cleerly | ISCHEMIA

TABLE OF CONTENTS

MAIN CLINICAL VALIDATION STUDY
CREDENCE[1]

Cleerly® ISCHEMIA™ accurately identified coronary ischemia as determined by invasive FFR.

In a retrospective analysis of symptomatic patients from the CREDENCE derivation and validation cohort (n=307 and n=305, respectively), the diagnostic performance by AUC on per-patient level was 0.80 for Cleerly ISCHEMIA, 0.69 for FFRcт and 0.65 for MPI; per-vessel data is below.

CREDENCE: Per vessel (n=868)

cleerly-cv-ischm-20240126
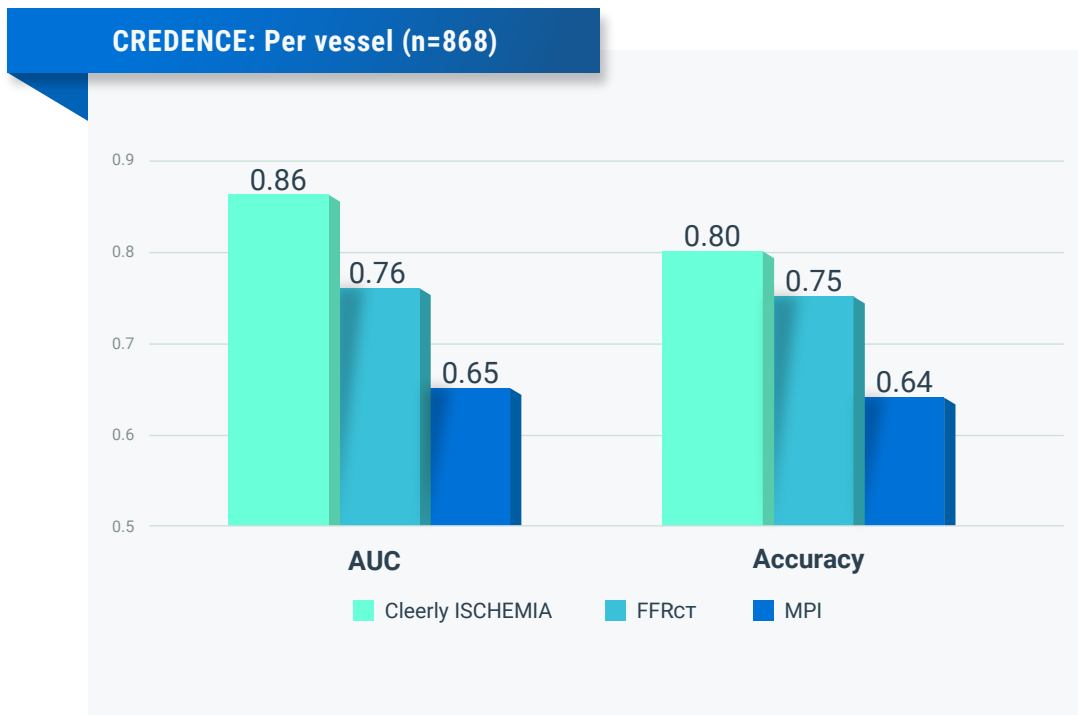
EXTERNAL VALIDATION STUDY #1
## (PACIFIC) [2]

Cleerly ISCHEMIA had higher diagnostic accuracy than myocardial perfusion imaging (mainly SPECT) and FFRCT.[1]

