Real-world Clinical Utility of a Multi-protein, Blood-based Biomarker Assay for Disease Activity Assessments in Multiple Sclerosis

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Introduction

Blood-based biomarkers have emerged as promising tools to optimize treatment decisions in multiple sclerosis (MS) including the initiation, switch, or cessation of disease modifying therapies (DMTs). The Octave MS Disease Activity (MSDA) test is a commercially available, analytically and clinically validated blood-based biomarker test that measures 18 proteins and adjusts for age and sex to determine four (4) disease pathway scores (i.e., immunomodulation, neuroinflammation, myelin biology, and neuroaxonal integrity) and an overall Disease Activity (DA) score scaled from 1.0-10.0 with thresholds corresponding to low (1-4), moderate (4.5-7), and high (7.5-10) levels of disease activity[1-3].

Objectives

The clinically validated MS Disease Activity Test measures 18 proteins and adjusts for age and sex to derive an overall disease activity score. This study investigates the clinical utility of MSDA for physician decision-making in real-world practice.

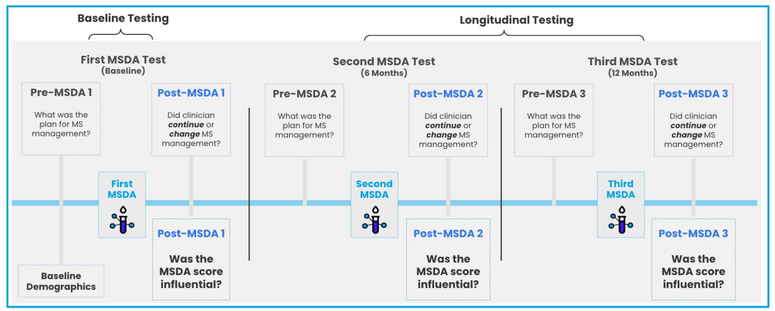


Figure 1: Study Design: A multicenter, retrospective chart review study with a pre-post test component was conducted in 14 clinics with MSDA in routine clinical use. Charts were reviewed to ascertain clinician decision-making before and after receipt of MSDA results. **Purple dashed text boxes** indicate time points for chart review by site staff. **Green dashed text boxes** indicate time points for the treating clinician.

Methods

Twenty clinicians from 14 clinics were involved in a chart review utilizing a retrospective, longitudinal design, with a pre-post component **(Figure 1)**. Chart reviews captured clinician decision-making before and after receipt of each MSDA result, while separate clinician assessments also captured the perceived impact of MSDA on MS management.

- **Inclusion criteria** | Patients aged 18 to 99 with a documented diagnosis of MS, CIS, or RIS, and at least 2 MSDA results from routine clinical care between March 1st, 2022 and January 8th, 2024.
- **Exclusion criteria** | Patients with incomplete data, pregnant or up to 6 weeks postpartum, or a major unrelated illness or comorbidity that affected MS management.
- **Chart Review** | Out of 412 charts screened for eligibility, a total of 352 charts were included in the final analysis. Data collected from charts include baseline demographics, standard of care assessments (i.e. MRI and clinical exam), and clinical recommendations before and after MSDA results.

Prompt: *Single MSDA test results influenced the decision to continue or change the MS management of this patient at this time.*

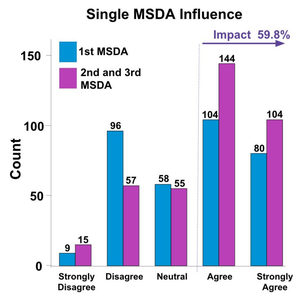


Figure 2: Clinician-reported influence of a single MSDA test to continue or change the MS management of a patient.

Prompt: *The change (or stability) across multiple MSDA test results influenced the decision to continue or change the MS management of this patient.*

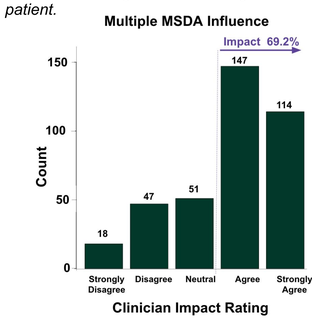
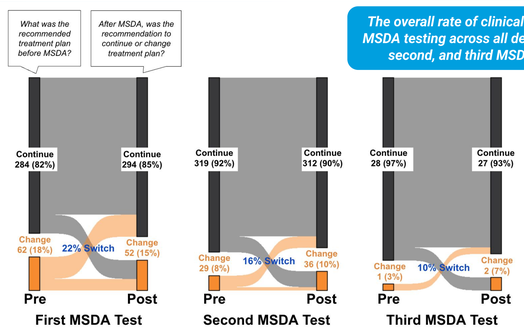


Figure 3: Clinician-reported influence of multiple MSDA tests to continue or change the MS management of a patient.



