EP1034

Longitudinal Testing with a Multivariate Blood Serum Biomarker Panel for Multiple Sclerosis Disease Activity: Patterns of Results in a Real-World Clinical Setting

Tammy Hoyt[1], James Eubanks[2], Ferhan Qureshi[2], John Foley[1]

1. Rocky Mountain Multiple Sclerosis Clinic, Salt Lake City, UT

2. Octave Bioscience, Menlo Park, CA, USA

BACKGROUND

A proteomic Multiple Sclerosis Disease Activity (MSDA) test which utilizes an algorithm consisting of 18 biomarkers to produce four disease pathway scores and an overall disease activity (DA) score has been analytically and clinically validated.[1,2] The disease pathway scores (immunomodulation, neuroinflammation, myelin biology and neuroaxonal integrity) are determined based on subsets of the 18 proteins and their established biological associations with one another. The pathway and DA scores are scaled from 1.0 - 10.0 with 0.5 intervals. The overall DA Score is utilized to define low, moderate, and high DA categories for each sample with ranges of 1.0 - 4.0, 4.5 - 7.0, and 7.5 - 10.0, respectively. DA score categories were established in a clinical validation study to correlate with the presence and count of gadolinium-enhancing lesions on an associated MRI: low = 0 lesions, moderate = 1 lesion, high = ≥ 2 lesions.[1]

OBJECTIVES

To characterize intra-patient variability of the MSDA test scores with longitudinal testing in a clinically stable real-world patient population.

METHODS

A total of 749 patient samples from Rocky Mountain Multiple Sclerosis Clinic were assayed using the MSDA test to generate DA and pathway scores. Of these, 13 relapsing-remitting patients had at least four MSDA tests performed over a maximum of a 20-month period. The average length between the first and second test was 12 months, 2 months between the second and third tests, and 1 month average for subsequent tests thereafter. All patients were considered steady state on therapy, having been administered natalizumab for at least 6 months with no gaps in treatment. All patients were considered both radiographically and clinically stable over the sample period. Descriptive statistics were used to characterize the relative stability of MSDA scores with longitudinal sampling.

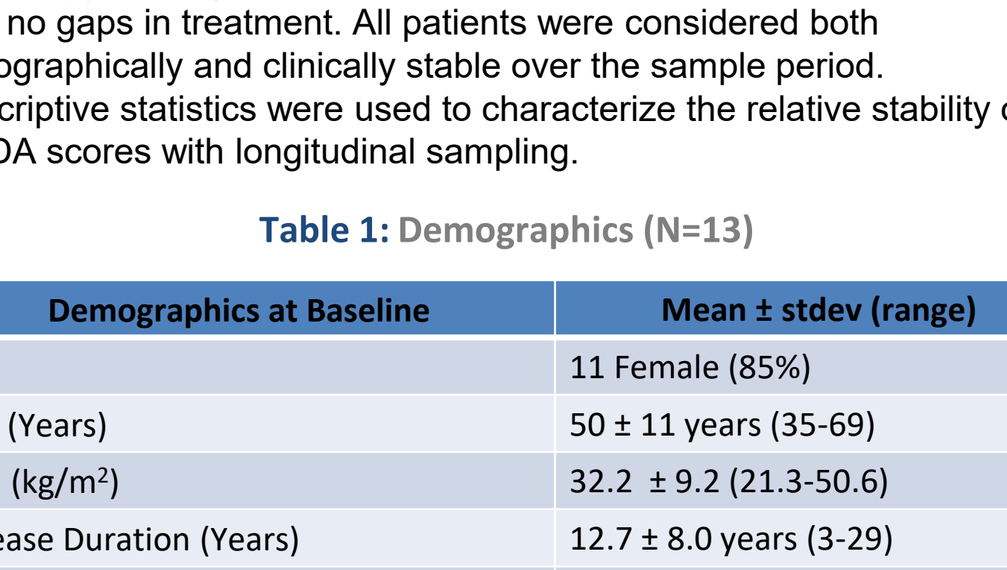
Table 1: Demographics (N=13)

