AlloMap® Variability: Long-Term Surveillance for Heart Transplant Patients

AlloMap®

Variability Report

AlloMap®
Variability Report

Now Available

Assessing Risk of Future Clinical Events in Heart Transplant Recipients

Need for Personalized Surveillance

Despite progress in the care and management of transplant patients, there remain challenges in optimizing long-term outcomes[1].

Service Offering to Assess Long-Term Risks

CareDx now provides AlloMap Score Variability (AMV) results for patients receiving AlloMap. AMV is a service offering from CareDx that aids in estimating the risk of one or more of the following future clinical events in heart transplant recipients:

- Graft dysfunction[2]
- Death from any cause
- Re-transplantation

Calculation of AMV

AMV is calculated using the standard deviation of four consecutive, AlloMap Scores. Qualifying AMV scores meet the following criteria:

- ≥315 days post transplant
- Time interval between the 1st and 4th score is ≥85 and ≤780 days.

Clinical Development of AMV

AMV was clinically developed over the course of more than five years and has been assessed in more than 600 patients:

- **Observation** — AlloMap score variability among clinically stable patients without rejection was lower than score variability in patients who experienced rejection; ISHLT[3].
- **Hypothesis** — retrospective analysis of randomized trial cohort demonstrated that AMV was predictive of future clinical events; IMAGE[4].
- **Performance** — evaluation of AMV in an independent patient population demonstrated that variability scores may be predictive of long-term risk; CARGO II[5].

[1]Starling et al. Multicenter Analysis of Immune Biomarkers and Heart Transplant Outcomes: Results of the Clinical Trials in Organ Transplantation-05 Study. *Am J Transplant* 2015 Aug 10 [Epub Ahead of print].

[2]Graft dysfunction is defined as a clinically significant hemodynamic compromise (left ventricular ejection fraction ≤40%, use of hemodynamic support such as inotropic medications and/or mechanical assist device, hospitalization for treatment of graft failure or dysfunction).

[3]Deng, et al. Low Variability of Intraindividual Longitudinal Leukocyte Gene Expression Profiling Cardiac Allograft Rejection Scores. *Transplantation*. 2010; 90(4): 459–461.

[4]Deng, et al. Utility of Gene Expression Profiling Score Variability to Predict Clinical Events in Heart Transplant Recipients. *Transplantation*. 2014; 97(6): 708–714.

[5]Crespo-Leiro, et al. Performance of gene-expression profiling test score variability to predict future clinical events in heart transplant recipients. *BMC Cardiovasc Disord* (2015).

AlloMap Variability Clinical Performance Characteristics[5]

Lower risk scores

Higher risk scores

Variability Score	NPV (95% CI)	% Scores Below	PPV (95% CI)
0.1	—	0.0	17.0 (—)
0.2	100.0 (—)	1.1	17.2 (11.6–23.8)
0.3	100.0 (—)	3.3	17.8 (12.3–24.7)
0.4	100.0 (—)	7.7	19.0 (13.1–26.9)
0.5	100.0 (—)	16.5	22.0 (15.2–30.8)
0.6	97.0 (91.4–100.0)	24.2	23.3 (15.7–33.0)
0.7	92.8 (85.4–97.8)	33.0	23.2 (15.4–33.7)
0.8	91.4 (84.2–96.5)	42.9	25.2 (16.3–37.1)
0.9	90.3 (83.9–95.2)	56.0	29.7 (18.5–46.0)
1.0	87.4 (80.1–92.9)	62.6	26.0 (14.8–41.8)
1.1	87.0 (80.4–92.4)	68.1	27.8 (15.3–46.5)
1.2	87.0 (80.3–92.2)	71.4	29.9 (16.3–51.0)
1.3	86.0 (79.3–91.3)	76.9	29.4 (14.6–53.4)
1.4	85.3 (78.7–90.6)	83.5	31.9 (13.5–63.2)
1.5	84.9 (78.5–90.1)	87.9	35.4 (13.5–75.8)
1.6	83.9 (77.1–89.4)	92.3	29.4 (5.9–100.0)
1.7	83.7 (77.1–89.1)	94.5	31.9 (0.0–100.0)
1.8	83.2 (76.6–88.6)	97.8	23.8 (—)
1.9	83.4 (77.0–88.7)	98.9	100.0 (—)
2.0	83.4 (77.0–88.7)	98.9	100.0 (—)
2.1	83.0 (76.6–88.4)	100.0	— (—)

