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Abstract Topic: - Clinical Genetics

Abstract Title: - CytoGenomic approach to identify genomic changes and their association with overall survival in Myelodysplastic syndromes

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Aims: - To identify genomic changes for accurate diagnosis and prognosis of the MDS using CGH in combination with SNP array.

Methods: - Study was carried out in 77 treatment naïve MDS subjects. CK/FISH in combination with high-resolution CNVs identification using CGH + SNP array and mutation profiling by targeted deep NGS

Results: - CGH+SNP array analysis revealed 82 clinically significant genomic lesions (losses/gains) in 49% of MDS patients. CGH + SNP array decreased the proportion of normal karyotype by 30%. SNP array in combination with NGS confirmed the biallelic loss of function of TP53 gene (2/6), which is a clinically relevant biomarker and new genetic based MDS entity i.e. MDS-biTP53 as per new WHO classification 2022. Genomic region 2p22.3 presented with frequent lesions and also with more hazard ratio (2.7, 95% CI 0.37 – 21) when analysed by Kaplan Meier survival analysis. CGH + SNP array changed the cytogenetic and IPSS-R risk group in 18% and 13% patients respectively with an improved prediction of prognosis. Multivariate analysis showed cytogenetic re-stratification, TP53 mutation and marrow blast percent independently predict survival of MDS patients.

Conclusions: - Our study suggests that the genomic region 2p22.3, is of importance in view of prognostication of patients and should be studied with good number of patients. SNP array in combination with NGS could successfully establish new MDS entity i.e. MDS-biTP53 during patient evaluation, hence CGH+SNP array along with NGS and conventional cytogenetics complement each other and should be combined to contribute to the study of genomic aberrations for better and more precise management of patients with MDS

Keywords: - CGH+SNP array analysis revealed 82 clinically significant genomic lesions (losses/gains) in 49% of MDS patients. CGH + SNP array decreased the proportion of normal karyotype by 30%. SNP array in combination with NGS confirmed the biallelic loss of function of TP53 gene (2/6), which is a clinically relevant biomarker and new genetic based MDS entity i.e. MDS-biTP53 as per new WHO classification 2022. Genomic region 2p22.3 presented with frequent lesions and also with more hazard ratio (2.7, 95% CI 0.37 – 21) when analysed by Kaplan Meier survival analysis. CGH + SNP array changed the cytogenetic and IPSS-R risk group in 18% and 13% patients respectively with an improved prediction of prognosis.

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