Science in the Service of Medicine

Unique Targets.
Novel Mechanisms.
New Medicines.

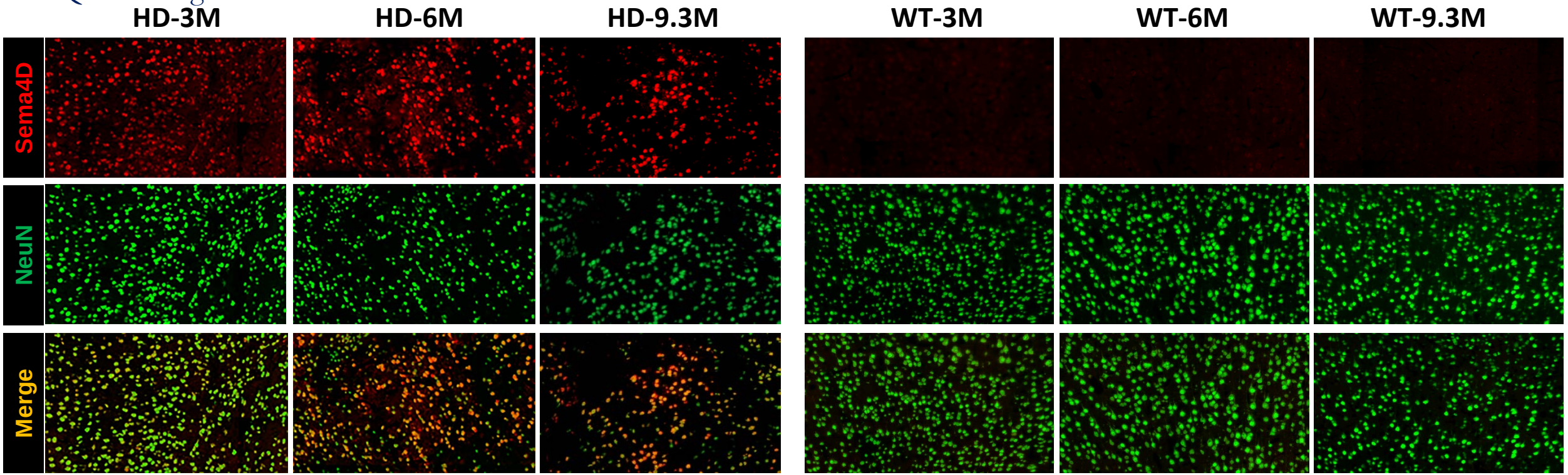
Learnings from SIGNAL Phase 2 Study

Forward Looking Statement

To the extent that statements contained in this presentation are not descriptions of historical facts regarding Vaccinex, Inc. (“Vaccinex,” “we,” “us,” or “our”), they are forward-looking statements reflecting management’s current beliefs and expectations. Such statements include, but are not limited to, statements about our plans, expectations and objectives with respect to the results and timing of our Phase 2 SIGNAL trial of pepinemab (VX15/2503) in Huntington’s disease and other clinical trials, the use and potential benefits of pepinemab in Huntington’s disease and other indications, and other statements identified by words such as “may,” “will,” “appears,” “expect,” “anticipate,” “estimate,” “intend,” “hypothesis,” “potential,” “advance,” and similar expressions or their negatives (as well as other words and expressions referencing future events, conditions, or circumstances). Forward-looking statements involve substantial risks and uncertainties that could cause the outcome of our research and pre-clinical development programs, clinical development programs, future results, performance, or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, uncertainties inherent in the execution, cost and completion of preclinical and clinical trials, uncertainties related to regulatory approval, risks related to our dependence on our lead product candidate pepinemab, the impact of the COVID-19 pandemic, and other matters that could affect our development plans or the commercial potential of our product candidates. Except as required by law, we assume no obligation to update these forward-looking statements. For a further discussion of these and other factors that could cause future results to differ materially from any forward-looking statement, see the section titled “Risk Factors” in our periodic reports filed with the Securities and Exchange Commission (“SEC”) and the other risks and uncertainties described in our Form 10-K dated March 9, 2020 and subsequent filings with the SEC.

SEMA4D is progressively upregulated in NeuN+ neurons of HD mice

Q175 transgenic mouse model of HD

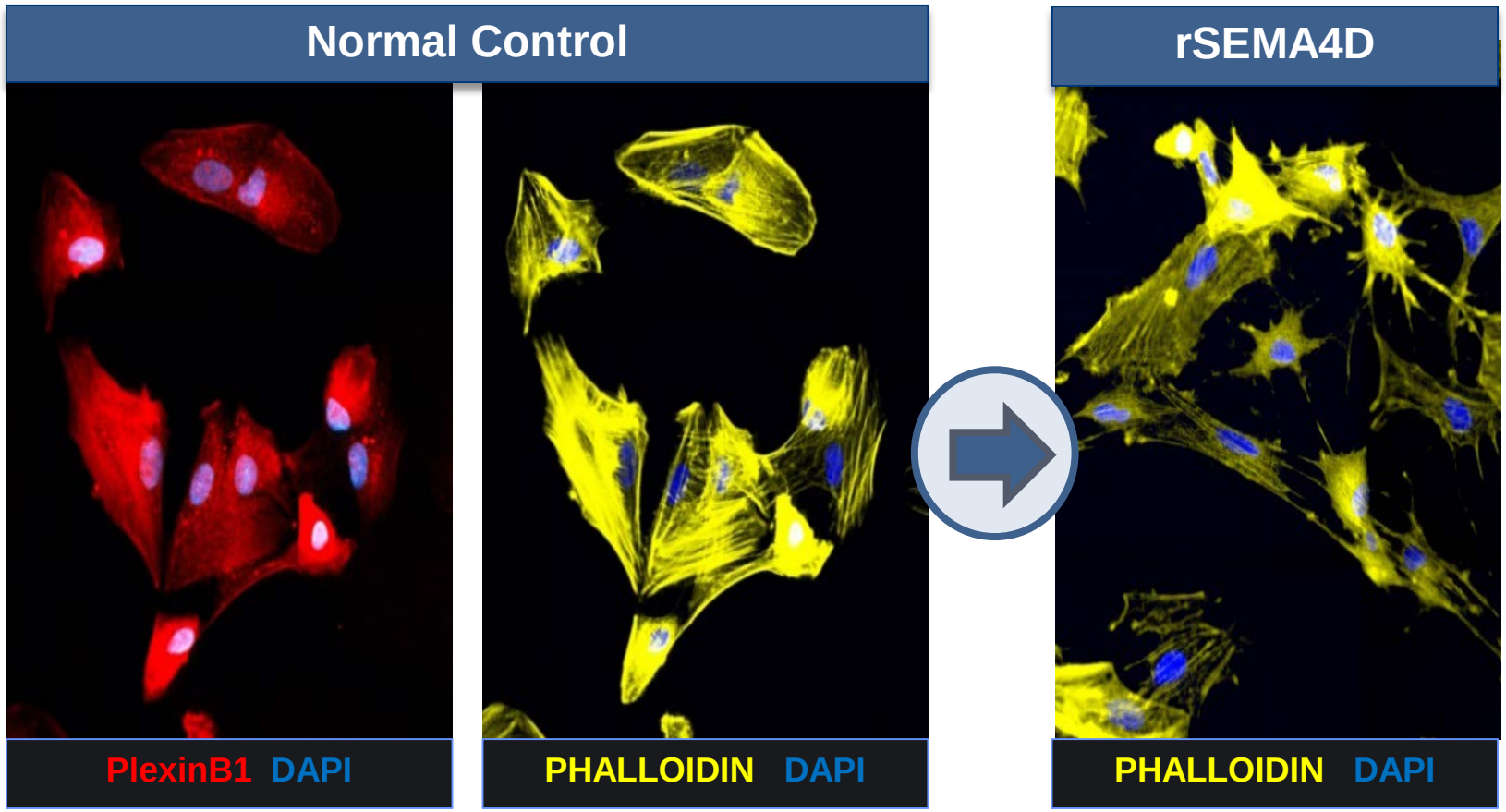


- **SEMA4D expression is upregulated in HD mice as disease progresses, compared to low expression in WT control.**
  - SEMA4D is upregulated early in disease, prior to onset of symptoms, which occurs ~ 5 months of age in Q175 HD transgenic mice.
- **SEMA4D co-localizes with NeuN+ neurons.**

NeuN/Sema staining of retrosplenial cortex region of Q175 knock-in mouse model of HD and age-matched wild type (WT) littermate controls. Representative images are shown from analysis of 3 mice/time-point. M = months of age.