In a post-hoc analysis of the PACIFIC study, Cleerly ISCHEMIA was compared to FFRcт, 15O-H2O PET and SPECT to predict invasive FFR≤ 0.8 as reference standard. On a per-patient basis Cleerly ISCHEMIA (AUC 0.91), FFRcт (AUC 0.90) and PET (AUC 0.88) performed similarly, outperforming SPECT (AUC 0.71) in predicting ischemia.
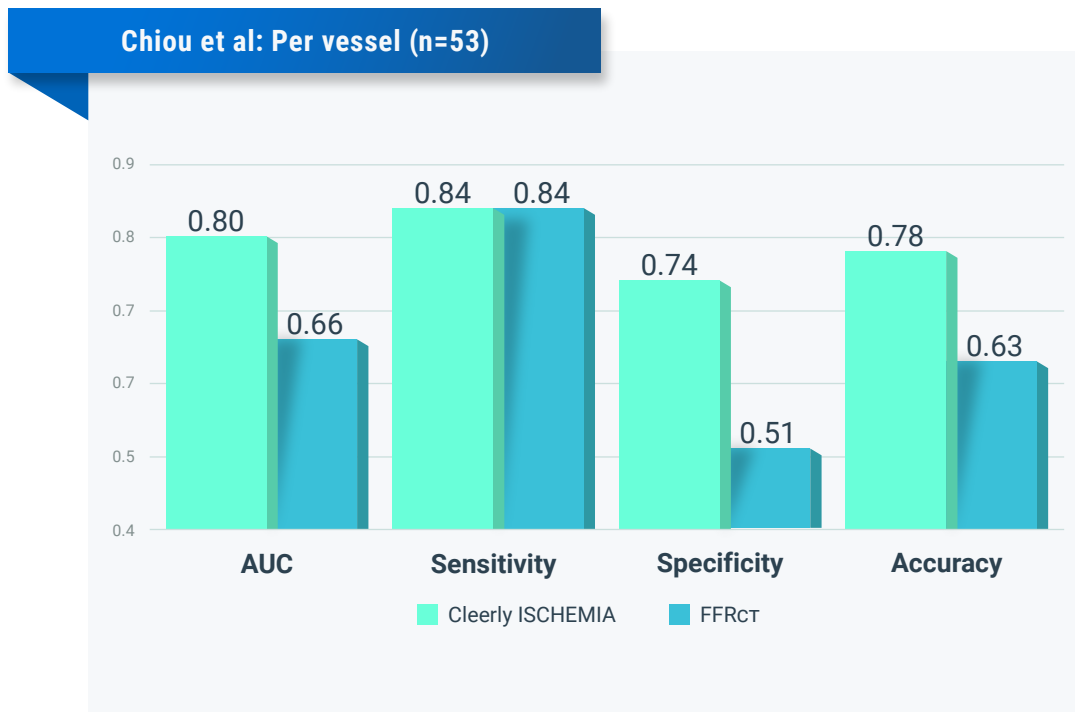
ROC for predicting FFR≤0.8 (per patient)
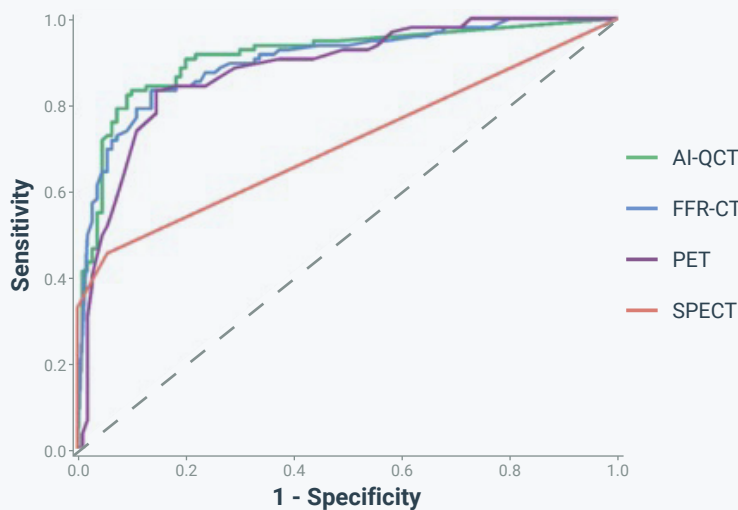
PACIFIC: Per vessel (n=612)
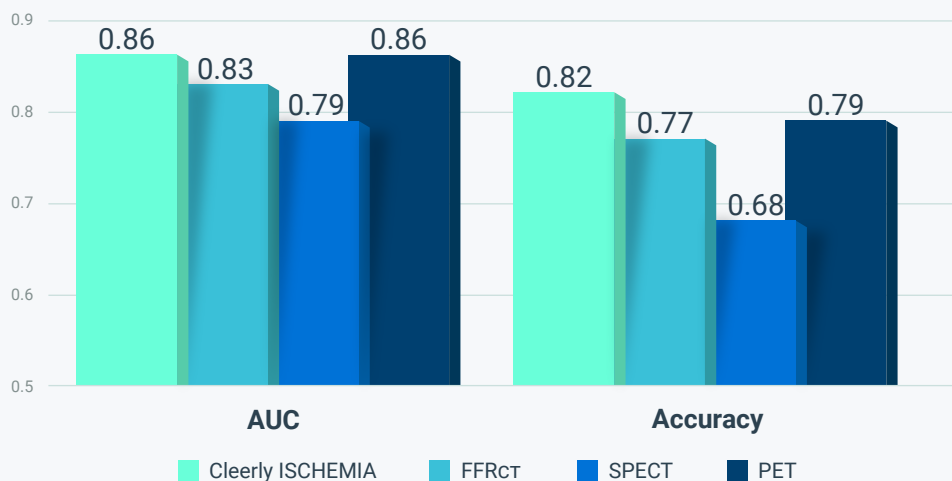
EXTERNAL VALIDATION STUDY #2
(CHIOU ET AL)[3]

