Real-world Utilization of the Octave® MSDA Test in Clinical Practice Across the US

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Disclosures

Dr. Okuda received personal compensation for consulting and advisory services from Biogen, Cortechs.ai, EMD Serono, Genentech, Genzyme/Sanofi, Moderna, Octave Bioscience, Pfizer, and Zenas BioPharma, and research support from Alexion, EMD Serono/Merck, and Novartis.

Dr. Okuda has issued national and international patents along with pending patents related to other developed technologies.

Dr. Okuda serves as a Senior Medical Advisor to Octave Bioscience, Medical Director to Cortechs.ai, and Medical Advisor to the MS Foundation.

Dr. Okuda received royalties for intellectual property licensed by The Board of Regents of The University of Texas System.

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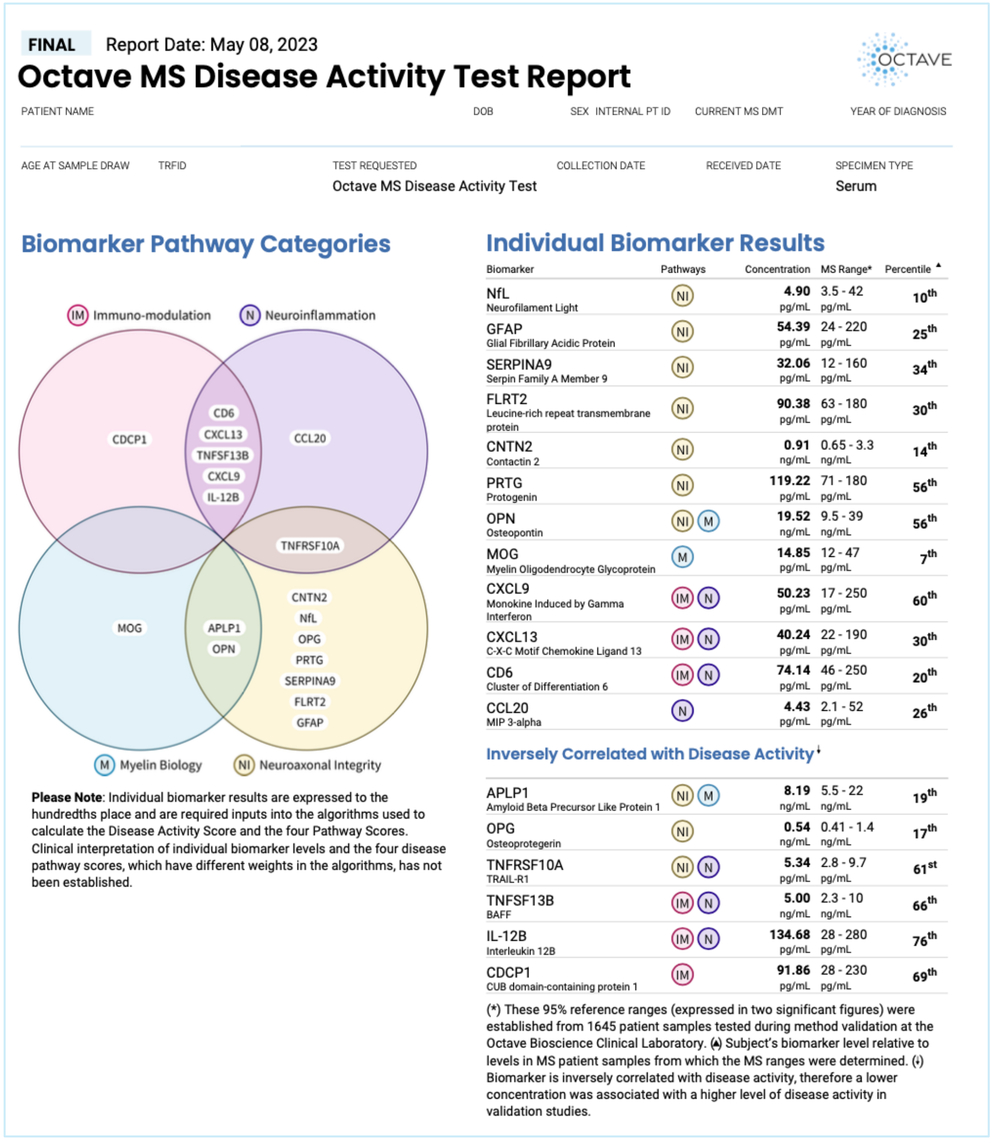
The Octave® MSDA test



FINAL Report Date: May 08, 2023

Octave MS Disease Activity Test Report

OCTAVE

PATIENT NAME	DOB	SEX	INTERNAL PT ID	CURRENT MS DMT	YEAR OF DIAGNOSIS

AGE AT SAMPLE DRAW	TRFID	TEST REQUESTED	COLLECTION DATE	RECEIVED DATE	SPECIMEN TYPE
		Octave MS Disease Activity Test			Serum

Biomarker Pathway Categories

Please Note: Individual biomarker results are expressed to the hundredths place and are required inputs into the algorithms used to calculate the Disease Activity Score and the four Pathway Scores. Clinical interpretation of individual biomarker levels and the four disease pathway scores, which have different weights in the algorithms, has not been established.