SEMA4D triggers collapse of actin cytoskeleton in astrocytes

A



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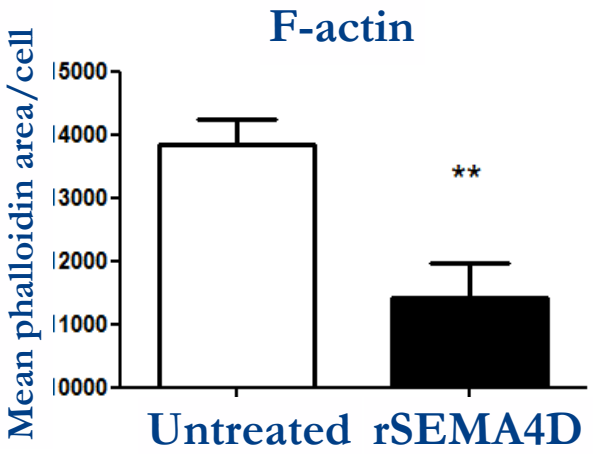
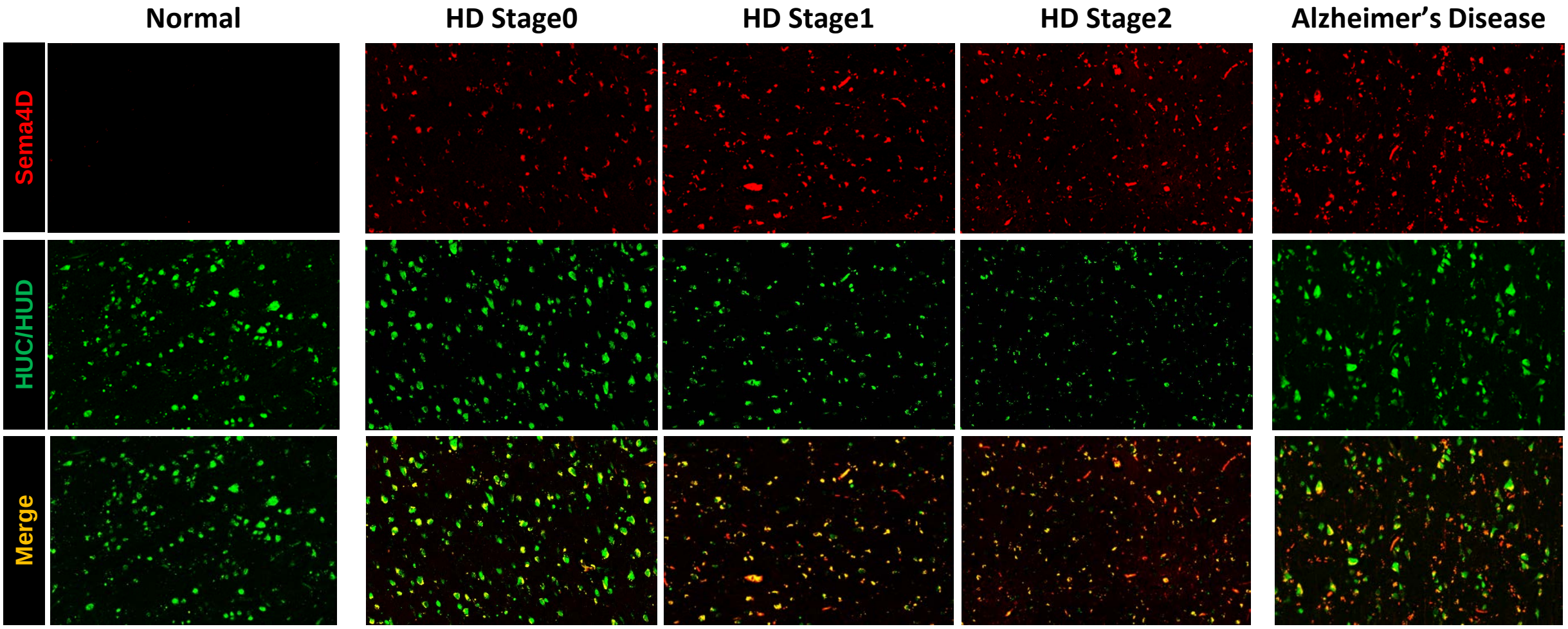
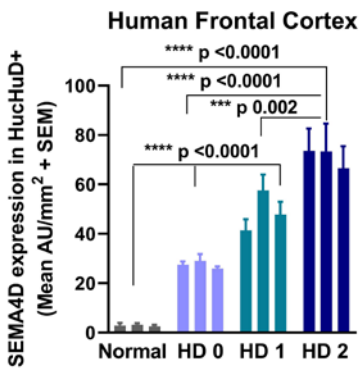
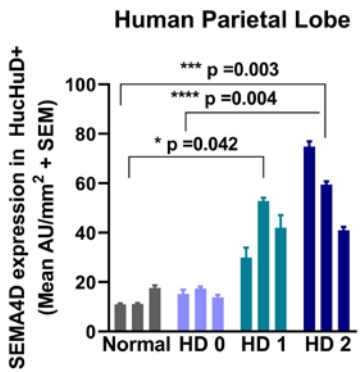
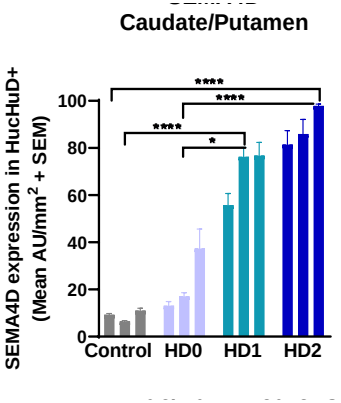
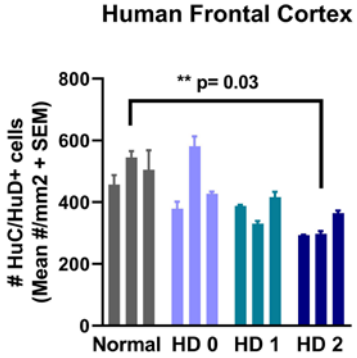
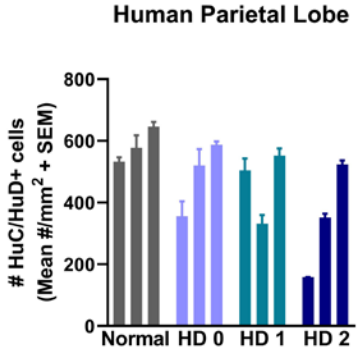
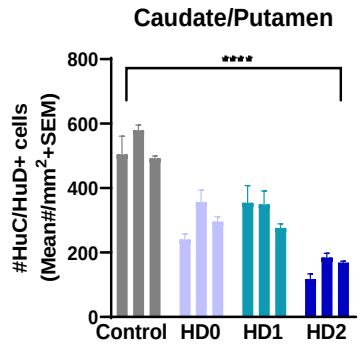
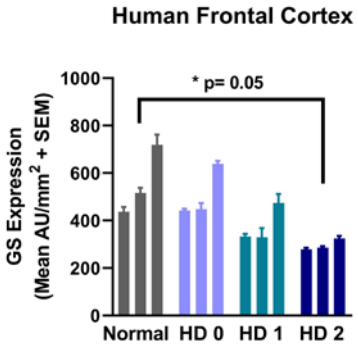
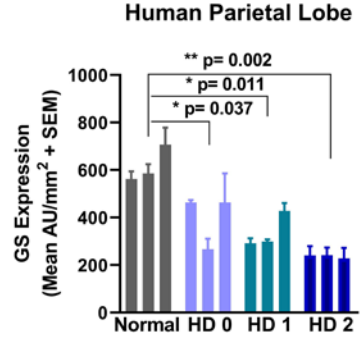
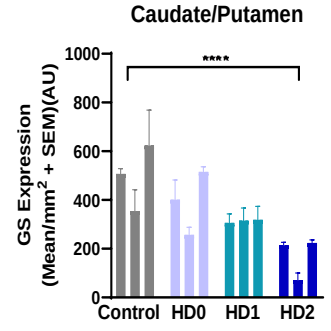


