

APPLE 2026

The 16th Asia-Pacific Primary Liver Cancer Expert Meeting

July 3-5, 2026 **Shanghai · China**

Networking Opportunities and Challenges

Chair Prof. Yi-Hsiang Huang

President, Taiwan Liver Cancer Association (TLCA)

Council member, Asia-Pacific Primary Liver Cancer Expert Association (APPLE)

Director, Department of Medical Research, Taipei Veterans General Hospital

Chair Professor, Institute of Clinical Medicine, National Yang Ming Chiao Tung University (NYCU), Taipei, Taiwan

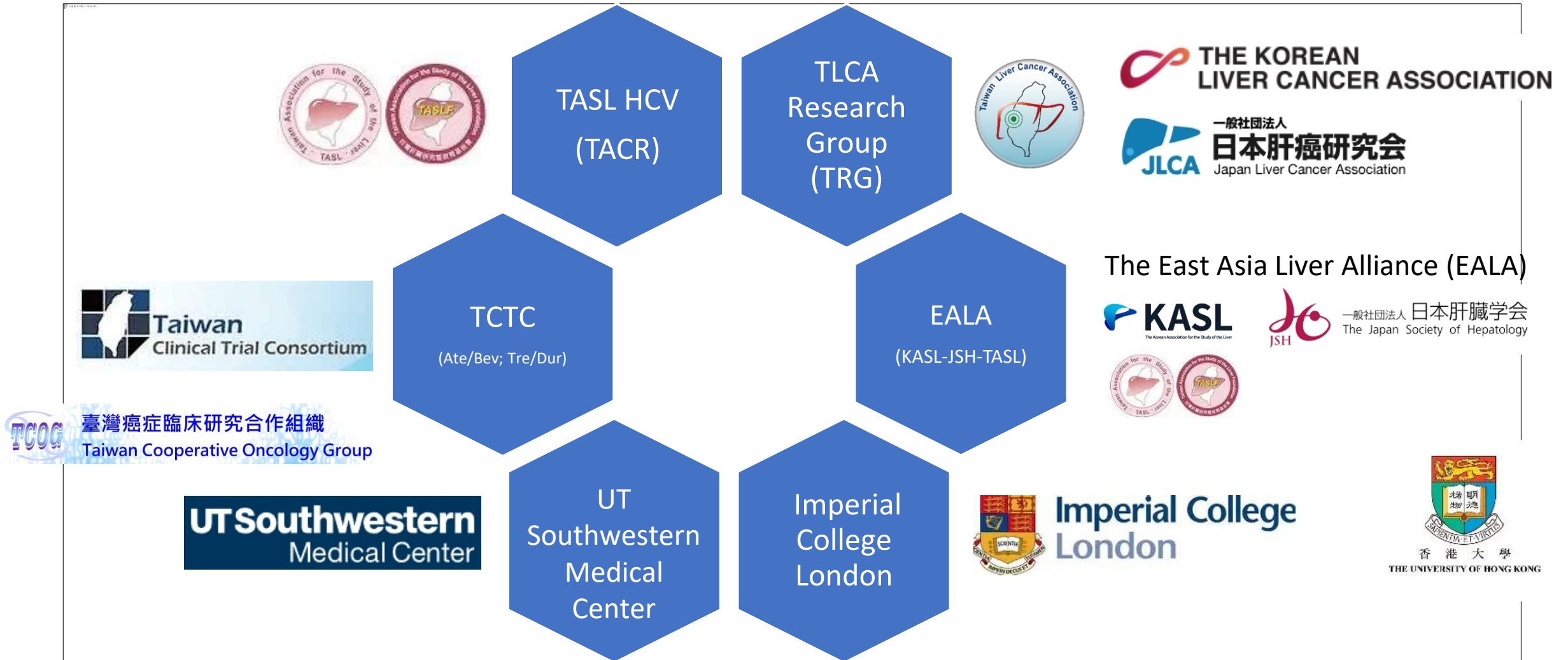


Disclosure of Conflict of Interest

- Advisory Board Membership: AstraZeneca, Gilead Sciences, Bristol-Meyers Squibb, Ono Pharmaceuticals, Eisai, Merck Sharp & Dohme and Roche.
- Research Grants: Gilead Sciences
- Speakership: AstraZeneca, Gilead Sciences, Bristol-Meyers Squibb, Ono Pharmaceutical, Merck Sharp & Dohme, Eisai, and Roche



Domestic and international consortium

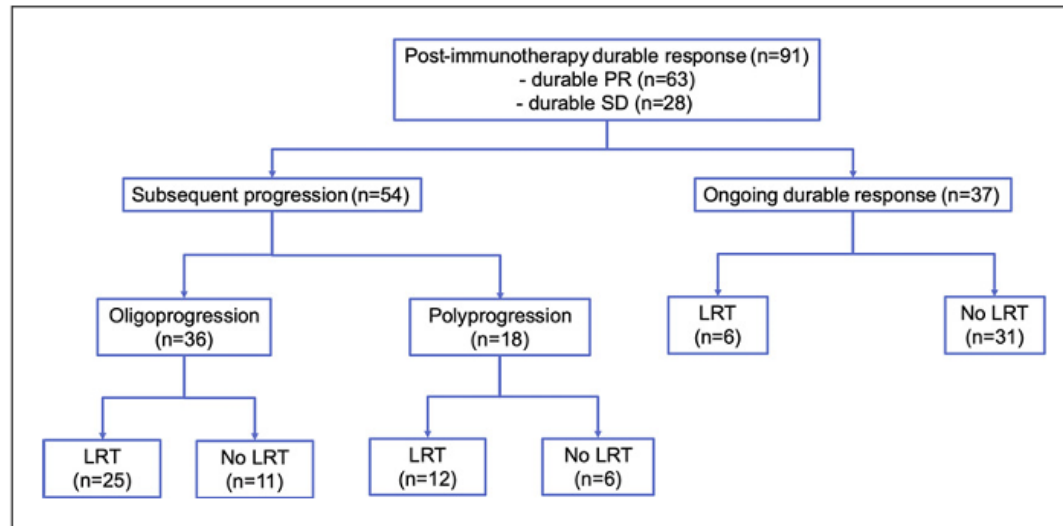


TLCA Research Group (TRG)

- Established in 2022
- A platform for investigators to propose study concepts and collect multicenter data supported by TLCA.

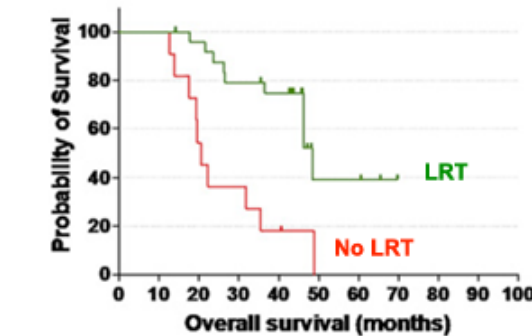
Outcomes of Post-Immunotherapy Durable Responders of Advanced Hepatocellular Carcinoma– with Emphasis on Locoregional Therapy for Oligoprogression

Tsung-Hao Liu^{a,b} San-Chi Chen^c Kun-Ming Rau^d Li-Chun Lu^{a,b}
Po-Ting Lin^{e,f} Yung-Yeh Su^g Wei Teng^{e,f} Shiue-Wei Lai^h Ren-Hua Yeh^h
Tsui-Mai Kaoⁱ Pei-Chang Lee^j Chi-Jung Wu^j Chien-Hung Chen^k
Chih-Hung Hsu^{a,b} Shi-Ming Lin^{e,f} Yi-Hsiang Huang^{j,l,m} Li-Tzong Chen^{g,h}
Ann-Lii Cheng^{a,b,n} Ying-Chun Shen^{a,b,n}
on behalf of Taiwan Liver Cancer Association Research Group (TRG)



Patients with oligoprogression

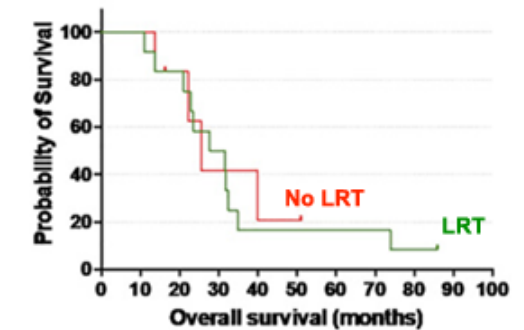
	Median OS (month)	P-value
LRT (n = 25)	48.4 (95% CI 38.7–58.0)	P<0.001
No LRT (n=11)	20.5 (95% CI 17.5–23.5)	



Patients at risk	25	25	23	18	16	3	3
	11	11	6	4	2		

Patients with polyprogression

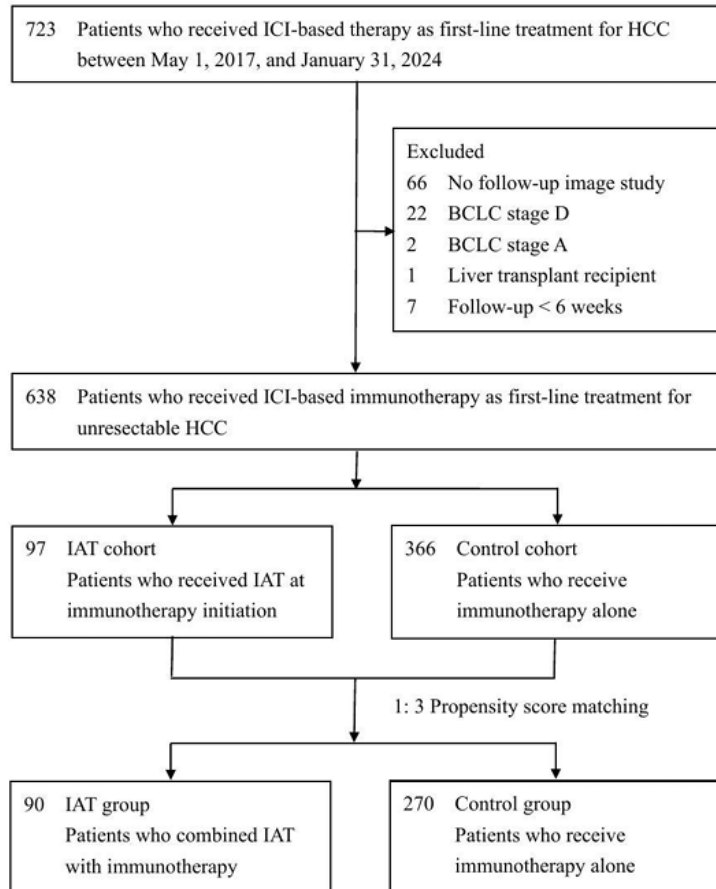
	Median OS (month)	P-value
LRT (n = 12)	27.7 (95% CI 13.8–41.6)	0.794
No LRT (n=6)	25.5 (95% CI 18.6–32.4)	



Patients at risk	12	12	10	7	3	2	2	2	1
	6	6	4	2	1	1			

Addition of Intra-arterial Therapy to Immunotherapy Improves Outcomes in uHCC: Taiwan Multicenter Cohort Study (TRG)

IAT cohort: patients received TACE, TARE, or HAIC within 4 weeks of initiating 1L immunotherapy



