

# In patients with hepatocellular carcinoma (HCC) (P), is Bevacizumab with Atezolizumab (I) more effective than Sorafenib (C) in long-term clinical prognosis (O)?

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## Abstract

Hepatocellular carcinoma (HCC) is the third leading cause of cancer death globally. China contributes to half of the global incidence of liver cancer, with about 70-85% being HCC. Definitive treatment for this condition would be surgical resection with liver transplant but for obvious reasons, the majority of affected patients are unable to meet the necessary criteria. Sorafenib is a form of chemotherapy that has been the mainstay treatment of HCC since its approval in 2007. More recently, the combination of Bevacizumab and Atezolizumab has shown greater efficacy in the treatment of unresectable HCC. Additionally, this new combination therapy shows favorable results in terms of long-term adverse effects. However, on an economic standpoint, the cost of long-term therapy may hinder its progression towards mainstay treatment.

## Introduction

- Sorafenib is a multikinase inhibitor associated with tumor cell proliferation and blood supply
- Bevacizumab is a selective VEGF inhibitor which demonstrates a more potent inhibitory effect on tumor angiogenesis than Sorafenib
- Atezolizumab is a checkpoint inhibitor of PDL1, which plays a role in T-cell suppression
- The combination of targeted therapy (Beverizumab) and checkpoint inhibition (Atezolizumab) has shown promising results through the IMbrave150 trials

## Methods

- A literature search was conducted via Pubmed and EBSCO on January, 2022.
  - “adults AND hepatocellular carcinoma AND bevacizumab”
- A total of six articles were chosen based on the following criteria
  - Publication within the past 5 years
  - Appropriate adjuvant therapy (Atezolizumab)
  - Randomized-Controlled Trial with intent-to-treat population
  - Access to the full-text article

## Results

- Cheng A-L, Qin S, Ikeda M, et al. Updated efficacy and safety data from IMBRAVE150: Atezolizumab plus bevacizumab vs. Sorafenib for unresectable hepatocellular carcinoma. *Journal of Hepatology*. 2021;76(4):862-873. doi:10.1016/j.jhep.2021.11.030
  - RCT of 501 patients designed to test the efficacy of Bevacizumab with Atezolizumab in the treatment of unresectable HCC when compared to Sorafenib (First-line)
- Finn RS, Qin S, Ikeda M, et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. *N Engl J Med*. 2020;382(20):1894-1905. doi:10.1056/NEJMoa1915745
  - RCT of 336 patients designed to test the efficacy of Bevacizumab with Atezolizumab in the treatment of unresectable HCC when compared to Sorafenib (First-line)
- Li D, Toh H, Merle P, et al. O-8 Atezolizumab + bevacizumab vs sorafenib for unresectable hepatocellular carcinoma: Results from older adults enrolled in IMbrave150. *Annals of Oncology*. 2020;31:234. doi:10.1016/j.annonc.2020.04.061
  - RCT of 252 patients designed to test the efficacy of Bevacizumab with Atezolizumab in the treatment of unresectable HCC when compared to Sorafenib (First-line)
- Qin S, Ren Z, Feng Y-H, et al. Atezolizumab plus bevacizumab versus sorafenib in the Chinese subpopulation with unresectable hepatocellular carcinoma: Phase 3 randomized, open-label IMBRAVE150 Study. *Liver Cancer*. 2021;10(4):296-308. doi:10.1159/000513486
  - RCT of 194 patients designed to test the efficacy of Bevacizumab with Atezolizumab in the treatment of unresectable HCC when compared to Sorafenib (First-line)
- Su D, Wu B, Shi L. Cost-effectiveness of Atezolizumab Plus Bevacizumab vs Sorafenib as First-Line Treatment of Unresectable Hepatocellular Carcinoma. *JAMA Netw Open*. 2021;4(2):e210037. doi:10.1001/jamanetworkopen.2021.0037
  - Partitioned survival model of 501 patients designed to test the cost-effectiveness of Bevacizumab with Atezolizumab in the treatment of unresectable HCC when compared to Sorafenib (First-line)

## Discussion

- Findings
  - 4/4 Studies concluded that Atezolizumab plus Bevacizumab therapy has greater efficacy than Sorafenib in the treatment of patients with unresectable HCC
  - The partitioned survival model concluded that Atezolizumab plus Bevacizumab therapy is not a cost-effective option when compared with Sorafenib in the treatment of patients with unresectable HCC
- Strengths
  - Blinded, independent review of imaging to prevent bias
  - Longevity of trials (12-28 months)
- Limitations
  - Open-label study design, lack of placebo infusions
  - Consistent patient population (Severity of HCC, comorbidities)
- Future Implications
  - Further cost-effective analysis
  - 5-Year survival rate follow-up

## Conclusion

- The research concluded that Atezolizumab and Bevacizumab demonstrated greater efficacy in terms of overall survival rate, safety profile, and secondary patient-reported outcomes
- However, the cost-effective analysis of both treatment arms demonstrated that Atezolizumab and Bevacizumab is not an economically sustainable option when compared with Sorafenib
- Potential future research include 3-5 year follow-up status post treatment and further cost-effective analysis as prices may be subjected to change
- Overall, if costs favor Bevacizumab and Atezolizumab in the future, it may serve as the new mainstay treatment for HCC.

	Sample Size (n)	Baseline Status	Control	Outcome Measures
Cheng et al	501	Systemic treatment-naive, U-HCC	Sorafenib	ORR, OSR, SP, SPRO
Finn et al.	336	Systemic treatment-naive, U-HCC	Sorafenib	OSR, SP, SPRO
Li et al.	252	Systemic treatment-naive, U-HCC	Sorafenib	OSR, SP, SPRO
Qin et al.	194	Systemic treatment-naive, U-HCC	Sorafenib	ORR, OSR, SP, SPRO
Su et al.	501	Systemic treatment-naive, U-HCC	N/A	QALY, ICUR, NHB, NMB

U-HCC: Unresectable hepatocellular carcinoma, ORR: Objective Response Rate, OSR: Overall Survival Rate, SP: Safety Profile, SPRO: Secondary Reported Patient Outcome, QALY: Quality Adjusted Life Years, ICUR: Incremental Cost-Utility Ratio, NHB: Net Health Benefits, NMB: Net Monetary Benefits