

SUPPLEMENTAL MATERIAL

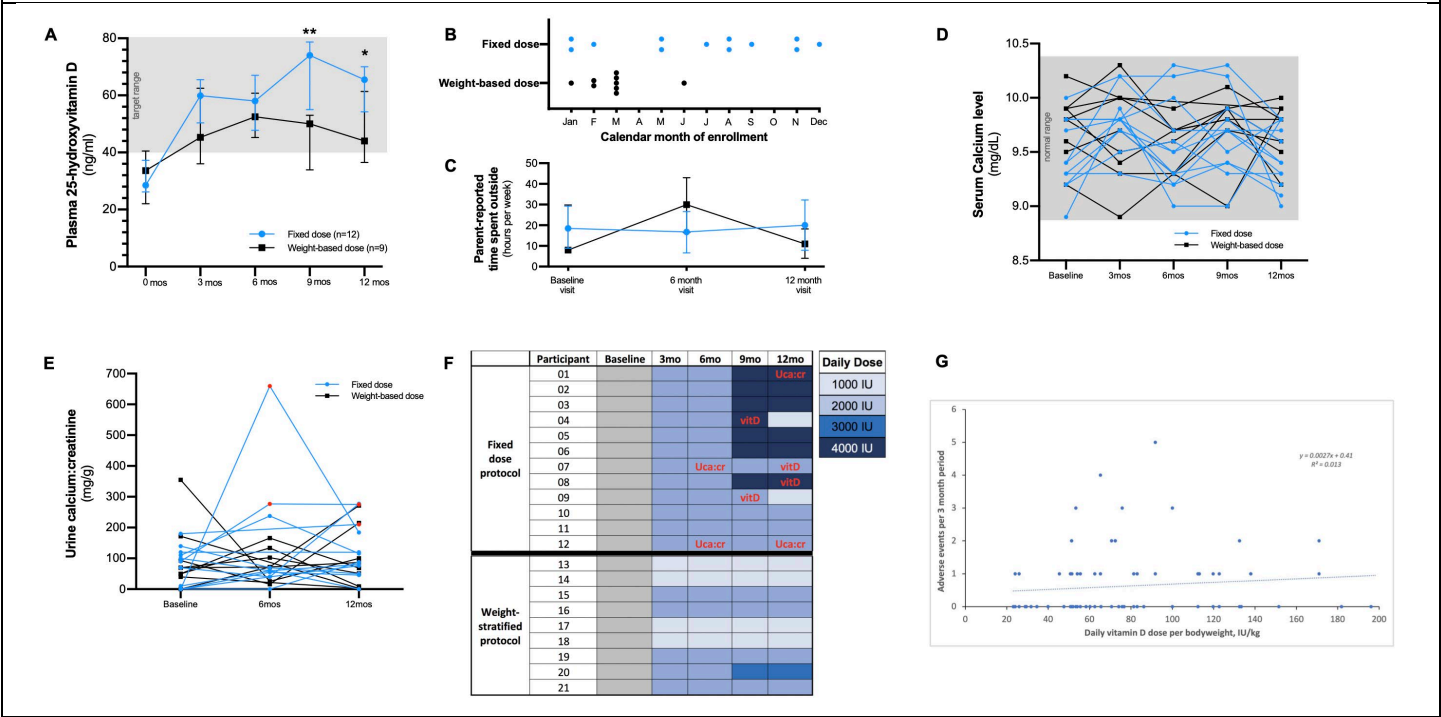
eTables:

eTable: Prescription and over-the-counter supplements at baseline and added during the study period		
	Baseline (unchanged through study)	Added during study
<i>Over-the-counter supplements</i>		
Multivitamin	5	0
Vitamin D supplement	2	0*
Omega-3 fatty acid supplement	2	1
Probiotic	2	1
Lorenzo's Oil	2	0
Cannabidiol	1	0
Walnut oil	1	0
N-acetyl cysteine	1	0
Vitamin C	0	1
<i>Prescription medications</i>		
Corticosteroid	11	1
Anti-depressant	3	0
Allergy/asthma medication	1	1
*no participants added vitamin D to their regimens except as specified within our study dosing protocol		

eFigures:

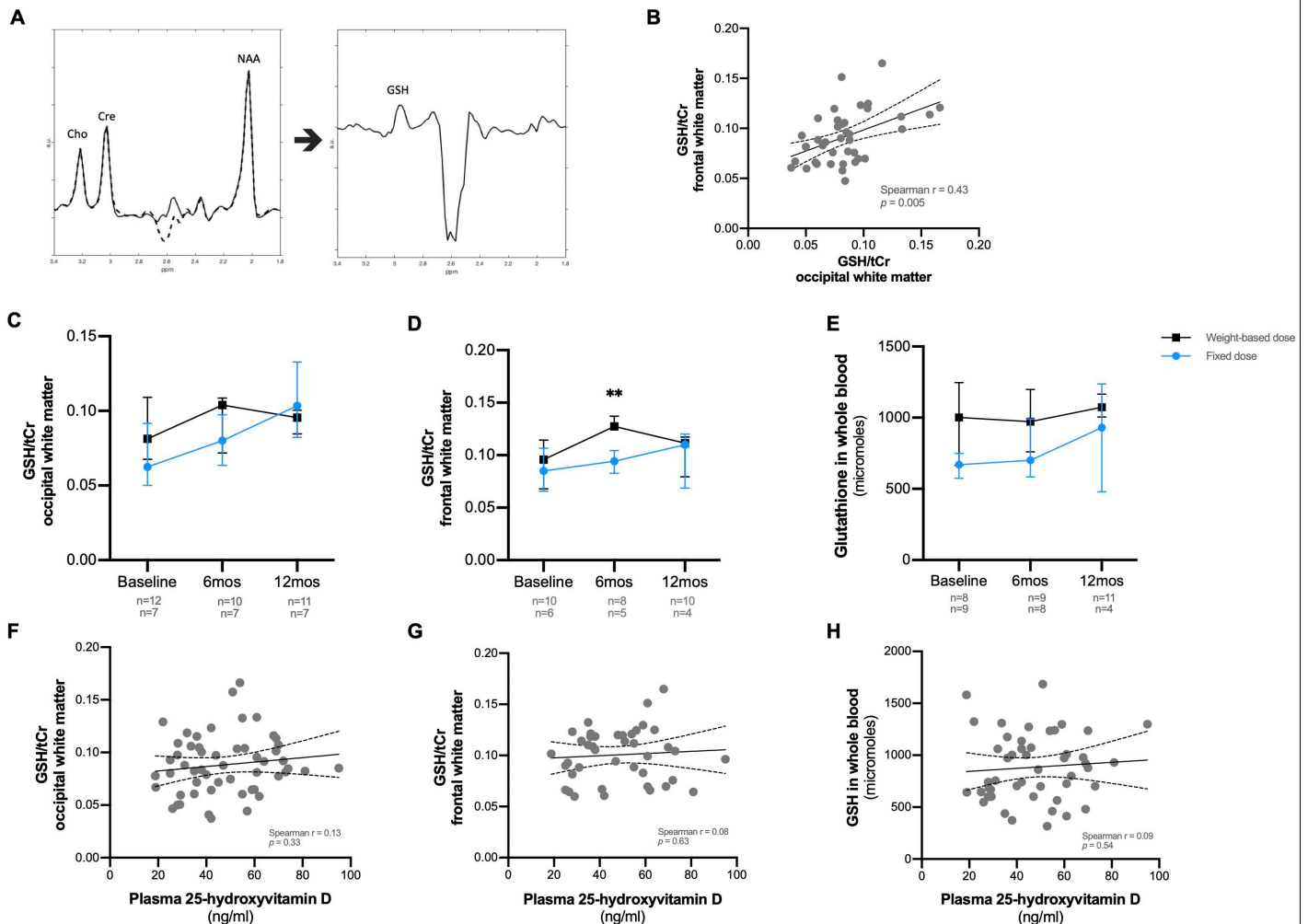
eFigure 1: Supplemental data relevant to pharmacokinetics and adverse events.

Median vitamin D levels were higher at 9-months and 12-months among participants allocated to Fixed-dose regimen (A). Most participants in the weight-stratified cohort were enrolled in the first quarter of 2019 (B). This enrollment pattern yielded a corresponding imbalance in time spent outdoors for the weight-stratified cohort (C). All patients maintained normal serum calcium levels throughout the study (D). Normal ranges for urine calcium:creatinine levels vary by age, but were elevated in three patients at four time points (red dots) (E). Laboratory threshold violations are shown according to patient, regimen, and dose where daily dose is indicated by cell color and red font indicates threshold violation for either plasma 25-hydroxyvitamin D level (vitD) or spot urine calcium:creatinine (Uca:cr); no laboratory threshold violations were observed among participants in the weight-stratified dosing regimen (F). A post-hoc analysis of participants in both dosing arms did not show a significant correlation between daily dose and adverse events (G).



eFigure 2: Supplemental data relevant to biomarkers.

MEGA-PRESS acquired spectra with editing on (dotted line) and editing off (solid line) are shown alongside the edited spectrum which delineates the GSH peak at 2.95 ppm (A). Measures of glutathione in frontal white matter correlated with measures in occipital white matter (B). Glutathione levels followed similar trajectories in the Fixed dose and Weight-based dosing groups. In a post-hoc analysis, GSH measures were similar between dosing groups in occipital white matter (C) and blood (E), differing between groups only within the frontal white matter and only at the 6-month timepoint (D). GSH/tCr ratios in the brain blood did not correlate with plasma vitamin D levels (F,G, H). Figures C, G, H, I display all available data. In Figures C, D, E median (dot) and interquartile range (bars) are shown.



Study Protocol and Statistical Analysis Plan:

eSAP: Our study protocol and statistical analysis plan is included for reference.