Individual Biomarker Results

Biomarker	Pathways	Concentration	MS Range*	Percentile ▲
NfL Neurofilament Light	NI	4.90 pg/mL	3.5 - 42 pg/mL	10th
GFAP Glial Fibrillary Acidic Protein	NI	54.39 pg/mL	24 - 220 pg/mL	25th
SERPINA9 Serpin Family A Member 9	NI	32.06 pg/mL	12 - 160 pg/mL	34th
FLRT2 Leucine-rich repeat transmembrane protein	NI	90.38 pg/mL	63 - 180 pg/mL	30th
CNTN2 Contactin 2	NI	0.91 ng/mL	0.65 - 3.3 ng/mL	14th
PRTG Protogenin	NI	119.22 pg/mL	71 - 180 pg/mL	56th
OPN Osteopontin	NI M	19.52 ng/mL	9.5 - 39 ng/mL	56th
MOG Myelin Oligodendrocyte Glycoprotein	M	14.85 pg/mL	12 - 47 pg/mL	7th
CXCL9 Monokine Induced by Gamma Interferon	IM N	50.23 pg/mL	17 - 250 pg/mL	60th
CXCL13 C-X-C Motif Chemokine Ligand 13	IM N	40.24 pg/mL	22 - 190 pg/mL	30th
CD6 Cluster of Differentiation 6	IM N	74.14 pg/mL	46 - 250 pg/mL	20th
CCL20 MIP 3-alpha	N	4.43 pg/mL	2.1 - 52 pg/mL	26th
Inversely Correlated with Disease Activity ⓘ				
APLP1 Amyloid Beta Precursor Like Protein 1	NI M	8.19 ng/mL	5.5 - 22 ng/mL	19th
OPG Osteoprotegerin	NI	0.54 ng/mL	0.41 - 1.4 ng/mL	17th
TNFRSF10A TRAIL-R1	NI N	5.34 pg/mL	2.8 - 9.7 pg/mL	61st
TNFSF13B BAFF	IM N	5.00 ng/mL	2.3 - 10 ng/mL	66th
IL-12B Interleukin 12B	IM N	134.68 pg/mL	28 - 280 pg/mL	76th
CDCP1 CUB domain-containing protein 1	IM	91.86 pg/mL	28 - 230 pg/mL	69th

(*) These 95% reference ranges (expressed in two significant figures) were established from 1645 patient samples tested during method validation at the Octave Bioscience Clinical Laboratory. (▲) Subject's biomarker level relative to levels in MS patient samples from which the MS ranges were determined. (↓) Biomarker is inversely correlated with disease activity, therefore a lower concentration was associated with a higher level of disease activity in validation studies.

What is the MSDA test?

- Minimally invasive **blood serum** test
- Developed specifically for **MS**
- Analytically and clinically **validated**
- **18 proteomic biomarkers** → single Disease Activity score
- Supports both **clinical practice**, clinical trials, and other research

MSDA Score Interpretation

LOW	MODERATE	HIGH
1.0 - 4.0	4.5 - 7.0	7.5 - 10.0

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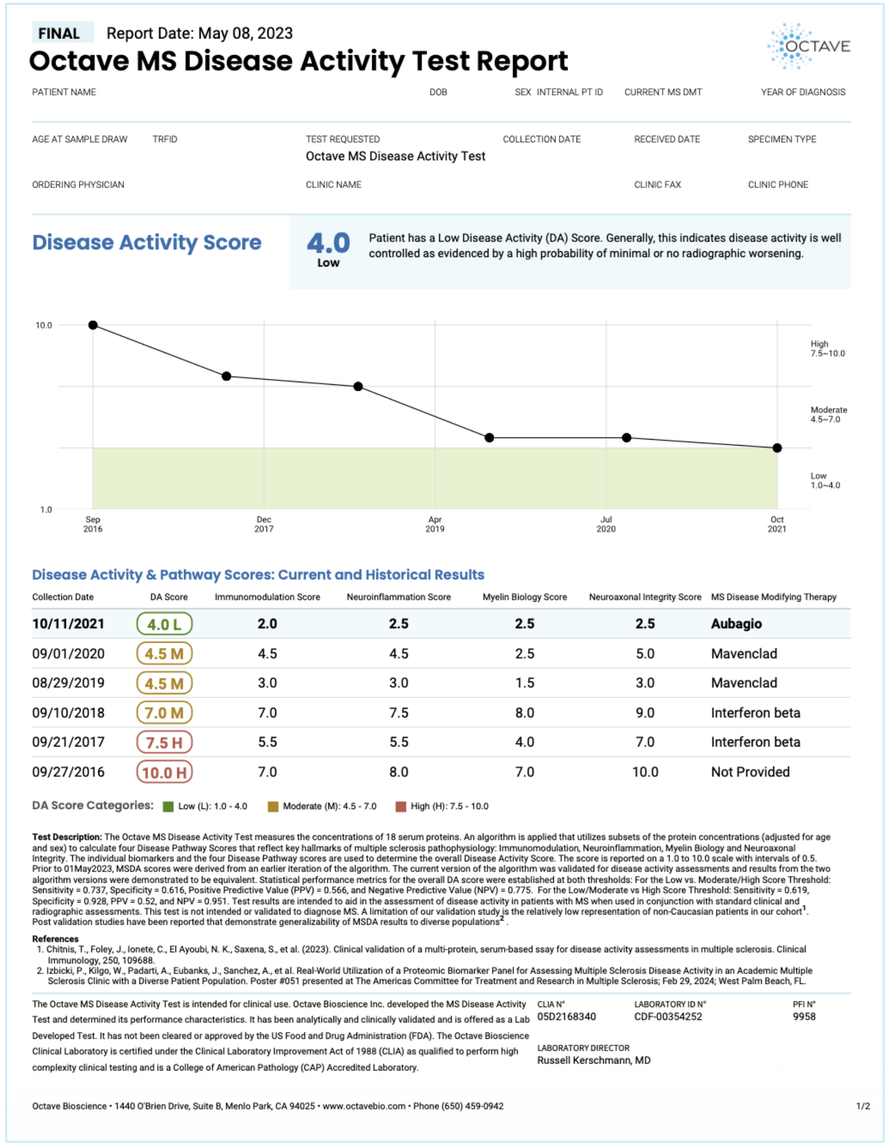
The Octave® MSDA test



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		Octave MS Disease Activity Test			

ORDERING PHYSICIAN	CLINIC NAME	CLINIC FAX	CLINIC PHONE

Disease Activity Score

4.0 Low

Patient has a Low Disease Activity (DA) Score. Generally, this indicates disease activity is well controlled as evidenced by a high probability of minimal or no radiographic worsening.

