

AlloSure Results Interpretation Guide

This guide is designed for clinicians and should be used as a supplement to the AlloSure Kidney results report. AlloSure results and allograft rejection status should always be considered in the context of other clinical factors and a clinician's judgement.

1 Current Test Result and Relative Change Value

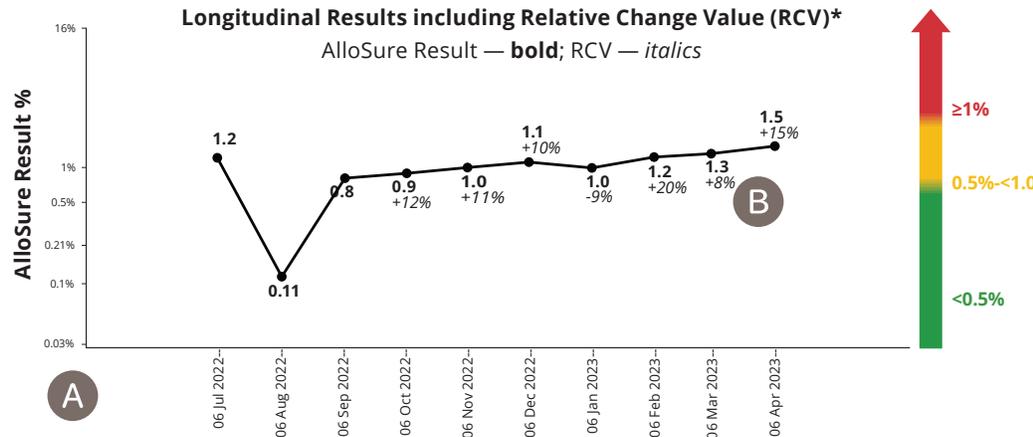
The Results Section reports the dd-cfDNA level obtained from the most recent AlloSure draw and the relative change value between results. Patients with dd-cfDNA levels $\geq 1.0\%$ have a higher risk of active rejection (AR) than patients with dd-cfDNA levels under 0.5% .¹ Increases between results, also known as Relative Change Value (RCV), of greater than 61% exceed normal biological variation and increases of 149% or more may indicate allograft injury.^{1,5}



2 Patient Test Summary

The Patient Test Summary depicts a patient's AlloSure results over time. For optimized clinical care, establishing a patient's baseline AlloSure level may be beneficial.

- 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** A solid line connects dd-cfDNA levels over time, and reflects the relative change value between results.*



* An increase of greater than 61% in consecutive AlloSure results is greater than the change that can be attributed to normal biological variation; additional clinical workup may be warranted. A median increase of 149% between results is indicative of graft injury; additional clinical workup is likely warranted. Please note that Relative Change Values will not be calculated anytime AlloSure results are under 0.20%.

AlloSure Result 1.5% **AlloSure Relative Change Value (RCV)** +15%

Interpretation:

- When interpreting AlloSure Result:
 - $\geq 1.0\%$ dd-cfDNA is associated with a higher probability of active rejection compared to scores less than 1.0% .^{1,2}
 - $\geq 2.2\%$ dd-cfDNA is the median observed in a reference population of stable recipients.^{1,2}
- When interpreting AlloSure RCV:
 - $>61\%$ increase in AlloSure Result from prior result may indicate a high likelihood of allograft injury.¹
 - $\geq 149\%$ increase in AlloSure Result from prior result may indicate a high likelihood of allograft injury.¹

NR - No Result, US - Unacceptable Sample, NA - RCV is not calculated due to AlloSure Result below 0.20%.

