

Evidence for Brain Energy Metabolic Support with CNM-Au8 Treatment: Results from the REPAIR Phase 2 Clinical Trials



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CONCLUSION: The REPAIR clinical trials demonstrate brain target engagement with CNM-Au8 treatment impacting brain energy metabolic support

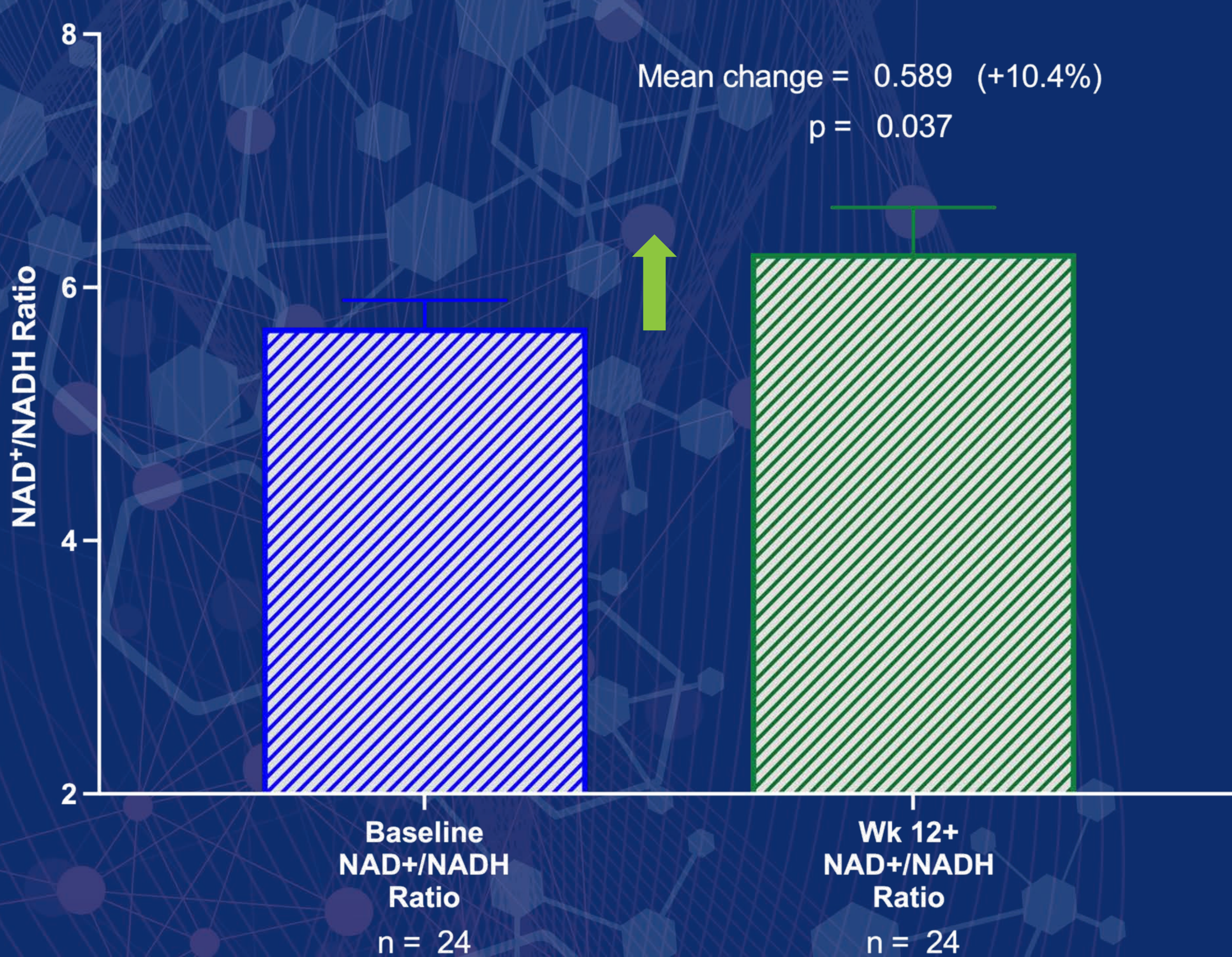
Design Scheme



1° Endpoint | NAD⁺/NADH Change at Week 12¹

REPAIR Integrated Analysis

