New Approach to Therapeutic Drug Monitoring of Mycophenolic Acid for Solid Organ Transplant Patients

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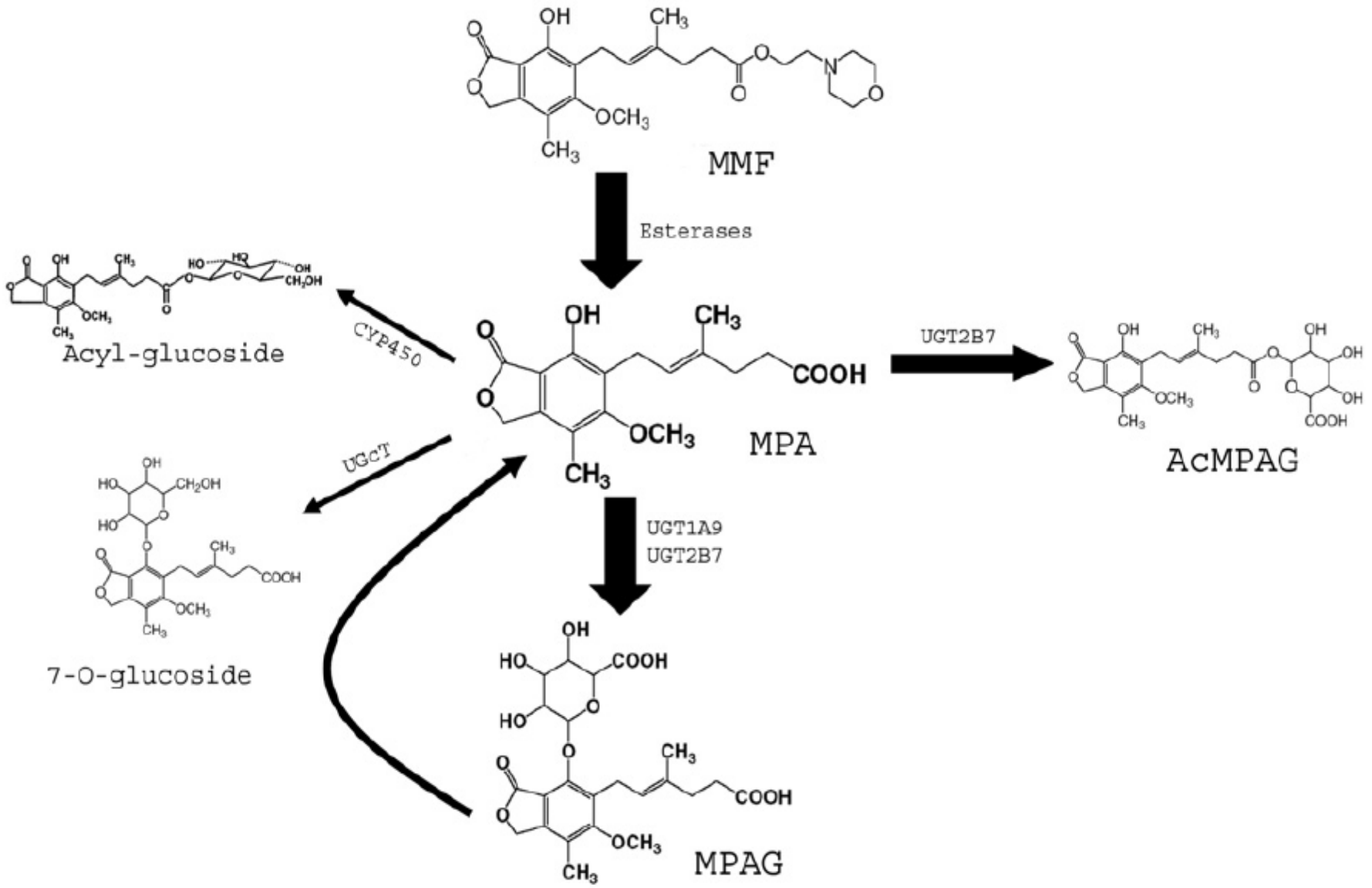
MPA and MPAG

- CellCept (Mycophenolate Mofetil) and Myfortic (Mycophenolate Sodium) are therapeutic drugs that are routinely administered to solid organ transplant patients to suppress the immune system and prevent organ rejection.

