ABSTRACT

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Title of diploma thesis: Effect of flubendazole on glioblastoma multiforme *in vitro* and *in vivo.*

Glioblastoma multiforme (GBM) is the most common malignant glioma of the central nervous system. Despite systematic complex treatment, the median survival of this malignity is 14 months. Anthelmintic and potential anticancer drug flubendazole (FLU) is recently studied for its antiproliferative effect in various tumor cells (1). The aim of our project was to investigate the effect of FLU on GBM cell lines U118MG (stabilized cell line) and GBM69 (primary cell line) *in vitro,* tumor growth *in vivo,* and its effect on mRNA and protein levels of selected markers of epithelial-mesenchymal transition and drug resistance. First-line chemotherapeutic temozolomide (TMZ) was used as a positive control. Both tested cell lines were more sensitive to FLU treatment in comparison with TMZ. Indeed, FLU caused more apparent morphological changes than TMZ in these cells. FLU significantly influenced mRNA and protein levels of E-cadherin, N-cadherin, vimentin, as well as resistance markers MGMT or MRP-1. In addition, subcutaneous ectopic implantation of U118MG cell line into the immunodeficiency athymic mouse xenograft models Nude-Foxn1^{nu} confirmed our *in vitro* data. FLU (10 mg/kg) significantly suppressed tumor growth in mice, which was also manifested in proliferation marker ki67. The level of mesenchymal marker N-cadherin in excised tumors was significantly decreased as well. In conclusion, FLU significantly affected GBM cell viability *in vitro*, as well as tumor growth in athymic immunodeficient mice. Moreover, FLU effect was mostly more prominent than the effect of TMZ.

Keywords: *Glioblastoma multiforme*, flubendazole, *in vitro* a *in vivo* effect, markers of epithelial-mesenchymal transition, markers of drug resistance