

Exagen[®]

Patient Focused. Discovery Driven.



Delivering Improved Care in Rheumatology

The impact of Advanced Laboratory Testing:
AVISE CTD

Overview

- ✘ Deficiencies of Standard Diagnostic Laboratory Tests (SDLTs) for differential diagnosis of SLE
- ✘ Value of an early and accurate SLE diagnosis
- ✘ Novel advances in differential diagnosis of SLE
 - Cell-bound Complement Activation Products (CB-CAPs)
 - AVISE Lupus/CTD – innovative two-tier multianalyte assay panel (MAP)

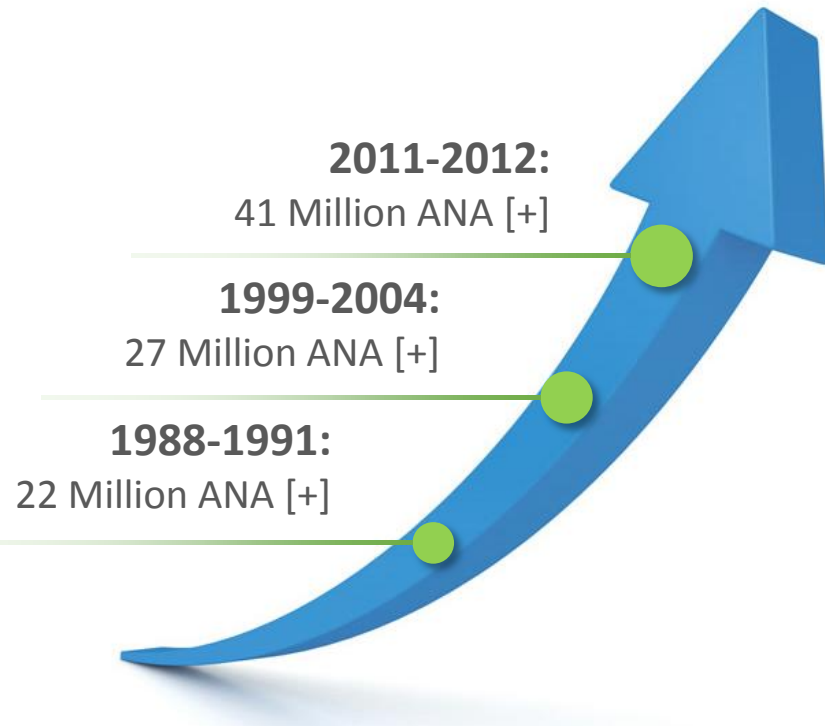
Exagen: A Lab Committed to Solutions for Autoimmune Diseases

Exagen Inc. is focused on accuracy

- ✘ Exclusive and specialized biomarkers including; EC4d, BC4d, PC4d, anti-C1q, anti-CarP and anti-PS/PT
- ✘ A powerful algorithm validated by over a decade of research
- ✘ Medical, clinical & technical consultation available
- ✘ Quality results you can trust from a central laboratory