Demographics at Baseline	Mean ± stdev (range)
Sex	11 Female (85%)
Age (Years)	50 ± 11 years (35-69)
BMI (kg/m^2)	32.2 ± 9.2 (21.3-50.6)
Disease Duration (Years)	12.7 ± 8.0 years (3-29)
Natalizumab Exposure (Years)*	6.5 ± 4.7 years (0.5-13.4)

*Time since initial exposure - may not represent continuous exposure

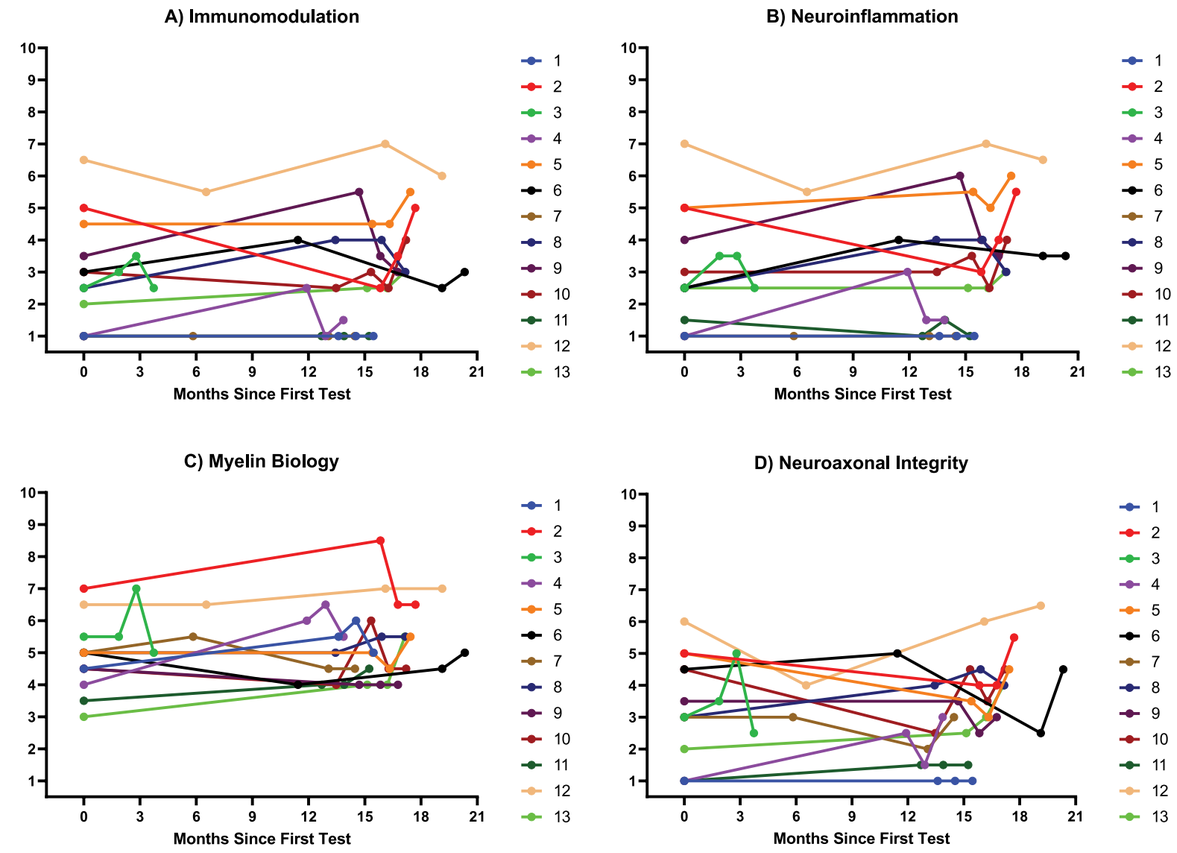
RESULTS

Figure 1:
MSDA Scores in Longitudinal Stable Natalizumab Cohort



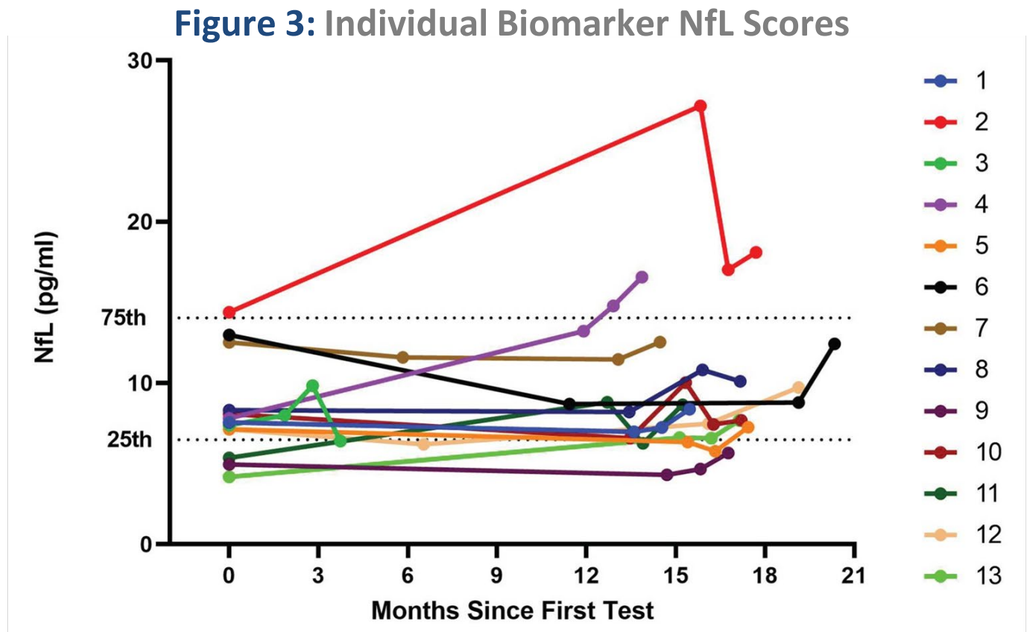
Longitudinal MSDA test results over a maximum of 20 months. The mean MSDA score at baseline was 3.5 ± 1.5 (range 1.5 - 6.5). The mean intra-patient variability was 1.0 ± 0.5 (range 0.5-2.0). The median intra-patient % CV for the