- Mycophenolate compounds are metabolized by recipients into Mycophenolic Acid (MPA), the active immunosuppressive compound.

- MPA is subsequently metabolized into Mycophenolic Acid Glucuronide (MPAG). MPAG is partially converted back to MPA by enterohepatic recirculation.

Metabolism of Mycophenolate Compounds



Betônico, Gustavo N., et al. Journal of nephrology 21.4 (2008): 503-509.

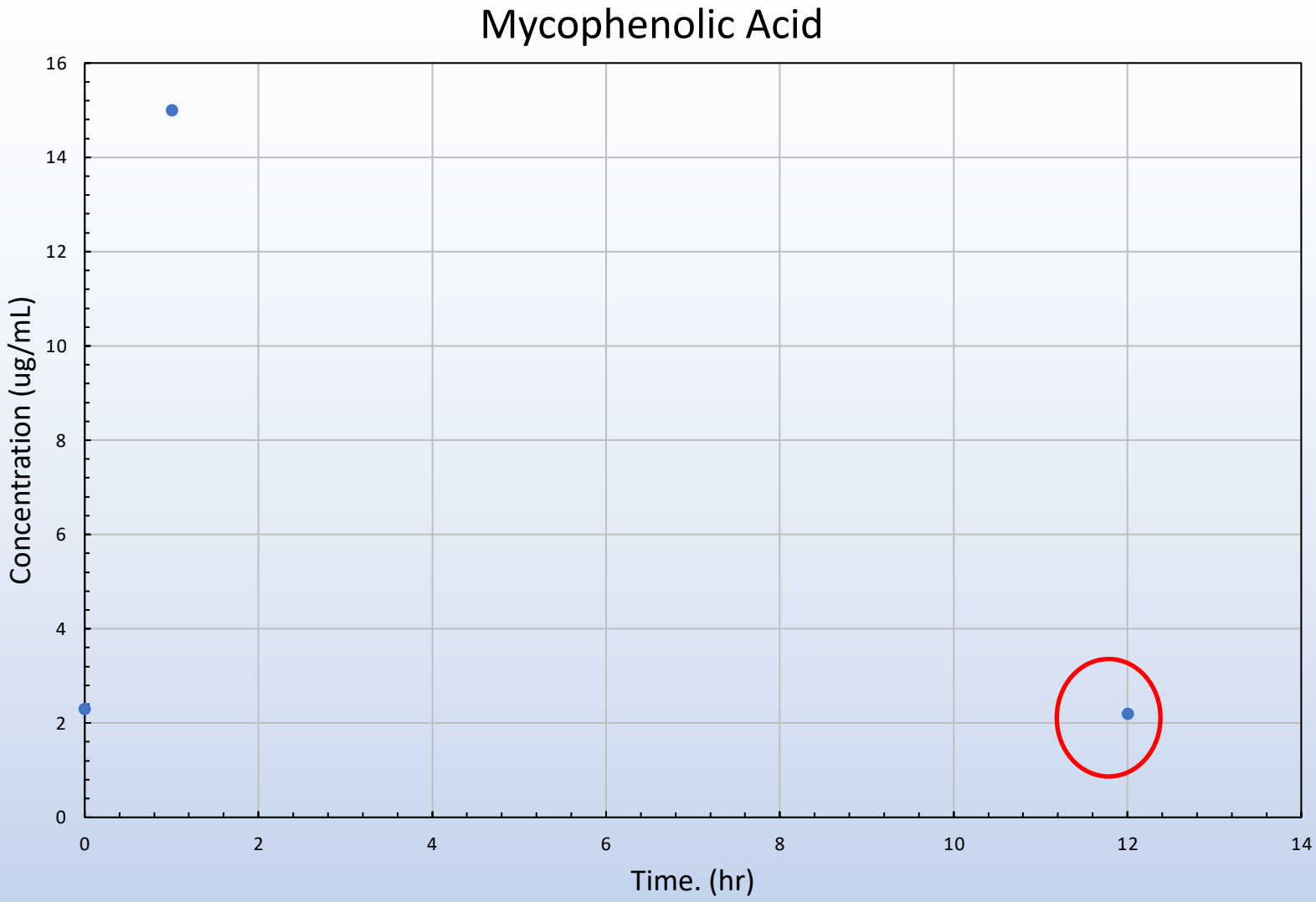
Reasons for Pharmacokinetic Variability

- Gender
- Ethnicity
- Hypoalbuminemia
- Hyperalbuminemia
- Pharmacogenetic variability
- Renal Impairment
- Hepatic Impairment
- Interaction with other drugs
- Co-Morbidities
- Time after transplant

Current Practices

Steady state analysis is the current standard in US for therapeutic drug monitoring of MPA and MPAG.