Use of AMV may enable clinicians to personalize patient surveillance and care > 315 days post-transplant. Current performance characteristics associated with AMV suggest that patients with scores[5]:

- ≤0.6 may be at a lower risk of future events
- ≥1.6 may be at a higher risk of future events

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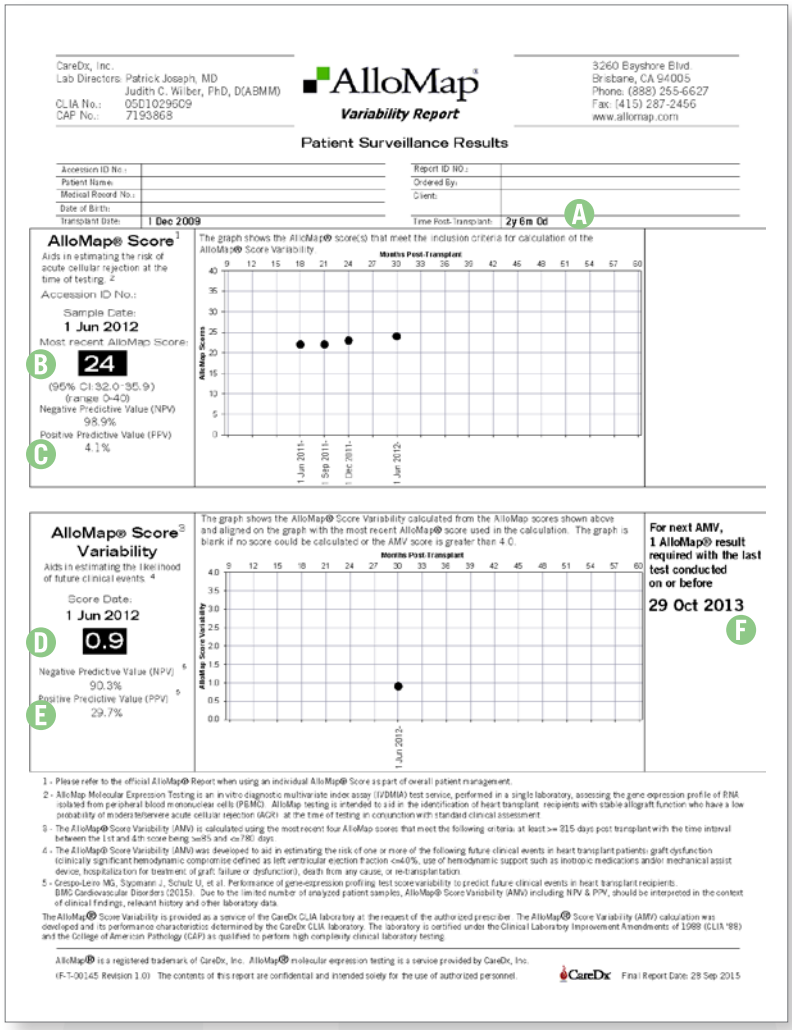
Variability Report

AMV Patient Report Features

- A Time Post Transplant
- B Most Recent AlloMap Score
- C AlloMap NPV and PPV*
- D Most Recent AMV Score
- E AMV NPV and PPV
- F Criteria for Next AMV Score

*NPV and PPV: negative & positive predictive value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AlloMap® Variability Report

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Patient Surveillance Results

Accession ID No.:
Patient Name:
Medical Record No.:
Date of Birth:
Transplant Date: 1 Dec 2009

Report ID NO.:
Ordered By:
Client:
Time Post-Transplant: 2y 6m 0d (A)

