Enzastaurin is a selective serine/threonine protein kinase inhibitor of protein kinase C (PKC). These PKC enzymes are responsible for tumor growth, proliferation, and apoptosis. Enzastaurin disrupts phosphotransferase activity of PKC isoforms via an interaction at the ATP binding site. Inhibition of this pathway by enzastaurin blocks tumor angiogenesis and growth.

In a phase II trial, Butowski et al. subjected 66 patients with newly diagnosed GBM to receive standard radiochemotherapy with TMZ with enzastaurin given once daily during RT and in the adjuvant period at 250 mg/day without dose modifications. The primary endpoint was OS. Median OS was 17.1 months, slightly more favorable than the standard treatment and median PFS was 9 months. The most common grade 3/4 adverse event was lymphopenia noted in 39.4% patients.

In another trial, enzastaurin was delivered before and concomitant with radiation therapy, followed by enzastaurin maintenance therapy in newly diagnosed GBM patients without MGMT promoter hyper-methylation. The primary endpoint was PFS at 6 months of at least 55%. However, the trial reported 53.6% PFS at 6 months (95% CI: 39.865.6) and median OS of 15.0 months (95% CI: 11.917.9) for all patients [1)].

1)
Mallick S, Gandhi AK, Rath GK. Therapeutic approach beyond conventional temozolomide for newly diagnosed glioblastoma: Review of the present evidence and future direction. Indian J Med Paediatr Oncol. 2015 Oct-Dec;36(4):229-37. doi: 10.4103/0971-5851.171543. Review. PubMed PMID: 26811592; PubMed Central PMCID: PMC4711221.