Myelodysplastic and Myeloproliferative Disorders Acute Myeloid Leukemia Evolution Risk Mutations Assessment in The Georgian population

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Content

Abbreviations:

MPN – Myeloproliferative disorder

MDS – Myelodysplastic syndrome

NCDC – National Center for Disease Control

MF – Primary myelofibrosis

PV – Polycythemia vera

ET – Essential thrombocytopenia

IPSS-R - Revised International Prognostic Scoring System

WPSS - WHO Prognostic Scoring System

PMF – Primary myelofibrosis

WHO – World health organization

RFU – Relative fluorescence unit

Abstract: Despite increased awareness, and healthcare quality for different types of cancers worldwide, as well, in Georgia and worldwide, the diagnosis and/or management of cancer remain challenging. As NCDC's (National Center for Disease Control) latest statistical analysis shows, in 2018, the incidence of hematological malignancies including myeloproliferative (MPNS) and myelodysplastic syndromes (MDS), remains steady at >500 cases/year. Unfortunately, the 5-year survival rate is <50%. MPNS and MDS are characterized by the uncontrolled proliferation of mature blood cells, the results of disease-causing alterations are occurring in the bone marrow stem cells. Both carry a 2-14% risk of leukemic transformation. Patients suffering from polycythemia vera (PV), essential thrombocytopenia (ET), and primary myelofibrosis (PMF) are known to have alterations in the *JAK2, CALR,* or *MPL* genes that predispose these patients to develop the cancer. These mutations have been used for diagnosis, classification of the disease, and prognosis, in conjunction with other markers. Additional markers (mutations in *ASXL1, EZH2, TET2, IDH1/2, SRSF2,* and *SF2B1*) can also be used for diagnosis and prognosis. Prognosis can be determined using the use of IPSS-R and/or WPSS scoring system. These scoring systems assess patients' personalized outcomes, as well as estimate risks of AML transformation. Early identification of selective mutation and/or biomarkers is vital for improving patient prognosis and survival. Totally, I have analyzed 152 samples, out of which only 82 were positive for MPN and MDS characteristic mutations. According to results, from these 82 mutations (JAK, CARL, KIT, RUNX1) positive patients nearly 7% of patients express additional risk mutations other than *JAK2* mutation. These mutations are identified as a marker for possible blastic evolution. Based on the limited number of samples I have analyzed in my thesis, I believe that in the Georgian population, there are more mutation than reported. Coffalyser.Net data sheet must identify the exact length of DNA molecules to detect mutation-specific probes and copy number mutations. Furthermore, false-negative results can be detected, due to the low starting concentration of genetic information from the cancerous cells. MLPA approach has some limitations in identifying concomitant mutations; Thus, further studies with more sensitive molecular method (sequencing of the regions of interest) are needed for identification of the specific mutations.