Vectra® Guided Care
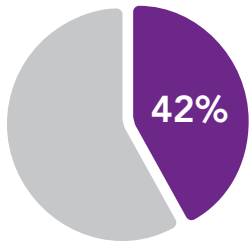
Evaluate success of controlling rheumatoid arthritis inflammation by using Vectra at initiation, change in drug therapy, and repeating to monitor response to therapy

Vectra®

Vectra® Can Help Guide Personalized Medical Management Decisions to Improve Patient Outcomes

42% of patients thought to be in low or moderate disease activity by traditional disease activity measure were in high disease activity measured by Vectra and thus were at risk for joint damage progression.

42%

In a combined analysis of patients from 3 studies, 42% of those with low or moderate disease activity by DAS28-CRP had a high Vectra Score[1]

Vectra Guided Care provides quantitative personalized insight to help guide disease management plan:

- Vectra is the **best predictor of radiographic progression**

- Provides scores ranging from 1 to 100 to categorize RA disease activity into low, moderate or high to **help guide medical management**

- The Vectra Score Interpretation found on the report **provides guidance to physicians**

- **Changes in the Vectra Score of 8 or more** in high and moderate patients represent a meaningful change in RA inflammation

The benefits of using Vectra in your office

✓ Objective Insight into Inflammation

✓ Improved Efficiency

✓ Patient Affordability

1. Curtis JR, et al. Curr Med Res Opin, 2019: March 14. **2.** 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. **3.** Arthritis Rheumatol. 2016 Jan;68(1):1-26.

Vectra® Provides Molecular Insights on the Inflammatory State of RA That Can Help Inform Your Medical Management Decisions.
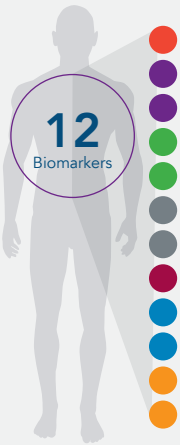
12 Biomarkers

- Vectra measures 12 biomarkers and combines them into a single score thus allowing providers to incorporate molecular insight from various inflammatory pathways driving RA disease activity

- Vectra incorporates information on age, gender and adiposity to provide a score that reflects a patient's personalized disease activity and inflammation level

- Vectra is an unsurpassed predictor of radiographic progression

Vectra is a **molecular measurement of disease activity and RA inflammation**

Adhesion Molecules	Growth Factors	Cytokines/ Receptors	Matrix Metalloproteinases	Skeletal-Related Proteins	Hormones	Acute-Phase Proteins
VCAM-1	EGF	IL-6	MMP-1	YKL-40	Leptin	SAA
	VEGF-A	TNF-RI	MMP-3		Resistin	CRP

Sample

Sample

Sample

Report Highlights

- Vectra provides a personalized measure of disease activity

- Vectra provides the risk of rapid radiographic progression within one year[2]

- Change in Vectra Score is assessed in relation to the Minimally Important Difference (MID). MID of 8 reflects the smallest absolute change in Vectra Score that likely reflects a change in disease activity and is not due only to random variation.[3]

- Vectra Score Interpretation calls out considerations for treatment decisions

- Patient Vectra Scores for the past three years are presented in one easy to read graph

1. Kay J, et al. Arthritis Res Therapy. 2014;16(1):R40. **2.** Curtis JR, et al. Validation of a novel multibiomarker test to assess rheumatoid arthritis disease activity. Arthritis Care Res. 2012; 64 (12): 1794-1803. **3.** Chernoff D, (February 2019). Determination of the Minimally Important Difference (MID) in Multi-biomarker Disease Activity (MBDA) Test Scores. Clinical Rheumatology

Vectra®

The Vectra® Report Gives Clear Perspective of RA Inflammation

Vectra Helps Identify a Patient's Future Risk of Radiographic Progression

PATIENT INFORMATION

Age	49
Gender	Female
Diagnosis	RA
Drug Therapy	MTX, Etanercept

VISIT NOTES

- Patient is 5'2", 178 lbs.
- Patient reports feeling okay and is resistant to changing therapy
- Patient has had RA for five years

Vectra Score

72

HIGH
(45-100)

{ Scores over time will show a trend and can **provide insight into a meaningful change** in the patient's disease activity }

Vectra® Report:
A Personalized Precision Tool

The Vectra Score is reported on a scale of 1-100. Patients in the high and moderate categories are considered to have uncontrolled inflammation, and may require treatment modification.

