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RhAP



Rheumatology Specialty Labs

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Rana Aoufe, PA-C:

• There are no relevant financial relationships to disclose.

Sylvia Phommalinh, PA-C:

• There are no relevant financial relationships to disclose.

RHEUMATOLOGY LABS

- It is important to note that our labs do not make any diagnosis.
- The PHYSICAL EXAM is our most important component.
- Labs help GUIDE US.

RHEUMATOID ARTHRITIS MARKERS

• Conventional markers used for RA are **RF** and **CCP** (98% specific, 70% sensitive)

 14.3.3eta protein- joint derived, proinflammatory mediator that is highly specific for established RA(77% sensitivity) and early RA(59-64% sensitivity). May provide 15% incremental benefit in identifying early RA in RF/CCP negative patients. Also associated with higher rates of joint damage measured by radiographic assessments.

RHEUMATOID ARTHRITIS MARKERS

- AntiCarP(anti-carbamylated protein antibodies) predicts development of RA independent of anti-CCP with sensitivity of from 36.2-47.7% and specificity from 92.9-97%. may be present years before onset of symptoms of RA, associated with more severe clinical and radiographic disease.
- Anti-Sa(citrullinated vimentin antibodies) nearly **100% specificity for RA** and sensitivities of **20-25% in early RA and 47% in establish RA**. May identify an additional 8.7% of RA that is anti-CCP negative. Predicts more severe disease and poor prognosis. Anti-Sa antibody titers correlate with higher disease activity.
- Anti-CEP-1(citrullinated alpha-enolase 1 antibody)– early marker that can predict the onset of symptoms in pre-clinical RA years before onset with **specificity of 98% and sensitivity of 37-67%**. Detected in 12.5% of RA patients who test negative for anti-CCP.



Vectra simultaneously measures 12 proteins that are involved in multiple key pathways of RA

12 Biomarkers Assess Systemic Disease Activity in RA								
Adhesion	Growth	Cytokines/	Matrix	Skeletal-Related	Hormones	Acute-Phase		
Molecules	Factors	Receptors	Metalloproteinases	Proteins		Proteins		
VCAM-1	EGF VEGF-A	IL-6 TNF-RI	MMP-1 MMP-3	YKL-40	Leptin Resistin	SAA CRP		
Cellular Infl	ux & Tissue	Inflammation	Cartilage Degradation	Stromal Activity	L Systemic In	flammatory		
Grov	wth	& Destruction	& Joint Damage	& Regulation	Resp	onse		

Clinical Remission (DAS28 <2.6) Does Not Eliminate the Risk for Radiographic Progression (RP)⁹

Structural damage can continue even when symptoms appear under control



19% of patients in clinically defined remission had progression of **radiographic joint damage** over one year

Four Cohorts with Requisite Data Were Identified and Combined (N=953) 11



- The four cohorts combined (N=953) included patients receiving biologic and non-biologic DMARDS
- In continuous and binary analyses, the Vectra Score was the most significant predictor of radiographic progression over one year compared to eight other variables
- The analysis demonstrated that RP aligned more closely with the adjusted Vectra Score than
 conventional measures, even when they were discordant
- A risk curve was created, showing RP increases continuously with an increasing Vectra Score, with RP risk of more than 40% among the highest adjusted Vectra Scores

Radiographic progression (RP; ∆TSS >5) by category of adjusted Vectra Score cross-classified with conventional disease activity measures

16.1%

(5/31)

15.8%

(86/544)

5.5%

>3

0%

(0/12)





A high Vectra Score correlates with a risk of higher future irreversible joint damage¹¹

The risk for radiographic progression over one year increases continuously with an increasing Vectra Score.



- Minimally Important Difference(MID) occurs when a patient's Vectra Score has a change that is greater or equal to 8.
 - Decrease of Vectra score of 8 or more shows a favorable response to treatment in patients in moderate of high disease activity
 - Increase of Vectra score of 8 or more presents an increase in disease activity and may require adjustment to treatment regimen

When would we use Vectra DA in clinical practice?