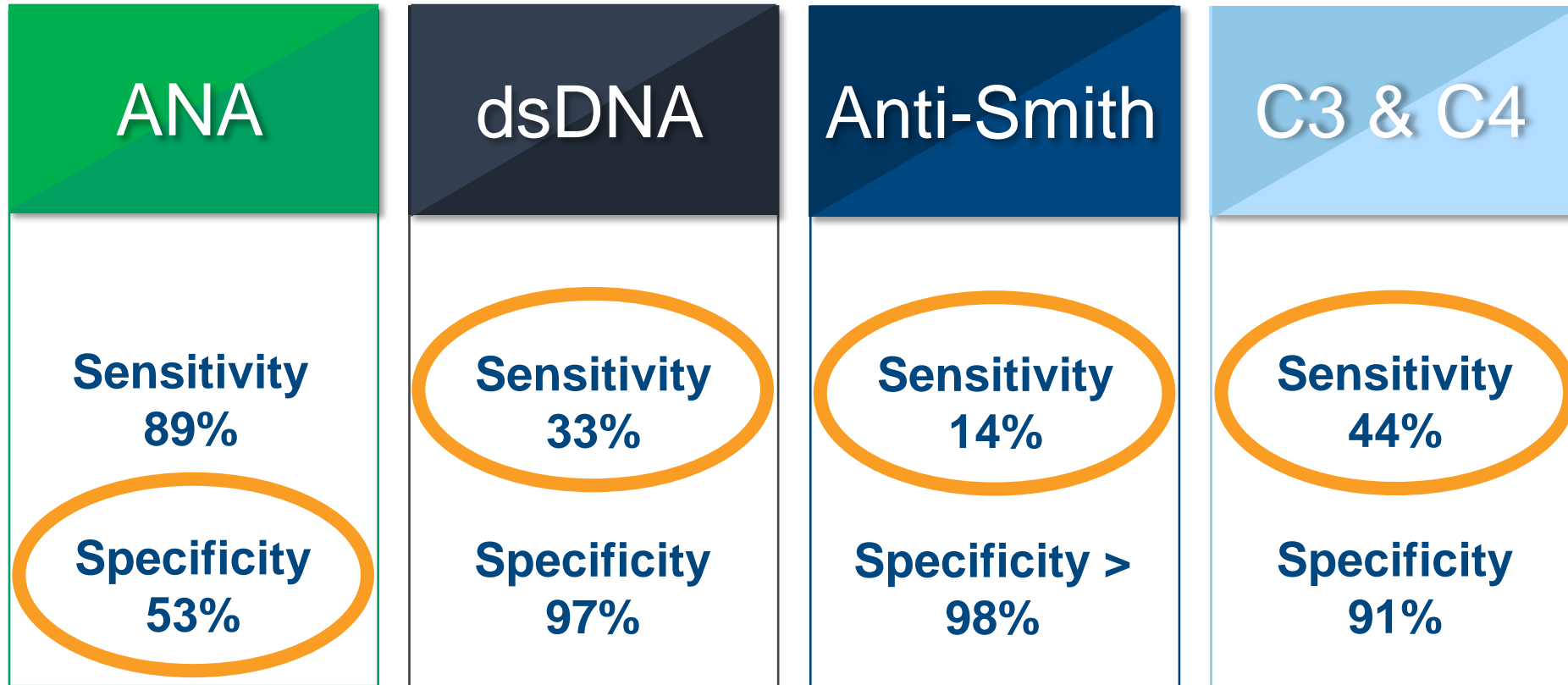


The Frequency of Autoantibodies in the U.S. Population is Rising



- ✕ Recent study findings suggests ANA prevalence reached 41 million in 2011-2012 up significantly from prior decades
- ✕ ANA prevalence is up significantly among
 - Both sexes (especially men)
 - Older adults (≥ 50 yrs.)
 - Non-Hispanic whites

Deficiencies of Standard Diagnostic Laboratory Tests (SDLTs)



None of these serological markers provides both sensitivity and specificity for the diagnosis of CTD or SLE

Value of an Early SLE Diagnosis

Early diagnosis of SLE (within 6 months of onset) is associated with:



Improved outcomes¹

- ✓ Fewer flares
- ✓ Less severe flares
- ✓ Lower rates of hospitalization
- ✓ Reduced SDI (Systemic Lupus Damage Index)



Reduced costs¹

- ✓ Reduced all-cause & SLE-related in-patient costs
- ✓ 53% reduction in total care costs over 10 years
- ✓ Diminished resource utilization

SLE - An Underestimated Cause of Death

CDC considers SLE as a “contributing factor”, not a cause of death. which leads to under-reporting. When SLE is considered the primary cause of death, statistics reveal:

#1

SLE is the number 1 single cause of death among females 15-24 years with chronic inflammatory diseases*

5th

Fifth leading cause of death for Black and Hispanic females 15-24 years*

Top
15

One of the top 15 leading causes of death among females between 10-44 years*

*When unintentional injury, homicide, and suicide are excluded from this analysis.

