MOLECULAR PROFILING OF PATIENTS WITH PHILADELPHIA CHROMOSOME-NEGATIVE MYELOPROLIFERATIVE NEOPLASMS (PH- MPN) FROM RN MACEDONIA

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Introduction

Initial understanding on the pathogenesis of Philadelphia (Ph) chromosome-negative myeloproliferative neoplasms (MPNs) has been achieved with the discovery of mutually exclusive driver somatic mutations in JAK2, CALR and MPL genes leading to constitutive activation of the JAK/STAT signaling pathway. Additional mutations, referred to as non-driver mutations, are assumed to have prognostic implications and are used as clonal markers in triple negative MPN cases.

Materials and methods

To observe the molecular profile of 59 patients with Ph-MPNs, we performed next generation sequencing (NGS) of bone marrow DNA using the Archer Variantplex Myeloid Core panel consisted of 37 MPN-associated genes.

Results

Driver mutations were present in 39/59 (66%) patients, of which 30/39 (77%), 6/39 (15.4%), 3/39 (7.7%) in the JAK2, CALR and MPL gene, respectively. Non-driver mutations were detected in 7/59 (11.9%) triple-negative cases (ASXL1 in 3 and DDX41, CBL, FLT3 and SCF3R in individual patients), while no mutations were detected in the remaining 13/59 (22%) patients. Additional mutations were detected in 9 JAK2V617F positive patients (ASXL1 in 4, DNMT3A and TET2 in 2 each, and RUNX1, TP53 and CBL mutations in one patient each). More than two non-driver mutations were present in only 3 patients associated with poor prognosis.

Conclusion

Our results support previous data on the role of molecular profiling for identifying high-risk MPN patients and for confirming the disease clonality. The fact that 22% of our patients did not show

presence of any mutation, raises the possibility that either reactive processes ware in the background of the MPN phenotype or that additional genes should be incorporated in the NGS myeloid panel.