Pharmacokinetics MPA



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Given the drastic variations in interpatient metabolisms of MPA and its glucuronide metabolite (MPAG).

It is important that more accurate and comprehensive methods of TDM are made available to transplant patients.

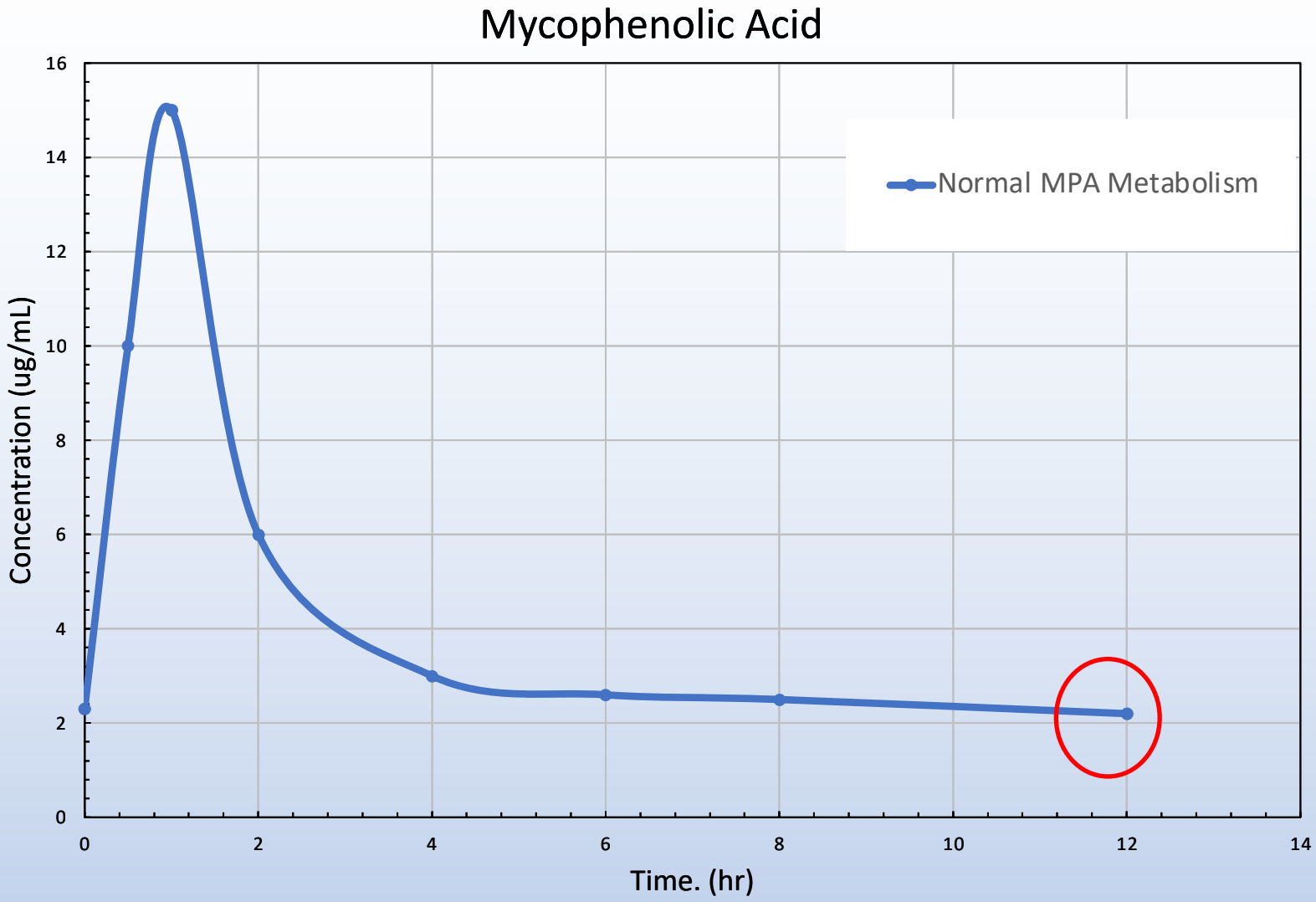
New approach to TDM of MPA

Our laboratory has developed an assay for therapeutic drug monitoring of MPA and MPAG using LC-MS/MS.