SEMA4D is upregulated in neurons during Human HD and AD disease progression

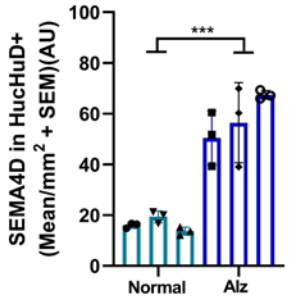
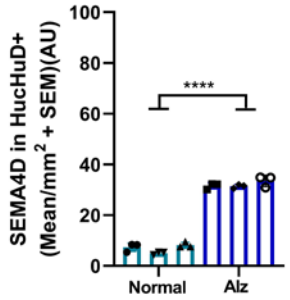
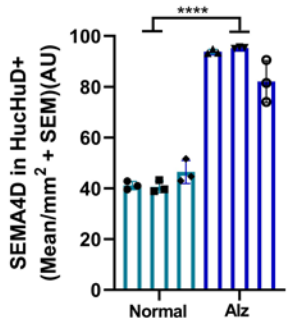
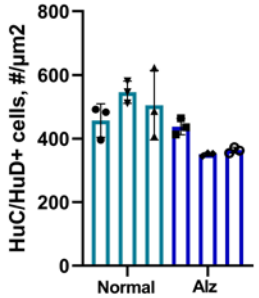
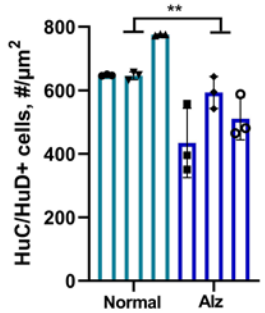
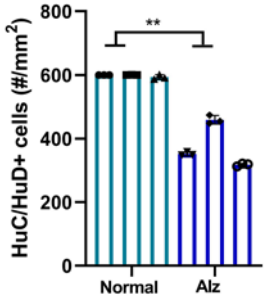
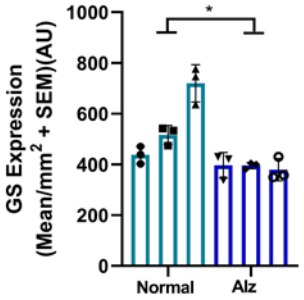
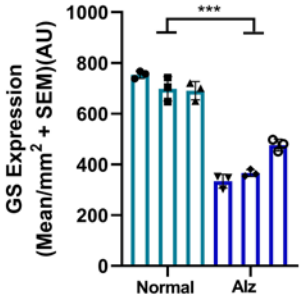
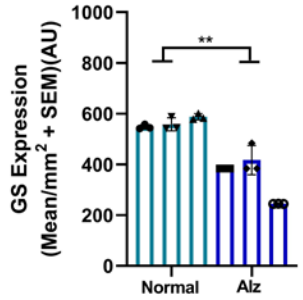
Frontal Lobe



SEMA4D Expression is Increased and Neuronal Survival is Reduced During HD Progression: Glutamine Synthetase, a marker of normal astrocyte function, is progressively reduced

	Frontal Cortex	Parietal Lobe	Striatum
SEMA4D in Neurons			
HuC/HuD+ Neurons			
Glutamine Synthetase			

SEMA4D Expression is Increased and Neuronal Survival is Reduced During Alzheimer's Progression

	Frontal Cortex	Temporal Lobe	Thalamus
SEMA4D in Neurons			
HuC/HuD+ Neurons			
Glutamine Synthetase			

wcg™ Statistics•Collaborative

SIGNAL (VX15-2503-N-131)

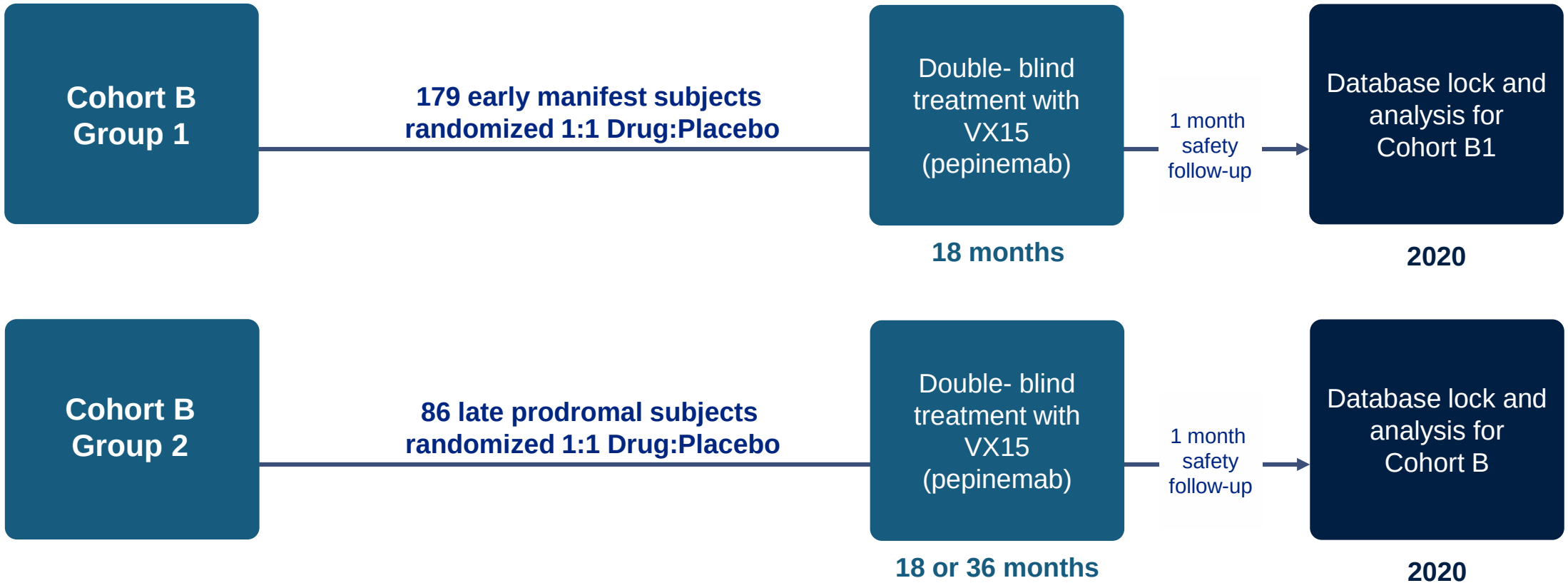
Cohort B Results

HUNTINGTON STUDY • GROUP

seeking treatments that make a difference

VACCINEX

Clinical Trial Design

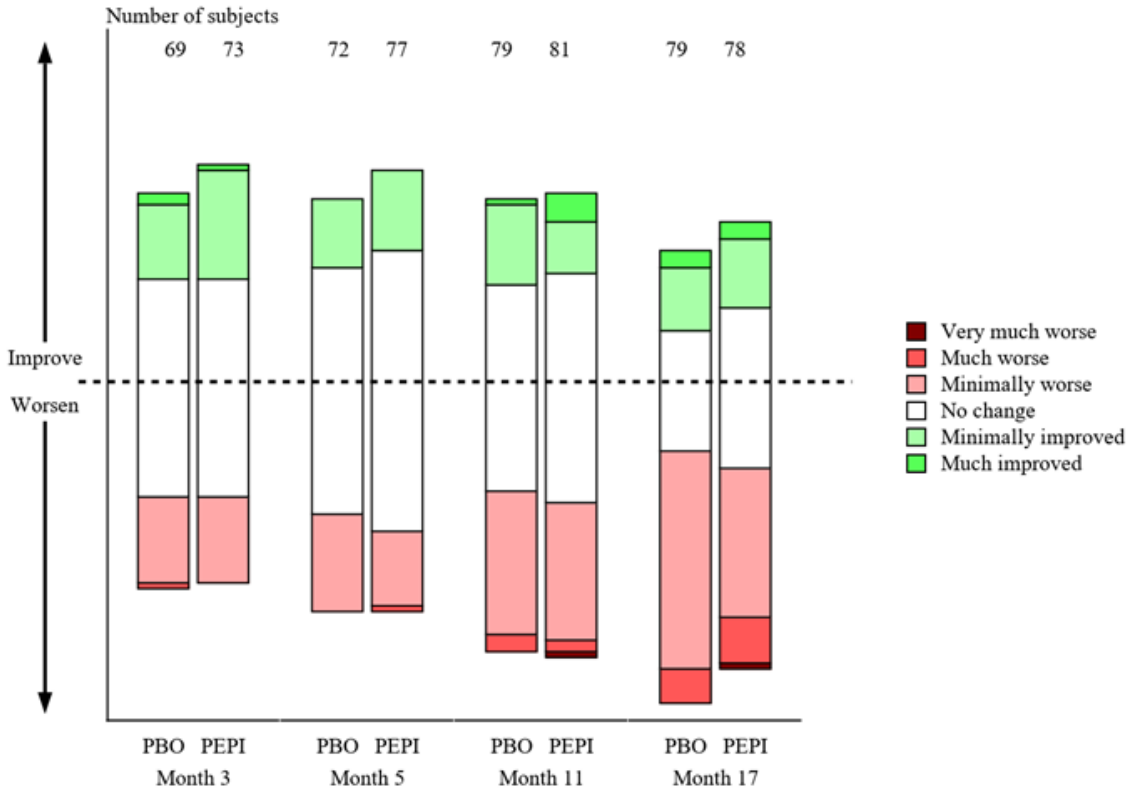


Abbreviated Baseline Characteristics - ITT Population

	Cohort B1 (N=179)		Cohort B2 (N=86)	
	PBO (N=88)	**PEPI (N=91)**	**PBO (N=45)**	**PEPI (N=41)**
Discontinued Treatment Early	10	13	2	0
Had Any SAE (*)	8	4	4	2
Had Any Grade 3+ AE (*)	14	17	6	8
CAG repeat length	44.1 (3.8)	43.5 (3.1)	42.8 (2.3)	42.4 (2.7)
CAP score (**)	470 (96)	466 (85)	374 (72)	404 (98)
UHDRS-DCL at screening, n(%)				
0,1 –Normal or non-specific signs	0	0	0	0
2 – May be HD (50%-89% confident)	0	0	31 (69%)	29 (71%)
3 – Likely HD (90%-98% confident	0	0	14 (31%)	12 (29%)
4 –Unequivocal HD (>99% confident)	88 (100%)	91 (100%)	0	0

