IATDMCT PRAGUE 2022

Objective and Methods

- To evaluate the rate of discrepancies between observed AUCs measured with a microsampling approach (AUC_{OBS}) and expected AUCs from C_{min} (AUC_{EXP})

- Microsampling AUC monitoring in SOT recipients from Dec 2019 to Feb 2022
- **AUC_{OBS}** : 8-time point profiles, Volumetric absorptive microsampling (VAMS) (Mitra©, Neoteryx, CA, USA), LC-MS/MS method by Tron et al.[1]. Non compartmental PK approach (PK solver)
- **AUC_{EXP}** : Equations developed by Marquet et al.[2] and Saint-Marcoux et al.[3,4]
- Discrepancy: **AUC_{EXP}** +/-20% from **AUC_{OBS}** Bland-altman

[1]Tron et al., J Chrom B 2021; [2]Marquet et al., Ther Drug Monit 2018, Saint-Marcoux et al., Ther Drug Monit 2013; [4]Brunet et al., Ther Drug Monit 2019

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Results

- Patients and treatment
  - 63 AUCs in 51 patients

Patients' characteristics (n=63 measurements)	
Age (median, range)	52 (21;80)
Sex (%H/F)	68 % H / 32 % F
Type of transplantation (% kidney, liver, heart)	78 % K / 20 % L / 2% H
C Reactive Protein ($mg.mL^{-1}$) (median, range) (n=46*)	3 (<1;26)
Serum Creatinine ($\mu mol.mL^{-1}$) (median, range) (n=62*)	134 (58;420)
Hematocrit (%) (median, range) (n=62*)	36 (25;47)
Prograf® Immediate-release tacrolimus (n)	31
Advagraf® Extended-release tacrolimus (n)	17
Envarsus®LCP-tacrolimus (n)	15

*data not available for all patients

Median POD = 467 days [7-4255]

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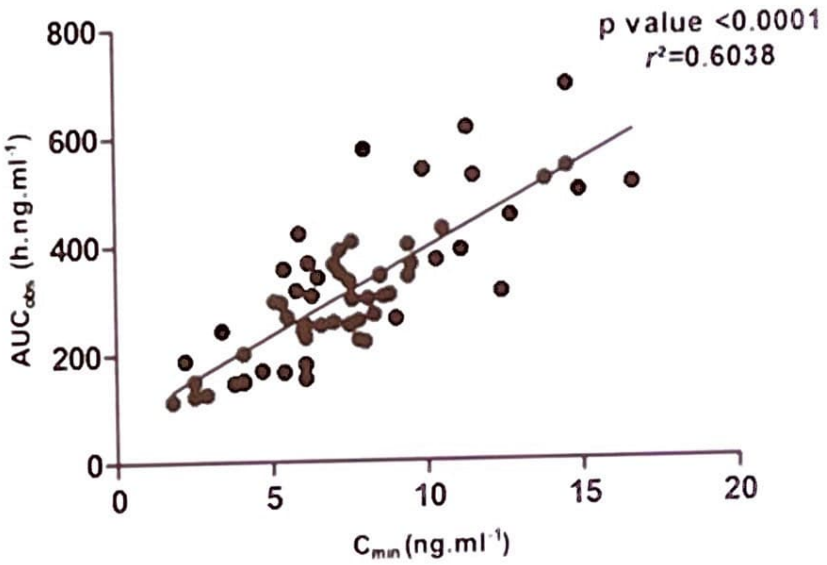
- AUC_{OBS} vs C_{min}



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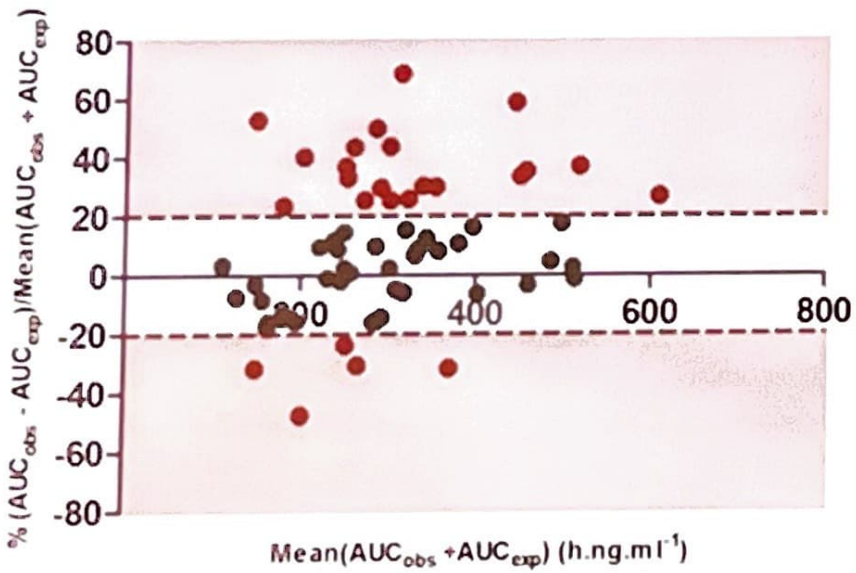
Results

- AUC_{EXP} vs AUC_{CALC}



Bias > 20% in 25/63 patients (39.6%)

20/63 (31.7%) C_{min} underestimated AUC
5/63 (7.9%) C_{min} overestimated AUC

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Discussion - Conclusion

- Cmin is not a adequate exposure index in ≈ 40% of patients
- Cmin mostly undersestimate AUC -> risk **adverse drug reactions**
- Cohort of patients with AUC for cause!
- No specific equation for LCP-Tacro

- Individualizing Cmin according to **AUC should be proposed to every SOT**
- AUC measured with a microsampling approach **might be the new gold standard**
- Frequent discrepancies might be **an explanation for unexpected drug effect**