Provide pharmacokinetic analysis that is personalized to each patient.

Determine the best drug regimen for lowering the risk of organ rejection and toxic side effects.

Pharmacokinetics MPA



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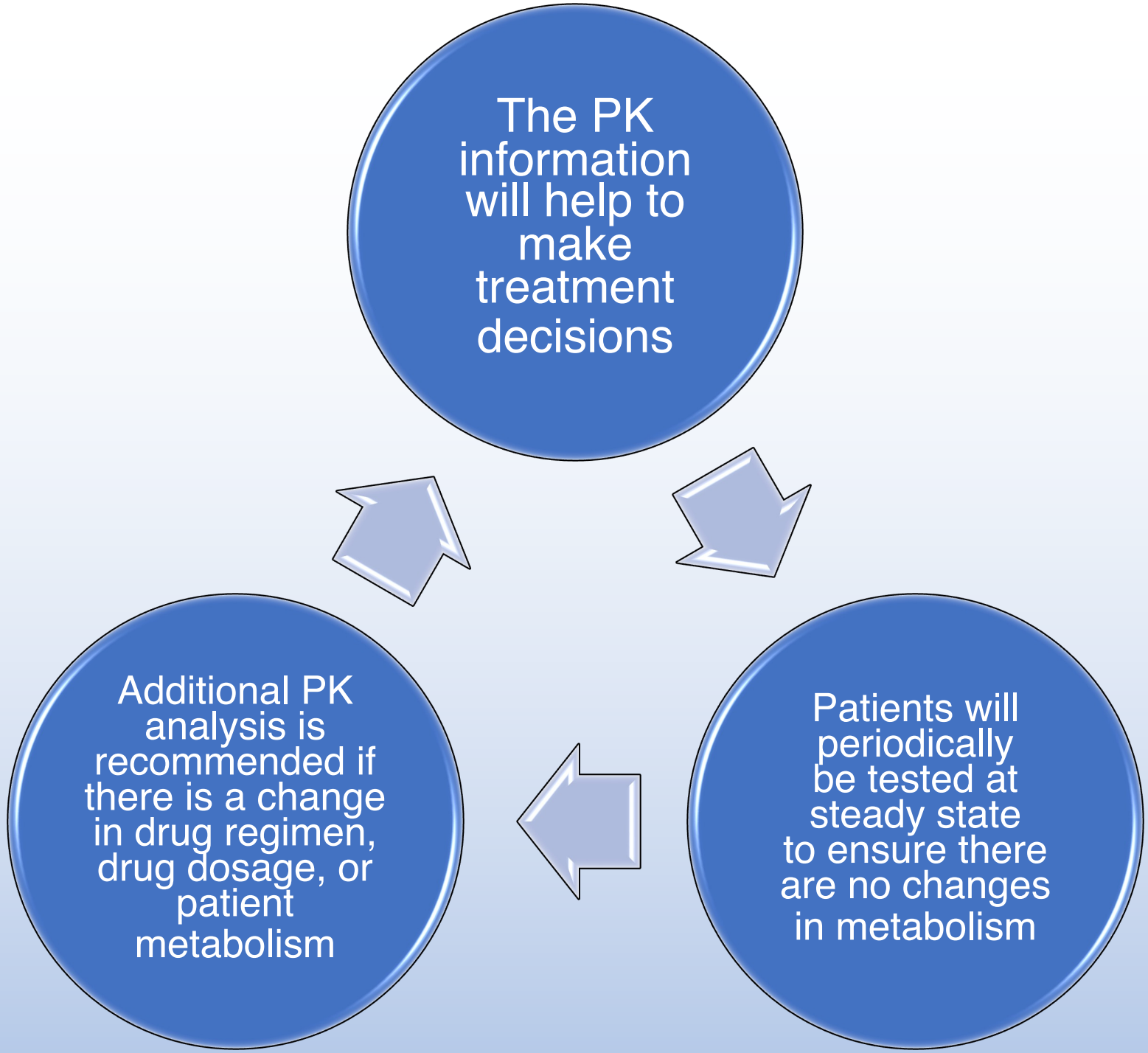