Cleerly ISCHEMIA compared favorably to FFRᴄᴛ against invasive adenosine FFR.

In a single center 43 month retrospective review of 442 patients referred for CCTA and CT-FFR. The per vessel ischemia prediction for Cleerly ISCHEMIA and FFRᴄᴛ, are shown.

Chiou et al: Per vessel (n=53)

Bar chart comparing Cleerly ISCHEMIA and FFRᴄᴛ:
- AUC: Cleerly ISCHEMIA 0.80, FFRᴄᴛ 0.66
- Sensitivity: Cleerly ISCHEMIA 0.84, FFRᴄᴛ 0.84
- Specificity: Cleerly ISCHEMIA 0.74, FFRᴄᴛ 0.51
- Accuracy: Cleerly ISCHEMIA 0.78, FFRᴄᴛ 0.63

Legend: Cleerly ISCHEMIA, FFRᴄᴛ

cleerly-cv-ischm-20240126

Cleerly ISCHEMIA performed well compared to FFRᴄᴛ in prediction of myocardial ischemia.

In a single center study of 35 patients and 42 vessels. Specificity was the only significantly different per-vessel measure between Cleerly ISCHEMIA and FFRᴄᴛ (76% vs 44%; p = 0.031).

Karlsberg et al: Per vessel (n=42)

Legend: Cleerly ISCHEMIA, FFRᴄᴛ
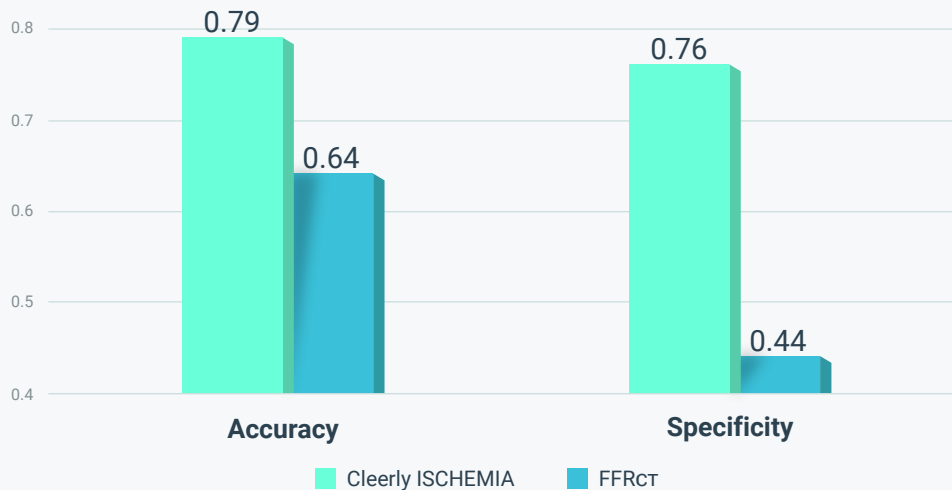
Performance for prediction of myocardial ischemia defined as FFR≤0.8 or iFR≤0.89
N=35 patients and 42 vessels