*pre-COVID era; **CAP score = age×(CAG repeat length – 33.66)

Clinical Global Impression of Change - CGIC
Post-hoc Categorical analysis– Early Manifest (Cohort B1)



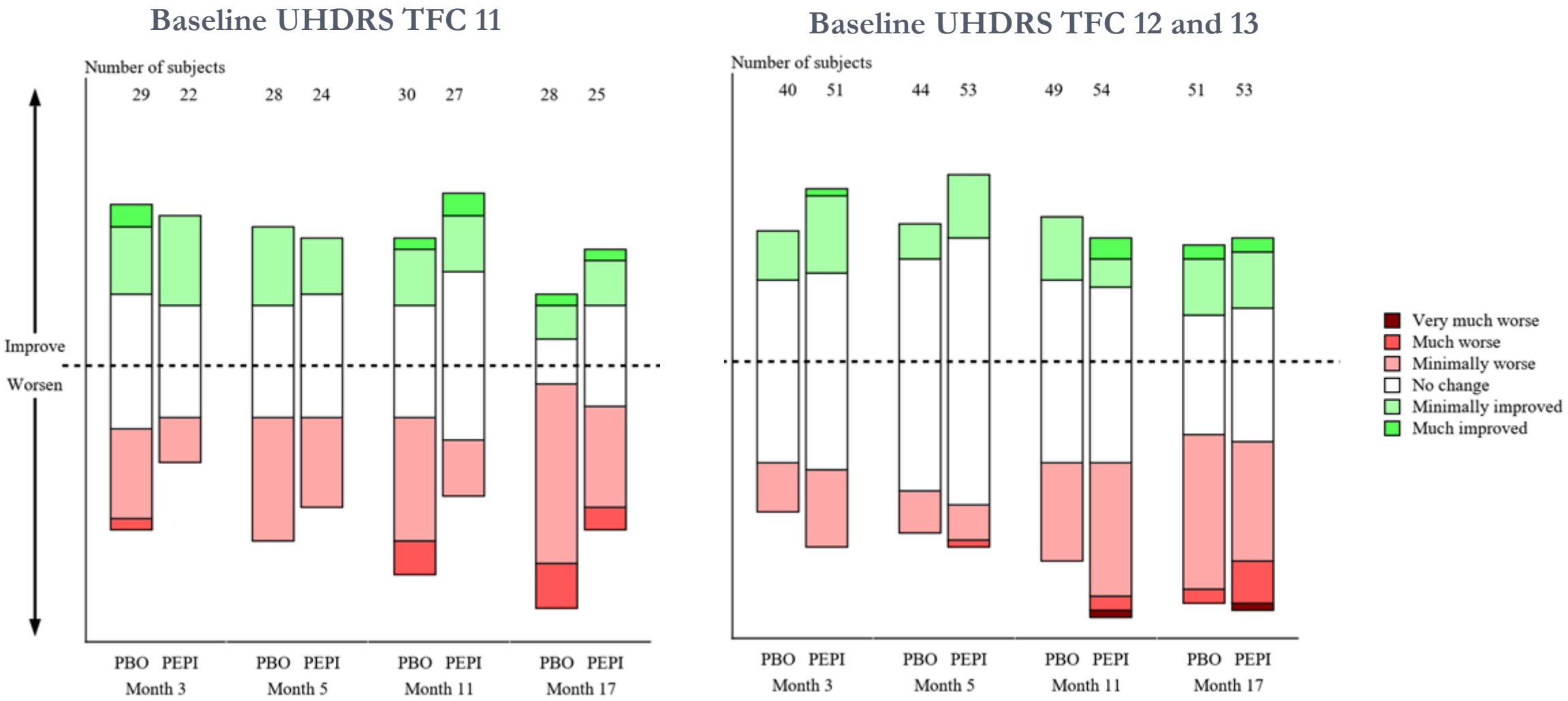
Abbreviations: CGIC=Clinical Global Impression of Change; mITT=modified intent-to-treat; PBO=placebo; PEPI=pepinemab;
Note(s): Figure inclues all subjects in CGIC population.
The sample sizes are the number of subjects in the CGIC population with non-missing data at the specified visit.
A seven-point Likert scale, ranging from very much worse (-3) to very much improved (+3).
Values are set to -3 following deaths judged by a Blinded Data Review Committee to be related to HD.

Month 17 categories	**Placebo** N=79	**Pepinemab** N=78
3—Very much improved	0	0
2—Much improved	3 (4%)	3 (4%)
1—Minimally improved	11 (14%)	12 (15%)
0—Not changed	21 (27%)	28 (36%)
-1—Minimally worse	**38** (48%)	**26** (33%)
-2—Much worse	**6** (8)%	**8** (10%)
-3—Very much worse	0	**1** (1%)
-1 to -3	**56%**	**45%**

nominal one-sided p= 0.12

Fisher's exact test for worsening score. Note that SAP proposed to evaluate change from baseline as a continuous variable, but CGIC is a categorical variable that is normally evaluated by Chi square or Fisher's exact test..

Clinical Global Impression of Change - CGIC
Post-hoc Subgroup Analysis– Early Manifest



Clinical Global Impression of Change - CGIC
Post-hoc Subgroup Analysis– Early Manifest

TFC 11

Month 17 categories	**Placebo** N=28	**Pepinemab** N=25
3—Very much improved	0	0
2—Much improved	1 (4%)	1 (4%)
1—Minimally improved	3 (11%)	4 (16%)
0—Not changed	4 (14%)	9 (36%)
-1—Minimally worse	**16** (57%)	**9** (36%)
-2—Much worse	**4** (14%)	**2** (8%)
-3—Very much worse	0	**0**
-1 to -3	**71%**	**44%**

