ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 17, Issue, 06, pp.33556-33557, June, 2025
DOI: https://doi.org/10.24941/ijcr.49191.06.2025

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

ATEZOLIZUMAB PLUS BEVACIZUMAB IN HEPATOCELLULAR CARCINOMA: A COMPREHENSIVE REVIEW OF EFFICACY, SAFETY, AND EMERGING EVIDENCE

Abhirami Rajasekhar[1], Amritha Krishna[1], Drishya, L., [2*] and Shaiju S Dharan[3]

[1]Ezhuthachan College of Pharmaceutical Sciences
[2]Assistant Professor, Department of Pharmacy Practice, Ezhuthachan College of Pharmaceutical Sciences
[3]Principal, Department of Pharmacy Practice, Ezhuthachan College of Pharmaceutical Sciences

ARTICLE INFO

Article History:
Received09th March, 2025
Received in revised form
21st April, 2025
Accepted 19th May, 2025
Publishedonline30th June,2025

Keywords:

Feronia limonia, properties, non-traditional fruit crop, food processing, medicinal values, proper utilization, Profit making, extension work, Awareness.

***Corresponding author:**
Drishya L

ABSTRACT

Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related mortality worldwide. Recent advances in immunotherapy have significantly altered the treatment landscape. Atezolizumab, a PD-L1 inhibitor, combined with Bevacizumab, a VEGF inhibitor, has demonstrated remarkable efficacy in advanced HCC. This review summarizes the mechanism, clinical data, safety, and guideline recommendations for this regimen. It also explores ongoing trials and future prospects. The IMbrave150 trial is the cornerstone for this therapeutic advance, establishing it as the first-line standard. Each section includes a focused discussion and reference citations for further understanding.

Citation: Abhirami Rajasekhar, Amritha Krishna, Drishya L and Shaiju S Dharan. 2025. "Atezolizumab plus Bevacizumab in Hepatocellular Carcinoma: A Comprehensive Review of Efficacy, Safety, and Emerging Evidence". *International Journal of Current Research, 17, (06), 33556-33557.*

INTRODUCTION

Hepatocellular carcinoma (HCC) stands as a major global health challenge, ranking as the sixth most prevalent malignancy and the third leading cause of cancer-related mortality worldwide. The disease predominantly arises in the context of chronic liver injury caused by hepatitis B and C virus infections, excessive alcohol intake, and more recently, non-alcoholic fatty liver disease and steatohepatitis. The pathogenesis involves a complex interplay between chronic inflammation, fibrosis, genetic alterations, and hepatocyte regeneration that ultimately leads to malignant transformation. Most patients present with advanced-stage disease, where curative options such as resection, transplantation, or ablation are no longer viable, necessitating systemic therapy. Hence, improving systemic therapeutic strategies for advanced HCC remains a critical need in oncology. (1,2)

Mechanism of Action: The rationale for combining Atezolizumab with Bevacizumab stems from their complementary mechanisms in modulating the tumor microenvironment. Atezolizumab is a fully humanized IgG1 monoclonal antibody that binds to PD-L1, thereby blocking its interaction with PD-1 and B7.1 receptors on T cells. This blockade reactivates suppressed cytotoxic T lymphocytes and promotes an effective anti-tumor immune response. Bevacizumab, on the other hand, is a recombinant humanized monoclonal antibody that targets VEGF-A, inhibiting angiogenesis which is essential for tumor growth and metastasis. Inhibition of VEGF also leads to normalization of the tumor vasculature, improving immune cell infiltration and drug delivery to tumor sites. Together, this synergistic interaction disrupts immune evasion and tumor neovascularization, enhancing the overall therapeutic efficacy in hepatocellular carcinoma. (3-5)

Clinical Evidence: IMbrave150 Trial: The IMbrave150 trial compared Atezolizumab-Bevacizumab with Sorafenib in unresectable HCC patients (6). Results showed significant improvement in overall survival (OS) and progression-free survival (PFS) for the combination therapy. Median OS was not reached in the experimental arm versus 13.2 months in the Sorafenib group, establishing a new first-line standard.

Dosing and Regimen: The standard regimen includes Atezolizumab 1200 mg and Bevacizumab 15 mg/kg administered intravenously every 3 weeks (7). Premedication and prophylactic management for bleeding risk are necessary. Endoscopic variceal screening is recommended before initiation due to the bleeding risk associated with Bevacizumab (8). Regular imaging and laboratory follow-up are required.

Real-World Evidence: Real-world studies reinforce the efficacy of the combination regimen in patients with varying liver functions and comorbidities (9). Outcomes in Child-Pugh B patients were less favorable but still showed benefit. Observational data support the use of this combination beyond the strictly selected clinical trial population, expanding its real-life applicability (10).