Disease Activity & Pathway Scores: Current and Historical Results

Collection Date	DA Score	Immunomodulation Score	Neuroinflammation Score	Myelin Biology Score	Neuroaxonal Integrity Score	MS Disease Modifying Therapy
10/11/2021	**4.0 L**	**2.0**	**2.5**	**2.5**	**2.5**	**Aubagio**
09/01/2020	4.5 M	4.5	4.5	2.5	5.0	Mavenclad
08/29/2019	4.5 M	3.0	3.0	1.5	3.0	Mavenclad
09/10/2018	7.0 M	7.0	7.5	8.0	9.0	Interferon beta
09/21/2017	7.5 H	5.5	5.5	4.0	7.0	Interferon beta
09/27/2016	10.0 H	7.0	8.0	7.0	10.0	Not Provided

DA Score Categories: Low (L): 1.0 - 4.0 Moderate (M): 4.5 - 7.0 High (H): 7.5 - 10.0

Test Description: The Octave MS Disease Activity Test measures the concentrations of 18 serum proteins. An algorithm is applied that utilizes subsets of the protein concentrations (adjusted for age and sex) to calculate four Disease Pathway Scores that reflect key hallmarks of multiple sclerosis pathophysiology: Immunomodulation, Neuroinflammation, Myelin Biology and Neuroaxonal Integrity. The individual biomarkers and the four Disease Pathway scores are used to determine the overall Disease Activity Score. The score is reported on a 1.0 to 10.0 scale with intervals of 0.5. Prior to 01May2023, MSDA scores were derived from an earlier iteration of the algorithm. The current version of the algorithm was validated for disease activity assessments and results from the two algorithm versions were demonstrated to be equivalent. Statistical performance metrics for the overall DA score were established at both thresholds: For the Low vs. Moderate/High Score Threshold: Sensitivity = 0.737, Specificity = 0.616, Positive Predictive Value (PPV) = 0.566, and Negative Predictive Value (NPV) = 0.775. For the Low/Moderate vs High Score Threshold: Sensitivity = 0.619, Specificity = 0.928, PPV = 0.52, and NPV = 0.951. Test results are intended to aid in the assessment of disease activity in patients with MS when used in conjunction with standard clinical and radiographic assessments. This test is not intended or validated to diagnose MS. A limitation of our validation study is the relatively low representation of non-Caucasian patients in our cohort[1]. Post validation studies have been reported that demonstrate generalizability of MSDA results to diverse populations[2].

References

1. Chitnis, T., Foley, J., Ionete, C., El Ayoubi, N. K., Saxena, S., et al. (2023). Clinical validation of a multi-protein, serum-based ssay for disease activity assessments in multiple sclerosis. Clinical Immunology, 250, 109688.
2. Izbicki, P., Kilgo, W., Padarti, A., Eubanks, J., Sanchez, A., et al. Real-World Utilization of a Proteomic Biomarker Panel for Assessing Multiple Sclerosis Disease Activity in an Academic Multiple Sclerosis Clinic with a Diverse Patient Population. Poster #051 presented at The Americas Committee for Treatment and Research in Multiple Sclerosis; Feb 29, 2024; West Palm Beach, FL.

The Octave MS Disease Activity Test is intended for clinical use. Octave Bioscience Inc. developed the MS Disease Activity Test and determined its performance characteristics. It has been analytically and clinically validated and is offered as a Lab Developed Test. It has not been cleared or approved by the US Food and Drug Administration (FDA). The Octave Bioscience Clinical Laboratory is certified under the Clinical Laboratory Improvement Act of 1988 (CLIA) as qualified to perform high complexity clinical testing and is a College of American Pathology (CAP) Accredited Laboratory.

