

REPAIR-MS Results | A Phase 2 Study of Magnetic Resonance Spectroscopy to Assess the Effects of CNM-Au8 for the Bioenergetic Improvement of Impaired Neuronal Redox State in Multiple Sclerosis

RepairMS

CNM-Au8
Oral nano-suspension



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Treatment with CNM-Au8 30 mg Resulted in Improved Brain Energy Metabolism NAD⁺/NADH Ratio: Evidences Novel Mechanism of Action for the Treatment of MS

Design Overview | Phase 2 Study | Open-Label Sequential Group Investigator-Blinded 12-Week Study Utilizing ³¹P-MRS Imaging of Brain Energy Metabolites with a 6-Week Post-Therapy Washout & Safety Follow-Up Period

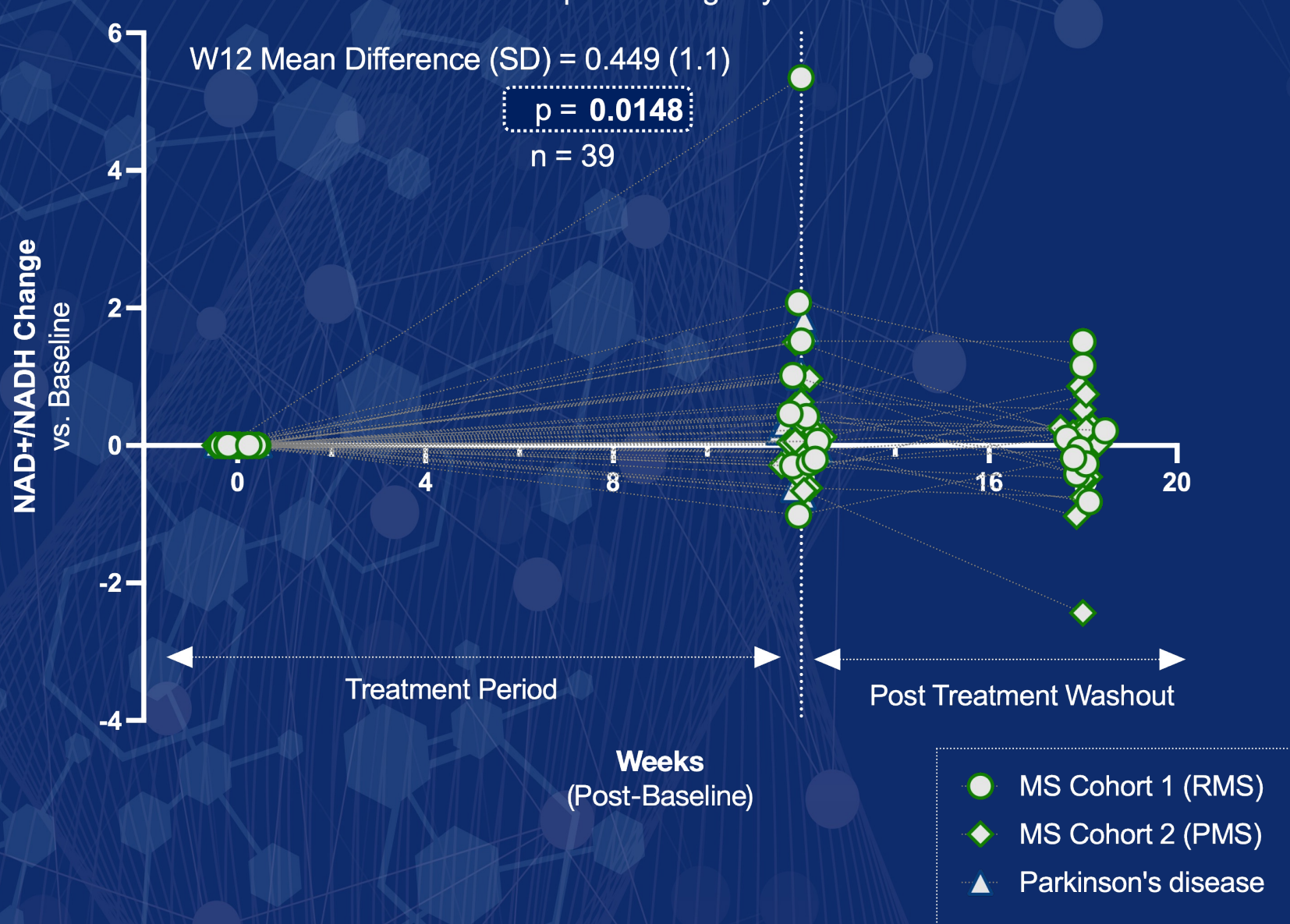
- REPAIR-MS Cohort 1 enrolled relapsing remitting MS, stable on natalizumab (n=13)
- REPAIR-MS Cohort 2 included non-active progressive MS (PMS) without relapse(s) or gadolinium enhancing lesion(s) within the previous 5 years, taking either a B-cell depleting therapy or an S1P-modulator (n=20)
- REPAIR-PD included participants diagnosed with Parkinson's disease within 3 years, Hoehn and Yahr stage ≤ 3 , and stable treatment with dopaminergic therapies (n=13)
- Prespecified integrated analysis of the combined cohorts (primary efficacy outcome); all evaluable with post-baseline ³¹P-MRS scans

