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A combined analysis of two prospective randomised studies exploring the impact of extended post-radiation temozolomide on survival outcomes in newly diagnosed glioblastoma

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Abstract

Purpose: The optimal duration of post-radiation temozolomide in newly diagnosed glioblastoma remains unclear, with no published phase III randomised trials. Standard-of-care stipulates 6 months. However, in routine care, it is often extended to 12 months, despite lacking robust supporting data.

Methods: GEINO14-01 (Spain) and EX-TEM (Australia) studies enrolled glioblastoma patients without progression at the end of 6 months post-radiation temozolomide. Participants were randomised 1:1 to six additional months of temozolomide or observation. Primary endpoint was 6-month progression free survival from date of randomisation (6mPFS). Secondary endpoints included overall survival (OS) and toxicity. 204 patients were required to detect an improvement in 6mPFS from 50 to 60% (80% power). Neither study recruited sufficient patients. We performed a combined analysis of individual patient data. Journal instruction requires a city for affiliations; however, these were missing in affiliations [1, 2, 11, 15, 16, 18, 20, 22, 23, 24, 25, 27, 30, 31, 32, 33, 34]. Please verify if the provided city is correct and amend if necessary. **Completed RESULTS:** 205 patients were recruited: 159 in GEINO14-01 (2014-2018) and 46 in EX-TEM (2019-2022). Median follow-up was 20.0 and 14.5 months. Baseline characteristics were balanced. There was no significant improvement in 6mPFS (57.2% vs 64.0%, OR0.75, $p = 0.4$), nor across any subgroups, including MGMT methylated; PFS (HR0.92, $p = 0.59$, median 7.8 vs 9.7 months); or OS (HR1.03, $p = 0.87$, median 20.1 vs 19.4 months). During treatment extension, 64% experienced any grade adverse event, mainly fatigue and gastrointestinal (both 54%). Only a minority required treatment changes: 4.5% dose delay, 7.5% dose reduction, 1.5% temozolomide discontinuation. **As keywords are mandatory for this journal, please provide 3-6 keywords:** glioblastoma; temozolomide; survival **CONCLUSION:** For glioblastoma patients, extending post-radiation temozolomide from 6 to 12 months is well tolerated but does not improve 6mPFS. We could not identify any subset that benefitted from extended treatment. Six months should remain standard-of-care.

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