JOURNAL ARTICLE

Optimal duration of adjuvant temozolomide in glioblastoma: An unsolved and unsolvable problem

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Extract

The standard treatment of glioblastoma with temozolomide concomitant with irradiation and followed by six cycles of adjuvant temozolomide, as initially described by Stupp et al, has not been replaced by any other treatment in more than 15 years, although it has been adjusted according to various patient characteristics, such as age or O^6-methylguanine-DNA methyltransferase (*MGMT*) promoter methylation status.[1,2] Median survival remains, however, clearly unsatisfactory.

Other treatment regimens have failed to improve outcomes, and some modifications of the standard temozolomide treatment have been investigated. A large phase III study compared standard doses of temozolomide with dose-dense schedules with the aim of reducing the levels of MGMT, the main repair protein of temozolomide DNA damage, and thus diminishing its activity. However, no advantage in progression-free survival (PFS) or overall survival (OS) was observed.[3] Another modification involves prolonging the number of cycles of adjuvant temozolomide to 12 or more, with the aim of increasing the PFS and OS of patients whose disease was controlled by the initial treatment. This approach is feasible due to the mild toxicity profile of temozolomide, as well as to its oral administration, which allows a continued administration without major patient discomfort or side effects, although it does involve a not inconsequential economic impact.

This extension of adjuvant temozolomide has been used in several clinical trials and has also been implemented in clinical practice despite a lack of clear indications of survival benefits. This extended use of adjuvant temozolomide is based not only on its high tolerability but also on the lack of effective rescue treatments and the somewhat arbitrary nature of using only six cycles in the initial study design.

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