

*Mohan M., Jeff R., Natalie M., and Ryan R., transplant recipients*

## The cutting edge solution to detect donor-derived cell-free DNA for transplant surveillance

**THE LATEST INNOVATION IN ORGAN TRANSPLANT SURVEILLANCE CAN DRIVE BETTER OUTCOMES FOR YOUR PATIENTS**

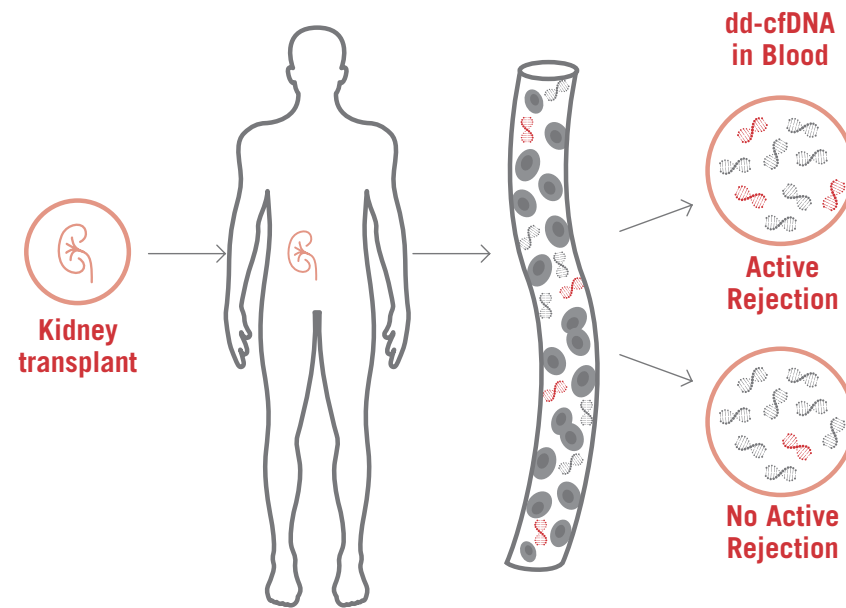
AlloSeq cfDNA is a **kit based solution** that enables measurement of dd-cfDNA through a blood test

# Cell-free DNA: a clear biomarker for organ injury

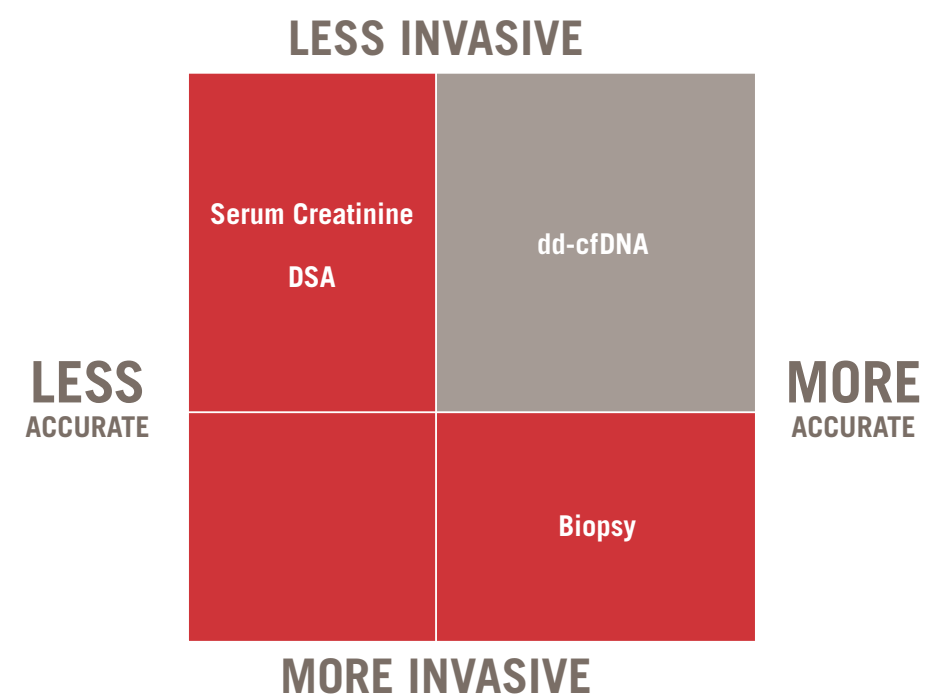
CELL-FREE (cfDNA) IS FRAGMENTED DNA IN THE BLOODSTREAM THAT ORIGINATES FROM CELLS UNDERGOING CELL INJURY AND DEATH