nominal one-sided p= 0.041

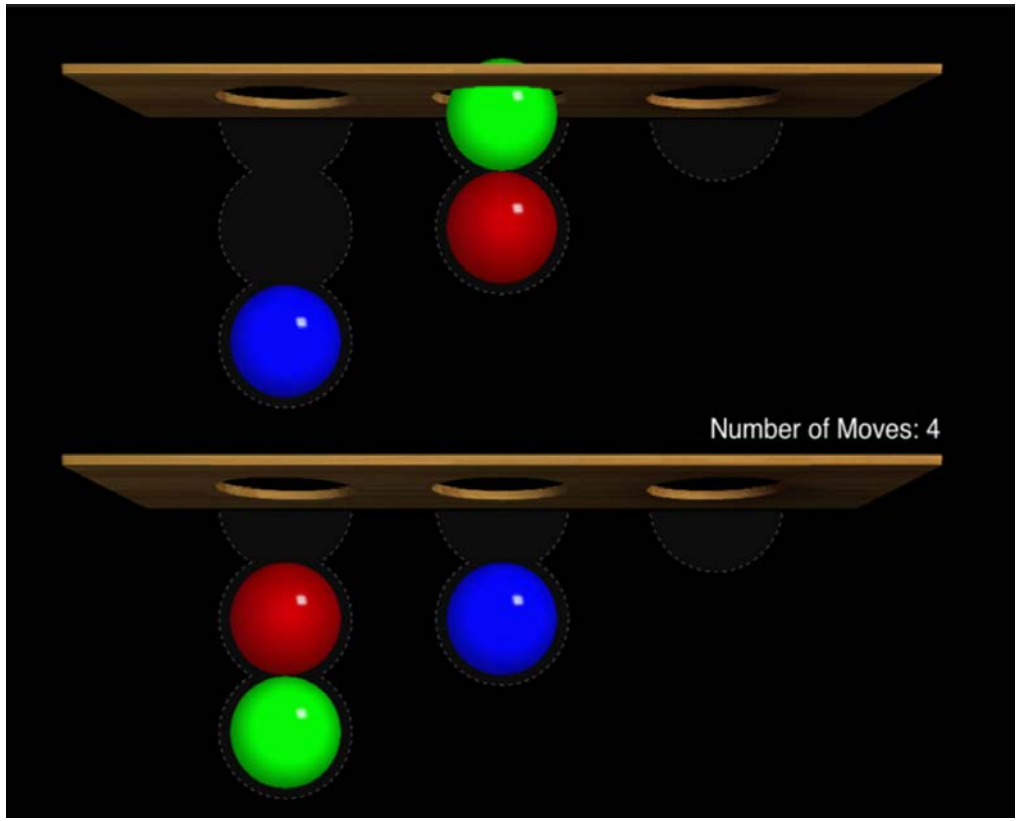
Fisher's exact test for worsening score

TFC 12-13

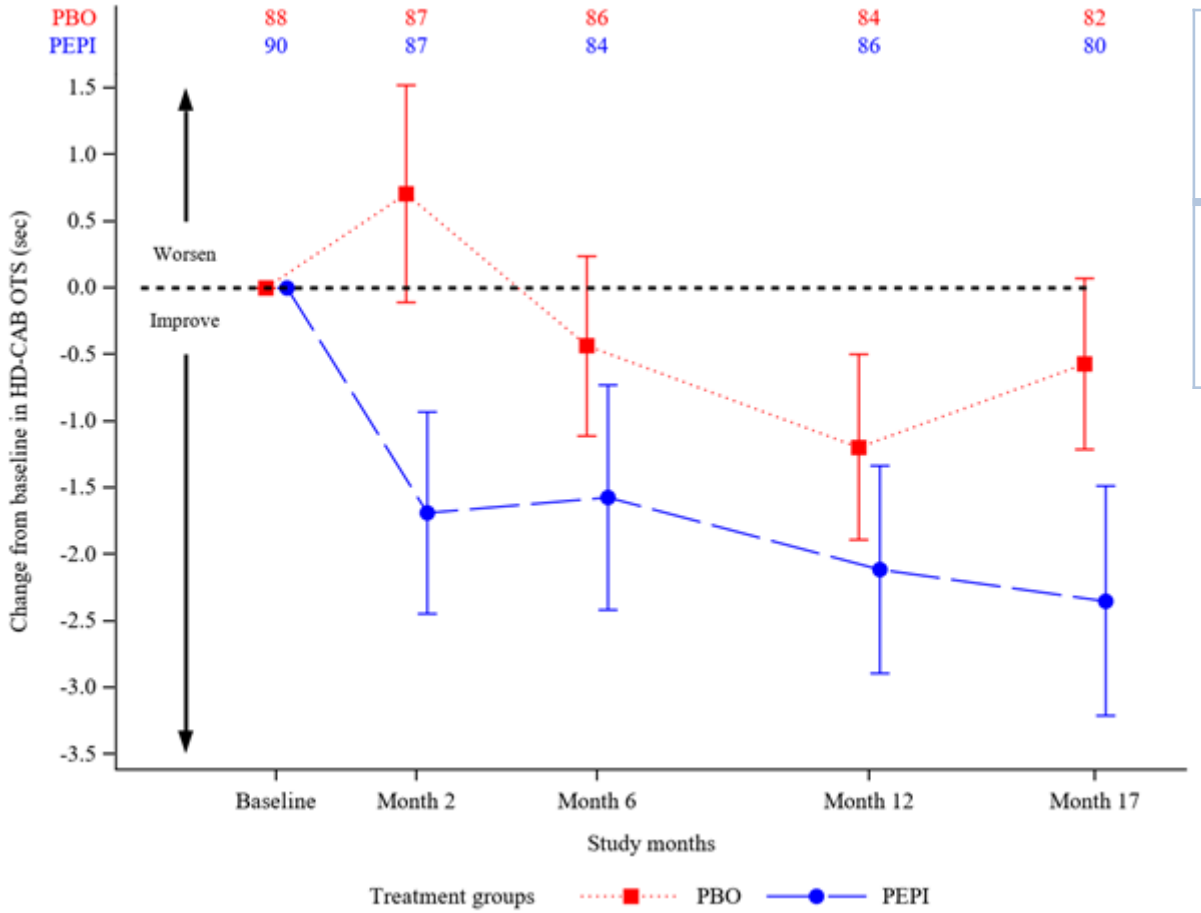
Month 17 categories	**Placebo** N=51	**Pepinemab** N=53
3—Very much improved	0	0
2—Much improved	2 (4%)	2 (4%)
1—Minimally improved	8 (16%)	8 (15%)
0—Not changed	17 (33%)	19 (36%)
-1—Minimally worse	**22** (43%)	**17** (32%)
-2—Much worse	**2** (4%)	**6** (11%)
-3—Very much worse	0	1 (2%)
-1 to -3	**47%**	**45%**

nominal one-sided p= no difference

OTS Assessment of Executive Function – Planning and Memory



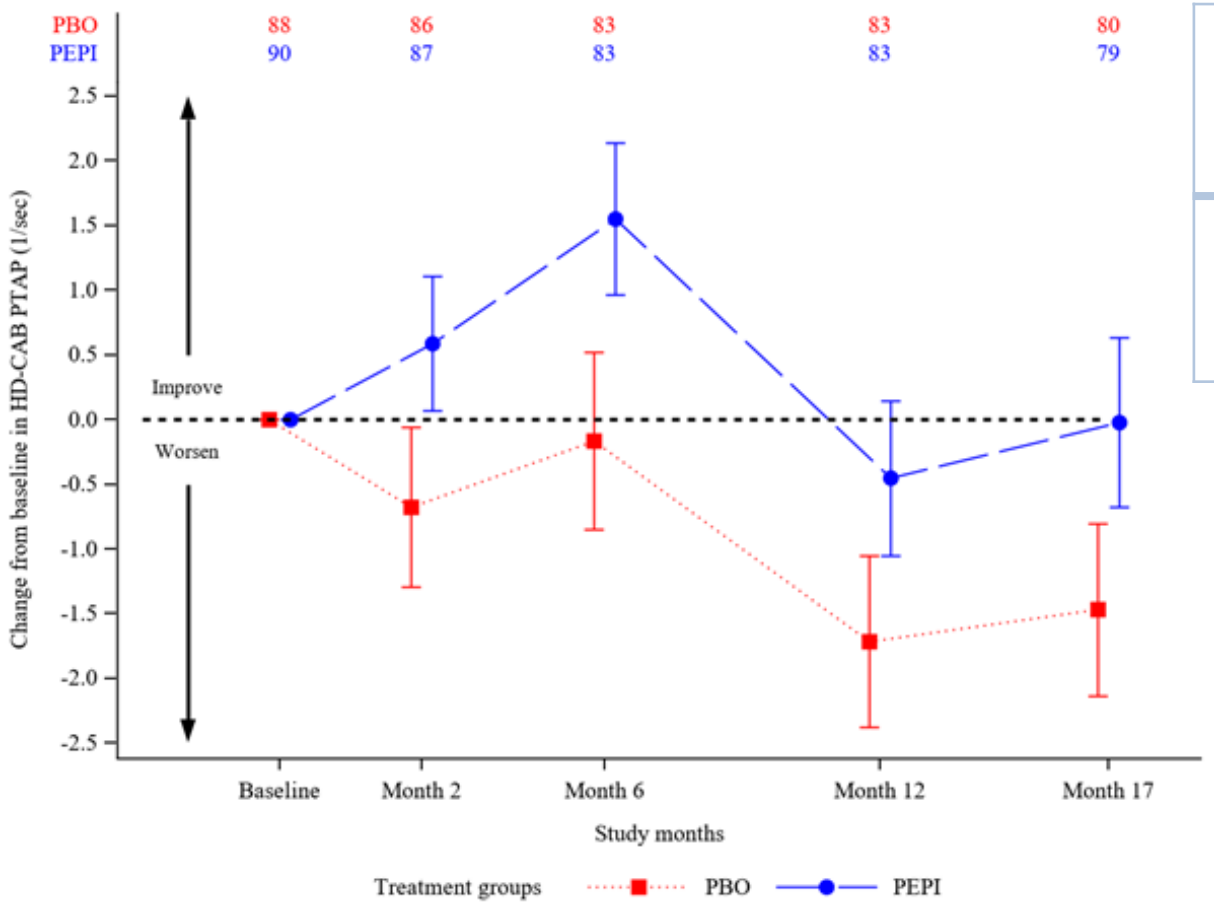
One Touch Stockings (OTS) – Cohort B1
Co-Primary 2a: Cognitive Assessment



One-sided p-value	Favors PEPI	Success [Critical value]
0.028	Yes	No [0.025] [0.0125]

Difference (PEPI – PBO)
Change from Baseline at Month 17 (95% CI) = -1.98 (-4.00, 0.05)

