



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

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Background

Conventional monitoring of patients with multiple sclerosis Demogra (MS) is performed using both clinical and radiographic assessments. The Multiple Sclerosis Disease Activity (MSDA) test is a commercially available multi-protein blood test. It has been analytically¹ and clinically validated².

The MSDA test measures 18 proteins to determine 4 disease pathway scores (i.e. Immune Modulation, Neuroinflammation, Myelin Biology, and Neuroaxonal Integrity) (Figure 2 & 3) and an overall Disease Activity score scaled from 1.0-10.0 with thresholds corresponding to Low, Moderate, and High disease activity.

Clinical validation is relative to gadolinium positive (Gd +) lesions on magnetic resonance imaging (MRI). The timing of utilizing the MSDA test and specific use cases/situations may depend on patient- and provider-specific preferences.

Objectives

The aim of the study was to assess the feasibility and real-world utility of the MSDA in diverse populations within the setting of an academic MS clinic in the southeastern United States.

Methods

Retrospective chart review was conducted at a single academic center. For all patients (n = 90) that received the MSDA from September 2022 to August 2023, relevant patient data was reviewed (see Table 1-3). A total of 90 blood samples were collected. Five samples were longitudinal (i.e. contained two data points). Data was reviewed including age, sex, race, age, EDSS, disease duration, DMT, presence or absence of recent evidence of disease activity by MRI change (new or active lesion), progressing symptoms, or recent clinical relapse. Patients were selected to receive the test at the discretion of the ordering provider.

Disclosures: William Kilgo serves on the speaker bureaus of Biogen, Genentech, and TG Therapeutics. Akhil Padarti has nothing to disclose. Patricia Izbicki, Jim Eubanks, Angela Sanchez, and Ferhan Qureshi are employees of Octave Bioscience.

References: 1. Qureshi F, Hu W, Loh L, et al. Analytical validation of a multi-protein, serum-based assay for disease activity assessments in multiple sclerosis. Proteomics *Clin Appl.* 2023;17(3):e2200018. doi:10.1002/prca.202200018 2. Chitnis T, Foley J, Ionete C, et al. Clinical validation of a multi-protein, serum-based assay for disease activity assessments in multiple sclerosis. *Clin Immunol*. 2023;253:109688. doi:10.1016/j.clim.2023.109688

Participants

Age (mean

Sex (% Fen

Ethnicity (% % Not Hisp

Race (% Af Asian, % Ca

BMI (mean

Smoking (Former)

Table 1: Participant Demographics. BMI = Body Mass Index

Radiog

Recent MF (% Yes, %

Gd+ Lesior 0 (%) 1 (%) ≥2 (%)

New or Enl Yes, % No)

Table 2: Radiographic Status. Recent MRI activity is defined
 as Gd+ and/or new T2 lesions \pm 60 days of MSDA draw.

Figure 1: Population breakdown of disease course. RIS, radiographically isolated syndrome; CIS, clinically isolated syndrome; RRMS, relapsing remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis; PPMS, primary progressive multiple sclerosis.

Presented at the Ninth Congress of the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS), February 29 - March 2, 2024, West Palm Beach USA

raphics (n = 90)	
n ± SD)	43 ± 12
male, % Male)	81%, 19%
(% Hispanic or Latino, panic or Latino)	0%, 100%
frican American, % Caucasian)	43%, 1%, 56%
n ± SD)	32 ± 8
(% Yes, % No, %	20%, 73%, 7%

raphic Status (n = 86)	
RI Activity (± 60 days) No)	15%, 85%
ons) %)	91% 2% 7%
nlarging T2 Lesions (%)	9%, 91%



Clinical Status (n = 90)

Type of DMT	070/
No Current DMT (%)	27%
Alemtuzumab (%)	3%
Dimethyl fumarate (%)	7%
Diroximel fumarate (%)	9%
Fingolimod (%)	2%
Glatiramer acetate (%)	2%
IFN beta 1a (%)	2%
Leflunomide (%)	1%
Natalizumab (%)	11%
Ocrelizumab (%)	23%
Ofatumumab (%)	7%
Ozanimod (%)	1%
Pegylated IFN (%)	1%
Siponimod (%)	1%
Teriflunomide (%)	3%
EDSS (mean ± SD)	3.97 ± 1.76
Disease Duration (mean ± SD years)	11 ± 9
Clinical Status (% Stable, % Recent Relapse, % Progressing)	71%, 15%, 14%

Table 3: Clinical Status. Recent relapse is defined as

 clinician-determined relapse ± 60 days of examination.EDSS = Expanded Disability Status Scale.

Case Series Highlights

High Score Preceding Relapse

33 year old female, newly diagnosed and started on treatment with dimethyl fumarate one year prior. Patient was clinically stable at time of MSDA, which was performed for a baseline score while on dimethyl fumarate. 12 days following the test, the patient reported new onset of bilateral lower extremity numbness and poor balance. MRI showed multiple enhancing lesions. The patient was transitioned to ocrelizumab.

MSDA Score



Conclusions

The MSDA test was a reliable indicator of recent objective disease activity when used in routine clinical practice within an academic MS clinic. All patients with high scores had evidence of recent disease activity, including two examples of elevated MSDA scores that preceded future clinical and radiographic manifestations of disease activity. Future directions with this research will include sub analyses of this diverse patient population.

Population Overview



Figure 4: Left = MSDA overall score and pathway scores (n = 90). The categories are defined as low, moderate, and high with ranges of 1.0 - 4.0, 4.5 - 7.0, and 7.5 - 10.0, respectively. A score in the moderate/high range is \sim 4.5 times more likely to have \geq 1 Gd+ lesion(s) as compared to the low range. A score in the high range is ~ 21 times more likely to have ≥ 2 Gd+ lesions. Right = Percent of participants (n = 90) in each MSDA category.

Concordance of Results

Of the twelve "High" MSDA scoring patients, seven of eleven with reviewable MRIs had evidence of recent Gd (+) MRI activity. Eleven of the twelve "High" scorers had either recent objective clinical disease activity and/or MRI activity. The single high scorer with no clinical or radiographic correlate was a few weeks post-partum, not on DMT, with a history of highly active disease, and new, nonenhancing T2 lesions on MRI. Two of the twelve "High" scorers had elevated MSDA scores prior to clinical or radiographic evidence of disease activity.

Minimally Symptomatic MS

31 year old female who presented to the emergency department for headache. MRI brain with and without contrast showed multifocal lesions in a classical distribution for a demyelinating process. Work-up was all suggestive of a demyelinating etiology. She subsequently reported a subacute onset of facial numbness, but was otherwise clinically asymptomatic at the time of initial imaging.

MSDA Score

Highly Active Disease

21 year old female presenting with recent onset left-sided optic neuritis and lower extremity weakness. She is naïve to treatment including steroids. MSDA was obtained six weeks after baseline MRI.

MSDA Score

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