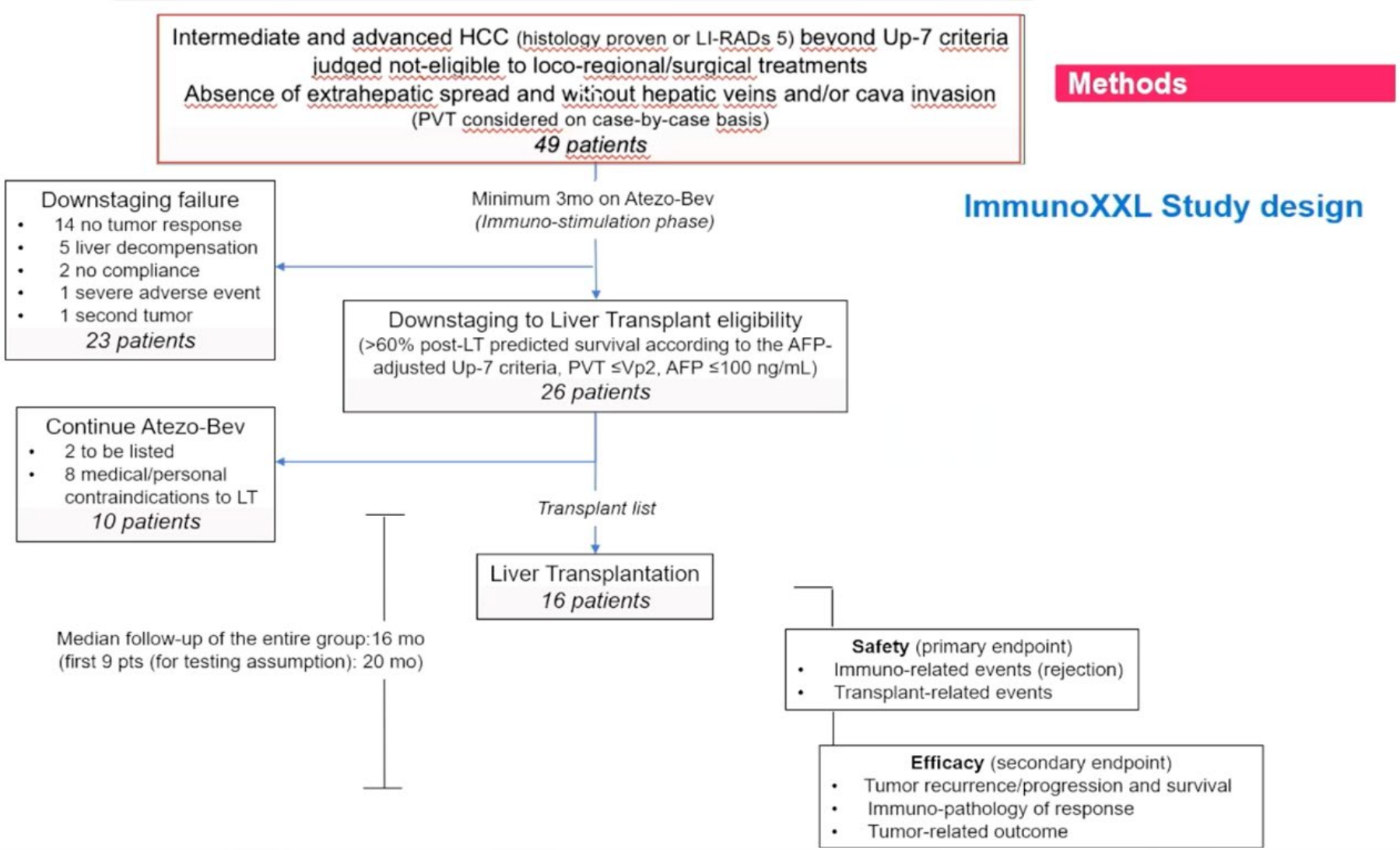






Trabizian P et al. J Hepatol. 2025 Mar;82(3):512-522.

Immune XXL trial



Methods

ImmunoXXL Study design

Bhoori S, et al. J Hepatol 2024;80: S70.

