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THE LIVER WEEK 2025
HIGHLIGHTS

In this landmark year, TLW 2025 reflected the 30-year legacy of KASL by advancing its four strategic pillars: Scientific Excellence, Educational Advancement, Multidisciplinary Collaboration, and Global Leadership.

The Korean Association for the Study of the Liver

THE KOREAN ASSOCIATION OF HBP SURGERY

THE KOREAN LIVER CANCER ASSOCIATION

The Korean Liver Transplantation Society

THE LIVER WEEK 2025 HIGHLIGHTS:

Celebrating the 30th Anniversary of the Korean Association for the Study of the Liver

Location: Hwabaek International Convention Center (HICO), Gyeongju, Korea
Date: May 29 to 31, 2025

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Running title: TLW 2025 highlights

Abbreviations

AFP, alpha-fetoprotein; AASLD, American Association for the Study of Liver Diseases; CIK, cytokine-induced killer; CHB, chronic hepatitis B; CR, calorie restriction; DFS, disease-free survival; EC, extended criteria; GPC-3, glypican-3; HCC, hepatocellular carcinoma; IL-15, interleukin-15; KASL, Korean Association for the Study of the Liver; LT, liver transplantation; KLCA, Korean Liver Cancer Association; MASLD, metabolic dysfunction-associated steatotic liver disease; MC, Milan criteria; NMA, network meta-analysis; OS, overall survival; SOC, standard care; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TRE, time-restricted eating; TLW, The Liver Week

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Celebrating the 30th Anniversary of the Korean Association for the Study of the Liver

Location Hwabaek International Convention Center (HICO), Gyeongju, Korea

Date May 29 to 31, 2025

In 2025, the Korean Association for the Study of the Liver (KASL) commemorated its 30th anniversary. Over the past three decades, KASL has made remarkable contributions to the advancement of hepatology through the development of evidence-based clinical practice guidelines, promotion of basic, translational, and clinical research, participation in health policy formation, and active collaboration with international liver associations worldwide.

The Liver Week (TLW) 2025, held in this landmark year, mirrored the spirit and legacy of KASL's 30-year journey. Since 2014, TLW has been jointly organized by KASL, the Korean Association of Hepato-Biliary-Pancreatic Surgery (KHBPS), the Korean Liver Cancer Association (KLCA), and the Korean Liver Transplantation Society (KLTS). As a multidisciplinary conference, TLW serves as a platform for collaboration and exchange among numerous professionals involved in liver diseases, including physicians, students, researchers, and specialized nurses. Held under the theme "A Big Welcome to the Liver Festival in Gyeongju, Korea," this year's comprehensive scientific congress convened 1,309 participants from 30 countries, transforming the symposium into a truly global celebration of hepatology. The congress featured a total of 45 sessions comprising 153 lectures, offering an in-depth exploration of diverse areas of liver diseases. A total of 724 abstracts were submitted, of which 8 were selected for plenary presentations, 102 for free paper presentations, 118 for oral poster presentations, and 276 abstracts were presented in the poster exhibition. Among them, 45 researchers were honored with the Best Presentation Award for their outstanding contributions. Beyond academic excellence, TLW 2025 was also a memorable social gathering. The welcome dinner, held in the serene outdoor garden of

Hwangryongwon, an iconic location set against the backdrop of a millennium-old capital, provided participants with a uniquely elegant and inspiring networking experience under the summer night sky. The scene vividly embodied the symposium's theme, a true festival of hepatology, alive with the spirit of shared inquiry.

