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PROGNOSTIC IMPACT OF NOVEL GENE POLYMORPHISMS IN NEWLY DIAGNOSED ACUTE MYELOID LEUKEMIA ADULTS UNDERGOING INDUCTION CHEMOTHERAPY

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Single nucleotide polymorphisms (SNPs) could lead to **interindividual differences in treatment outcome.**

A recent study (*Gamazon et al. Blood. 2013;121(21):4366-76*) reported several **novel SNPs** involved in cytarabine cytotoxicity using a whole-genome approach, that were **associated with clinical outcomes in AML pediatric population**.

OBJECTIVE: impact of the SNPs in **effectiveness & toxicity** of therapy in **AML adults**

METHODS

SNPs: rs12036333, rs10758713, rs9883101, rs6550826, rs2897047, rs7729269

Patients: 109 adults of a single center at initial diagnosis from AML, induction with idarubicin plus cytarabine (PETHEMA-LMA 99, 2007 & 2010 trials)

Technique: Sequenom® mass spectrometry–based multiplex genotyping assay

Efficacy: complete remission (CR) vs. partial remission/resistance (deaths were excluded)

Toxicity: grade 0-1 vs. grade 2-4 (maximum grade of all the specific toxicities), WHO scale

Hematologic toxicity: time to neutropenia and thrombocytopenia recovery since first day of chemotherapy

Statics: χ2 test with (Yates correction if needed) and Mann–Whitney U test

RESULTS

Patients: median age 53 years (range 17-78 years)

Baseline characteristics *(age, gender, leukocyte count, hemoglobin level, platelet count and percentage of peripheral or BM blasts)*: was **significant difference** with the **genotype distributions** regarding **age** (wild allele carriers of rs9883101 were older, P=0.02) and **gender** (men had higher proportion of variant alleles for rs6550826 and rs7729269, P=0.003 and 0.006; and wild allele for rs2897047, P=0.005).

Effectiveness: SNPs were **not associated** with the CR rates

Toxicity: toxicities were more frequent in **variant alleles** of several SNPs (table)

SNP	Cardiac	Hepatic	Skin	G3-4	Thrombocytopenia recovery (days)	Neutropenia recovery (days)
rs12036333					GG/GA:32.7 AA:57.5 (0.004)	
rs10758713				GG:51.9-GA/AA: 73.3% (0.043)		GG/GA:34.0 AA:68.0 (0.029)
rs9883101					AA:28.4-AC/CC: 38.6 (0.036)	
rs6550826					CC:28.2-CG/GG: 38.9 (0.027)	
rs2897047		CC/CT:52.0 TT:88.9% (0.04)				CC/CT:32.9 TT:51.1 (0.015)
S7729269	TT:8.2-TC/CC: 22.9% (0.031)		TT:16.4-TC/CC: 39.6% (0.003)			TT/TC:35.9 CC:16.3 (0.029)

TABLE 1. Association between SNPs and different toxicities, expressed in % (wild vs variant allele) and P value

DISCUSION

We obtained **new associations** of these **novel polymorphisms with toxicity**, not previously studied in **adult AML patients**, but not in effectiveness. Further studies with larger population are needed to validate these associations and to elucidate the molecular mechanism.

CONCLUSION

In future, these SNPs could be **useful biomarkers in clinical practice**.

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