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Association of temozolomide with progressive multifocal leukoencephalopathy: a disproportionality analysis integrated with network pharmacology

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Abstract

Background: Temozolomide (TMZ) is an alkylating agent, approved for the management of glioblastoma. The TMZ is not known for Progressive Multifocal Leukoencephalopathy (PML). The main objective of the current study is to find out the association of TMZ with PML using disproportionality analysis of FDA Adverse Event Reporting System (FAERS) data integrated with network pharmacological approaches.

Research design and methods: OpenVigil tool was used to query FAERS database. The disproportionality measures were calculated. The network has been constructed using Cytoscape. Finally, the possible binding interactions was studied using Glide, Schrödinger Inc.

Results: A total number of 3502 cases of PML were reported in the FAERS database. Out of these, 10 cases were found with TMZ. The subgroup analysis results have shown a greater number of cases in females. The network has indicated the involvement of human mitogen-activated protein kinase, 3-phosphoinositide-dependent protein kinase 1 protein, human mTOR complex protein, Phosphatidylinositol 4,5-bisphosphate 3-kinase protein, and glycogen synthase kinase-3 beta protein. The docking results have indicated good interactions of TMZ with active site of glycogen synthase kinase-3 beta and mitogen-activated protein kinase 1 as compared to other identified targets.

Conclusion: The PML is identified as novel signal with temozolomide.

Keywords: OpenVigil 2.1; Temozolomide; disproportionality analysis; docking study; network pharmacology; progressive multifocal leukoencephalopathy.