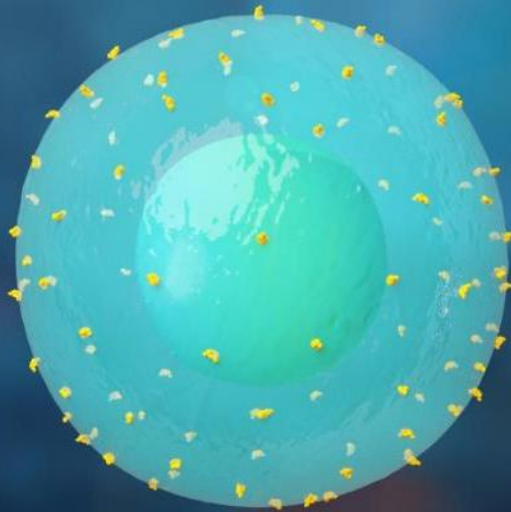
Cell-Bound Complement Activation Products (CB-CAPs) Video

CB-CAPs

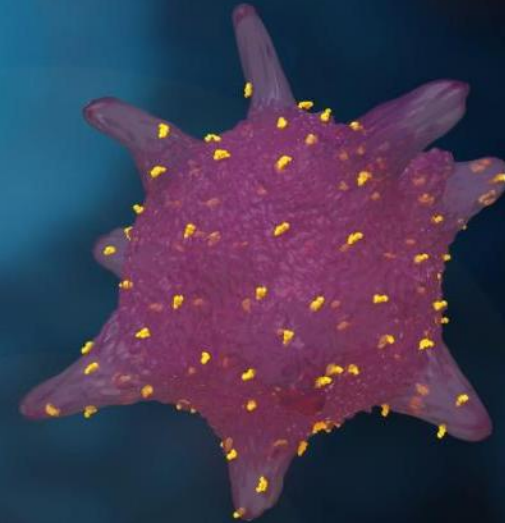
Cell-bound Complement Activation Products



