Symposium

# [S-10] S-10: Progress of TDM for hematopoietic stem cell transplantation

Chairs: Tomohiro Terada, Japan / Erik van Maarseveen, The Netherlands

Tue. Sep 26, 2017 10:30 AM - 12:00 PM Room D (1F)

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## [S-10-2] Therapeutic drug monitoring (TDM) in paediatric and adult patients on high dose busulfan conditioning therapy: a retrospective analysis including outcomes

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### Background

Busulfan is used in conditioning regimens prior to haematopoietic stem cell transplantation (HSCT). Body-weight based busulfan doses were supposed to meet the targeted area under the concentration versus time curve (AUC). However, series of observations indicate existing inter/intra-individual variability challenging the body-weight based fixed busulfan dosing scheme.

**Aim:** The purpose of this retrospective analysis was to describe to what extent body-weight based busulfan dosing fails to meet efficacious and safe drug exposure, thus demanding TDM in paediatric and adult patients regardless of route of administration.

### Methods

Data of 195 patients (133 children and 62 adults), who received High dose busulfan for myeloablative target before HSCT is included. Trough concentration (immediately before the $5^{th}$ dose), samples immediately after the end of 2 hour lasting infusion or 1hour after oral form (peak),4hr, and 6hr from the starting time of administration, respectively were retrieved. Busulfan plasma concentrations were determined by high performance liquid chromatography and the AUC was calculated using the trapezoidal rule

### Results

Following body weight-based busulfan dosing, We recorded wide range of trough levels 25–1244 g/L and peak levels 679–4586 g/L resulting in wide range of AUC requiring dose adjustment in about 60 % paediatric and 50% adult cases, respectively. Concerning outcomes, post transplant survival rate is around 80% in paediatric patients, versus 60% in adults. Transplant related mortality, disease progression, and relapse were among main causes of mortality in paediatric patients. In contrast, sinusoidal obstruction syndrome(SOS) associated multi-organ failure was the leading cause of mortality(6/23) followed by sepses(5/23), relapse(5/23), and other different reasons(5/23) including 2 cases of disease progression among adults, whereas SOS record as cause of mortality was absent in our paediatric patients. Nevertheless, no direct causal relations found for SOS and AUC indicating that other factors may play major role.

## Conclusions

Although AUC doesn’ t necessarily correspond with outcomes due to co-factors, our results demonstrate that busulfan, PK/PD inter/intra-individual variability challenge remains. The fact that doses in more than half of the cases were to be adjusted underlines the importance of TDM as mandatory care regardless of route of administration both in paediatric and adult patients.