Adverse Effects and Safety: The combination is generally well tolerated. Common adverse events include hypertension, proteinuria, fatigue, and bleeding (11). Immune-related toxicities such as hepatitis and colitis may occur with Atezolizumab (12). Gastrointestinal bleeding is a major concern, warranting close monitoring and variceal management before therapy initiation (13).

Predictors of Response: Currently, no validated biomarkers predict response to this regimen in HCC. Investigations are ongoing into PD-L1 expression, tumor mutation burden, and immune gene signatures (14). Clinical parameters like performance status and liver function remain key determinants of benefit. Research continues to identify molecular markers to better guide patient selection.

Comparison with Other Regimens: Atezolizumab-Bevacizumab has shown superior outcomes compared to Sorafenib (6). Other regimens like Lenvatinib and STRIDE (Durvalumab + Tremelimumab) offer alternatives (15,16). However, the IMbrave150 combination remains the preferred first-line option due to survival benefit and tolerability, with current trials exploring optimal sequencing strategies.

Guideline Recommendations: Leading guidelines from AASLD, EASL, and NCCN endorse Atezolizumab-Bevacizumab as first-line treatment for unresectable HCC (17–19). They emphasize pre-treatment screening for varices, preserved liver function (Child-Pugh A), and appropriate patient selection. Integration into clinical algorithms reflects its established efficacy and safety across diverse populations.

Future Directions: Future research aims to evaluate this regimen in adjuvant and neoadjuvant settings. Trials like IMbrave050 assess recurrence prevention after resection (20). Combination strategies with TKIs or dual immune checkpoint inhibitors are being explored. Additionally, cost-effectiveness and accessibility remain critical for global implementation in routine clinical practice.

CONCLUSION

The Atezolizumab-Bevacizumab combination represents a paradigm shift in HCC management. It offers survival and response advantages with manageable toxicity. It is now the standard of care for eligible patients with advanced disease. Ongoing research will define its expanded roles and improve personalization through biomarker integration and real-world optimization.

REFERENCES

Brahmer JR, *et al*. Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy. *Journal of Clinical Oncology.* 2018;36(17):1714–1768.

Casadei-Gardini A, *et al*. Atezolizumab–bevacizumab combination in real-life: A multicenter study. Liver Cancer. 2021;10(6):615–624.

Chen DS, Mellman I. Oncology meets immunology: the cancer-immunity cycle. Immunity. 2013;39(1):1–10.

D'Alessio A, *et al*. Outcomes in patients with Child-Pugh B HCC treated with atezolizumab-bevacizumab. *Journal of Hepatology.* 2022;77(4):896–907.

European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. *Journal of Hepatology.* 2018;69(1):182–236.

Ferrara N, Gerber HP, LeCouter J. The biology of VEGF and its receptors. *Nature Medicine.* 2003;9(6):669–676.

Finn RS, *et al*. Lenvatinib vs. sorafenib in first-line treatment of unresectable HCC. *Journal of Clinical Oncology.* 2020;38(15):193–202.

Finn RS, Qin S, Ikeda M, *et al*. Atezolizumab plus Bevacizumab in unresectable hepatocellular carcinoma. *The New England Journal of Medicine.* 2020; 382(20):1894–1905.

Genentech. Tecentriq (atezolizumab) prescribing information. 2020.

Harding JJ, *et al*. Biomarker landscape for HCC treated with immunotherapy. JCO Precision Oncology. 2019;3:PO.18.00206.

Heimbach JK, *et al*. Endoscopic screening recommendations before systemic therapy in HCC. Hepatology. 2020;72(1):289–290.

Kelley RK, *et al*. Durvalumab–tremelimumab STRIDE regimen in HCC: HIMALAYA trial. *Journal of Clinical Oncology.* 2023;41(9):1898–1907.

Kudo M, *et al*. IMbrave050 trial: Adjuvant use of atezolizumab and bevacizumab. *Journal of Clinical Oncology.* 2023;41(Suppl 4):327.

Kudo M, *et al*. Safety profile of atezolizumab plus bevacizumab in unresectable HCC: Global safety update. Liver Cancer.

Marrero JA, *et al*. AASLD guidelines for diagnosis and treatment of HCC. Hepatology. 2018;68(2):723–750.

McGlynn KA, Petrick JL, El-Serag HB. Epidemiology of hepatocellular carcinoma. Hepatology. 2021;73(S1):4–13.

National Comprehensive Cancer Network. NCCN Guidelines for Hepatobiliary Cancers. Version 2.2024.

Reig M, Forner A, Rimola J, *et al*. Real-world implementation of atezolizumab and bevacizumab in advanced HCC. *Journal of Hepatology.* 2021;75(3):670–679.

Sung H, Ferlay J, Siegel RL, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2021;71(3):209–249.

Voron T, Colussi O, Marcheteau E, *et al*. VEGF-A modulates expression of inhibitory checkpoints on CD8+ T cells in tumors. *Journal of Experimental Medicine.* 2015;212(2):139–148.

****