CNS tumours

MGMT METHYLATION IN TISSUE AND SERUM FROM UNRESECTABLE GlioBLASTOMA (GBM) PATIENTS (P) INCLUDED IN THE GENOM 009 STUDY, A MULTICENTER RANDOMIZED STUDY BY THE GEINO GROUP COMPARING TEMOZOLOMIDE (TMZ) VERSUS TMZ-PLUS-BEvacizumab (BEV). (CLINICALTRIALS.GOV NCT01102595)


1Medical Oncology, Catalan Institute of Oncology, Hospital Germans Trias i Pujol, Badalona (Barcelona), SPAIN
2Pathology, Hospital Germans Trias i Pujol, Badalona (Barcelona), SPAIN
3Medical Oncology, Catalan Institute of Oncology, LHospitalitat (Barcelona), SPAIN
4Medical Oncology, University Hospital 12 de Octubre, Madrid, SPAIN
5Medical Oncology, Hospital Provincial de Castellon, Castellon, SPAIN
6Medical Oncology Unit, Hospital Universitario Virgen de las Nieves, Granada, SPAIN
7Medical Oncology, Hospital Sant Pau, Barcelona, SPAIN
8Medical Oncology, Hospital Universitari i Politècnic La Fe, Valencia, SPAIN
9Pathology, Hospital Germans Trias i Pujol, Badalona (Barcelona), SPAIN
10Medical Oncology, Hospital Miquel Servei, Zaragoza, SPAIN
11Medical Oncology, Hospital General Universitario Valencia, Valencia, SPAIN
12Medical Oncology, Hospital Clinico Universitario San Carlos, Madrid, SPAIN
13Medical Oncology, Hospital Universitario Marques de Valdecilla, Santander, SPAIN
14Medical Oncology, Hospital Sant Joan de Reus, Tarragona, SPAIN
15Medical Oncology, Hospital Universitario Lucus Augusti de Lugo, Lugo, SPAIN
16Medical Oncology, Hospital Xeral Cies Vigo, Vigo, SPAIN
17Medical Oncology, Hospital del Mar, Barcelona, SPAIN

Aim: We compared treatment with TMZ versus TMZ + BEV prior to and concomitant with radiotherapy in unresectable GBM p. The potential prognostic role of MGMT methylation was examined in p with available tissue and/or serum samples.

Methods: Patients were randomly assigned to receive either TMZ (200 mg/m², days 1–5, for two 28-day cycles), followed by TMZ with concomitant radiotherapy (60Gy) (TMZ Arm) or the same regimen with the addition of BEV (10mg/kg /15 days) (BEV Arm). Both arms then received adjuvant TMZ for 6 cycles. The primary endpoint was overall response rate (ORR) according to RANO criteria after the two pre-radiotherapy cycles. Secondary endpoints included the analysis of MGMT methylation in serum and/or tissue as a potential prognostic marker. MGMT methylation was analyzed in a blinded fashion in two separate molecular biology laboratories using identical techniques.

Results: 93 p were randomized – 45 to the TMZ Arm and 48 to the BEV Arm. ORR was higher in the BEV Arm (P = 0.001). Progression-free survival (PFS), overall survival (OS) and 1-year survival were longer in the BEV Arm but differences did not reach statistical significance. MGMT methylation was analyzed in tissue samples from 60 p, 55 of whom were evaluable for response and survival; MGMT was methylated in 28 and unmethylated in 29 (3 no evaluable). MGMT methylation was analyzed in serum sample from 77 p; 72 of whom were evaluable for response and survival; MGMT was methylated in 11 and unmethylated in 61 p. In 40 p with MGMT methylation results in both tissue and serum, no significant concordance between tissue and serum methylation was observed. Tissue MGMT methylation was associated with longer PFS (P = 0.01), OS (P = 0.001) and 1-year survival (P = 0.004), but no association between serum MGMT methylation and outcome was observed: PFS (P = 0.72), OS (P = 0.84) or 1-year survival (P = 0.98).

Conclusions: MGMT methylation in serum is not useful to predict outcome in GBM p. The low proportion of p with serum MGMT methylation suggests a possible contamination of DNA with lymphocytes.

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