Level of Disease Activity	LOW	MODERATE	HIGH
Vectra Score	1 to 29	30 to 44	45 to 100
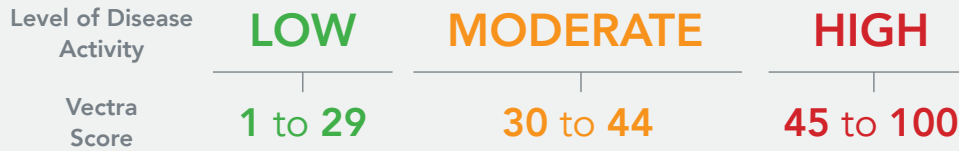
REPORT PAGE 1

Vectra Score factors in age, gender and adiposity of the patient to provide personalized measurement of inflammation

Risk of RP patient's risk of rapid radiographic progression within one year

Change in Score will show the difference between multiple scores and indicate if there has been a meaningful change, or no change in disease activity

Vectra Scores Over Time is a rolling 3.5 year date range plus initial score consisting of 7 half-year periods

Vectra Score Interpretation provides a more detailed explanation of the Vectra Score, disease activity category, risk of radiographic progression and treatment plan consideration

Risk of RP Graph gives a patient's future risk of radiographic progression based on their Vectra Score

As of 12/4/2017 Vectra Score has been adjusted based on **age, gender** and **adiposity** of the patient

Meaningful Change: MID of 8 is the smallest absolute change in the Vectra Score that is likely to reflect change in disease activity

---

SAMPLE

ORDERING PHYSICIAN: Physician Name, MD

RECEIVING HEALTHCARE PROVIDER
Clinic United Partnership Example of Oklahoma University
1234 Pennsylvania Ave, Bldg 100, Ste 123, Dept of Rheumatology
Anytown, OK 12345
Phone: 555-555-1234 / Fax: 555-555-1234

SPECIMEN
Collection Date: JUL-24-2020
Receipt Date: JUL-25-2020

REPORT
Report Date: JUL-30-2020

PATIENT
Name: Jane Doe
Date of Birth: NOV-1-1970
Patient ID: 000-000-0000
Gender: Female
TRF ID: 00000000-00

Vectra Molecular Result

Vectra Score	Risk of RP	Change in Score	Vectra Score Interpretation
72 HIGH (45-100)	**20%** 1-Year Risk of Radiographic Progression	⬆ Meaningful Increase ≥8 Units	■ High Vectra Score: 72 — Patient has a High Vectra Score that increased by 8 or more units from the previous score, which was also in the High category. Patient is at increased risk for radiographic progression. Consider adjusting treatment regimen to reduce inflammation, and retesting at the next clinical visit.

VECTRA SCORE DESCRIPTION

Vectra Disease Activity Levels: ■ Low: 1 to 29 ■ Moderate: 30 to 44 ■ High: 45 to 100

Vectra Score measures the concentrations of 12 serum proteins. An algorithm is applied to these concentrations to calculate a disease activity score on a scale of 1 to 100. The Vectra Score is personalized based on the age, gender, and adiposity of the patient.

RISK OF RADIOGRAPHIC PROGRESSION (RP)

The risk of RP is shown as a function of Vectra Score (see graph, right). The definition of RP is a 1-year total Sharp score change of >5 units. Increased risk of RP means a greater chance of irreversible joint damage.

