GraftAssure CORE™
Personalized Transplant Monitoring

Liver

Clinical Publication Summary

Use of Graft-Derived Cell-Free DNA as an Organ Integrity Biomarker to Reexamine Effective Tacrolimus Trough Concentrations After Liver Transplantation

Oellerich M, Schütz E, Kanzow P, et al. (2014) Ther Drug Monit 36(2):136

Practical Clinical Utility

Donor-derived cell-free DNA (dd-cfDNA) may aid in determining the minimum effective immunosuppressive dose for liver transplant patients

Endpoints and Goals

To understand if dd-cfDNA can be used to re-examine currently accepted minimally effective tacrolimus trough blood concentrations in liver transplant patients.

Methods

A total of 103 paired tacrolimus and dd-cfDNA measurements from samples collected between days 5 and 30 after liver transplantation were analyzed in this study.

- **Number of patients** = 10 immunologically high-risk patients (comorbidities include: HCV+, cirrhosis, re-transplants, hepatocellular carcinoma, sclerosing cholangitis)
- **Number of samples** = 103

Droplet digital polymerase chain reaction (ddPCR) was used to assess dd-cfDNA concentration (%).

Tacrolimus whole blood concentrations were measured using mass spectrometry and dosing was based on previously-established therapeutic ranges.

- Tacrolimus thresholds used in this study were based on therapeutic ranges (8-12 mg/L) accepted by liver transplant surgeons and hepatologists
- A dd-cfDNA value of ≤10% indicated organ integrity (graft in good health)

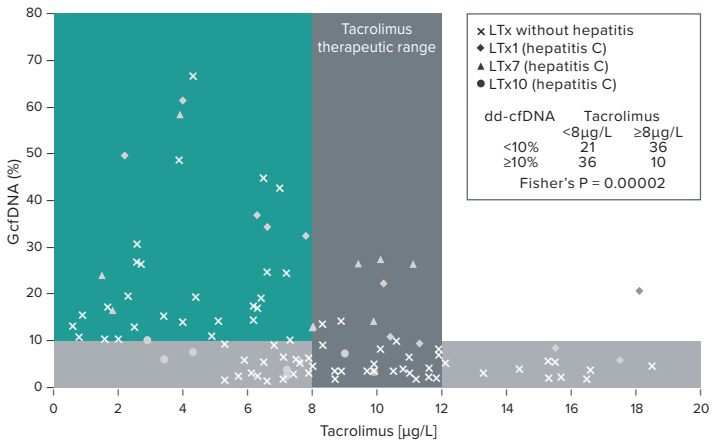

FIGURE 1. Comparison of predose Tacro concentrations in micrograms per liter versus the percentages of cell-free DNA coming from the donor liver (GcfDNA) in adult patients (n=10) during the first 5-30 days after LTx.

GcfDNA = graft-derived cell-free DNA (equivalent to dd-cfDNA).

Results

There was a highly significant segregation towards patients with elevated dd-cfDNA (≥10%) and tacrolimus concentrations below the target concentration of 8–12 mg/L.

dd-cfDNA ≤10% gave the best separation for the evaluation of effective tacrolimus concentrations, supporting its use as the cutoff for defining graft integrity from graft damage.

Conclusion

dd-cfDNA (%) measurement may be helpful in achieving more effective personalized immunosuppression and, in particular, may better aid clinical care in finding the minimum effective immunosuppressive dose for liver transplant patients.

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