Lenvatinib

- Comparison of survival benefit and safety profile between lenvatinib and donafenib as conversion therapy in patients with hepatocellular carcinoma
- Stereotactic body radiotherapy versus lenvatinib for hepatocellular carcinoma with portal vein tumor thrombosis: a propensity matching score analysis
- Stereotactic Body Radiotherapy Combined With Lenvatinib With or Without PD-1 Inhibitors as Initial Treatment for Unresectable Hepatocellular Carcinoma
- Convexal subarachnoid haemorrhage in a patient under pembrolizumab-lenvatinib combination therapy
- Lenvatinib with or without stereotactic body radiotherapy for hepatocellular carcinoma with portal vein tumor thrombosis: a retrospective study
- Comparison of stereotactic body radiotherapy with and without lenvatinib for advanced hepatocellular carcinoma: a propensity score analysis
- Lenvatinib or anti-VEGF in combination with anti-PD-1 differentially augments antitumor activity in melanoma
- Posterior Reversible Encephalopathy Syndrome after Lenvatinib Therapy in a Patient with Olfactory Neuroblastoma

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While lenvatinib is primarily used in systemic oncology (especially hepatocellular carcinoma, thyroid cancer, and renal cell carcinoma), it has limited but growing relevance in neurosurgery, particularly in the context of neuro-oncology.

 Potential Neurosurgical Applications 1. Brain Metastases Management Lenvatinib, often in combination with immune checkpoint inhibitors (e.g., pembrolizumab), is being explored in patients with brain metastases, especially from renal cell carcinoma or thyroid cancer.

In cases where metastases are not amenable to surgery or radiosurgery, lenvatinib may serve as adjunct systemic therapy to stabilize extracranial disease or reduce intracranial burden.

2. Anaplastic Thyroid Cancer (ATC) with CNS Involvement Lenvatinib has shown modest efficacy in ATC, a highly aggressive tumor that can invade the skull base or metastasize to the brain.

For neurosurgeons dealing with skull base erosion or cord compression from ATC, systemic control with lenvatinib may complement decompressive surgery.

3. Glioblastoma (GBM) – Experimental Role Lenvatinib has been tested in early-phase trials for recurrent GBM due to its anti-angiogenic profile (VEGFR inhibition).

So far, the results are limited and inconclusive, and it is not part of standard GBM protocols.

⚠ Considerations for Neurosurgeons High risk of hypertension, hemorrhage, and wound healing complications—important in the perioperative context.

Should be discontinued before surgery and reintroduced with caution postoperatively.

Watch for tumor necrosis or hemorrhage when used preoperatively.

 Takeaway Message Lenvatinib is not a neurosurgical drug, but neurosurgeons should be aware of its

use in systemic management of cancers with CNS involvement or skull base extension. Coordination with oncology is essential when planning surgery in patients receiving lenvatinib.

Retrospective comparative cohort studies

In a retrospective comparative cohort study, Hou et al. [1)] published in the American Journal of Translational Research, the authors—affiliated with the Department of Oncology, Department of Gynaecology and Obstetrics, and Department of Neurosurgery at Shijiazhuang People's Hospital (Hebei, China), as well as Beijing Water Conservancy Hospital—compared the survival benefit and safety profile of lenvatinib versus donafenib as conversion therapy in patients with hepatocellular carcinoma (HCC) at China National Liver Cancer (CNLC) stages I–III.

Lenvatinib demonstrated significantly superior survival outcomes—both in overall survival and progression-free survival—compared to donafenib. It also showed better tolerability, with fewer grade ≥3 adverse events.

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 1. Study Design: Retrospective = Weak Evidence

This is yet another retrospective single-center analysis, plagued by inherent biases—selection, reporting, and confounding—that no amount of statistical massaging can resolve. No randomization, no blinding, and no control for treatment timing or physician discretion. In oncology, where treatment nuances matter, such designs should be considered hypothesis-generating at best, not guidance for clinical practice.

 2. Sample Size: Statistically Thin, Clinically Hollow

The study included only 76 patients (40 lenvatinib vs. 36 donafenib). Such a low-powered cohort raises major concerns:

PFS difference (4.6 vs. 2.9 months), though statistically significant, is barely clinically relevant.

ORR difference (15% vs. 5.6%) is not even statistically significant (P=0.551) — but still emphasized in the discussion as if it mattered.

Multivariate analysis with such a small dataset is mathematically questionable and likely overfitted.