Endpoint	Cleerly ISCHEMIA	FFRᴄᴛ	p-value
Per-vessel			
Accuracy	79% (33/42)	64% (27/42)	0.133
Sensitivity	82% (14/17)	94% (16/17)	0.308
Specificity	76% (19/25)	44% (11/25)	0.031
Per-patient			
Accuracy	83% (29/35)	66% (23/35)	0.134
Sensitivity	88% (14/16)	88% (14/16)	1.000
Specificity	79% (15/19)	47% (9/19)	0.083

cleerly-cv-ischm-20240126

DIAGNOSTIC PERFORMANCE AND PROGNOSTIC COMPARISON WITH $^{15}O\text{-}H_2O\text{-}PET$ [5]

Cleerly ISCHEMIA improves risk stratification.

This study compared the prognostic value of Cleerly ISCHEMIA for clinical events among 864 patients undergoing $^{15}O\text{-}H_2O\text{-}PET$ perfusion imaging with 7.7 years of mean follow-up. A positive Cleerly ISCHEMIA score was associated with a 1.5-fold increased adjusted rate of long-term death, MI, or unstable angina. Positive Cleerly ISCHEMIA score was also associated with a significantly higher rate of MACE among patients with normal perfusion.

Adjusted Kaplan-Meier Curves of the Primary Endpoint and Components

Death, MI, uAP

HR 1.96 (95% CI 1.50-2.57), p<0.001

Normal AI-ischemia result — Abnormal AI-ischemia result
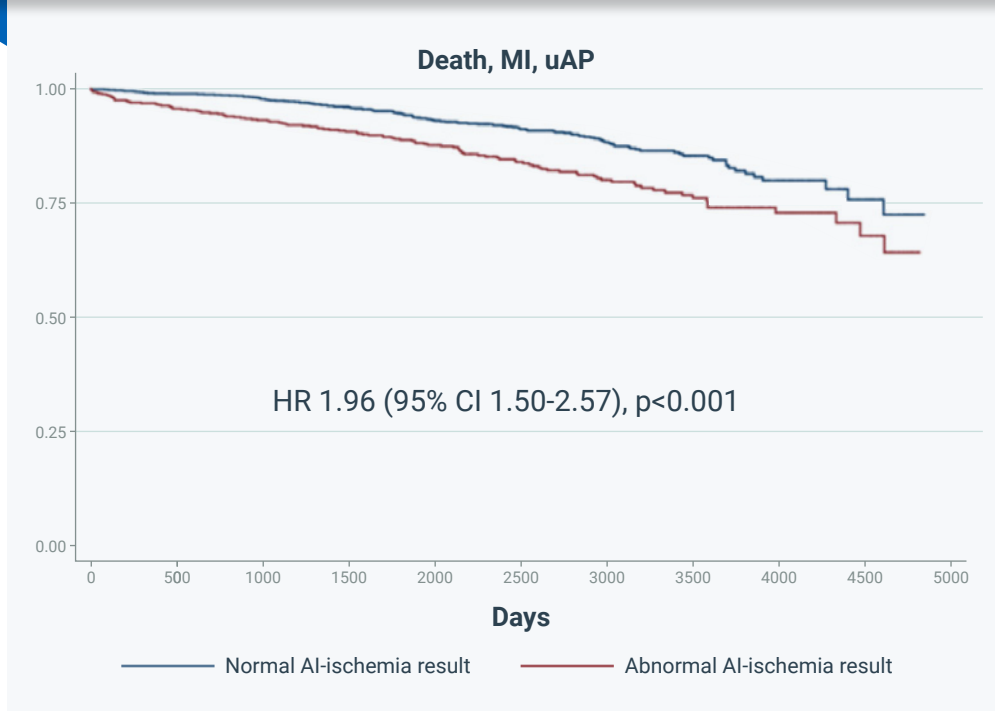
DIAGNOSTIC PERFORMANCE AND PROGNOSTIC COMPARISON WITH $^{15}O\text{-}H_2O\text{-}PET$ [6]

Cleerly ISCHEMIA showed similar long-term prognostic value as $^{15}O\text{-}H_2O\text{-}PET$ perfusion imaging.