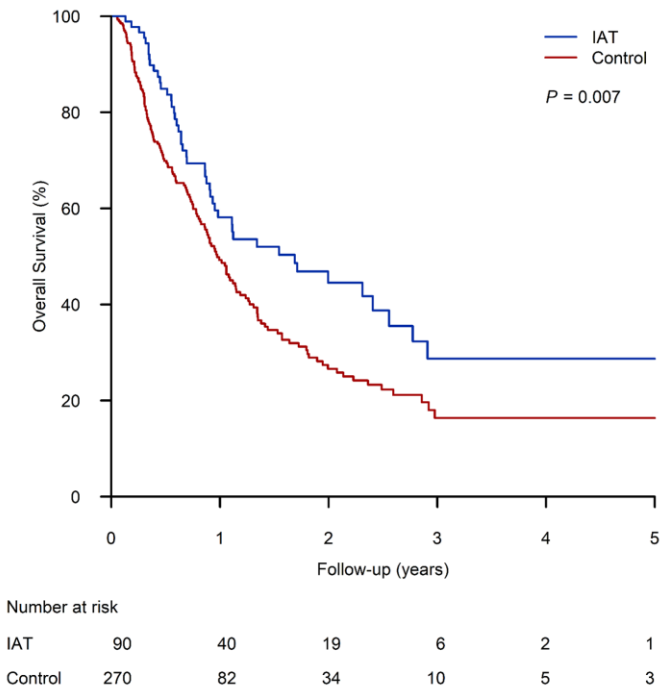
Liver Cancer

Liver Cancer , DOI: 10.1159/000552375
Received: November 13, 2025
Accepted: April 20, 2026
Published online: May 5, 2026

Addition of Intra-arterial Therapy to Immunotherapy Improves Outcomes in Unresectable Hepatocellular Carcinoma: Taiwan Multicenter Cohort Study

Lee T-Y, Lee P-C, Shen Y-C, Hsu W-F, Lai S-W, Chang C-W, Su Y-Y, Su T-H, Lin P-T, Dai C-Y, Hsu C-S, Chen S-C, Rau K-M, Lee I-C, Jhan S-R, Liu T-H, Lai H-C, Wang T-E, Lin S-M, Liang P-C, Tseng C-H, Chang P-Y, Wu S-C, Wang H-W, Lee S-W, Huang Y-H

Variables	IAT group (n= 90)	Control group (n= 270)	P value
Tumor response, n (%) ¹			0.003
CR	13 (14.4)	15 (5.6)	
PR	29 (32.2)	56 (20.7)	
SD	26 (28.9)	95 (35.2)	
PD	22 (24.4)	99 (36.7)	
ORR	42 (46.7)	71 (26.3)	<.001
DCR	68 (75.6)	166 (61.5)	0.022
Clinical CR ²	11 (12.2)	12 (4.4)	0.018
Curative conversion ³	9 (10.0)	7 (2.6)	0.006
Curative conversion by hepatectomy	6 (6.7)	5 (1.9)	0.032
Clinical CR with drug-free status	6 (6.7)	10 (3.7)	0.376
Duration of response, week	19.0 (9.7-36.6)	11.0 (8.4-23.1)	0.009
Immune therapy duration, week	20.5 (11.0-43.1)	15.6 (7.5-28.6)	0.011
Discontinuation due to TRAE, n (%)	8 (8.9)	30 (11.1)	0.692
Subsequent systemic therapy, n (%)	19 (21.1)	47 (17.4)	0.529



Lee TY, Huang YH*, TLCA Research Group (TRG). Liver Cancer Liver Cancer , DOI: 10.1159/000552375

TRG and Japan Multicenter Collaboration

Lenvatinib was associated with significantly longer PFS than Atezo+Bev in patients with a baseline CRAFITY score of 2.

Liver Cancer

Liver Cancer, DOI: 10.1159/000552808
Received: February 6, 2026
Accepted: May 3, 2026
Published online: June 1, 2026

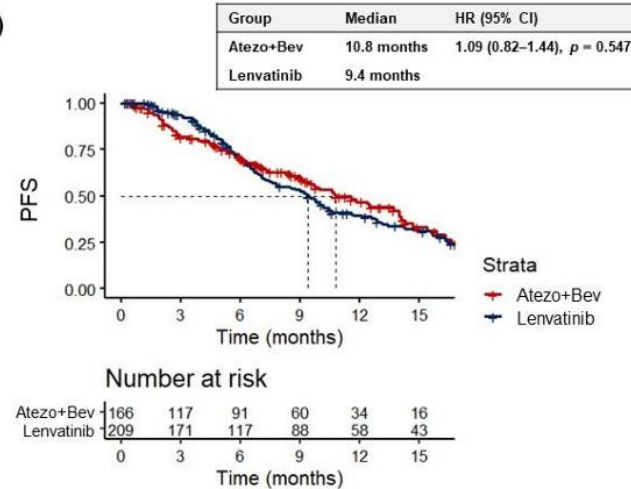
Atezolizumab Plus Bevacizumab Versus Lenvatinib as First-Line Treatment for Unresectable Hepatocellular Carcinoma Stratified by the CRAFITY Score: An International Multicenter Study

Ueno M, Su Y-Y, Takai A, Huang Y-H, Morimura H, Nishijima N, Lin S-M, Chang C-W, Iwamoto S, Nagatomo S, Lai H-C, Mitani T, Ikeda A, Uenoyama Y, Umeda M, Chen S-C, Chuang C-H, Lai S-W, Lee T-Y, Nakano S, Dai C-Y, Goto T, Su T-H, Hsu CS, Lo C-C, Takeda H, Osaki Y, Hatano E, Lee P-C, Lin P-T, Wang H-W, Hsu W-F, Liu T-H, Seno H

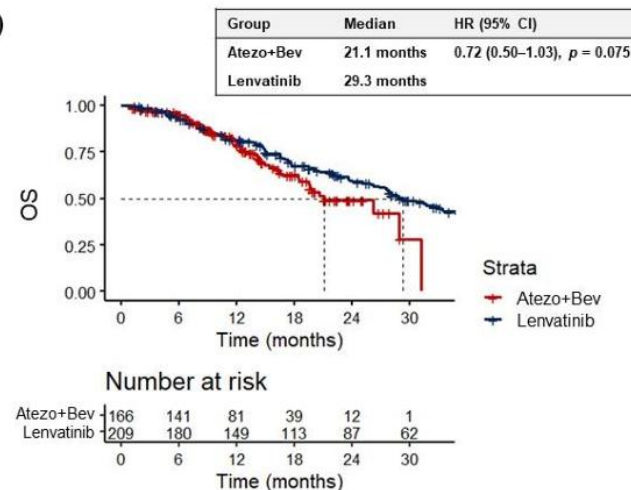
	Atezo+Bev (n=354)	Lenvatinib (n=640)	p-value
Age, years	71 [62–78]	71 [63–78]	0.564
Sex			0.320
Male	281 (79.4%)	489 (76.4%)	
Female	73 (20.6%)	151 (23.6%)	
Performance status			0.001*
0	254 (71.8%)	385 (61.6%)	
1	87 (24.6%)	186 (29.8%)	
2	13 (3.7%)	54 (8.6%)	
BCLC stage			0.419
Early	18 (5.1%)	56 (8.8%)	
Intermediate	128 (36.2%)	216 (33.8%)	
Advanced	208 (58.8%)	368 (57.5%)	
Macrovascular invasion	104 (31.2%)	161 (26.9%)	0.187
Extrahepatic metastasis	120 (36.0%)	236 (39.5%)	0.336
Child–Pugh score			0.272
5	183 (51.7%)	317 (49.5%)	
6	115 (32.5%)	198 (30.9%)	
7	39 (11.0%)	80 (12.5%)	
8	13 (3.7%)	26 (4.1%)	
≥9	4 (1.1%)	19 (3.0%)	
ALBI score	-2.45 [-2.73 to -2.04]	-2.42 [-2.70 to -2.02]	0.323
Etiology of liver diseases			
Viral			
Non-viral			
CRP, mg/dL	0.34 [0.11–1.64]	0.70 [0.20–2.69]	<0.001*
AFP, ng/mL	35.3 [4.7–824.1]	61.9 [6.3–964.0]	0.056
DCP, mAU/mL	560 [84–7229]	309 [44–3223]	0.005*
CRAFITY score			<0.001*
0	166 (46.9%)	209 (32.7%)	
1	126 (35.6%)	276 (43.1%)	
2	62 (17.5%)	155 (24.2%)	



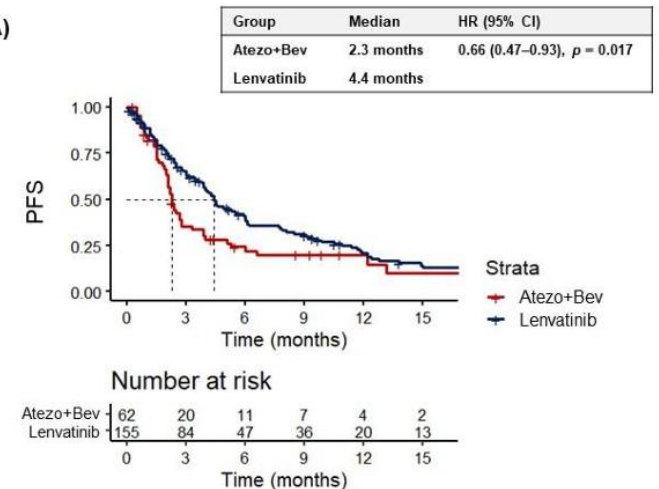
(A)



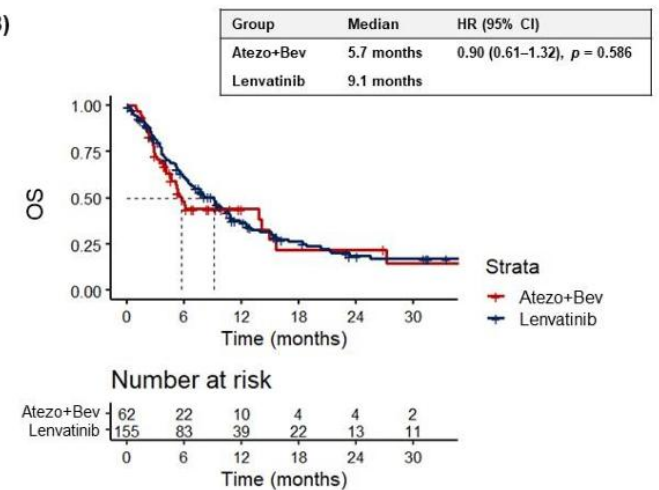
(B)



(A)



(B)