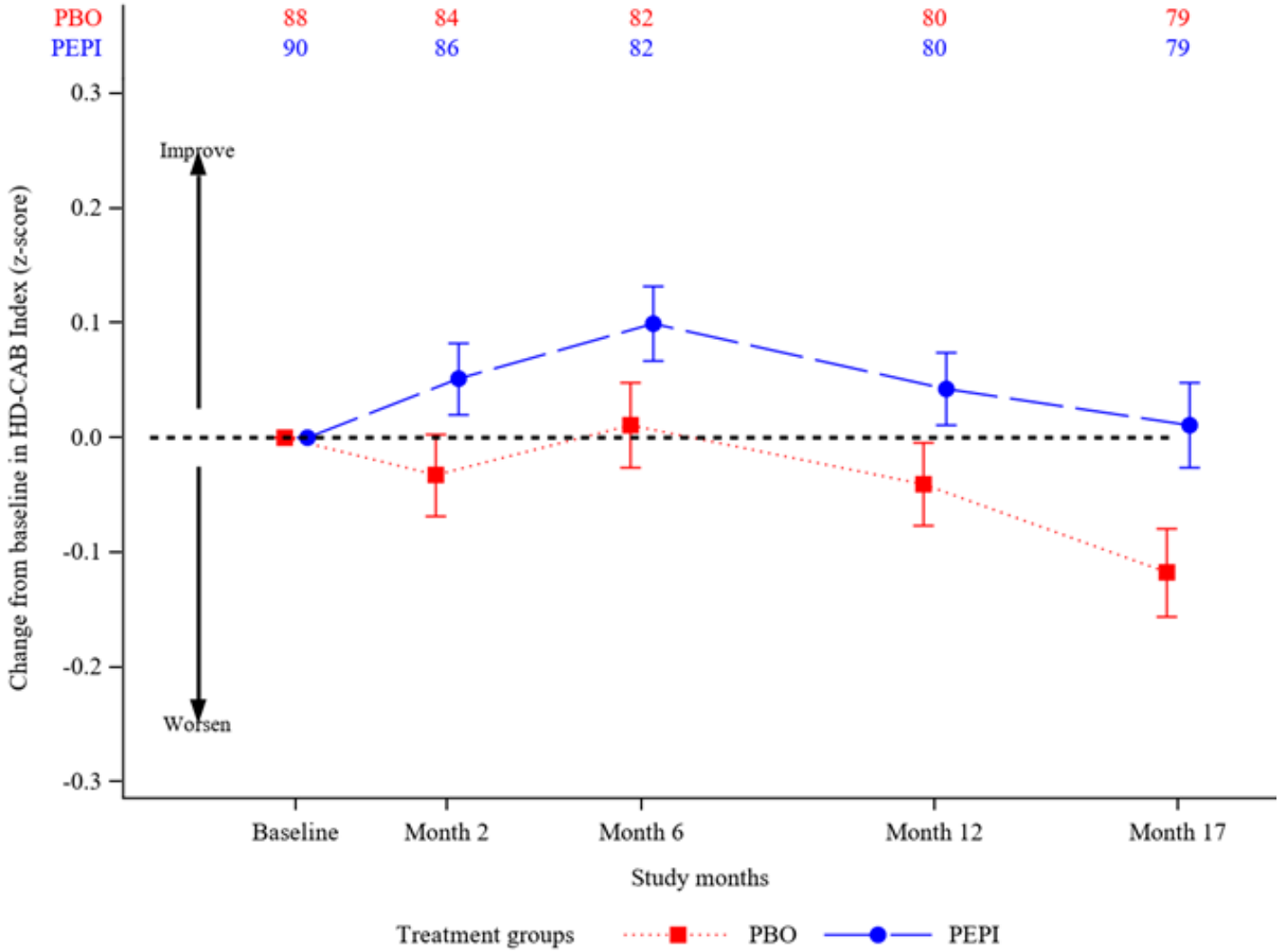
Paced Tapping (PTAP) – Cohort B1
Co-Primary 2b: Cognitive Assessment



One-sided p-value	Favors PEPI	Success [Critical value]
0.06	Yes	No [0.025] [0.0125]

Difference (PEPI – PBO)
Change from Baseline at Month 17 (95% CI) = 1.43 (-0.37, 3.23)

Post-hoc analysis of HD-CAB Index – Cohort B1



One-sided p-value	Favors PEPI	Critical value
0.007	Yes	Yes [0.025]

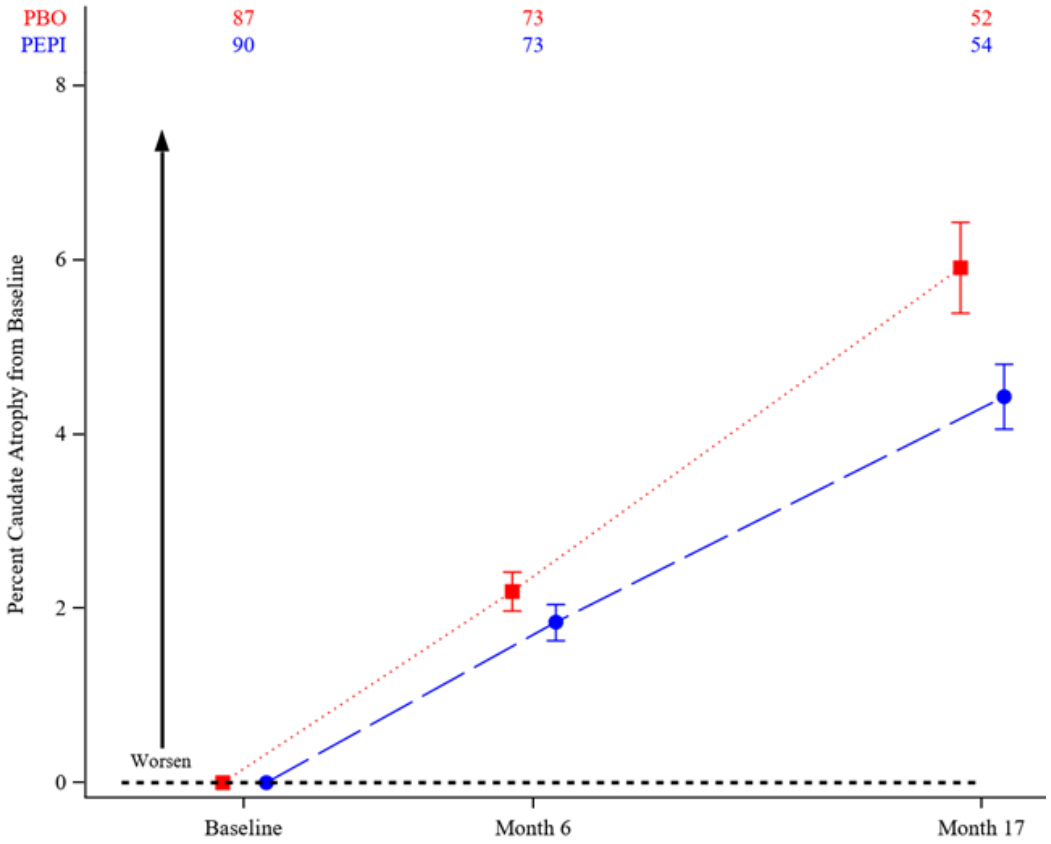
Baseline to Month 17 Analysis for HD-CAB with MMRM: Cohort B1 mITT Population

	PBO		PEPI		Difference, PEPI - PBO	
Population / Parameter	**N[a]**	**Mean (SE)**	**N[a]**	**Mean (SE)**	**Estimate (95% CI)**	**One-Sided p-value (+ Favors PEPI)[b]**
Cohort B1 mITT (N=178)	88		90			
OTS (sec)[c]	88	-0.33 (0.72)	89	-2.30 (0.73)	-1.98 (-4.00, 0.05)	0.028 (+)
PTAP (1/sec)[d]	87	-1.67 (0.65)	89	-0.24 (0.64)	1.43 (-0.37, 3.23)	0.060 (+)
SDMT[e]	88	-3.59 (0.70)	89	-2.97 (0.71)	0.62 (-1.35, 2.59)	0.27 (+)
EMO[f]	88	-0.09 (0.33)	89	0.28 (0.33)	0.37 (-0.55, 1.30)	0.22 (+)
HVLT-R[g]	88	0.21 (0.73)	89	0.65 (0.73)	0.44 (-1.59, 2.47)	0.34 (+)
TMT-B (sec)[h]	88	8.27 (4.24)	89	1.06 (4.26)	-7.21 (-19.09, 4.66)	0.12 (+)
HD-CAB Index (Cohort B1 reference)[i]	**87**	**-0.12 (0.04)**	**89**	**0.01 (0.04)**	**0.13 (0.03, 0.23)**	**0.007 (+)**

