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Phase 2 Study of Radiation Therapy Plus Low Dose Temozolomide Followed by Temozolomide and Irinotecan for Glioblastoma: NRG Oncology RTOG Trial 0420.

[Lieberman FS](#)¹, [Wang M](#)², [Robins HJ](#)³, [Tsien CI](#)⁴, [Curran WJ Jr](#)⁵, [Werner-Wasik M](#)⁶, [Smith RP](#)⁷, [Schultz C](#)⁸, [Hartford AC](#)⁹, [Zhang P](#)¹⁰, [Mehta MP](#)¹¹.

- 1 University of Pittsburgh Medical Center, University of Pittsburgh Physicians, Department of Neurology, Department of Medicine, Pittsburgh, PA. Electronic address: liebermanf@upmc.edu.
- 2 Merck & Co.
- 3 University of Wisconsin, Madison, WI.
- 4 Washington University School of Medicine, St. Louis, MO.
- 5 Emory University, Atlanta, GA.
- 6 Thomas Jefferson University Hospital, Philadelphia, PA.
- 7 University of Pittsburgh UPMC Shadyside, Pittsburgh, PA.
- 8 Medical College of Wisconsin, Milwaukee, MI.
- 9 Dartmouth-Hitchcock Medical Center, Lebanon, NH.
- 10 NRG Oncology Statistics and Data Management Center - American College of Radiology, Philadelphia, PA.
- 11 University of Maryland Medical Systems, Baltimore, MD (during trial) - Miami Cancer Institute, Coral Gables, FL (current).

PURPOSE: Evaluate the toxicity and efficacy of adjuvant temozolomide (TMZ) and irinotecan (CPT-11) for 12 months following concurrent chemo-radiation in newly diagnosed glioblastoma (GBM).

METHODS: Trial XXXX, a single arm, multi-institutional phase 2 trial was designed to determine the efficacy and toxicity of concomitant TMZ and radiation (RT) followed by adjuvant TMZ combined with CPT-11 given for 12 cycles compared to historical controls of adjuvant TMZ alone given for 6 cycles.

RESULTS: A total of 170 patients were enrolled, of which 152 were eligible. Adjuvant CPT-11 combined with TMZ was more toxic than expected. A higher rate of hematologic and gastrointestinal toxicities was most frequently noted with the combination regimen compared to adjuvant TMZ alone. Grade 3/4 hematologic toxicity was 38% compared to 14% reported in the Stupp trial. Following an early interim analysis, adjuvant CPT-11 dose was reduced to 100 mg/m² D1 and D15 for the first cycle. CPT-11 dose escalation proceeded over first 3 cycles if tolerated.

Median overall survival (OS) for all eligible patients was 16.9 months compared to 13.7 months of the historical control ($p=0.03$). Post-hoc subgroup analysis suggested an improvement in OS for patients with RTOG recursive partitioning analysis (RPA) Class III although limited to 22 patients (14% of eligible patients).

CONCLUSIONS: Although Irinotecan and TMZ for 12 cycles given after chemoradiation for patients with newly diagnosed GBM significantly improved median survival compared to historical control data at the time the study was conducted, the historical control median survival time of 13.7 months does not represent the current benchmark for this patient population. Treatment intensification does prolong overall survival compared to the current standard.

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