WHEN GRAFT INJURY OCCURS, DONOR-DERIVED CELL-FREE DNA (dd-cfDNA) INCREASES IN THE BLOOD

**dd-cfDNA** IS A POWERFUL, MINIMALLY INVASIVE TOOL FOR ORGAN TRANSPLANT SURVEILLANCE

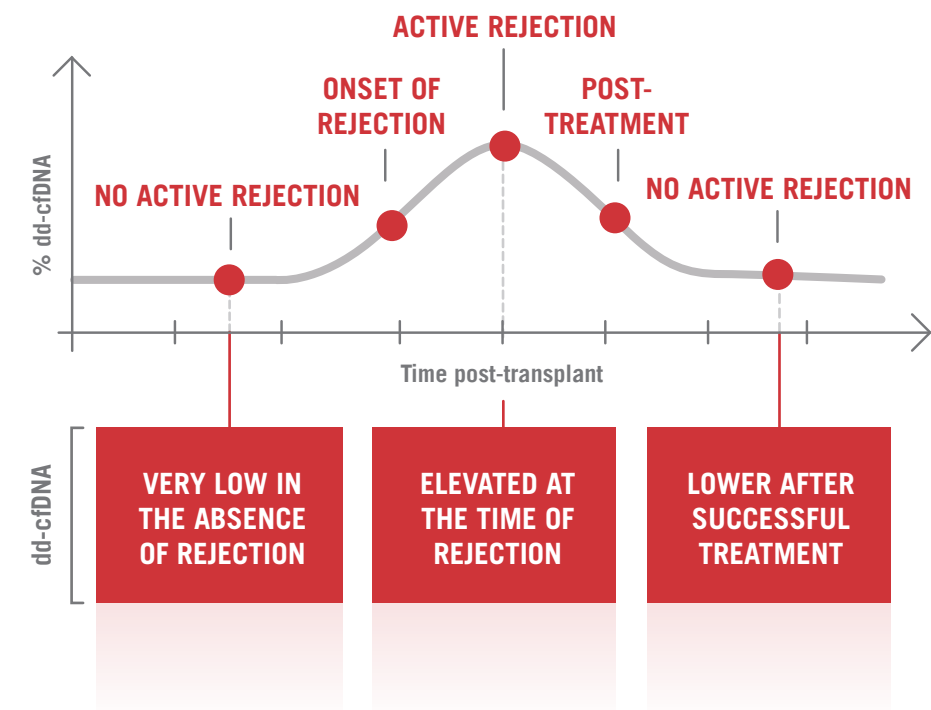


## AlloSeq cfDNA, innovation in action



## What is AlloSeq cfDNA?

- + A minimally invasive blood test that measures dd-cfDNA
- + A kit based test to run in your own lab and does not require prior genotyping
- + A simple workflow that provides sample to report solution within 24 hours



AlloSeq cfDNA can be added to these current research protocols with ease:



# AlloSeq cfDNA was developed after the successful clinical validation of AlloSure

**ALLOSURE IS THE dd-cfDNA SURVEILLANCE SERVICE THAT HAS BEEN CLINICALLY AND ANALYTICALLY VALIDATED FOR IDENTIFYING KIDNEY INJURY.<sup>4</sup>**

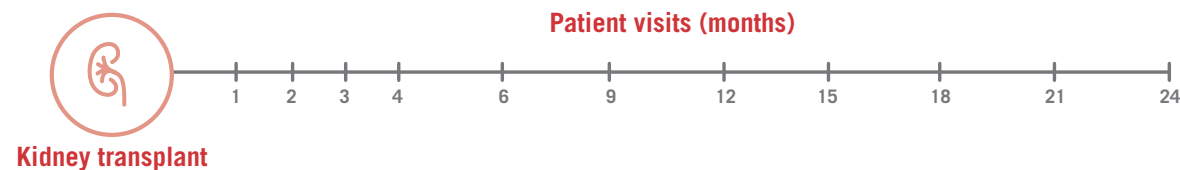
AlloSure's dd-cfDNA clinical study, DART, demonstrated clear conclusions in a prospective multi-center study