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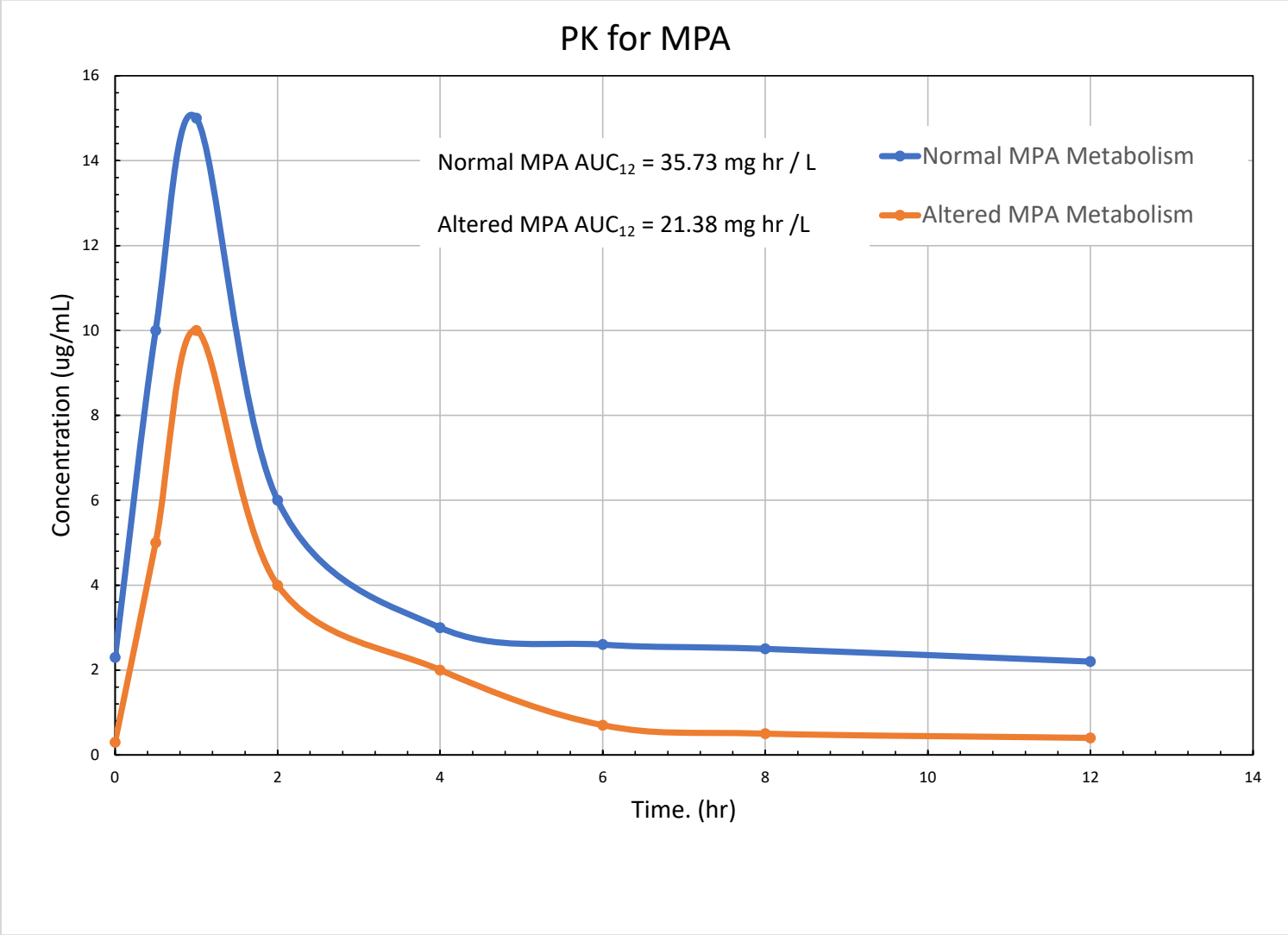
PHARMACOKINETIC RESULTS



