

EVALUATION OF DANUSERTIB EFFECTS ON CELL VIABILITY AND CITOMORPHOLOGICAL PARAMETERS IN CANCER STEM CELL LINES FROM GLIOBLASTOMA MULTIFORME

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Glioblastoma multiforme (GBM) is a grade IV astrocytoma and the least successfully treated solid tumor: current therapies provide a median survival of 12-15 months after diagnosis, due to the high recurrence rate. Glioma stem cells (GSCs) are believed to be the real driving force of tumor initiation, progression and relapse. Better therapeutic strategies GSC-targeted are needed.

A number of potential molecular targets for the identification of novel anticancer drugs interferes with the cell cycle. Danusertib is a small molecule with strong activity against Aurora kinases, a protein kinases family overexpressed in a variety of human cancers and correlated, also in GBM, with chromosomal instability, tumor aggressiveness and poor prognosis.

In this study, we analyzed the effect of Danusertib exposure on cell viability, proliferation and cytomorphological parameters, by means of different assays (MTT, trypan blue and clonogenic assays, mitotic index and ploidy determination, morphological analysis), in four GSC lines from GBM. GBM2 cell line showed a loss and G166 a gain of Aurora kinases genes, while GliNS2 and G179 cell lines showed no variation.

Results showed that response to Danusertib exposure was heterogeneous among GSC lines. Cell viability and proliferation were significantly reduced in GBM2 and G179 cell lines, while G166 and GliNS2 were resistant. The analysis of cell and nuclear morphology in GBM2 and G179 cell lines highlighted the presence of large multinucleated cells and an increase in the number of polymorphic nuclei and micronuclei. At last conventional cytogenetics evidenced a significant increase in ploidy in GBM2 and G179.

Expression and mutational analysis of Aurora kinases and the study of chromosome segregation errors are in progress in order to deeply understand the heterogeneous response to Danusertib treatment on our GSC lines.