natera | Prospera™ Transplant assessment

Highlights from Prospera's clinical validation

Prospera™ is clinically validated to assess active rejection with great accuracy in the largest published donor-derived cell-free DNA (dd-cfDNA) validation study on renal transplant patients.

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COHORT

Diverse patient population studied with a trusted partner

- Partnered with the University of California, San Francisco
- 217 biopsy-matched renal allograft samples
- Variety of ethnic and racial demographics
  - Hispanic/Latino (n=50)
  - Caucasian (n=74)
  - African American (n=31)
  - Asian (n=31)

DESIGN

Blinded, retrospective analysis using gold standard of kidney biopsy as truth

- Blinded pathology readings and analysis of blood samples
- Included same-day biopsy matched samples in primary analysis
- Reviewed by a single pathologist to ensure consistency and quality in the data
- Used prospectively selected, previously published cut-off of 1% dd-cfDNA to discriminate between active rejection and not active rejection

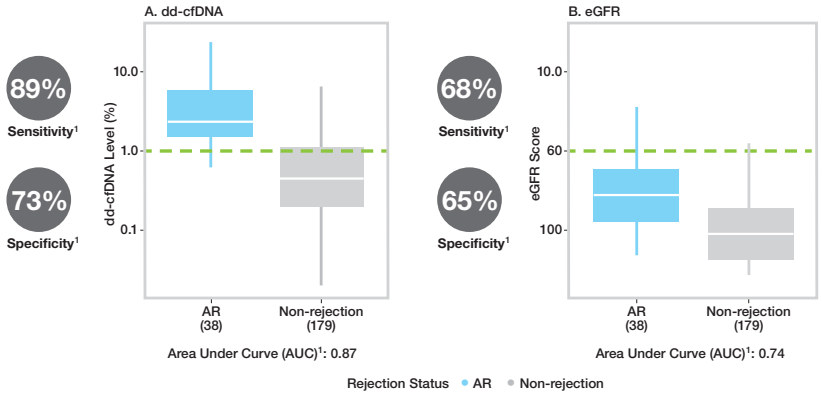
ANALYSIS

Classification based on recent guidelines

- Assessed active rejection in the following categories: antibody-mediated rejection (ABMR), T cell-mediated rejection (TCMR ≥ 1a) and mixed (ABMR/TCMR)
- Categorized biopsies with "borderline rejection" in the non-rejection group instead of active rejection, consistent with the latest BANFF 2017 criteria

Clinical Validation Results

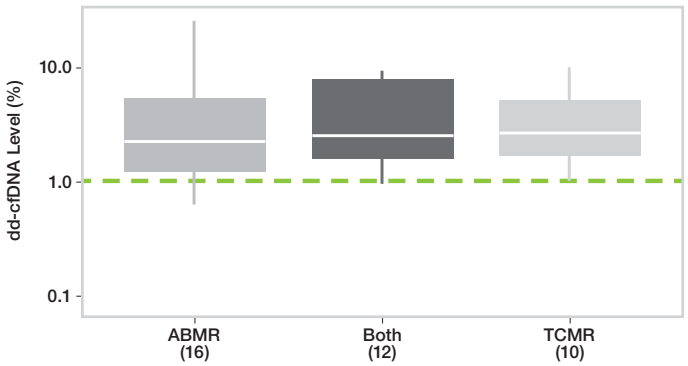
More sensitive and specific than standard screening tools[1]



Subanalysis:
Consistent performance regardless age

- Similar performance of sensitivity (89%), specificity (76%) and AUC (0.88) an **adults-only cohort** to the overall study population[4]
- Significantly higher predictive power (AUC of 0.84) compared to serum creatinine (AUC of 0.58) in assessing active rejection in an **adults-only, for-cause sub-cohort**. This serum creatinine performance of 0.58 AUC is in-line with other previously published serum creatinine performance metrics (0.542[2], 0.633[3])

Robust to all rejection types



- In contrast to other dd-cfDNA studies, Natera was able to differentiate T cell-mediated rejection from no rejection
- Median dd-cfDNA did not differ significantly between ABMR, TCMR and mixed rejection

Similar performance in stable and those with clinical signs of rejection

	Sensitivity	Negative predictive value*
Clinical AR	86%	93.8%
Subclinical AR	92%	98.3%**

* Assuming 25% AR Prevalence (higher risk population)
** Assuming 10% AR Prevalence in a low risk population

- Prospera is the first commercial cfDNA assay to publish performance in renal transplant surveillance situations, providing results that can enable physicians to manage patients with previously unsuspected rejection[1,2]

References:

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. *Journal of Clinical Medicine*. 2019;8(1):19.
2. Bloom RD, et al. *J Am Soc Nephrol*. 2017 Jul;28(7):2221-2232.
3. Kaplan, et al. *Am Journal of Transplantation*. 2003; 3:1560-1565
4. Sigdel TK, Acosta Archila F, Navarro S, et al. Rapid Detection of Kidney Transplant Injury by Quantifying Donor-Derived Cell-Free DNA via Massively Multiplex PCR. Poster presented at: American Transplant Congress (ATC); 2019 June 01-05, Boston, MA.

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