- Baseline data with new RA diagnosis and repeat every 6-12 months
- RA vs OA disease activity since joint pain subjectively assess by patients
- Deciding if change in therapy is indicated, patient reports their RA is not controlled but physical exam is benign

What is the recommended frequency for ordering this test?

- High disease activity : Q3 months to ensure response to treatment
- Moderate disease activity: Q3-6 months to ensure patient is not moving into high disease activity category
- Low disease activity: Annually

VECTRA DA SAMPLE RESULTS

Vectra Molecular Result

Vectra Score	Risk of RP	Change in Score	Vectra Score Interpretation
74 . ^{HIGH} (45-100)	21% 1-Year Risk of Radiographic Progression	Meaningful Change Not Calculated Multiple Vectra scores required for meaningful change calculation	High Vectra Score: 74 Patient has a High Vectra Score and 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 ace. cender, and adjoosity of the patient.

RISK OF RADIOGRAPHIC PROGRESSION (RP)

The risk of RP is shown as a function of Vectra Score (see chart, 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.



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.



PRISM RA

What is the test used for?

 Helps determine suitable treatment options for your patients

When is the test used in clinical practice?

- At baseline to determine if TNFi is a good first line therapy after failure of MTX
- Moderate RA disease activity after starting TNFi
- Switching to another class after failure of TNFi
- LOMN when appealing for another class of medication



How was PRISM RA developed?

- The human interactome was used to identify genes relevant to RA disease biology
- Clinical data from patients were analyzed with Sciphers AI platform to rank biological features by their ability to differentiate patients that would respond to therapy from those that would not
- The 23 features most predictive of non-response were use in PrismRA algorithm



- What is the recommendation for when this test is ordered?
 - RA patients naïve to treatment
 - RA patients prior to starting TNFi
 - RA patients on a TNFi and considering dose change or medication change

PRISM RA

₩90%

of patients with rheumatoid arthritis (RA) are treated with TNFi therapies as first-line b/tsDMARD^{1,2} of patients with RA reach ACR50 at 6 months with b/tsDMARD after failing methotrexate^{3,4}

ABOUT 1/3



• How accurate is this test?

- PrismRA has a 90% positive predictive value
- 10% of patients with results that they are nonresponders will respond to a TNFi inhibitor
- This should be used along with clinical judgement

PRISM RA RESULTS

Incorporating PrismRA into your practice





• Comprehensive test used for evaluation and monitoring of many rheumatological conditions



- Conditions being evaluated:
 - SLE
 - -RA
 - Sjogren's
 - Scleroderma
 - PM/DM
 - APS
 - Autoimmune thyroid disease



When to order AVISE?

- Further evaluate a +ANA with symptoms that could be related to multiple conditions
- Useful when patients are adamant they have CTD because of a +ANA
- Used to use for cash patient because it was cost effective

- AVISE CTD
- AVISE APS
- AVISE SLE
- AVISE Vasculitis

- AVISE SLE prognostic
- AVISE PC4d
- AVISE AntiCarP

- AVISE SLE monitor
- AVISE MTX
- AVISE HCQ

• AVISE CTD

 Useful in evaluating patients with +antibodies and overlapping symptoms of different disease states



• AVISE SLE

- Improves accuracy by using assays with greater sensitivity and specificity in their Cell-Bound Complement Activation Products
- Conducting multiple tests simultaneously to combine results into a single index score (Lupus index score)
- Allows for earlier diagnosis which in turn decreases risk of organ involvement

• AVISE SLE

Order ID	739811	0	Specimen Collected Received	01/19/2023	Patient	Sample, Susan S.
Provider	Exagen	Provider MD	Test Order Created Reported	01/20/2023 01/25/2023	Gender - DOB Identifier Received Exagen ID	Female - 01/01/1996 541163

AVISE Lupus Test Report



				Tier 1
Tier 1 Analytes	Value	Interpretation	Reference Range	Assessment
Anti-dsDNA IgG	20.00 IU/mL	Negative	<201 - Negative 201-<302 - Equivocal 2302 - Positive	1
Confirmation by Crithidia luciliae		N/A		
Anti-Smith IgG	<0.7 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive	Negative
CB-CAP: EC4d - Erythrocyte-bound C4d	25 Net MFI	POSITIVE	<15 - Negative 15 -75 - Positive >75 - Strong Positive	
CB-CAP: BC4d - B-lymphocyte-bound C4d	100 Net MFI	POSITIVE	<61 - Negative 61-200 - Positive >200 - Strong Positive	
Note:				
Criteria for Tier 1 Positive not met.				

