



Comprehensive Connective
Tissue Disease Assessment

Order ID
739813
Provider
Exagen
Provider MD

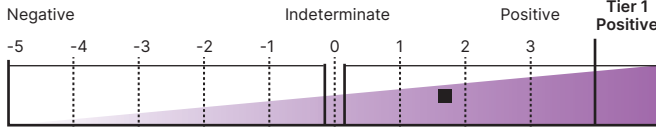
Specimen
Collected
07/21/2025
Received
07/22/2025

Test Order
Created
07/22/2025
Reported
07/24/2025

Patient
Gender
Female
MRN
AB123450

Sample,
Susan S.
DOB
01/01/1996

AVISE Lupus Result: Positive - Index: 1.8



INDEX INTERPRETATION: A Lupus Index score of 1.8 is associated with an increased likelihood of SLE. Positive results are driven by ANA (ELISA) positivity as well as classical complement activation, as indicated by the level of EC4d and/or BC4d. Results should be interpreted by a provider in conjunction with all available clinical findings.

Lupus Index Score Biomarkers	Value	Interpretation	Reference Range
Anti-dsDNA IgG (ELISA)	18.04 IU/mL	Negative	<201 - Negative 201 - <302 - Equivocal ≥302 - Positive
Confirmation by Crithidia luciliae (IFA)		N/A	
Anti-Smith IgG (ELFA)	<0.7 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive
CB-CAP: EC4d - Erythrocyte-bound C4d (FC)	11 Net MFI	Negative	<15 - Negative 15-75 - Positive >75 - Strong Positive
+ CB-CAP: BC4d - B-lymphocyte-bound C4d (FC)	192 Net MFI	POSITIVE	<61 - Negative 61-200 - Positive >200 - Strong Positive
+ ANA IgG (ELISA)	22.93 Units	POSITIVE	<20 - Negative 20-<60 - Positive ≥60 - Strong Positive
Anti-SSB/La IgG (ELFA)	0.8 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive
Anti-Scl-70 IgG (ELFA)	<0.6 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive
Anti-Centromere Protein B (CENP) IgG (ELFA)	0.7 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive
Anti-Jo-1 IgG (ELFA)	<0.3 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive
Anti-CCP IgG (ELFA)	1.2 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive

T Cell Biomarkers	Value	Interpretation	Reference Range
+ CB-CAP: TC4d (FC)	235 Net MFI	POSITIVE	<200 - Negative ≥200 - Positive
+ T Cell autoantibody: TlgG (FC)	198 Net MFI	POSITIVE	<170 - Negative ≥170 - Positive
+ T Cell autoantibody: TlgM (FC)	277 Net MFI	POSITIVE	<230 - Negative ≥230 - Positive

ANA (Immunofluorescence)	Value	Interpretation	Reference Range
+ ANA by HEp-2 (IFA)	Titer: 1:320	POSITIVE	<1:80 - Negative ≥1:80 - Positive
	Nuclear Pattern: Speckled		
	Cytoplasmic Pattern: Not Observed		

Comments:

- BC4d and TC4d are markers of classical complement activation with greater than 95% specificity against healthy individuals. In the positive range, BC4d is present in 53% of SLE patients and in low percentages of patients with Sjögren's disease, myositis, systemic sclerosis, RA, APS, and vasculitis. When positive, TC4d is observed in 58% of SLE patients. It is also present in 28% of Sjögren's disease, 13% of spondyloarthropathies, 13% of PsA, and 5% of RA patients. [Kyttaris et al. 2025]. **A positive result alone does not establish a diagnosis. Results must be interpreted by a healthcare provider in the context of all available clinical findings.**
- TlgG and TlgM autoantibodies are 95% specific against healthy individuals. When positive, TlgG is observed in 31% of SLE patients. It is also present in 10% of Sjögren's disease and 10% of RA patients. When positive, TlgM is observed in 30% of SLE patients. It is also present in 14% of Sjögren's disease, 4% of PsA, 7% of fibromyalgia, and 6% of RA patients. Additionally, TlgM is elevated in up to 21% of patients exposed to COVID-19, though levels typically do not persist beyond six months in mild (non-hospitalized) cases. [Kyttaris et al. 2025 and Perez-Diez et al. 2024]. **A positive result alone does not establish a diagnosis. Results must be interpreted by a healthcare provider in the context of all available clinical findings.**

In a study of 794 subjects comprising 304 SLE patients, 285 patients with other rheumatic diseases and 205 normal healthy controls, positivity for Tier 1 markers (anti-dsDNA by ELISA, confirmed with Crithidia by IFA, anti-Sm by Enzyme Linked Fluorescent Immunoassay (ELFA) or elevated EC4d and BC4d by Flow Cytometry yielded a sensitivity of 46% and a specificity of 95% for SLE vs. other autoimmune rheumatic diseases (ORD). Among the 164 SLE subjects negative in Tier 1, a positive index score composite of ANA (by ELISA), EC4d/BC4d and positivity for anti-CCP, SS-B/La, CENP, Jo-1 or Scl-70 (by ELFA) resulted in sensitivity of 62% for SLE and specificity of 89% for SLE vs. ORD. The overall two-tier algorithm result yielded 80% sensitivity for SLE and 86% specificity vs. ORD diseases (98% specificity for SLE vs. healthy individuals).