EC4d



BC4d



PC4d

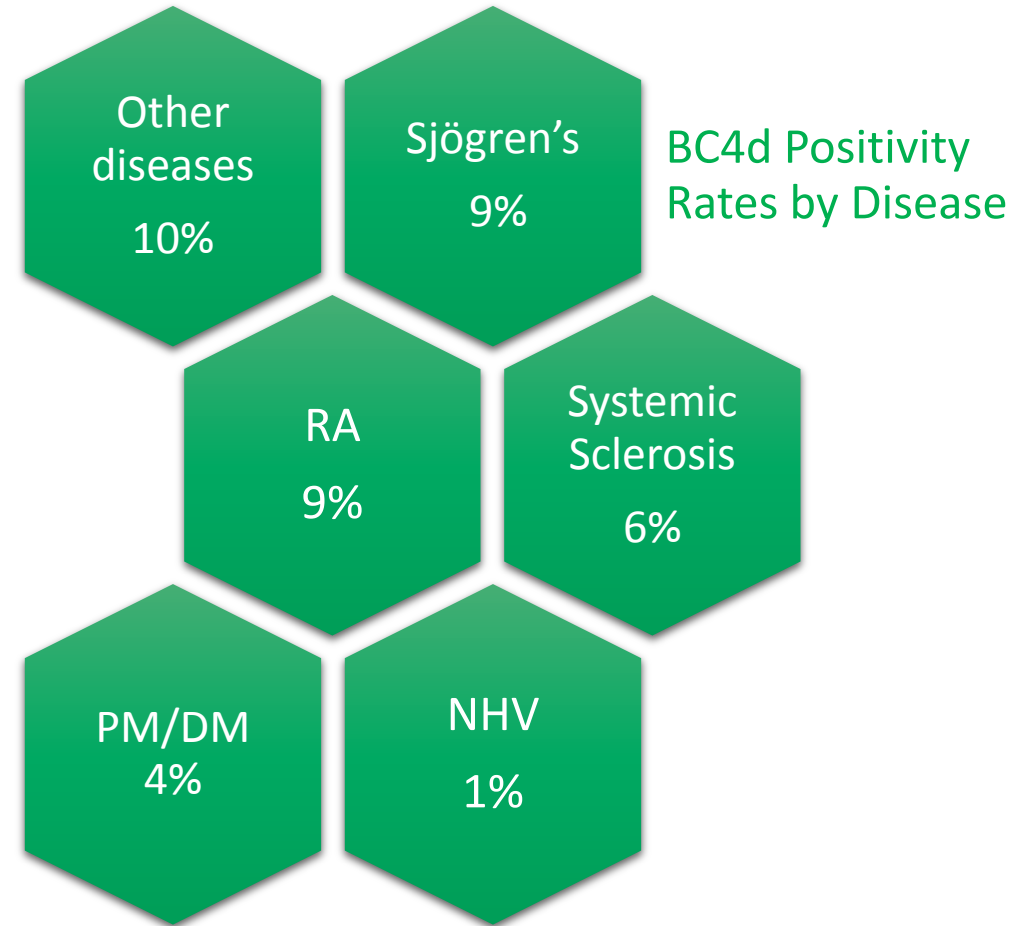
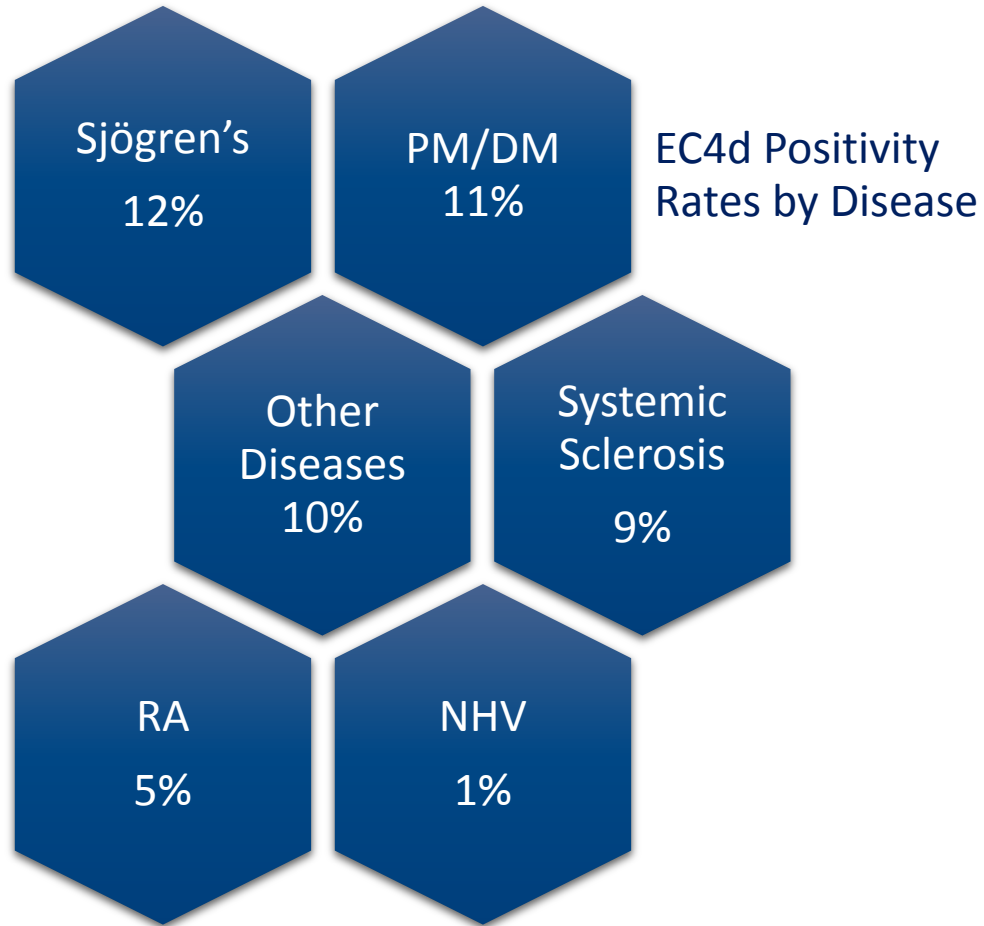