CLIA N°	LABORATORY ID N°	PFI N°
05D2168340	CDF-00354252	9958

LABORATORY DIRECTOR
Russell Kerschmann, MD

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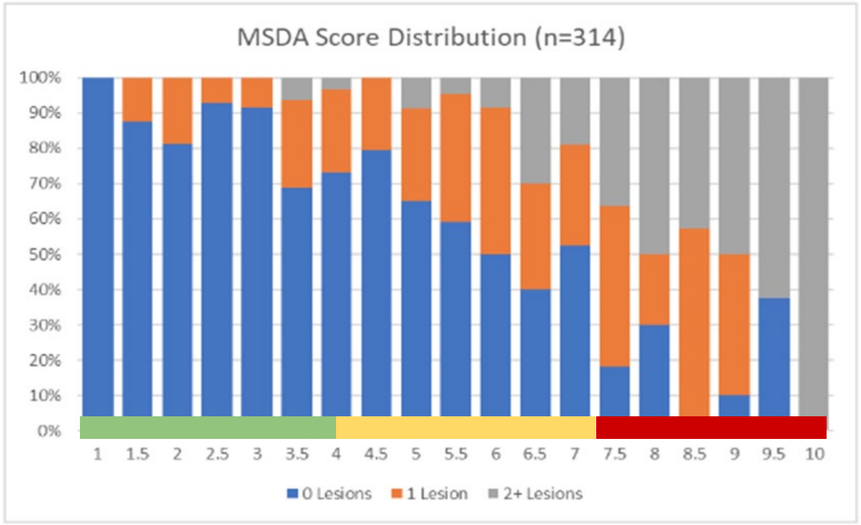
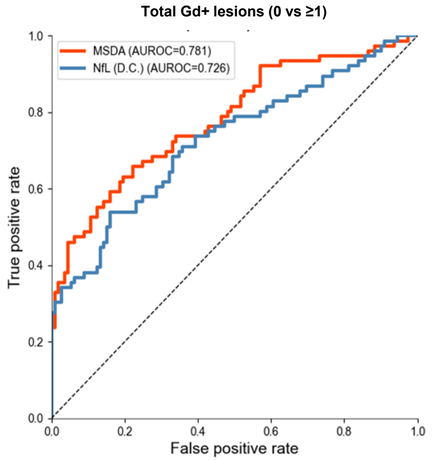
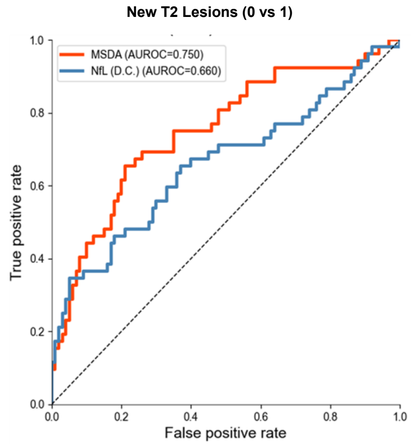
Octave® MSDA test: risk assessment of MS disease activity and severity

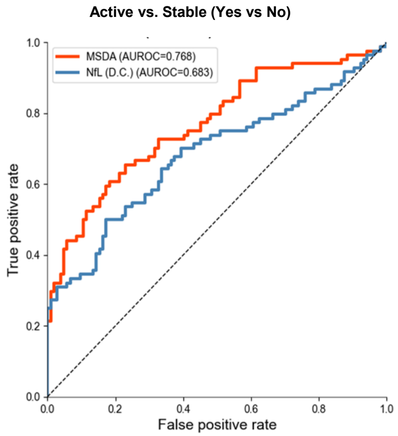




MSDA AUROC=0.781
MSDA without NfL = .698
NfL AUROC=0.694
NfL with DC* AUROC=0.726
p=0.0337



MSDA AUROC=0.750
MSDA without NfL = .695
NfL AUROC=0.619
NfL with DC* AUROC=0.660
p=0.0041



MSDA AUROC=0.768
MSDA without NfL = .714
NfL AUROC=0.645
NfL with DC* AUROC=0.683
p=0.0039

Group	Compare To	Clinical Validation Odds Ratio
Moderate/High	Low	**4.49** times more likely to have ≥1 Gd+ lesions
High	Low/moderate	**20.99** times more likely to have ≥2 Gd+ lesions

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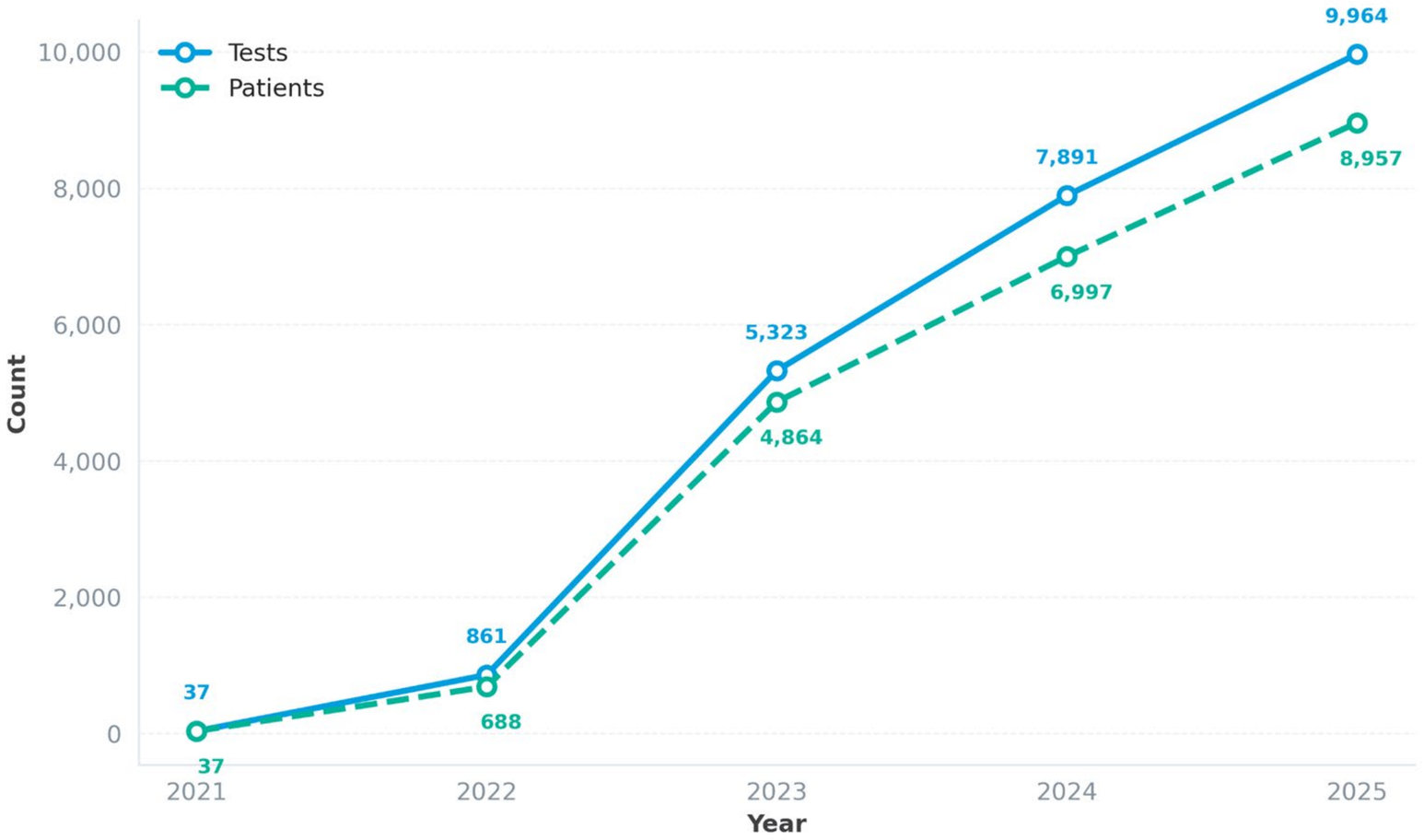
Chitnis, T. *et al.* Clinical validation of a multi-protein, serum-based assay for disease activity assessments in multiple sclerosis. *Clin. Immunol.* **253**, 109688 (2023).
*DC = Demographic correction using Octave MSDA Test methodology

