Precision Oncology Across the Spectrum of Liver Tumours: Highlights from the Liver Tumours–Clinical Session at EASL Congress 2026

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PRIMARY LIVER cancers pose substantial clinical challenges despite significant advances in surveillance, diagnosis, and systemic therapy. Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related mortality worldwide, while rarer malignancies such as intrahepatic cholangiocarcinoma (ICC) and fibrolamellar carcinoma (FLC) continue to be diagnosed at advanced stages with limited curative options.[1] The Liver Tumours–Clinical session at European Association for the Study of the Liver (EASL) Congress 2026 highlighted how innovations in supportive care, biomarker development, AI, microbiome science, and immunotherapy can be used to reshape the management of liver malignancies. Although the studies varied in scope and methodology, a common theme of all the presentations was the transition from a conventional one-size-fits-all approach to a more pragmatic, precision-based approach guided by tumour biology, host factors, and technological advances.

IMPROVING OUTCOMES BEYOND TUMOUR CONTROL

Cancer cachexia remains a major yet often under-recognised contributor to morbidity and mortality in patients with advanced HCC.[2] In a multicentre RCT, Biswas et al.[3] evaluated the use of oral olanzapine as an adjunct to nutritional counselling in patients with intermediate or advanced HCC and cachexia. The study demonstrated significant improvements in appetite, weight gain, and quality of life among patients receiving olanzapine, without major safety concerns.

Importantly, the benefits extended beyond just weight gain. Improvements in anorexia scores, caloric intake, and patient-reported quality of life suggest that supportive care interventions can meaningfully influence daily functioning and symptom burden. While no significant changes were observed in muscle mass or functional performance, these findings reinforce that

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clinically relevant outcomes in advanced cancer extend beyond radiological response and survival. As systemic therapies continue to prolong survival in HCC, interventions addressing cachexia and quality of life will become increasingly important components of comprehensive cancer care.

ADVANCING EARLY DETECTION THROUGH LIQUID BIOPSY

Early diagnosis remains the cornerstone of improving HCC outcomes, yet current surveillance strategies based on ultrasound with/without α-fetoprotein (AFP) remain suboptimal. Oussalah and colleagues presented results from a prospective Phase III validation study evaluating circulating methylated SEPT9 (mSEPT9), a cell-free DNA-based epigenetic biomarker, in patients with cirrhosis undergoing HCC surveillance.[4]

The study demonstrated superior diagnostic performance of mSEPT9 compared with AFP alone and showed that combining both biomarkers substantially enhanced sensitivity for early-stage disease. Particularly noteworthy was the marked improvement in detecting Barcelona Clinic Liver Cancer (BCLC) Stage 0–A tumours, a stage at which curative interventions remain feasible.

These findings reflect the growing influence of liquid biopsy technologies in hepatology. Rather than replacing existing surveillance approaches, mSEPT9 may complement current algorithms by improving risk stratification and reducing missed opportunities for early intervention. However, implementation will require assessment of cost-effectiveness, integration with imaging pathways, and validation across diverse patient populations. Nevertheless, this study represents a major prospective evaluation of an epigenetic biomarker for HCC surveillance presented in recent years.

OVERCOMING IMMUNOTHERAPY RESISTANCE THROUGH GUT MICROBIOME MODULATION

Resistance to immune checkpoint inhibition is a major obstacle in the management of advanced HCC. One of the most innovative studies in the session explored whether modulation of the gut

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microbiome could restore treatment sensitivity to immune checkpoint inhibition.

The FAB-HCC pilot study evaluated faecal microbiota transplantation via the colonic route combined with continued atezolizumab and bevacizumab therapy in patients whose disease had progressed on the same regimen. Although limited by its single-arm design and small sample size, the study reported encouraging response rates and demonstrated successful microbiome engraftment following faecal microbiota transplantation.[5]

Beyond clinical activity, the investigators documented alterations in microbial composition, bile acid profiles, and systemic immune responses, providing mechanistic evidence that microbiome modulation may influence antitumour immunity. These findings align with a growing body of evidence linking gut microbial diversity to immunotherapy responsiveness across multiple tumour types.[6]

While larger randomised studies are needed before clinical adoption, the work highlights an emerging paradigm in oncology: therapeutic manipulation of the host ecosystem rather than the tumour alone. If confirmed, microbiome-based interventions could become an important strategy for overcoming resistance to immunotherapy in HCC.

