HG-17. THE HISTONE DEACETYLASE INHIBITOR PCI-24781 SHOWS ANTIPROLIFERATIVE, PRO-APOPTOTIC AND RADIOSENSITIZING EFFECTS ON PEDIATRIC GLIOBLASTOMA CELL-LINES
Pamela Viani Andrade, Augusto Faria Andrade, Rosane Gomes de Paula Queiroz, Carlos Alberto Scrideli, Luiz Gonzaga Tone, and Elvis Terci Valera; Faculdade de Medicina de Ribeirão Preto, USP., Ribeirão Preto / SP, Brazil

The acetylation of DNA can modulate the expression of genes involved in the development and progression of malignancies. Histone deacetylase (HDACs) inhibitors are clinically active and well tolerated in the treatment of a wide variety of tumors. HDACs inhibitors can sensitize cell response to ionizing radiation, potentially reducing treatment doses and side effects. OBJECTIVES: To assess the potential radiosensitizer effect of abexinostat (PCI-24781), a new and potent pan-HDAC inhibitor in two pediatric glioblastoma cell-lines (SF188 and KNS42). METHODS: The effect of PCI-24781 on proliferation rates, clonogenic capacity and apoptosis were compared prior and following cell irradiation. The clonogenic assay was performed without irradiation (48h of incubation) at the doses of 0.25, 0.5, 1 and 2μM of PCI-24781. The clonogenic assay combined with irradiation was performed at 48h using the inhibitor IC50 for each cell-line in combination with irradiation doses of 0.5, 1, 2 and 4Gy. For cell proliferation assays, the intervals of 24h, 48h, 72h and 96h at the doses of 0.5, 1, 2, 4, 8 and 16μM of PCI-24781 were selected for study. Apoptosis were evaluated at 48h-cultures at the doses of 2, 4, 8 and 16μM. RESULTS: The HDAC inhibitor repressed cell proliferation, displaying a more significant effect at 48h in the dose of 2μM (p < 0.05). PCI-24781 also induced apoptosis (p < 0.05); the percentage of cell death for SF188 and KNS42 (at 16μM) was 40% and 55% respectively. Cells demonstrated massive decrease in colony formation with PCI-24781; this effect was more pronounced when drug was combined with irradiation (p < 0.001). CONCLUSION: These data demonstrate potential radiosensitizer and antiproliferative effects of PCI-24781 on pediatric glioblastoma cell-lines. This study will now focus on key proteins responsible for the double-strand breaks repair caused by irradiation, trying to elucidate epigenetic pathways potentially involved in the therapy with PCI-24781. Financial Support: Fapesp (process no. 2013/13891-8).