Real-world utilization of the MSDA test

Growth in MSDA Test volume for MS patients



Year To Date (YTD): 25,242 total tests
through January 31, 2026

Test volume increased by **>1,000%** from 2022 to 2025
(1,032 tests in January 2026)

17,945 unique patients
through January 31, 2026
(1,032 unique patients in January 2026)

MSDA score distribution: 66% Low, 28% Moderate, 6% High

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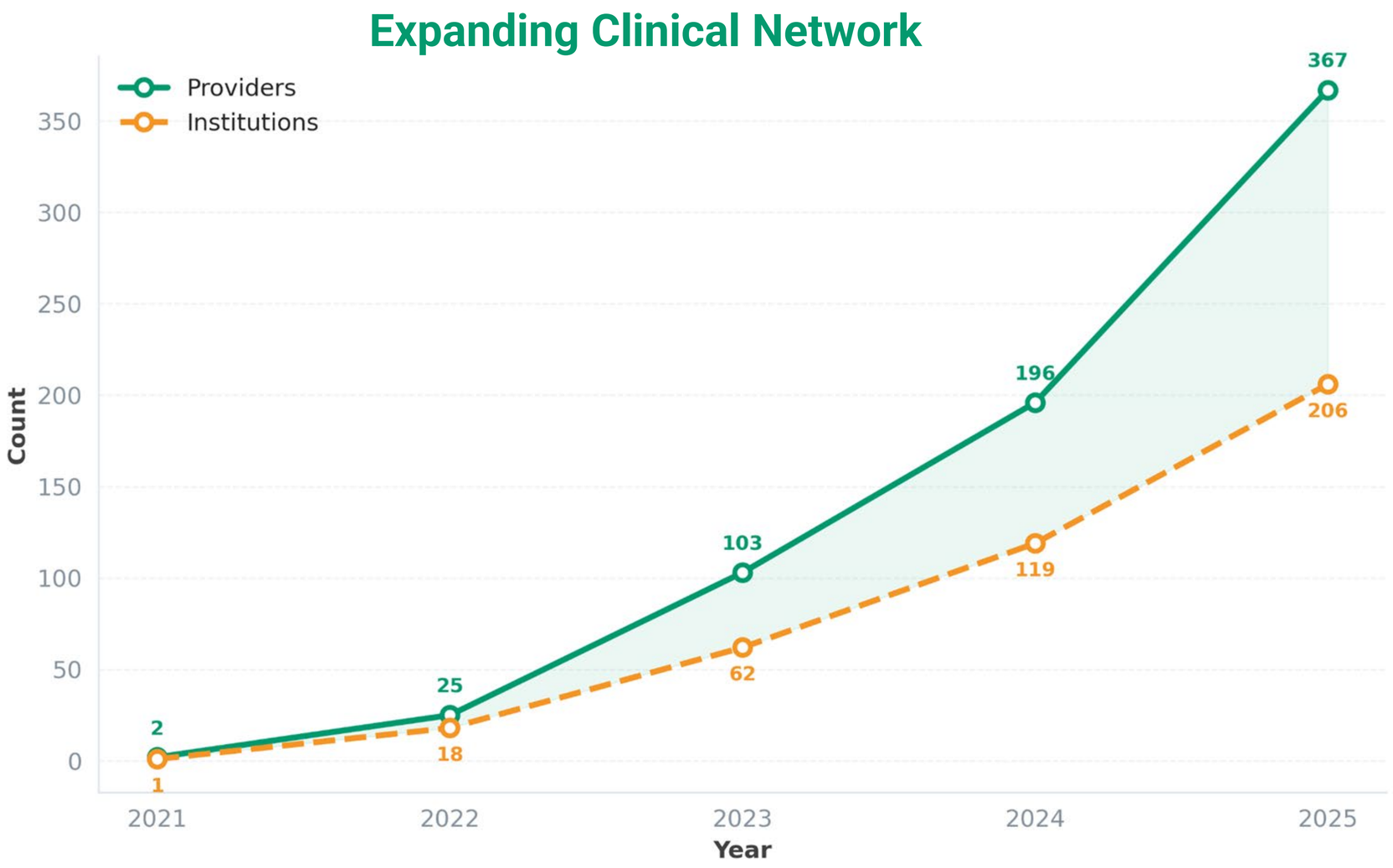
Expanding Provider and Clinic Utilization