This year, TLW 2025 prominently featured dedicated programs for young investigators, underscoring its commitment to cultivating future leaders in hepatology. The postgraduate course included sessions designed for beginners in basic research, where mentors shared their practical experiences in establishing research frameworks. Additionally, participants engaged in learning new approaches in translational hepatology. The Data Science Camp session featured cutting-edge lectures on statistical methodologies commonly employed in hepatology and the application of artificial intelligence in liver disease research, attracting particular attention for its practical relevance.
TLW 2025 demonstrated the KASL's active collaboration with other international liver associations, emphasizing their collective commitment to advancing hepatology. Notably, KASL and the American Association for the Study of Liver Diseases (AASLD) held their third consecutive joint symposium in this TLW 2025, fostering collaborative discussions on liver-related topics. Beyond scientific exchanges, the partnership was further highlighted by a special commemorative gift from AASLD to celebrate KASL's 30th anniversary, which was received with great appreciation. The congratulatory video sent from the AASLD President, Professor Grace Su, was a delightful surprise. Additionally, the KLCA– Japanese Liver Cancer Association (JLCA) joint session focused on the shared theme of "Pre- and post-liver transplantation management for hepatocellular carcinoma (HCC)," providing a platform for focused discussion on advancing research strategies in HCC. Under the theme "Innovating and expanding surgical horizons for HCC in the immunotherapy era," the KLCA–Taiwan Liver Cancer Association (TLCA) engaged in several intense discussions.

This year, early morning sessions (Special Interest Groups) enabled in-depth discussions on specific topics, including steatotic liver disease, abdominal ultrasound, autoimmune hepatitis, and portal hypertension. The congress also introduced the updated 2025 clinical guidelines on "metabolic dysfunction-associated steatotic liver disease," introducing revised terminologies and new

pharmacological therapies. Additionally, the 2025 clinical guidelines on “Hepatitis C virus” were presented, outlining simplified treatment strategies and specific recommendations for special populations.

The scientific innovations and inclusive collaborations demonstrated at TLW 2025 will be long cherished, along with the KASL’s 30-year spirit and joint mission to improve the lives of patients with liver diseases. Subsequently, we would like to highlight several distinguished papers presented at TLW 2025.

Time-restricted eating: A promising alternative to calorie restriction for managing hepatic steatosis in metabolic dysfunction-associated steatotic liver disease

This study, which was the largest randomized controlled trial presented at TLW 2025, demonstrated that time-restricted eating (TRE) significantly reduced hepatic steatosis compared to standard care (SOC) and showed similar benefits to calorie restriction (CR). TRE can be considered a promising alternative dietary strategy for managing metabolic dysfunction-associated steatotic liver disease (MASLD).[1]

This study evaluated the efficacy of TRE versus CR and SOC in reducing hepatic steatosis and improving metabolic outcomes in patients with MASLD (Figure 1). In a 16-week trial involving 333 participants, SOC participants were instructed to consume at least 500 kcal less than their usual meal, and they received

