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721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Pharmacokinetic-Targeting and Dose-Adjustment of I.V. Busulfan for Myeloablative Conditioning in Allogeneic Hematopoietic Cell Transplantation

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Introduction: Pharmacokinetically (PK)-targeting intravenous busulfan improves outcomes following allogeneic hematopoietic cell transplantation (HCT). However, the optimal busulfan area under the curve (AUC) likely differs based on the specific conditioning regimen, and the target busulfan exposure is unknown in combination with fludarabine and low-dose total body irradiation (TBI).
Methods: This study included 1019 adult HCT recipients that received myeloablative conditioning including fludarabine, busulfan, anti-thymocyte globulin, and low-dose (4cGy) TBI. Busulfan was administered as a total dose of ~3.2mg/kg given equally from days -5 to -2 pre-transplant. Total AUC was estimated using measurements of serial serum samples. Multivariate Cox and Fine-Gray regression were used for comparison of AUC subgroups. The primary outcomes of interest were relapse-free survival (RFS) and overall survival (OS).
Results: Median AUC was 62.3 mg•hr/L (range: 39.4-128.0 mg•hr/L). Total AUC exposure of 49.3-57.5 mg•hr/L was associated with greater RFS (67% vs. 47%, HR=1.82, P=0.014) and OS (71% vs. 46%, HR=1.99, P=0.008) compared to patients with higher AUCs of 57.5-73.9 mg•hr/L. Although very low (<49.3 mg•hr/L) or very high (>73.9 mg•hr/L) AUCs trended towards worse RFS and OS compared to 49.3-57.5 mg•hr/L, this analysis was limited by the small number of patients with extreme AUCs and did not reach statistical significance. Except potentially for patients with a high/very high HCT disease risk index, 49.3-57.5 mg•hr/L appeared to be the optimal AUC regardless of patient sex, age, or primary disease.
Conclusion: Within the evaluated AUC range, 49.3-57.5 mg•h/L appeared to be associated with the most favourable survival. Pharmacokinetic-targeting to this range may improve outcomes.

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