Patient serostatus may affect the risk of radiographic progression. Thus, the actual risk of radiographic progression may be higher if this patient is seropositive and lower if this patient is seronegative.

This Patient 20%

CHANGE IN SCORE DESCRIPTION

Change in Score is assessed in relation to the Minimally Important Difference (MID) for Vectra. The MID for patients with a Moderate or High Vectra Score is 8.0.

VECTRA SCORES OVER TIME Complete score history shown on last page.

■ Low ■ Moderate ■ High

Meaningful Change (≥8 MID)

44 — 11/15/19
63 — 3/25/20
72 — 7/30/20

Jan, 2018   Jan, 2019   Jan, 2020   Jan, 2021

*As of December 4, 2017 the Vectra Score is adjusted based on the age, gender and adiposity of the patient.

Sample

Vectra®

The Vectra Score is calculated from the concentrations of the 12 biomarkers shown on this page, which represent different biological pathways involved in RA pathophysiology. The clinical application of individual biomarker values, which have different weighting in the Vectra algorithm, has not been established.

Includes the leptin range for all RA patients.

Result/Units: Concentrations of the individual biomarkers

The RA range refers to the reference range for each biomarker based on a reference set of RA patients. This is the concentration range that contains the central 95% of results for that biomarker.

Patient biomarker level relative to levels in all patients in the RA reference set.

Includes a complete list of your patient's historical Vectra Scores

Includes comments and details relevant to Vectra samples and patient care (e.g., reason behind sample rejection).

Vectra® — SAMPLE

PATIENT: Jane Doe	DOB: NOV-1-1970	PATIENT ID: 000-000-0000	GENDER: Female

Individual Biomarker Results

TYPE	BIOMARKER	RESULT / UNITS	RA RANGE†	RA PERCENTILE‡
ACUTE PHASE PROTEINS	SAA	1.1 ug/mL	0.29 - 85	8%
	CRP	0.32 mg/L	0.19 - 92	64%
ADHESION MOLECULES	VCAM-1	0.41 ug/mL	0.39 - 1.2	68%
CYTOKINE-RELATED PROTEINS	IL-6	2.9 pg/mL	2.5 - 200	6%
	TNF-RI	1.2 ng/mL	0.8 - 3.9	2%
GROWTH FACTORS	EGF §	190 pg/mL	12 - 410	17%
	VEGF-A	330 pg/mL	75 - 790	26%
HORMONES	LEPTIN	10 ng/mL	1.5 - 120	18%
	RESISTIN	5.7 ng/mL	3.5 - 21	51%
MATRIX METALLOPROTEINASES	MMP-1	5.6 ng/mL	1.3 - 23	21%
	MMP-3	17 ng/mL	7.9 - 160	10%
SKELETAL-RELATED PROTEINS	YKL-40	45 ng/mL	22 - 540	3%

† These 95% reference ranges were established from 325,781 patient samples tested at Crescendo Bioscience Clinical Laboratory.
§ Inversely correlated with disease activity.
‡ Subject's biomarker level relative to levels in RA patient specimens from which the RA ranges were determined.

Please note: The individual biomarker results, which are expressed to two significant figures, are required inputs into the algorithm used to calculate the Vectra Score. Clinical interpretation of individual biomarker levels, which have different weights in the Vectra algorithm, has not been established.

Complete Vectra Score History

COLLECTION DATE	SCORE	NOTES
Feb. 10, 2017	56	Unadjusted*
Nov. 15, 2019	44	
Mar. 25, 2020	63	
Jul. 30, 2020	72	

*As of December 4, 2017 the Vectra Score is adjusted based on the age, gender and adiposity of the patient.

