AUC of Micophenolate mofetil as a tool to avoid over and under exposure.

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Introduction
Micophenolate mofetil (MMF) is used concomitantly with Tacrolimus to prevent rejection after transplantation. No correlation between C0 and AUC is shown and AUCs are mandatory to know MMF exposure. In our center, kidney transplant patients receive 2000mg total daily dose (TDD) after transplantation and doses are reduced to 1000 mg TDD at discharge (7-10 days). In clinical practice, MMF TDD is decreased to 500 mg in case of: adverse effect, renal disfunction, infectious disease. The aim of the study was to correlate MMF doses with on target AUCs (30-50 µg.h/ml) and clinical variables.

Methods
MMF AUCs were performed in adult kidney transplant recipients (N=65). Pharmacokinetic data were analyzed from 2000 (N=31), 1000 (N=17) and 500 (N=17) mg MMF TDD. Blood samples were collected at pre-dose and 0.5, 1, 1.5, 2, 4, 6, 8 and 12-hours after MMF intake. Biochemical and clinical data were collected.

Results
The AUCs mean (µg.h/ml) depending on the dose were: 57.12±25.30 (24.77-114.4), 37.70±24.73 (10,89-107.61) and 24.59±17.79 (6.26-70.26) respectively for 2000, 1000 and 500 mg MMF TDD. Values of C0 (µg/ml): 2.99±2.044, 1.69±1.12 and 1.56±1.21, Cmax (µg/ml): 12.25±7.24 (2.4-32.1), 10.68±7.77 (2.65-28.9) and 5.8±3.97 (1.21-15); and Tmax (h): 1.8±1.54, 1.32±1.10, 2±1.89 were detailed respectively for 2000, 1000 and 500 mg MMF TDD. A percentage of 51,61% (n=16) of patients resulted overexposed after a TDD of 2000mg at the first week after transplantation and 12,9% (n=4) were underexposed. Only 23,52% and 11.76% were over-exposed after 1000 and 500 MMF TDD. Conversely, a high percentage of under-exposure of 52,94% and 88.23% was observed respectively. A Total of 35.48% of viral infections were observed and 72.72% of the infections occurred in patients over-exposed and 2000mg MMF TDD (33% showed CMV infection in the first-year post-TR; p=0.049). An interesting inverse correlation between weight and MMF exposure was found (r= -0,4693, p= 0,0089).

Conclusions
A higher number of over-exposure patients were observed after 2000 mg MMF TDD and with under-exposure after 1000 and 500 MMF TDD. Pharmacokinetic studies to individualize MMF treatment are needed to increase the number of patients on target.