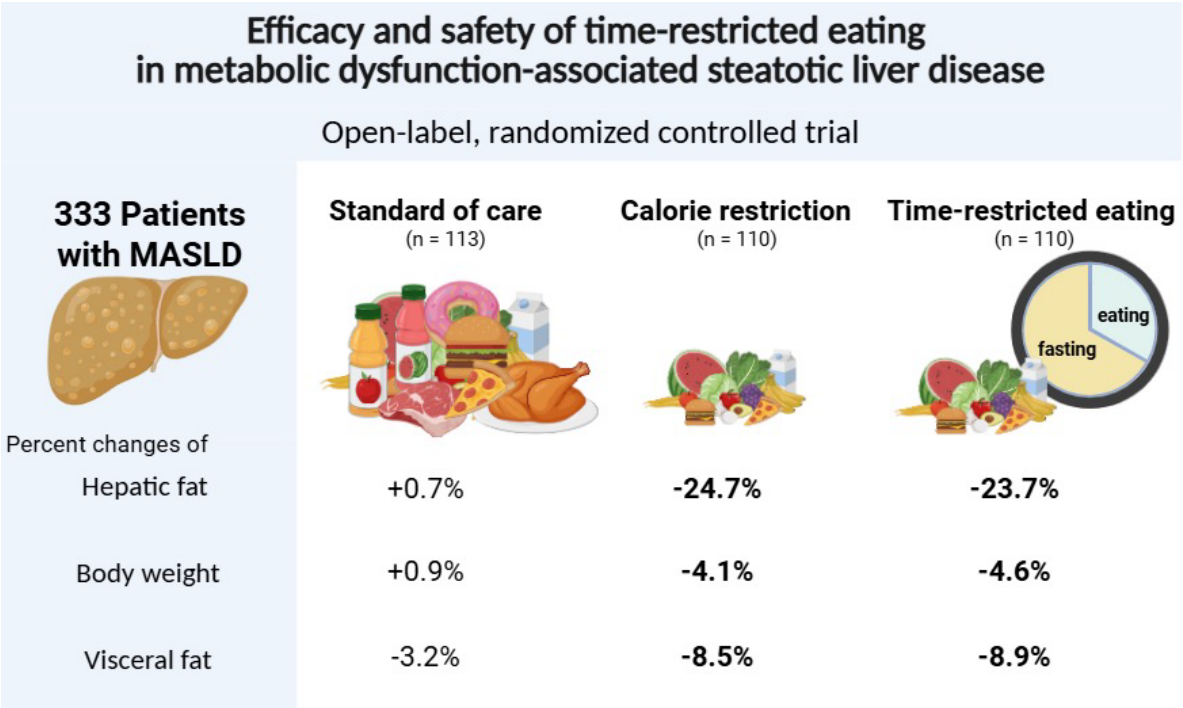


Figure 1

monthly feedback via standard text messaging. Participants in the CR and TRE groups followed the same caloric restriction as the SOC group but received more intensive monitoring and guidance. TRE participants additionally adhered to an 8-hour daily eating window. As a result, TRE significantly reduced hepatic steatosis (-25.8%) compared with SOC (0.7%, $p<0.001$), with similar reductions observed in the CR group (-24.7%). Improvements in body weight, waist circumference, body fat mass, and visceral fat were also comparable between the TRE and CR groups. No significant differences were found between the TRE and CR groups regarding glucose homeostasis, liver stiffness, or sleep quality.

TRE is a feasible and practical option in treating patients with MASLD, particularly in settings where major dietary modifications (e.g., Mediterranean diet) are less practical. Its simplicity may support better adherence, positioning TRE as a valuable part of lifestyle modification-based MASLD management.

Lower hepatocellular carcinoma risk observed with tenofovir alafenamide vs. tenofovir disoproxil fumarate

This Korean nationwide study presented in TLW 2025 demonstrated that tenofovir alafenamide (TAF) was associated with a lower risk of developing hepatocellular carcinoma (HCC) compared to tenofovir disoproxil fumarate (TDF) in treatment-naive patients with chronic hepatitis B (CHB).[2]

This nationwide, population-based cohort study utilized Korean National Health Insurance claims data to compare HCC incidence in treatment-naive patients with CHB initiating either TAF or TDF. Among 87,355 adults who began TAF or TDF between 2017 and 2022, a total of 54,185 treatment-naive patients who received either agent as first-line therapy (TAF, n=20,994; TDF, n=33,191) for at least 6 months were included.

Over a median follow-up of 3.27 years, the annual HCC incidence rate was significantly lower in the TAF group than in the TDF group (7.5 vs. 10.3 per 1,000 patient-years [PYs]; subdistribution hazard ratio [SHR], 0.74; 95% confidence interval [CI], 0.66–0.83; p <0.001, Figure 2A). After propensity score-matching with 19,013 pairs, the TAF group had a lower annual HCC incidence rate than the TDF group (7.5 vs. 9.9 per 1,000 PYs; SHR, 0.77; 95% CI 0.67–0.87; p<0.001, Figure 2B). In a multivariable analysis, TAF was significantly associated with a reduced HCC incidence (SHR, 0.76; 95% CI, 0.67–0.85; p<0.001).