Comments

While the Vectra Score provides important objective data, it is intended for informational purposes only and does not constitute a recommendation. Medical management decisions should be made by a healthcare provider with an understanding of the full medical history and clinical assessment of the patient. For full test specifications and related publications, please visit **VectraScore.com.**

Laboratory Director: Bruce F Arnold, MD, FCAP
Crescendo Bioscience, Inc. a Myriad Genetics Company
320 Wakara Way, Salt Lake City, UT 84108
VectraScore.com | F: 1-877-743-8640 | P: 1-877-743-8639

The Vectra test is intended for clinical use. Crescendo Bioscience Inc. and Myriad Genetics Inc. developed Vectra and determined its performance characteristics. The Crescendo Bioscience Clinical Laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical testing and is a College of American Pathologists Accredited Laboratory.

2 of 2

Sample

Technical Specifications at VectraScore.com

Vectra® Guided Care

Vectra is a Validated Prognostic Test for Radiographic Progression[1,2]
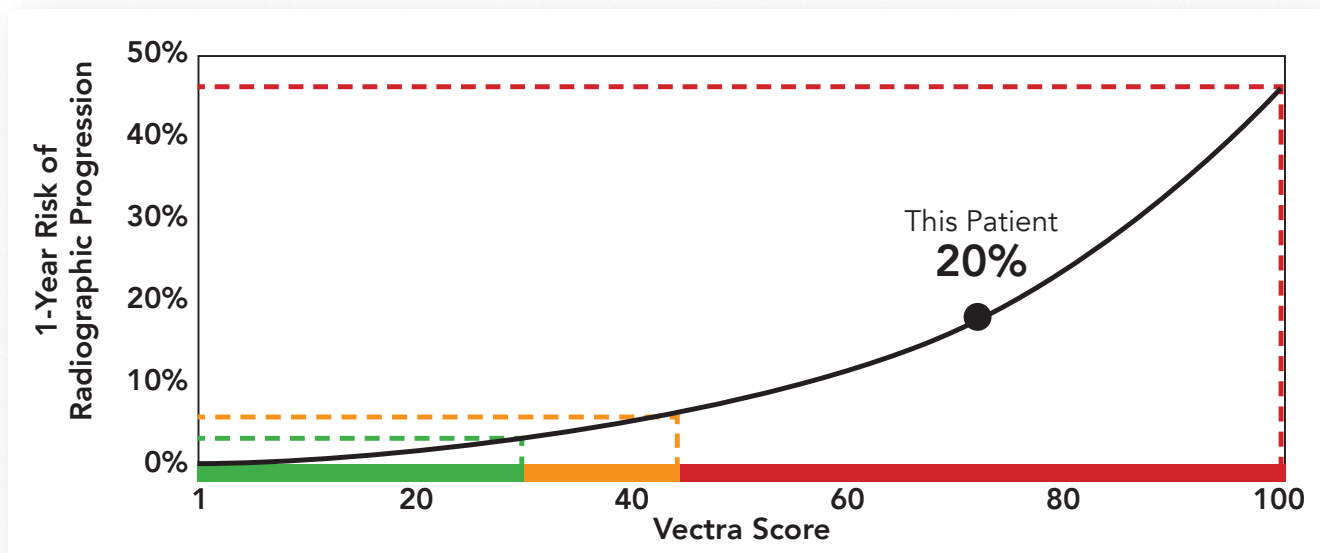
The Vectra Score correlates to the risk of radiographic progression (RP), which leads to permanent joint damage. As the Vectra Score increases the risk of RP increases. Sharp Score is used to evaluate radiographic progression. A Sharp Score change of 5 or more within one year is considered rapid radiographic progression.[2]

Patient serostatus may effect the risk of radiographic progression. The actual risk of radiographic progression may be higher if this patient is seropositive and lower if this patient is seronegative.

How was the Radiographic Progression Risk developed?