In 1233 patients (45% male, median age 63.0 years) with 7.9 yrs of

follow-up, PET found 26% patients had ischemia, Cleerly ISCHEMIA 28%, with 83% concordance (Cohen's kappa 0.58). Both PET (HR 1.82 (95%CI 1.30-2.56), p<0.001) and Cleerly ISCHEMIA (HR 1.99 (95%CI 1.42-2.81), p<0.001) were predictive of MACE.
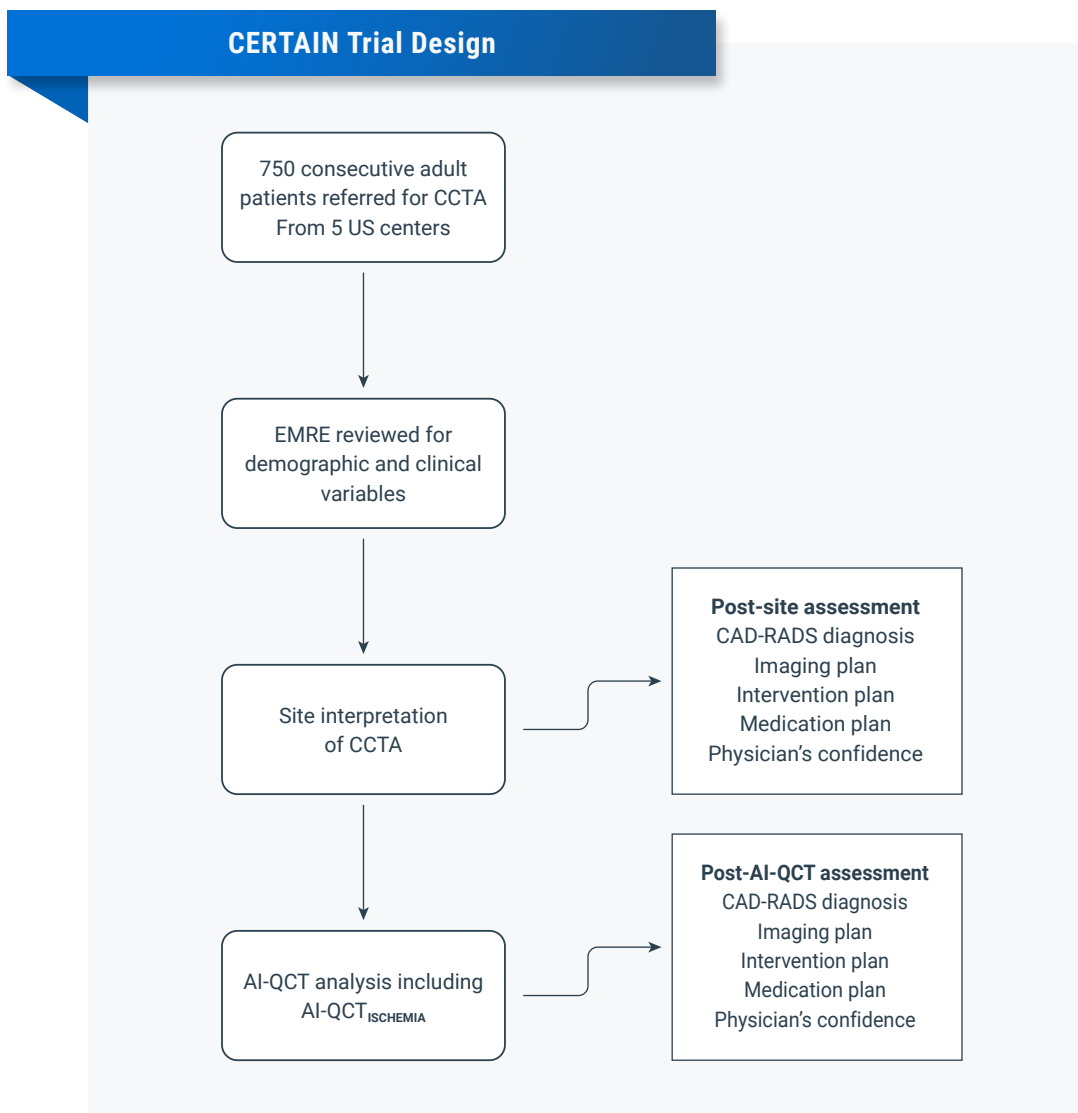
AI-based ischemia algorithm

