Highlights of the Validation of the Corus® CAD Blood Test

CORUS CAD

Multicenter Validation of the Diagnostic Accuracy of a Blood-Based Gene Expression Test for Assessing Obstructive Coronary Artery Disease in Nondiabetic Patients

CARDIODX®

Highlights of the Validation of the Corus® CAD Blood Test[1]

PREDICT STUDY OVERVIEW
(Personalized Risk Evaluation and Diagnosis In the Coronary Tree)

- 1,343 nondiabetic patients with suspected coronary artery disease (CAD) from 39 U.S. clinical sites, enrolled between July 2007 and April 2009, were included in the development and prospective validation of the Corus CAD blood test for obstructive CAD* based on age, sex, and RNA levels from the patients' blood sample
  - Patients were divided into independent development (N=694) and validation (N=649) sets
  - Principal Investigator: Eric Topol, MD, Scripps Research Institute

- The PREDICT validation set included the following types of stable patients,[†] all of whom had been referred for invasive coronary angiography (ICA):
  - Symptomatic (chest pain or suspected anginal-equivalent) or asymptomatic high risk
  - Nondiabetic
  - No known obstructive CAD, prior myocardial infarction, or prior revascularization procedure
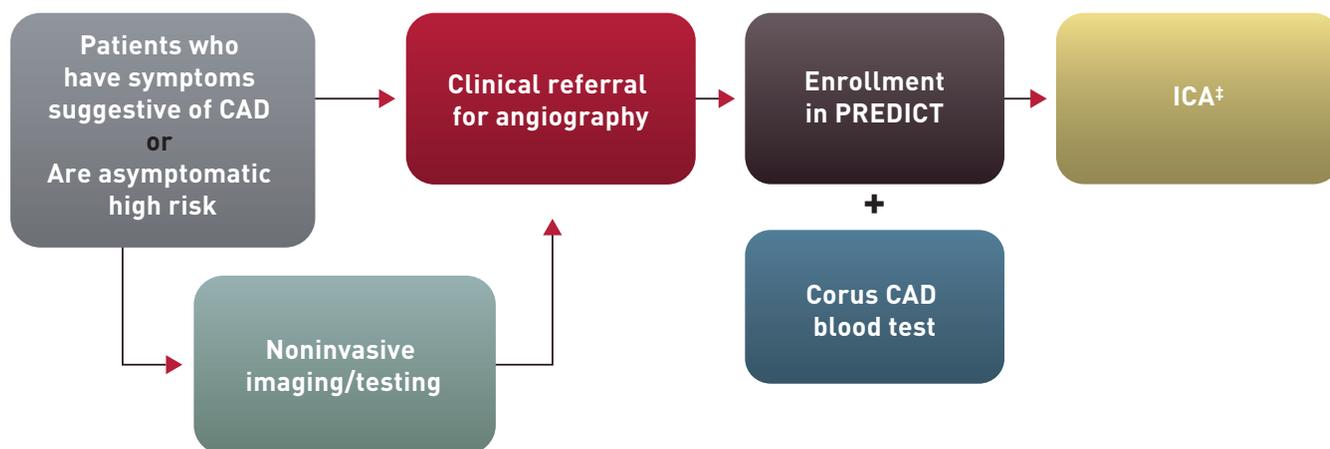 - No known chronic inflammatory disorders, elevated white blood cell counts, or cardiac protein markers

Patients who have symptoms suggestive of CAD **or** Are asymptomatic high risk → Clinical referral for angiography → Enrollment in PREDICT → ICA[‡]

Noninvasive imaging/testing

Enrollment in PREDICT **+** Corus CAD blood test

FIGURE 1: PREDICT study design

*Obstructive CAD is defined as at least one atherosclerotic plaque causing ≥50% luminal diameter stenosis in a major coronary artery (≥1.5 mm lumen diameter) as determined by invasive quantitative coronary angiography or coronary computed tomography angiography (≥2.0 mm lumen diameter).
†For full eligibility criteria, refer to Appendix 2 of Rosenberg S, Elashoff MR, Beineke P, et al. *Ann Intern Med.* 2010;153:425-434.
‡Data analyzed by quantitative coronary angiography core lab.

KEY FINDINGS

Majority of Patients Sent for Invasive Coronary Angiography Did Not Have Obstructive CAD

- Only 37% of all patients in PREDICT were found to have obstructive CAD by quantitative coronary angiography (QCA) **(SEE FIGURE 2)**

  - In women, the rate of obstructive CAD was particularly low (26%)

- These findings from the PREDICT study are consistent with those reported by Patel, et al. in a study of 398,978 patients published in the *New England Journal of Medicine* in 2010[2]

Corus® CAD Test Has High Sensitivity and Negative Predictive Value (NPV)

- Test sensitivity and NPV are 85% and 83%, respectively[§]

Corus CAD Test Score is Proportional to the Presence and Extent of Obstructive CAD

- The higher the test score, the higher the likelihood of obstructive CAD **(SEE FIGURE 3)**

- The Corus CAD score is significantly correlated with coronary atherosclerotic plaque burden as measured by maximum percent stenosis **(SEE FIGURE 4)**

