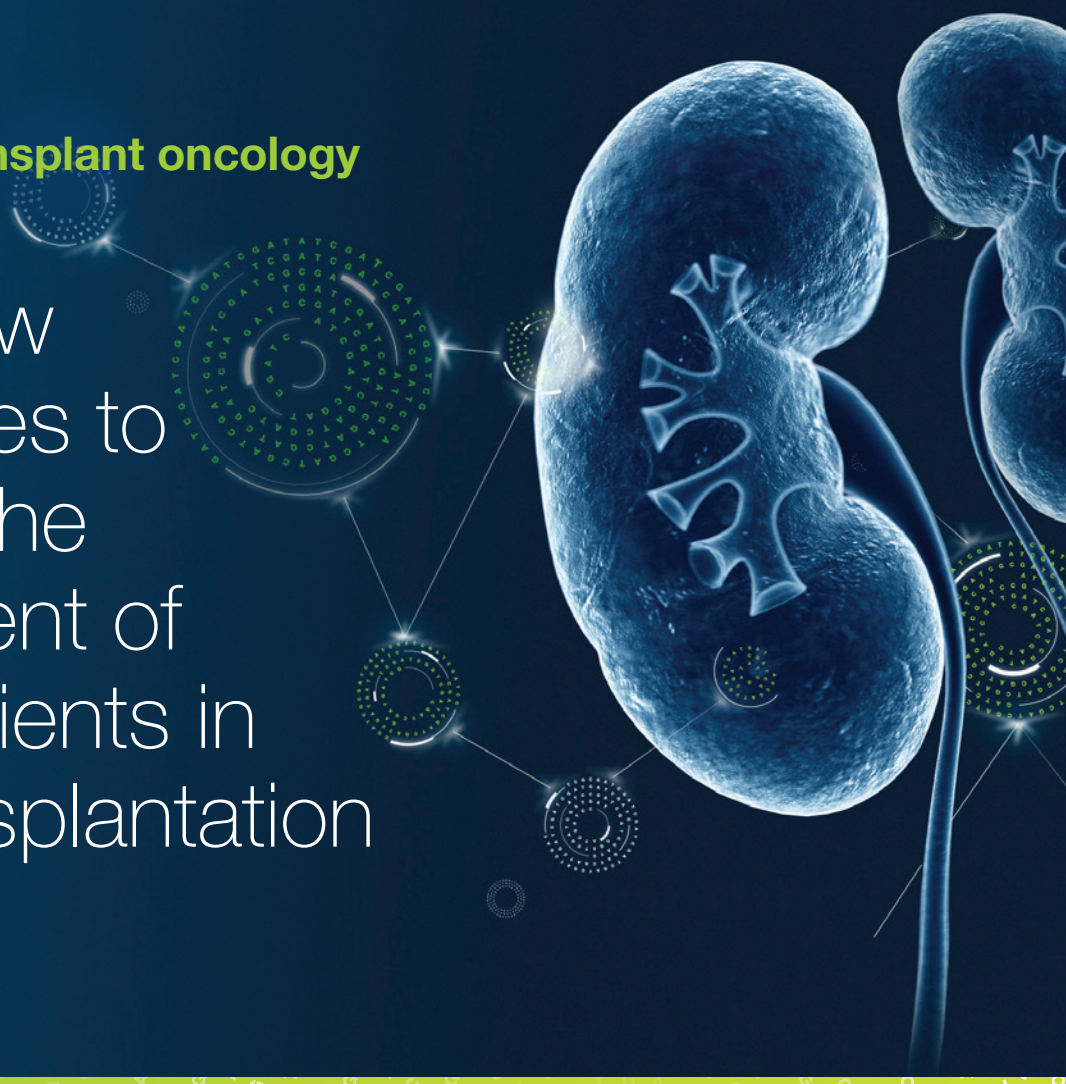
natera™ | Prospera™ Transplant assessment | Signatera™ Residual disease test (MRD)

Innovations in transplant oncology

Explore new technologies to transform the management of cancer patients in organ transplantation



Join us in understanding how Signatera™ and Prospera™ can improve decision-making at the complex intersection of organ transplantation and oncology.

