

## **BUSULFAN THERAPEUTIC DRUG MONITORING (TDM) FOR CONDITIONING REGIMEN IN PAEDIATRIC HSCT PATIENTS TO ACHIEVE RECENTLY HARMONIZED CUMULATIVE EXPOSURE (cAUC): A RETROSPECTIVE ANALYSIS RESULTS OF SINGLE CENTRE**

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**Background:** One of the significant progress in human medicine is haematopoietic stem cell transplantation (HSCT). Pre-transplantation conditioning therapy is a rigorous step, where cytotoxic agents like busulfan are widely used. However, there are drawbacks of conditioning therapies and busulfan-containing protocol is not without challenge. It is well known that both under exposure and over exposure to busulfan is one of the factors influencing overall outcomes. The aim of this contribution is to demonstrate that previous belief that first dose prediction of busulfan exposure may be enough is now challenged indicating necessity of close monitoring of exposure in-between doses especially in paediatric patients presenting significant variability. **Patients and methods:** Cohort of 102 paediatric subjects of age between 4 month and 18 years, actual body weight 6-82 in kilo grams with varieties diagnosis across ALL, AML, Lymphoma, malignity of different tissues and immunity disorders as well as congenital metabolic errors suggested to benefit from HSCT were included. Gender distribution was of 62 male and 40 females. Analysis of TDM outcomes post so-called harmonized unit for busulfan exposure measure given as cAuc in conditioning therapy at single centre was performed. The drug concentration were determined by LC/MS from four samples (trough, 2, 4, 6 hours) from the start time of the fifth infusion given in 2 hours and then after relevant dose adjustment while the dose is given at 6 hours interval according to local protocol to complete 16 doses within four days. AUC was calculated using the trapezoidal rule and MWPHARM++ version 20.3.329 MEDIWARE a.s. Czech Republic has been used for pharmacokinetic simulation and fitting dose adjustments. **Results:** The majority (92%) of paediatric patients need busulfan dose escalation by 16-125%, whereas less than 5% remained without dose change or needed dose reduction by 13% based on TDM results. **Conclusion:** Our results strongly confirm the necessity of TDM to keep the patients within target of 78-101 mg/L\*hr. cAUC recently published. The results unequivocally demonstrate that traditional initial protocol maybe under dose majority of paediatric patients unless the dose is adjusted individually utilizing therapeutic drug monitoring.

**KEY-Words:** Busulfan, TDM, Cumulative AUC, Paediatric Patients