Immune XXL trial

3F, 13M; HBV 19%; HCV 7 (44%), HBV 3 (19%), ETOH 3 (19%), MASLD 4 (25%)

15 out 16 pts received LRT prior to immunotherapy (12 intra-arterial treatments)

median AFP 283 (IQR: 6-1080); 12% had AFP >1000

median size of the largest lesion at diagnosis: 6.5 cm (IQR: 2.9-7)

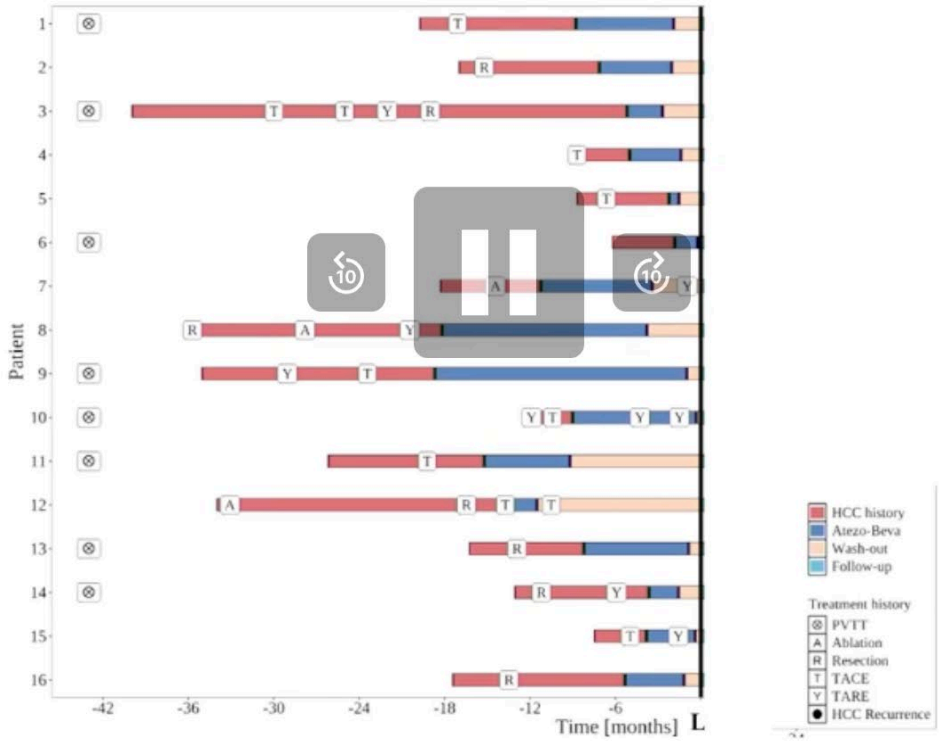
8 out of 16 pts (50%) had multifocality

8 out 16 pts (50%) had PVT:
6 Vp2
1 Vp3
1 Vp4

median Atezo-Bev duration: 4.7 months (IQR:2.4-7.6)

median wash-out period: 57.5 days (IQR:29-87)

Individual patients' treatment and history



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Bhoori S, et al. J Hepatol 2024;80: S70.

Immune XXL trial

Results

Post-LT adverse events (grade> 3, clinically relevant)

25% of ATCR

Surgery-related severity of complications was mainly due to vascular and biliary complications

2 re-transplantations (12.5%); one for hepatic artery thrombosis and one for delayed malfunction

1 death due to mixed delayed malfunction + mild rejection + marginal graft sepsis

90-days morbidity and mortality after transplant were 62.5% and 6.3% respectively

Post-LT (50%)

