View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by Firenze University Press: E-Journals

IJAE
Vol. 122, n. 1 (Supplement): 21, 2017
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

PI3Kα-selective inhibitor alpelisib (BYL719), may be effective as anticancer agents in Rhabdomyosarcoma

Alberto Bavelloni[1], Manuela Piazzi[3], Giulia Ramazzotti[2], Roberta Fiume[2], William Blalock[3] and Irene Faenza[2]

[1] SC Laboratory of Musculoskeletal Cell Biology, Rizzoli Orthopedic Institute (IOR), Bologna, Italy
[2] Department of Biomedical Sciences, University of Bologna, Bologna, Italy
[3] Institute of Molecular Genetics-National Research Council of Italy (IGM-CNR), UOS Bologna, Bologna, Italy

Rhabdomyosarcoma (RMS) is a highly malignant and metastatic pediatric cancer that arises from the skeletal muscle. Recent studies have identified an important role of AKT signaling in RMS progression. This suggests targeting components of the PI3K/Akt pathway may be an effective therapeutic strategy. Here, we investigated the in vitro activity of the class I PI3K inhibitors [1] in human rhabdomyosarcoma cell lines (embryonal rhabdomyosarcoma RD and A204, alveolar rhabdomyosarcoma SJCRH30). We used a panel of four compounds which specifically target PI3K isoforms including the PI3Kα-selective (p110α) inhibitor alpelisib BYL719, currently in clinical development by Novartis Oncology, the p110β TGX-221 inhibitor, the p110γ CZC24832, the p110δ CAL-101inhibitor and the dual p110α/p110δ inhibitor AZD8835. The effects of single drugs and of several drug combinations were analyzed to assess cytotoxicity by MTT assays, cell cycle by flow cytometry , apoptosis by caspase 3/7 assay and Western blot, as well as the phosphorylation status of the pathway. BYL719 treatment resulted in G1 phase cell cycle arrest and apoptosis. BYL719 administered in combination with CAL-101, for 48 h and 72h, decreased cell viability and induced apoptosis in a marked synergistic manner. Taken together, our findings indicate that BYL719, either alone or in combination with p110δ CAL-101inhibitor, may be an efficient treatment for human rhabdomyosarcoma cells that have aberrant upregulation of the PI3K signaling pathway for their proliferation and survival.

References

[1] PI3K inhibitors as new cancer therapeutics: implications for clinical trial design. Massacesi C Di Tomaso E Urban P Germa C Quadt C et. al. OncoTargets and Therapy 2016 vol: 9 pp: 203

Keywords
Rhabdomyosarcoma, PI3K/Akt pathway, cancer

© 2017 Firenze University Press
http://www.fupress.com/ijae