natera™ | Prospera™
Transplant assessment


CASE STUDIES

## How quantifying background cell-free DNA enables even greater precision with Prospera for rejection assessment

As the experts in cell-free DNA (cfDNA) testing, Natera has refined our workflow based on findings from two million cfDNA tests to now include **a first-in-class technique capable of quantifying background cfDNA** in a streamlined manner.

When assessing rejection via the Prospera™ transplant assessment test, this pioneering enhancement provides additional information, which may enable an even more precise and confident assessment—particularly in flagging patients at-risk of false-negative interpretations.

PROSPERA CASE STUDIES*

# Even more precise, holistic assessment with background cfDNA

## PATIENT 1

### Meet Kirk

- Male
- Late 70s
- End-stage renal disease (ESRD)
- Transplant in mid-2018

**THE JOURNEY**

| Transplant surgery | Post-transplant | | |
|---|---|---|---|
| | 6 months | 7 months | 14 months |
| Mid 2018 | Elevated creatinine levels, indicating acute T cell-mediated rejection (TCMR) | Tested positive for BK viremia, which was immediately treated and resolved | Admitted for herpetic and cytomegalovirus (CMV) esophagitis and was treated with intravenous ganciclovir |

**CLINICAL ASSESSMENT WITH PROSPERA**

The Prospera result revealed a low **donor-derived cell-free DNA (dd-cfDNA) fraction at 0.38%**, indicating a decreased risk for active rejection.

Further Prospera analysis quantified background cfDNA, **revealing a level 21x the median**—and thereby flagging an increased risk of a false-negative interpretation.

Based on Prospera's enhanced reporting, percutaneous kidney transplant biopsy was performed; the result **confirmed chronic cellular rejection** (via Banff criteria).

**THE TAKEAWAY**

**Viral infections can cause an atypical increase in recipient background cfDNA. This inflation may lead to an artificially deflated percentage of dd-cfDNA.**

**Prospera's novel ability to quantify background cfDNA highlighted an increased risk for a false-negative interpretation.**

## PATIENT 2

### Meet Janice

- Female
- Early 60s
- End-stage renal disease (ESRD)
- Transplant in early 2017

**THE JOURNEY**

| Transplant surgery | Post-transplant |
|---|---|
| | 3 years |
| Early 2017 from a deceased donor | Assessed with Prospera during a routine visit |

**CLINICAL ASSESSMENT WITH PROSPERA**

Prospera result showed a **dd-cfDNA of 0.28%**, potentially a decreased risk for active rejection.

The report also flagged atypical background cfDNA levels that were elevated at **~7x the median.**

The resulting percutaneous kidney transplant biopsy **revealed BK virus-associated nephropathy and T cell-mediated rejection.**

**THE TAKEAWAY**

**BK virus-associated active injury may contribute to atypical background cfDNA levels.**

**Prospera's latest enhancement allows for physicians to more effectively identify active rejection that would have otherwise been missed.**

## PATIENT 3

### Meet Scotty

- Male
- Late 70s
- End-stage renal disease (ESRD)
- Transplant in mid-2018

**THE JOURNEY**

| Transplant surgery | Post-transplant | |
|---|---|---|
| | 1 month | 6 months |
| Late 2019 from an unrelated, living donor | Diagnosed with dengue fever, followed by acute allograft dysfunction | A biopsy was performed revealing active antibody-mediated rejection. He was then treated with plasmapheresis and intravenous immunoglobulin with clinical resolution |

**CLINICAL ASSESSMENT WITH PROSPERA**

At 7 months post-transplant, he received a Prospera result of **0.16% dd-cfDNA level**, indicative of a decreased risk for active rejection.

The Prospera result also revealed a heightened level of background cfDNA at **~13X the median**.

A biopsy thereafter **showed resolution of ABMR and borderline acute cellular rejection.**

**THE TAKEAWAY**

**For the first time, further evaluation of background cfDNA levels enabled the physician to identify signs of borderline acute cellular rejection.**

**This additional information by Prospera can provide a more complete clinical assessment of your transplant patient.**

## PATIENT 4

### Meet Sharon

- Female
- Late 50s
- End-stage renal disease (ESRD)
- secondary to PKD

**THE JOURNEY**

| Transplant surgery | Post-transplant | | |
|---|---|---|---|
| | 11 months | 11 months, 1 week | 11 months, 1.5 weeks |
| Late 2018 from a deceased donor | Presented with four days of worsening diffuse muscle pain | Progressed to a temperature of 101°F (asymptomatic previously). Visited her local emergency room | Tested positive for COVID-19 and intubated at her transplant center. Renal function deteriorated, immunosuppression was closely managed |

**CLINICAL ASSESSMENT WITH PROSPERA**

Prospera was used to assess rejection status on the 20th day of her hospital stay.

The Prospera result showed **0.07% dd-cfDNA** with a heightened level of background cfDNA at **~57X the median.**

A second Prospera test was drawn on the 25th day of her hospital stay with a result of **0.25% dd-cfDNA** and a decreased level of background cfDNA at **~15x the median.**

**THE TAKEAWAY**

**COVID-19 may cause very elevated background cfDNA. Therefore, patients are at-risk for a false negative interpretation, especially when immunosuppression is reduced in response to the infection.**

**By reporting high background level, Natera proactively alerts the physician if the result may yield a false negative in a high-risk patient.**

* Deidentified patient names and details

# About Prospera, Transplant Assessment Test

## Powered by highly optimized, proprietary cfDNA technology, Prospera enables you to:

**Catch all rejection types in a single blood draw:** Prospera's unique ability to identify T cell-mediated rejection (TCMR) gives a more holistic view of your patient's rejection status.[1]

**Minimize risk of missing active rejection:** Prospera is three times less likely to miss an active rejection** than the first-generation donor-derived cell-free DNA test (Negative Predictive Value of 95% vs 84%).[1, 2]

**More accurately classify active rejection:** Prospera demonstrated better performance than the first-generation dd-cfDNA test (sensitivity of 89% vs 59%) to identify patients with active rejection.[1, 2]


**References**

** 25% prevalence of active rejection

1 Sigdel TK, Archila FA, Constantin T, et al. Optimizing detection of kidney transplant injury by assessment of donor-derived cell-free DNA via massively multiplex PCR. J Clin Med. 2019;8(1):19.

2 Bloom RD, Bromberg JS, Poggio ED, et al. Cell-free DNA and active rejection in kidney allografts. J Am Soc Nephrol. 2017;28(7):2221-2232. doi: 10.1681/ASN.2016091034.



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