LEVIATHAN

2ND LINE TREATMENT POST ATEZOLIZUMAB + BEVACIZUMAB FOR HCC:
A quick reference on key findings and clinical impact

PUBLICATION SNAPSHOT

Lenvatinib versus sorafenib as second-line treatment post atezolizumab plus bevacizumab for hepatocellular carcinoma: the LEVIATHAN study[1]

A multicentre, observational study

Key eligibility criteria

Patients with HCC who received 1st line atezolizumab + bevacizumab (A+B)

- Progression on or discontinuation of A+B
- Child-Pugh liver class A
- ECOG PS ≤2
- No locoregional therapies during or between treatment lines
- No prior CTLA-4 inhibitors

2nd line treatment

Lenvatinib
(N = 125)
Dosed per REFLECT trial guidelines[2]

Sorafenib
(N = 105)
Dosed per SHARP trial guidelines[3]

Endpoints[a]

- mOS and mPFS from 2nd line start
- OS from the start of A+B
- Disease control rate
- Exploratory subgroup analyses by primary vs secondary resistance to A+B

LEVIATHAN met its endpoints in survival outcomes

After a median follow-up of 29.5 months, **lenvatinib** was associated with **superior survival outcomes** compared to **sorafenib**

Lenvatinib maintained a **consistent benefit** in the propensity score–matched cohort, compared to **sorafenib**

mPFS	mOS	mOS From the start of A+B
5.5 mo	11.9 mo	22.4 mo
vs	vs	vs
2.6 mo	7.4 mo	14.3 mo
HR 0.41, p < 0.001	HR 0.67, p = 0.018	HR 0.51, p < 0.001

Understanding LEVIATHAN in clinical context

Although the approval of **1st line IO-based therapies** has transformed HCC treatment, **patients who progress** on these therapies remain **without established 2nd line treatment options**

LEVIATHAN aims to close this gap in 2nd line by advancing **understanding of how to optimise treatment** after intolerance or progression to atezolizumab + bevacizumab in 1st line

Not all TKIs are equal when it comes to treatment **after** progression or discontinuation on **atezolizumab + bevacizumab** 1st line

STUDY LIMITATIONS

- Observational
- Not randomised

Further studies are needed

- To validate current observations
- Including other VEGFR-targeting multikinase inhibitors
- To identify predictive biomarkers

KEY CLINICAL TAKEAWAYS

Lenvatinib showed **improved overall survival** compared with sorafenib when used as a 2nd line treatment **after disease progression on A+B**

The **advantages persisted** after **propensity score matching** and in patients with **primary resistance** to IO-based therapy, challenging the assumption of **TKIs equivalence**

LEVIATHAN supports **lenvatinib** as a **more effective 2nd line option** than **sorafenib** following **atezolizumab + bevacizumab** in unresectable HCC, including patients with primary resistance to immunotherapy

[a] To reduce bias and balance prognostic factors, a propensity score–matched analysis was performed, incorporating ECOG status, AFP level, neutrophil-to-lymphocyte ratio, portal vein thrombosis, and type of resistance to 1st line A+B

1. Lombardi P, et al. JHEP Reports. 2025: 101595; 2. Kudo M, et al. Lancet. 2018;391:1163-1173; 3. Llovet JM, et al. N Engl J Med. 2008;359:378-390;

AFP, alpha-fetoprotein; A+B, atezolizumab + bevacizumab; CTLA-4, cytotoxic T-lymphocyte–associated protein 4; ECOG PS, Eastern Cooperative Oncology Group performance status; HCC, hepatocellular carcinoma; HR, hazard ratio; IO, immuno-oncology; mo, months; mOS, median overall survival; mPFS, median progression-free survival; OS, overall survival; TKI, tyrosine kinase inhibitor; VEGFR, vascular endothelial growth factor receptor;

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