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A multicenter phase I trial of combination therapy with interferon- β and temozolomide for high-grade gliomas (INTEGRA study): the final report.

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Abstract

Our previous study demonstrated that interferon- β markedly enhanced chemosensitivity to temozolomide; one of the major mechanisms is downregulation of O(6)-methylguanine DNA-methyltransferase transcription via p53 induction. This effect was also observed in an experimental animal model. The results of these studies suggest that compared to temozolomide-based chemotherapy performed concomitantly with radiotherapy, chemotherapy with interferon- β and temozolomide and concomitant radiotherapy might further improve the clinical outcomes of patients with malignant gliomas. A multicenter phase I clinical trial-the Integrated Japanese Multicenter Clinical Trial: a Phase I Study of Interferon- β and Temozolomide for Glioma in Combination with Radiotherapy (INTEGRA Study)-was conducted in patients with high-grade gliomas in order to evaluate the safety, feasibility, and preliminary clinical effectiveness of combination therapy with interferon- β and temozolomide. The primary endpoint was the incidence of adverse events. The exploratory endpoints were progression-free survival time and overall survival time. The study population comprised 16 patients with newly diagnosed and 7 patients with recurrent high-grade gliomas. Grades 3-4 leukocytopenia and neutropenia were observed in 6.7 and 13.3% of patients, respectively. Overall, 40% of patients showed an objective response to therapy. In patients with newly diagnosed glioblastoma, the median overall survival time was 17.1 months and the rate of 1-year progression-free survival was 50%. We conclude that this regimen is safe and well tolerated and may prolong survival of patients with glioblastoma. A phase II clinical study is essential to corroborate our findings.

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