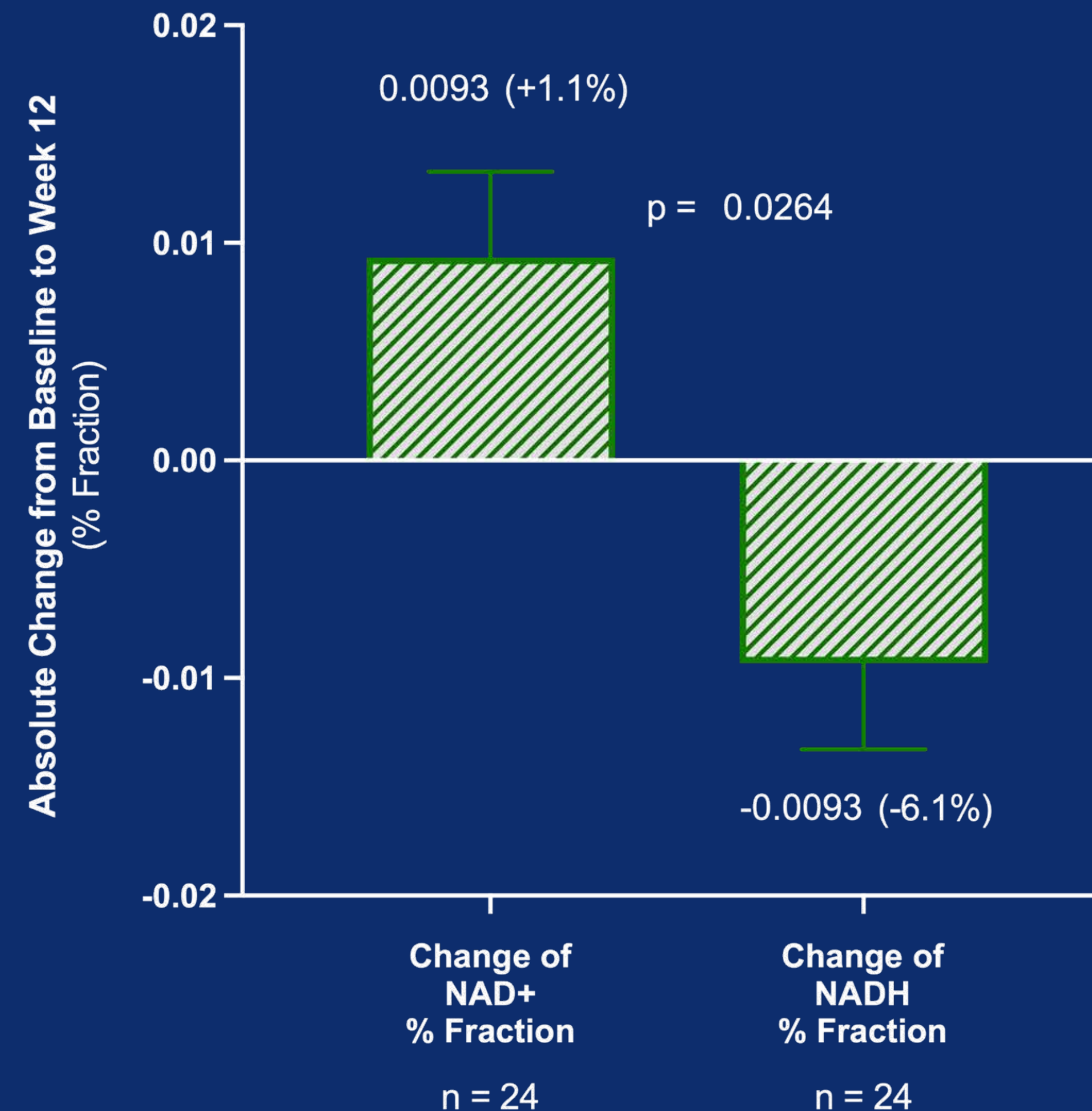
³¹P-MRS Change in Brain NAD⁺/NADH Ratio at End of Treatment
 Partial Volume Coil; Ratio of NAD⁺/NADH (% Fraction of NAD⁺, NADH Couple)
Primary Endpoint, (Paired t-test), Mean ± SEM



2° Endpoint | NAD⁺ & NADH Fraction

REPAIR Integrated Analysis

³¹P-MRS Average Change in Brain NAD & NADH (% Fraction)
 Partial Volume Coil; % Fraction of NAD⁺ and NADH
Secondary Endpoint, Mean ± SEM (Paired t-test)