Hybrid CCTA/PET imaging
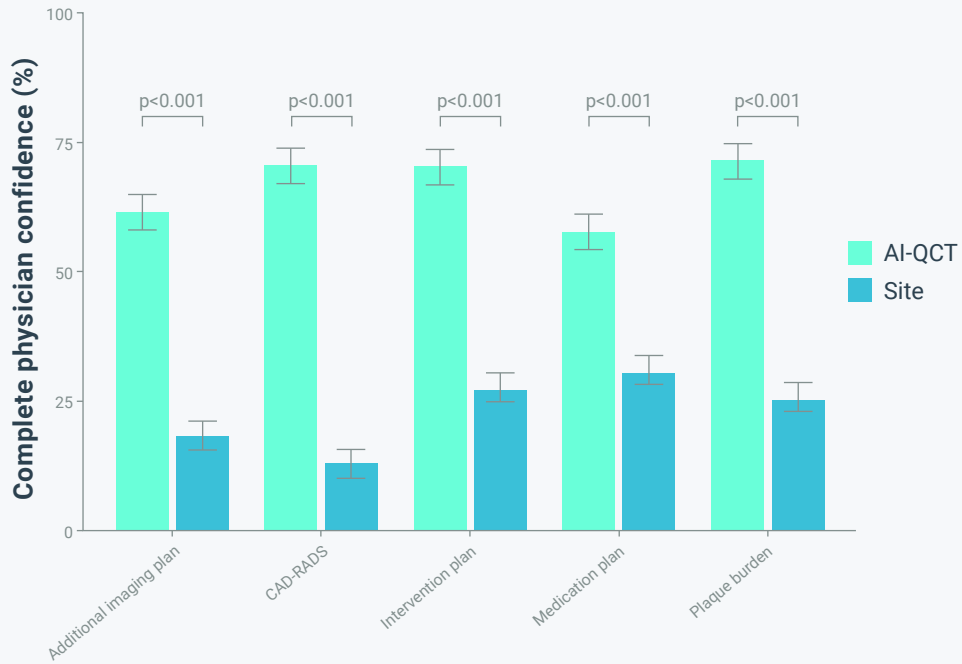
cleerly-cv-ischm-20240126

CLINICAL UTILITY COMPARED WITH CCTA ALONE[8]