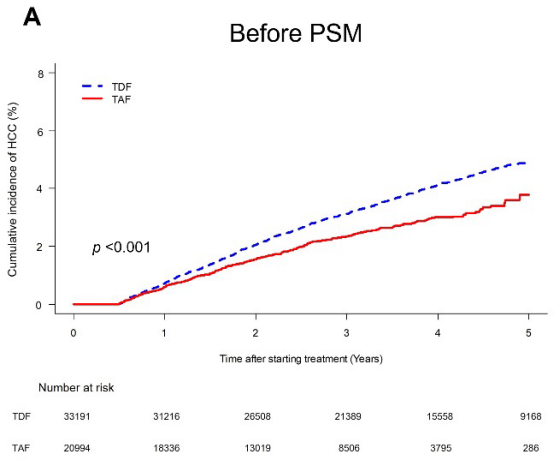


Figure 2A

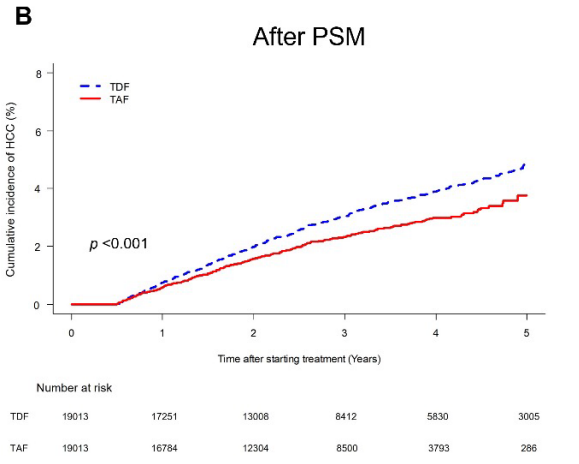
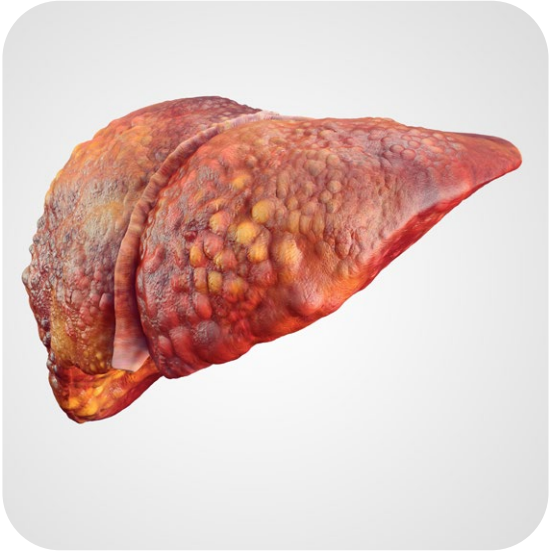


Figure 2B



In subgroup analysis, TAF demonstrated a significantly lower annual incidence of HCC compared to TDF, regardless of the presence of cirrhosis at baseline; 4.5 vs. 6.1 per 1,000 PYs in the non-cirrhosis subgroup (p=0.002) and 21.3 vs. 27.1 per 1,000 PYs in the cirrhosis subgroup (p=0.005).

This study highlights that TAF was associated with a lower risk of HCC development compared to TDF in treatment-naive patients with CHB. These findings may provide useful guidance for clinicians to select first-line antiviral therapy; however, prospective validation is warranted.

Durable benefits of adjuvant CIK cell immunotherapy in HCC: Long-term RCT follow-up and insights into immune mechanisms

In this 9-year follow-up of a randomized controlled trial, adjuvant cytokine-induced killer (CIK) cell therapy significantly prolonged recurrence-free and cancer-specific survival in patients with hepatocellular carcinoma (HCC) after curative treatment. Immune profiling revealed expansion of CD8+ memory T cells, suggesting long-term immunological control.[3]

This study aimed to evaluate whether autologous CIK cell therapy could provide long-term recurrence prevention and to elucidate the immunological mechanisms after curative HCC treatment. In this 9-year extended follow-up of a multicenter randomized controlled trial including 226 patients with stage I/II HCC who underwent curative resection or ablation, patients received either standard follow-up (n=112) or adjuvant CIK cell therapy (n=114). The CIK group demonstrated significantly