Elevated CB-CAPs are Primarily Associated with SLE

CB-CAPs (EC4d & BC4d) are sensitive for SLE at low positive threshold levels

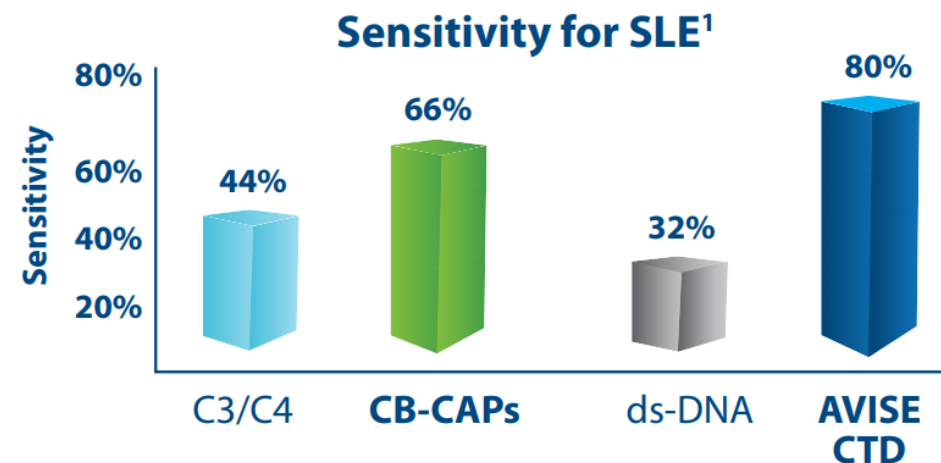
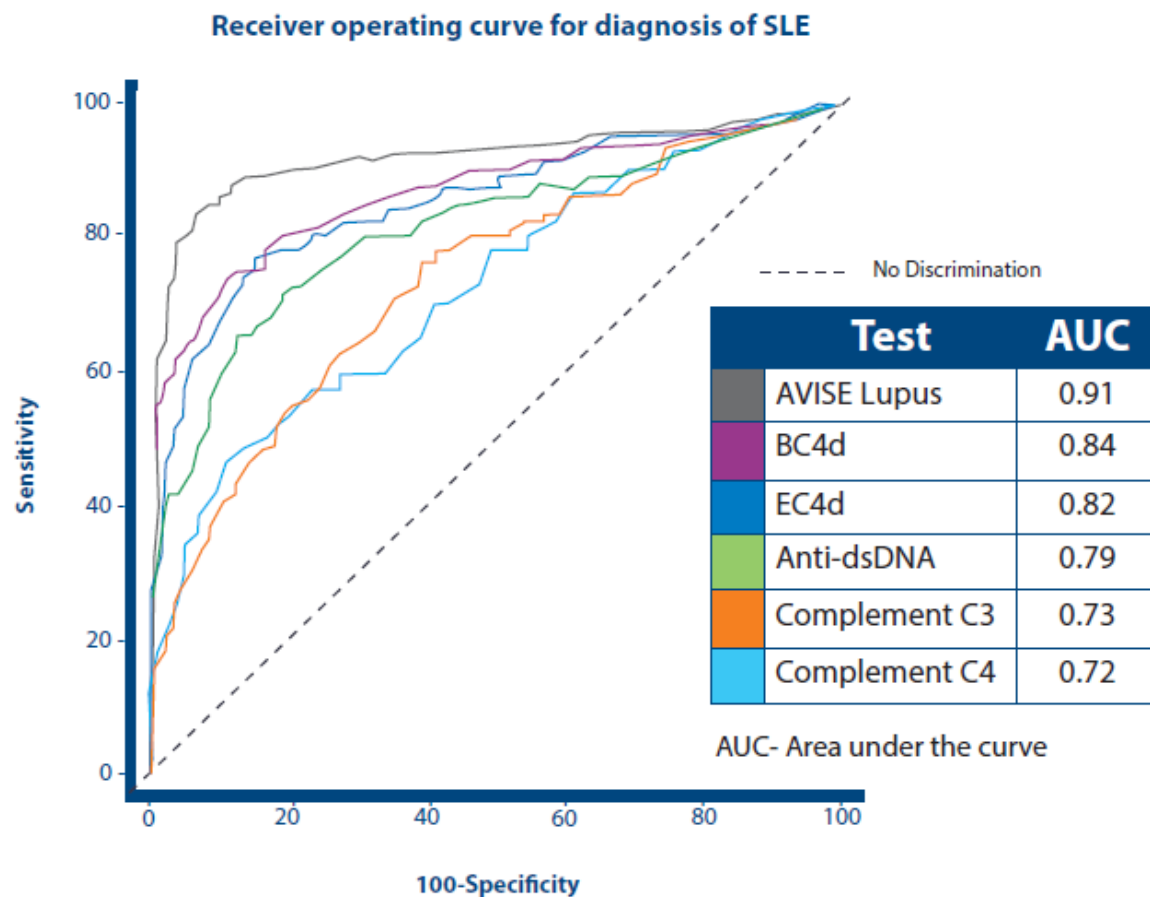
Low Positive	SLE
EC4d > 14 Units	46%
BC4d > 60 Units	53%
EC4d > 14 Units <u>and/or</u> BC4d > 60 Units	66%