Category	REPAIR-MS Cohort 1	REPAIR-MS Cohort 2	REPAIR-MS (Total)
Participants: (n)	13	20	33
Age: Mean (SD)	41.6 (10.0)	54.1 (9.9)	49.2 (11.6)
Sex (female): n (%)	9 (69%)	13 (65%)	22 (67%)
Relapsing MS / PPMS / SPMS: (n)	13 / 0 / 0	0 / 12 / 8	13 / 12 / 8
Baseline EDSS: Mean (SD)	2.7 (1.9)	4.9 (1.7)	4.0 (2.1)

Primary Endpoint | Improved NAD⁺/NADH Ratio (Combined REPAIR Program)

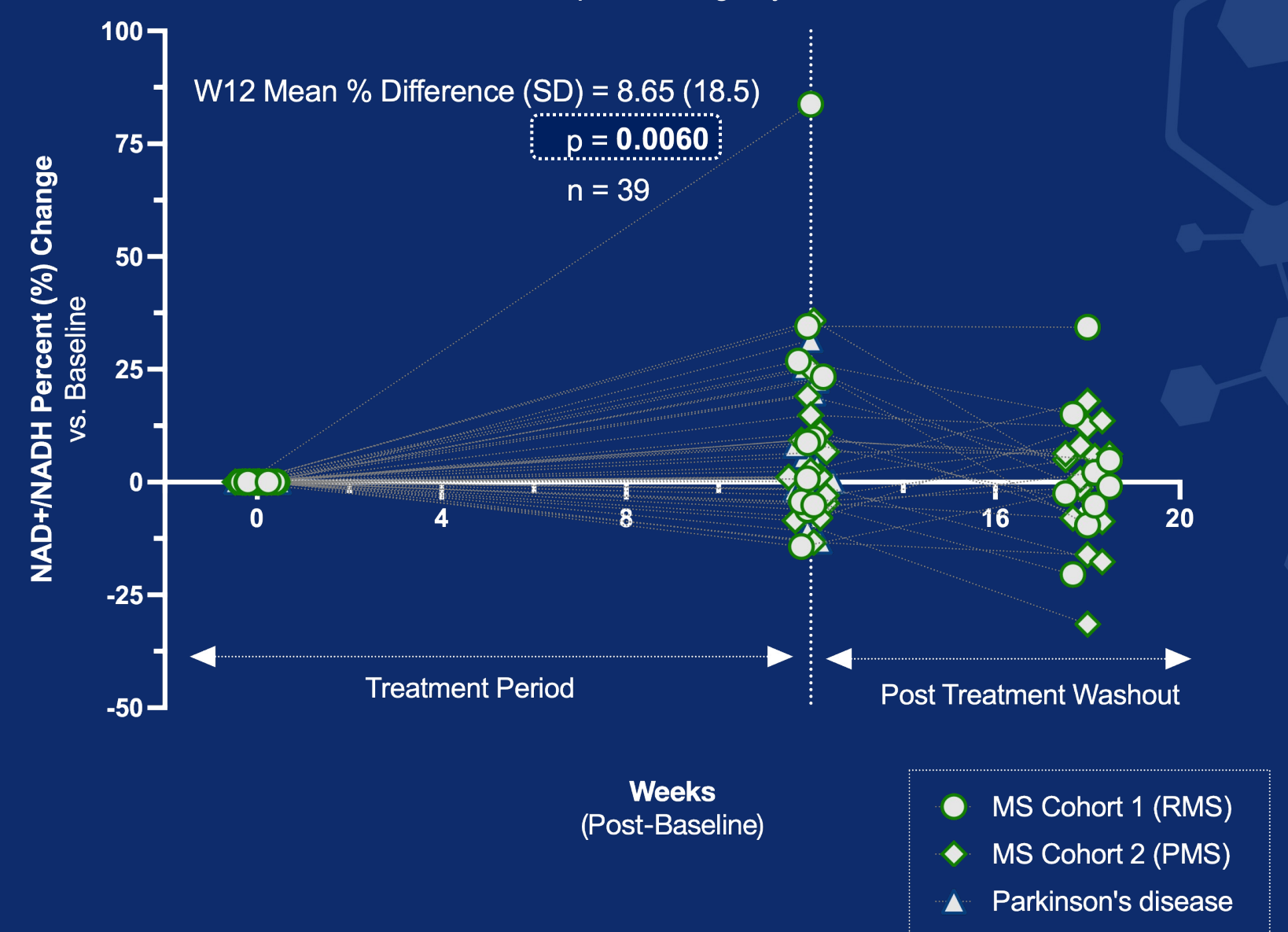
NAD⁺/NADH Ratio (Unit Change)

