ABSTRACT

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Efficacy of Anti-VEGF Drugs Based Combination Therapies in Recurrent Glioblastoma: Systematic Review and Meta-Analysis.

Solipuram V(1), Soltani R(2), Venkatesulu BP(3)(4), Annam S(5), Alavian F(6), Ghasemi S(2).

Author information:
(1)Department of Medicine, Saint Agnes Hospital, Baltimore, MD, USA.
(2)Cellular and Molecular Research Center, Basic Health Sciences Institute, Shahrekord University of Medical Sciences, Shahrekord, Iran.
(3)Department of Radiation Oncology, Loyola University Stritch School of medicine, Chicago, IL, USA.
(4)Edward Hines VA Hospital, Chicago, IL, USA.
(5)Osmania Medical College, Hyderabad, Telangana, India.
(6)Department of Biology, School of Basic Sciences, Farhangian University, Tehran, Iran.

BACKGROUND: Recurrent glioblastoma multiforme (rGBM) has a grim prognosis with current therapies offering no survival benefit. Several combination therapies involving anti-VEGF agents have been studied with mixed results.

METHODS: A systematic search was performed using five electronic databases: PubMed, Scopus, ISI, Embase, and the Cochrane Library without language limitations. The primary outcome of interest was progression free survival (PFS). Secondary outcomes were overall survival (OS), objective response ratio (ORR), and grade ≥ 3 adverse events. Estimates for PFS, OS were calculated as random effects hazard ratio (HR) with 95% confidence intervals (CIs) using the generic inverse variance method. Estimates for ORR, grade ≥ 3 adverse events were calculated using a random-effects risk ratio (RR) with 95% confidence intervals (CIs) using the Mantel-Haenszel method.

RESULTS: Thirteen studies met the inclusion criteria and a total of 1994 patients have been included in the analysis. There was no statistically significant improvement in PFS (HR 0.84; 95% CI (0.68, 1.03); I2=81%), OS (HR 0.99; 95% CI (0.88, 1.12); I2=0%), ORR (RR 1.36; 95% CI (0.96, 1.92); I2=61%) in the combination therapy group when compared to the control group. Significantly higher grade ≥ 3 adverse events (RR 1.30; 95% CI (1.14, 1.48); I2=47%) were seen in the combination therapy when compared to the control group.

CONCLUSION: Our analysis showed that the use of combination therapy with anti-VEGF agents did not offer any benefit in PFS, OS, or ORR. In contrast, it had significantly higher grade 3-5 adverse events. Further studies are needed to identify effective therapies in rGBM that can improve survival.

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