Elevated CB-CAPs Are Rarely Found in Other CTDs



*Other disease patients include Fibromyalgia, Vasculitis, Granulomatosis with Polyangiitis and Antiphospholipid Syndrome, NHV = Normal Healthy Volunteers

AVISE Lupus is an Integrated Result with High Diagnostic Yield



- The ideal diagnostic marker will have a curve nearing the upper left corner
- AVISE Lupus is a 10 marker sub-component of AVISE CTD including: ANA, anti-dsDNA, anti-Sm, EC4d, BC4d, plus 5 ENA autoantibodies
- AVISE Lupus and CB-CAPs outperform traditional biomarkers

What is AVISE CTD?



AVISE CTD is the only test incorporating CB-CAPs technology making it ideal for ANA positive patients or anyone suspected of having an autoimmune rheumatic disease

Markers Included in AVISE CTD

SLE Associated Markers

EC4d*, BC4d*, AVISE Lupus Index*,
ANA by ELISA & HEp-2, Anti-dsDNA Confirmation by Crithidia, Anti-Smith

ENA Panel to help distinguish specific CTD

Anti-Smith	Anti-U1RNP
Anti-Ro52	Anti-RNP70
Anti-Ro60	Anti-Scl-70
Anti-SS-B/LA	Anti-CENP
Anti-Jo-1	Anti-RNA Pol III

Anti-Histone and anti-CarP available by request

RA Panel to help rule-in Rheumatoid arthritis

RF IgM
RF IgA
Anti-CCP

APS Panel to help assess risk for thrombosis

Anti-Cardiolipin IgM
Anti-Cardiolipin IgG
Anti-B2-GP1 IgM
Anti-B2-GP1 IgG

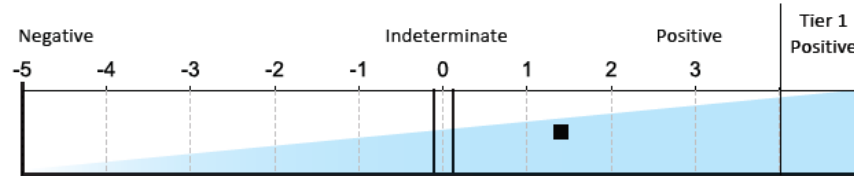
Thyroid Panel to help diagnose autoimmune disorders