Tier 2 Analytes	Value	Interpretation	Reference Range	Tier 2 Assessment
ANA IgG	40.00 Units	POSITIVE	<20 - Negative 20-<60 - Positive 260 - Strong Positive	1
CB-CAP: EC4d - Erythrocyte-bound C4d	25 Net MFI	POSITIVE	<15 - Negative 15-75 - Positive >75 - Strong Positive	
CB-CAP: BC4d - B-lymphocyte-bound C4d	100 Net MFI	POSITIVE	<61 - Negative 61-200 - Positive >200 - Strong Positive	
Anti-SS-B/La IgG	1.0 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive	Positive
Anti-ScI-70 IgG	1.0 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive	
Anti-Centromere Protein B (CENP) IgG	1.0 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive	
Anti-Jo-1 IgG	1.0 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive	
Anti-CCP IgG	1.0 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive	
Note: This assessment is associated with an incr	reased likelihood	of SLE.		

Order ID 739811 Provider Exagen Provider MD		Specimen Collected Received Test Order Created Reported	01/19/2023 01/20/2023 01/20/2023 01/25/2023	Patient Gender - DOB Identifier Received Exagen ID	Sample, Susan S. Female - 01/01/1996 541163
SLE-Associated Analytes	Value	Interpretati	ion Refer	ence Range	
+ ANA IgG	40.00 Un	nits POSITIVE	ELISA	<20 - Negative 20-<60 -	Positive 260 - Strong Positive
+ ANA by HEp-2 Titer:	1:320	POSITIVE	IFA: +	1:80 - Negative 21:80 - Pr	ositive
Nuclear Pattern: Speckled					
Cytoplasmic Pattern: Not Observed	1				
Anti-dsDNA IgG	20.00 IU/	/mL Negative	EUSA	<201 - Negative 201-<30	02 - Equivocal (a302 - Positive
Confirmation by Crithidia luciliae	N/A		IFA: 1	legative	
Anti-Smith IgG	<0.7 U/	mL Negative	ELFA	<7 - Negative 7-10 - Equi	vocal >10 - Positive
+ CB-CAP: EC4d - Erythrocyte-bound C4d	25 Ne	t MFI POSITIVE	FACS	<15 - Negative 15-75 - Pr	ositive >75 - Strong Positive
+ CB-CAP: BC4d - B-lymphocyte-bound C4d	100 Net	t MFI POSITIVE	FACS	<61 - Negative 61-200 - I	Positive >200 - Strong Positive
Other Autoimmune Disease Auto-Antibodies	Volue	Interpretati	ion Refer	ence Range	
Anti-SS-B/La IgG	1.0 U/	mL Negative	ELFA	<7 - Negative 7-10 - Equi	vocal >10 - Positive
Anti-ScI-70 IgG	1.0 U/	mL Negative	ELFA	«7 - Negative 7-10 - Equi	vocal >10 - Positive
Anti-Centromere Protein B (CENP) IgG	1.0 U/	mL Negative	ELFA	<7 - Negative 7-10 - Equi	vocal >10 - Positive
Anti-Jo-1 IgG	1.0 U/	mL Negative	ELFA	<7 - Negative 7-10 - Equi	vocal >10 - Positive
Anti-CCP IgG	1.0 U/	mL Negative	ELFA	<7 - Negative 7-10 - Equi	vocal >10 - Positive
Optional Analytes Ordered	Value	Interpretati	ion Refer	ence Range	