The risk of RP was determined by combining data from 4 cohorts (OPERA, BRASS, SWEFOT, and Leiden) to evaluate the ability of the Vectra Score to predict radiographic progression and to compare this ability with those of DAS28-CRP and CRP. Vectra was 3x better at predicting RP in one year than DAS28-CRP.[2]

{ An increased risk of radiographic progression means **greater chance of irreversible joint damage** }

1. Curtis JR, et al. Validation of a novel multibiomarker test to assess rheumatoid arthritis disease activity. Arthritis Care Res. 2012; 64 (12): 1794-1803. **2.** Huizinga T, et al. Predicting Risk of Radiographic Progression for Patients with Rheumatoid Arthritis [abstract]. Arthritis Rheumatol. 2019; 71 (suppl 10). https://acrabstracts. org/abstract/predicting-risk-of-radiographic-progression-for-patients-with-rheumatoid-arthritis/. Accessed October 24, 2019.

Vectra®

Vectra® Guided Care

Minimally Important Difference (MID) Can Help Guide Your Decision Making

Meaningful Change
(≥8 MID)

63 3/25/20

72 7/30/20
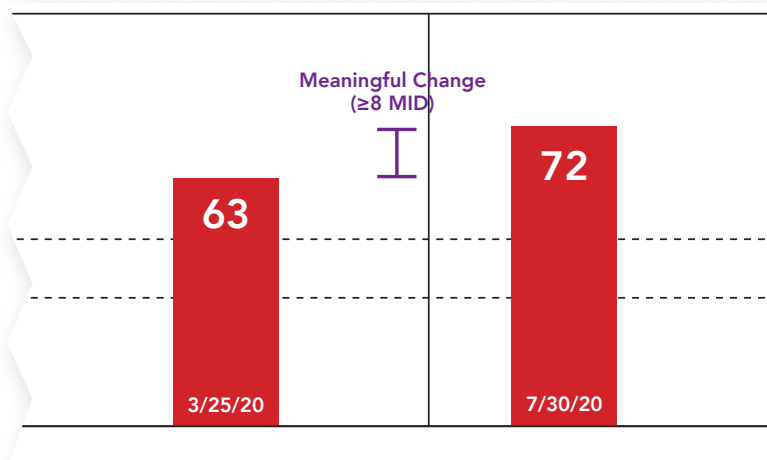
Changes of Vectra Scores of 8 or more help guide medical management decisions by representing meaningful changes in rheumatoid arthritis inflammation

How was the Minimally Important Difference established? The minimally important difference (MID) was determined by conducting a clinical study. This clinical study evaluated daily and diurnal variation in Vectra Scores in order to determine the minimally important change in score that is clinically meaningful. Having this information will help aid in your ability to make treatment decisions.

Vectra Score Interpretation

VECTRA SCORE	MEDICAL MANAGEMENT RECOMMENDATION‡
Low (<30)	**CONSIDER ONE OF THE FOLLOWING:** • **No treatment change** (re-test in 6-12 months or sooner if indicated) • **Reduce treatment if Vectra Score is low at two consecutive measures** (re-test in 6-12 months or sooner if indicated)* *See ACR Guidelines for therapy reduction in clinically well controlled patients

Moderate (30-44)	**CONSIDER ONE OF THE FOLLOWING:**
	• **Change or intensify treatment**
	  • If the Vectra Score has increased by ≥ 8 units since previous Vectra (re-test in 3 months)
	  • If the Vectra Score has decreased by <8 units since the most recent RA treatment change use clinical judgment (re-test when indicated)
	• **No treatment change**
	  • If the Vectra Score has decreased by >8 units since baseline or the most recent RA treatment change (re-test when indicated)
	  • If therapy was recently changed but no previous Vectra Score is available (re-test in 3 months)

High (>44)	**CONSIDER ONE OF THE FOLLOWING:** • **Change or intensify treatment** (re-test in 3 months) • **No treatment change if the Vectra Score has decreased by >8 units when a change in therapy has recently occurred** (re-test in 3 months)

This medical management guidance provides recommendations only. The treatment management decisions can only be done by a medical professional with the full information of patients medical status and medical history. These recommendations are currently being tested in clinical trial "VIVID" listed on clintrials.gov (NCT03810144).

