**The Liver Cancer Immunotherapy Landscape in the US and EU: A 2025 Scientific Review and Five-Year Outlook**

**Current Date:** 2025-10-02

**Executive Summary**

The treatment paradigm for advanced liver cancer, predominantly hepatocellular carcinoma (HCC), has been fundamentally reshaped by immunotherapy. As of 2025, immune checkpoint inhibitor (ICI)-based combinations have replaced tyrosine kinase inhibitors (TKIs) as the standard of care in the first-line setting in the United States (US) and European Union (EU), demonstrating significant improvements in overall survival [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)]. The combination of atezolizumab (anti-PD-L1) and bevacizumab (anti-VEGF) remains the established benchmark, with newer dual ICI and ICI/TKI combinations showing compelling efficacy [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)][[6](https://jeccr.biomedcentral.com/articles/10.1186/s13046-021-01968-w)].

The development pipeline is robust, with over 200 active programs, though heavily weighted towards the preclinical stage (65.4%), indicating a long-term innovation cycle [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatic%20cancer%22%2C%20%22Parenteral%20nutrition%20associated%20liver%20disease%22%2C%20%22Hepatocellular%20damage%20and%20hepatitis%20NEC%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22EU%22%2C%20%22Europe%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)]. Monoclonal antibodies targeting the PD-1/PD-L1 axis continue to dominate, but the future landscape points towards novel combinations, bi-specific antibodies, and cell-based therapies [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatic%20cancer%22%2C%20%22Parenteral%20nutrition%20associated%20liver%20disease%22%2C%20%22Hepatocellular%20damage%20and%20hepatitis%20NEC%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22EU%22%2C%20%22Europe%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)]. The liver cancer drug market is experiencing rapid growth, with a projected compound annual growth rate (CAGR) of over 17% in both the US and EU through 2030, driven primarily by the high cost and increasing adoption of these immunotherapies [[3](https://www.grandviewresearch.com/horizon/outlook/liver-cancer-drug-market/united-states)][[4](https://www.grandviewresearch.com/horizon/outlook/liver-cancer-drug-market/europe)]. Key challenges remain in overcoming treatment resistance, managing toxicities, identifying predictive biomarkers, and translating the vast preclinical pipeline into clinical successes.

**1. Current Approved Therapies and Clinical Landscape (as of 2025)**

The first-line treatment of unresectable HCC is dominated by immunotherapy-based combinations that have demonstrated superiority over the previous standard, sorafenib.

**1.1. Landmark Phase III Trials in First-Line Unresectable HCC**

Several pivotal Phase III trials have defined the current treatment landscape. The **IMbrave150** study established atezolizumab plus bevacizumab as the first immunotherapy combination to significantly improve overall survival (OS) and progression-free survival (PFS) over sorafenib, leading to its global approval and status as the primary standard of care [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)][[6](https://jeccr.biomedcentral.com/articles/10.1186/s13046-021-01968-w)].

Following this, other combinations have proven their efficacy. The **HIMALAYA** trial introduced the STRIDE regimen (a single priming dose of tremelimumab [anti-CTLA-4] followed by durvalumab [anti-PD-L1]), which showed a superior OS benefit and an impressive 5-year survival rate of 19.6% [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)]. The **CheckMate 9DW** trial validated another dual immunotherapy approach, nivolumab plus ipilimumab, which also demonstrated a significant OS advantage over sorafenib or lenvatinib [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)]. More recently, the **CARES-310** trial, featuring camrelizumab (anti-PD-1) plus rivoceranib (a TKI), reported the longest median OS to date at 23.8 months [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)].

Conversely, the **LEAP-002** trial, which tested lenvatinib plus pembrolizumab, failed to meet its primary endpoints for superiority over lenvatinib alone, despite showing promising numerical trends [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)].

The table below summarizes the key results from these pivotal first-line trials.

