Intelligencia AI

Liver Cancer

We analyzed our data at Intelligencia AI to generate a high-level view of liver cancer's current and potential future state of drug development.

Globally, liver cancer is the sixth-most frequent cancer and the fourth-leading cause of death from cancer[1]. It is more commonly encountered as a metastasis rather than a primary tumor.

The leading causes of liver cancer are cirrhosis due to hepatitis B, hepatitis C or alcohol and non-alcoholic fatty liver disease.

Due to the variability in liver cancer causes, significant focus is given not only on treatment but also on prevention (hepatitis immunizations, alcohol use decrease, diabetes management)[2,3].

Reported global liver cancer incidence is about 8.6 per 100,000 person-years[4].

Overall, it has a five-year survival estimate of 22%: 37% for localized liver cancer, 14% for regional liver cancer and 4% for distant metastatic liver cancer[5].

HOW IS LIVER CANCER CURRENTLY TREATED?

Commonly used types of treatment[6]:

- Surgery
- Liver transplant
- Ablation therapy
- Embolization therapy
- Targeted therapy
- Immunotherapy
- Radiation therapy

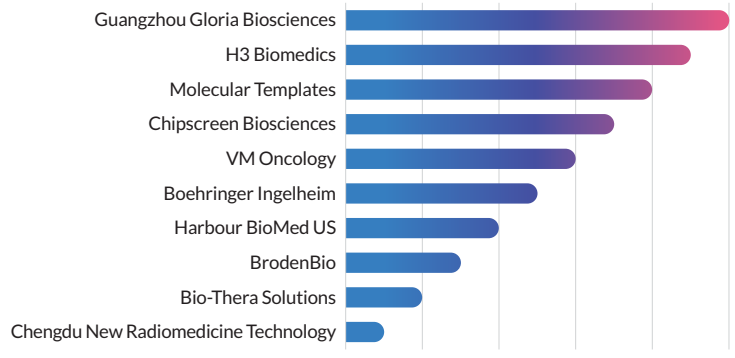
In the past five years, the following drugs have received regulatory approval by the FDA: atezolizumab, nivolumab, durvalumab/tremelimumab, cabozantinib, and ramucirumab. Atezolizumab and nivolumab are both monoclonal antibodies (mAbs) that target the Programmed Cell Death Protein 1 (PD-1)/Programmed Cell Death Ligand 1 (PDL-1) pathway. The durvalumab/tremelimumab regimen targets the same pathway but also cytotoxic T-lymphocyte associated protein 4 (CTLA-4). Cabozantinib is a small molecule tyrosine kinase inhibitor (TKI). Ramucirumab is a mAb that targets vascular endothelial growth factor receptor 2 (VEGFR-2).

DETAILS IN THE DATA: HERE'S WHAT WE LEARNED ABOUT LIVER CANCER

In analyzing our data[7], we identified:

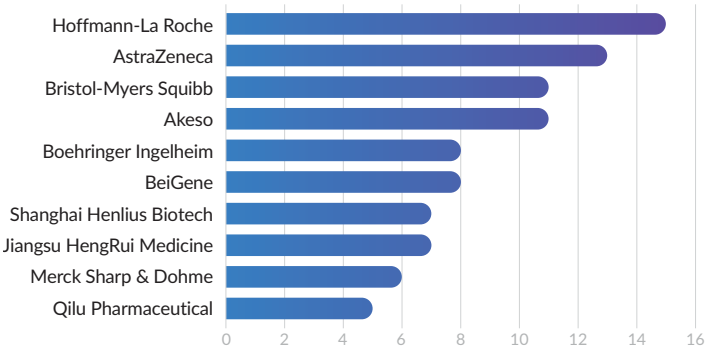
- 238 **ongoing** industry-led, FDA-track interventional clinical development programs* among which:
  - *68 are in Phase 1 or 1b,*
  - *134 are in Phase 2 or 1/2 and*
  - *36 are in Phase 2/3 or Phase 3.*
- The programs mentioned above are conducted by 111 different primary sponsors and correspond to 208 investigational drugs/drug combinations, covering 71 different drug modalities/modality combinations.

Top 10 Sponsors in Liver Cancer - Ranked by Intelligencia AI Pipeline Performance Score



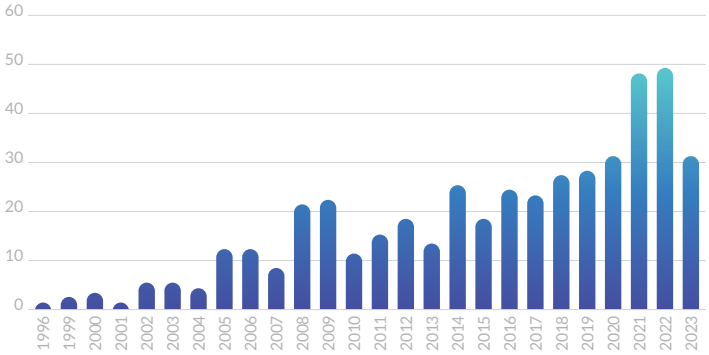
Our pipeline performance score leverages our patented AI-driven probability of technical and regulatory success (PTRS) assessments.

Sponsors With the Highest Number of Active Liver Cancer Clinical Programs



These are the top sponsors based on the number of ongoing liver cancer clinical programs.*

Distribution of Liver Cancer Clinical Programs by Year of Initiation Since 1996



Over the past two decades, liver cancer clinical development has seen a slow, upward trend, with 2021 and 2022 being significant outliers.