Anti-Thyroglobulin
Anti-Thyroid Peroxidase

* EXCLUSIVE TO EXAGEN

AVISE CTD Test Results

AVISE Lupus Result: **Positive - Index: 1.4**



Tier 1 Analytes	Value	Interpretation	Reference Range	Tier 1 Assessment
Anti-dsDNA IgG	20 IU/mL	Negative	<302 - Negative ≥302 - Positive	Negative
Confirmation by Crithidia luciliae				
Anti-Smith IgG	1 U/mL	Negative	<5 - Negative 5-10 - Equivocal >10 - Positive	
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 Units	POSITIVE	<20 - Negative 20-59 - Positive ≥60 - Strong Positive	Positive
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 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive	
Anti-Scl-70 IgG	<1 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive	
Anti-CENP IgG	1 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive	
Anti-Jo-1 IgG	<1 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive	
Anti-CCP IgG	2 U/mL	Negative	<7 - Negative 7-10 - Equivocal >10 - Positive	
Note:				
This assessment is associated with an increased likelihood of SLE.				

AVISE Lupus Result is illustrated on a gradient of increasing likelihood for the presence of SLE*

AVISE Result Report

Page 2 contains values for all analytes with positives flagged for easy review

SLE Associated Analytes	Value	Interpretation
ANA IgG	40 Units	POSITIVE
ANA by HEp-2	<i>Titer:</i> 1:320	POSITIVE
<i>Nuclear Pattern: Speckled</i>		
<i>Cytoplasmic Pattern: Not Observed</i>		
Anti-dsDNA IgG	20 IU/mL	Negative
Anti-dsDNA by Crithidia (confirmatory)	N/A	
Anti-Smith IgG	1 U/mL	Negative
CB-CAP: EC4d - Erythrocyte-bound C4d	25 Net MFI	POSITIVE
CB-CAP: BC4d - B-lymphocyte-bound C4d	100 Net MFI	POSITIVE
Other Autoimmune Disease Auto-Antibodies	Value	Interpretation
Anti-U1RNP IgG	1 U/mL	Negative
Anti-RNP70 IgG	5 U/mL	Negative
Anti-Ro52 IgG	8 CU	Negative
Anti-Ro60 IgG	5 CU	Negative
Anti-SS-B/La IgG	1 U/mL	Negative
Anti-Scl-70 IgG	<1 U/mL	Negative
Anti-RNA Pol III IgG	15 Units	Negative
Anti-Centromere Protein B (CENP) IgG	1 U/mL	Negative
Anti-Jo-1 IgG	<1 U/mL	Negative

RA Auto-Antibodies	Value	Interpretation
Rheumatoid Factor IgM	2.0 U/mL	Negative
Rheumatoid Factor IgA	1 U/mL	Negative
Anti-CCP IgG	2 U/mL	Negative
APS Auto-Antibodies	Value	Interpretation
Anti-Cardiolipin IgM	2 CU	Negative
Anti-Cardiolipin IgG	<6 CU	Negative
Anti-β2 Glycoprotein 1 IgM	1 CU	Negative
Anti-β2 Glycoprotein 1 IgG	<6 CU	Negative
Thyroid Auto-Antibodies	Value	Interpretation
Anti-Thyroglobulin IgG	<12 IU/mL	Negative
Anti-Thyroid Peroxidase IgG	<4 IU/mL	Negative

Clinical Applications

Many clinical scenarios can benefit from the AVISE CTD test.

