
Oral

[O25-1] O25-1: Biomarkers for transplantation

Chairs: Mercè Brunet, Spain / Hirofumi Jono, Japan

Mon. Sep 25, 2017 1:30 PM - 2:30 PM Main Hall (1F)

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[O25-1-1] Naturally regulatory T cell-specific demethylated region in FOXP3 as a biomarker to predict acute rejection in kidney transplant patients under immunosuppression with tacrolimus, mycophenolic acid and steroids

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Keywords: Kidney Transplantation, Individualization, Biomarker, Regulatory T Cells, Immunosuppression

Background

Individualization of the immunosuppressive therapy after kidney transplantation (KTx) beyond therapeutic drug monitoring (TDM) is desirable. The search for biomarkers to complement TDM is ongoing and regulatory T cells (Tregs) are considered promising because they reflect the immune status of graft recipients. The current study aimed to see whether Tregs in the first month (M1) after KTx are associated with the occurrence of acute rejection (AR) events later in the .first year post NTx.

Methods

Naturally Tregs in whole blood were determined by the demethylation status of the Tregs Specific Demethylated Region (TSDR) of the Forkhead-Box-P3 (FOXP3) gene using quantitative PCR (qPCR). Seventy patients (23 females, age 17-78 y) in M1 post KTx were included. AR was recorded up to M12. Percentile ranks of TSDR demethylation were established and ROC curves as well odds ratios were calculated. Tacrolimus (Tac) in whole blood was determined by LC-MS/MS, mycophenolic acid (MPA) in plasma by HPLC. Diagnosis of AR was established by clinical symptoms and/or biopsy.

Results

Tregs in M1 predicted AR (n=7) between M2 and M6 below a 45.8th percentile cut-off with a sensitivity of 87.5% and a specificity of 69.4% (area 0.781, P=0.009). Tregs at M1 were not associated with AR (n=5) in M7 to M12 but Tregs in M2 and M3 with a sensitivity of 80%, and a specificity of 60% (area 0.797, p=0.0007). Odds ratios using the cut-offs established by ROC analysis were 15.8 (95% CI 1.8-137.9, p=0.012) and 6.0 (95% CI 0.63-56.8, p=0.12), respectively. There was no association between Tregs and either Tac or MPA concentrations. Tac and MPA concentrations in M1 were predictive for the occurrence of AR between M2 and M6, too.

Conclusions

Low Tregs determined by qPCR of the TSDR early after transplantation seem to be promising to predict AR in the consecutive months after KTx with a lead time of about 1-5 months as well as to be used in combination with other biomarkers to complement TDM for better individualizing immunosuppression. The results of this single center study need confirmation in a greater cohort of KTx patients and in other centers.