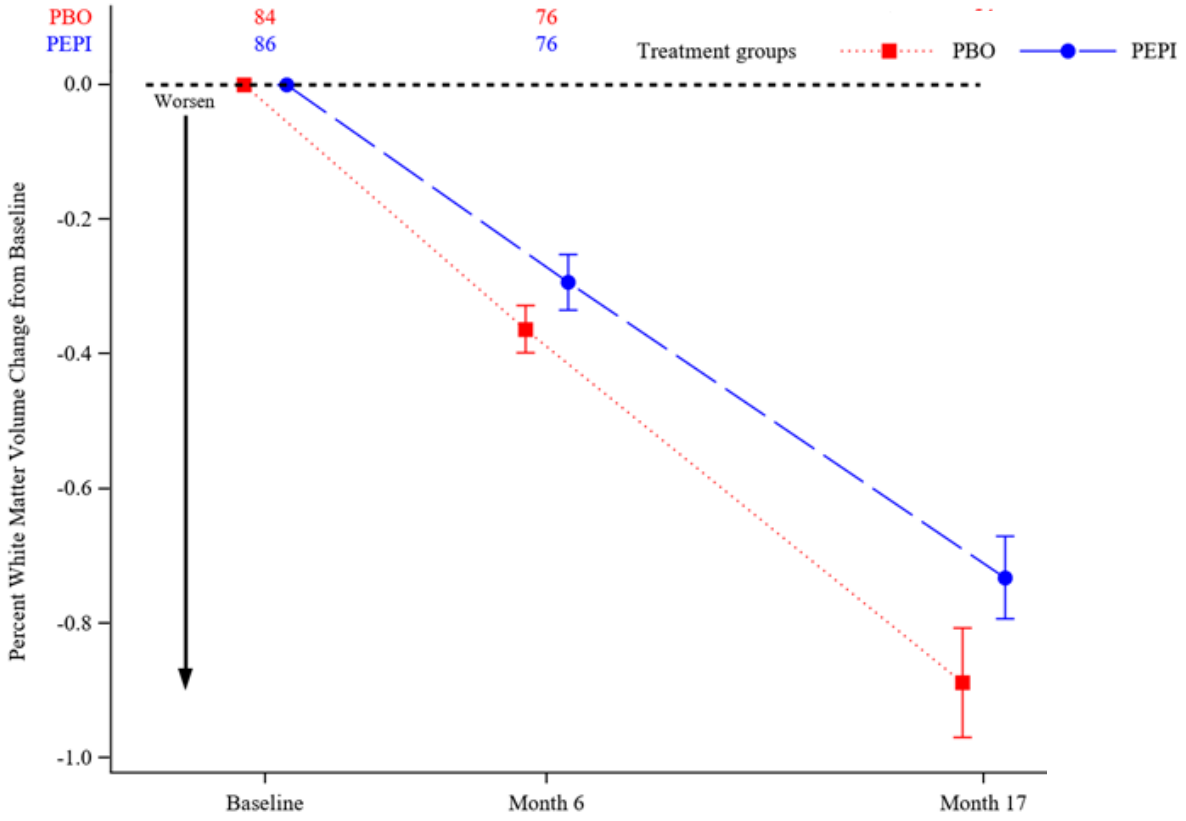
The HD-CAB Composite Index is the average z-score of the 6 component assessments. If, as is the case here, all components change in the direction of patient benefit (+), this increases significance relative to the individual assessments.

Pre-specified exploratory volumetric MRI analysis – Cohort B1

CBSI (caudate atrophy)