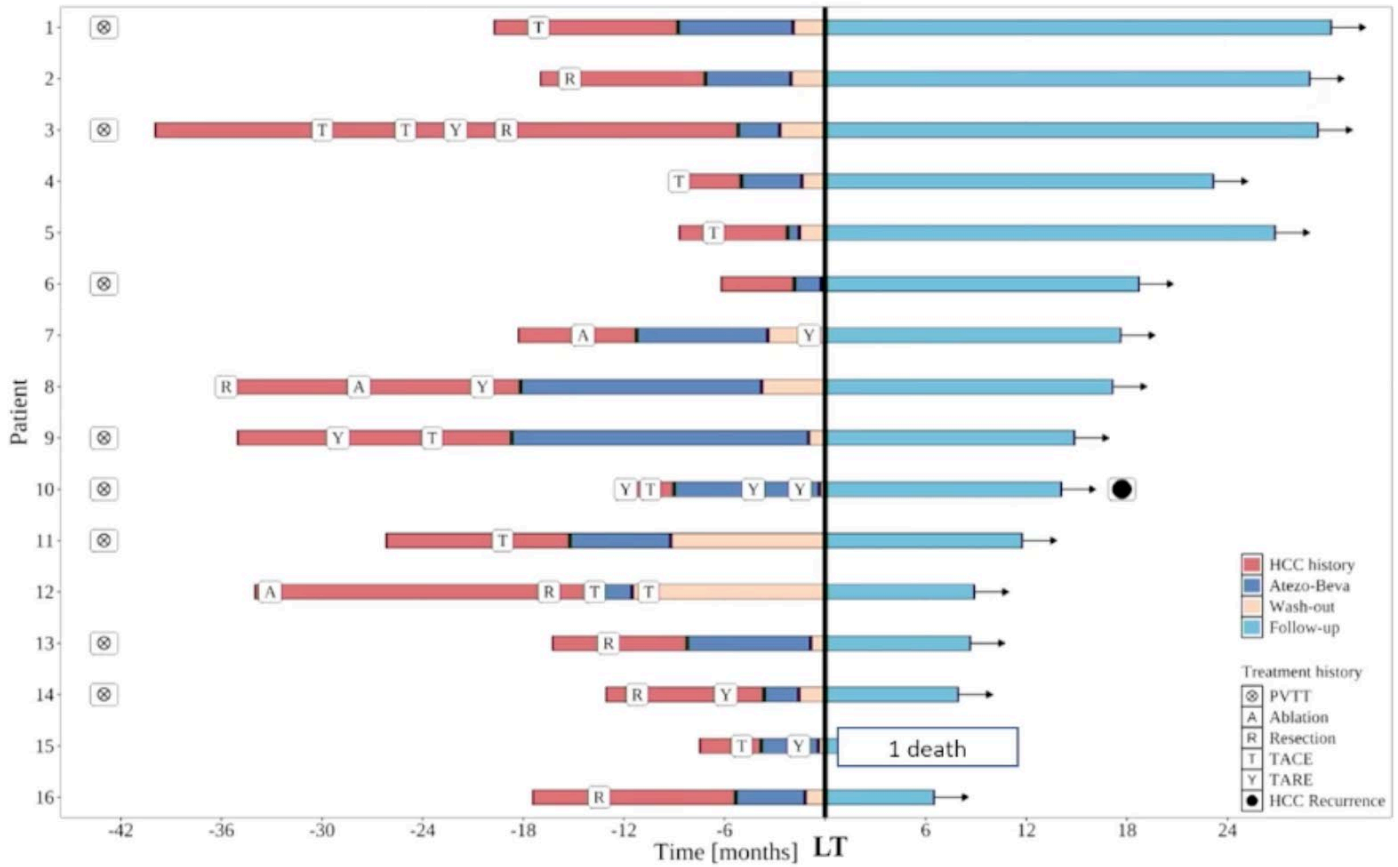
	Grade 3	Grade 4	Grade 5
- Immune mediated AEs (25%)	4	0	0
Acute rejection requiring biopsy and steroids treatment			
RAI 5	1		
RAI 6	2		
RAI 7	1		
- Technical			
Hepatic artery thrombosis-stenosis	2 (12%)	0	0
Biliary fistula-stenosis	4 (25%)	0	0
Incisional hernia	1 (6%)	0	0
Chylous fistula	1 (6%)	0	0
- Medical			
Drug-induced liver injury	1 (6%)	0	0
MINOCA	0	1 (6%)	0
- Mixed			
Multiorgan failure	1 (6%)	0	1 (6%)
Re-transplantation	0	2 (12.5%)	0

Submitted data, please do not post

Bhoori S, et al. J Hepatol 2024;80: S70.