Use of Cleerly® LABS™ and Cleerly ISCHEMIA has a major impact on physicians' confidence, changing diagnosis and patient management in more than 57% of cases.
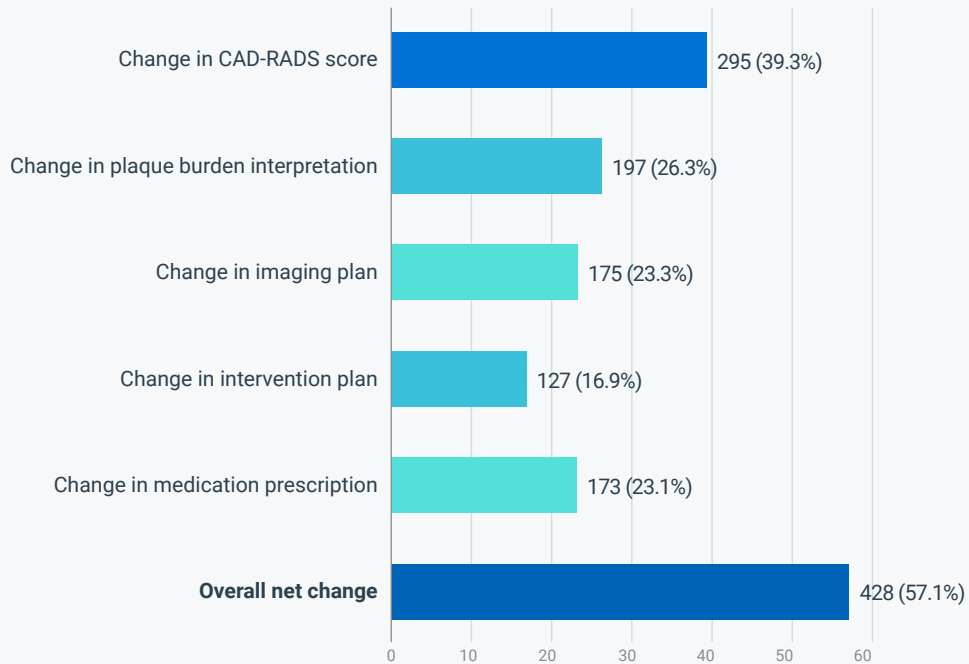
CERTAIN was a multicenter study recruiting consecutive CCTA patients. After CCTA, physicians assessed 750 patients' diagnosis, imaging, intervention and medication management plans. This was repeated after using Cleerly LABS + ISCHEMIA. Use of Cleerly LABS + ISCHEMIA improved physician complete confidence 2-5x in every step of the care pathway. Cleerly LABS + ISCHEMIA was associated in at least one clinical category change in >57% of patients.

CERTAIN Trial Design

750 consecutive adult patients referred for CCTA From 5 US centers

↓

EMRE reviewed for demographic and clinical variables

↓

Site interpretation of CCTA →

Post-site assessment
CAD-RADS diagnosis
Imaging plan
Intervention plan
Medication plan
Physician's confidence

↓

AI-QCT analysis including AI-QCT$_{ISCHEMIA}$ →

Post-AI-QCT assessment
CAD-RADS diagnosis
Imaging plan
Intervention plan
Medication plan
Physician's confidence

Physician's confidence in care pathway with site CCTA assessment compared with Cleerly assessment

Complete physician confidence (%)

AI-QCT
Site

p<0.001 (Additional imaging plan)
p<0.001 (CAD-RADS)
p<0.001 (Intervention plan)
p<0.001 (Medication plan)
p<0.001 (Plaque burden)

Change Following Cleerly Compared with CCTA

Change in CAD-RADS score	295 (39.3%)
Change in plaque burden interpretation	197 (26.3%)
Change in imaging plan	175 (23.3%)
Change in intervention plan	127 (16.9%)
Change in medication prescription	173 (23.1%)
Overall net change	428 (57.1%)

Diagnostic Performance Comparison with FFRcт, MPI

[1] Nurmohamed N, Danad I, Jukema R, et al. Development and validation of a quantitative coronary CT angiography model for diagnosis of vessel-specific coronary ischemia. In Press *JACC CV Imaging* 2024.

[2] Nurmohamed NS, Danad I, Jukema R. High Diagnostic Accuracy Of AI-Ischemia in Comparison To PET, FFR-CT, SPECT, and Invasive FFR: A Pacific Sub-Study. Presented at the American College of Cardiology Annual Scientific Meeting New Orleans LA 2023.

[3] Chiou A, Hermel M, Miller G et al. Cleerly™ Vs. Heartflow™ vs. Site Read in The Per-Vessel Prediction of Adenosine FFR ≤0.80 With Plaque Features Associated with False Positives. Presented at the American College of Cardiology Annual Scientific Meeting New Orleans LA 2023.

