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Unlocking Hope: Anti-VEGFR inhibitors and their potential in glioblastoma treatment

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HIGHLIGHTS

- *VEGFR* plays a fundamental role in Glioblastoma Multiforme (GBM) angiogenesis.
- *VEGFR* mutations and increased expression are often found in GBM and are correlated with tumor grade.
- Anti-VEGFR TKIs produced moderate outcomes in treating GBM patients.
- Multiple adjustments can be made to enhance the efficacy of anti-VEGFR TKIs.

ABSTRACT

Purpose

This systematic review summarizes evidence of VEGFR gene mutations and VEGF/VEGFR protein expression in glioblastoma multiforme (GBM) patients, alongside the efficacy and safety of anti-VEGFR tyrosine kinase inhibitors (TKIs) for GBM treatment.

Methods

A comprehensive literature review was conducted using PubMed up to August 2023. Boolean operators and MeSH term "glioma," along with specific VEGFR-related keywords, were utilized following thorough examination of existing literature.

Results

VEGFR correlates with glioma grade and GBM progression, presenting a viable therapeutic target. Regorafenib and axitinib show promise among studied TKIs. Other multi-targeted TKIs (MTKI) and combination therapies exhibit potential, albeit limited by blood-brain barrier penetration and toxicity. Combining treatments like radiotherapy and enhancing BBB penetration may benefit patients. Further research is warranted in patient quality of life and biomarker-guided selection.

Conclusion

While certain therapies hold promise for GBM, future research should prioritize personalized medicine and innovative strategies for improved treatment outcomes.

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INTRODUCTION

Glioblastoma multiforme (GBM) is a primary malignant brain cancer that occurs in all parts of the central nervous system, affecting mostly the brain, especially the frontal and temporal lobes (Larjavaara et al., 2007, Davis, 2016). While the incidence of glioblastoma increases with age, it mostly occurs in older adults and in males (Ostrom et al., 2013). Glioblastomas were previously classified as primary or secondary. The new classification is based on the IDH mutation status in the tumor,...

MATERIALS AND METHODS

Using the PubMed database until August 2023, a complete review of the literature was undertaken. Using Boolean operators, the MeSH term ‘glioma’, and the keywords “glioblastoma”, “VEGFR”, “axitinib”, “regorafenib”, “sorafenib”, “pazopanib”, “cabozantinib”, “cediranib”, “sunitinib”, “vandetanib”, “tivozanib”, “vatalanib”, “aee788”, and “nintedanib” were used after a thorough study of the existing literature to identify the anti-VEGFR TKIs relevant to glioblastoma.

Overall, 513 papers were...

Glioblastoma and the VEGF pathway

VEGFRs represent prototypical tyrosine kinase receptors (RTKs) that encompass essential components, including an extracellular segment responsible for ligand recognition, a transmembrane segment, and an intracellular domain that contains a tyrosine kinase domain (Shibuya, 1995). VEGFR receptors are divided into 3 types, each binding to different sets of ligands: VEGFR1 that binds VEGFA, VEGFB, and PlGF; VEGFR2 that also binds VEGFA in addition to VEGFE, VEGFC, and VEGFD; and finally, VEGFR3...

DISCUSSION

Glioblastoma multiforme is a primary malignant tumor that targets the central nervous system and especially the brain. Its angiogenesis, which fuels its growth, may or may not be linked to hypoxia.

The goal of this review was to identify the most promising tyrosine kinase inhibitors in the treatment of glioblastoma multiforme while determining the most effective strategies to pair TKIs with other interventions.

Extensive research has actively demonstrated the validity of targeting VEGFR in GBM,...

CONCLUSION

GBM is an aggressive primary malignant tumor with limited treatment options, with angiogenesis as an important factor fueling its growth. Numerous research projects have explored TKIs, especially those targeting angiogenesis and VEGFRs. Regorafenib and axitinib have shown clinical promise, with regorafenib demonstrating improved survival and safety. Ongoing phase III trials for regorafenib hold promise. Approaches to enhance therapy success are also being developed, such as using personalized...

Conflict of interest statement

The authors declare no conflicts of interest....

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