Review

<https://doi.org/10.3350/cmh.2025.0724>

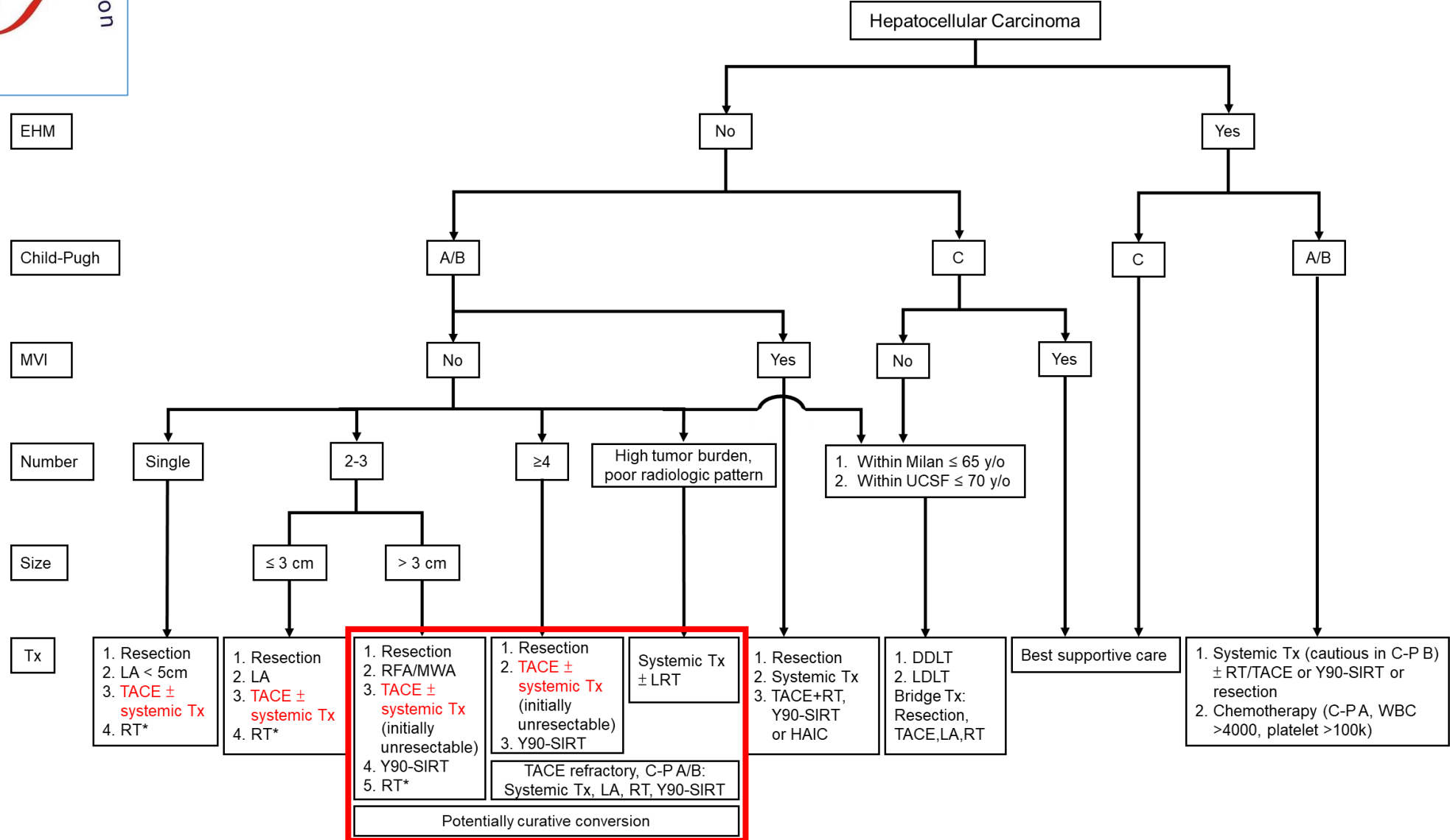
Clinical and Molecular Hepatology 2025;31:1213-1232

Taiwan liver cancer association management consensus guidelines for intermediate-stage hepatocellular carcinoma

I-Cheng Lee^{1,2,*}, Hung-Wei Wang^{3,4,*}, Wei Teng^{5,6,*}, Tsung-Jung Lin^{7,*}, Chien-Hung Chen^{8,9,10}, Hsueh-Chou Lai^{3,4}, Teng-Yu Lee^{11,12}, Ching-Wei Chang^{13,14}, Chao-Hung Hung¹⁵, Chia-Yen Dai^{16,17}, Yi-Ping Hung^{2,18}, Ying-Chun Shen^{19,20,21}, Chien-Wei Su^{1,2,22}, Ming-Chih Ho^{23,24}, Wei-Chen Lee^{6,25}, Gar-Yang Chau²⁶, Chin-Tsung Ting^{27,28}, Po-Chin Liang^{29,30}, Chien-An Liu^{2,31}, Pi-Yi Chang^{32,33}, Kuan-Yang Chen⁷, Shi-Ming Lin^{5,6}, Li-Tzong Chen^{34,35}, and Yi-Hsiang Huang^{1,22,36};
TLCA Intermediate Stage HCC Working Group



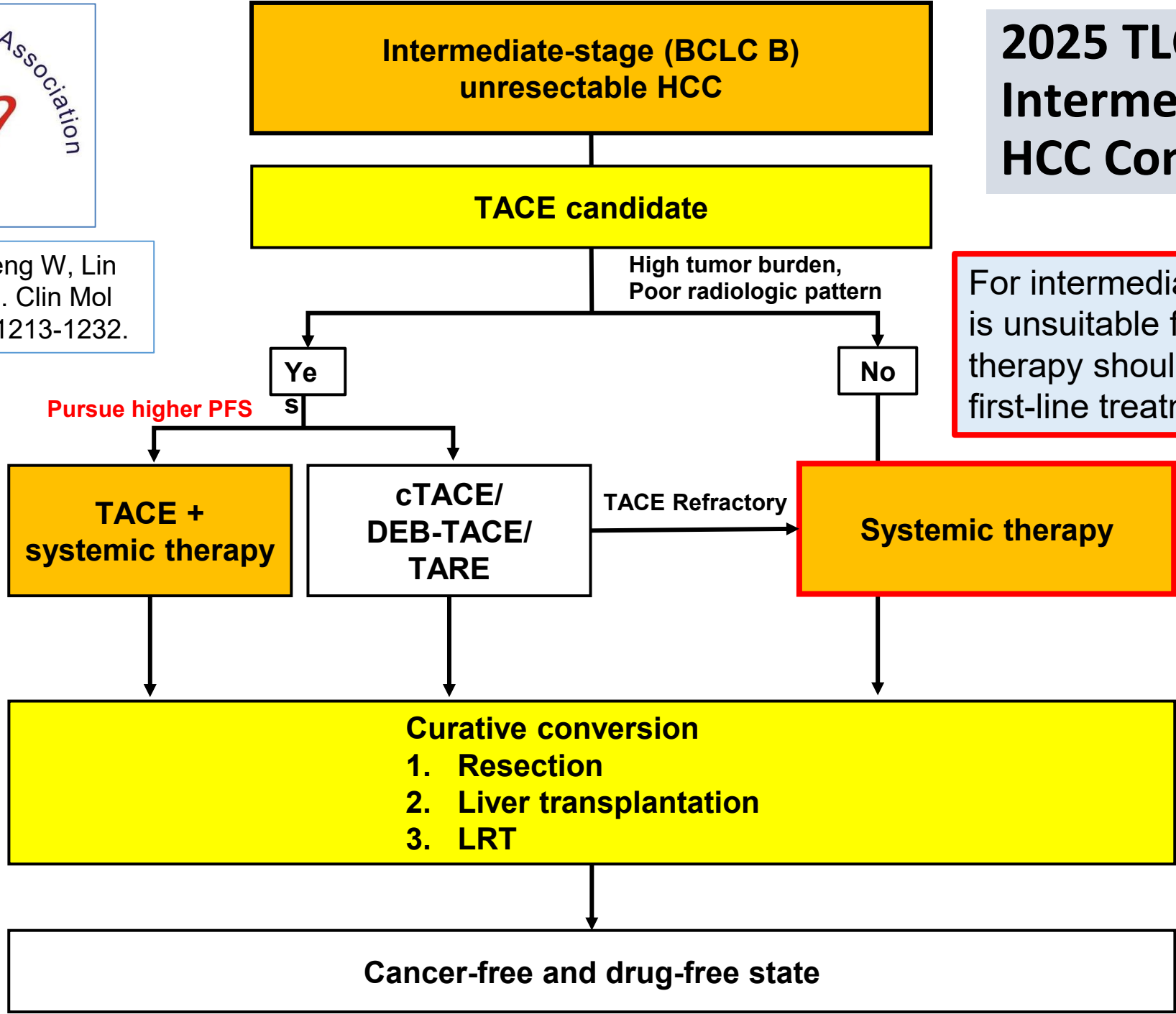
TLCA Consensus Guidelines for Intermediate Stage HCC





Lee IC, Wang HW, Teng W, Lin TJ,...Huang YH*, et al. Clin Mol Hepatol. 2025;31(4): 1213-1232.

2025 TLCA Intermediate-stage HCC Consensus



For intermediate-stage HCC that is unsuitable for TACE, systemic therapy should be initiated as the first-line treatment.



1,163 patients from 14 Hospitals

1	National Taiwan University Hospital	國立臺灣大學醫學院附設醫院
2	Taipei Veterans General Hospital	臺北榮民總醫院
3	Mackay Memorial Hospital	馬偕紀念醫院
4	Taipei Municipal Wanfang Hospital	臺北市立萬芳醫院
5	Taipei City Hospital	臺北市立聯合醫院
6	Taipei Medical University Hospital	臺北醫學大學附設醫院
7	China Medical University Hospital	中國醫藥大學附設醫院
8	Taichung Veterans General Hospital	臺中榮民總醫院
9	Chia-Yi Christian Hospital	嘉義基督教醫院
10	National Cheng Kung University Hospital	國立成功大學醫學院附設醫院
11	Kaohsiung Chang Gung Memorial Hospital	高雄長庚紀念醫院
12	Kaohsiung Medical University Chung-Ho Memorial Hospital	高雄醫學大學附設中和紀念醫院
13	E-Da Hospital	義大醫院
14	E-Da Cancer Hospital	義大癌治療醫院

