A multicenter randomized study comparing temozolomide (TMZ) versus TMZ-plus-bevacizumab (BEV) before standard treatment in unresectable glioblastoma (GBM) patients (p): The GENOM 009 study by the GEINO group.

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Abstract

Abstract

Background: We compared the efficacy and safety of treatment with TMZ or TMZ+BEV prior to and concomitant with radiotherapy in unresectable GBM patients. Methods: Between December 2009 and April 2013, p with unresectable GBM, PS<3 and MMS ≥25 were randomly assigned to receive either TMZ (85 mg/m², days 1–21, for 2, 28-day cycles), followed by standard TMZ with concomitant radiotherapy (60Gy) and then adjuvant TMZ for 6 cycles (TMZ Arm), or the same regimen but with the addition of BEV (10mg/kg/15 days) during pre-radiotherapy and concomitant treatment (BEV Arm). The primary endpoint was response according to RANO criteria after the 2 pre-radiotherapy cycles. The study was powered to detect a 30% difference between arms (α and β errors of 0.05 and 0.20). Secondary endpoints included toxicity, neurological deterioration before radiation, progression-free survival (PFS), overall survival (OS) and 1-year survival. Results: 103 p were registered and 93 randomized – 45 to the TMZ Arm, or the same regimen but with the addition of BEV (10mg/kg/15 days) during pre-radiotherapy and concomitant treatment (BEV Arm). The primary endpoint was response according to RANO criteria after the 2 pre-radiotherapy cycles. The study was powered to detect a 30% difference between arms (α and β errors of 0.05 and 0.20). Secondary endpoints included toxicity, neurological deterioration before radiation, progression-free survival (PFS), overall survival (OS) and 1-year survival. Results: 103 p were registered and 93 randomized – 45 to the TMZ Arm, 48 to the BEV Arm. Partial response (PR) was attained in 7.1% of p in the TMZ Arm vs 25.6% in the BEV Arm (P=0.001), and clinical benefit (PR + stable disease) in 26.1% vs 65%, respectively Neurological deterioration before radiotherapy was more frequent in the TMZ Arm (48.9% vs 20.8% of p; P=0.004). PFS was 2.2 months (m) in the TMZ Arm vs 4.8 m in the BEV Arm (HR, 0.79; P=0.29). OS was 7.7 m vs 10.8 m (HR, 0.71; P=0.12) and 1-year survival was 29.6% vs 48.9% (HR, 0.60; P=0.08), respectively. MGMT methylation was an independent prognostic factor for longer PFS (P=0.01), OS (P=0.001) and 1-year survival (P=0.004). More toxicities occurred in the BEV Arm, but a significant difference was observed only for stomatitis (P=0.02). Conclusions: The primary endpoint was met. The response rate was significantly higher in the BEV Arm. A tendency towards improved PFS, OS and 1-year survival was also observed in the BEV Arm, but the trial was not powered to detect statistical significance for these outcomes. TMZ+BEV is a feasible and effective option for unresectable GBM p. Clinical trial information: NCT01105386.