367 providers
through end of 2025
(444 by January 31, 2026)

206 institutions
through end of 2025
(237 by January 31, 2026)

MSDA tests ordered in
41/50 states

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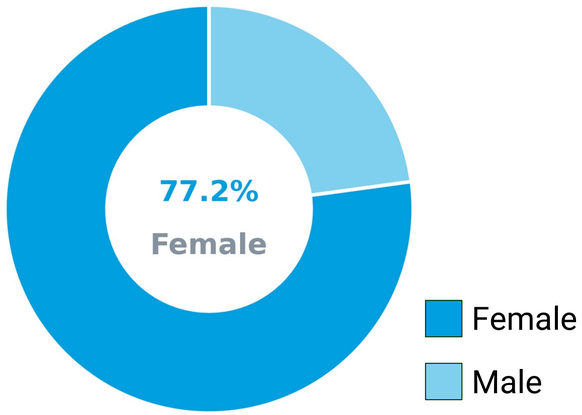
Patient Demographics

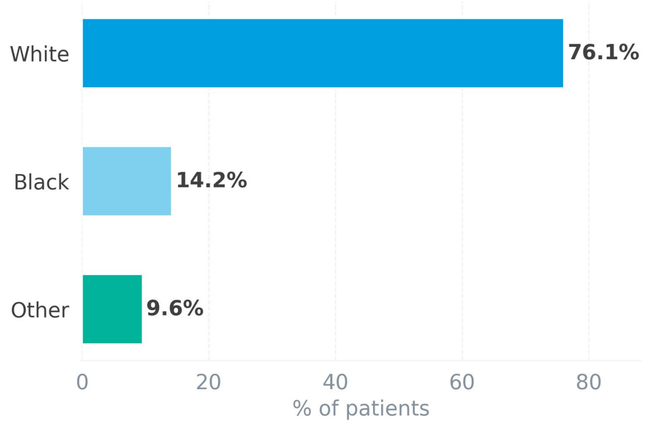
Age	**52.4 ± 13.6 yrs** **18-92 yrs range**
Disease Duration	**13.8 ± 8.9 yrs**

GENDER



RACE (n=10,769)

*** Excludes 7,176 not entered**



ETHNICITY (n=9,857)

*** Excludes 8,088 not entered**

4.7%
HISPANIC/LATINO

95.3% Non Hispanic

DMT EFFICACY AT LAST TEST (n=12,770)

High 44.5% **Moderate 14.8%** **Low 5.6%** **No DMT 34.7%**

**** Excludes 5,150 not entered and 25 other/no match**

High Efficacy = anti-CD20s, natalizumab, alemtuzumab, cladribine; Moderate Efficacy = S1Ps, fumarates, teriflunomide; Low Efficacy = interferons, glatiramer acetate

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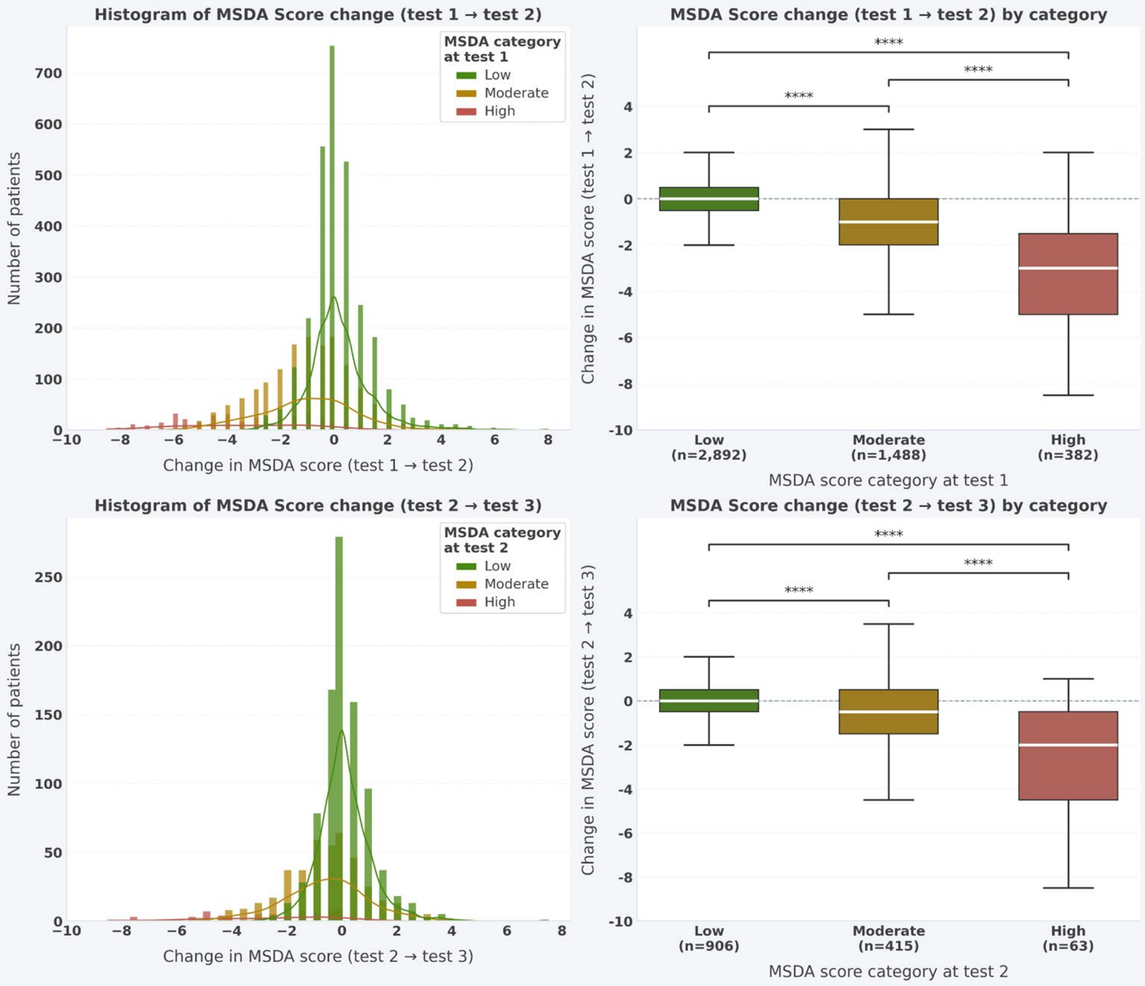
Longitudinal changes in MSDA scores



