

Highlights of the PREDICT Trial 12 Month Follow-Up

CORUS^{CAD}
Gene Expression Test By CardioDx

Whole Blood Gene Expression Testing for
Coronary Artery Disease in Nondiabetic
Patients: Major Adverse Cardiovascular
Events and Interventions in the PREDICT Trial

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CARDIODX[®]

Highlights of Corus[®] CAD Gene Expression Test Clinical Utility at 12 Months

Rosenberg S, Elashoff MR, Lieu HD, et al. Whole Blood Gene Expression Testing for Coronary Artery Disease in Nondiabetic Patients: Major Adverse Cardiovascular Events and Interventions in the PREDICT Trial. *J Cardiovasc Transl Res.* 2012;5:366-374.

BACKGROUND

Corus CAD is a blood-based gene expression test that uses peripheral blood to quickly and safely assess whether or not a patient's symptoms are due to obstructive coronary artery disease (CAD)* by measuring the RNA levels of 23 genes that significantly correlate with obstructive CAD.¹ Alterations in gene expression in peripheral blood cells have been shown to be sensitive to the presence and extent of obstructive CAD.

In 2010, Rosenberg et al. published results from the PREDICT Trial, a prospective trial at 39 centers to validate the Corus CAD gene expression test for the assessment of obstructive CAD in stable nondiabetic patients with symptoms suggestive of CAD that were clinically referred for elective invasive coronary angiography (N=526).

Key finding from the PREDICT Trial:²

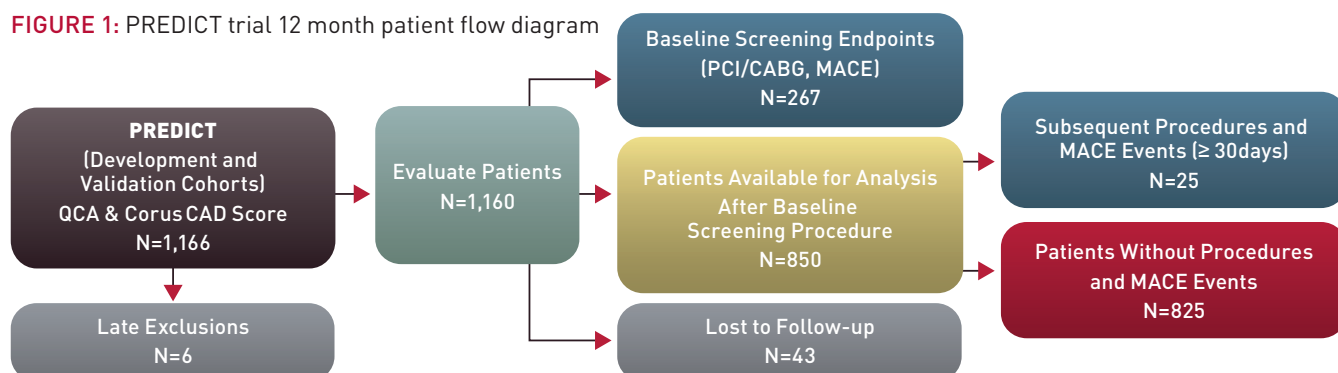
- Corus CAD demonstrated high sensitivity at 85% and negative predictive value (NPV) at 83% for excluding obstructive CAD as the cause of a patient's symptoms

PREDICT TRIAL 12 MONTH FOLLOW-UP

The objective of this prospective trial was to determine if patients with a low Corus CAD score have significant risk of major adverse events 12 months after Corus CAD testing. To assess this risk, the trial monitored the clinical event rates of patients in the 12 months post-index invasive coronary angiography and Corus CAD testing.

- 1,160 patients from the Corus CAD development and validation cohorts of the PREDICT Trial (SEE FIGURE 1)
 - All patients had quantitative coronary angiography (QCA) results and Corus CAD gene expression scores. Follow-up achieved with 96% of patients (n=1,116)
 - Clinical endpoints measured within 12 months post-Corus CAD test score:
 - Revascularization procedures associated with index and subsequent catheterizations**
 - Major adverse cardiovascular events (MACE)***
 - Among 292 procedures and events within one year, 267 (92%) occurred within the first 30 days which included procedures at the time of index catheterization. Only 25 (8%) of the procedures or events (14 and 11, respectively) occurred between 30 days and 12 months post-index coronary angiography

FIGURE 1: PREDICT trial 12 month patient flow diagram



KEY FINDINGS

Low Corus CAD Scores (≤ 15) Correlate to Less Than 1% Likelihood of MACE in 12 Months

- Less than 1% of patients with low Corus CAD scores had a major adverse cardiovascular event (MI, stroke, or death) within 12 months that was not associated with the index coronary angiography (SEE FIGURE 2)
- Less than 10% of patients with low Corus CAD scores had a revascularization within 12 months, which included any revascularization done as part of the index coronary angiography (SEE FIGURE 2)
- PREDICT 12 month results provide evidence for the clinical utility of Corus CAD for safely excluding obstructive CAD in stable patients with low Corus CAD scores, even in this high risk cohort (36% prevalence of CAD) where all patients were clinically referred to invasive coronary angiography

