

9th International Conference on

LEUKEMIA AND HEMATOLOGIC ONCOLOGY

October 05-06, 2017 London, UK

New opportunities in hematologic malignancy treatment: Therapeutic application of PI3K inhibitors

Ava Safaroghli Azar, Davood Bashash and Seyed H Ghaffari
Hahid Beheshti University of medical sciences, Iran

Statement of the problem: Among signaling pathways involved in the pathogenesis of hematologic malignancies, constitutive activation of phosphatidylinositol 3-kinase (PI3K) has been observed in a high proportion of patients, largely as a result of genetic mutation. Here, we have evaluated and compared the effects of two PI3K inhibitors, which are currently being tested in clinical trials on hematologic malignancies.

Methodology: To define the effect of the isoform-specific PI3K δ inhibitor CAL-101 and pan-PI3K inhibitor BKM120 in different types of hematologic malignancies, a panel of cell lines consist of multiple myeloma, acute lymphoblastic leukemia, and acute promyelocytic leukemia were chosen. Cell viability, apoptosis and caspase-3 activity were determined during incubation with either the inhibitors. The molecular mechanism was also evaluated by RQ-PCR and Western blot analysis.

Findings: Our results showed that both BKM120 and CAL-101 effectively reduced the cell viability of all malignant cells, independent of mutational status of p53, by causing cell cycle arrest and promoting ROS-mediated apoptosis. Despite favorable cytotoxic effects, we found differences in the ability of CAL-101 and BKM120 to decrease cell survival. As compared to CAL-101, BKM120 evidently blocked Akt phosphorylation and caused a more pronounced apoptosis induction through both p53 and NF- κ B-dependent pathways, introducing BKM120 as a more potent inhibitor. This study suggests that that probably complete inhibition of class I PI3K activity more effectively abrogated leukemic cell proliferation and survival.

Conclusion & Significance: Our data indicate a potential application for PI3K inhibitors in the treatment of hematologic malignancies, irrespective of the adverse prognostic markers and support the clinical development of these PI3K inhibitors for patients.

Biography

Ava Safaroghli-Azar completed her master's degree in 2016 from Shahid Beheshti University of medical sciences, school of allied medical sciences, Tehran, Iran. She has studied the effect of the several targeted anti-cancer agents and their mechanism of action on different hematologic malignancies. She has published several papers in the field between the years 2016 and 2017.

ava.s.azar@gmail.com

Notes: