

New Approaches to Brain Tumor Therapy CNS Consortium, Baltimore, MD.

**PURPOSE:** Recent data suggest that the glutamatergic system is important in the proliferation and migration of glioblastoma. Talampanel is a well-tolerated, oral alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor blocker that could be beneficial in this disease. **PATIENTS AND METHODS:** This trial was designed to estimate overall survival in adults with newly diagnosed glioblastoma treated with talampanel in addition to standard radiation (RT) and temozolomide (TMZ). A secondary purpose was to evaluate talampanel toxicity in this setting. Talampanel was initiated with RT + TMZ and discontinued for toxicity or disease progression. Survival was compared with historical controls. **RESULTS:** Seventy-two patients were enrolled from December 2005 to July 2006. Their median age was 60 years (range, 37 to 85 years, with 17% > 70 years), median Karnofsky performance score was 90 (range, 70 to 100), and 77% had a debulking procedure. With a median follow-up time of 18 months, 55 patients (76%) have died, yielding a median survival time of 18.3 months (95% CI, 14.6 to 22.5 months). When the 60 patients who were 18 to 70 years old were compared with the European Organisation for Research and Treatment of Cancer (EORTC) RT + TMZ data, the median survival (20.3 v 14.6 months, respectively) and percentage of patients surviving at 24 months (41.7% v 26.5%, respectively; P = .02) seemed superior. The percentage of patients methylated at O(6)-methylguanine-DNA methyltransferase was lower than on the EORTC study (29% v 43%, respectively). Talampanel was well tolerated and did not increase the known hematologic or nonhematologic toxicities of TMZ. **CONCLUSION:** Talampanel can be added to RT + TMZ without significant additional toxicity. The encouraging survival results in methylated and unmethylated patients suggest that blocking AMPA receptors may be a useful strategy in newly diagnosed glioblastoma.

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