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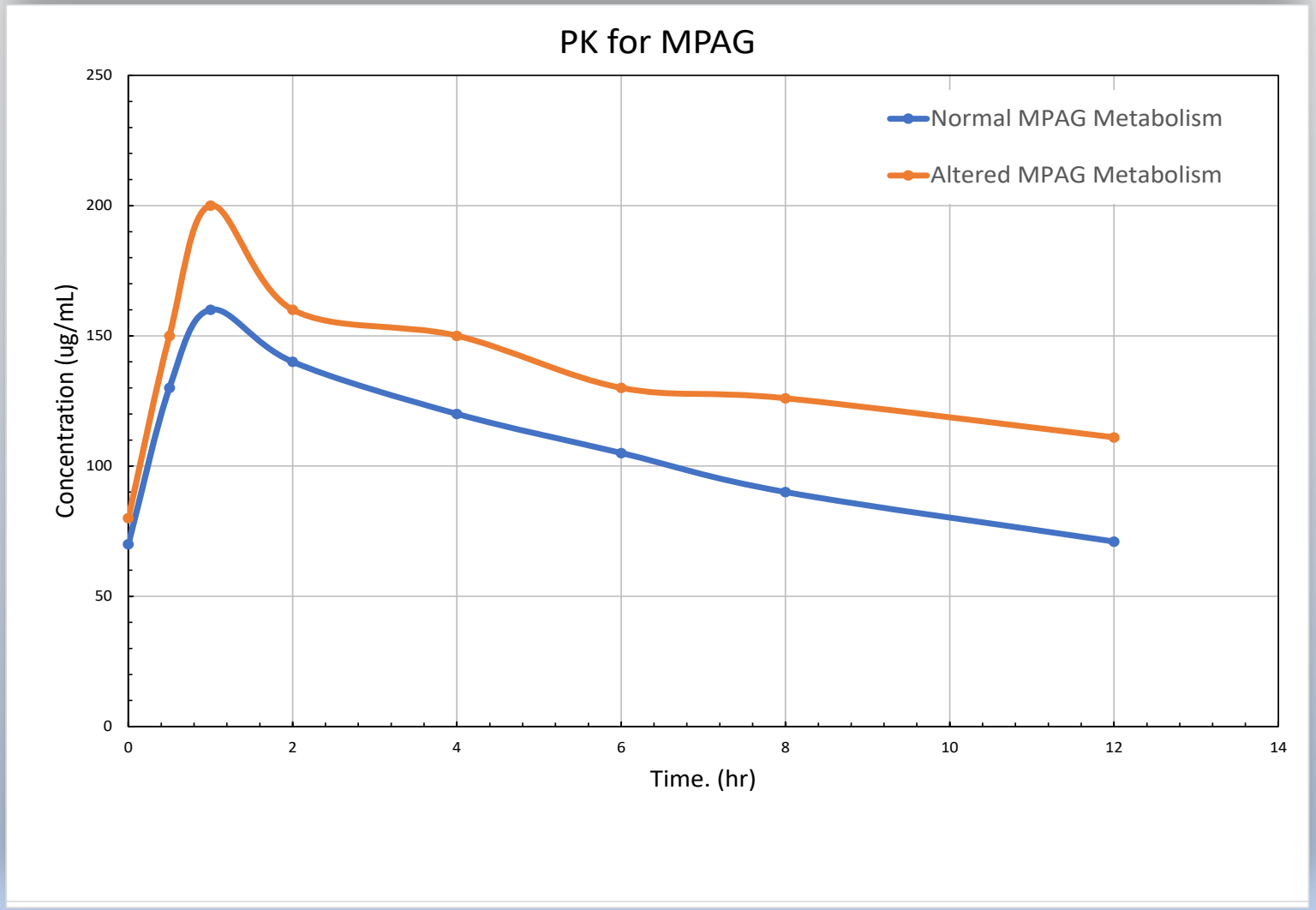
PHARMACOKINETIC RESULTS



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Interpretation MPA AUC_{12}

Target: Total MPA AUC from 0-12 hours (AUC_{12}) of **30-60 mg hr /L**

Low AUC is associated with increase incidence of biopsy-proven acute rejection.

