ABSTRACT

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Tailored therapy for recurrent glioblastoma. Report of a personalized molecular approach.

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BACKGROUND: Failure of clinical trials with targeted therapies in glioblastoma (GBM) is probably related to the enrollment of molecularly unselected patients. In this study we report the results of a precision medicine protocol in recurrent GBM.
METHODS: We prospectively evaluated 34 patients with recurrent GBM. We determined the expression of vascular endothelial growth factor (VEGF), epidermal growth factor receptor variant III (EGFRvIII), and phosphatase and tensin homolog (PTEN). According to the molecular pattern we administered bevacizumab alone in patients with VEGF overexpression, absence of EGFRvIII, and

normal PTEN (group A; n=16); bevacizumab + erlotinib in patients with VEGF overexpression, expression of EGFRvIII, and normal PTEN (group B; n=14); and bevacizumab + sirolimus in patients with VEGF overexpression and loss of PTEN, irrespective of the EGFRvIII status (group C; n=4). We evaluated the response rate, the clinical benefit rate, the 6-month progression-free survival (PFS-6), the 12-month PFS (PFS-12) and the safety profile of the treatment. Moreover we compared our results with the ones of EORTC 26101 trial.
RESULTS: Response rate was 50% in the whole cohort with the highest rate in group C (75%). Clinical benefit rate was 71% with the highest rate in group C (75%). PFS-6 was 56% in the whole cohort with the highest rate in group B (64%).

PFS-12 was 21% in the whole cohort with the highest rate in group B (29%). When comparing our results with those from the combination arm of the EORTC 26101 trial we found a significantly higher PFS-6 and PFS-12 in our cohort.
CONCLUSIONS: The precision medicine protocol for recurrent GBM is feasible and leads to improved results if compared with studies lacking molecular selection.

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