 3. Conversion Therapy? Or Rebranding a Failure?

The term “conversion therapy” is misleading here. These drugs were administered in the hope of downstaging HCC — yet no actual conversion to surgery or local treatment is reported. The authors exploit a term that evokes curative intent without backing it up. This is not conversion therapy — it's systemic palliation repackaged in euphemism.

 4. Outcome Inflation: OS vs. PFS Discrepancy

While OS doubled (14.9 vs. 7.9 months, P=0.010), PFS barely improved by 6 weeks (4.6 vs. 2.9 months). This disparity suggests that post-progression treatments may have confounded OS — but the study gives no data on subsequent lines of therapy, making the OS benefit unverifiable and potentially misleading.

⚠ 5. Safety Reporting: Cherry-Picking by Omission

The claim that lenvatinib is “more tolerated” is based on selective listing of fewer grade ≥3 events. But the paper:

Doesn’t define how adverse events were graded.

Doesn’t give the absolute rates of common toxicities (hypertension, proteinuria).

Doesn’t report dose adjustments, interruptions, or treatment duration.

This paints an incomplete and biased picture of safety — likely underpowered to detect real toxicity differences.

 6. Biomarker Analysis: Statistical Necromancy

Hazard ratios for AFP and hepatic vein invasion are presented as independent prognostic factors. However, these are well-established predictors and add nothing novel to the study. Worse: interpreting these from a cohort of 76 patients with multiple covariates is statistical overreach bordering on negligence.

 7. Institutional Echo Chamber

All four departments involved belong to one hospital. No external validation, no multicenter inclusion. The study reflects local practice, local bias, and perhaps local drug availability policies — not generalizable conclusions for global hepatology or oncology communities.

 Final Verdict

This is a fragile, underpowered, and poorly contextualized study that tries to extract clinical meaning from statistical noise. It overstates the benefits of lenvatinib, mislabels its purpose as “conversion therapy,” and cherry-picks safety data — all wrapped in the false authority of multivariate modeling over 76 patients.

Calling this “evidence” is dangerous.

Using it to guide therapy is reckless.

 Takeaway Message from the Study for a Neurosurgeon

Although this study focuses on systemic therapy for hepatocellular carcinoma (HCC), a neurosurgeon—especially one involved in neuro-oncology or metastatic brain disease—can extract the following key message:

Systemic therapies like lenvatinib may extend survival modestly in solid tumors such as HCC, but their actual impact on neurosurgical decision-making (e.g., eligibility for resection of brain metastases

or control of neurological symptoms) remains indirect, unmeasured, and largely speculative.

⚠ Critical Insight: The study uses the term “conversion therapy” without demonstrating any actual conversion to surgery, which is a red flag for neurosurgeons who base treatment on resectability and local disease control.

Such papers illustrate the growing pressure to rebrand palliative systemic treatments as potentially curative, despite limited supporting evidence—highlighting the need for neurosurgeons to remain critical readers and decision-makers when systemic therapies are proposed in multidisciplinary settings.

Case reports

A 57-year-old man presented with seizures. Until the seizure onset, he had been treated for thyroid cancer and its metastasis to the thoracic vertebral body with the multi-receptor tyrosine kinase inhibitor (RTK) lenvatinib for 4 years. MRI revealed a slightly high intensity lesion in the left frontal base area on T2-weighted or fluid-attenuated inversion recovery (FLAIR) images, and the lesion showed only faint enhancement on T1-weighted images after gadolinium administration. Total resection was performed and the histopathological diagnosis was glioblastoma. However, grade IV histology was observed in only a limited area, and the majority of the specimen showed lower grade histology with moderate vascularization that lacked microvascular proliferation.

Lenvatinib, which is anti-angiogenic, might have affected the radiological characteristics, as well as the pathology of the tumor. Brain tumors arising during treatment with RTKs for other cancers could show atypical imaging findings [2].

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Hou Y, Gao Z, Han Y, Liu C, Su X, Zhang D. Comparison of survival benefit and safety profile between lenvatinib and donafenib as conversion therapy in patients with hepatocellular carcinoma. Am J Transl Res. 2025 May 15;17(5):3496–3504. doi: 10.62347/PBLA2928. PMID: 40535653; PMCID: PMC12170375.
2)
Arai N, Sasaki H, Tamura R, Obara K, Yoshida K. Unusual magnetic resonance imaging findings of a glioblastoma arising during treatment with lenvatinib for thyroid cancer. World Neurosurg. 2017 Aug 10. pii: S1878-8750(17)31314-1. doi: 10.1016/j.wneu.2017.08.017. [Epub ahead of print] PubMed PMID: 28804045.