High AUC is associated with toxic side effects.

MPA AUC_{12} is the most useful exposure measure for individualization.

Individualization of mycophenolate therapy leads to improved patient outcomes.

Staatz, Christine E., and Susan E. Tett. "Archives of toxicology 88.7 (2014): 1351-1389.
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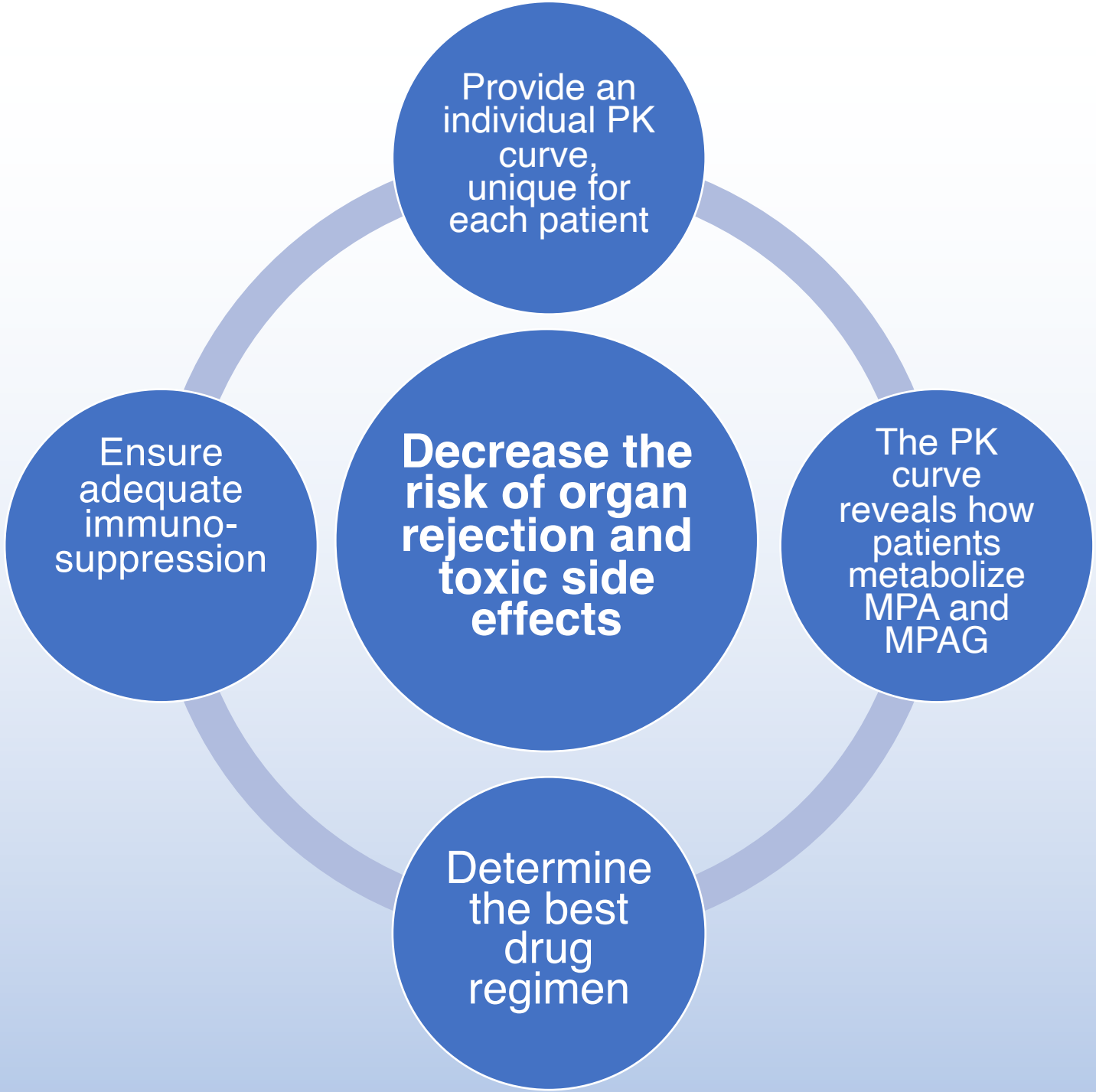

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