Most common points of utility include:

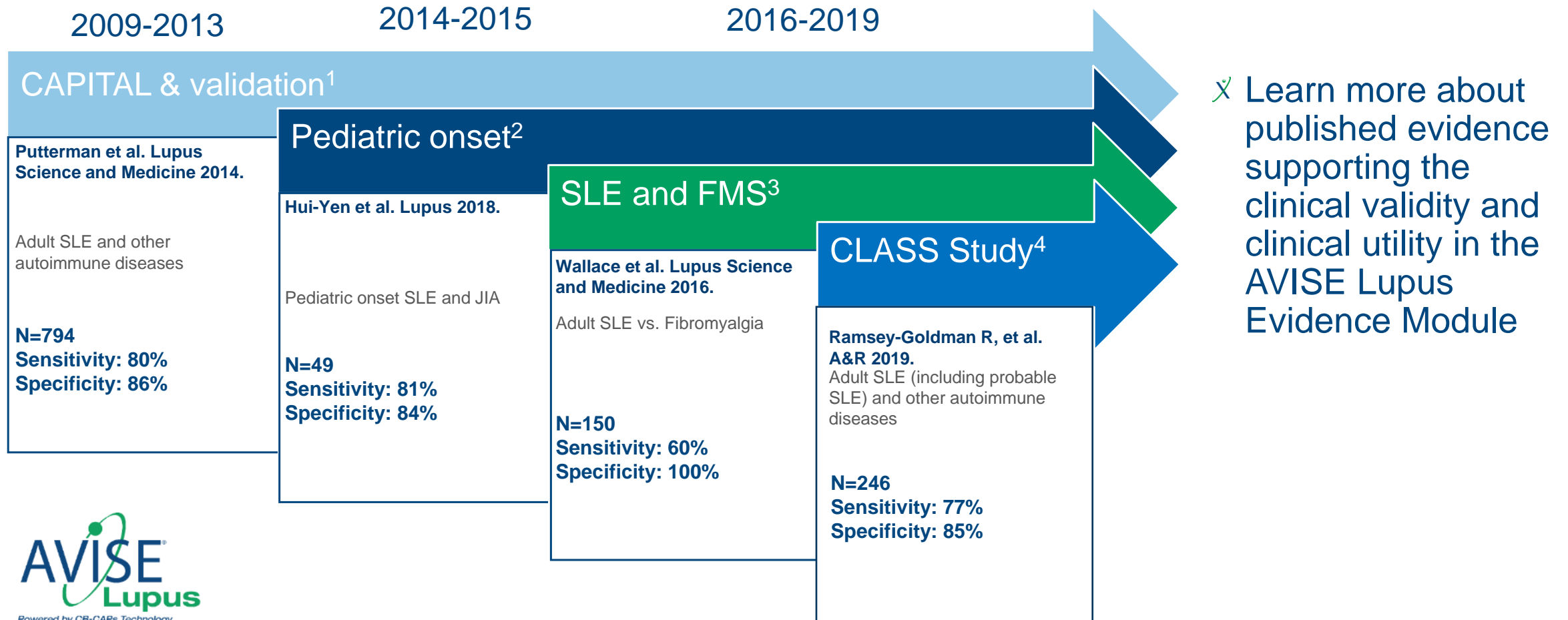
ANA+ Referrals

Overlapping
Symptoms/fibro

New Patient
Triage

Observation of
undifferentiated
CTD

AVISE Lupus: A Test Backed by Extensive Validation



AVISE Lupus Clinical Evidence Overview

ANALYTICAL VALIDITY

1. Dervieux et al., *J. Immunol. Methods*, 2016

CLINICAL VALIDITY

1. Putterman et al., *Lupus Science & Medicine*, 2014 (n=304 SLE, 490 controls), Sens.: 80%; Spec: 86%
2. Ramsey-Goldman et al., *Arthritis & Rheumatology*, 2019 (n=53 SLE, 92 pSLE, 101 other diseases), Sens.: 77%; Spec: 85%

CLINICAL UTILITY

1. Mossell et al., *Open Rheumatology J.*, 2016 (n=23 SLE, 23 controls)
2. Wallace et al., *Lupus Science & Medicine*, 2019 (n=145, 72 randomized to AVISE Lupus, 73 to SDLT arm)
3. Liang et al., *Lupus Science & Medicine*, 2020 (n=138) 2-year chart review. AVISE exhibited PPV=65% & NPV=90%

Questions about AVISE CTD?