Natera's innovations in transplant oncology

Prospera™
Transplant assessment

Signatera™
Residual disease test (MRD)

Advances in Cell-Free DNA Testing

Transform the management of cancer patients in organ transplantation

Pre-Transplant Evaluation

- A significant number of patients evaluated for transplantation have a history of cancer.
- Patients with end-stage renal disease have a 20% higher rate of colorectal cancer than the general population.[1]
- A history of cancer makes it difficult for patients to receive a transplant due to the uncertain risk of recurrence.

Post-Transplant Monitoring

- Transplant recipients also require immunosuppressive medications to avoid rejection, which can increase the risk of new or recurring cancers.

Signatera™
Cancer Recurrence Monitoring

Rejection VS **Cancer and Infection**

Prospera™
Rejection Monitoring

Signatera™
Cancer Recurrence Monitoring

A Balance of Immunosuppression

CONCERT STUDY

Colorectal Neoplasm in Candidates Enlisting for Renal Transplantation

A study to accelerate clearance for renal transplantation in molecular residual disease (MRD)-negative patients with a history of colorectal cancer

PARC STUDY

Prospera in Renal Allograft Recipients with Cancer

A study to understand how malignancies and cancer therapy affect background cell-free DNA levels in renal allograft recipients.

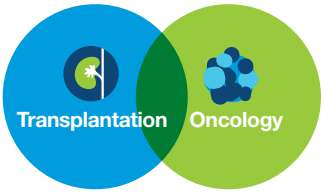
SIGNAL STUDY

Signatera in Liver Cancer

An observational study of Signatera in patients with liver cancer to determine molecular residual disease (MRD) rates before and after liver transplant.

The goal of Natera's Innovation in Transplant Oncology initiative is to understand how Signatera and Prospera can be used to improve decision-making at the complex intersection of organ transplantation and oncology, and to respond to the unmet needs within these communities.
For more information and to participate in these studies, please contact us at nito@natera.com.

Prospera™ transplant assessment test is a noninvasive blood test that can comprehensively identify all types of active organ rejection with great precision.

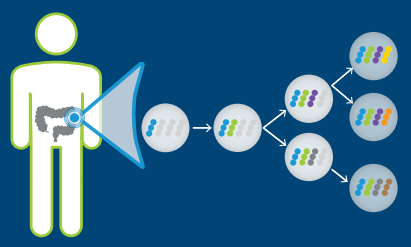


Signatera™ is a personalized, tumor-informed assay optimized to detect circulating tumor DNA (ctDNA) for molecular residual disease (MRD) assessment and recurrence monitoring for cancer patients.

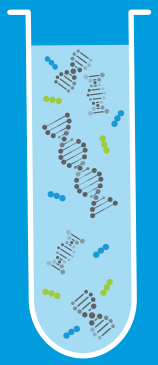
Signatera residual disease test (MRD): the personalized and tumor-informed approach

Signatera is a customized molecular residual disease assessment that can detect recurrence, on average, 8.15 months earlier than imaging tools, with high sensitivity and high specificity.

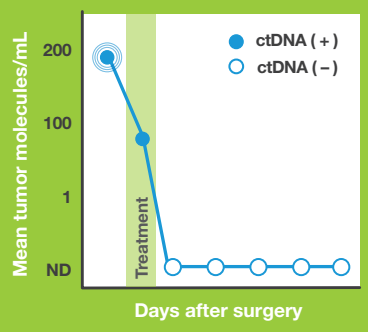
Sequence tumor tissue to identify unique signature of tumor mutations



Custom design and manufacture personalized mPCR assay for each patient, targeting the top 16 clonal mutations found in the tumor



Use personalized assay to test patient's blood for presence of circulating tumor DNA (ctDNA)



The personalized, tumor-informed approach behind Signatera

Signatera is the only commercially available test that can detect MRD and assess disease recurrence in solid tumors.

