

# Time-Dependent Apparent Increase in dd-cfDNA Percentage in Clinically Stable Patients Between One and Five Years Following Kidney Transplantation

Schütz E, Asendorf T, Beck J, et al. (2020) Clin Chem 66(10):1290.

# **Practical Clinical Utility**

For long-term surveillance, measurement of absolute dd-cfDNA (cp/mL) concentrations appears to be superior to the fractional abundance of dd-cfDNA (%)

# **Endpoints and Goals**

- Assess changes in dd-cfDNA (%) reference values by measuring total cfDNA dynamics over several years following kidney transplantation
- Determine whether dd-cfDNA (%) is as effective as absolute dd-cfDNA (cp/mL) for long-term graft surveillance
- Evaluate a possible relationship between cfDNA and tacrolimus

### **Methods**

- Single-center, cross-sectional study cohort (part of a prospective clinical validation trial) evaluated 929 plasma samples from 303 clinically stable kidney transplant patients at nine defined time points from 12 to 60 months following kidney transplantation
- dd-cfDNA (%) and dd-cfDNA (cp/mL) were directly compared along with additional laboratory values from routine monitoring (creatinine, white blood cell count, eGFR, and ISD)

# Results

#### Total cfDNA median values steadily decreased over

**time** among the 303 clinically stable patients during the observation period, resulting in increasing dd-cfDNA (%) that was independent of graft health.

There was a sustained significant difference in total cfDNA compared to healthy controls (HC) and patients with other medical conditions (OC) not receiving immunosuppression



**FIGURE 1.** Time course of total cell-free DNA (cf-DNA) during the 60 months study period. Boxes depict the 25th and 75th percentiles as a box and a median line; whiskers extend to minimum or maximum, but at most 1.5 x IQR; Left side with restricted y-axis; Right side with y-axis covering all outliers.

# Absolute dd-cfDNA (cp/mL) was stable during

**observation period**, along with median plasma creatinine and eGFR, confirming that absolute quantification accurately reflected the 303 healthy stable patients.



**FIGURE 2.** Regression analyses of study variables vs log-months after kidney transplant. Time dependencies are given as slope coefficients of quantile regression for given parameters (y-axes) vs log-months for the different percentiles (x-axis). A deviation of the 95%-pointwise confidence intervals (shaded area) from 0 indicates a significant change of values with time. cfDNA: cell-free DNA; dd-cfDNA: donor derived cell-free DNA.

Conclusion

Calcineurin inhibitor (CNI) therapy increased the amount of total cfDNA, which decreased during drug tapering and led to an

increase in dd-cfDNA (%). The absolute amount (cp/mL) and the established threshold remained stable.

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