Objective

Demonstration of CNS target engagement with ³¹P-magnetic resonance spectroscopy (³¹P-MRS)

Design

Open-label, dose blinded 12-week treatment (Enrolled: REPAIR-PD n=13, REPAIR-MS, n=13)

Endpoints

- Primary: change of NAD⁺/NADH ratio based on pre-specified integrated analyses of PD & MS cohorts
- Secondary: change of NAD⁺ and NADH fractions of NAD pool

Safety

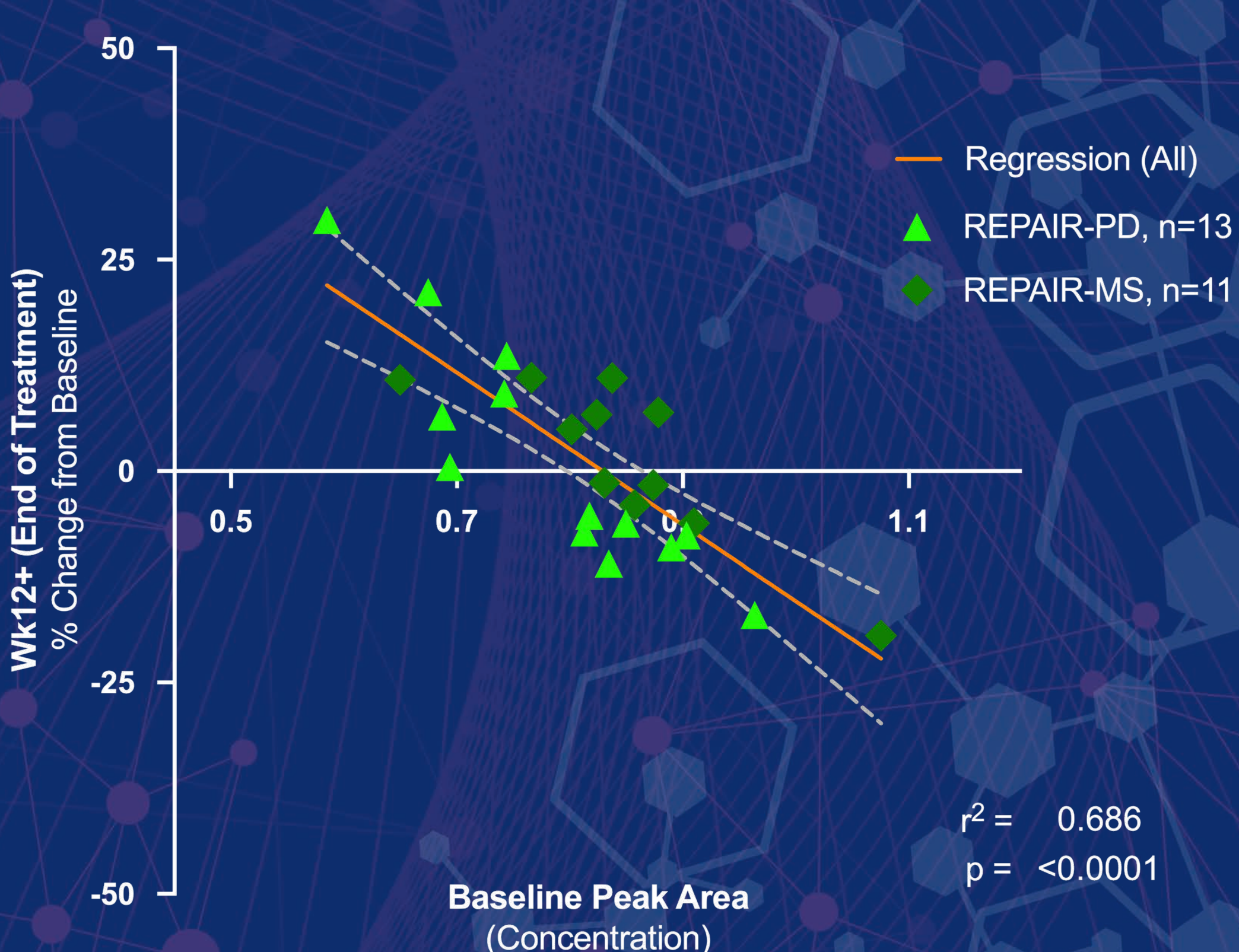
- Well tolerated; 97% treatment compliance
- TEAEs were all mild-to-moderate severity and transient
- No SAEs