- Among industry-led, FDA-track historical programs, 39% transitioned from Phase 1 to Phase 2 and 15% from Phase 2 to Phase 3.
- 16 drugs (run by 14 different sponsors) have not received prior FDA approval in liver cancer and are being tested in Phase 3 trials.
  - *The majority of these 16 drugs are mAbs. The exceptions are: the small molecule inhibitors (SMIs) Namodenoson, Anlotinib and Rivoceranib, the recombinant protein Pegargiminase and the T-cell vaccine Allostim.*
- In terms of Mechanism of Action (MoA), the most common targets for mAbs are the PD-1/PD-L1 pathway and CTLA-4. Namodenoson targets adenosine receptor A3, Anlotinib targets vascular endothelial growth factor receptor (VEGFR), fibroblast growth factor receptor (FGFR), platelet-derived growth factor receptor (PDGFR), and c-kit, while Rivoceranib targets vascular endothelial growth factor receptor 2 (VEGFR-2).

PERSPECTIVE: WHAT DOES THIS ALL MEAN?

Due to the majority of liver cancer causes being conditions that provide multiple avenues for detection and/or treatment, significant industry focus has been given on preventative measures. Taking into account, however, the small number of recent approvals, as well as the disease's 5-year survival rate, liver cancer indeed constitutes an unmet patient need. It is a need that the pharmaceutical industry seems eager to address, especially because almost every non-approved Phase 3 asset currently in development is run by a different sponsor.

Boehringer Ingelheim appears to be among the most prolific companies in liver cancer and one of the most promising ones, based on Intelligencia AI's pipeline performance score. However, the same targets that have proven successful in recent years are also the ones that are currently in the latest stages of development (VEGFR, PD1/PD-L1). There appear to be opportunities for further developing these pathways, but it is imperative to identify more biomarkers. For the foreseeable future, most of the industry will focus on already established targets and pathways.

About Intelligencia AI

Intelligencia AI™ leads the way in leveraging proprietary data, biomedical expertise and artificial intelligence (AI) with its patented technology to address significant challenges in the pharmaceutical industry. These challenges include lengthy drug development timelines, excessive costs, and unsustainable return on investment (ROI). Its suite of AI-powered solutions delivers actionable insights crucial in mitigating risks and enhancing decision-making associated with drug development by providing an accurate, unbiased assessment of a drug's probability of success. Founded in 2017, Intelligencia AI is headquartered in New York, NY, with offices in Athens, Greece, and employs 110 individuals globally. Visit intelligencia.ai to discover more.

References

1 Global Burden of Disease Liver Cancer Collaboration; Akinyemiju T, Abera S, Ahmed M, Alam N, Alemayohu MA, Allen C, Al-Raddadi R, Alvis-Guzman N, Amoako Y, Artaman A, Ayele TA, Barac A, Bensenor I, Berhane A, Bhutta Z, Castillo-Rivas J, Chitheer A, Choi JY, Cowie B, Dandona L, Dandona R, Dey S, Dicker D, Phuc H, Ekwueme DU, Zaki MS, Fischer F, Fürst T, Hancock J, Hay SI, Hotez P, Jee SH, Kasaeian A, Khader Y, Khang YH, Kumar A, Kutz M, Larson H, Lopez A, Lunevicius R, Malekzadeh R, McAlinden C, Meier T, Mendoza W, Mokdad A, Moradi-Lakeh M, Nagel G, Nguyen Q, Nguyen G, Ogbo F, Patton G, Pereira DM, Pourmalek F, Qorbani M, Radfar A, Roshandel G, Salomon JA, Sanabria J, Sartorius B, Satpathy M, Sawhney M, Sepanlou S, Shackelford K, Shore H, Sun J, Mengistu DT, Topór-Mądry R, Tran B, Ukwaja KN, Vlassov V, Vollset SE, Vos T, Wakayo T, Weiderpass E, Werdecker A, Yonemoto N, Younis M, Yu C, Zaidi Z, Zhu L, Murray CJL, Naghavi M, Fitzmaurice C. The Burden of Primary Liver Cancer and Underlying Etiologies From 1990 to 2015 at the Global, Regional, and National Level: Results From the Global Burden of Disease Study 2015. JAMA Oncol. 2017 Dec 1;3(12):1683-1691. doi: 10.1001/jamaoncol.2017.3055. PMID: 28983565; PMCID: PMC5824275.

2 Bruix J, Han KH, Gores G, Llovet JM, Mazzaferro V. Liver cancer: Approaching a personalized care. J Hepatol. 2015 Apr;62(1 Suppl):S144-56. doi: 10.1016/j.jhep.2015.02.007. PMID: 25920083; PMCID: PMC4520430.

3 Mantovani A, Targher G. Type 2 diabetes mellitus and risk of hepatocellular carcinoma: spotlight on nonalcoholic fatty liver disease. Ann Transl Med. 2017 Jul;5(13):270. doi: 10.21037/atm.2017.04.41. PMID: 28758096; PMCID: PMC5515814.

4 https://www.wcrf.org/cancer-trends/liver-cancer-statistics/

5 https://www.cancer.org/cancer/types/liver-cancer/detection-diagnosis-staging/survival-rates.html

6 https://www.cancer.gov/types/liver/what-is-liver-cancer/treatment

7 Data as of September 27, 2024

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**A program (also known as clinical pipeline or drug pipeline) is the clinical development of a drug (or a set of drugs in case of combination therapies) by a pharmaceutical company (alone or in collaboration with other partners) for an indication. A program consists of a set of clinical trials with the ultimate goal of approval for marketing. Each program has unique and specific parameters that can potentially justify a separate regulatory approval. Specifically, the definition of a clinical program is one of unique drug(s), drug dosage, mode of administration, adjuvant state, indication, sponsor, disease severity (e.g. stage of disease), line of treatment and biomarker information used as inclusion criteria.*