‡ Chernoff D, (February 2019). Determination of the Minimally Important Difference (MID) in Multi-biomarker Disease Activity (MBDA) Test Scores. Clinical Rheumatology.
Curtis JR, et al. Update and Clinical Utility of Multi-Biomarker Disease Activity Testing in the U.S. The Journal of Rheumatology November 2018, jrheum. 180071

MANAGEMENT DECISION
Patient and Provider agree to make a treatment change

- Baseline at time of treatment change decision

  Therapy Initiation or Change: Until the desired treatment target is reached drug therapy should be adjusted every 3-6 months

THERAPY MONITORING
Evaluate if treatment is working

- Test at 3-6 months after treatment change to evaluate if treatment is working

  Achieving a state of disease remission in RA is considered a primary treatment goal

LOW DISEASE ACTIVITY MONITORING
Evaluate that patient remains within disease goal

- Continue to test patient two times a year once in low activity

  Monitor that patient is remaining in treatment goal

Vectra®

Provider & Patient Resources

VectraScore.com

Your online resource to learn more about Vectra, patient and provider testimonials and access the clinician portal

VectraView®

VectraView® is an online analytical tool that enables you to draw insights from Vectra results at the individual patient or practice level. VectraView allows you to:

- Access all of your patients' Vectra results in one place through a convenient online portal
- Store and access disease activity measurements alongside Vectra results
- View Vectra Scores displayed in the context of your patients' medications
- View Vectra results for all tested patients in one view and filter to identify patients for follow-up
- Save time – Order subsequent Vectra tests using prefilled test requisition forms

CARE — Vectra Financial Assistance Program

If you encounter any financial hardship, we will work directly with you toward your complete satisfaction. If you have any questions regarding the cost of testing, please contact Myriad.

myriadpromise.com

billinghelp@myriad.com
877-743-8639

myVectra™

myVectra™ provides patients access to their test results

- Go to VectraScore.com
- Click on myVectra link at top of page
- Use the fillable form to complete your profile information
- myVectra App is available for free in the Apple App store or Google Play

GHLF creakyjoints

Is a non-profit digital arthritis community that can provide your patients with:

- Educational resources to manage their disease
- Support and advice
- Advocacy opportunities
- Patient-centered research with ArthritisPower®

Find out more at creakyjoints.org

Patient & Provider Medical Support

A team of highly-trained medical liaisons is available by phone or email to help answer questions regarding Vectra results.

Phone: 877-743-8639 x1984 // **Email:** VectraMed@myriad.com

Vectra® CARE Financial Assistance

Vectra Customer Service and Billing will work directly with patients to make Vectra accessible

✔ **Medicare & Medicaid Patients***

Medicare patients have no out of pocket patient responsibility, and thus do not qualify for financial assistance. Medicaid patients are fully covered due to federal income requirements.

What if the Patient has Out-of-Pocket Concerns?

If the patient cannot afford their copay, deductible, or other out-of-pocket costs related to the test, they may be eligible for assistance through Vectra CARE Financial Assistance if their household income meets guidelines.

Vectra CARE Income Guidelines example based on a household of four**	
INCOME	**PATIENT RESPONSIBILITY**
Less than $52,400	$0
$52,401 - $78,600	$45
$78,601 - $104,800	$90

Patients can apply for financial assistance here:
VectraScore.com/Care

We are committed to helping all patients have access to Vectra testing to guide their rheumatoid arthritis treatment. We encourage all patients to fill out the Vectra CARE form to request financial assistance.

Vectra Customer Service **877-743-8639** and **VectraCS@myriad.com**

{ If a patient has ANY questions associated with their bill, have them contact Vectra Customer Service and we will work directly with the patient. }

*Medicare Advantage plans may require a copay   **Based on 0-4x federal poverty levels and household size of 4, https://aspe.hhs.gov/2020-poverty-guidelines 5/20

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