MSDA score was 13.6%. Five patients had scores after baseline that resulted in a DA score category change (all between the low and moderate categories). No patients had scores at baseline or for subsequent timepoints that were in the high disease activity category.
CV = coefficient of variation

Figure 2: Longitudinal Disease Pathway Scores



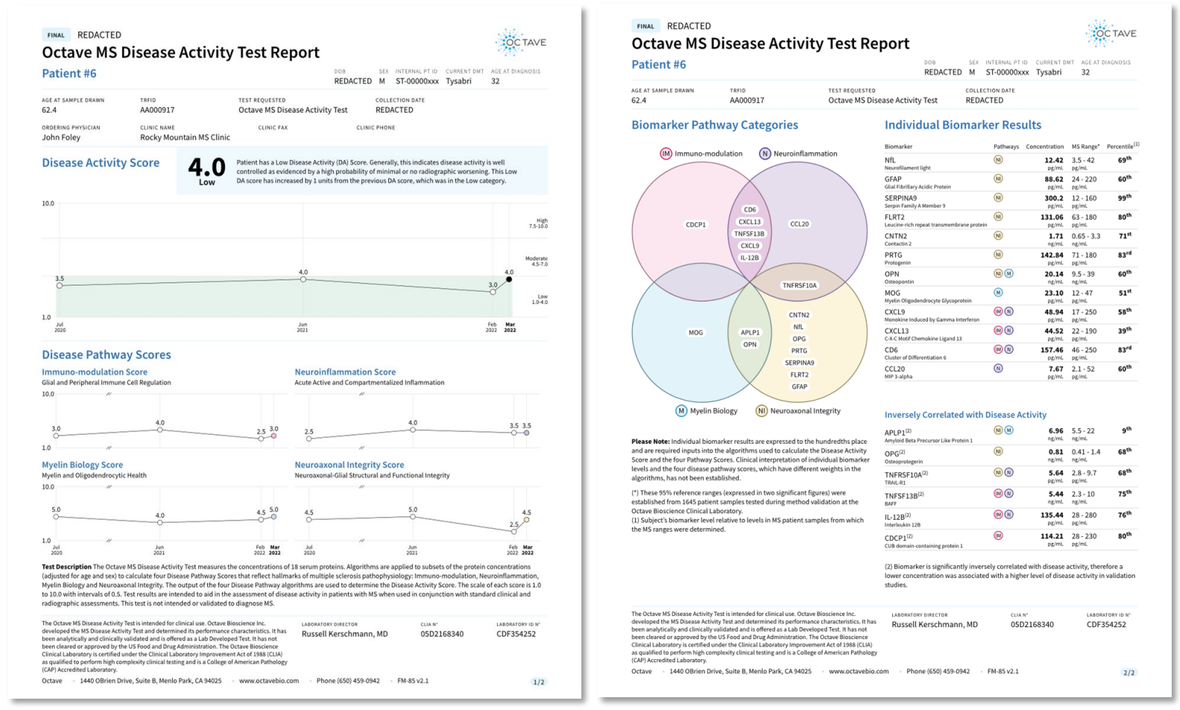
Longitudinal pathway scores over maximum 20 months. The mean ± sdev (range) at baseline for the individual pathway scores are as follows: A) Immunomodulation 2.8 ± 1.7 (1.0 - 6.5), B) Neuroinflammation 3.0 ± 1.8 (1.0 – 7.0), C) Myelin Biology 4.8 ± 1.1 (3.0 – 7.0) and D) Neuroaxonal Integrity 3.3 ± 1.7 (1.0- 6.0),