Corus CAD Test Improves Classification of Patient Disease Status

- The combination of test score and clinical factor assessment[3] is significantly better than clinical factor assessment alone

- Independent of myocardial perfusion imaging result or clinical risk, increasing test score is associated with increasing likelihood of obstructive CAD

Low Yield of Obstructive CAD at ICA for Patients in the PREDICT Study
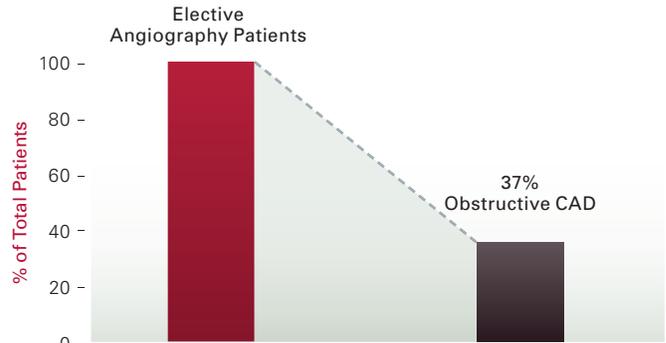

FIGURE 2: Percent of patients in PREDICT found to have obstructive CAD by QCA

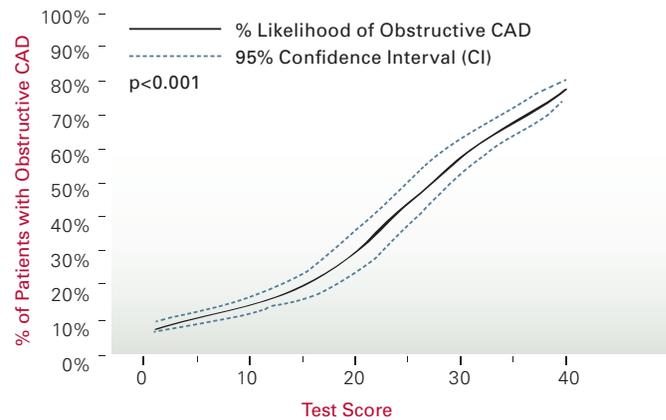**Test Score Correlates with Percentage of Patients in PREDICT Who Had Obstructive CAD**

— % Likelihood of Obstructive CAD
---- 95% Confidence Interval (CI)
$p < 0.001$

FIGURE 3: Relationship between test score and likelihood of obstructive CAD

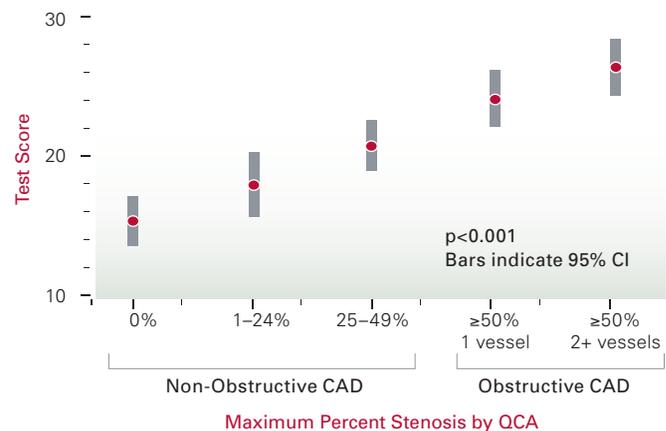**Test Score Correlates with Coronary Atherosclerotic Plaque Burden in PREDICT by Maximum Percent Stenosis**

$p < 0.001$
Bars indicate 95% CI

Non-Obstructive CAD   Obstructive CAD

Maximum Percent Stenosis by QCA

FIGURE 4: Correlation between test score and plaque burden

[§]This performance correlates to patients in PREDICT who had a likelihood of obstructive CAD of approximately 20% at a score threshold of 14.75. At this likelihood, test specificity and positive predictive value are 43% and 46%, respectively.

CardioDx®

CardioDx, Inc., a molecular diagnostics company specializing in cardiovascular genomics, is committed to developing clinically validated tests that empower clinicians to better tailor care to each individual patient. Strategically focused on coronary artery disease, CardioDx is committed to expanding patient access and improving 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 age, sex, and the gene expression profile of cells found in peripheral blood specimens to help a clinician identify the likelihood that a patient has 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 (CAD), 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, 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 age, sex, and the expression levels of multiple genes using an algorithm with weighted gene expression levels to generate a quantitative score. The results of the test should be used by clinicians in conjunction with other tests and clinical information when assessing a patient's CAD.

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 CAD, to predict or detect response to therapy, or to help select the optimal therapy for patients.

REFERENCES:
1. 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. **2.** Patel MR, Peterson ED, Dai D, et al. Low Diagnostic Yield of Elective Coronary Angiography. *N Engl J Med.* 2010;362(10):886-895. **3.** Diamond GA, Forrester JS. Analysis of Probability as an Aid in the Clinical Diagnosis of Coronary Artery Disease. *N Engl J Med.* 1979;300(24):1350-1358.

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