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Rheumatoid Arthritis Biomarkers	Value	Interpretation	Reference Range
Anti-CCP IgG (ELFA)	1.2 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive
Anti-PAD4 IgA (ELISA)	3.5 U/mL	Negative	<25 - Negative ≥25 - Positive
Anti-PAD4 IgG (ELISA)	4.6 U/mL	Negative	<13 - Negative ≥13 - Positive
Anti-RA33 IgA (ELFA)	0.8 U/mL	Negative	<5 - Negative ≥5 - Positive
Anti-RA33 IgG (ELFA)	1.8 U/mL	Negative	<8 - Negative ≥8 - Positive
Anti-RA33 IgM (ELFA)	2.1 U/mL	Negative	<42 - Negative ≥42 - Positive
Rheumatoid Factor IgA (ELFA)	0.9 IU/mL	Negative	<14 - Negative 14-20 - Equivocal >20 - Positive
Rheumatoid Factor IgM (ELFA)	<1.1 IU/mL	Negative	<3.5 - Negative 3.5-5 - Equivocal >5 - Positive

Sjögren's Disease Biomarkers	Value	Interpretation	Reference Range
Anti-SSA/Ro52 IgG (ELFA)	0.5 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive
Anti-SSA/Ro60 IgG (ELFA)	<0.4 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive
Anti-SSB/La IgG (ELFA)	1.7 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive

Mixed Connective Tissue Disease Biomarkers	Value	Interpretation	Reference Range
+ Anti-U1RNP IgG (ELFA)	22.8 U/mL	POSITIVE	<5 - Negative 5-10 - Equivocal >10 - Positive
Anti-RNP70 IgG (ELFA)	0.3 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive

Antiphospholipid Syndrome Biomarkers	Value	Interpretation	Reference Range
+ Anti-Cardiolipin IgG (ELFA)	82.6 GPL	POSITIVE	<10 - Negative 10-40 - Weak Positive >40 - Positive
Anti-Cardiolipin IgM (ELFA)	<1.7 MPL	Negative	<10 - Negative 10-40 - Weak Positive >40 - Positive
+ Anti-β2 Glycoprotein 1 IgG (ELFA)	19.3 U/mL	POSITIVE	<7 - Negative 7-10 - Equivocal >10 - Positive
Anti-β2 Glycoprotein 1 IgM (ELFA)	<2.4 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive

Systemic Sclerosis Biomarkers	Value	Interpretation	Reference Range
Anti-Scl-70 IgG (ELFA)	<0.6 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive
Anti-RNA Pol III IgG (ELFA)	<0.7 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive
Anti-Centromere Protein B (CENP) IgG (ELFA)	0.7 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive

RA33 autoantibodies are highly specific (>95%) for RA against healthy individuals. In a cohort of 161 diagnosed RA patients (60 seropositive and 101 seronegative based anti-CCP and RF), IgG, IgM, and IgA RA33 autoantibodies were collectively present in 32% of seropositive RA patients and 16% of seronegative RA patients. PAD4 autoantibodies are highly specific (>95%) for RA against healthy individuals. In a cohort of 379 RA patients (220 seropositive and 159 seronegative) IgA and IgG antibodies were collectively observed in 50% of seropositive RA and 14% of seronegative RA.



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Myositis Biomarkers	Value	Interpretation	Reference Range
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Anti-Jo-1 IgG (ELFA)	<0.3 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive
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Thyroid Biomarkers	Value	Interpretation	Reference Range
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Anti-Thyroglobulin IgG (ELFA)	<12 IU/mL	Negative	<40 - Negative 40-60 - Equivocal >60 - Positive
Anti-Thyroid Peroxidase IgG (ELFA)	<4 IU/mL	Negative	<25 - Negative 25-35 - Equivocal >35 - Positive

FC: Flow Cytometry
IFA: Immunofluorescence Assay
ELISA: Enzyme-Linked Immunosorbent Assay
ELFA: Enzyme-Linked Fluorescent Assay