³¹P-MRS Change in Brain NAD⁺/NADH Ratio at End of Treatment
Partial Volume Coil; Ratio of NAD⁺/NADH (% Fraction of NAD⁺, NADH Couple)
REPAIR Studies (Integrated Analyses: All Cohorts), Primary Endpoint
Participant Change by Visit



NAD⁺/NADH Ratio (% Change)

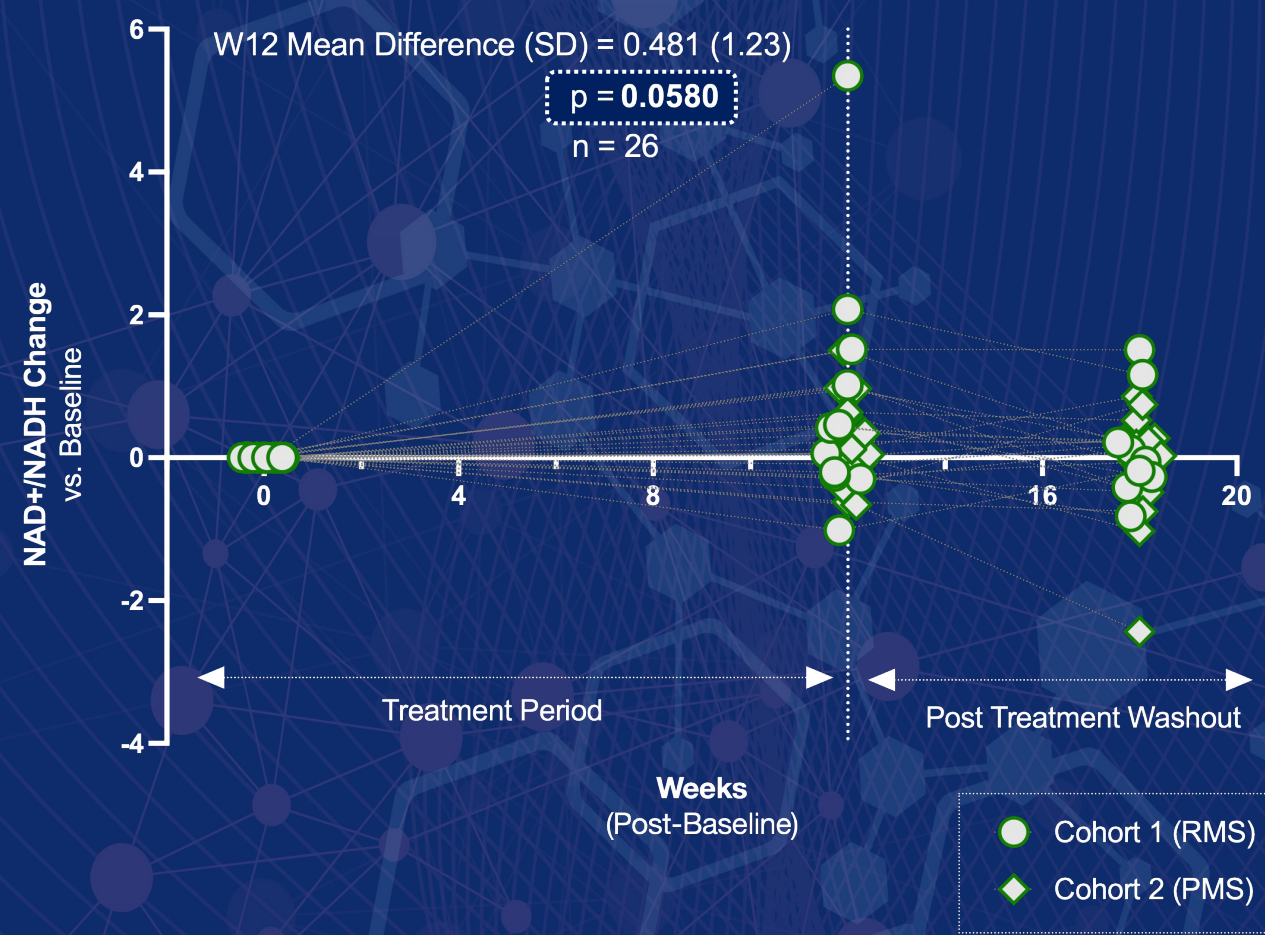
³¹P-MRS Percent (%) Change in Brain NAD⁺/NADH Ratio at End of Treatment
Partial Volume Coil; Ratio of NAD⁺/NADH (% Fraction of NAD⁺, NADH Couple)
REPAIR Studies (Integrated Analyses: All Cohorts), Primary Endpoint (Sensitivity Analysis)
Participant Change by Visit