Immune XXL trial

Follow-up, tumor recurrence, OS

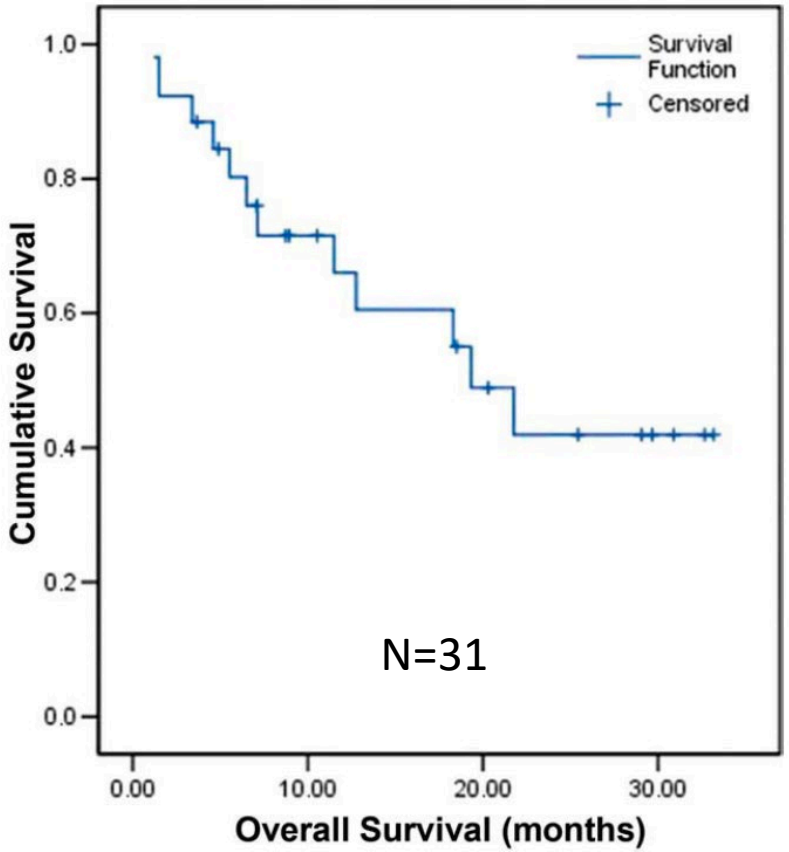


- Median follow-up 16 months
- 1 patient recurred (6.2%)
- **RFS and OS: 94% and 90% respectively at 2 yrs**

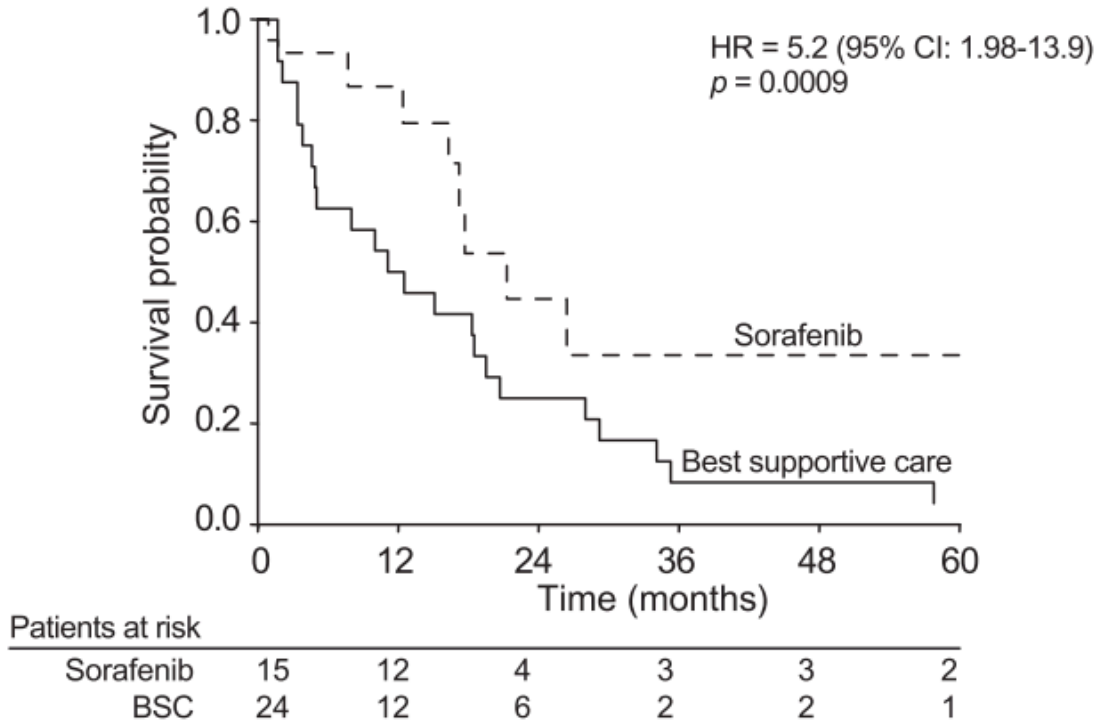
Bhoori S, et al. J Hepatol 2024;80: S70.

