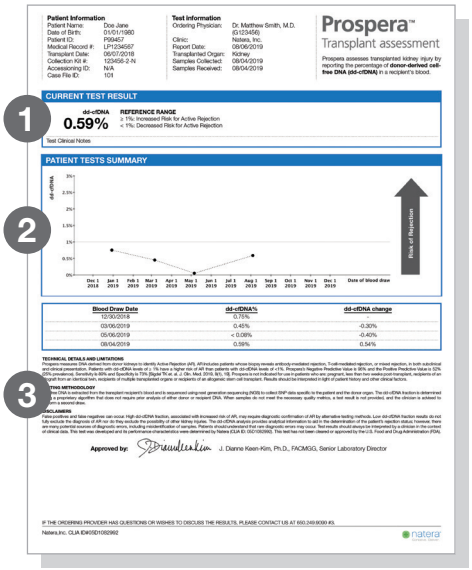
natera | Prospera™ Transplant assessment



Clinician's guide to results

This guide is designed for clinicians and should be used as a supplement to the Prospera™ results reports. Prospera uses single-nucleotide polymorphism (SNP)-based technology to assess for active rejection (AR) by measuring the DNA derived from transplanted donor kidneys. AR includes antibody-mediated rejection, T-cell-mediated rejection, and mixed rejection in both subclinical and clinical presentations, as revealed in the biopsy. The Prospera result represents the percent of cell-free DNA in the recipient's blood that originates from the allograft. Prospera results and transplant rejection status should always be considered in the context of other significant clinical factors and physician judgment.

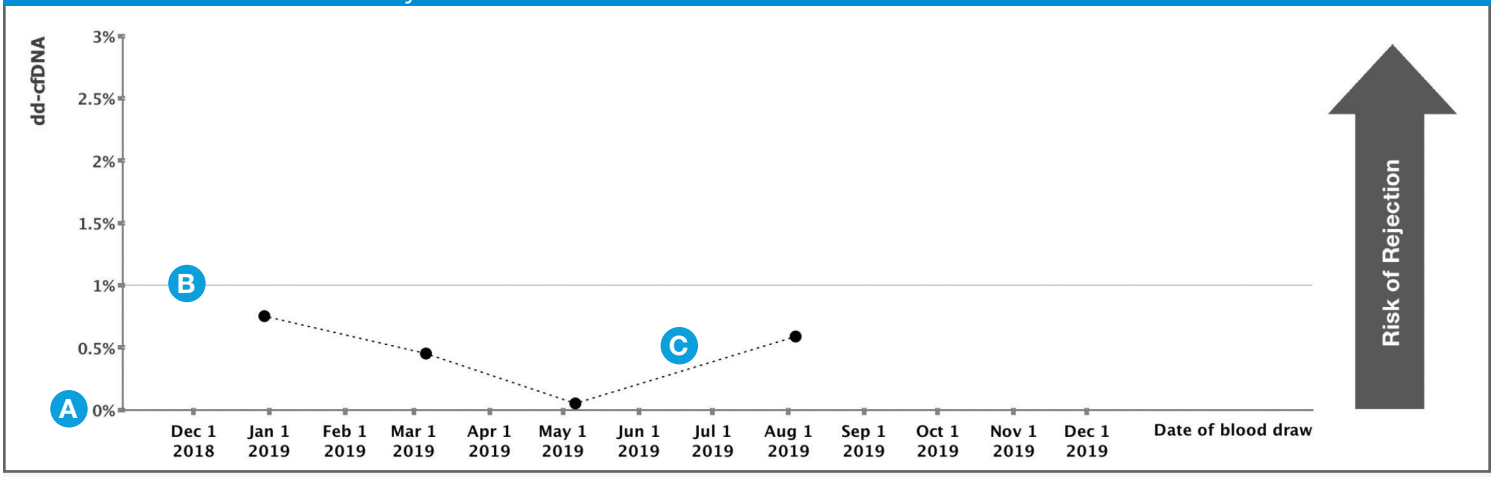
1 Current Test Result

dd-cfDNA
0.59%

REFERENCE RANGE
≥ 1%: Increased Risk for Active Rejection
< 1%: Decreased Risk for Active Rejection