Primary & Secondary Endpoints | REPAIR-MS

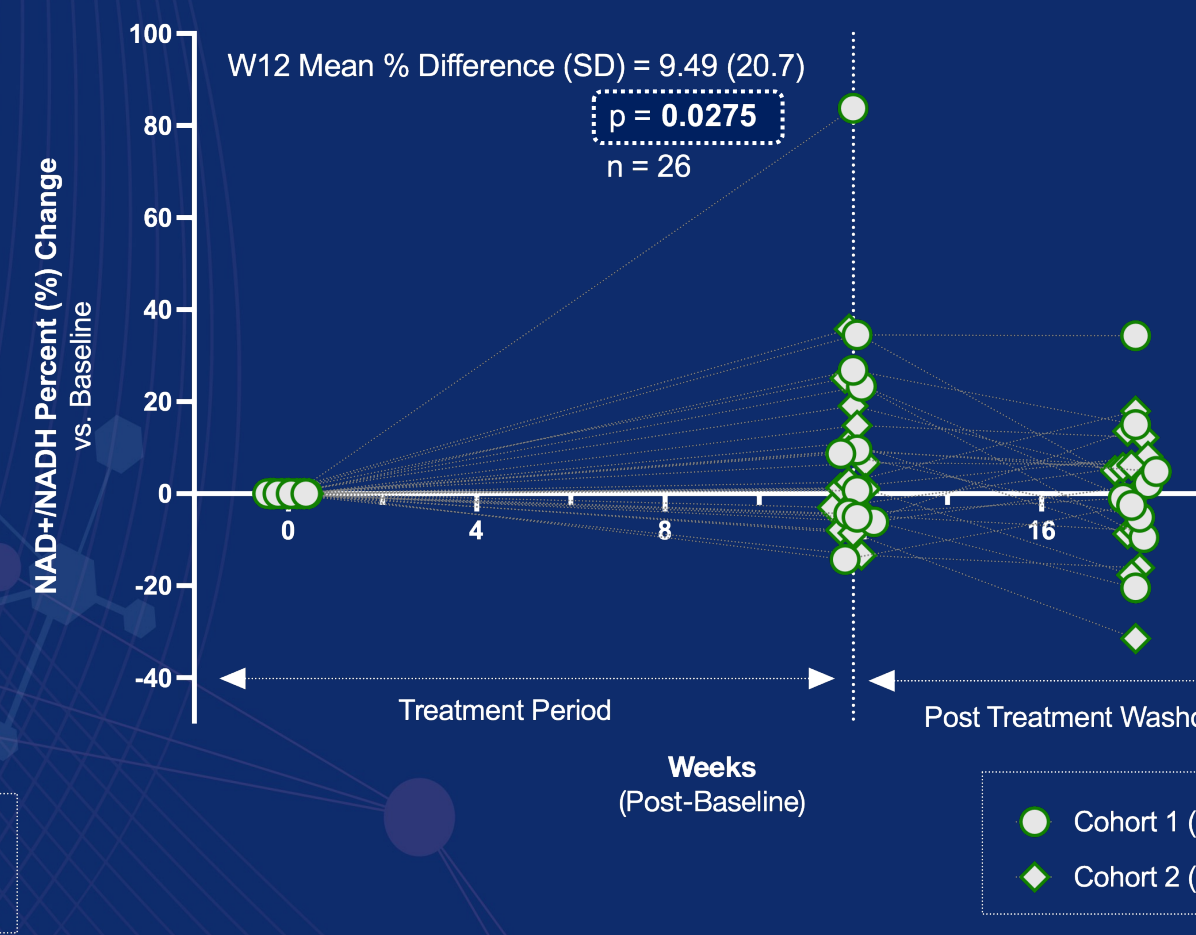
Primary | NAD⁺/NADH Ratio (Unit Change)

