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CLINICAL STUDY - PATIENT STUDY

ACNU-based chemotherapy for recurrent glioma in the temozolomide era

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Abstract No standard of care for patients with recurrent glioblastoma has been defined since temozolomide has become the treatment of choice for patients with newly diagnosed glioblastoma. This has renewed interest in the use of nitrosourea-based regimens for patients with progressive or recurrent disease. The most commonly used regimens are carmustine (BCNU) monotherapy or lomustine (CCNU) combined with procarbazine and vincristine (PCV). Here we report our institutional experience with nimustine (ACNU) alone ($n = 14$) or in combination with other agents ($n = 18$) in 32 patients with glioblastoma treated previously with temozolomide. There were no complete and two partial responses. The progression-free survival (PFS) rate at 6 months was 20% and the survival rate at 12 months 26%. Grade III or IV hematological toxicity was observed in 50% of all patients and led to interruption of treatment in 13% of patients. Non-hematological toxicity was moderate to severe and led to interruption of treatment in 9% of patients. Thus, in this cohort of patients pretreated with temozolomide, ACNU failed to induce a substantial stabilization of disease in recurrent glioblastoma, but caused a notable hematotoxicity. This study does not commend ACNU as a therapy of first choice for patients with recurrent glioblastomas pretreated with temozolomide.

Keywords Glioma · Chemotherapy · Nimustine · Recurrence · Temozolomide

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Introduction

The introduction of temozolomide as the standard of care for patients with newly diagnosed glioblastoma [1] has resulted in an increased use of temozolomide as the first chemotherapy of choice for glioma patients in general. Previously, nitrosourea-based regimens had been considered the most active chemotherapy for patients with glioma, although their value had remained controversial [2]. The British Medical Research Council (MRC) trial had failed to demonstrate superior activity of PCV added to radiotherapy compared with radiotherapy alone [3]. The NOA-01 trial of the Neurooncology Working Group of the German Cancer Society as well as two smaller series from Japan had reported very promising median survival data exceeding 16 months using ACNU-based primary radiochemotherapy regimens, but these trials lacked an appropriate control arm [4–6]. A recent meta-analysis also proposed a significant survival gain for ACNU in newly diagnosed high-grade gliomas [7]. The widespread use of temozolomide in patients with newly diagnosed disease, mostly glioblastoma, resulted in a reevaluation of nitrosoureas at progression or recurrence. Larger patient series