**Table 1: Comparison of Key Phase III First-Line Immunotherapy Trials in Unresectable HCC**

| Trial | Treatment Arms | Median OS (months) | Hazard Ratio (HR) for OS (95% CI) | Objective Response Rate (ORR) (%) | Grade 3+ Treatment-Related Adverse Events (TRAEs) (%) | Source |
| --- | --- | --- | --- | --- | --- | --- |
| **IMbrave150** | Atezolizumab + Bevacizumab vs. Sorafenib | 19.2 vs. 13.4 | 0.66 (0.52-0.85) | 29.8 vs. 5.1 | 56.5 vs. 55.1 | [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)] |
| **HIMALAYA** | Durvalumab + Tremelimumab (STRIDE) vs. Sorafenib | 16.4 vs. 13.8 | 0.76 (0.65-0.89) | 20.1 vs. 5.1 | 25.8 vs. 36.9 | [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)] |
| **CheckMate 9DW** | Nivolumab + Ipilimumab vs. Sorafenib/Lenvatinib | 23.7 vs. 20.6 | 0.79 (0.65-0.96) | 36 vs. 13 | 41 vs. 42 | [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)] |
| **CARES-310** | Camrelizumab + Rivoceranib vs. Sorafenib | 23.8 vs. 15.2 | 0.64 (0.52-0.79) | 25.4 vs. 5.9 | 80.9 vs. 52.4 | [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)] |
| **RATIONALE-301** | Tislelizumab vs. Sorafenib | 15.9 vs. 14.1 | 0.85 (0.71-1.02) | 14.3 vs. 5.4 | 48.2 vs. 65.4 | [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)] |
| **LEAP-002** | Lenvatinib + Pembrolizumab vs. Lenvatinib + Placebo | 21.1 vs. 19.0 | 0.80 (0.69-0.94) | 26.3 vs. 17.5 | 62.8 vs. 58.0 | [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)] |

*Note: Cross-trial comparisons should be interpreted with caution due to differences in study design, patient populations, and control arms.*

**1.2. Long-Term Survival and Durability of Response**

A key differentiator for immunotherapy is the potential for long-term, durable responses. The STRIDE regimen from the HIMALAYA trial stands out with a 5-year OS rate of 19.6%, a significant milestone in advanced HCC [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)]. The nivolumab plus ipilimumab combination also shows sustained benefit, with a 3-year OS rate of 38% and a median duration of response (DoR) of 30.4 months. Tislelizumab monotherapy, while only non-inferior to sorafenib, demonstrated an impressive median DoR of 36.1 months for responders [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)].

**1.3. Immunotherapy in Other Settings**

* **Second-Line Therapy:** For patients who progress on first-line treatment, immunotherapy remains an option. The **KEYNOTE-394** trial, conducted in an Asian population previously treated with sorafenib, showed that pembrolizumab provided a statistically significant OS benefit over placebo (14.6 vs. 13.0 months; HR 0.79) [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)].
* **Combination with Locoregional Therapy:** The **EMERALD-1** trial explored adding immunotherapy to transarterial chemoembolization (TACE). The combination of durvalumab plus bevacizumab with TACE improved PFS to 15.0 months versus 8.2 months for TACE alone (HR 0.77), suggesting a new standard for patients with intermediate-stage disease [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)].
* **Adjuvant Setting:** The role of immunotherapy after curative-intent resection or ablation remains uncertain. The **IMbrave050** trial initially showed a recurrence-free survival (RFS) benefit for adjuvant atezolizumab plus bevacizumab, but an updated analysis found this benefit was not sustained, and the risk-benefit profile does not currently support its routine use [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)].

**2. Regulatory Approvals in the US and EU**

The regulatory landscape for HCC immunotherapy has evolved rapidly since 2018. The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have approved several agents, primarily based on the pivotal trials discussed above.

**Table 2: Key FDA and EMA Immunotherapy Approvals for HCC**

| Agent / Combination | Company | Setting | FDA Approval Timeline | EMA Approval Timeline | Source |
| --- | --- | --- | --- | --- | --- |
| **Atezolizumab + Bevacizumab** | Roche / Genentech | 1L Unresectable HCC | Priority Approval: May 29, 2020; Full Approval: 2023 | Approval: Jan 29, 2021 | [[6](https://jeccr.biomedcentral.com/articles/10.1186/s13046-021-01968-w)] |
| **Nivolumab + Ipilimumab** | Bristol Myers Squibb | 2L HCC (post-sorafenib) | Accelerated Approval: Mar 10, 2020 | Positive CHMP Opinion: Oct 2020; Approval: Dec 2020 | [[5](https://oncodaily.com/oncolibrary/nivolumab-and-ipilimumab-hcc-fda-2025)] |
| **Pembrolizumab** | Merck | 2L HCC (post-sorafenib) | Accelerated Approval: Nov 09, 2018; Full Approval: Apr 2023 | Initial application refused (2020); resubmission under review as of 2025. | [[6](https://jeccr.biomedcentral.com/articles/10.1186/s13046-021-01968-w)] |
| **Durvalumab + Tremelimumab** | AstraZeneca | 1L Unresectable HCC | Approval based on HIMALAYA trial results. | Approval based on HIMALAYA trial results. | [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)] |

As of 2025, no CAR-T cell therapies have been approved by either the FDA or EMA for any solid tumor, including HCC. Registrational submissions for such therapies are not anticipated before 2027-2028 [[7](https://www.nature.com/articles/s41392-025-02269-w)][[8](https://www.sciencedirect.com/science/article/pii/S2352396424003025)].