The RCV reported for AlloSure Transcatheter Kidney (TK) has not been established. Clinical validity of the AlloSure test was established in kidney transplant recipients who were at least 14 days post-transplant. AlloSure should be interpreted in the context of clinical findings and relevant patient history for more information about AlloSure, please visit [allo.sure.com](#). Specimens from kidney transplant recipients in whom the prior kidney allograft(s) remain in situ and from SPK recipients³ are acceptable for testing. AlloSure is not intended for use in kidney transplant recipients who are pregnant, recipients of a transplant from a allogeneic fetus, recipients of allogeneic bone marrow transplant, or the recipients of multiple transplants (eg, other than simultaneous pancreas at time of transplant). Transfusion of blood components containing white blood cells in the 30 days prior to blood draw may lead to elevated result. Renal biopsies performed in the 24 hours prior to AlloSure specimen collection may elevate dd-cfDNA. ¹Crivello et al., *Am J Surg* 2016; ²Bloom et al., *Am Soc Nephrol* 2017; ³Polyzou et al., *Pediatric Transplantation* 2020; ⁴Bloembergen et al., *J Appl Lab Med* 2017; ⁵Ito et al., *Kidney International* 2013; ⁶Winkler et al., *Transplantation Direct* 2022; ⁷Yee et al., *Transplantation Direct* 2023. The AlloSure donor-derived cell-free DNA test was developed and its performance characteristics were determined by the CareDx laboratory. The test has not been cleared or approved by the U.S. Food and Drug Administration, nor is it currently registered by the laboratory as certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88) and accredited by the College of American Pathologists (CAP) as qualified to perform high complexity clinical laboratory testing. The contents of this report are confidential and intended solely for the use of authorized personnel.

3 Interpretation of AlloSure Test Results

>2.9% AlloSure dd-cfDNA is associated with a higher risk of active rejection

AlloSure results over 2.9% with the presence of DSAs is highly predictive of antibody-mediated rejection with a PPV of 89%.⁴

≥1.0% AlloSure dd-cfDNA is associated with a higher risk of active rejection

AlloSure dd-cfDNA levels greater than or equal to 1% may indicate a probability of active rejection (antibody-mediated rejection or T cell-mediated rejection). For dd-cfDNA ≥1.0%, there is a positive predictive value (PPV) of 54% and a negative predictive value (NPV) of 84% for active rejection. The positive and negative predictive values for antibody-mediated rejection at an AlloSure result of 1.0% are 49% and 85%, respectively.¹⁻⁴

>0.5% AlloSure dd-cfDNA is an early signal of graft injury and dysfunction

AlloSure dd-cfDNA levels greater than 0.5% may indicate a high risk for recurrent rejection, detection of DSAs, and loss of eGFR, with a PPV for all rejection of 50% and an NPV of 90%.¹⁻³

0.21-0.23% AlloSure dd-cfDNA is the median observed in a reference population of stable recipients

Patients with AlloSure dd-cfDNA levels of 0.21% have an NPV of 95% for active rejection.²

>61% increase in AlloSure dd-cfDNA from a prior sample exceeds normal biological variability and ≥149% is indicative of allograft injury

An increase of greater than 61% between results is larger than the change that may be attributable to normal biological variation.⁵ An increase of greater than or equal to 149% between results is indicative of allograft injury.¹ Additional clinical workup is warranted. Please note that Relative Change Values will not be calculated anytime AlloSure results are under 0.20%.

Considerations for Simultaneous Pancreas-Kidney (SPK) Patients

- AlloSure levels in stable patients were between 0.18% to 0.29%.^{6,7}
- Patients with rejection had AlloSure levels elevated from their baseline^{6,7}
- 97% of patients without rejection had a AlloSure levels < 0.5%⁶
- The RCV in Section 1 and thresholds in Section 3 have not been validated in SPK

Contraindications and Limitations

DO NOT USE AlloSure testing for

- Recipients of transplanted organs other than kidney transplant(s) (SPK transplants are acceptable)
- Recipients of a bone marrow transplant
- Recipients of a transplant from a monozygotic (identical) twin
- Recipients who are pregnant
- Recipients who are less than 14 days post-transplant

Limitations

AlloSure should not be used within:

- 30 days after a blood transfusion that contains white blood cells (washed or leukocyte-depleted RBCs are acceptable)
- 24 hours following a biopsy

References:

1. Bu, L et al. *Kidney International* 2021
2. Bloom RD et al. *J Am Soc Nephrol*. 2017; 28:2221–2232
3. Stites E, et al. *Am J Transplant*. 2020; 00:1–8
4. Jordan SC et al. *Transplantation Direct* 2018; 4:e379
5. Bromberg JS et al. *J Appl Lab Med*. 2017; 2:309–321
6. Williams MD, Fei M, Schadde E, et al. *Transplantation Direct* 2022; 8:e1321. doi: 10.1097/TXD.0000000000001321.
7. Yoo A, Riedel A, Qian I, et al. *Transplantation Direct* 2023; 9:e1459. doi: 10.1097/TXD.0000000000001459