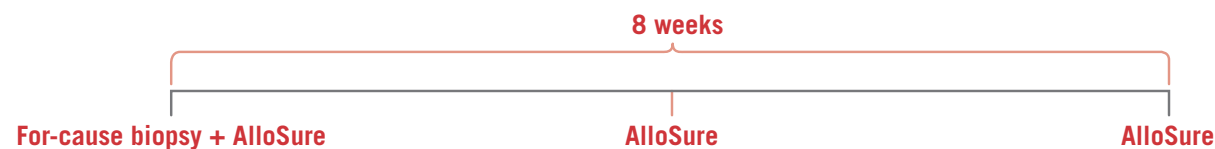
- 14** DART study centers nationwide in the US
- US** Renal demographic represented
- 384** Patients were enrolled
- 102 & 27** For cause biopsy cohort: 102 patients (107 samples with both biopsy and AlloSure), 27 with active rejection

## TWO DART STUDY PROTOCOLS:

**Surveillance** - newly transplanted recipients with AlloSure tests at 11 surveillance visits



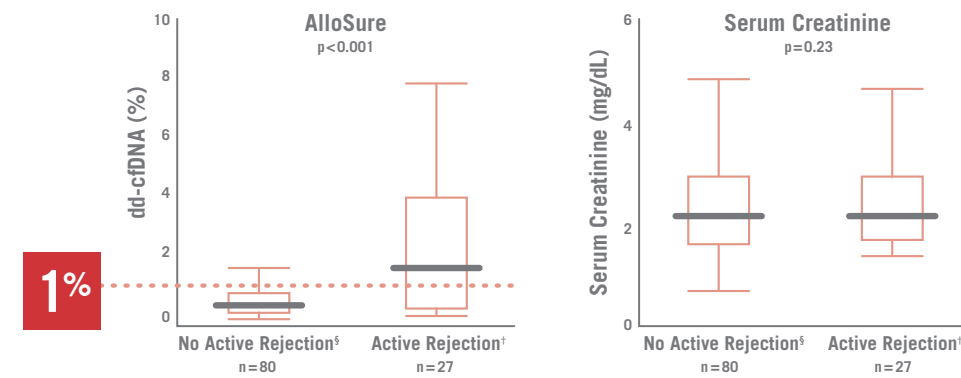
**Clinically Indicated For Cause biopsy\*** - with AlloSure tests at time of biopsy and 1-2 follow-ups



\*An elevated level of serum creatinine was the most common clinical indication for the biopsy

# The AlloSure DART study conclusions are clear.

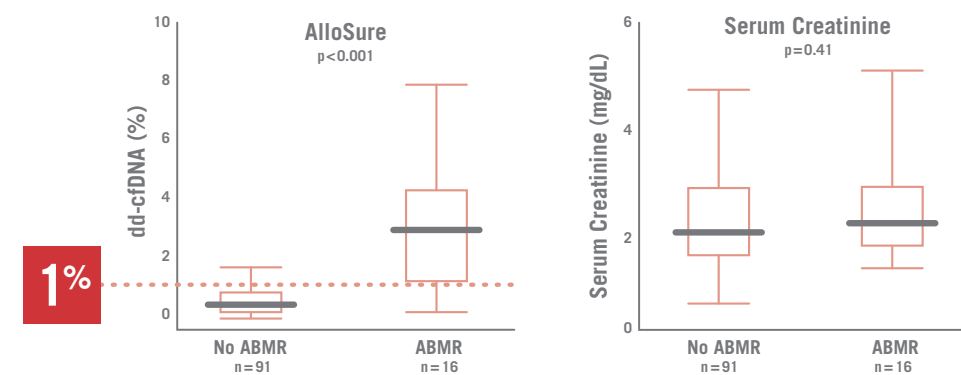
## ALLOSURE OUTPERFORMS SERUM CREATININE FOR DETECTING ACTIVE REJECTION



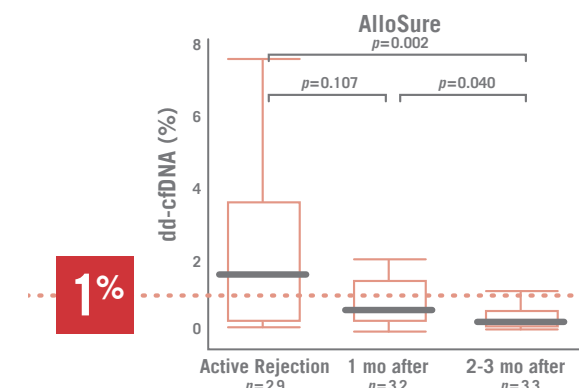
<sup>§</sup> No active Rejection, n=80 samples from 75 patients

<sup>†</sup> Active Rejection = acute/active ABMR; chronic, active ABMR; and TCMR IA and greater, n=27 samples from 27 patients.