Therapy of HCC recurrence after Liver transplantation

Systemic therapy with sorafenib (and mTOR)



The median OS was 19.3 months [95%CI: 13.4–25.1], and the median TTP was 6.77 months (95% CI: 2.3–11.1).



Gomez-Martin C,et al. Liver Transplant. 2012;18:45–52.

Sposito C, et al. J Hepatol. 2013;59:59–66.

Therapy of HCC recurrence after Liver transplantation

Systemic therapy with sorafenib (and mTOR)

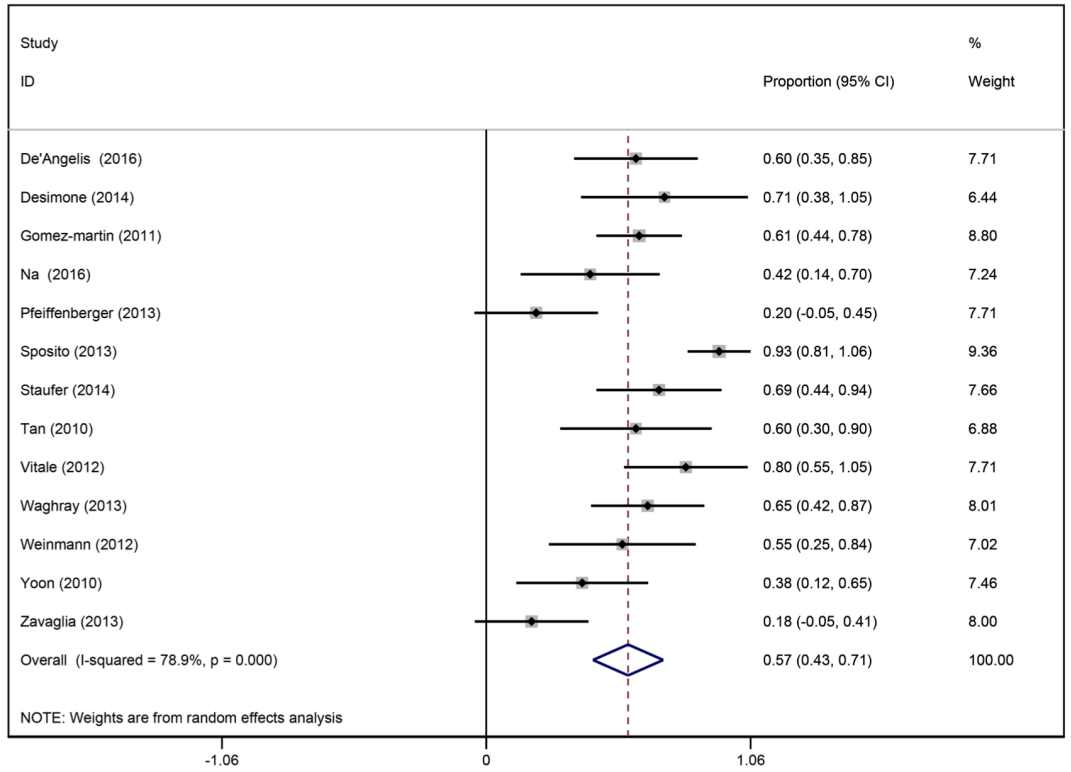
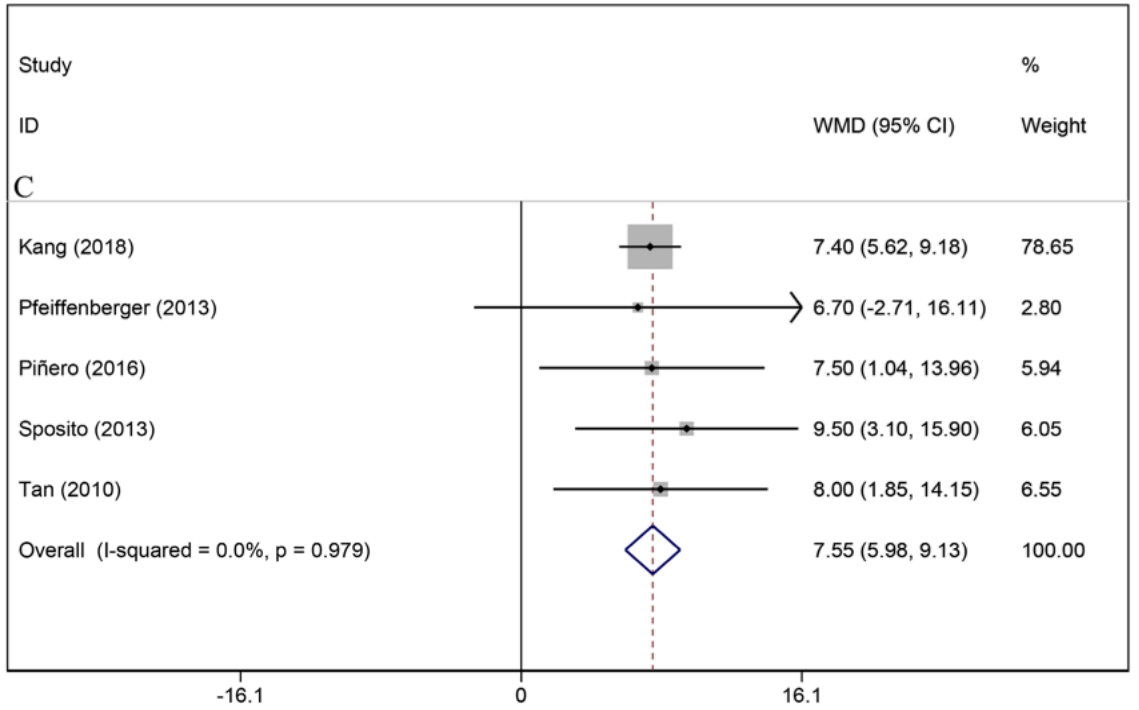