AlloMap® Score[1]
Aids in estimating the risk of acute cellular rejection at the time of testing.[2]
Accession ID No.:
Sample Date: 1 Jun 2012
Most recent AlloMap Score: (B) 24
(95% CI:32.0-35.9)
(range 0-40)
Negative Predictive Value (NPV) 98.9%
Positive Predictive Value (PPV) 4.1% (C)

The graph shows the AlloMap® score(s) that meet the inclusion criteria for calculation of the AlloMap® Score Variability
Months Post-Transplant
AlloMap Scores
1 Jun 2011 · 1 Sep 2011 · 1 Dec 2011 · 1 Jun 2012

AlloMap® Score[3] Variability
Aids in estimating the likelihood of future clinical events.[4]
Score Date: 1 Jun 2012
(D) 0.9
Negative Predictive Value (NPV)[6] 90.3%
Positive Predictive Value (PPV)[5] 29.7% (E)

The graph shows the AlloMap® Score Variability calculated from the AlloMap scores shown above and aligned on the graph with the most recent AlloMap® score used in the calculation. The graph is blank if no score could be calculated or the AMV score is greater than 4.0.
Months Post-Transplant
AlloMap Score Variability
1 Jun 2012

For next AMV, 1 AlloMap® result required with the last test conducted on or before
29 Oct 2013 (F)

1 - Please refer to the official AlloMap® Report when using an individual AlloMap® Score as part of overall patient management.
2 - AlloMap Molecular Expression Testing is an in vitro diagnostic multivariate index assay (IVDMIA) test service, performed in a single laboratory, assessing the gene expression profile of RNA isolated from peripheral blood mononuclear cells (PBMC). AlloMap testing is intended to aid in the identification of heart transplant recipients with stable allograft function who have a low probability of moderate/severe acute cellular rejection (ACR) at the time of testing in conjunction with standard clinical assessment.
3 - The AlloMap® Score Variability (AMV) is calculated using the most recent four AlloMap scores that meet the following criteria: at least >= 315 days post transplant with the time interval between the 1st and 4th score being >=85 and <=780 days.
4 - The AlloMap® Score Variability (AMV) was developed to aid in estimating the risk of one or more of the following future clinical events in heart transplant patients: graft dysfunction (clinically significant hemodynamic compromise defined as left ventricular ejection fraction <=40%, use of hemodynamic support such as inotropic medications and/or mechanical assist device, hospitalization for treatment of graft failure or dysfunction), death from any cause, or re-transplantation.
5 - Crespo-Leiro MG, Stypmann J, Schulz U, et al. Performance of gene-expression profiling test score variability to predict future clinical events in heart transplant recipients. BMC Cardiovascular Disorders (2015). Due to the limited number of analyzed patient samples, AlloMap® Score Variability (AMV) including NPV & PPV, should be interpreted in the context of clinical findings, relevant history and other laboratory data.

The AlloMap® Score Variability is provided as a service of the CareDx CLIA laboratory at the request of the authorized prescriber. The AlloMap® Score Variability (AMV) calculation was developed and its performance characteristics determined by the CareDx CLIA laboratory. The laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88) and the College of American Pathology (CAP) as qualified to perform high complexity clinical laboratory testing.

AlloMap® is a registered trademark of CareDx, Inc. AlloMap® molecular expression testing is a service provided by CareDx, Inc.
(F-T-00145 Revision 1.0) The contents of this report are confidential and intended solely for the use of authorized personnel.
CareDx Final Report Date: 28 Sep 2015

To receive AMV contact your CareDx representative or send an email to CareDx Customer Service (customercare@caredx.com).

Upon opting in to receive AMV, a Transplant Center Summary Report (TCSR) will be sent. The TCSR will include the four most recent AlloMap scores and current AMV score (if available) for all active patients in your practice for the current year and previous three calendar years.

You will also receive individual AMV score reports for each patient who receives a traditional AlloMap. Please note that AMV reports will arrive separate from traditional AlloMap Score reports.

CareDx®

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