¹NAD⁺/NADH ratio declines approximately 0.5% per decade in cross-sectional observational studies

Exploratory | Equilibration of Energetic Metabolites

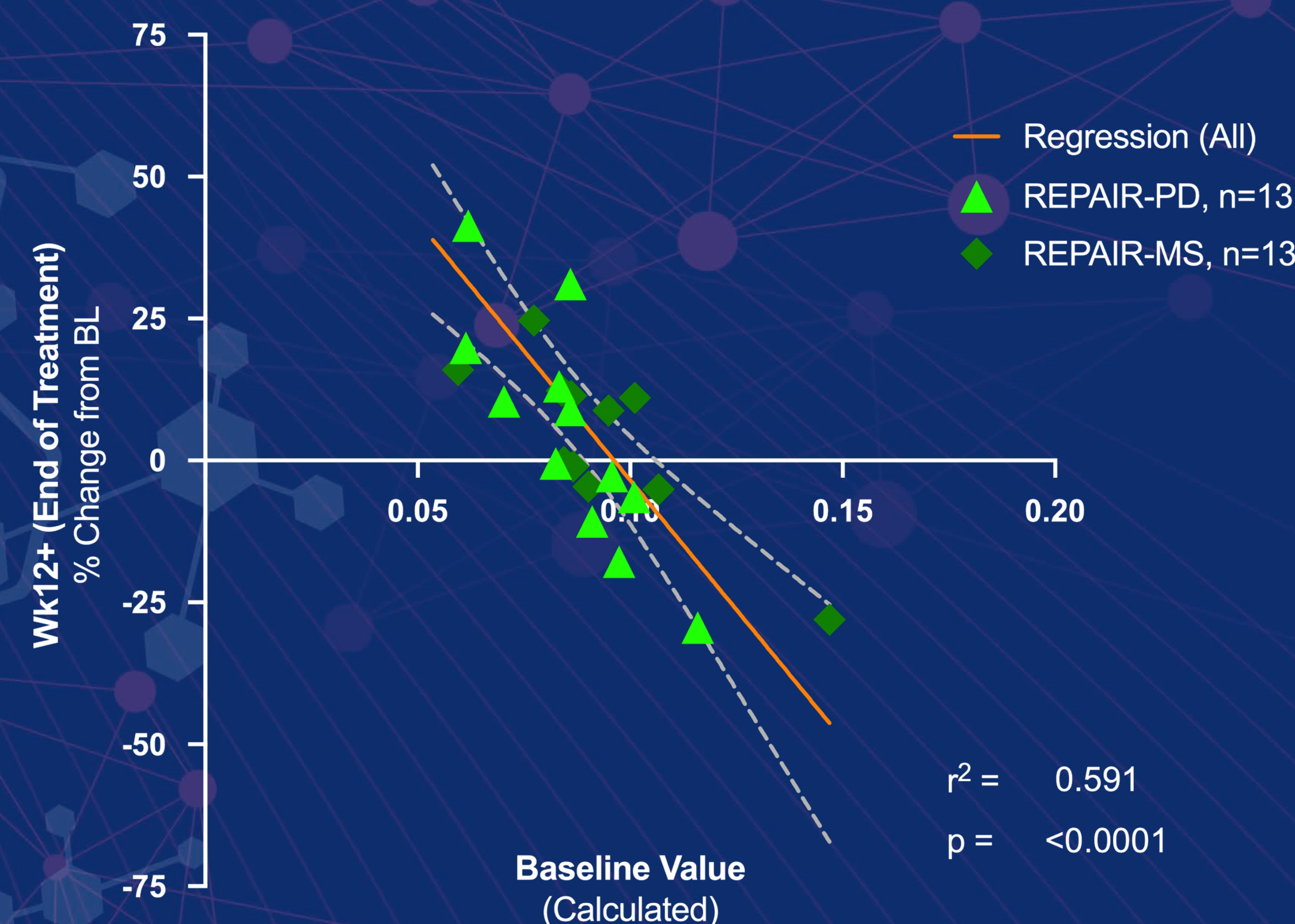
REPAIR Integrated

³¹P-MRS Change in β-ATP at End of Treatment
 Full Volume Coil ³¹P Signal Area (Integral)
 Percent (%) Change vs. Baseline Value