Personalized, tumor-informed assay (turnaround time = 2–3 weeks)

- A primary tissue sample and a blood sample are required for whole-exome sequencing and personalized test design.

Ultrasensitive ctDNA detection

- Signatera is designed to detect ctDNA of somatic and truncal variants to optimize sensitivity.
- This tumor-informed method enables filtering of germline and CHIP mutations to decrease false positive rates.

Optimized for longitudinal monitoring (turnaround time = 1 week)

- Only a blood sample is needed each time Signatera is ordered for the adjuvant or surveillance settings.

Prospera™
Transplant assessment

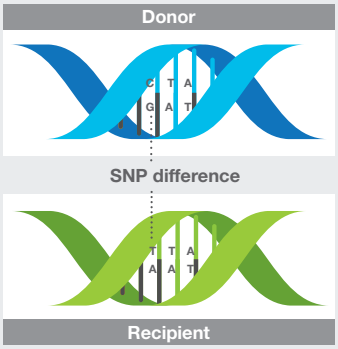
Developed by Natera with our trusted legacy in cell-free DNA, Prospera is thoughtfully optimized to be a precise and reliable tool for early, clinically meaningful rejection assessment.[2,3]

How Prospera works

Recipient blood sample

The sample is a mix of donor and recipient cell-free DNA (cfDNA)

Precise identification:



M ore than 13,000 single-nucleotide polymorphisms (SNPs) and advanced bioinformatics are used to differentiate recipient and donor cfDNA

Test results

NO active rejection: Minimal donor-derived cell-free DNA (dd-cfDNA) is released in a stable patient's blood.

OR

Active rejection: Upon cell injury, more dd-cfDNA is released from the donor kidney.

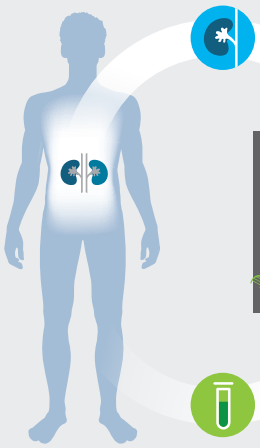
Prospera reports the percentage of dd-cfDNA in a transplant recipient's blood

As experts in cell-free DNA (cfDNA) testing, we have refined our workflow based on our findings from two million cfDNA tests to now include **a proprietary technique to quantify absolute background cfDNA** in a streamlined manner.

This enhancement provides additional information to the physician when assessing rejection and may assist in identifying patients who are at risk of a false negative interpretation.

Defining background cell-free DNA and its influence on your result

Background cell-free DNA originates from the transplant recipient and is naturally occurring in variable amounts within the plasma.



$$\frac{\text{Amount of donor-derived cfDNA from the transplanted kidney}}{\text{Background (total) cfDNA in the blood sample}} = \left(\text{\% donor-derived cfDNA (dd-cfDNA)}\right)$$

When the amount of background cfDNA is atypical, it impacts the percentage of dd-cfDNA and may compromise the depiction of risk for active rejection.

Factors that may influence background DNA may include:

- High body mass index (BMI)[4]
- Sepsis[5]
- Age[6]
- Surgery[7]
- Shipment and storage of sample[8]
- Chemotherapy[9]
- Normal variation[10]
- Myocardial infarction[11]
- Hemodialysis[12]
- Rejection

Signatera™
Cancer Recurrence Monitoring

Colorectal neoplasm in candidates enlisting for renal transplantation (CONCERT)

Unmet need

The average wait time for a kidney transplant is three to five years in the US, according to the National Kidney Foundation,[13] but that time can increase depending on certain factors, including a history of cancer.

There is a lack of standardization and consistent rationale in the determination of transplant eligibility—especially the requirements pertaining to demonstrating cancer clearance.