[4] Karlsberg RP, Gonzalez Quesada C, Samuels B et al. High diagnostic accuracy of a novel artificial intelligence guided quantitative coronary computed tomography algorithm for predicting myocardial ischemia. Presented at the Society of Cardiovascular Computed Tomography Annual Scientific Meeting Boston MA 2023. *Journal of Cardiovascular Computed Tomography* Vol. 17 Issue 4 Supplement S28−S29 Published in issue: July, 2023.

Diagnostic Performance Comparison with FFRcт, MPI

[5] Bär S, Nabeta T, Maanitty T. Prognostic Value of a Novel Artificial Intelligence-Based Coronary Computed Tomography Angiography-Derived Ischemia Algorithm for Patients with Suspected Coronary Artery Disease. Presented at the European Society of Cardiology Annual Scientific Meeting Amsterdam NE 2023. *In Submission European Heart Journal Cardiovascular Imaging* 2023.

[6] Maanitty T, Bär S, Nabeta T. Prognostic value of a novel artificial intelligence-based CCTA-derived ischemia algorithm in patients with suspected coronary artery disease: comparison against hybrid CCTA/PET perfusion imaging. Presented at the Society of Cardiovascular Computed Tomography Annual Scientific Meeting Boston MA 2023. Winner Best Abstract Award. *Journal of Cardiovascular Computed Tomography* Vol. 17I Issue 4 Supplement S2 Published in issue: July, 2023.

[7] Bär S, Maanitty T , Nabeta T, et al. Incremental Prognostic Value Of A Novel Artificial Intelligence-Based CCTA-Derived Ischemia Algorithm Among Patients With Normal And Reduced Myocardial Perfusion. Presented at the Society of Cardiovascular Computed Tomography Annual Scientific Meeting Boston MA 2023. *Journal of Cardiovascular Computed Tomography* Vol. 17 Issue 4 Supplement S59 Published in issue: July, 2023.

Clinical Utility Compared with CCTA

[8] Nurmohamed NS, Cole J, Budoff M et al. Changes in CAD Diagnosis, Imaging, Intervention and Medication with AI-QCT: the CERTAIN trial. Presented at the Society of Cardiovascular Computed Tomography Annual Scientific Meeting Boston MA 2023. In Submission (invited) Circulation Cardiovascular Imaging. *Journal of Cardiovascular Computed Tomography* Vol. 17 Issue 4 Supplement S56−S57 Published in issue: July, 2023

　　cleerly-cv-ischm-20240126

Cleerly is the company on a mission to eliminate heart attacks by creating a new standard of care for the diagnosis of heart disease. Through its AI-empowered solutions, Cleerly supports comprehensive phenotyping of coronary artery disease, through its evaluation of advanced non-invasive CT imaging. Cleerly's approach is grounded in nearly 20 years of science from landmark multi-center clinical trials. Cleerly enhances health literacy for each and every stakeholder in the coronary care pathway.

For more information, please visit: www.cleerlyhealth.com.

Cleerly LABS is a web-based software application that is intended to be used by trained medical professionals as an interactive tool for viewing and analyzing cardiac computed tomography (CT) data for determining the presence and extent of coronary plaque (i.e. atherosclerosis), stenosis and evaluates the likelihood of ischemia in patients who underwent Coronary Computed Tomography Angiography (CCTA) for evaluation of CAD or suspected CAD. Rx Only.

Cleerly ISCHEMIA™

Cleerly ISCHEMIA analysis software is an automated machine learning-based decision support tool, indicated as a diagnostic aid for patients undergoing CT analysis using Cleerly LABS software. When utilized by an interpreting healthcare provider, this software tool provides information that may be useful in detecting likely ischemia associated with coronary artery disease. Patient management decisions should not be made solely on the results of the Cleerly ISCHEMIA analysis. Rx Only.

Learn more about Cleerly ISCHEMIA
cleer.ly/ischemia-reinvented

cleerly-cv-ischm-20240126