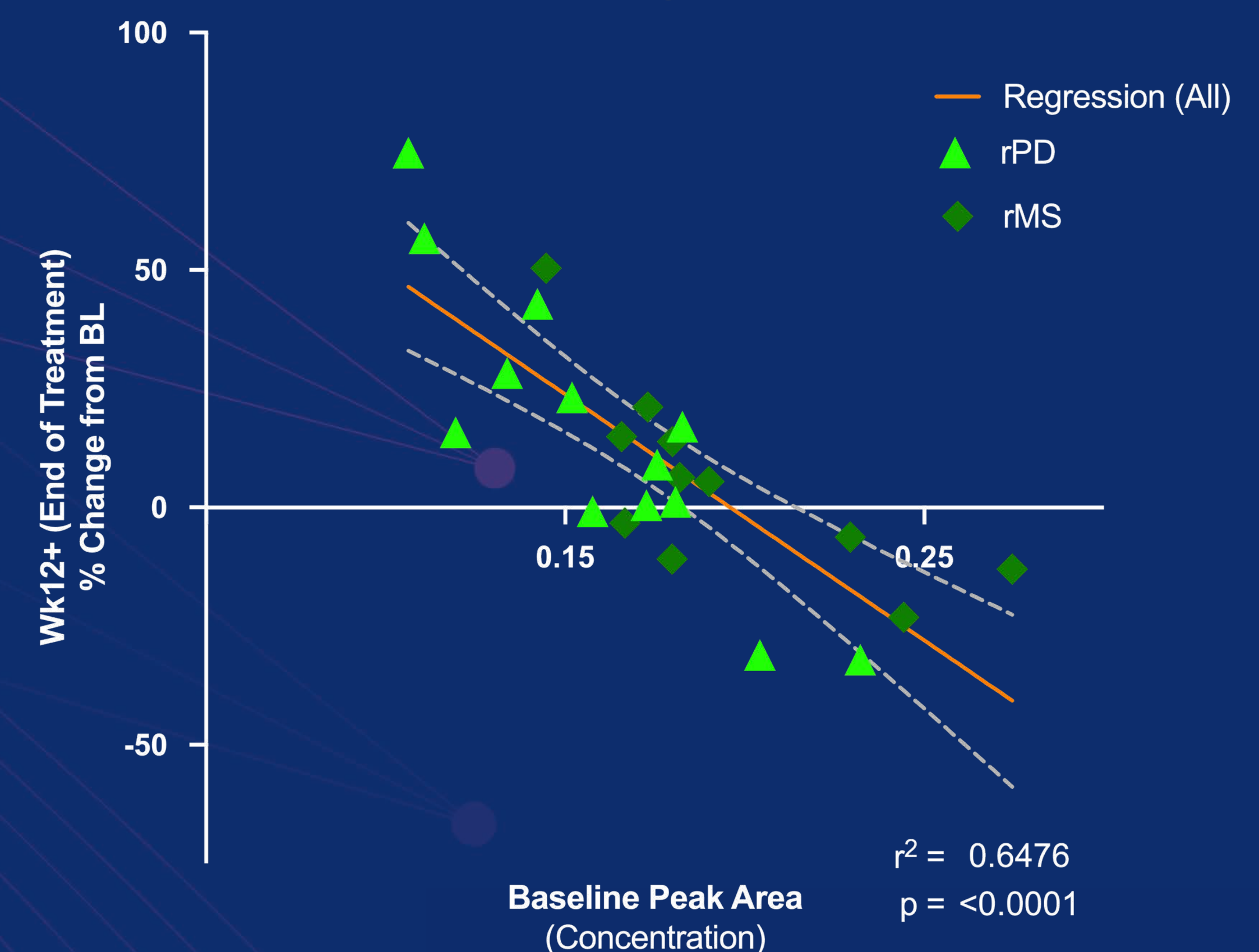
REPAIR Integrated

³¹P-MRS Change in Phosphorylation Potential at End of Treatment
 Full Volume Coil ³¹P Signal Area (β-ATP, Pi^(m))
 β-ATP/ADP * Intracellular Phosphate [Pi^(m)]
 Percent (%) Change from Baseline to End of Study



REPAIR Integrated

³¹P-MRS Change in Phosphocholine (PC) at End of Study
 Full Volume Coil ³¹P Signal Area (Integral)
 Percent % change vs. BL value



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