NILOTINIB INDUCES APOPTOSIS THROUGH JAK/STAT PATHWAY MEMBER STAT5A, STAT5B IN K562 CML CELL MODEL

T. Guliyeva¹, B. T. Kaymaz¹, M.C. Ozkan¹, A. O. Uysal¹, B. Kosova², F. Sahin¹, G. Saydam¹
¹Hematology, Ege University Hospital, Turkey; ²Medical Biology, Ege University Hospital, Turkey

AIM: In the current study, we aimed to determine transcriptional and translational differences of STAT5A and STAT5B and also apoptosis rates following nilotinib treatment in CML model K562 cells.

METHODS: Cell proliferation was assessed by WST assay in order to determine cytotoxicity of nilotinib upon leukemic cells. While mRNA expression levels of STAT5A and STAT5B were analyzed by real time qRT-PCR; protein expressions were detected via western-blot method following nilotinib treatment for duration of 24 – 96 hours also with untreated control group. Apoptosis was performed by “Caspase-3” and “Cell Death Detection” assays following the same treatments with same time intervals. Statistical analyses were done by GraphPad prism software with a significance of p<0.05.

RESULTS: While number of apoptotic cells were increased by 2.1 fold, 47.36% (p=0.045) as a result of measurement of caspase 3 activity; a 1.89 fold, 52.8% increase was detected in apoptosis rate following Cell Death assay (p=0.0012) in nilotinib treated group. As for mRNA expression results, while STAT5A expression was significantly decreased by 65.12% [(2.87 fold; p=0.0033)] and by 90.9% [(10.99 fold; p=0.0001)] at 72th – 96th hours respectively; STAT5B was downregulated by 80.95% [(5.25 fold; p=0.0032)], and 93.36% (15.08 fold; p=0.0001)] for 72th and 96th hours in nilotinib treated group compared to control group. As for protein results, both STAT5A and STAT5B protein expression levels were inhibited in a time dependent manner but dramatic suppressions were detected especially at 96th hour for each protein.

CONCLUSION: In conclusion, target genes STATs expressions were suppressed at mRNA and protein levels and also leukemic cell apoptosis was induced following nilotinib treatment of IC50 dose. Therefore, targeting JAK/STAT pathway components and evaluating new candidate target genes responsible for CML pathogenesis has an accelerating importance in therapeutic application area.