No optional analytes ordered

- AVISE APS
 - Combination of biomarkers to assess a patient's risk for APS and thrombosis
 Order ID 739810 Provider Examp Provider MD
 Specimen Collected 01/19/2023 Received 01/19/2023
 Patient Sample, Susan S.

ider	Exagen	Provider MD	Received	01/20/2023	Constant DOD	Eemole 01/01/1006
			Test Order		Gender - DOB	Female - 01/01/1990
			Created	01/20/2023	Identifier Received	
			Reported	01/25/2023	Exagen ID	541163

AVISE APS Test Report

	Analyte	Value		Interpretation	Reference Range
+	Anti-Cardiolipin IgM	42.1	MPL	POSITIVE	ELFA: <10 - Negative 10-40 - Weak Positive >40 - Positive
	Anti-Cardiolipin IgG	8.0	GPL	Negative	ELFA: <10 - Negative 10-40 - Weak Positive >40 - Positive
	Anti-Cardiolipin IgA	8.0	APL	Negative	ELFA: <14 - Negative 14-20 - Equivocal >20 - Positive
	Anti-β2 Glycoprotein 1 IgM	6.0	U/mL	Negative	ELFA: <7 - Negative 7-10 - Equivocal >10 - Positive
	Anti-β2 Glycoprotein 1 IgG	6.0	U/mL	Negative	ELFA: <7 - Negative 7-10 - Equivocal >10 - Positive
+	Anti-β2 Glycoprotein 1 IgA	11.0	U/mL	POSITIVE	ELFA: <7 - Negative 7-10 - Equivocal >10 - Positive
+	Anti-Phosphatidylserine/Prothrombin IgM	45.50	Units	POSITIVE	ELISA: <30 - Negative >30 - Positive
	Anti-Phosphatidylserine/Prothrombin IgG	20.50	Units	Negative	ELISA: ≤30 - Negative >30 - Positive

AVISE Vasculitis

Complete panel of ANCA-associated biomarkers

Order ID Provider	204187 Example Provider MD	Specimen Collected Received	08/20/2020 08/20/2020	Patient	Sample, Robert S
		Test Order Created Reported	08/20/2020 08/24/2020	Identifier Received Exagen ID	302583

AVISE VASCULITIS AAV

AVISE VASCULITIS RESULT:	p-ANCA Positive >	1:1280	Anti-MPO Positive		
ANCA by IFA Titer:	>1:1280	Positive	IFA:<1:20-Negative I ≥20 Positive		

Pattern: Perinuclear (p-ANCA)

Positive ANCAs are useful in the diagnosis of small vessel vasculitis - granulomatosis with polyangiitis, microscopic polyangiitis and eosinophilic granulomatosis with polyangiitis. However, they can also be seen in connective tissue disease, IBD, some infections, malignancy, and as a reaction to drugs. Therefore, they should be interpreted with care in light of the clinical findings and workup.

Vasculitis-Associated Analytes:	Value	Interpretation	Reference Range
Anti-MPO IgG	>740 CU	Positive	CIA: <20-Negative I ≥20-Positive
Anti-PR3 IgG	<2 CU	Negative	CIA: <20-Negative I ≥20-Positive
Anti-GBM IgG	3 CU	Negative	CIA: <20-Negative I ≥20-Positive

AVISE SLE prognostic

10-marker panel to assess risk for thrombosis, CV events. lupus nephritis and neuropsychiatric lupus.

Order ID	739810	Specimen Collected	01/15/2022	Patient	Sample, Susan S
Provider	Exagen Provider MD	Test Order Created	01/16/2022	Gender - DOB Identifier Received	Female - 01/01/1996
		Reported	01/20/2022	Exagen ID	541163