* Only patients with at least 90 days between consecutive tests included in the figure.

Significant differences in MSDA scores between consecutive tests across all categories ($p<0.0001$).

Mean score changes
Test 1 -> Test 2:
+0.2 for low
−1.0 for moderate
−3.3 for high

Mean score changes
Test 2 -> Test 3:
+0.1 for low
−0.6 for moderate
−2.6 for high

High MSDA scores: **mean decrease exceeded the detectable change threshold (−1.24)**, suggesting effective treatment.[1]

* Score category defined at the first test of each consecutive pair

Number of Patients: **12,835** pts (1 test);
3,556 pts, 19.8% (2 tests); **1,554** pts, 8.7%(3+ tests)

Days between tests	Average	Median
Test 1 -> Test 2	**310 days**	**260 days**
Test 2 -> Test 3	**267 days**	**216 days**

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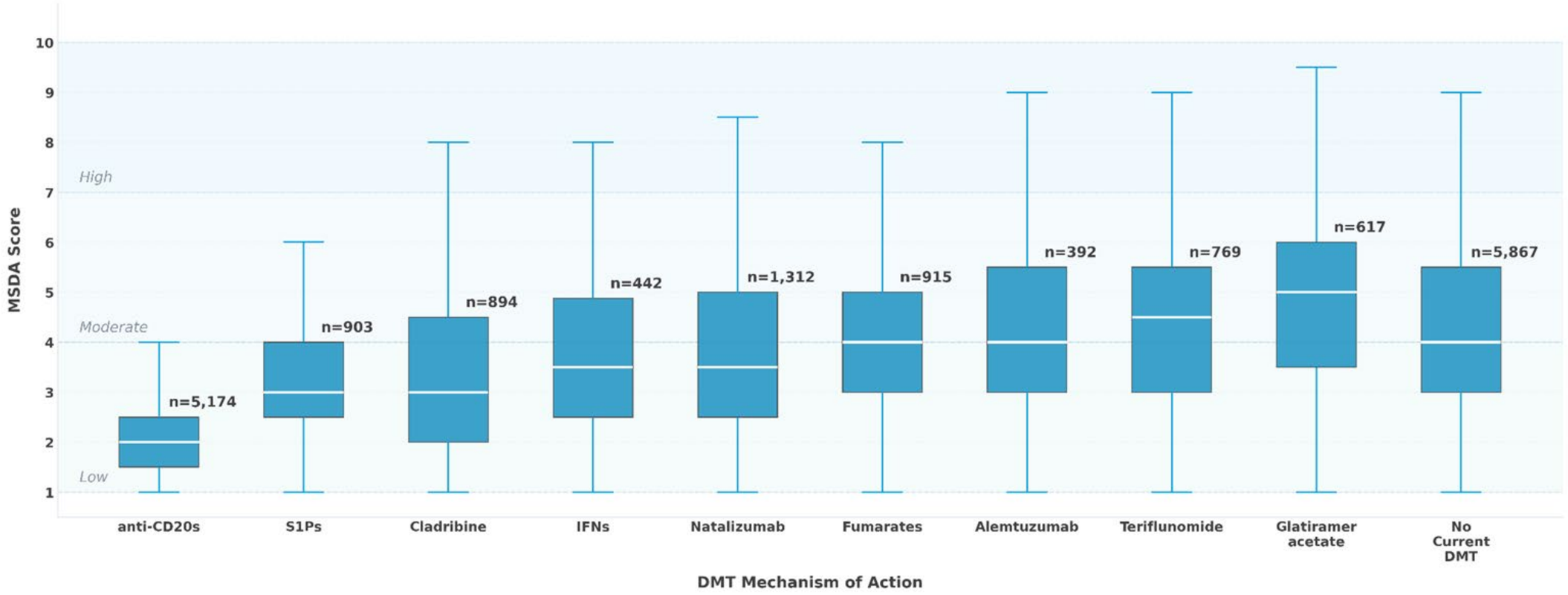
1. McCurdy S et al. ECTRIMS 2025, Barcelona, Spain, P1544