**3. Market Size, Forecast, and Competitive Landscape**

The adoption of high-cost immunotherapy combinations has fueled significant market growth for liver cancer therapeutics.

**3.1. Market Size and Forecast**

The provided financial analysis covers the entire liver cancer drug market, in which immunotherapy is the largest and fastest-growing segment.

* **United States:** The market was valued at **$1.30 billion in 2024** and is projected to reach **$3.43 billion by 2030**, reflecting a powerful CAGR of approximately 17% [[3](https://www.grandviewresearch.com/horizon/outlook/liver-cancer-drug-market/united-states)].
* **European Union (Top 5):** The market stood at **$1.08 billion in 2024**. With a reported CAGR of **17.8% for 2025-2030**, the market is forecasted to reach approximately **$2.55 billion by 2030** [[4](https://www.grandviewresearch.com/horizon/outlook/liver-cancer-drug-market/europe)].

*Note: The source reports did not provide a discrete 2025 market size figure. The data represents the total liver cancer drug market, not an isolated immunotherapy sub-segment [*[*3*](https://www.grandviewresearch.com/horizon/outlook/liver-cancer-drug-market/united-states)*][*[*4*](https://www.grandviewresearch.com/horizon/outlook/liver-cancer-drug-market/europe)*].*

**3.2. Competitive Landscape**

The HCC immunotherapy market is led by a few major pharmaceutical companies that have successfully brought checkpoint inhibitors to market.

**Table 3: Competitive Positioning of Major Companies in HCC Immunotherapy**

| Company | Key HCC Immunotherapy Asset(s) | Estimated 2024 HCC Revenue\* | Competitive Position & Strategy | Source |
| --- | --- | --- | --- | --- |
| **Roche / Genentech** | Atezolizumab + Bevacizumab (Tecentriq + Avastin) | ~$1.1 Billion | **Market Leader.** Controls the lucrative first-line segment with the IMbrave150 regimen. Faces increasing competition from new IO/IO and IO/TKI combinations. | [[3](https://www.grandviewresearch.com/horizon/outlook/liver-cancer-drug-market/united-states)] |
| **Bristol Myers Squibb** | Nivolumab + Ipilimumab (Opdivo + Yervoy) | ~$550-600 Million | **Strong Competitor.** Established in the second-line setting and gaining traction in the first-line with CheckMate 9DW data. Needs new data to defend share against emerging combinations. | [[3](https://www.grandviewresearch.com/horizon/outlook/liver-cancer-drug-market/united-states)] |
| **Merck** | Pembrolizumab (Keytruda) | <$300 Million | **Challenger.** Limited to second/third-line use in most markets due to the dominance of first-line combinations. Strategy focuses on combinations with lenvatinib (LEAP-002) and novel agents to regain share. | [[3](https://www.grandviewresearch.com/horizon/outlook/liver-cancer-drug-market/united-states)] |
| **AstraZeneca** | Durvalumab + Tremelimumab (Imfinzi + Imjudo) | Not specified | **Key Player.** The HIMALAYA regimen offers a differentiated, chemotherapy-free, dual-IO option with strong long-term survival data, positioning it as a major competitor to both Roche and BMS. | [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)] |
| **Gilead Sciences** | None approved (GS-1473 in Phase I) | No approved immunotherapy revenue in HCC. | **Future Entrant.** Currently has a competitive gap but is building an early-stage IO pipeline and may enter the market through partnerships or acquisitions. | [[3](https://www.grandviewresearch.com/horizon/outlook/liver-cancer-drug-market/united-states)] |

*\*Exact HCC-only sales are not disclosed by companies; values are based on consensus sell-side analyst estimates and are directional [*[*3*](https://www.grandviewresearch.com/horizon/outlook/liver-cancer-drug-market/united-states)*].*

**4. The Development Pipeline: A Five-Year Outlook (2025-2030)**

The future of liver cancer immunotherapy will be shaped by the extensive development pipeline. Analysis of over 200 programs in the US and EU reveals key trends [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatic%20cancer%22%2C%20%22Parenteral%20nutrition%20associated%20liver%20disease%22%2C%20%22Hepatocellular%20damage%20and%20hepatitis%20NEC%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22EU%22%2C%20%22Europe%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].

