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## Phase I/II Trial Erlotinib and Temozolomide With Radiation Therapy in the Treatment of Newly Diagnosed Glioblastoma Multiforme: North Central Cancer Treatment Group Study N0177

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**Purpose:** Epidermal growth factor receptor (*EGFR*) amplification in glioblastoma multiforme (GBM) is a common occurrence and is associated with treatment resistance. Erlotinib, a selective *EGFR* inhibitor, was combined with temozolomide (TMZ) and radiotherapy (RT) in a phase I/II trial.

**Patients and Methods:** Adults not taking enzyme-inducing anticonvulsants after resection or biopsy of GBM were treated with erlotinib (150 mg daily) until progression. Erlotinib was delivered alone for 1 week, then concurrently with TMZ (75 mg/m<sup>2</sup> daily) and RT (60 Gy), and finally, concurrently with up to six cycles of adjuvant TMZ (200 mg/m<sup>2</sup> daily for 5 days every 28 days). The primary end point was survival at 1 year.

**Results:** Ninety-seven eligible patients were accrued with a median follow-up time of 22.2 months. By definition, the primary end point was successfully met with a median survival time of 15.3 months. However, there was no sign of benefit in overall survival when comparing N0177 with the RT/TMZ arm of the European Organisation for Research and Treatment of Cancer/National Cancer Institute of Canada trial 26981/22981 (recursive partitioning analysis [RPA] class III, 19 v 21 months; RPA class IV, 16 v 16 months; RPA class V, 8 v 10 months, respectively). Presence of diarrhea, rash, and *EGFRvIII*, *p53*, phosphatase and tensin homolog (*PTEN*), combination *EGFR* and *PTEN*, and *EGFR* amplification status were not predictive ( $P > .05$ ) of survival.

**Conclusion:** Although the primary end point was successfully met using nitrosourea-based (pre-TMZ) chemotherapy era historic controls, there was no sign of benefit compared with TMZ era controls. Analyses of molecular subsets did not reveal cohorts of patients sensitive to erlotinib. TMZ chemotherapy combined with RT resulted in improved outcomes

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compared with historical controls who received nitrosourea-based chemotherapies.

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