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-10-3] Pharmacokinetic analysis of once-daily intravenous busulfan in combination with fludarabine for elderly AML/MDS patients

Shingo Yamazaki[1], Takaaki Suzuki[2], Takatsuka Hirokazu[3], Yusuke Takeda[4], Emiko Sakaida[5], Chikako Ohwada[6], Katsuhiro Shono[7], Akira Yokota[8], Chiaki Nakaseko[9], Itsuko Ishii[10] (1.Division of Pharmacy, Chiba University Hospital, 2.Chiba University Hospital, 3.Chiba University Hospital, 4.Chiba University Hospital, 5.Chiba University Hospital, 6.Chiba University Hospital, 7.Chiba University Hospital, 8.Chiba University Hospital, 9.Chiba University Hospital, 10.Chiba University Hospital)

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Background

Therapeutic drug monitoring (TDM) of once-daily i.v. Buslfan (BU) is reported that it minimizes the variations in intra- and inter-individual systemic exposure and provides improved dose estimation. Lee et al. reported that the clearance (CL) of BU decreased from day1 to day4 in pediatric patients. On the other hand, pharmacokinetic parameters of BU in elderly Japanese patients were not reported. Therefore it is important to clarify the pharmacokinetic parameters and understanding characteristics of BU pharmacokinetics (PK).

Methods

This study is designed as a prospective and multicenter trial. All patients received 3.2 mg/kg of BU as initial dosage, 4 points of blood sampling were measured on day1 (1, 3, 5, 9 h after the end of infusion). Pharmacokinetic parameters of BU was analyzed and adjusted the dosing schedule as the target area under the concentration-time curve (AUC) up to 6,000 mM*min/L on day2. The validity of the AUC was checked by the basis of blood sampling (trough, 1, 5 h after the end of infusion) on day4. The PK of BU was analyzed as 1-compartment model, AUC was calculated as AUC = dose / CL. The potential covariates affecting the pharmacokinetic parameter were explored.

Results

We enrolled 21 patients. The elimination half-life and distribution volume were similar between the day1 and day4 (2.9±0.4 vs 3.0±0.4 h, 0.67±0.08 vs 0.61±0.09 L/kg, respectively, mean±SD), on the other hand, the CL was significantly reduced (0.165±0.031 vs 0.145±0.025 L/kg/hr, p=0.002). The AUC increased after dosing adjustment (4823±881 vs 6026±78 mM*min/L). When we compared with the decreasing rate of CL in diagnosis between day1 and day4, the CL of myelodysplastic syndrome was a declining trend relative to acute myeloid leukemia.

Conclusions

Our results suggested that the PK profiles in elderly Japanese patients were similar to those in pediatric patients reported by Lee et al. On the other hand, we consider that it needs larger scale study for exploring the intra- and inter-covariate factors of PK parameters. In conclusion, the CL of BU may decrease when administrating to elderly AML or MDS patients.