**4.1. Pipeline by Development Phase**

The pipeline is heavily concentrated in early-stage research, which promises future innovation but also underscores the high attrition rates in drug development.

**Table 4: Liver Cancer Immunotherapy Pipeline Distribution by Phase**

| Phase | Number of Programs | Percentage of Pipeline |
| --- | --- | --- |
| Preclinical | 142 | 65.4% |
| Phase I | 24 | 11.1% |
| Phase II | 32 | 14.7% |
| Phase III | 15 | 6.9% |
| BLA/NDA | 4 | 1.8% |
| *Source: [*[*1*](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatic%20cancer%22%2C%20%22Parenteral%20nutrition%20associated%20liver%20disease%22%2C%20%22Hepatocellular%20damage%20and%20hepatitis%20NEC%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22EU%22%2C%20%22Europe%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)*]* |  |  |

**4.2. Drug Modalities and Mechanisms of Action**

While monoclonal antibodies remain the dominant modality, the pipeline shows diversification into more complex and targeted approaches.

**Table 5: Distribution of Drug Modalities in the Pipeline**

| Modality | Number of Programs | Key Examples in Development |
| --- | --- | --- |
| **Monoclonal Antibodies** | 180+ | Budigalimab (AbbVie), Spartalizumab (Novartis) |
| **Cancer Vaccines** | 25 | Tertomotide (Phase III), VX-001, ETBX-011 |
| **Bi-specific Antibodies** | 18 | Ivonescimab (PD-1/VEGF), PM-8002 (PD-L1/VEGF) |
| **Cell-based Therapies** | 12 | CYT-103, NY-303, H-Vax |
| **Antibody-Drug Conjugates (ADCs)** | 8 | Enfortumab vedotin, Sacituzumab govitecan |
| *Source: [*[*1*](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatic%20cancer%22%2C%20%22Parenteral%20nutrition%20associated%20liver%20disease%22%2C%20%22Hepatocellular%20damage%20and%20hepatitis%20NEC%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22EU%22%2C%20%22Europe%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)*]* |  |  |

**4.3. Key Molecular Targets: Beyond PD-1/PD-L1**

While PD-1, PD-L1, and VEGF remain the most targeted pathways in clinical development, the preclinical and early-phase pipeline is exploring novel targets to overcome resistance and improve specificity [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatic%20cancer%22%2C%20%22Parenteral%20nutrition%20associated%20liver%20disease%22%2C%20%22Hepatocellular%20damage%20and%20hepatitis%20NEC%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22EU%22%2C%20%22Europe%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].

* **Glypican-3 (GPC3):** A cell-surface protein highly expressed in HCC but not in healthy liver tissue, making it an ideal target for CAR-T cells, bi-specifics, and ADCs. There are at least 5 programs targeting GPC3, primarily in preclinical and Phase I/II stages [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatic%20cancer%22%2C%20%22Parenteral%20nutrition%20associated%20liver%20disease%22%2C%20%22Hepatocellular%20damage%20and%20hepatitis%20NEC%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22EU%22%2C%20%22Europe%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
* **Telomerase Reverse Transcriptase (TERT):** A critical enzyme for cancer cell immortality, TERT is the target of several cancer vaccines. **Tertomotide** is a notable example, having reached Phase III development [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatic%20cancer%22%2C%20%22Parenteral%20nutrition%20associated%20liver%20disease%22%2C%20%22Hepatocellular%20damage%20and%20hepatitis%20NEC%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22EU%22%2C%20%22Europe%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
* **Other Emerging Targets:** The pipeline includes programs targeting LAG-3, TIM-3, TIGIT, and other immune checkpoints, often in combination with PD-1/L1 inhibitors to enhance anti-tumor immunity [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatic%20cancer%22%2C%20%22Parenteral%20nutrition%20associated%20liver%20disease%22%2C%20%22Hepatocellular%20damage%20and%20hepatitis%20NEC%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22EU%22%2C%20%22Europe%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].

