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Mutations in IDH1 and its prognostic role for patients with glioblastoma

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Introduction: Glioblastoma multiforme (GBM) is the most malignant primary brain tumor in adults with high mortality. Standard therapy (surgery, radiotherapy and chemotherapy with temozolomide) has only limited effectiveness with the median survival of patient with GBM 12.1-14.6 months. Recent GBM whole-genome studies revealed some novel prognostic and predictive biomarkers. The recurrent mutations in metabolic enzyme IDH - isocitrate dehydrogenase (isoforms IDH1 and IDH2) were identified in about 70%-80% of low-grade gliomas, in 50% of anaplastic gliomas and in approximately 5% of glioblastomas. The distinctive mutation IDH1 R132H was uncovered to be a strong prognostic biomarker for patients with malignant gliomas. Therefore we investigated the prognostic role of IDH1 R132 mutation in our GBM patients.

Methods: The IDH1 R132H mutation status was studied in the tumor samples from 55 patients with GBM that were treated by the standard GBM protocol in the Faculty Hospital in Pilsen. The real-time PCR with TaqMan® Mutation Detection Assays and TaqMan® Mutation Detection IPC Reagent Kitwas used. The IDH1 R132 mutation status was compared with the progression free survival (PFS) and overall survival (OS) of patients.

Results: The IDH1 R132H mutation was identified in 20 from 55 GBM tumor samples (36.4%). Patients with IDH R132H mutation had longer PFS-275 vs. 115 days (P<0.027, Log Rank), as well as longer OS - 390 vs. 235 days (P<0.05, Log Rank) than patients with wild-type IDH1.

Summary: The IDH1 R132H mutation was observed in the interestingly higher number of patients with GBM that was previously published by other groups. The prognostic value of this mutation was also observed in our study. Patients with IDH1 R132 mutation had significantly longer PFS and OS than patients with wild-type IDH1. The IDH1 mutation status could be used as a strong prognostic factor for patients with GBM.

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