³¹P-MRS Change in Brain NAD⁺/NADH Ratio at End of Treatment
Partial Volume Coil; Ratio of NAD⁺/NADH (% Fraction of NAD⁺, NADH Couple)
REPAIR-MS (Combined Cohorts), Primary Endpoint
Participant Change by Visit



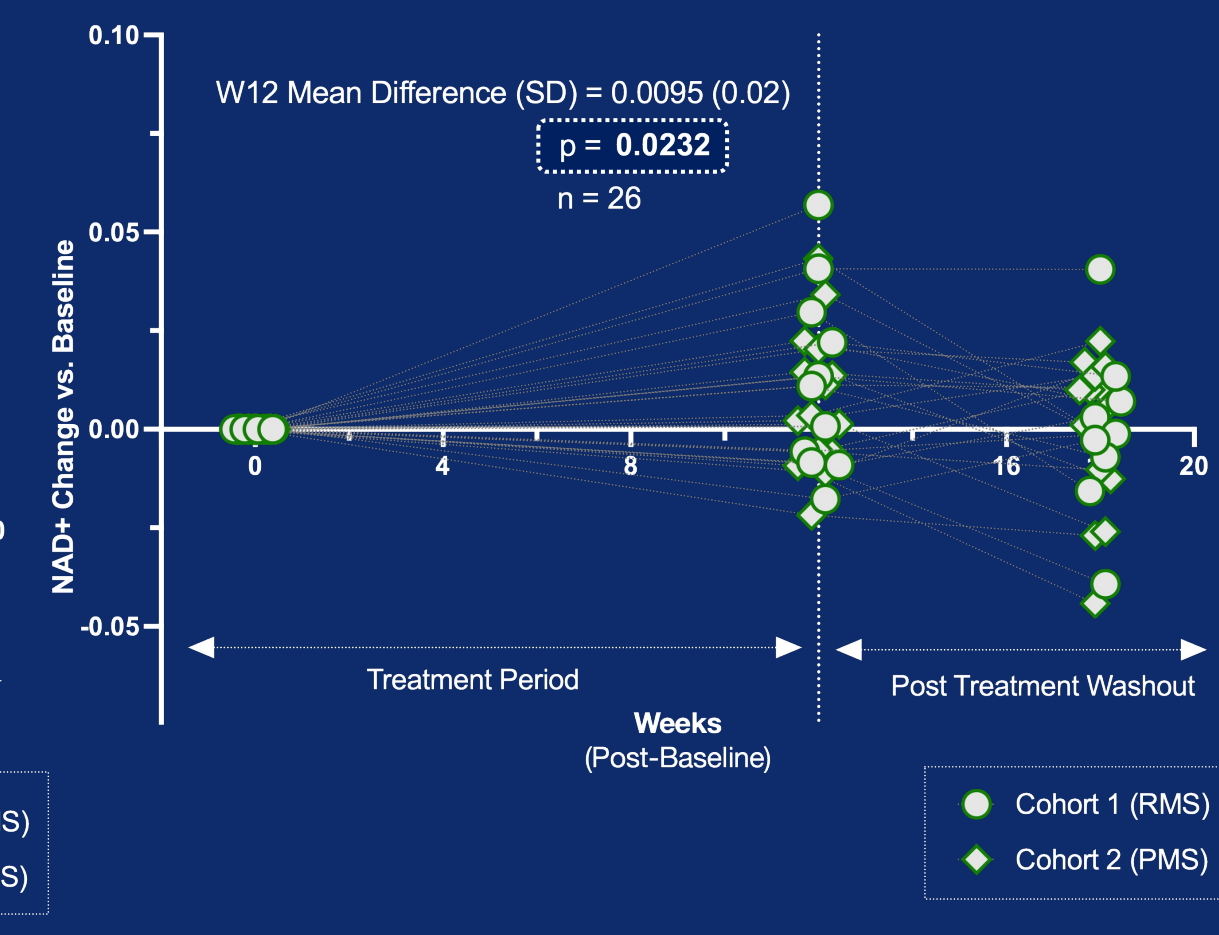
Primary | NAD⁺/NADH Ratio (% Change)