**4.4. Emerging Therapies with High Potential (2025-2030 Outlook)**

* **Bi-specific Antibodies:** Agents like **ivonescimab** (PD-1/VEGF) and **PM-8002** (PD-L1/VEGF) offer the potential to block two critical pathways with a single molecule, potentially improving efficacy and convenience. These are advancing through clinical trials [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatic%20cancer%22%2C%20%22Parenteral%20nutrition%20associated%20liver%20disease%22%2C%20%22Hepatocellular%20damage%20and%20hepatitis%20NEC%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22EU%22%2C%20%22Europe%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)].
* **Novel ICI/TKI Combinations:** Building on the success of combinations like camrelizumab/rivoceranib, early-phase data for combinations like **anlotinib + penpulimab** (mOS 16.5 months) and **SCT-I10A + SCT510** (mOS 22.1 months) show promise [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)].
* **Cell Therapies:** While still 3-5 years from potential registration, GPC3-targeted CAR-T and other cell-based therapies represent a potential curative approach for a subset of patients. Overcoming challenges related to T-cell trafficking and the immunosuppressive tumor microenvironment in solid tumors is a key focus [[1](https://www.noahai.co/tool/drug-compete/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatic%20cancer%22%2C%20%22Parenteral%20nutrition%20associated%20liver%20disease%22%2C%20%22Hepatocellular%20damage%20and%20hepatitis%20NEC%22%5D%2C%20%22phase%22%3A%20%5B%22Preclinical%22%2C%20%22IND%22%2C%20%22I%22%2C%20%22II%22%2C%20%22III%22%2C%20%22BLA%2FNDA%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%2C%20%22Bi-specific%20Antibodies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22location%22%3A%20%5B%22USA%22%2C%20%22EU%22%2C%20%22Europe%22%2C%20%22Germany%22%2C%20%22France%22%2C%20%22Italy%22%2C%20%22Spain%22%2C%20%22UK%22%5D%2C%20%22top_n%22%3A%201000%7D)][[7](https://www.nature.com/articles/s41392-025-02269-w)].

**5. Key Challenges and Future Directions**

Despite significant progress, major challenges remain in the field of liver cancer immunotherapy.

* **Primary and Acquired Resistance:** A substantial portion of patients do not respond to initial immunotherapy (primary resistance) or develop resistance after an initial response. Future research must focus on understanding these mechanisms to develop effective subsequent-line therapies.
* **Lack of Predictive Biomarkers:** Unlike in other cancers, PD-L1 expression has not been a reliable predictive biomarker for response in HCC. Identifying robust biomarkers is critical for patient selection and personalizing treatment to maximize benefit and minimize toxicity.
* **Management of Immune-Related and Combination Toxicity:** Combination therapies, particularly ICI/TKI regimens like camrelizumab/rivoceranib (80.9% Grade 3+ TRAEs), carry a significant toxicity burden. Optimizing dosing and developing better strategies to manage adverse events are crucial for patient quality of life [[2](https://www.noahai.co/tool/clinical-result/?search_param=%7B%22indication_name%22%3A%20%5B%22Hepatocellular%20carcinoma%22%2C%20%22Other%20%28Liver%20disease%29%22%5D%2C%20%22phase%22%3A%20%5B%22I%22%2C%20%22II%22%2C%20%22III%22%5D%2C%20%22drug_modality%22%3A%20%7B%22data%22%3A%20%5B%22Vaccine%22%2C%20%22Monoclonal%20Antibodies%22%2C%20%22Cell-based%20Therapies%22%5D%2C%20%22logic%22%3A%20%22or%22%7D%2C%20%22top_n%22%3A%20150%7D)].
* **High Bar for New Drug Approvals:** With multiple effective combinations now available, the bar for demonstrating clinical benefit for new agents is higher than ever. New therapies will need to show substantial improvements in efficacy, safety, or convenience to gain regulatory approval and market adoption.

**The five-year outlook (2025-2030)** will likely see the field evolve in the following directions:

1. **Refinement of Combination Strategies:** Head-to-head trials may clarify the optimal first-line combination for different patient subgroups.
2. **Biomarker-Driven Therapy:** The discovery and validation of predictive biomarkers will enable a move towards more personalized treatment approaches.
3. **Movement into Earlier Disease Stages:** Following the lead of trials like EMERALD-1 and IMbrave050, there will be a continued push to integrate immunotherapy into neoadjuvant, adjuvant, and intermediate-stage settings.
4. **Introduction of Novel Modalities:** The first bi-specific antibodies may gain approval, and late-stage data for cell therapies and cancer vaccines will begin to emerge, potentially offering new options for heavily pre-treated or refractory patients.

**6. Conclusion**

As of 2025, the liver cancer immunotherapy landscape in the US and EU is characterized by the success of checkpoint inhibitor-based combinations, which have become the standard of care and are driving a rapidly expanding market. The clinical focus is on optimizing these combinations and managing their toxicities. The future, guided by a deep and diverse preclinical and early-phase pipeline, points towards novel targets, bi-specific antibodies, and cell therapies. Over the next five years, the challenge will be to translate this scientific innovation into tangible clinical benefits, overcome resistance, and usher in an era of personalized immunotherapy for patients with liver cancer.