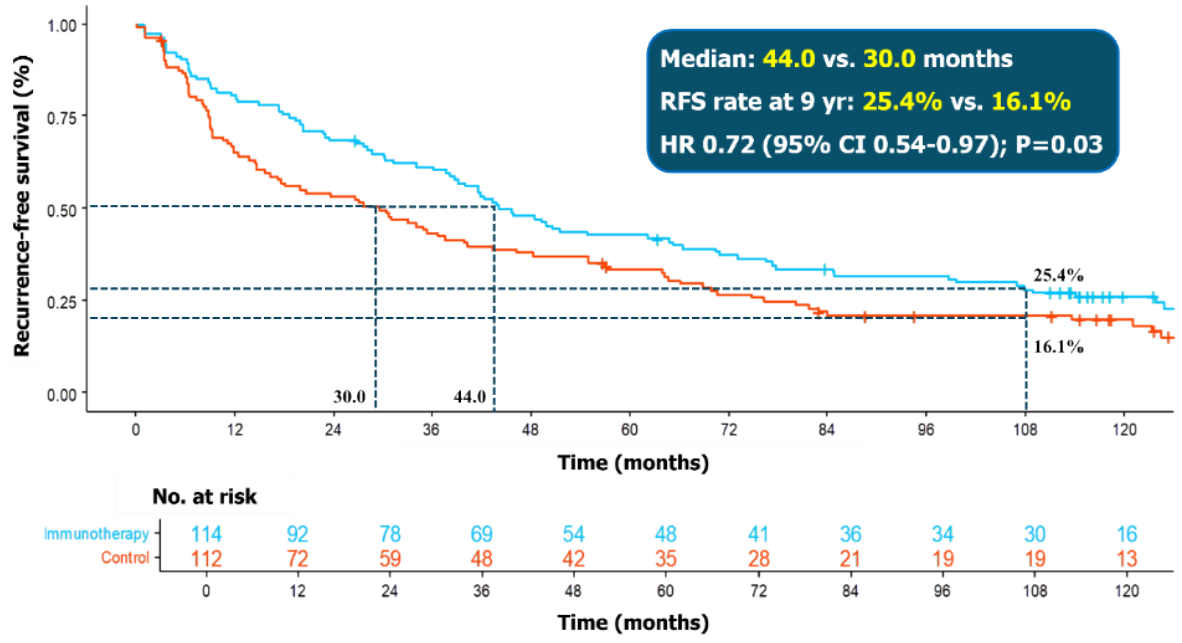


Figure 3

improved recurrence-free survival (median 44.0 vs. 30.0 months; HR=0.72, p=0.033) and cancer-specific survival (HR=0.49, p=0.036) (Figure 3). Overall survival also favored the CIK group (HR=0.70), though this was not statistically significant (p=0.13). In a prospective immune profiling study of 19 patients, repeated CIK cell transfer led to a significant increase in CD8+ classical memory T cells (p=0.03), suggesting a long-term immune modulation.

This study is the first to demonstrate long-term survival benefits of adjuvant immunotherapy in early-stage HCC. The observed expansion of memory T cells suggests that repeated CIK infusions may establish sustained anti-tumor immune surveillance. Given its feasibility and favorable safety profile, CIK therapy emerges as a promising adjuvant immunotherapeutic strategy for HCC, warranting further investigation into its long-term efficacy and underlying mechanisms.

