breast cancer, metastatic

THE EFFECTS OF THE BKM120 COMBINATION WITH DOCETAXEL ON BREAST CANCER CELLS AND BREAST CANCER STEM CELLS

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Aim: Buparlisib (BKM120) is an oral pan-phosphatidylinositol 3-kinase inhibitor, targeting all four isoforms of class I PI3K (α, β, γ, and δ). This study evaluated the effects of the inhibitor on breast cancer normal cell lines (MDA-MB-231, MCF-7, SK-BR-3) and the BCSCs in vitro.

Methods: The BCSCs were typically enriched via mammosphere culture. The inhibition of drugs on cancer cells were tested by MTT assay. The tumorigenicities and invasion abilities were detected by wound-healing assay and plate clone formation assay. The mammosphere-forming efficiency of breast cancer cells treated with different concentrations of the BKM120, an operational surrogate of BCSCs, were also performed. The nature of the drug interaction of was evaluated by using the combination index (CI) according to the method of Chou and Talalay. The impact of BKM120 and combined with docetaxel on PI3K/AKT/mTOR pathway was assessed by Western blotting.

Results: All three kinds of BCSCs were appeared resistant to BKM120 in vitro, compared with the non-tumorigenic cancer cells. In addition, when three cancer cells treated with the IC50 dose of BKM120, the invasion abilities of cancer cells significantly decreased (P < 0.05). The number of cloning were all dropped compared with the control group (P < 0.05), and the trend of MCF-7 cells was more obvious among the others. Compared with control group, the volume of mamospheres and MFE of BKM120 group significantly decreased. The combination effect of BKM120 and docetaxel, which called as Combination Index, showed synergism in three cancer lines. When the activities of BKM120 on PI3K pathway signaling were assessed by western blotting in the presence of series of doses of drug BKM120, the drug showed inhibited the phosphorylation of both Akt and S6 in all tested lines and all BCSCs.

Conclusions: BKM120 can inhibit the growth of normal cancer cells and BCSCs, by inhibiting cell proliferation, descenting the invasion abilities, and reducing the expression of pAKT and pS6 indicating that treatment with BKM120 and docetaxel may be an efficient therapy for normal cancer cells and BCSCs.

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