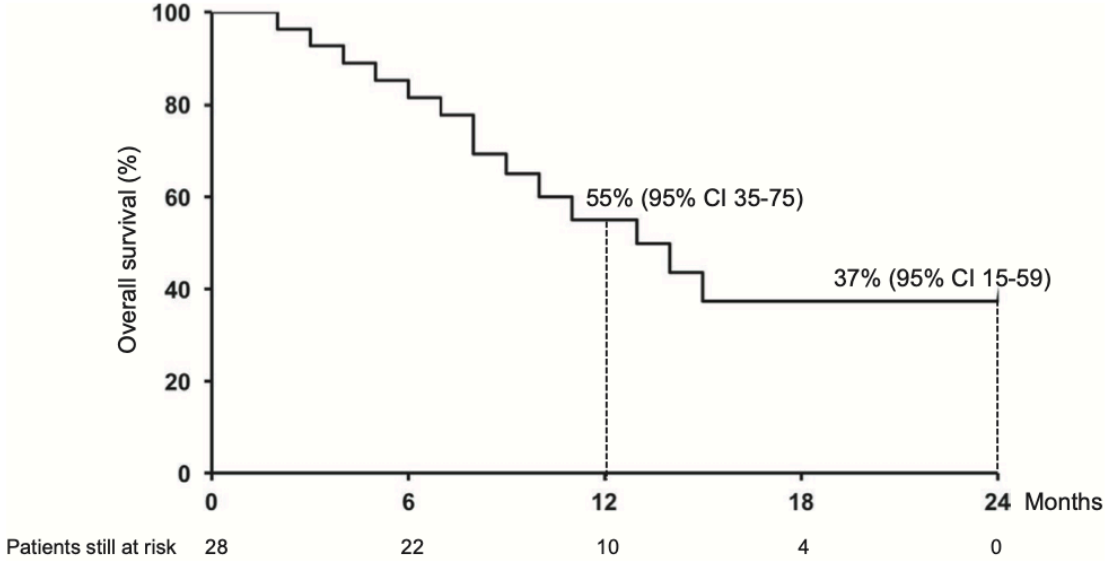
Figure 2. Forest plot of 1-year survival rates of patients treated with sorafenib for hepatocellular carcinoma recurrence after liver transplantation in 13 studies.