The overall rate of clinical decision changes after MSDA testing across all decision time points (first, second, and third MSDA tests) was 19.4%.

Figure 4: Paired pre/post MSDA decision impact responses for up to 3 MSDA tests per patient chart reviewed.

Results

A total of 352 charts which included 723 MSDA tests were reviewed. The proportion of decision time points where clinicians "strongly agreed" or "agreed" that MSDA results influenced their decision-making was greater when multiple longitudinal MSDA results were available compared to a single MSDA result: 69.2% (p<0.001; 95%CI: [60.2, 78.3]%) vs. 59.8% (p=0.217; 95%CI: [43.7, 76]%), respectively **(Figures 2 & 3)**. The overall rate of clinical decision changes after MSDA testing (19.4%) exceeded predefined benchmarks **(Figure 4)**[4].

Three patterns in clinician MS management were observed following receipt of MSDA results : 1) A low MSDA score supported the clinician's plan to continue the current treatment plan, 2) A low MSDA score helped determine when a patient could discontinue a DMT, and 3) A high MSDA score identified when a patient should initiate a DMT **(Figure 5)**.

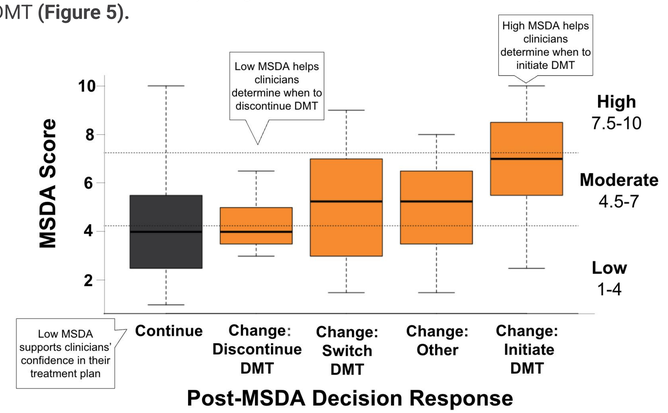


Figure 5: Relationships between MSDA scores and post-MSDA decisions from study site staff chart review.

Conclusions

When used in combination with standard of care, MSDA demonstrates clinical utility for real-world decision-making in MS management, based on the observed changes in treatment plan and clinician-reported impact, which increases with longitudinal use. MSDA results significantly influence clinical decision changes at a rate higher than established benchmarks, and also provide added confidence to clinicians when maintaining the patient's current treatment plan.

References: [1]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, [2]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, [3]Chitnis T, Qureshi F, Gehman VM, et al. Inflammatory and neurodegenerative serum protein biomarkers increase sensitivity to detect clinical and radiographic disease activity in multiple sclerosis. Nat Commun 2024. [4]Bajus, L., Leyden, K. M. & Graziera, C. Variability in Clinical Impressions and Decisions by Neurologists Interpreting MS MRI Brain Reports. Poster presented at CMSC 2023.

Disclosures: ES, SE, SM, MB, FQ, and KR are employees of Octave Bioscience. AS, JE, PI, and AG are former employees of Octave Bioscience. MW is a consultant for Sanofi, Horizon/Amgen, Cycle Pharma, Octave Bioscience and on the speakers bureau at Sanofi, Horizon/Amgen, BMS, Biogen, and TG Therapeutics. AO has received consultant/speaking fees from Alexion, Biogen, EMD Serono, Novartis, Roche, Genentech, Sanofi Genzyme, TG Therapeutics, and research support from Alexion, EMD Serono, Novartis, Octave Bioscience, Roche Genentech, Sanofi Genzyme, and TG Therapeutics. MS has received consulting fees from Roche, Astra Zeneca, Octave Biosciences, and Pliant Therapeutics. TG is a consultant for Horizon Therapeutics, Sanofi, Genentech and EMD Serono. MB has received research support from Biogen, EMD Serono, Sanofi, and Genentech and speaker and consultant fees from Biogen, EMD Serono, Sanofi, Genentech, Alexion, Bristol Myers Squibb, TG Therapeutics, and Octave Bioscience. WK serves on the speaker bureaus of Biogen, Genentech, and TG Therapeutics. MJW has provided Research Support for EMD Serono, Genentech, Novartis; Advisory Committee/Consultant for Biogen Idec, Bristol Myers Squibb, EMD Serono, Genentech, Novartis, Sanofi Genzyme, Janssen, Alexion, TG Therapeutics; Speaker Bureau for Biogen Idec, Bristol Myers Squibb, EMD Serono, Genentech, Novartis, Sanofi Genzyme, Janssen. YJ has provided Research Support for Novartis, SANOFI-GENZYME, Genentech, TG Therapeutics, Octave Bioscience; Speaker Bureau of Amgen, Alexion-AstraZeneca and TG Therapeutics and participated in an Octave Bioscience advisory board.

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