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NRG-BN002: Phase I Study of Ipilimumab, Nivolumab, and the Combination in Patients with Newly Diagnosed GBM

Andrew E Sloan [1 2], Kathryn Winter [3 4], Mark R Gilbert [5], Kenneth Aldape [5], Serah Choi [2], Patrick Y Wen [6], Nicholas Butowski [7], Fabio M Iwamoto [8], Raju R Raval [9], Alfredo D Voloschin [10], Carlos Kamiya-Matsuoka [11], Minhee Won [2 3], Minesh P Mehta [12]

Affiliations

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Abstract

Background: Immune checkpoint inhibitors (ICIs) have efficacy in several solid tumors but limited efficacy in glioblastoma (GBM). This study evaluated the safety of anti-CTLA-4 and anti-PD-1 ICIs alone or in combination in newly diagnosed GBM after completion of standard radiochemotherapy with the subsequent intent to test combinatorial ICIs in this setting.

Methods: The primary endpoint was dose limiting toxicity (DLT) for adults with unifocal, supratentorial newly diagnosed GBM after resection and chemoradiation. Ipilimumab and nivolumab were tested separately and in combination with a planned expansion cohort dependent upon DLT results.

Results: Thirty-two patients were enrolled at 9 institutions; 6 to each DLT assessment cohort and 14 to the expansion cohort. Median age: 55 years, 67.7% male, 83.9% white. Treatment was well tolerated with a 16% Grade 4 events; the combination did not have unexpectedly increased toxicity, with no Grade 5 events. One DLT was seen in each single-agent treatment; none were observed in the combination, leading to expanded accrual of the combined treatment. Median follow-up was 19.6 mo. For all patients receiving combination treatment, median overall survival (OS) and progression-free survival (PFS) were 20.7 mo. and 16.1 mo., respectively.

Conclusions: IPI and NIVO are safe and tolerable with toxicities similar to those noted with other cancers when given in combination with adjuvant TMZ for newly diagnosed GBM. Combination IPI+NIVO is not substantially more toxic than single agents. These results support a subsequent efficacy trial to test the combination of ICIs in a phase II/III for patients with newly diagnosed GBM.

Keywords: GBM; Immune checkpoint Inhibitor; Ipilimumab; Nivolumab; Phase I.

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