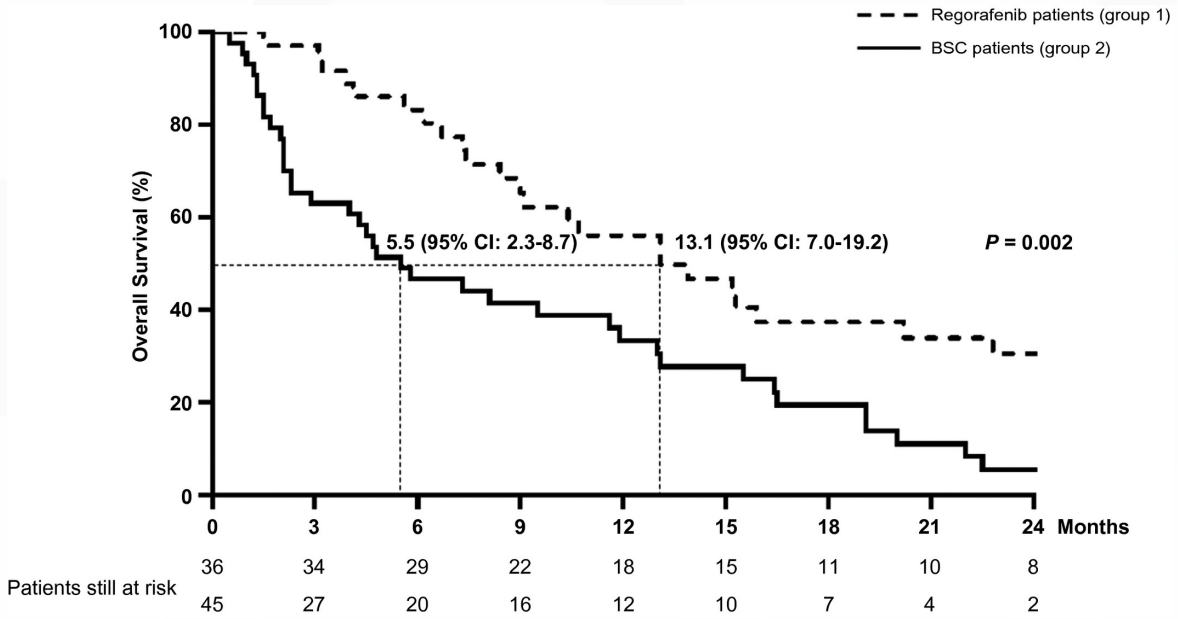
Li et al. Turk J Gastroenterol. 2021 Jan;32(1):30-41

Therapy of HCC recurrence after Liver transplantation

Systemic therapy with regorafenib



The median OS was 12.9 months (95% CI, 6.7-19.1)



- The median OS was 13.1 (versus 5.5 months; P < 0.01)
- The use of Regorafenib had a HR, 0.37; (CI95%, 0.16-0.89; P = 0.02).
- The median OS calculated from sorafenib start was 28.8 months (95% CI, 17.6-40.1) in group 1 versus 15.3 months (95% CI, 8.8-21.7) in group 2 (P < 0.01)

Iavaronne M et al. Am J Transplant. 2019 Nov;19(11):3176-3184.

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Allograft rejection in liver transplant recipientes treated with ICI

Allograft rejection in liver transplant recipientes treated with ICI: case series with > 3 patients

N of LT recipientes who developed acute rejection	Organ failure after acute rejection	Reference
4/11 (36%)	3 /4 (75%)	Gassmann, Transpl Direct 2018
9/24 (37.5%)	6 / 8 (75%)	D´Izarny-Gargas, Am J Tranaspl 2020
7/19 (39%)	Non-reported	Kumar, The Oncologist 2020
2/8 (25%)	0	Owoyemi, Cancer 2020
7/20 (35%)	6/7 (86%)	Fisher, J Am Acad Dermatol, 2020

- The average time to graft rejection from first ICI use was 3 weeks;
- Most graft rejection after ICI therapy occurred in patients who had transplant within 3 years;

ICI: Immune checkpoint inhibitors; LT: liver tranasplant

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Outcomes of postLT rrecurrent patients receiving Immunotherapy