³¹P-MRS Percent (%) Change in Brain NAD⁺/NADH Ratio at End of Treatment
Partial Volume Coil; Ratio of NAD⁺/NADH (% Fraction of NAD⁺, NADH Couple)
REPAIR-MS (Combined Cohorts), Primary Endpoint (Sensitivity)
Participant Percent (%) Change by Visit



Secondary | NAD⁺ % Fraction (Unit Change)

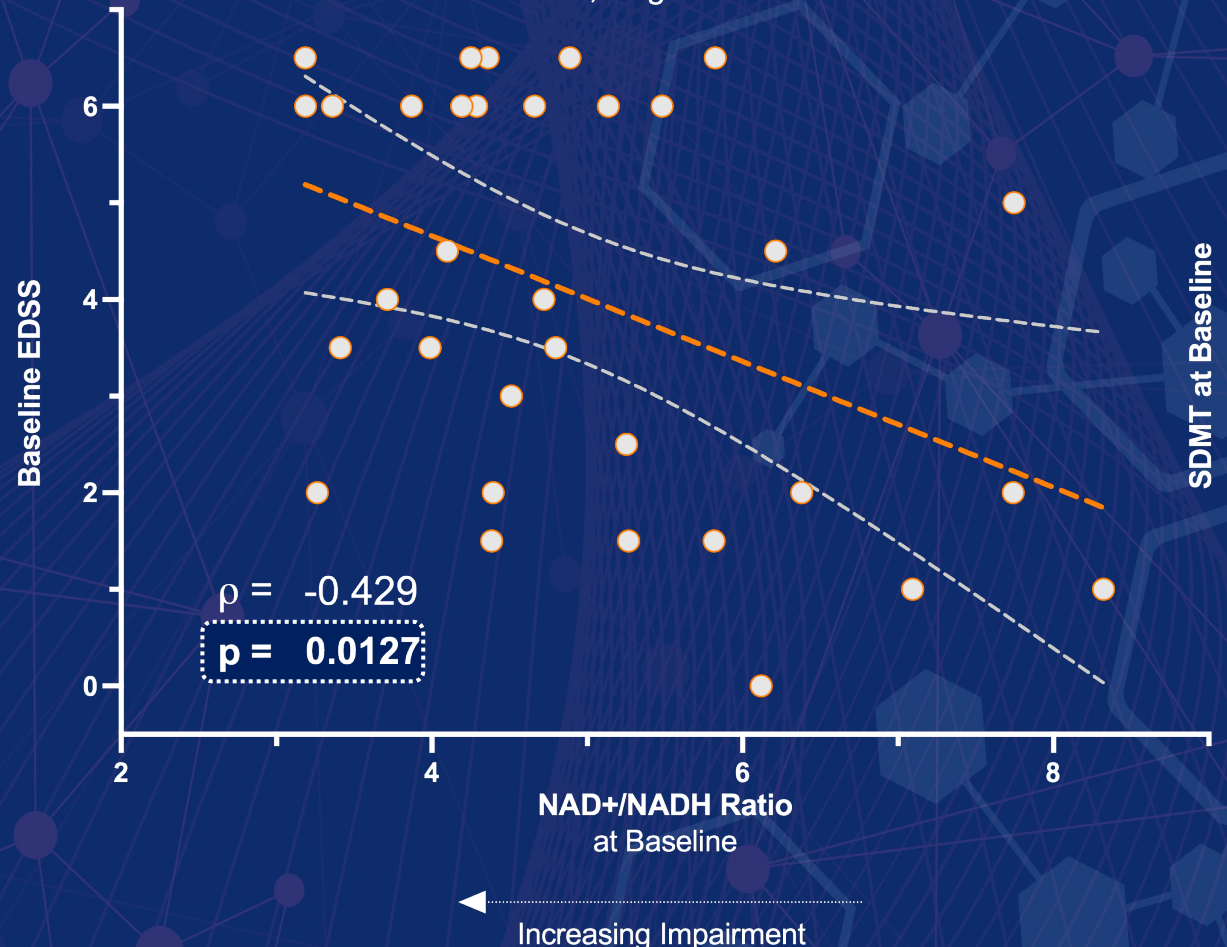
³¹P-MRS Percent Change in Brain NAD⁺ at End of Treatment
Partial Volume Coil; NAD⁺ (% Fraction of NAD⁺, NADH Couple)
REPAIR-MS (Combined Cohorts), Secondary Endpoint
Participant Change by Visit