Negative Predictive Value and Sensitivity for Procedures and Events in 12 Months

Duration & Endpoints	NPV	Sensitivity	p-value
12-Month Procedures & MACE	90%	86%	<0.001
12-Month MACE	99%	82%	0.16 [†]

FIGURE 2: Negative predictive value (NPV) and sensitivity for procedures and events in 12 months. All values calculated at a threshold Corus CAD score of 15

High Corus CAD Test Scores Were Associated with Higher Revascularization and MACE Rates

- When patients were stratified to low (1–15), medium (16–27), and high (28–40) Corus CAD scores, higher scores were positively correlated at 12 months to increased likelihood of procedures (CABG or PCI) and all procedures and events (SEE FIGURE 3)
- Low Corus CAD scores (≤ 15) were associated with decreased event likelihood ($p < 0.001$)
- High Corus CAD scores (> 27) yielded 3 times the event rates as compared to low Corus CAD scores (≤ 15)

Dependence of Event Likelihood on Corus CAD Scores in 12 Months

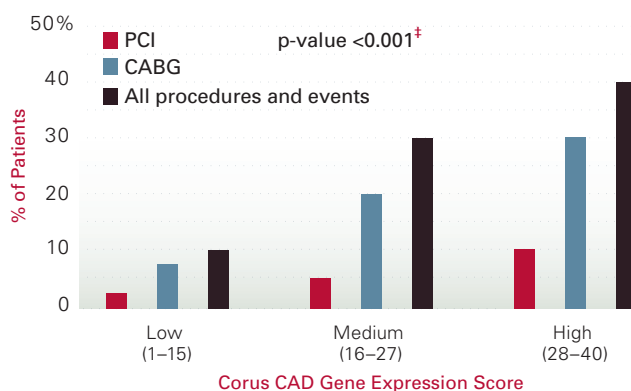


FIGURE 3: The percentage of patients who had procedures or events within 12 months of the index catheterization are shown stratified by test score. Results are shown for the entire cohort of 1,160 patients

* Obstructive CAD was defined in the study as at least one atherosclerotic plaque causing $\geq 50\%$ luminal diameter stenosis in a major coronary artery (≥ 1.5 mm lumen diameter) as determined by quantitative coronary angiography (QCA).

** Procedure was defined in the study as any percutaneous coronary interventions (PCI) regardless of angioplasty, bare metal stent, drug-eluting stent, or coronary arterial bypass grafting (CABG).

*** MACE was defined in the study as stroke or transient ischemic attack (TIA), myocardial infarction (MI), or all-cause death.

[†] p-value not statistically significant at 12-month MACE alone, due to small sample size.

[‡] p-value < 0.001 for “All Procedures and Events” between low, medium, and high Corus CAD scores. “All Procedures and Events” includes those procedures at index catheterization.

CardioDx®

CardioDx, Inc., a pioneer in the field of cardiovascular genomic diagnostics, is committed to developing clinically validated tests that empower clinicians to better tailor care to each individual patient. Strategically focused on coronary artery disease, cardiac arrhythmia and heart failure, CardioDx is poised to expand patient access and improve healthcare quality and efficiency through the commercialization of genomic technologies.

Corus® CAD Intended Use

The Corus CAD test is a quantitative in vitro diagnostic test performed in a single laboratory, using the gene expression profile of cells found in peripheral blood specimens to be used as an aid to identify patients who are likely to have coronary artery stenosis of at least 50%. The test should be performed on patients with a history of chest pain, with suspected anginal equivalent to chest pain, or with a high risk of coronary artery disease, but with no known prior myocardial infarction or revascularization procedures. The test is not intended for patients with acute myocardial infarction, high risk unstable angina, systemic infectious or systemic inflammatory conditions, diabetes, and/or who are currently taking steroids, immunosuppressive agents, or chemotherapeutic agents.

The test is performed on a blood specimen obtained from the patient. The test incorporates the expression levels of multiple genes using an algorithm with weighted functions to generate a quantitative score. The results of the test should be used by clinicians in conjunction with other tests and clinical information in their assessment of a patient's coronary artery disease.

The Corus CAD test is for prescription use only. The test is not intended to be used to screen for stenosis among patients who are asymptomatic and not considered at high risk for coronary artery disease, to predict or detect response to therapy, or to help select the optimal therapy for patients.

REFERENCES:

- 1 Wingrove JA, Daniels SE, Sehnert AJ, et al. Correlation of Peripheral-Blood Gene Expression With the Extent of Coronary Artery Stenosis. *Circ Cardiovasc Genet*. 2008;1:31-38.
- 2 Rosenberg S, Elashoff MR, Beineke P, et al. Multicenter Validation of the Diagnostic Accuracy of a Blood-Based Gene Expression Test for Assessing Obstructive Coronary Artery Disease in Nondiabetic Patients. *Ann Intern Med*. 2010;153:425-434.

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