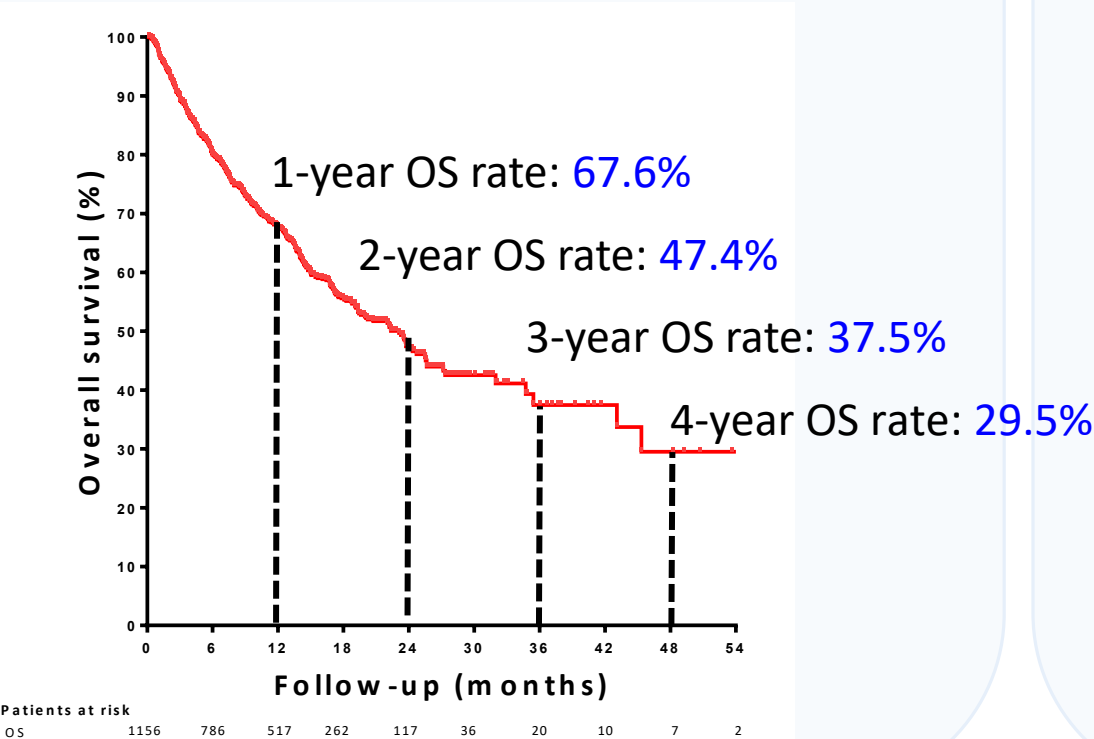
Primary Endpoints: Overall Survival and Progression-Free Survival

Median follow-up: 10.5 months (IQR, 4.7–17.2)

Overall Survival

Median OS: 23.1 months

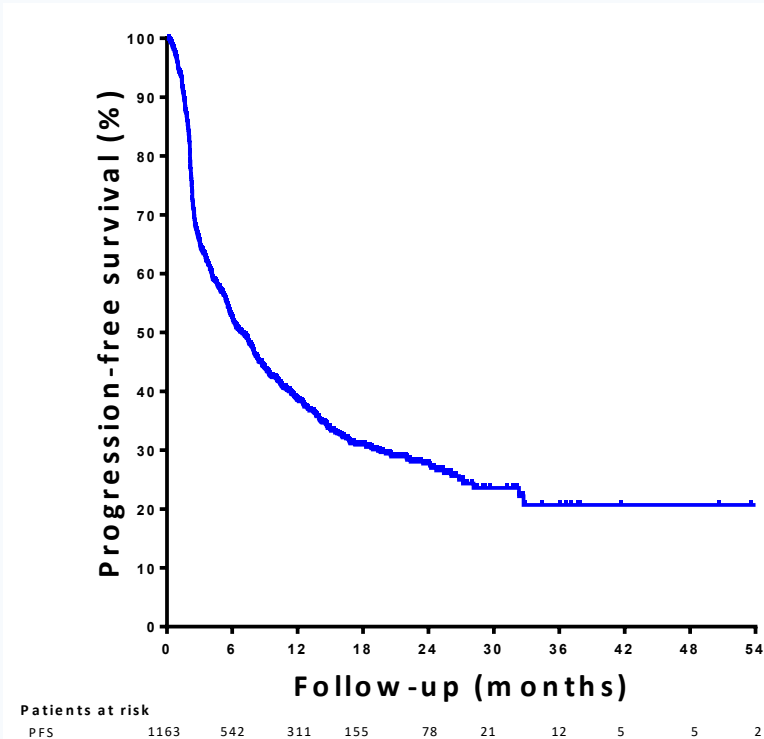
95% CI: 20.5–25.7



Progression-Free Survival

Median PFS: 6.9 months

95% CI: 6.0–7.8



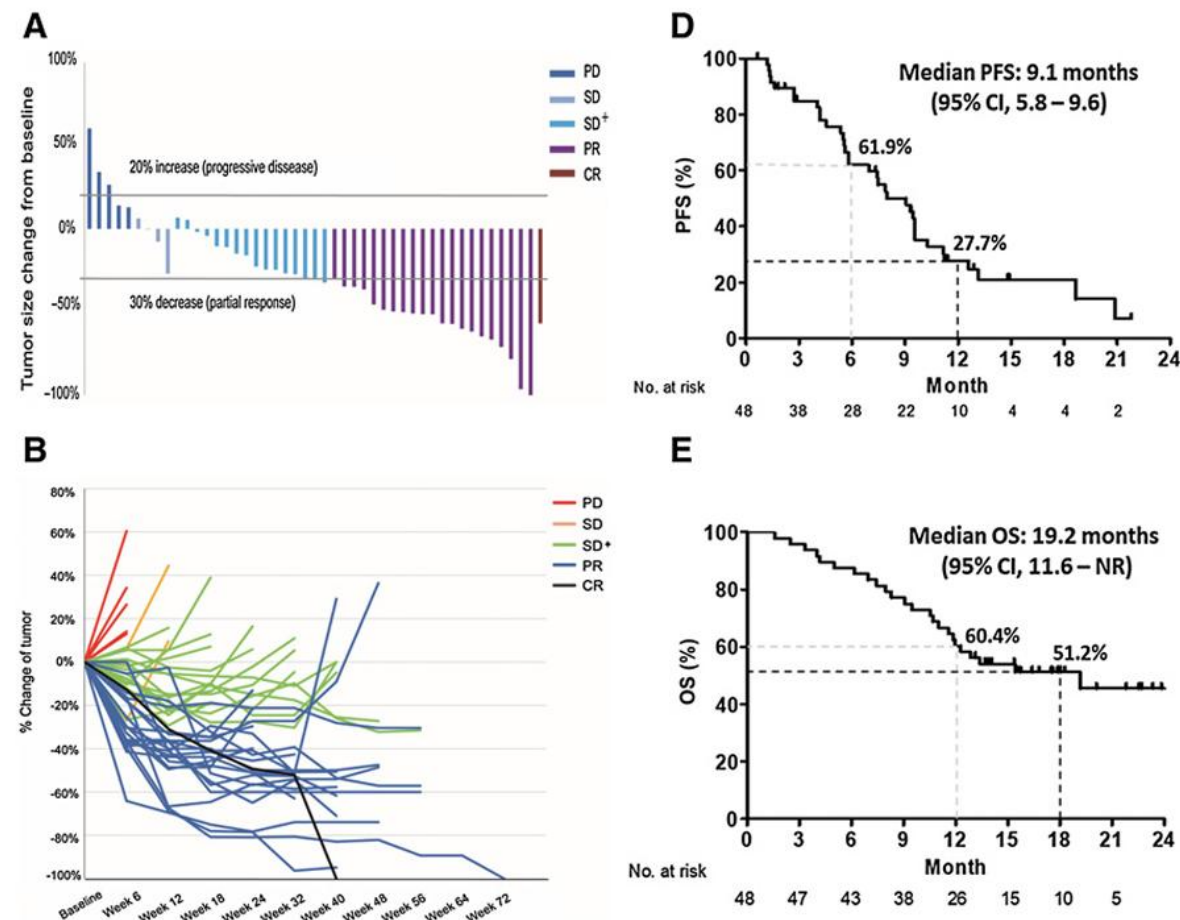
Phase II T1219 Study: a single-arm phase II of nivolumab plus modified GS (NGS) as first-line treatment in advanced BTC

CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

Impaired Chromatin Remodeling Predicts Better Survival to Modified Gemcitabine and S-1 plus Nivolumab in Advanced Biliary Tract Cancer: A Phase II T1219 Study

Nai-Jung Chiang^{1,2,3}, Kien Thiam Tan⁴, Li-Yuan Bai^{5,6}, Chin-Fu Hsiao⁷, Chung-Yu Huang⁴, Yi-Ping Hung^{1,2}, Chien-Jui Huang⁸, San-Chi Chen^{1,2}, Yan-Shen Shan^{9,10}, Yee Chao^{1,2}, Yi-Hsiang Huang^{2,11}, I-Cheng Lee^{2,11}, Pei-Chang Lee^{2,11}, Yung-Yeh Su^{3,12}, Shu-Jen Chen⁴, Chun-Nan Yeh^{13,14}, Li-Tzong Chen^{3,12,15}, and Ming-Huang Chen^{1,2}

- Fixed-dose 240 mg nivolumab and 800 mg/m² gemcitabine on day 1, plus oral administration of S-1 80/100/120 mg daily, according to the initial body surface area (<1.25/m²; ≥1.25/m² and <1.5/m²; or ≥1.5/m²) on days 1 to 10 in a 2-week cycle.



Chiang NJ, et al. Clin Cancer Res. 2022 Oct 3;28(19):4248-4257.

A Preliminary Real-World Cohort Analysis of Atezolizumab/Bevacizumab versus Durvalumab/Tremelimumab as First-Line Therapy in Unresectable HCC: The East Asia Liver Alliance Study

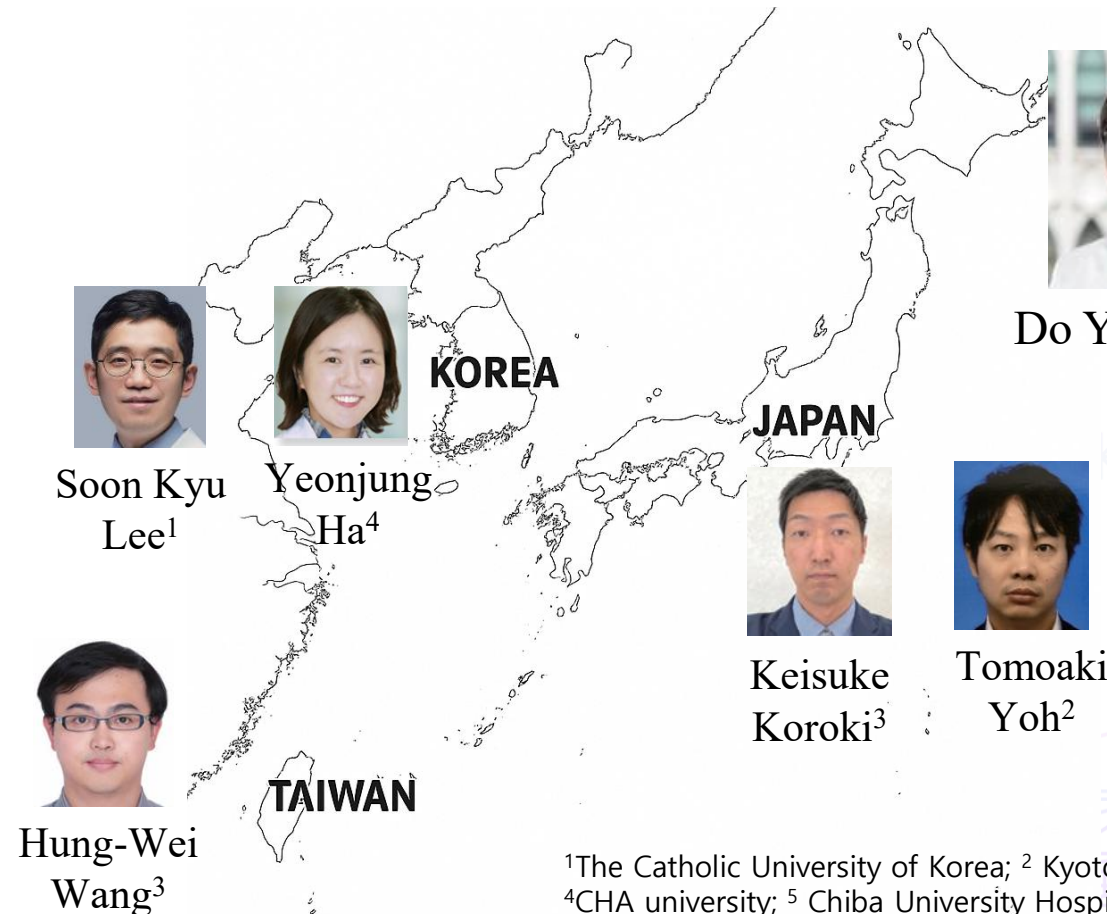
Soon Kyu Lee^{1*}, Tomoaki Yoh^{2*}, Hung-Wei Wang^{3*}, Yeonjung Ha^{4*}, Keisuke Koroki^{5*}, Jeong Won Jang¹, Pei-Chang Lee⁶, Masayuki Ueno², Atsushi Takai², Sadahisa Ogasawara⁵, Dong Yun Kim⁷, Pei-Chang Lee⁶, Etsuro Hatano^{2#}, Do Young Kim^{7#}, Yi-Hsiang Huang^{6#}

