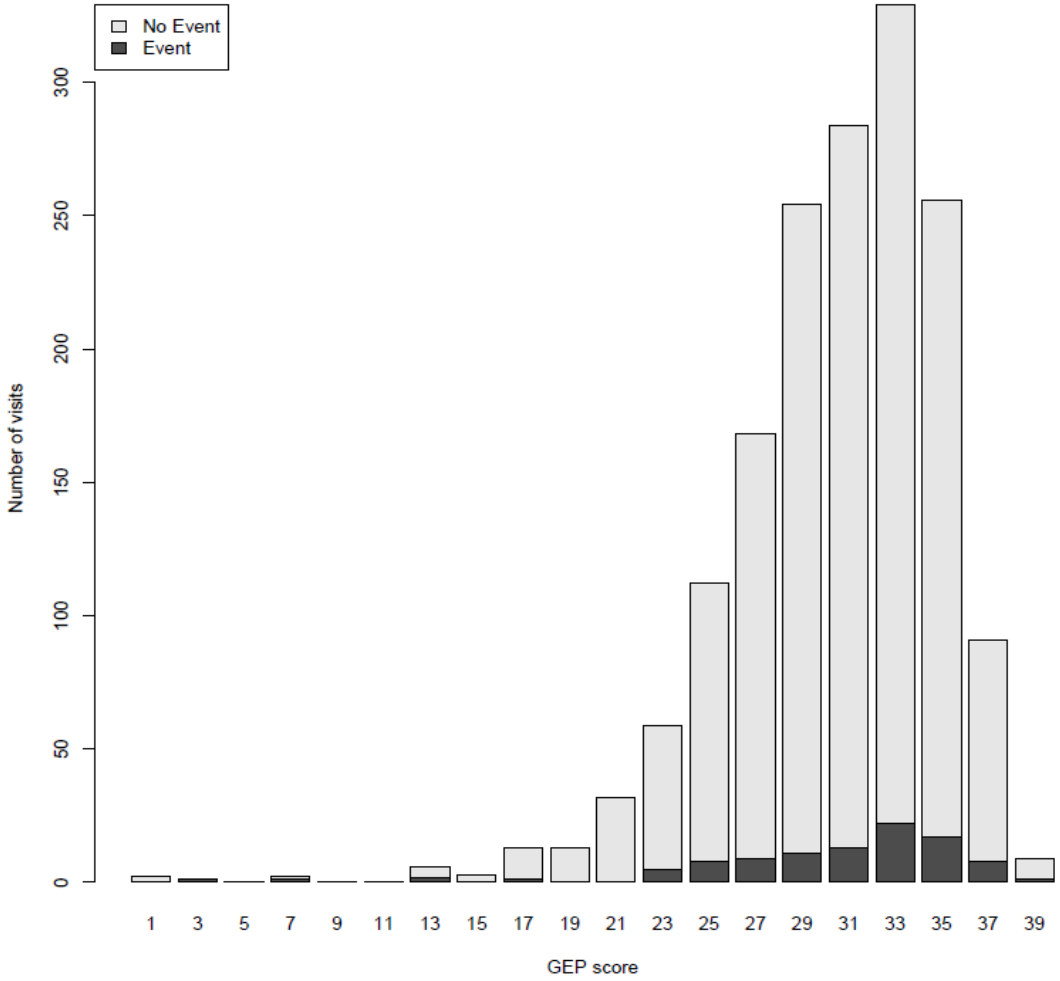
SUPPLEMENTAL DIGITAL CONTENT

SDC Figure S1. Distribution of Gene Expression Profiling Ordinal Scores



SDC Fig.S1. Distribution of Gene expression profiling ordinal scores (AlloMap scores). The gene-expression profiling score is an integer between 0 and 39. Each score has an associated negative predictive value for acute cellular rejection.

SDC Table S1

	Multivariate Analysis Study Cohort	Event Patients	No Event Patients
Number of Patients	369	30	339
Number of Tests	1634	99	1535
Test Interval, Mean ± SD (range), in months	4.4 ± 2.3 (0.4, 24.1)	3.6 ± 1.2 (0.8 – 7.1)	4.4± 2.4 (0.4, 24.1)
Tests/Patient, Mean± SD (range)	4.4±1.7 (2, 10)	3.3 ± 1.2 (2-6)	4.5 ± 1.6 (2-10)
Gene-expression profiling test ordinal score, Mean ± SD (range)	30.9 ± 4.5 (2 - 39)	30.6 ± 6.2 (4 - 39)	30.9 ± 4.4 (2 - 39)
Gene-expression profiling score variability , Mean ± SD (range)	1.0 ± 0.8 (0.01 - 5.9)	1.6 ±1.4 (0.2 - 5.9)	1.0 ± 0.7 (0.01, 5.2)

SDC **Table S2. Multivariate Models to Predict Future Clinical Events**[*]

Cox Proportional Hazards Regression Results of Surveillance Information Added to Base Clinical Model*					
	Regression Coefficient (SE)	**p-value**	**Hazard Ratio (95% CI)**[†]	**AIC**	**C-Index (95% CI)**
Base Clinical Model				329.5	0.68 (0.59,0.78)
Gene-expression profiling test score variability: (standard deviation of gene-expression profiling ordinal scores)[‡]	0.57 (0.12)	<0.001	1.76 (1.38, 2.25)	318.0	0.69 (0.61,0.76)
Gene-expression profiling test ordinal score (0-39)[‡]	-0.078 (0.10)	0.43	0.92 (0.76, 1.12)	330.9	0.68 (0.59,0.77)
Gene-expression profiling test threshold score ≥ 34	0.12 (0.43)	0.77	1.13 (0.48, 2.65)	331.5	0.68 (0.59,0.78)
Gene-expression profiling test score variability, controlling for ordinal score	0.63 (0.15)	<0.001	1.87 (1.39, 2.52)	319.5	0.70 (0.62, 0.77)

[*] Clinical events of rejection with hemodynamic compromise, graft dysfunction due to other causes, death, or re-transplantation.
[†] Hazard Ratio: values less than 1indicate risk decreases as variable increases; the associated regression coefficient is negative.
[‡] Uses transformed gene-expression profiling scores. If x is the AlloMap gene-expression profiling ordinal score, we use y = 2.451(log(x/(40-x))-0.234)

SDC Table S2 adds information to what is found in Table 3 in the main report. Because the Spearman rank correlation between score variability and median score was relatively small, but highly significant, a model was also constructed which controls for within-patient average score when estimating/testing the effect of within-person standard deviation on event rates. The results are shown in the bottom row of SDC Table 2. The regression coefficient for gene-expression score variability remains highly significant ($p < 0.001$) when the model includes adjustment for ordinal scores (see SDC). The C-Index is slightly better (0.70) when controlling for the average score than the model which uses only the variability score added to the base clinical factors (C-Index =0.69.)

The C-Index values are not very different among the 5 models summarized in SDC Table 2, however, the 95 % confidential intervals range from 0.59 to 0.78, so it is possible that with a future larger dataset, a significant difference in the C-Index may be demonstrated. With the current dataset, which is limited by a relatively small number of event endpoints (n=30), the variability model appears to have promise, based on its highly significant regression coefficient and its favorable AIC score.