Case Remarks:

Signed by: Prashanti Reddy, MD

Prashanti Reddy MD

Date: 10/25/2024

References

1. Kyttaris V, et al. Front Immunol. 2025; 16:1518208. doi: 10.3389/fimmu. 2025.1518208.
2. Concoff A, Warsi T, Taghavi S, et al. Arthritis Rheumatol. 2024; 76 (suppl 9). Abstract #2232.
3. Concoff A, Warsi T, Taghavi S, et al. Arthritis Rheumatol. 2024; 76 (suppl 9). Abstract #2233.
4. Ramsey-Goldman R, et al. ACR Open Rheumatol. 2021 Feb;3(2):116-123. doi: 10.1002/acr2.11219.
5. Arriens C, et al. Lupus Sci Med. 2020 Apr; 7(1). doi: 10.1136/lupus-2019-000377.
6. Ramsey-Goldman R, et al. Arthritis Rheumatol. 2020 Jan;72(1):78-88. doi: 10.1002/art.41093.
7. Hui-Yuen J, et al. Lupus. 2018 Dec;27(14):2262-2268. doi: 10.1177/0961203318809181.
8. Sieghart D, Platzer A, Studenic P, et al. Front Immunol. 2018;9:876. doi:10.3389/fimmu.2018.00876.
9. Wallace D, et al. Lupus Sci Med. 2016 Feb;3(1):e000127. doi: 10.1136/lupus-2015-000127.
10. Putterman C, et al. Lupus Sci Med. 2014 Oct;1(1):e000056. doi: 10.1136/lupus-2014-000056.



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Prashanti Reddy, MD

Provider Relations: 888.452.1522
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What's NEW in this AVISE CTD Report



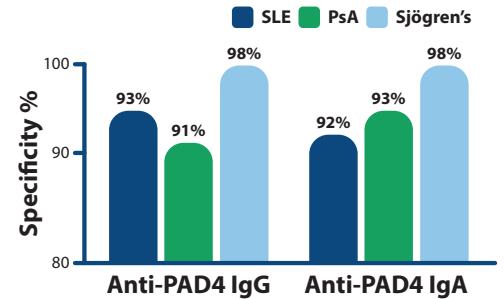
NEW Anti-PAD4 Biomarkers for Rheumatoid Arthritis

Peptidylarginine deiminases (PADs) play a crucial role in the pathogenesis of RA by generating citrullinated proteins, which are the hallmark autoantigens of the disease. Anti-PAD4 autoantibodies specifically target one of these enzymes involved in this pathogenic process. **Unlike traditional markers, anti-PAD4 can be present in patients who are seronegative by RF and anti-CCP**, helping clinicians identify RA earlier in the disease course.

Anti-PAD4 autoantibodies are observed in 14% of seronegative RA patients and 50% of seropositive RA patients.



Anti-PAD4 autoantibodies are also **highly specific against healthy individuals (>95%) and other autoimmune rheumatic diseases** including systemic lupus erythematosus (SLE), psoriatic arthritis (PsA), and Sjögren's disease.



Anti-PAD4 autoantibodies can develop pre-clinically and **are associated with heightened risk for severe joint damage**. The use of seronegative RA biomarkers with high specificity provides an opportunity to substantiate clinical suspicion of RA, aiding earlier diagnosis and treatment.

Other Recently Added Biomarkers for RA and SLE

Unique Value of T Cell Biomarkers for Systemic Lupus Erythematosus

T Cell-bound C4d (TC4d) and antibodies targeting T Cells (TlgM and TlgG) demonstrate superior diagnostic performance compared to conventional SLE biomarkers such as anti-dsDNA, anti-Smith, and complement C3/C4. **TC4d is elevated in approximately 60% of SLE patients** and is positive in about 50% of SLE patients who test negative for all conventional SLE biomarkers. TlgM and TlgG autoantibodies are also primarily sensitive for SLE, with **approximately 30% of SLE patients showing positive TlgM and TlgG**. TC4d, TlgM, and TlgG are 95% specific for SLE against healthy individuals and are rarely elevated in patients with other autoimmune diseases.

Unique Clinical Value of RA33 Biomarkers for Rheumatoid Arthritis

Seronegative RA makes up approximately 30% of diagnosed RA and up to 50% of early RA cases. Novel RA biomarkers such as anti-RA33, PAD4 and anti-CarP can provide evidence of systemic autoimmunity when conventional biomarkers are negative. Autoantibodies to the RA33 antigen are highly specific (>95%) for RA against healthy individuals. Collectively, IgG, IgM, and IgA antibodies to RA33 are found in 32% of seropositive RA and 16% of seronegative RA patients.



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