S4-3 BX-795, A PDK1 INHIBITOR, INHIBITS THE GROWTH OF ORAL SQUAMOUS CARCINOMA CELL LINES

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BX-795, A PDK1 INHIBITOR, INHIBITS THE GROWTH OF ORAL SQUAMOUS CARCINOMA CELL LINESLi-Yuan Bai1,2, Yu-Chen Tsai,3 Jing-Ru Weng31College of Medicine; 3Department of Biological Science and Technology, College of Life Sciences; China Medical University, Taichung, Taiwan;2Division of Hematology and Oncology, Department of Internal Medicine; China Medical University Hospital, Taichung, TaiwanIntroduction: The phosphoinositide 3-kinase/3-phosphoinositide-dependent kinase 1 (PDK1)/Akt signaling plays an important role in cancer cell growth, survival, metastasis and has been implicated in cancer cell drug resistance. It is well recognized that activation of Akt pathway is a significant prognostic factor for oral cancer. Here, we test the antitumor effect of a PDK1 inhibitor, BX-795, in a panel of oral squamous cell carcinoma (OSCC) cell lines. Procedures: The antiproliferative activity of BX795 was tested in 4 OSCC cell lines, HSC3, SCC2095, SCC4 and Ca922 first. SCC2095 was selected for the following parts of the study. Findings: The IC50 of BX-795 for HSC3, SCC2095, SCC4 and Ca922 was 4.6 μM, 5.5 μM, >7.5 μM and 6.6 μM in 24 h, and 1.8 μM, 3.1 μM, 6.5 M and 4.8 μM in 48 h, respectively. BX-795 induced a dose-dependent apoptotic change of SCC2095 as demonstrated in DAPI dye staining and Comet tail assay. Cell cycle analysis showed G2/M arrest of cells treated with BX-795 for 48 h. Furthermore, BX-795 induced dephosphorylation of Akt and IKK. For cell cycle related proteins, BX795 down regulated the expression of cyclin A, cdc25c and cdc2. Conclusions: BX-795 exhibited high potency in suppressing OSCC growth. In addition to inhibiting PDK1, it also induced G2/M cell cycle arrest. Further investigations are needed to determine the clinical application of BX-795 in the treatment of OSCC.