A Pilot Safety Study of Lenalidomide and Radiotherapy for Patients with Newly Diagnosed Glioblastoma Multiforme

Jan Drappatz M.D., Eric T. Wong M.D., David Schiff M.D., Santosh Kesari M.D., Ph.D., Tracy T. Batchelor M.D., M.P.H., Lisa Doherty, Debra Conrad LaFrankie, Naren Ramakrishna M.D., Ph.D., Stephanie Weiss M.D., Sharon T. Smith, Abigail Ciampa, Jennifer Zimmerman, Louis Ostrowsky, Karly David, Andrew Norden M.D., Loretta Barron, Christine Sceppa, Peter M. Black M.D., Ph.D. and Patrick Y. Wen M.D.

Department of Neurosurgery, Brigham & Women's Hospital, Harvard Medical School, Boston, MA

Pappas Center for Neuro-Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, Boston, MA

Division of Cancer Neurology, Department of Neurology, Brigham & Women's Hospital, Harvard Medical School, Boston, MA, Boston, MA

Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA

Center for Neuro-Oncology, Dana Farber/Brigham & Women's Cancer Center, Dana Farber Cancer Institute, Harvard Medical School, Boston, MA, Boston, MA

Neuro-Oncology Center, Department of Neurology, University of Virginia, Charlottesville, VA

Department of Radiation Oncology, Dana Farber/Brigham and Women's Cancer Center, Harvard Medical School, Boston, MA, Boston, MA


Purpose
To define the maximum tolerated dose (MTD) of lenalidomide, an analogue of thalidomide with enhanced immunomodulatory and antiangiogenic properties and a more favorable toxicity profile, in patients with newly diagnosed glioblastoma multiforme (GBM) when given concurrently with radiotherapy.

Patients and Methods

Patients with newly diagnosed GBM received radiotherapy concurrently with lenalidomide given for 3 weeks followed by a 1-week rest period and continued lenalidomide until tumor progression or unacceptable toxicity. Dose escalation occurred in groups of 6. Determination of the MTD was based on toxicities during the first 12 weeks of therapy. The primary endpoint was toxicity.

Results

Twenty-three patients were enrolled, of whom 20 were treated and evaluable for both toxicity and tumor response and 2 were evaluable for toxicity only. Common toxicities included venous thromboembolic disease, fatigue, and nausea. Dose-limiting toxicities were eosinophilic pneumonitis and transaminase elevations. The MTD for lenalidomide was determined to be 15 mg/m²/d.

Conclusion

The recommended dose for lenalidomide with radiotherapy is 15 mg/m²/d for 3 weeks followed by a 1-week rest period. Venous thromboembolic complications occurred in 4 patients, and prophylactic anticoagulation should be considered.

Author Keywords: Lenalidomide; Glioblastoma; Angiogenesis; Radiotherapy; Immunomodulatory

Note to users: The section "Articles in Press" contains peer reviewed accepted articles to be published in this journal. When the final article is assigned to an issue of the journal, the "Articles in Press" version will be removed from this section and will appear in the associated published journal issue. The date it was first made available online will be carried over. Please be aware that although "Articles in Press" do not have all bibliographic details available yet, they can already be cited using the year of online publication and the DOI as follows: Author(s), Article Title, Journal (Year), DOI. Please consult the journal's reference style for the exact appearance of these elements, abbreviation of journal names and the use of
There are three types of "Articles in Press":

- **Accepted manuscripts**: these are articles that have been peer reviewed and accepted for publication by the Editorial Board. The articles have not yet been copy edited and/or formatted in the journal house style.
- **Uncorrected proofs**: these are copy edited and formatted articles that are not yet finalized and that will be corrected by the authors. Therefore the text could change before final publication.
- **Corrected proofs**: these are articles containing the authors' corrections and may, or may not yet have specific issue and page numbers assigned.