¹The Catholic University of Korea; ² Kyoto University Hospital; ³ China Medical University Hospital; ⁴ CHA university;
⁵ Chiba University Hospital; ⁶ Taipei Veterans General Hospital; ⁷ Yonsei University

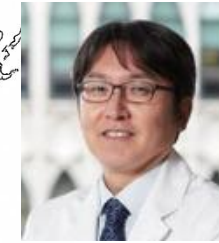


Methods – proposal at EALA 2025

- This study planned to analyze medical records of patients with HCC who received Atezo/Bev or Durva/Treme between January 2022 and December 2025 across seven medical centers in Japan, Korea, and Taiwan.



[Mentors]



Do Young Kim⁷



Yi-Hsiang Huang⁶

¹The Catholic University of Korea; ² Kyoto University Hospital; ³ China Medical University Hospital; ⁴CHA university; ⁵ Chiba University Hospital; ⁶ Taipei Veterans General Hospital; ⁷ Yonsei University

Methods – Extension of study population

- This study planned to analyze medical records of patients with HCC who received Atezo/Bev or Durva/Treme between January 2022 and December 2025 across seven medical centers in Japan, Korea, and Taiwan.
- Following the inclusion of an additional 12 institutions in Japan, the study ultimately enrolled patients from 19 university hospitals across three countries, including 3 in Korea, 2 in Taiwan, and 14 in Japan.



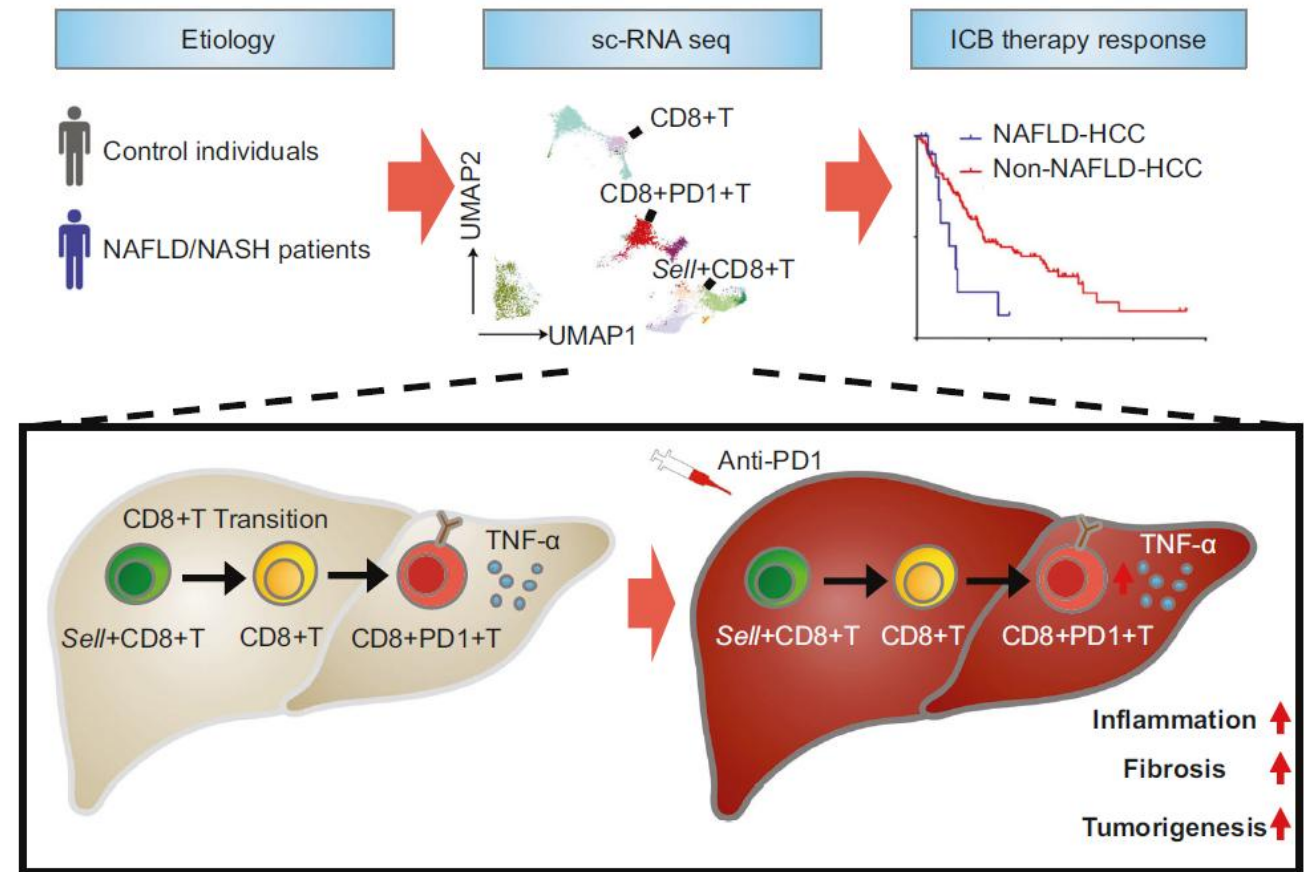
Joint Research with Dr. David Pinato (>30 publications)

- NASH limits anti-tumour surveillance in immunotherapy-treated HCC. *Nature*. 2021 Apr;592(7854):450-456. doi: 10.1038/s41586-021-03362-0.
- A myeloid immunosuppressive phenotype defines primary refractoriness to atezolizumab Plus bevacizumab in hepatocellular carcinoma. *J Hepatol*. 2026 Jun 15:S0168-8278(26)02605-X. doi: 10.1016/j.jhep.2026.05.018.
- Characteristics and outcomes of immunotherapy-related liver injury in patients with hepatocellular carcinoma versus other advanced solid tumours. *J Hepatol*. 2024 Mar;80(3):431-442. doi: 10.1016/j.jhep.2023.10.040
- The use of advanced machine learning to predict outcomes after atezolizumab plus bevacizumab for advanced hepatocellular carcinoma: a retrospective cohort study. *Lancet Digit Health*. 2026 Feb;8(2):100952. doi: 10.1016/j.landig.2025.100952.
- Immunotherapy vs Best Supportive Care for Patients With Hepatocellular Cancer With Child-Pugh B Dysfunction. *JAMA Oncol*. 2024 Sep 1;10(9):1253-1258. doi: 10.1001/jamaoncol.2024.2166.
- Hepatic decompensation is the major driver of mortality in patients with HCC treated with atezolizumab plus bevacizumab: The impact of successful antiviral treatment. *Hepatology*. 2025 Mar 1;81(3):837-852. doi: 10.1097/HEP.0000000000001026.
- Outcome and management of patients with hepatocellular carcinoma who achieved a complete response to immunotherapy-based systemic therapy. *Hepatology*. 2025 Jun 1;81(6):1714-1727. doi: 10.1097/HEP.0000000000001163.
- Preliminary evidence of safety and tolerability of atezolizumab plus bevacizumab in patients with hepatocellular carcinoma and Child-Pugh A and B cirrhosis: A real-world study. *Hepatology*. 2022 Oct;76(4):1000-1012. doi: 10.1002/hep.32468.

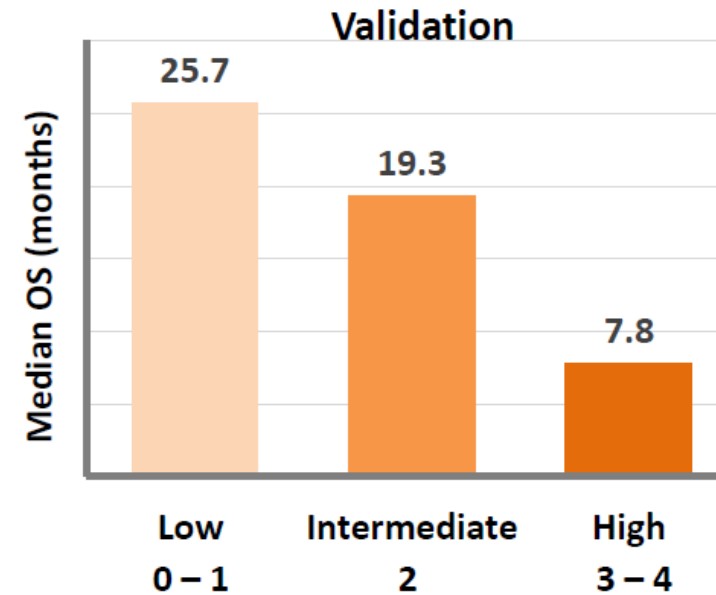
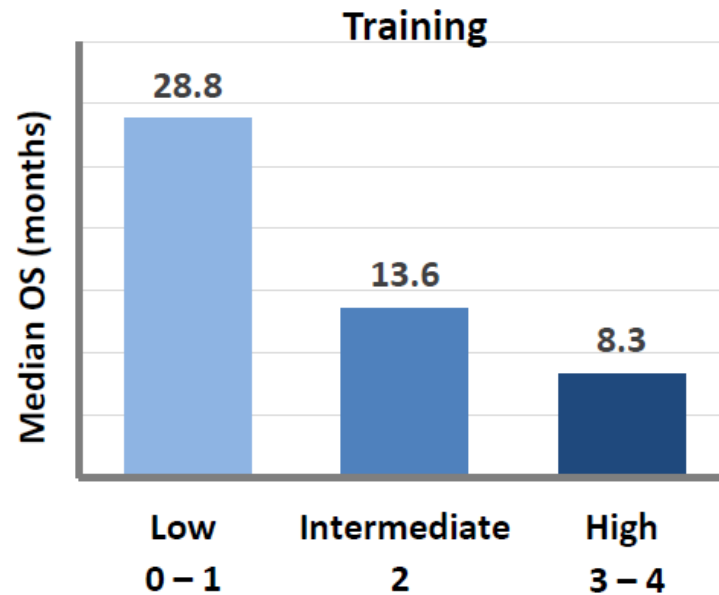
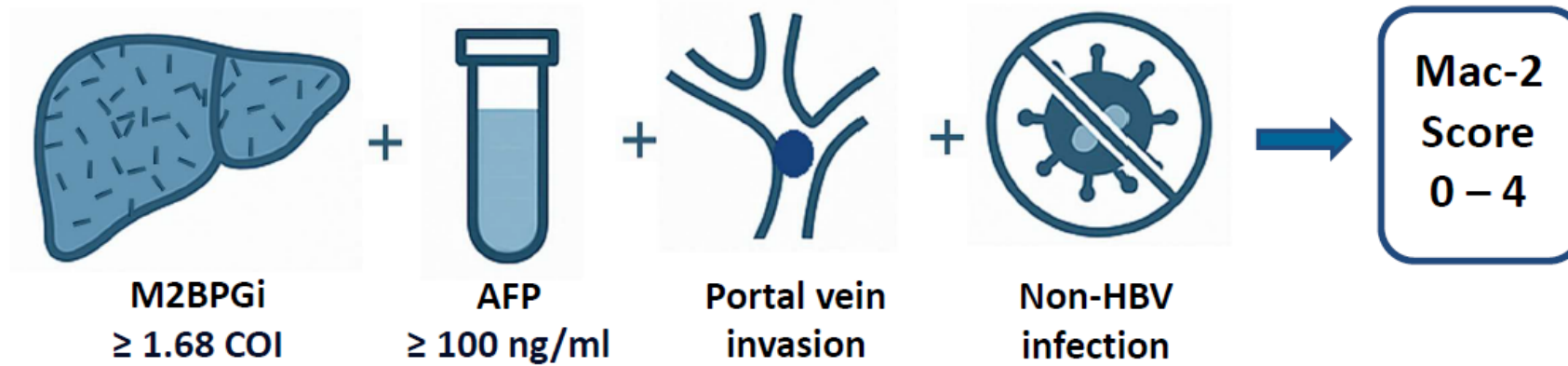