The Current Test Result section reports the dd-cfDNA level obtained from the most recent Prospera draw. The reference range provides a general risk assessment derived from our published clinical validation study. Patients with dd-cfDNA levels ≥1% have a higher risk of AR than patients with dd-cfDNA levels of <1%.[1]

2 Patient Test Summary



A The X-axis highlights the date of blood draw; the Y-axis represents the % dd-cfDNA level at the date of the blood draw.

B The 1% dd-cfDNA cutoff is marked as a reference.

C A dotted line connects dd-cfDNA values over time, but does not necessarily reflect a rate of change.

The Patient Test Summary depicts the patient's Prospera results over the previous 12-month period. For optimized clinical care, establishing a patient's baseline dd-cfDNA level may be beneficial. The chart below conveys the same information as in the graph above, but it adds specific draw dates and % dd-cfDNA change between draws.

Blood Draw Date	dd-cfDNA%	dd-cfDNA change
12/30/2018	0.75%	-
03/06/2019	0.45%	-0.30%
05/06/2019	< 0.08%	-0.40%
08/04/2019	0.59%	0.54%

3 Technical Details

	dd-cfDNA level ≥1.00(%)
Sensitivity – the ability of the test to correctly identify those patients **with** active rejection (true positives)	**88.7**
Specificity – the ability of the test to correctly identify those patients **without** active rejection (true negatives)	**72.6**
Positive predictive value (PPV)* – the chance that an individual is experiencing active rejection, given an increased risk result	**51.9**
Negative predictive value (NPV)* – the chance that the individual is truly stable, given a low-risk result	**95.1**

*PPV and NPV calculated based on a 25% prevalence of AR.

Limitations

Prospera is contraindicated:

- less than 24 hours after a biopsy or dialysis
- less than two weeks after transplant
- in pregnant women
- in recipients of multi-organ transplants or allogeneic stem cells
- in patients who have received an allograft from a genetically identical twin.

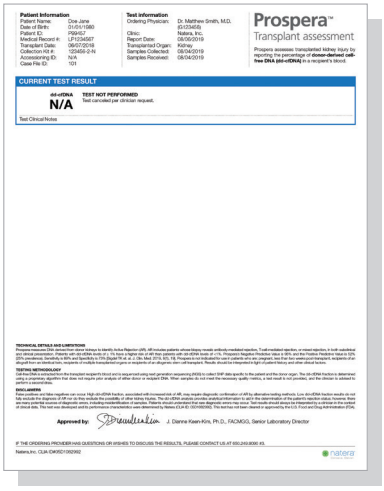
Results should be interpreted in the context of the entire clinical presentation because it is possible that other factors may influence dd-cfDNA results

Other Results

Test not performed (TNP)
The reason the test was not performed is indicated in the Current Test Result section and may include: sample receipt >8 days post draw; low blood volume (only one tube received instead of two); incorrect tube; or damaged sample. *If the test was not performed due to missing required information, please contact Natera to update. Otherwise, a new sample is required for testing.*

No results — submission of repeat specimen is required for testing
This result may be due to issues with laboratory processing or limitations of the testing algorithm. This result is likely sample-specific and is expected to resolve with a new sample.

No results — repeat sample is not indicated
These rare cases occur when an individual has a DNA pattern that cannot be interpreted clearly by this assay. This can be due to normal variation or to other clinical factors that may impact analysis. Please contact the Prospera clinical team with any additional patient information.


Prospera™
Transplant assessment
CURRENT TEST RESULT
dd-cfDNA
N/A
TEST NOT PERFORMED
Test cancelled per clinician request.

For additional assistance, you are encouraged to contact Prospera clinical support at **1.650.480.5007** or **transplantclinical@natera.com**.

References:
1. Sigdel TK, Acosta Archila F, 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. doi: 10.3390/jcm8010019

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