

## THE INFLUENCE OF RFC1 A80G GENE POLYMORPHISMS ON METHOTREXATE TOXICITY IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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**Introduction:** The reduce folate carrier (RFC1) is the main transporter of methotrexate (MTX) and folate in the cell and his malfunction might be a reason for incidence of toxicities during antifolate therapy. In our study we investigated the clinical relevance of SLC19A1 A80G polymorphism for high dose methotrexate(HD-MTX) related toxicities in children with acute lymphoblastic leukaemia (ALL)

**Material and methods:** Our study comprised of 65 children with ALL treated with high doses of MTX (5g/m<sup>2</sup>). Genotyping for RFC1 A80G polymorphisms was performed using the PCR-based RFLPA. Toxic effects were analyzed according to the criteria for toxicity from the protocol ALL BFM 2000 (absence or presence of toxic effects) in correlation with the type of present polymorphism.

**Results:** In our study patients with AG + GG polymorphisms of RFC1 gene had higher probability for developing anemia as compared with carriers of AA polimorphism [ OR (95%CI) 3,400 (0,77 - 14,93), RR (95%CI) 2,125 (0,76 - 5,97)p=0,095], but without statistical significance. Nevertheless, there were not any association between the other types of toxicity and RFC1 A80G polymorphisms

**Conclusion:** The present study suggests that analyzing RFC1 A80G gene polymorphisms could provide additional information for predicting MTX toxicities. Further multicenter studies with larger data should be performed for future individualization of treatment in childhood ALL.

**Key words:** RFC1 A80G, polymorphism, methotrexat, toxicities, lymphoblastic leukemia