NASH limits anti-tumour surveillance in immunotherapy-treated HCC

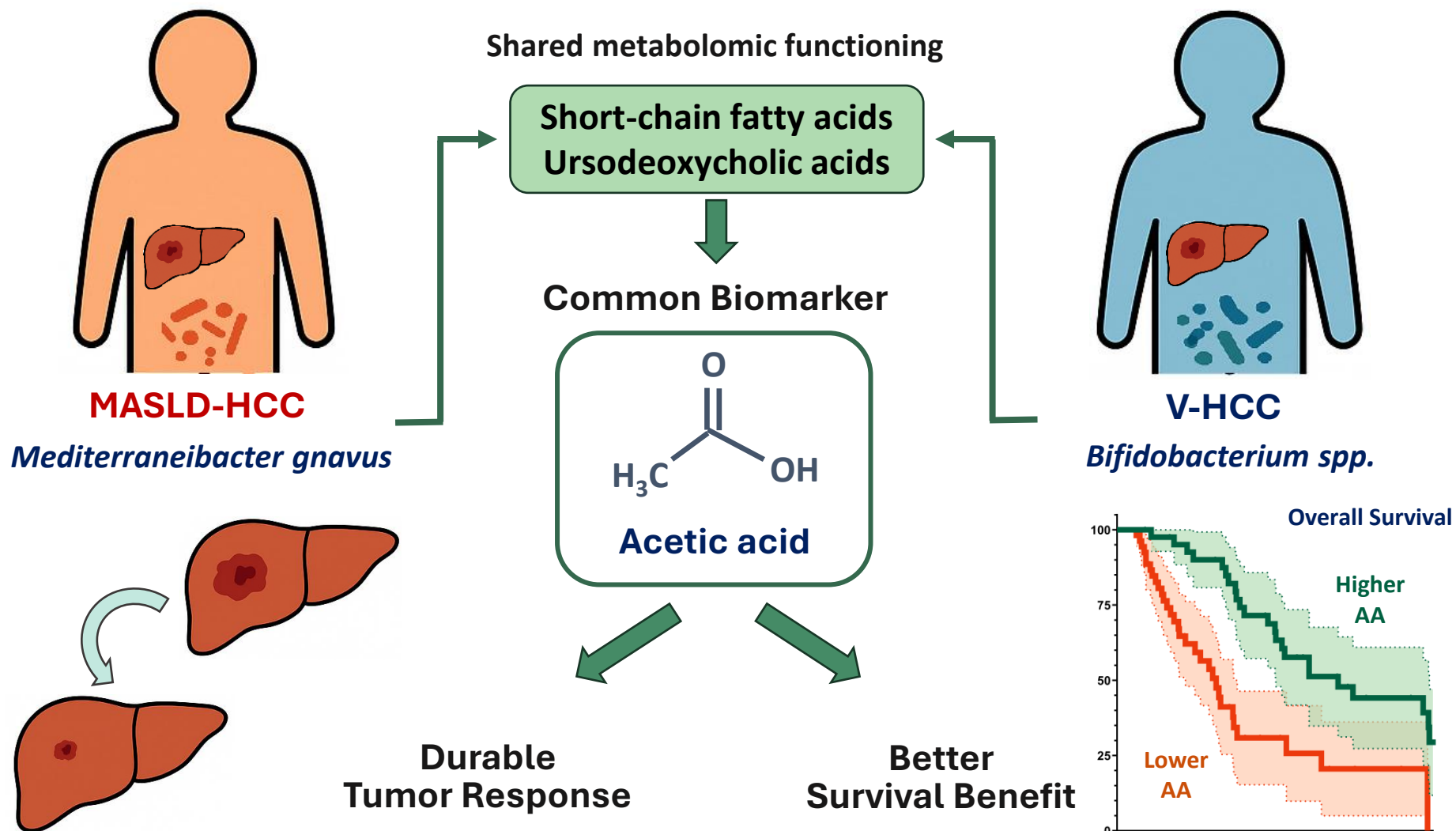
Dominik Pfister^{1,82}, Nicolás Gonzalo Núñez², Roser Pinyol³, Olivier Govaere⁴, Matthias Pinter^{5,6}, Marta Szydlowska¹, Revant Gupta^{7,8}, Mengjie Qiu⁹, Aleksandra Deczkowska¹⁰, Assaf Weiner¹⁰, Florian Müller¹, Ankit Sinha^{11,12}, Ekaterina Frie Thomas Engleitner^{13,14,15}, Daniela Lenggenhager¹⁶, Anja Moncsek¹⁷, Danijela Heide¹, Kristin Stirm¹, Jan Kosla¹, Eleni Kotsiliti¹, Valentina Leone^{1,18}, Michael Dudek¹⁹, Suhail You Donato Inverso^{20,21}, Indrabahadur Singh^{1,22}, Ana Teijeiro²³, Florian Castet³, Carla Montirc Philipp K. Haber²⁴, Dina Tiniakos^{4,25}, Pierre Bedossa⁴, Simon Cockell²⁶, Ramy Younes^{4,27}, Michele Vacca²⁸, Fabio Marra²⁹, Jörn M. Schattenberg³⁰, Michael Allison³¹, Elisabetta Bugianesi²⁷, Vlad Ratziu³², Tiziana Pressiani³³, Antonio D'Alessio³³, Nicola Personeni^{33,34}, Lorenza Rimassa^{33,34}, Ann K. Daly⁴, Bernhard Scheiner^{5,6}, Katharina Pomej^{5,6}, Martha M. Kirstein^{35,36}, Arndt Vogel³⁵, Markus Peck-Radosavljevic³⁷, Florian Huckle³⁷, Fabian Finkelmeier³⁸, Oliver Waidmann³⁸, Jörg Trojan³⁸, Kornelius Schulze³⁹, Henning Wege³⁹, Sandra Koch⁴⁰, Arndt Weinmann⁴⁰, Marco Buete Fabian Rössler⁴¹, Alexander Siebenhüner⁴², Sara De Dosso⁴³, Jan-Philipp Mallm⁴⁴, Viktor Umansky^{45,46}, Manfred Jugold⁴⁷, Tom Luedde⁴⁸, Andrea Schietinger^{49,50}, Peter Schirmacher⁵¹, Brinda Emu¹, Hellmut G. Augustin^{20,21}, Adrian Billeter⁵², Beat Mülle Stich⁵², Hiroto Kikuchi⁵³, Dan G. Duda⁵³, Fabian Kütting⁵⁴, Dirk-Thomas Waldschmidt⁵⁴, Matthias Philip Ebert⁵⁵, Nuh Rahbari⁵⁶, Henrik E. Mei⁵⁷, Axel Ronald Schulz⁵⁷, Marc Ringelhan^{58,59,60}, Nisar Malek⁶¹, Stephan Spahn⁶¹, Michael Bitzer⁶¹, Marina Ruiz de Galarreta^{24,62}, Amaia Lujambio^{24,62,63}, Jean-Francois Dufour^{64,65}, Thomas U. Marron^{24,66}, Ahmed Kaseb⁶⁷, Masatoshi Kudo⁶⁸, **Yi-Hsiang Huang^{69,70}**, Nabil Djouder²³, Katharina Wolter^{71,72}, Lars Zender^{71,72,73}, Parice N. Marche^{74,75}, Thomas Decaens^{74,75,76}, David J. Pinato^{77,78}, Roland Rad^{13,14,15}, Joachim C. Mertens¹⁷, Achim Weber^{16,79}, Kristian Unger¹⁸, Felix Meissner¹¹, Susanne Roth⁹, Zuzana Macek Jilkova^{74,75,77}, Manfred Claassen^{7,8}, Quentin M. Anstee^{4,80}, Ido Amit¹⁰, Percy Knolle¹⁹, Burkhard Becher Josep M. Llovet^{3,24,81} & Mathias Heikenwalder¹



Mac-2 Score: A Serum Fibrosis Marker-Based Model Predicts Survival of uHCC under Immunotherapy



Distinct gut microbiota but common metabolomic signatures between Viral and MASLD HCC contribute to outcomes of combination immunotherapy



Lee PC, Huang YH* Hepatology. 2025 Jun 30. doi: 10.1097/HEP.0000000000001446. Online ahead of print.

Journal Pre-proof

A myeloid immunosuppressive phenotype defines primary refractoriness to atezolizumab Plus bevacizumab in hepatocellular carcinoma.

