ABSTRACT

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Early postoperative treatment versus initial observation in CNS WHO grade 2 and 3 oligodendroglioma: clinical outcomes and DNA methylation patterns.

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PURPOSE: The treatment of oligodendroglioma consists of tumor resection and radio-chemotherapy. The timing of radio-chemotherapy remains unclear and predictive biomarkers are limited.

METHODS: Adult patients diagnosed with isocitrate dehydrogenase (IDH)-mutated, 1p/19q-codeleted CNS WHO grade 2 and 3 oligodendroglioma at the Medical University of Vienna and the Kepler University Hospital Linz (Austria) in 1992-2019 were included. Progression-free (PFS) and overall survival (OS) between early postoperative treatment and initial observation were compared using propensity score-weighted Cox regression models. DNA methylation analysis of tumor tissue was performed using Illumina MethylationEPIC 850k microarrays.

RESULTS: 131/201 (65.2%) patients with CNS WHO grade 2 and 70/201 (34.8%) with grade 3 oligodendroglioma were identified. 83/201 (41.3%) patients underwent early postoperative treatment, of whom 56/83 (67.5%) received radio-chemotherapy, 15/84 (18.1%) radiotherapy (RT) only and 12/83 (14.5%) chemotherapy only. Temozolomide-based treatment was administered to 64/68 (94.1%) patients, while RT + procarbazine, lomustine (CCNU) and vincristine (PCV) was applied in 2/69 (3.5%) patients. Early treatment was not associated with PFS (adjusted hazard ratio (HR) 0.74; 95%CI: 0.33-1.65, p=0.459) or OS (adjusted HR: 2.07; 95%CI: 0.52-8.21, p=0.302) improvement. Unsupervised clustering analysis of DNA methylation profiles from patients receiving early treatment revealed two methylation clusters correlating with PFS, whereas no association of clustering with O6-methylguanine methyltransferase (MGMT) promoter methylation, CNS WHO grade, extent of resection, and treating center could be observed.

CONCLUSIONS: In this retrospective study, early postoperative treatment was not associated with improved PFS/OS in oligodendroglioma. The potentially predictive value of whole-genome methylation profiling should be validated in prospective trials.

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