Figure 3: Individual Biomarker NfL Scores



The average baseline NfL concentration was 8.3 ± 3.1 (4.2 - 14) pg/mL, with a mean intra-patient variability of 9.3 ± 3.7 (4.9-19.2) pg/mL. The median intra-patient %CV for NfL concentration across the 13 patients was 18.3%. NfL concentrations are adjusted for age prior to being used as an input in the MSDA algorithm.

Figure 4: Octave MSDA Patient Report



Patient #6 Octave MSDA report which features the longitudinal MSDA and disease pathway scores as well as the most recent individual biomarker concentrations with percentiles relative to the MS population.

CONCLUSIONS

Thirteen MS patients on a high efficacy disease modifying therapy had only minor fluctuations in MSDA score with repeated longitudinal testing. Although we observed a range of baseline MSDA scores between patients, intra-patient changes were on average within the reported analytical precision for the DA score (3 SD = 1.5 score units).[2] The variability (median intra-patient %CV) observed for the MSDA score over 20 months of longitudinal testing was less than that observed for NfL, illustrating the value of a proteomic panel vs a single marker in ascertaining the pathophysiological correlates of clinical status. These results complement the extensive clinical validation of the MSDA test with real world examples of repeated testing. Use of the MSDA test as a clinical adjunct for longitudinal monitoring of patients may help inform the degree of biologic disease stability.

References and Disclosures

Tammy Hoyt is a paid consultant for Octave Bioscience.
Jim Eubanks and Ferhan Qureshi are employees of Octave Bioscience.
John Foley has received research support from Biogen, Novartis, Adamas, Octave, Genentech, and Mallinckrodt.
He received speakers' honoraria and acted as a consultant for EMD Serono, Genzyme, Novartis, Biogen, and Genentech. He has equity interest in Octave. He is the founder of InterPro Bioscience.

1. Chitnis, T., Foley, J., Ionete, C., El Ayoubi, N., Saxena, S., Gaitan-Walsh, P., Lokhande, H., Paul, A., Saleh, F., Weiner, H., Qureshi, F., Becich, M.J., Rubio da Costa, F., Gehman, V.M., Khoury, S. J. Clinical validation study results of a multivariate proteomic serum-based assay for disease activity assessments in multiple sclerosis. Presented at: 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 13-15, 2021
2. Hu, W., Loh, L., Patel, H. , DeGuzman, H., Zhou, K. , Rubio da Costa, F., Gehman, V.M. , Zhang, F. , Qureshi, F. Analytical Validation of the Disease Activity Score and 4 Disease Pathway Scores for a Multivariate Proteomic Multiple Sclerosis Disease Activity Test. P006, Presented at the 7th Congress of the Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS); February 24-26, 2022