Pasquale Lombardi, Erik Ramon-Gil, Rabial Q. Raja, Leonardo Brunetti, Giulia Francesca Manfredi, Zhongguo Zhou, George Mercus, Sarah Cappuyns, Claudia Angela Maria Fulgenzi, Antonio D'Alessio, Aria Torkpour, Ciro Celsa, Bernardo Stefanini, Hannah Yang, Fionnuala Crowley, Thomas U. Marron, Anwaar Saeed, Matthias Pinter, Bernhard Scheiner, Yi-Hsiang Huang, Pei-Chang Lee, Naoshi Nishida, Ryan Po-Ting Lin, Andrea Dalbeni, Caterina Vivaldi, Gianluca Masi, Natascha Rohlen, Johann von Felden, Ahmed Kaseb, Peter R. Galle, Masatoshi Kudo, Wei-Fan Hsu, Lorenza Rimassa, Alessandro Parisi, Robin Kate Kelley, Hidenori Toyoda, Mario Pirisi, Falah Jabar, Mehrdad Rakaee, Giuseppe Cabibbo, Calogero Cammà, Fabio Piscaglia, Sohyun Hwang, Dong Jun Shin, Michael Li, Jeroen Dekervel, Nadia Guerra, Tim Meyer, Helen L. Reeves, Bertram Bengsch, Gennaro Daniele, Derek A. Mann, Hong Jae Chon, Jack Leslie, David J. Pinato

PII: S0168-8278(26)02605-X

DOI: <https://doi.org/10.1016/j.jhep.2026.05.018>

Reference: JHEPAT 10553



Characteristics and outcomes of immunotherapy-related liver injury in patients with hepatocellular carcinoma versus other advanced solid tumours

Ciro Celsa^{1,2,†}, **Giuseppe Cabibbo**^{2,†}, Claudia A.M. Fulgenzi^{1,3}, Bernhard Scheiner^{1,4}, Antonio D'Alessio^{1,5}, Giulia F. Manfredi^{1,5}, Naoshi Nishida⁶, Celina Ang⁷, Thomas U. Marron⁷, Anwaar Saeed⁸, Brooke Wietharn⁹, Matthias Pinter⁴, Jaekyung Cheon¹⁰, Yi-Hsiang Huang¹¹, Pei-Chang Lee¹², Samuel Phen¹³, Anuhya Gampa¹⁴, Anjana Pillai¹⁵, Caterina Vivaldi¹⁶, Francesca Salani^{15,16}, Gianluca Masi¹⁵, Natascha Roehlen¹⁷, Robert Thimme¹⁷, Arndt Vogel^{18,19}, Martin Schönlein²⁰, Johann von Felden²¹, Kornelius Schulze²¹, Henning Wege²¹, Peter R. Galle²², Masatoshi Kudo⁶, Lorenza Rimassa^{23,24}, Amit G. Singal¹³, Paul El Tomb²⁵, Susanna Ulahannan²⁵, Alessandro Parisi²⁶, Hong Jae Chon¹⁰, Wei-Fan Hsu²⁷, Bernardo Stefanini²⁸, Elena Verzoni²⁹, Raffaele Giusti³⁰, Antonello Veccia³¹, Annamaria Catino³², Giuseppe Aprile³³, Pamela Francesca Guglielmini³⁴, Marilena Di Napoli³⁵, Paola Ermacora³⁶, Lorenzo Antonuzzo³⁷, Ernesto Rossi³⁸, Francesco Verderame³⁹, Fable Zustovich⁴⁰, Corrado Ficorella⁴¹, Francesca Romana Di Pietro⁴², Nicola Battelli⁴³, Giorgia Negrini⁴⁴, Francesco Grossi⁴⁵, Roberto Bordonaro⁴⁶, Stefania Pipitone⁴⁷, Maria Banzi⁴⁸, Serena Ricciardi⁴⁹, Letizia Laera⁵⁰, Antonio Russo⁵¹, Ugo De Giorgi⁵², Luigi Cavanna⁵³, Mariella Soraru⁵⁴, Vincenzo Montesarchio⁵⁵, Paola Bordi⁵⁶, Leonardo Brunetti³, Carmine Pinto⁴⁸, Melissa Bersanelli⁵⁶, Calogero Cammà², Alessio Cortellini^{1,3,†}, David J. Pinato^{1,5,*,†}

The use of advanced machine learning to predict outcomes after atezolizumab plus bevacizumab for advanced hepatocellular carcinoma: a retrospective cohort study



Mathew Vithayathil, Giulia Francesca Manfredi, Antonio D'Alessio, Claudia Angela Maria Fulgenzi, Ciro Celsa, Pasquale Lombardi, Aria Torkpour, Bernardo Stefanini, Peter R Galle, Naoshi Nishida, Bernhard Scheiner, Fionnuala Crowley, Linda Wu, Celina Ang, Thomas U Marron, Wei-Fan Hsu, Chun-Yen Lin, Ryan Po-Ting Lin, Susanna V Ulahannan, Haripriya Andanamala, Noha Soror, Ahmed Kaseb, Michael Lapelusa, Yehia I Mohamed, Martin Schönlein, Johann von Felden, Kornelius Schulze, Henning Wege, Brooke Wietharn, Caterina Vivaldi, Francesca Salani, Gianluca Masi, Tiziana Pressiani, Andrea Dalbeni, Leonardo Natola, Mariarosaria Marseglia, Fabio Piscaglia, Yi-Hsiang Huang, Pei-Chang Lee, Mario Pirisi, Alessandro Parisi, Natascha Rohlen, Robert Thimme, Marianna Silletta, Emanuela Di Giacomo, Bruno Vincenzi, Luca Galbato, Arndt Vogel, Giuseppe Cabibbo, Calogero Camma, Hong Jae Chon, Matthias Pinter, Alessio Cortellini, Masatoshi Kudo, Valentina Zanuso, Lorenza Rimassa, David J Pinato, Eric O Aboagye, Rohini Sharma



Summary

Background Combination immune checkpoint inhibitors are recommended as first-line therapy for advanced hepatocellular carcinoma. However, only a third of patients respond to treatment, and improved approaches to predict response are required. Using baseline clinical data, we aimed to use advanced machine learning models to predict overall survival and progression-free survival in patients with advanced hepatocellular carcinoma receiving atezolizumab plus bevacizumab.

Lancet Digit Health 2026;
8: 100952

Published Online February 12,
2026
[https://doi.org/10.1016/
j.landig.2025.100952](https://doi.org/10.1016/j.landig.2025.100952)



ELSEVIER

Contents lists available at ScienceDirect

European Journal of Cancer

journal homepage: www.ejccancer.com

Original Research

Determinants of long-term survival from atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma



Pei-Chang Lee^{a,b,c}, Alessio Cortellini^{a,d}, Bernardo Stefanini^{a,e}, Changhoon Yoo^f, Hong Jae Chon^g, Jaekyung Cheon^g, Masatoshi Kudo^h, Naoshi Nishida^h, Bernhard Scheinerⁱ, Matthias Pinterⁱ, Pasquale Lombardi^{a,j}, Claudia Angela Maria Fulgenzi^a, Antonio D'Alessio^a, Leonardo Brunetti^a, Aria Torkpour^a, Elena Valenzi^{k,l}, Fionnuala Crowley^m, Thomas U. Marron^m, Wei-Fan Hsuⁿ, Ciro Celsa^{a,o}, Giuseppe Cabibbo^{o,p}, Calogero Cammà^o, Peter Robert Galle^q, Caterina Vivaldi^{r,s}, Gianluca Masi^{r,s}, Rohini Sharma^a, Ryan Po-Ting Lin^{t,u}, Chun-Yen Lin^{t,u}, Brooke Wietharn^v, Anwaar Saeed^w, Francesco Tovoli^e, Fabio Piscaglia^{e,x}, Andrea Dalbeni^{y,z}, Alessandra Auriemma^{y,z}, David Sacerdoti^{y,z}, Alessandro Parisi^{aa}, Giulia Francesca Manfredi^{a,ab}, Andrea Dondo^{ab}, Lorenza Rimassa^{k,l}, Mario Pirisi^{ab}, Martin Schönlein^{ac}, Johann von Felden^{ac,ad}, Amit G. Singal^{ae}, Neehar Dilip Parkih^{af}, Haripriya Andanamala^{ag}, Susanna Ulahannan^{ag}, Natascha Roehlen^{ah}, Robert Thimme^{ah}, Yi-Hsiang Huang^{b,c,ai,aj,*}, David James Pinato^{a,ab,**}

ORIGINAL ARTICLE

Outcome and management of patients with hepatocellular carcinoma who achieved a complete response to immunotherapy-based systemic therapy

Bernhard Scheiner^{1,2}  | Beodeul Kang³ | Lorenz Balcar^{1,2}  |
 Iuliana-Pompilia Radu⁴ | Florian P. Reiter⁵  | Gordan Adžić⁶ | Jiang Guo⁷ |
 Xu Gao^{8,9} | Xiao Yuan⁸ | Long Cheng⁷ | Joao Gorgulho¹⁰ |
 Michael Schultheiss¹¹ | Frederik Peeters¹² | Florian Huckle¹³ |
 Najib Ben Khaled¹⁴ | Ignazio Piseddu¹⁴ | Alexander Philipp¹⁴ | Friedrich Sinner¹⁵ |
 Antonio D'Alessio^{16,17} | Katharina Pomej^{1,2} | Anna Saborowski¹⁸ |
 Melanie Bathon¹⁸ | Birgit Schwacha-Eipper⁴ | Valentina Zarka⁵ |
 Katharina Lampichler¹⁹ | Naoshi Nishida²⁰ | Pei-Chang Lee²¹ | Anja Krall²² |
 Anwaar Saeed²³ | Vera Himmelsbach²⁴ | Giulia Tesini^{25,26} | Yi-Hsiang Huang^{27,28} |
 Caterina Vivaldi^{29,30} | Gianluca Masi³⁰ | Arndt Vogel^{31,32,33} | Kornelius Schulze³⁴ |
 Michael Trauner¹ | Angela Djanani³⁵ | Rudolf Stauber²² | Masatoshi Kudo²⁰ |
 Neehar D. Parikh³⁶ | Jean-François Dufour³⁷ | Juraj Prejac^{6,38} | Andreas Geier⁵ |
 Bertram Bengsch^{11,39} | Johann von Felden³⁴ | Marino Venerito¹⁵ |
 Arndt Weinmann⁴⁰ | Markus Peck-Radosavljevic¹³ | Fabian Finkelmeier²⁴ |
 Jeroen Dekervel¹² | Fanpu Ji^{8,41} | Hung-Wei Wang⁴² | Lorenza Rimassa^{25,26} |
 David J. Pinato^{16,17} | Mohamed Bouattour⁴³ | Hong Jae Chon³ | Matthias Pinter^{1,2}

ORIGINAL ARTICLE

Hepatic decompensation is the major driver of mortality in patients with HCC treated with atezolizumab plus bevacizumab: The impact of successful antiviral treatment

Ciro Celsa^{1,2}  | Giuseppe Cabibbo²  | Claudia Angela Maria Fulgenzi¹ |
 Salvatore Battaglia³ | Marco Enea⁴ | Bernhard Scheiner⁵ |
 Antonio D'Alessio^{1,6} | Giulia F. Manfredi^{1,6} | Bernardo Stefanini^{1,7} |
 Naoshi Nishida⁸ | Peter R. Galle⁹ | Kornelius Schulze¹⁰ | Henning Wege¹⁰ |
 Roberta Ciccia² | Wei-Fan Hsu¹¹ | Caterina Vivaldi¹² | Brooke Wietharn¹³ |
 Ryan Po-Ting Lin^{14,15} | Angelo Pirozzi^{16,17} | Tiziana Pressiani¹⁷ |
 Andrea Dalbeni^{18,19} | Leonardo A. Natola¹⁹ | Alessandra Auriemma²⁰ |
 Cristina Rigamonti⁶ | Michela Burlone⁶ | Alessandro Parisi²¹ |
 Yi-Hsiang Huang^{22,23,24} | Pei-Chang Lee^{23,25} | Celina Ang²⁶ |
 Thomas U. Marron²⁷ | Matthias Pinter⁵ | Jaekyung Cheon²⁷ | Samuel Phen²⁸ |
 Amit G. Singal²⁸ | Anuhya Gampa²⁹ | Anjana Pillai²⁹ | Natascha Roehlen³⁰ |
 Robert Thimme³⁰ | Arndt Vogel^{31,32} | Noha Soror³³ | Susanna Ulahannan³³ |
 Rohini Sharma¹ | David Sacerdoti¹⁹ | Mario Pirisi⁶ | Lorenza Rimassa^{16,17} |
 Chun-Yen Lin^{14,15} | Anwaar Saeed³⁴ | Gianluca Masi¹² | Martin Schönlein³⁵ |
 Johann von Felden¹⁰ | Masatoshi Kudo⁸ | Alessio Cortellini^{1,36} |
 Hong Jae Chon²⁷ | Calogero Cammà² | David James Pinato^{1,6} 

