MGMT methylation status with pyrosequencing PSQ assessment: the cut-off value correlated with good favorable prognostic outcome in patients with newly diagnosis of glioma

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BACKGROUND: O6-methylguanine-DNA-methyltransferase (MGMT) has emerged as a relevant predictor of therapeutic response and good prognosis in patients with glioblastoma (GBM). Studies with pyrosequencing (PSQ) showed that this technique has a higher reproducibility and sensitivity than other techniques. However, the definition of a prognostically relevant threshold for the percentage of MGMT methylation remains one of the most critical issues in the use of PSQ analysis.

OBJECTIVE: The aim of this study was to define the cut-off value of PSQ-detected MGMT promoter hypermethylation which correlated with the most favourable prognostic outcomes.

METHODS: Data of patients affected by newly diagnosed primary GBM who underwent surgery or biopsy and followed at the Neuro-Oncology Unit of Regina Elena National Cancer Institute were retrospectively analyzed. Tissue samples were matched with a comprehensive set of clinical data collected in the database of IRE Neuro-Oncology Unit for each patient. Tissue samples were analyzed by means of PSQ for methylation status of MGMT assessment according to standardized procedure.

RESULTS: In total, 177 patients (102 men, 75 women) diagnosed as affected by Malignant Glioma from June 2013 to september 2016 were included in this study. Table 1 shows the characteristics of the study sample. There were no significant differences between women and men in terms of baseline demographic and clinical characteristics. The mean and median percentage of MGMT methylation, as detected by PSQ, were 21.5% and 16% (ranging from 2 to 85). No significant relationships were observed between gender, age at diagnosis, time from disease onset to diagnosis and percentage of MGMT methylation.

CONCLUSIONS: ROC analysis shows that MGMT>31% should be considered as the best cut off (sensitivity 70% specificity 77% p=0,0054) (sensibility 70%, specificity 60% p=0,057)