AVISE SLE Prognostic Test Report

_	Analyte	Value	Interpretation	Reference Range
+	Anti-C1q IgG	90.0 Units	POSITIVE	<20 - Negative ≥20 - Positive
	Anti-Ribosomal P IgG	8.00 Units	Negative	<20 - Negative ≥20 - Positive
÷	Anti-Phosphatidylserine/Prothrombin IgM *	45.00 Units	POSITIVE	≤30 – Negative >30 – Positive
÷	Anti-Phosphatidylserine/Prothrombin IgG *	34.00 Units	POSITIVE	≤30 – Negative >30 – Positive
	Anti-Cardiolipin IgM *	2.0 U/mL	Negative	<10 - Negative 10-40 - Weak Positive >40 - Positive
	Anti-Cardiolipin IgG *	4.0 U/mL	Negative	<10 - Negative 10-40 - Weak Positive >40 - Positive
	Anti-Cardiolipin IgA *	8.0 U/mL	Negative	<14 - Negative 14-20 - Equivocal >20 - Positive
	Anti-β2 Glycoprotein 1 IgM *	3.0 U/mL	Negative	<7 – Negative 7-10 – Equivocal >10 – Positive
	Anti-β2 Glycoprotein 1 IgG *	2.0 U/mL	Negative	<7 – Negative 7-10 – Equivocal >10 – Positive
	Anti-β2 Glycoprotein 1 IgA *	5.0 U/mL	Negative	<7 – Negative 7-10 – Equivocal >10 – Positive

- AVISE PC4d
 - Useful in aiding risk of thrombosis in SLE patients

- AVISE AntiCarP
 - Useful detection of RA patients before onset of symptoms
 - Can be used with significant family history of RA
 - Useful in patients who do not test + for RF/CCP

- AVISE SLE monitor
 - Useful for monitoring disease progression
 - Assess treatment efficacy
 - Help prevent organ involvement and joint damage

• AVISE MTX

- Measures active MTX metabolites
- Helps assess adherence to medication
- Helps assess appropriate dosing levels



• AVISE HCQ

- Measurement of HCQ levels
- Helps determine drug adherence
- Helps assess appropriate dosing levels
 - HCQ induced toxic retinopathy



PRISM RA CASE STUDY

- 39 y.o female diagnosed with SPRA in 2016. Failed MTX, HCQ, Adalimumab and Certolizumab pegol
- Do we switch to another TNFi or different mechanism of action?
- Decided to obtain PRISM RA

PRISM RA CASE STUDY

YOUR PATIENT'S PrismRA® RESULTS



RESULTS INTERPRETATION

A patient with a very high signal of non-response has a \geq 95% likelihood of not responding adequately to anti-TNF therapies. Thus, your patient has a \leq 5% likelihood of responding to anti-TNF therapies.



PRISM RA CASE STUDY

- RESULTS: High Non-Responder
- Patient was switched to biologic with different mechanism of action with great benefits

CASE STUDY

- 49 y.o female diagnosed with SNRA(4/2020) with synovitis, elevated APRs and fhx of RA.
- Tried MTX, LEF and HCQ. She has sulfa allergy.
- VECTRA DA 38 ; moderate disease activity(8/2/2021)
- PRISM RA 12.9 ; high non-response to TNFi (1/4/2022)
- Started on Adalimumab 40mg/0.4mL SQ biweekly 4/20/2022
- She reports joint pain and considering switch to another med
- VECTRA DA 19 ; low disease activity (6/19/2023) and normal APRs
- She continues with current therapy for RA, discussed OA is likely cause of joint pain

CASE STUDY

YOUR PATIENT'S PrismRA® RESULTS







CASE STUDY

Vectra Molecular Result



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 chart, 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.



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.



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

AVISE CASE STUDY

- 72 y.o female with history of stroke in 2018, fibromyalgia and OA. She presents with symptoms of joint pain, fatigue, prolonged AM stiffness.
- Labs showed +ANA no titer and dsDNA 11, CRP 7 (<4.9).
- AVISE test ordered
 - Results showed +ANA and +anti-TPO 433.
 - Lupus index: low likelihood of SLE

AVISE CASE STUDY

- Patient was assured that lupus diagnosis was less likely
- Discussed that her +ANA was likely due to Hashimoto's disease
- Advised regular evaluation of TSH levels through PCP

CONCLUDING REMARKS

- Specialty labs can be helpful in combination with clinical judgement
- It is important to consider cost to patients
- Patient cost may vary depending on insurance
- Most of these specialty tests have available assistance to patients





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