Impaired Brain Energy Metabolism Correlates with Baseline EDSS and Functional Clinical Scores

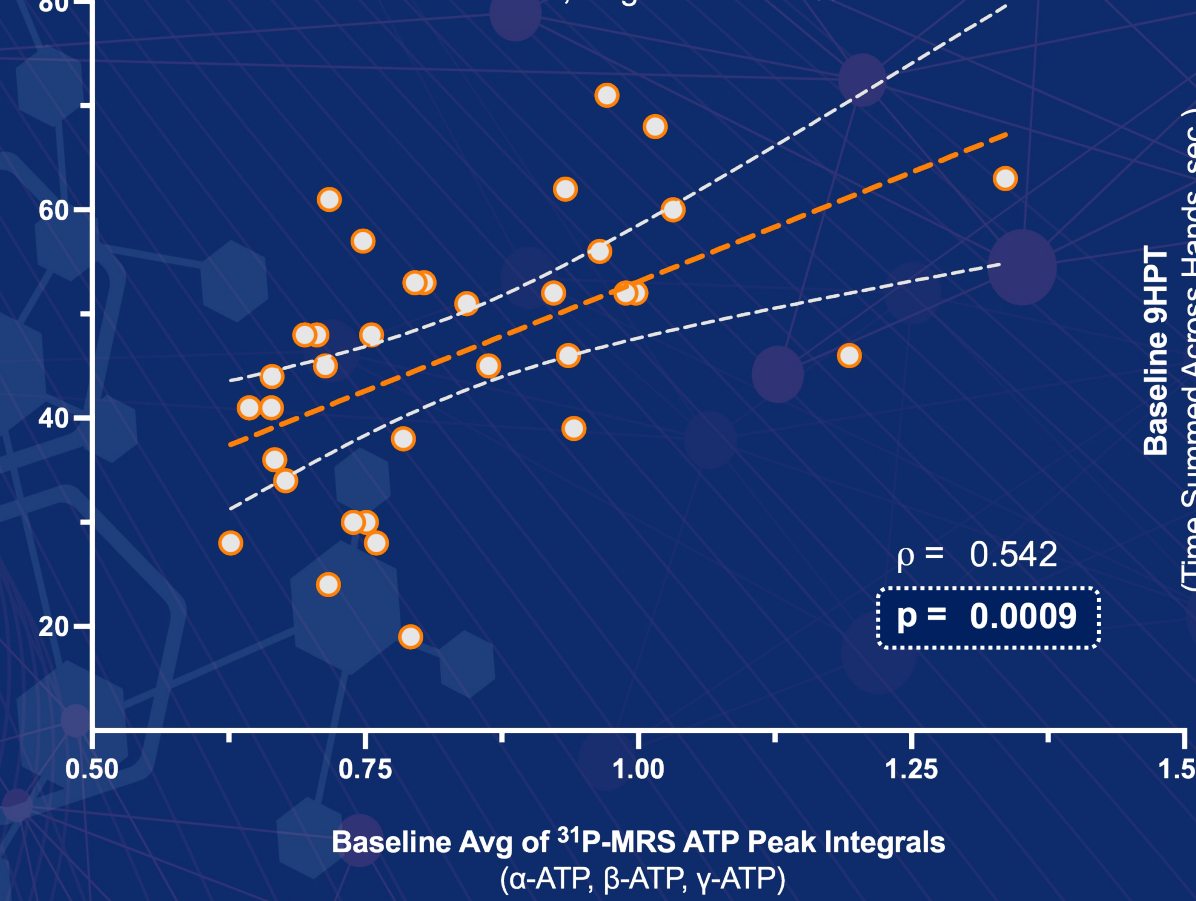
Baseline NAD⁺/NADH vs. EDSS

Baseline ³¹P-MRS NAD⁺/NADH Ratio Correlated with EDSS Severity
Partial Volume Coil; NAD⁺/NADH (Ratio of NADH Couple)
REPAIR-MS (Combined Cohorts)
Pearson Correlation, Regression \pm 95% CI Bounds