Study aims

The aims of this study are to:

- Provide quick, reliable assessment of colorectal cancer molecular residual disease (MRD) to better assess transplant eligibility
- Enable precise, early assessment of post-transplant recurrence

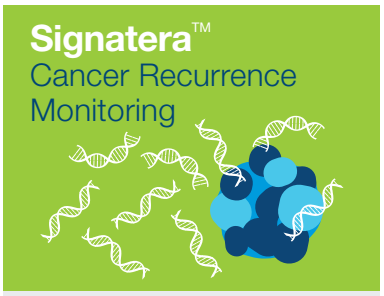
Study eligibility

Inclusion criteria:

- A history of colorectal cancer in patients who are considered cancer-free by current diagnostic tests and who are getting evaluated for kidney transplantation, regardless of cancer stage and duration
- Eligible for active listing based on glomerular filtration rate or because renal replacement therapy is currently in progress
- Available formalin-fixed, paraffin-embedded tumor tissue for a Signatera assay

Exclusion criteria:

- History of an organ transplant other than the renal allograft
- Clinical or radiological evidence of ongoing cancer
- Younger than 18 years of age



Observational study of Signatera in liver cancer (SIGNAL)

Unmet need

- Hepatocellular carcinoma (HCC) is the fifth most common and second most lethal malignancy worldwide.
- Liver transplantation is the best treatment for patients with early-stage HCC arising in cirrhosis selected according to Milan Criteria.[14]
- In 2015, HCC was the indication for 24% of liver transplant registrants and 27% of liver transplants.[15]
- Recurrences of HCC following liver transplants occur in 6% to 18% of patients and are difficult to predict.[16]
- There is no consensus on what the ideal cancer surveillance strategy and schedule should be after liver transplant.

Study aims

The aim of this study is to identify molecular residual disease (MRD) after liver transplantation to correlate it with risk of recurrence.

- Absence of MRD can allow for de-escalation of surveillance in low risk-patients (ctDNA-).
- Identification of MRD can lead to incorporation of intense surveillance in high-risk patients (ctDNA+) for whom locoregional therapy could improve survival.

Study eligibility

Inclusion criteria:

- Either underwent a liver transplant within the past 90 days or received a diagnosis of HCC and a liver transplant will be scheduled
- Available and sufficient tumor tissue on liver explant for whole-exome analysis

Exclusion criteria:

- Documented distant metastatic HCC
- Younger than 18 years of age

Prospera™
Rejection Monitoring

Prospera in renal allograft recipients with cancer (PARC)

Unmet need

- Kidney transplant recipients have a higher cancer risk than the general population, largely because of the side effects of induction therapy and immunosuppression maintenance medications.
- There is no strong data or consensus on how to adjust immunosuppressant regimens and monitor renal allograft function during and after cancer treatment.
- The main modes of monitoring for renal allograft rejection are serum creatinine and biopsy. Serum creatinine remains the most commonly monitored biomarker for renal allograft rejection, but though it is noninvasive, it is not particularly sensitive or specific.
- Biopsy with detailed pathology is the “gold-standard” for the diagnosis of organ rejection. Unfortunately, its clinical utility is significantly limited because of invasiveness, cost, inadequate sampling, and poor reproducibility.

Study aims

- Cell-free DNA is an effective monitoring tool as a marker for renal allograft rejection and injury.
- Both cancer and cancer-treatment regimens can affect cell-free DNA levels by increasing background cell-free DNA.
- Given the importance of monitoring for allograft rejection in patients with a renal allograft and any solid organ, hematopoietic, or lymphatic malignancy, the study aims to measure Prospera performance in these patients and to better understand the effect of cancer and cancer treatment on cfDNA in the blood.

Study eligibility

Inclusion criteria:

- Have a functioning kidney transplant in vivo
- Diagnosed with solid tumor malignancy, hematopoietic malignancy, or lymphoid tissue malignancy (either de novo or recurrence) within the prior year
- Have not received any treatment with curative intent prior to enrollment
- Intend to begin treatment for cancer within three months of enrollment

Exclusion criteria:

- Younger than 18 years of age
- Received a kidney from an identical twin
- Received any organ transplant other than a kidney
- Received a recent blood transfusion

Alongside our collaborators, we hope to bring significant innovation in personalized care for transplant patients with cancer or a history of cancer.

For more information and to participate in these studies, please contact us at nito@natera.com.

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