ORIGINAL ARTICLE

Surrogate and modified endpoints for immunotherapy in advanced hepatocellular carcinoma

Mir Lim¹ | Maishara Muquith¹ | Bernadette Miramontes¹ | Chieh-Ju Lee² |
Magdalena Espinoza³ | Yi-Hsiang Huang^{2,4} | David Hsiehchen¹

¹Division of Hematology and Oncology,
Department of Internal Medicine, University of
Texas Southwestern Medical Center, Dallas,
Texas, USA

²Division of Gastroenterology and Hepatology,
Department of Medicine, Taipei Veterans
General Hospital, Institute of Clinical Medicine,
Faculty of Medicine, National Yang Ming Chiao
Tung University, Taipei, Taiwan

³Division of Digestive and Liver Diseases,
Department of Internal Medicine, Texas
Southwestern Medical Center, Dallas, Texas,
USA

⁴Healthcare and Services Center, Taipei
Veterans General Hospital, Taipei, Taiwan

Abstract

Background and Aims: Immunotherapies have altered the treatment paradigm in HCC. Surrogate and modified endpoints are used to assess early success in clinical studies and guide clinical practice. We sought to determine whether surrogate endpoints and modifications to the conventional criteria for tumor response (RECIST), including modified RECIST (mRECIST) and immune-modified RECIST (imRECIST), are valid measures to predict overall survival (OS) in HCC treated with immunotherapies.

Approach and Results: We performed an individual-level post hoc analysis of patients treated with atezolizumab and bevacizumab in the IMbrave150 trial (N = 279) and a cross-sectional analysis of a multicenter real-world patient



Original Investigation | Oncology

Complete Response to Immunotherapy in Patients With Hepatocellular Carcinoma

Mir Lim, MD; Magdalena Espinoza, MD; Yi-Hsiang Huang, MD, PhD; Joseph Franses, MD; Hao Zhu, MD; David Hsiehchen, MD

Abstract

IMPORTANCE Immunotherapies are the preferred frontline treatment for most hepatocellular carcinomas (HCCs), but only a small subset of patients attain complete responses to immunotherapies, resulting in an absence of radiographic apparent disease. The clinical importance of these complete responses is unclear, and whether clinical or molecular features may define HCCs that are exquisitely sensitive to immunotherapies is ambiguous.

OBJECTIVE To describe the long-term survival outcomes of complete responders to immunotherapies, and to examine whether clinical and genomic characteristics are associated with complete response.

DESIGN, SETTING, AND PARTICIPANTS This cohort study includes a post hoc analysis of the IMbrave150 trial (which enrolled patients across 17 countries in North America, Europe, Asia, and Australia) and a multicenter cohort analysis of patients with advanced HCC treated with frontline immunotherapies across 3 institutions (2 in the US and 1 in Asia). Complete responders were defined as patients with a complete response according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 or modified RECIST. Statistical analyses were conducted from January to May 2024.

MAIN OUTCOMES AND MEASURES The main outcome was overall survival measured as the time

Key Points

Question What are the long-term survival outcomes and characteristics of patients with advanced hepatocellular carcinoma who attain a complete response while receiving immunotherapy?

Findings In this cohort study, a post hoc analysis of the IMbrave150 trial (279 patients) and a multicenter cohort analysis (194 patients) found that, in a subset of patients, complete responders to immunotherapy had prolonged overall survival and durable response while not receiving therapy. Complete responders also had greater immune cell programmed cell death 1 ligand 1 expression and lower circulating tumor DNA levels.



香港大學
THE UNIVERSITY OF HONG KONG

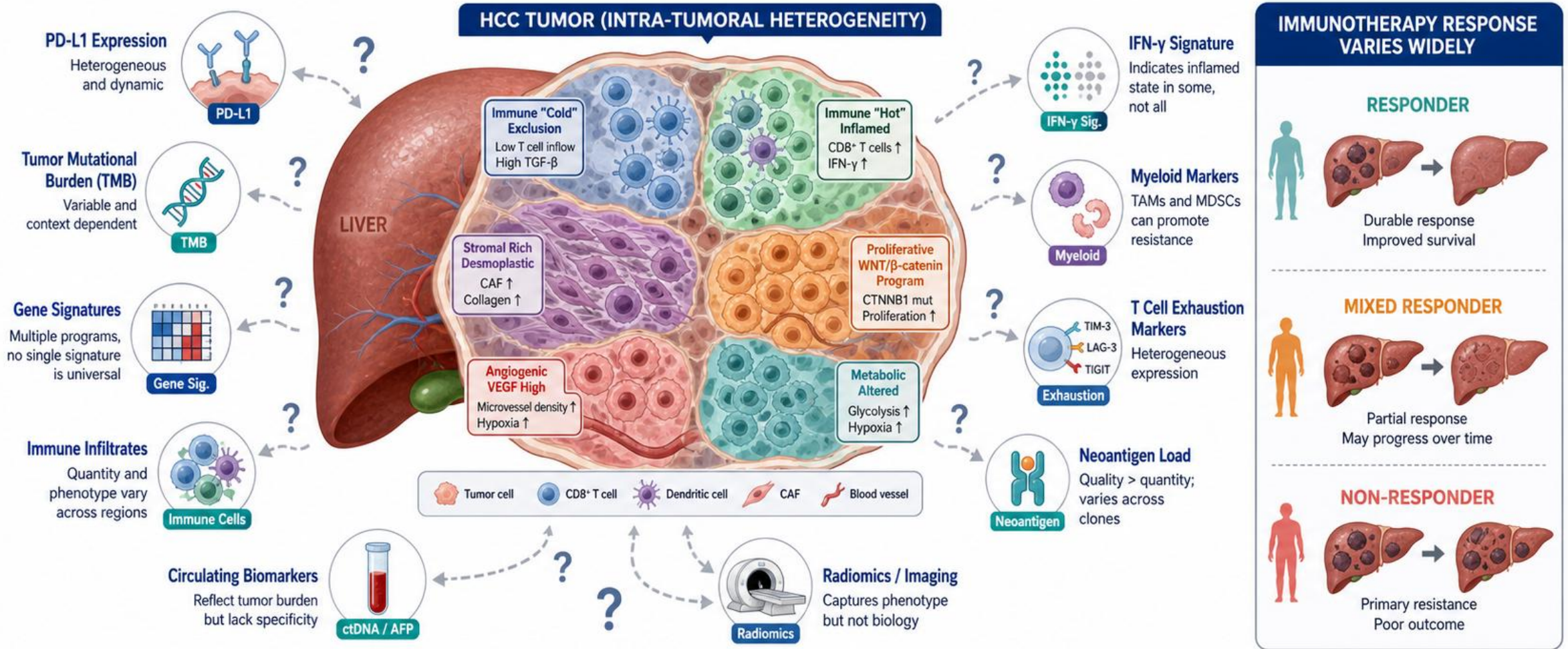


ORIGINAL ARTICLE

Multimodal multiphasic preoperative image-based deep-learning predicts HCC outcomes after curative surgery

Rex Wan-Hin Hui¹  | Keith Wan-Hang Chiu² | I-Cheng Lee^{3,4} | Chenlu Wang⁵ |
Ho-Ming Cheng¹ | Jianliang Lu¹ | Xianhua Mao¹ | Sarah Yu¹ | Lok-Ka Lam¹ |
Lung-Yi Mak^{1,6} | Tan-To Cheung^{6,7} | Nam-Hung Chia⁸ | Chin-Cheung Cheung⁹ |
Wai-Kuen Kan¹⁰ | Tiffany Cho-Lam Wong^{6,7} | Albert Chi-Yan Chan^{6,7} |
Yi-Hsiang Huang^{3,4,11} | Man-Fung Yuen^{1,6} | Philip Leung-Ho Yu⁵ |
Wai-Kay Seto^{1,6,12} 

Intra-tumoral Heterogeneity and the Absence of a Universal Predictive Biomarker in HCC Immunotherapy



TAKE-HOME MESSAGE

HCC exhibits marked intra-tumoral heterogeneity across immune, genomic, stromal, and metabolic dimensions. Current biomarkers are important but partially informative and lack universality—no single biomarker reliably predicts immunotherapy response.



NO UNIVERSAL PREDICTIVE BIOMARKER (YET)

A YI career pathway

1

Show up repeatedly

Choose a niche: IO biomarkers, radiomics, TACE combinations, surgery, or survivorship.

2

Offer usable work

Bring data cleaning, slide drafting, statistics coordination, IRB preparation, or manuscript writing.

3

Join TRG output

Aim for consensus papers, multicenter retrospective studies, or serial real-world cohorts.

4

Become outward-facing

Use the domestic record to pitch a cross-border substudy or validation cohort.

Domestic collaboration is where reputations are built: people first remember whether you are responsive, rigorous, and generous before they remember your h-index.

Challenge: The barriers YI will face

Methodology

Different staging systems, TACE heterogeneity, local practice variation, and mixed endpoints can make pooled analyses unstable.

Regulation

Data sharing, ethics amendments, privacy review, biospecimen export, and contract negotiation often move slower than scientific enthusiasm.

Access and reimbursement

Trial and real-world results are shaped by uneven access to systemic therapies, especially across healthcare systems.

Human factors

Authorship expectations, delayed replies, inconsistent data entry, and unclear leadership can silently kill good projects.

The challenge is not simply to find collaborators; it is to build trust around definitions, deadlines, and fairness.

Checklist

Domestically

- Join one your TRG-like theme and contribute actual work.
- Create one multicenter dataset with a clear dictionary.
- Volunteer for abstract drafting, slide synthesis, or manuscript coordination.
- Build a reputation for speed, rigor, and reliability.

Internationally

- Map one global consortium or senior collaborative group in your niche.
- Offer a concrete contribution: validation cohort, biomarker assay, imaging review, or regional comparator group.
- Ask for a small first project, not immediate leadership.
- Convert that project into long-term serial participation.

Young investigators do not need to wait for a perfect invitation; they need to become obviously useful collaborators.



From attendance to alliance

The task for the next generation is to turn meetings into datasets, datasets into papers, and papers into durable networks.



★
★
★
★
★
★

WORLD'S BEST HOSPITALS

2024-2026

Newsweek

POWERED BY
statista



TAIPEI VETERANS GENERAL HOSPITAL