Targeting HCC with precision: GPC3-directed, IL-15-enhanced CAR-NK cells demonstrate potent and durable anti-tumor activity

This study highlights the potential of glypican-3 (GPC3)-targeted, interleukin-15 (IL-15)-secreting chimeric antigen receptor-natural killer (CAR-NK) cells as an innovative and highly specific immunotherapeutic strategy for hepatocellular carcinoma (HCC), paving the way for more effective and persistent cell-based treatments in patients who are unresponsive to current therapies.[4]

This study aimed to develop CAR-NK cells specifically targeting GPC3, a heparan sulfate proteoglycan overexpressed in HCC but rarely found in healthy liver tissue. To enhance cell persistence and anti-tumor activity within the tumor microenvironment, the CAR-NK cells were engineered to secrete IL-15. High-affinity scFvs for GPC3 were identified via phage display, cloned, and expressed in the NK92 cell line using lentiviral vectors. Engineered GPC3 CAR-NK cells showed robust, specific cytotoxicity against GPC3-positive HCC cell lines, and the addition of the IL-15 cassette supported the long-term persistence and expansion of CAR-NK cells in vitro. In mouse xenograft models, IL-15-producing GPC3 CAR-NK cells achieved superior tumor volume reduction, higher rates of tumor cell lysis, and prolonged survival compared to control groups. Histological analysis confirmed greater intratumoral infiltration of NK cells in tumors treated with the IL-15-secreting GPC3 CAR-NK cells (Figure 4).

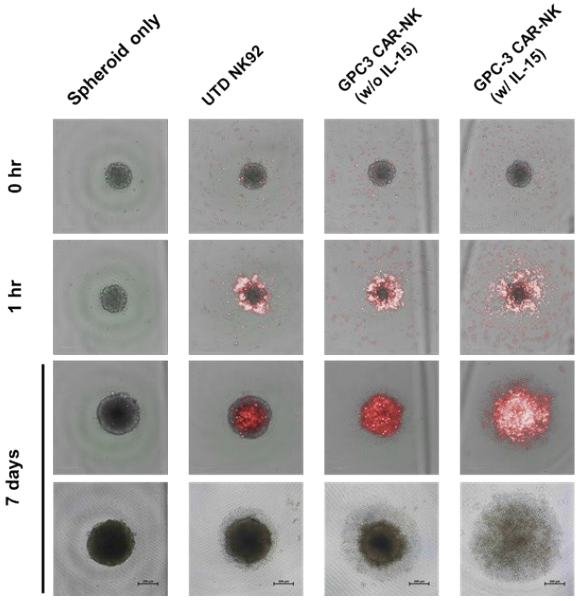


Figure 4

This pioneering work demonstrates that GPC3-targeted, IL-15-secreting CAR-NK cells are a promising next-generation immunotherapeutic candidate for HCC. The study provides strong preclinical evidence supporting further clinical development and highlights the potential of cell-based therapy

as a transformative strategy in the management of advanced HCC.

AFP-based models in expanded liver transplant criteria for HCC: A network meta-analysis and validation

A network meta-analysis (NMA) presented in TLW 2025 demonstrated that Metroticket 2.0 and the alpha-feto protein (AFP) model outperformed other expanded criteria (EC) in predicting prognosis, highlighting the clinical utility of AFP-based models in selecting patients with hepatocellular carcinoma (HCC) awaiting liver transplantation (LT).[5]

This NMA compared the performance of various EC between patients within the Milan criteria (MC) and those exceeding MC but meeting EC. The findings were validated using a large in-house cohort of liver transplant recipients.

Participants were adult patients diagnosed with HCC who underwent LT. Patients exceeding the MC but meeting EC formed the intervention group, while those within the MC comprised the control group. Outcomes were overall survival (OS), disease-free survival (DFS), and recurrence rate. Nine different LT eligibility criteria were included: AFP model, Asan, Hangzhou, Metroticket 2.0, MC, R4 T3, Shanghai, University of California San Francisco (UCSF), and Up-to-Seven. Of 22,466 articles identified, 35 studies contained 45 pairwise

