Poster

[P26-5] P26-5: Immunosuppressive drugs (4): Individualized dosage adjustment

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[P26-5-4] Twenty-four hour tacrolimus pharmacokinetics in renal transplant recipients on twice-daily dosing

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Background

We have previously shown that computer based dosing of tacrolimus (Tac) results in significantly better target achievement in renal transplant recipients compared to standard dosing by experienced transplant physicians. The computer model is however based on the assumption of similar Tac pharmacokinetics (PK) following morning and evening doses, which is questionable. Diurnal differences in systemic exposure may be due to different absorption rate and/or oral bioavailability of Tac following the morning and evening dose.

Methods

Full 24-hour PK was investigated in renal transplant recipients in the early phase following transplantation. In total, 26 whole blood Tac concentrations were measured per patient during the investigations: before and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, 10 and 12 hours after administration of the morning dose and additionally at 0.5, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 10 and 12 hours after the evening dose. Estimation of PK variables and parameters were performed by non-compartmental analyses. The recipients were instructed to administer Tac as in their everyday routine with regards to food and concomitant medication.

Results

This is an ongoing study, where 22 out of 30 patients have been included. Complete data will be presented. Preliminary results (n=3) show a more rapid absorption and higher bioavailability of Tac following the morning dose; AUC_{0-12} (75.3g*h/L) compared to AUC_{12-24} (66.3 g*h/L), C_{max} of 9.42 g/L compared to 6.32 g/L, and a shorter T_{max} following the morning dose (4.0 h) compared to the evening dose (6.1 h).

Conclusions

Preliminary results indicate a difference in the PK patterns following the morning and evening dose of Tac. Data from the present study will be valuable to improve the current understanding of Tac PK in the everyday treatment of renal transplant recipients.