Median MSDA score by DMTs



Real-world data suggests emerging proteomic DMT signatures based on MOA of DMTs

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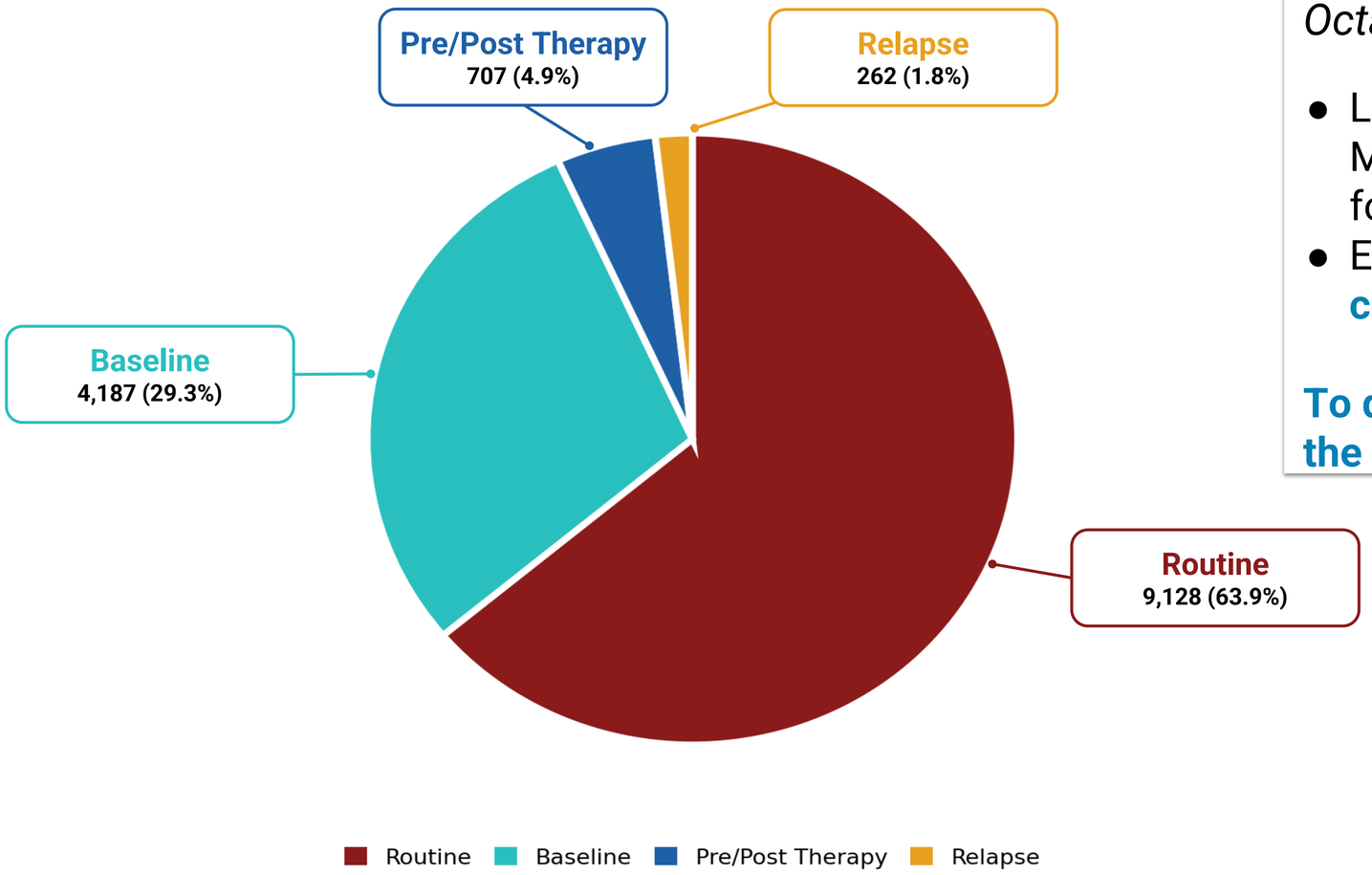
Why do clinicians use the MSDA test

Indications for use (n=14,284 tests)

* Excludes 10,958 other



Octave Cares

Octave's Financial Aid Program

- Launched in Q1 2025 to make the MSDA test **accessible and affordable** for all patients
- Empowers physicians to **order with confidence**

To date of those patients who received the test, 90% have paid $0

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Clinical Applications for the MSDA Test at UTSW

1. **Risk stratification at diagnosis:**
   - Guides treatment decisions and enhances patient counseling, especially when conservative care is favored
   - For individuals with radiologically isolated syndrome who are diagnosed with MS

2. **Relapse confirmation:** Patient-reported symptoms can be non-specific and may reflect pseudo-exacerbations triggered by heat, minor infections, or stress rather than true inflammatory disease activity

3. **Routine disease activity surveillance:**
   - For individuals on FDA-approved disease-modifying therapies, the MSDA Test offers objective insight into ongoing disease activity
   - For untreated individuals previously exposed to alemtuzumab, oral cladribine, etc.
   - DMT discontinuations due to factors such as infections, treatment fatigue, insurance changes, or perceived risk outweighing the benefit (i.e., age $\geq$65 years)

4. **Disease monitoring during high-risk periods:**
   - For women with multiple sclerosis who are trying to conceive, during pregnancy, and throughout the postpartum period
   - Disease rebound surveillance

5. **Alternative to MRI:** Surveillance MRI studies can result in substantial out-of-pocket costs and care delays due to limited access. In addition, these studies are often perceived as uncomfortable and anxiety provoking

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Conclusions

The Octave® MSDA Test: Driving a New Standard in MS Management

01

Broad Adoption

Significant uptake across U.S. clinical practices, reflecting growing confidence in blood-based biomarker tests

02

Actionable Biological Insight

High-scoring patients showed **meaningful MSDA score decreases** (−3.3 at Test 2), exceeding the 1.24 minimum detectable change threshold

03

Clinical Utility and Paradigm Shift

A **versatile, blood-based tool** for longitudinal MS management, relapse assessment and treatment optimization — signaling a shift toward **proactive, biomarker-driven MS care**

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