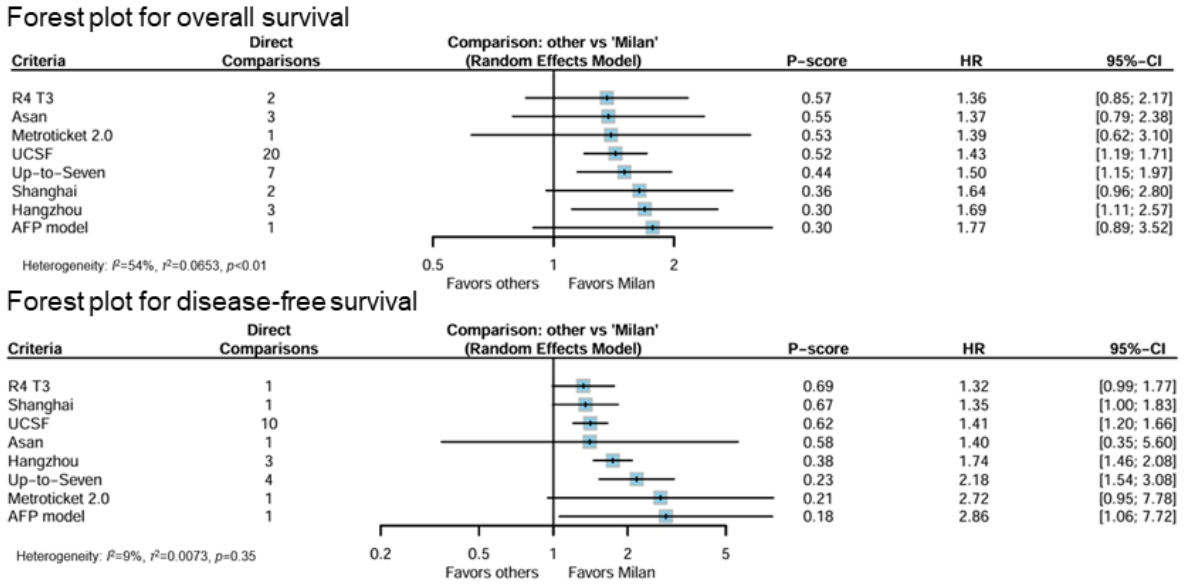


Figure 5

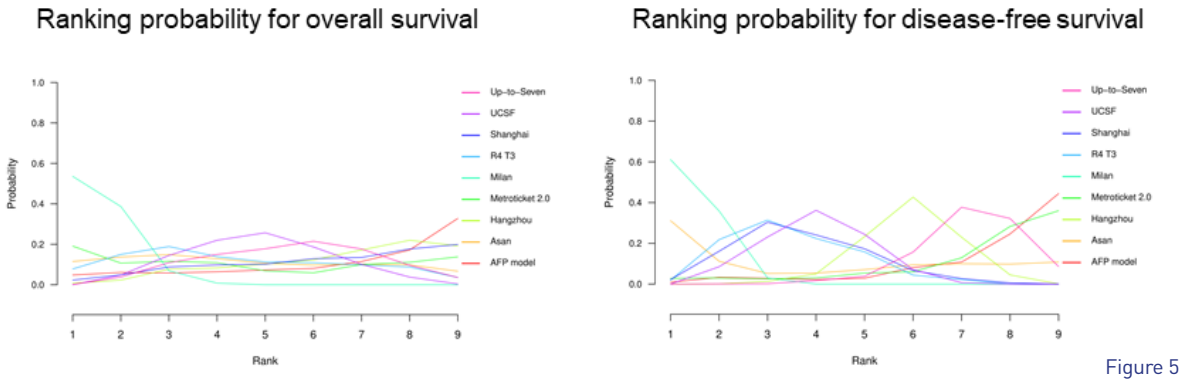


Figure 5

comparisons and were included in the NMA along with eight different EC.
This NMA comparing patients within the MC to those exceeding the MC but within EC showed that several EC had comparable efficacies in terms of OS and DFS (Figure 5), and that there was a tendency for the UCSF and Up-to-Seven criteria to be associated with worse outcomes, probably due to differences in the patient populations. Additionally, Metroticket 2.0 and the AFP model yielded more favorable HCC-specific mortality than other EC in a validation cohort, supporting the NMA findings. This study supports the clinical application of EC to LT, notably AFP-based models such as Metroticket 2.0 and the AFP model.

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