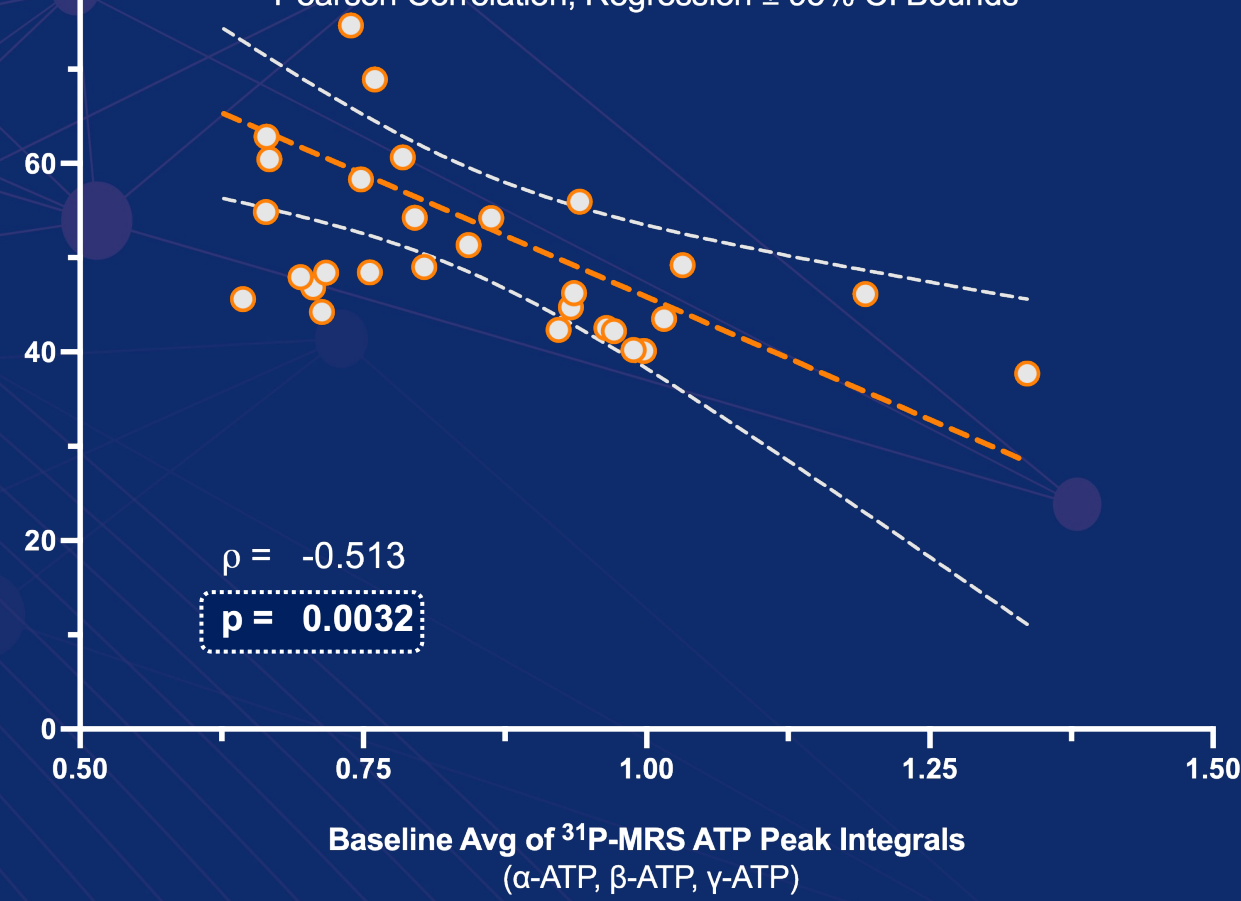
Baseline SDMT vs. Brain ATP Levels

Baseline ³¹P-MRS Whole Brain ATP Levels Correlated with SDMT
Full Volume Coil; Average of Peak Integrals for α -ATP, β -ATP, γ -ATP
REPAIR-MS (Combined Cohorts)
Pearson Correlation, Regression \pm 95% CI Bounds



Baseline 9HPT vs. Brain ATP Levels

Baseline ³¹P-MRS Whole Brain ATP Levels Correlated with 9HPT
Full Volume Coil; Average of Peak Integrals for α -ATP, β -ATP, γ -ATP
REPAIR-MS (Combined Cohorts)
Pearson Correlation, Regression \pm 95% CI Bounds



Safety Findings | REPAIR-MS

- 64 TEAEs were reported in 24 participants (73%)
 - Top 3 most frequently reported TEAEs: headache (15%), COVID-19 (12%), upper respiratory tract infection (9%)
- All TEAEs were assessed as mild-to-moderate severity (100%)
- 2 SAEs occurred in 2 participants (syncope, pneumonia)
- 2 (6%) participants discontinued due to TEAEs; headache (n=1), pneumonia (n=1)
- 1 laboratory safety finding was assessed as related to drug (hypertransaminasaemia, ALT & AST $< 1.5 \times$ ULN), which resolved

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