Table 2 **Characteristics and reported outcomes of published cases with hepatocellular carcinoma recurrence receiving immunotherapy after liver transplantation.**

No.	Ref.	Age	Sex	HCC recurrence	Immunosuppression protocol before immunotherapy	Compound	Duration of IMT (wk)	Interval from LT to IMT (yr)	Graft rejection	Tumor respon-se	Follow-up (mo)	Cause of death
1	De Toni and Gerbes[27]	41	M	IR and ER	Low-dose tacrolimus	Nivolumab	30	1	No	PD	10	-
2	Friend *et al*[59]	20	M	ER	Sirolimus	Nivolumab	4	4	Yes, lethal (17 d)	NA	1	OF (4 wk after ICI initiation)
3	Friend *et al*[59]	14	M	ER	Tacrolimus	Nivolumab	2	3	Yes, lethal (7 d)	NA	1	OF (5 wk after ICI initiation)
4	Varkaris *et al*[25]	70	M	ER	Low-dose tacrolimus	Pembrolizumab	11.3	8	No	PD	3	PD
5	DeLeon *et al*[60]	57	M	HCC recurrence	Tacrolimus	Nivolumab	5.1	2.7	No	PD	1.2	Probably PD
6	DeLeon *et al*[60]	56	M	HCC recurrence	Sirolimus + MMF	Nivolumab	4.7	7.8	No	PD	1.1	Probably PD
7	DeLeon *et al*[60]	35	F	HCC recurrence	Tacrolimus	Nivolumab	5.6	3.7	No	PD	1.3	Probably PD
8	DeLeon *et al*[60]	64	M	HCC recurrence	Tacrolimus	Nivolumab	1.3	1.2	No	NA	0.3	MOF
9	DeLeon *et al*[60]	68	M	HCC recurrence	Sirolimus	Nivolumab	3.9	1.1	Yes (27 d)	NA	0.9	PD
10	Gassmann *et al*[58]	53	F	ER	Everolimus + MMF + steroids	Nivolumab	2	3	Yes, lethal (7 d)	NA	0.8	OF (2 wk after ICI initiation)
11	Rammohan *et al*[32]	57	M	ER	Tacrolimus + MMF + steroid + mTOR inhibitor	Pembrolizumab	42.9	4.3	No	CR	10	Alive
12	Zhuang *et al*[90]	54	M	ER	Tacrolimus	Nivolumab	62	2.7	No	PD	20	PD
13	Al Jarroudi *et al*[91]	70	M	IR	Tacrolimus	Nivolumab	8	> 3.0	Yes (45 d)	NA	4	PD
14	Al Jarroudi *et al*[91]	62	F	ER	Tacrolimus	Nivolumab	10	2.5	No	PD	2.5	Alive
15	Al Jarroudi *et al*[91]	66	M	IR and ER	Tacrolimus	Nivolumab	12	> 4.75	No	PD	3	Alive
16	Amjad *et al*[24]	62	F	IR and ER	-	Nivolumab	82.7	1.3	No	CR	20	Alive
17	Wang *et al*[92]	48	M	ER	Sirolimus + tacrolimus	Pembrolizumab	3	1	Yes (5 d)	NA	8	Alive
18	Qiu *et al*[93]	54	M	IR and ER	Sirolimus	Camrelizumab	39	4.3	No	PD	11	PD
19	Tan *et al*[21]	56	M	ER	Tacrolimus + MMF	HBV-TCR T cells	52	1.1	No	PR	12	Alive
20	Tan *et al*[21]	45	M	IR and ER	Sirolimus	HBV-TCR T cells	16	4.4	No	PD	3.7	Alive

ICI: Immune checkpoint inhibitors; LT: liver tranasplant

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Risks and benefits of TKIs and ICIs in the pre- and post-LT

Take home messages

- The application of transplant oncology should be done if the local dynamics of the waiting list does not harm the other included patients (both the HCC patients and those with advanced liver disease)

- Urgent need to define homogeneous criteria for downstaging

- The use of TKIs pre-LT is not supported. However, TKIs are safe in post-LT setting. The use of ICIs post-LT is associated with high risk of acute rejection

- Future challenges:
- Assess the risk of rejection and strategies for prevention
- Evaluate the real benefit of LT in those with CR (or deep response) after ICI

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