AI MOVES CLOSER TO CLINICAL PRACTICE

Diagnostic uncertainty remains a significant challenge in liver pathology, particularly when distinguishing ICC from metastatic adenocarcinoma on limited biopsy specimens. Cheng et al.[7] addressed this problem through development of a confidence-aware AI pathology model capable of differentiating ICC from metastatic tumours using routine digital histopathology slides.

A notable feature of the model was its incorporation of confidence estimation. Rather than generating a binary prediction for every case, the algorithm identified situations in which it was most likely to be correct, thereby improving reliability and reducing false-positive classifications. Prospective validation across European and Asian

cohorts demonstrated excellent diagnostic performance.

The concept of confidence-aware AI may ultimately prove as important as diagnostic accuracy itself. One of the major barriers to clinical implementation of AI tools has been the 'black box' nature of predictions. By explicitly quantifying uncertainty, this approach offers a more realistic framework for integrating AI into pathology workflows, where human expertise and machine learning can operate synergistically rather than competitively.

Although widespread deployment will require regulatory approval and real-world validation, the study provides a glimpse into how digital pathology may streamline diagnostic pathways, reduce unnecessary investigations, and accelerate treatment decisions.

NOVEL BIOMARKERS FOR RARE LIVER TUMOURS

The session concluded with an important contribution addressing FLC, a rare liver cancer that predominantly affects young individuals and lacks reliable biomarkers. Nault et al.[8] identified serum procalcitonin (PCT) as a highly sensitive and specific biomarker for FLC.

Across independent European and North American cohorts, serum PCT levels were markedly elevated in most patients with FLC, but rarely in conventional HCC or cholangiocarcinoma. Furthermore, longitudinal analyses suggested that PCT levels could be used to assess disease response and progression, supporting a potential role in treatment monitoring.

Mechanistic investigations strengthened the biological plausibility of the findings. Tumour-specific expression of the *CALCA* gene and localisation of procalcitonin production to tumour cells harbouring the characteristic *DNAJB1-PRKACA* fusion provide evidence that elevated PCT is directly linked to tumour biology rather than a nonspecific inflammatory phenomenon.

For a disease that often lacks effective biomarkers, these findings could have substantial clinical implications. Future studies will determine whether PCT can facilitate earlier diagnosis, improve surveillance following treatment, or serve as a surrogate marker in therapeutic trials.

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FUTURE PERSPECTIVES

Collectively, the studies presented in this session highlight the multidimensional nature of innovation in liver tumour research. Developments in anticancer therapy are being paralleled by advances in supportive care, molecular diagnostics, microbiome science, computational pathology, and biomarker discovery.

Several themes warrant particular attention. First, precision medicine is expanding beyond tumour genomics to include epigenetic biomarkers, host immune responses, and microbiome composition. Second, AI is moving from proof-of-concept studies toward clinically deployable tools capable of supporting diagnostic decision-making. Third, patient-centred outcomes such as quality of life and symptom burden are receiving greater recognition as meaningful therapeutic targets.

Despite these advances, important challenges remain. Most promising biomarkers require broader validation before incorporation into routine practice. Microbiome-based therapies demand randomised evaluation and mechanistic clarification. AI applications must demonstrate robustness across diverse healthcare settings. Nevertheless, the studies presented at EASL 2026 illustrate a field rapidly embracing interdisciplinary approaches to improve outcomes for patients with liver tumours.

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CONCLUSION

The Liver Tumours–Clinical session showcased how liver cancer management is increasingly becoming personalised, biologically informed, and technologically enabled. From improving quality of life in advanced HCC to enhancing early detection, overcoming immunotherapy resistance, refining pathological diagnosis, and identifying novel tumour biomarkers, the presented studies collectively underscore the evolution of liver oncology research. While many findings remain investigational, they provide a compelling roadmap for future research and offer optimism that more precise and effective care for patients with liver tumours is within reach.

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