soho2023
ELEVENTH ANNUAL MEETING

# DIVERSITY OF *DNMT3A*, *TET2*, AND *ASXL1* GENE VARIANTS IN PATIENTS WITH ACUTE MYELOID LEUKEMIA (AML)

Anastasia Kashlakova MD, Bella Biderman MD, PhD, Yulia Sidorova MD, PhD, Irina Lukianova MD, PhD, Dmitry Bessmertnyy MD, Zalina Fidarova MD, PhD, Tatyana Obukhova MD, PhD, Hunan Julhakyan MD, PhD, Andrey Sudarikov MD, PhD, Elena Parovichnikova MD, PhD
National Medical Research Center for Hematology, Moscow, Russian Federation

## INTRODUCTION

*DNMT3A*, *TET2*, and *ASXL1* gene mutations can occur in healthy individuals without hematologic malignancies. Some studies show they are also common in patients with AML and associated with poor outcomes.

## AIM

To evaluate the frequency and identify different genetic variants of *DNMT3A*, *TET2*, and *ASXL1* in AML patients.

## METHOD

The study included 61 patients with newly diagnosed AML and a median age of 37 years (range 18 – 59). Regarding the cytogenetics, 11.5% of patients (n = 7) had favorable-risk aberrations, 80.3% of patients (n = 49) had intermediate-risk and 8.2% (n = 5) had adverse cytogenetics. Mutational status of *DNMT3A* (exons 7 – 23), *TET2* (exons 2 – 10), and *ASXL1* (exon 12) genes were determined with NGS at the disease onset for all patients.

## RESULTS

Gene variants in *DNMT3A* were detected in 31.1% of patients (n = 19). Hotspot mutations in R882H were the most common (42.1%, n = 8). Four additional (likely) pathogenic missense mutations were found, all unique: R749C, T834A, G707D, and S337L. Frameshift indels were found in 15.8% of patients (n = 3). One patient had a stopgain mutation (Q696X), one had a splicing mutation (c.2174-1G>A) and one had stopgain and splicing mutations (W581* and c.1122+1G>A). In addition, one patient had a missense mutation of unknown significance (R379H). *TET2* variants were detected in 9.8% (n = 6) of patients. Three of them had frameshift indels (E783Mfs*5, L1816Vfs*6, and R1440Tfs*38) and one had stopgain mutation (C987X). Two missense mutations in *TET2* were identified as variants with unknown significance (R1261C and P1894T). Gene variants in *ASXL1* were rare enough and were detected only in 4.9% of patients (n = 3). One had a stopgain mutation (S770X) and two had (likely) pathogenic missense mutations (A746T and C594R). All variants except splicing mutation (c.2174-1G>A) of *DNMT3A* were found among patients from either intermediate or favorable cytogenetic risk groups.

## CONCLUSIONS

There is a great diversity of possible genetic alterations in *DNMT3A*, *TET2*, and *ASXL1* genes, which requires detailed investigation. Further studies in dynamics will evaluate their prognostic impacts in AML patients.

## CONTACT INFORMATION

Hunan Julhakyan
oncohematologist@mail.ru