## ALLOSURE IS HIGHLY SENSITIVE IN DISTINGUISHING ABMR FROM NO ABMR



## ALLOSURE LEVELS DECREASE FOLLOWING REJECTION TREATMENT



In patients with clinical suspicion of active rejection, the most common cause for the clinical suspicion of active rejection was elevated serum creatinine. The horizontal grey line is the median, and the top and bottom of the box represent the 75th and 25th percentile. Applicable to all 5 charts.

# dd-cfDNA surveillance testing can be added to previously established protocols



## MONTHS 1, 2 POST-TRANSPLANT

- + Baseline to be established during this time
- + dd-cfDNA is associated with changes immediately post-transplant (ischemia reperfusion injury, DGF or medication dose changes) and may be a potential surrogate marker for these changes
- + Results may contribute to treatment decisions

## MONTHS 3, 4 POST-TRANSPLANT

- + dd-cfDNA changes can be used as an associated surrogate marker to monitor the waning of induction immunosuppressants
- + Continue to monitor changes from baseline
- + Maintain continuity in surveillance for patients who transition to a general nephrologist

## MONTHS 6, 9, 12 POST-TRANSPLANT

- + Monitor for acute rejection
- + Test along with DSA to improve the positive predictive value for antibody mediated rejection<sup>8</sup>

## YEAR 2 ONWARD: QUARTERLY TESTING THROUGH LIFE OF TRANSPLANT

- + Monitor for changes in dd-cfDNA results that may occur before the onset of symptoms
- + Rejection due to ABMR increases over time and monitoring may provide an early warning of rejection<sup>9</sup>
- + A significant increase in dd-cfDNA may provide early insight into medication non-adherence

### TIME POST-TRANSPLANT

Biomarker	Condition Tested	TIME POST-TRANSPLANT					
		1 week	1 Month	2-3 Months	4-6 Months	7-12 Months	12+ Months
Creatinine	Indirect graft function	Daily	2-3 per Week	Weekly	Every 2 Weeks	Monthly	Every 2-3 Months
BK Virus	Viral infection	Monthly			Every 3 Months		-
DSA	Donor Specific Antibody formation	Weekly	Monthly	-	Every 6 Months		
<b>dd-cfDNA</b>	<b>Active allograft injury</b>	<b>Monthly</b>			<b>Every 2 Months</b>	<b>Every 3 Months</b>	

## ORDERING INFORMATION

Product	Product number	Description
AlloSeq cfDNA	ASCF-1(24)-IVD	Includes all the reagents required to make 24 NGS libraries

## REFERENCES

1. Matas et al. Am J Transplant 14:S11-S44, 2014.
2. Jordan et al. J Am Soc Nephrol 28:Suppl, 2017.
3. Grskovic M et al. J Mol Diagn 18:890-902, 2016.
4. Bloom RD et al. J Am Soc Nephrol 28, 2017.
5. Jordan S, et al. Transplant Direct. 2018 Aug 20;4(9):e379.
6. Mehta S, et al. Am J Transplant. 2018; 1-2.
7. Tanriover B, et al. Clin J Am Soc Nephrol. 2016; 11: 1650-1661.
8. Mehta R, et al. Transplantation. 2016 Aug; 206: 100 (8): 1610-1618.
9. Djamali A, et. al. Am J Transplant. 2014; 14(2): 255-71.
10. Ma T, et al. ASN 2018 Abstract FR-P0885. "Donor-Derived Cell-Free DNA in Renal Transplant Recipients with Delayed Graft Function"
11. Tanaka S, et al. Sci Rep. 18;8(1):15366, 2018.



### Want to order dd-cfDNA surveillance tests?

- **AlloSure:** Send in samples to CareDx central lab, email [customercare@caredx.com](mailto:customercare@caredx.com) or call 1-888-255-6627
- **AlloSeq cfDNA:** To learn more about how to bring AlloSeq cfDNA to your own lab, contact your CareDx representative or reach out to us:

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EMEA [orders-at@caredx.com](mailto:orders-at@caredx.com)  
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Nordic [orders-se@caredx.com](mailto:orders-se@caredx.com)

The cutting edge solution to detect donor-derived cell-free DNA for transplant surveillance

[www.caredxinc.com/alloseq-cfdna](http://www.caredxinc.com/alloseq-cfdna)