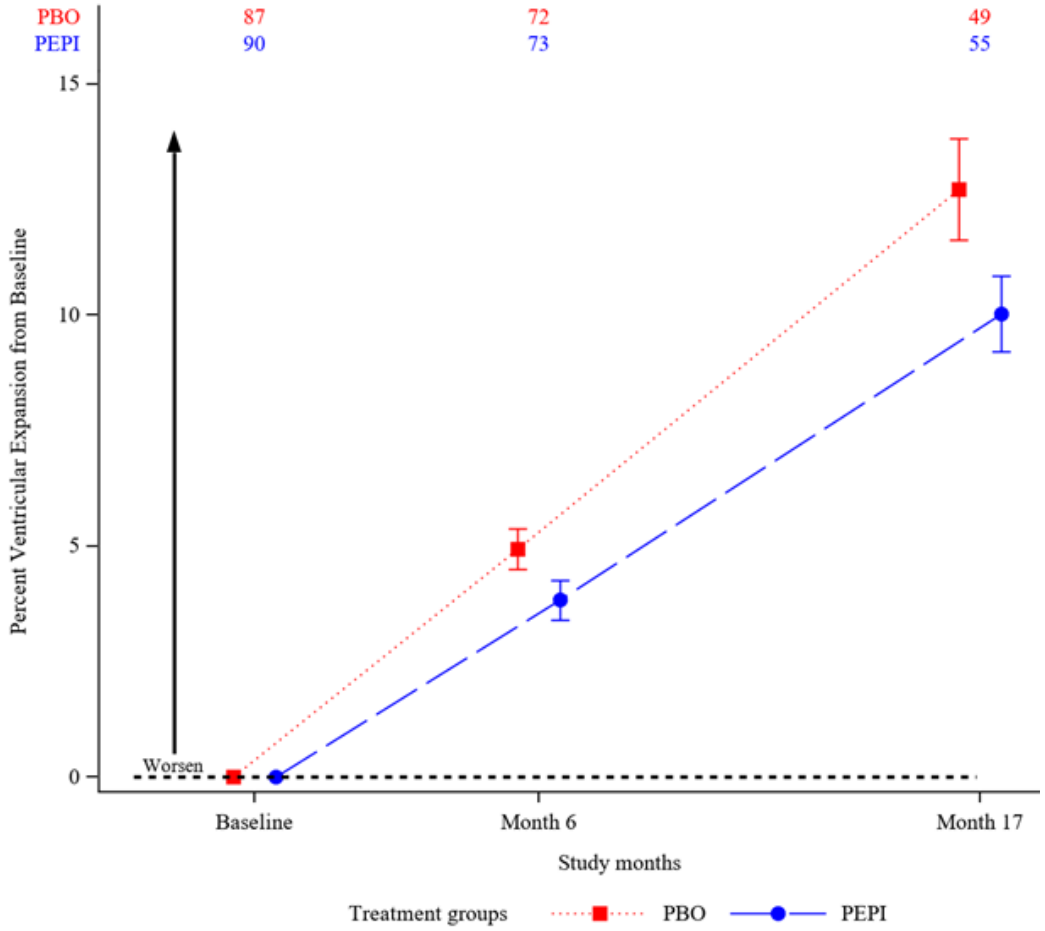


White matter volume

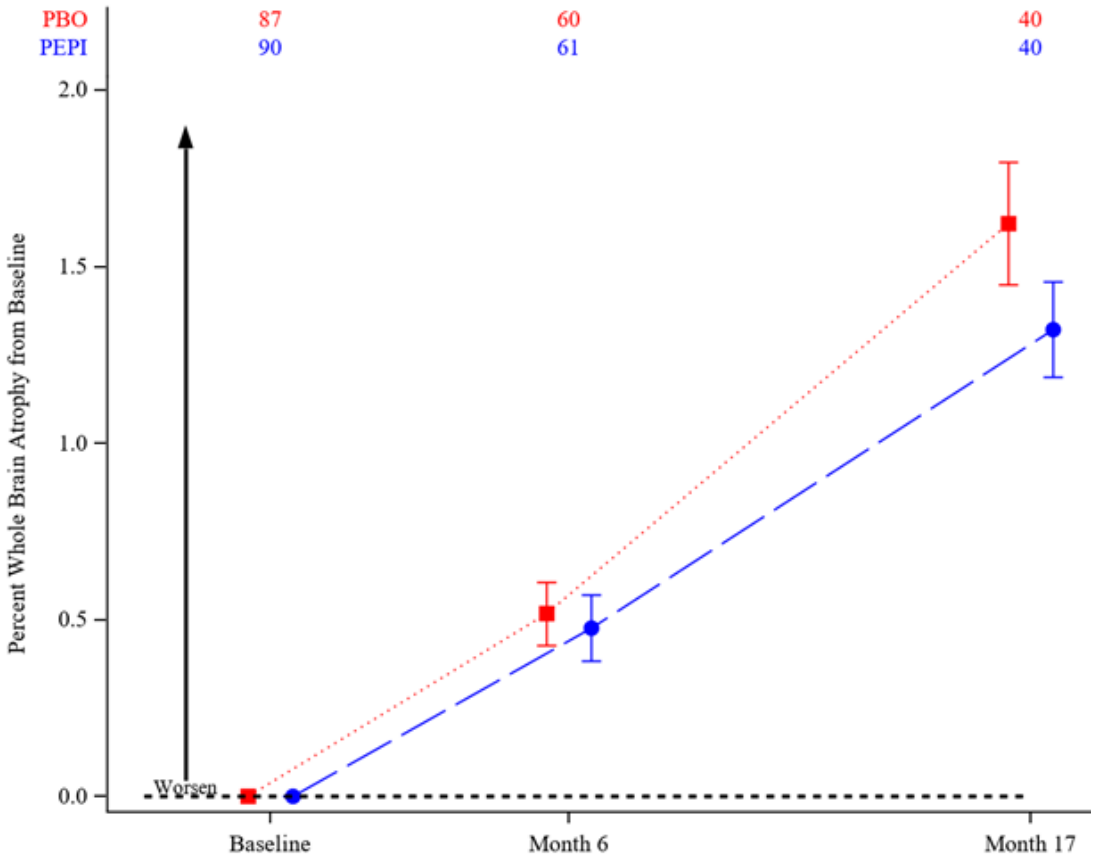


Pre-specified exploratory volumetric MRI analysis – Cohort B1

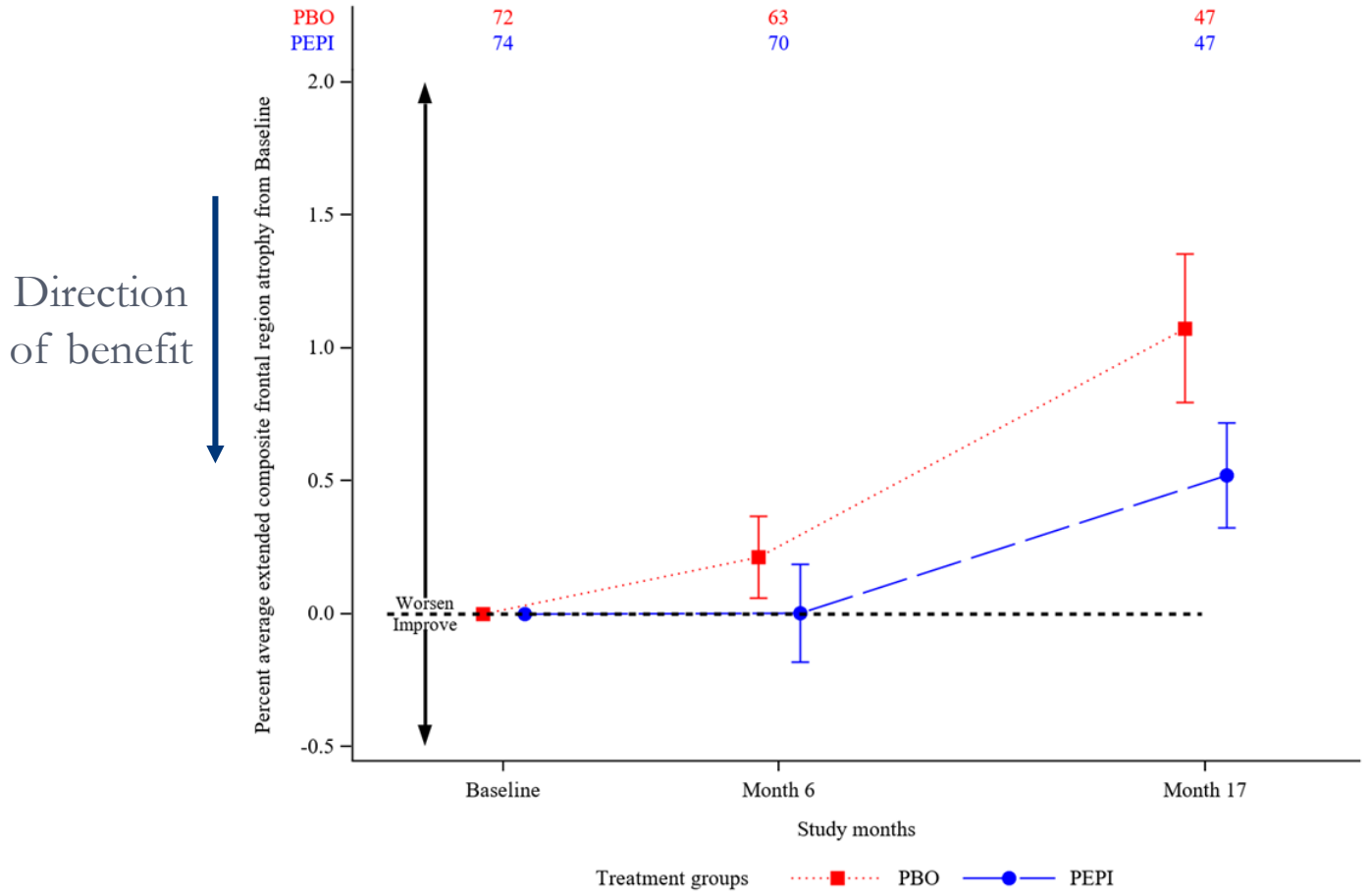
VBSI (ventricular expansion)



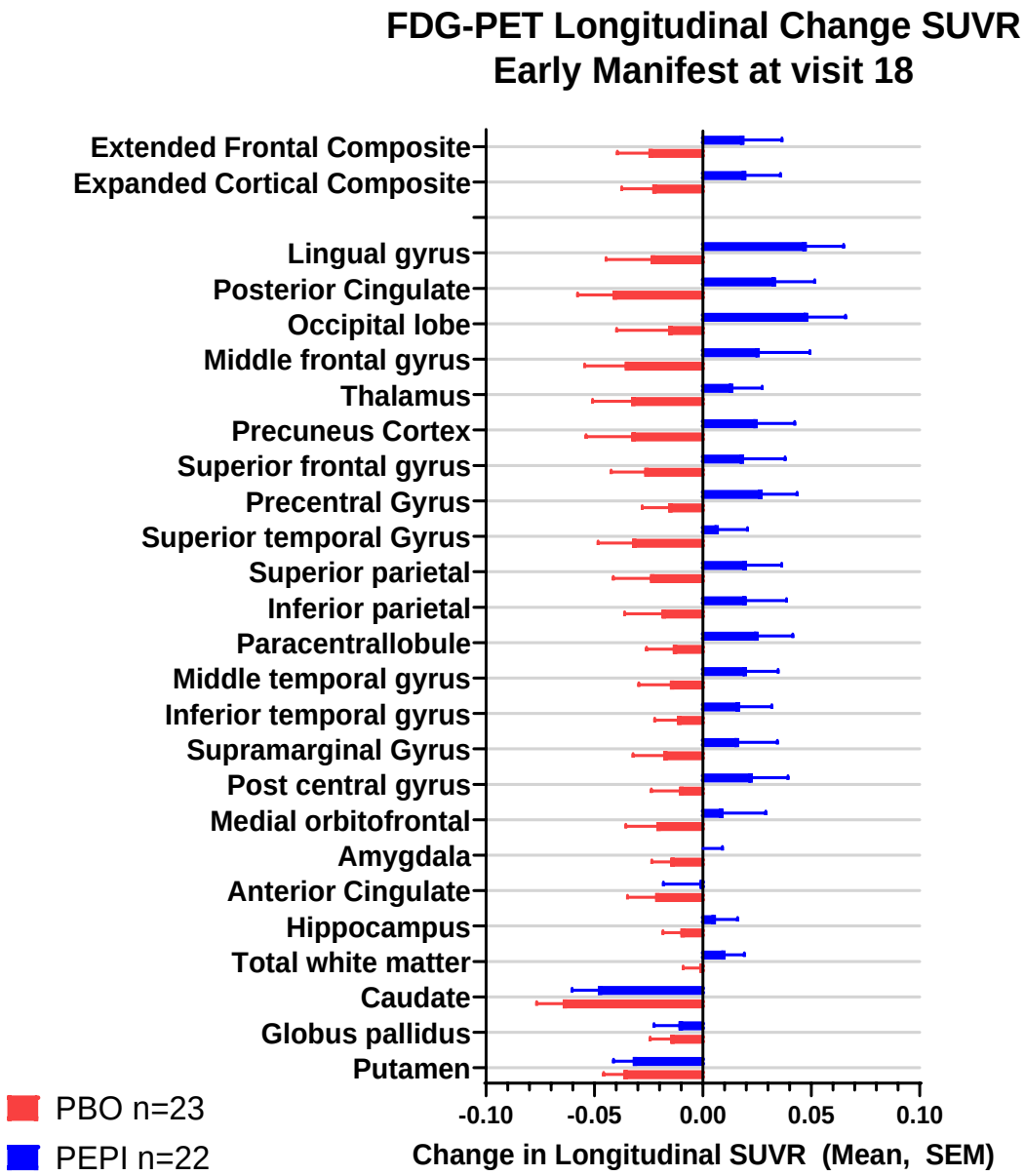
BBSI (whole brain atrophy)

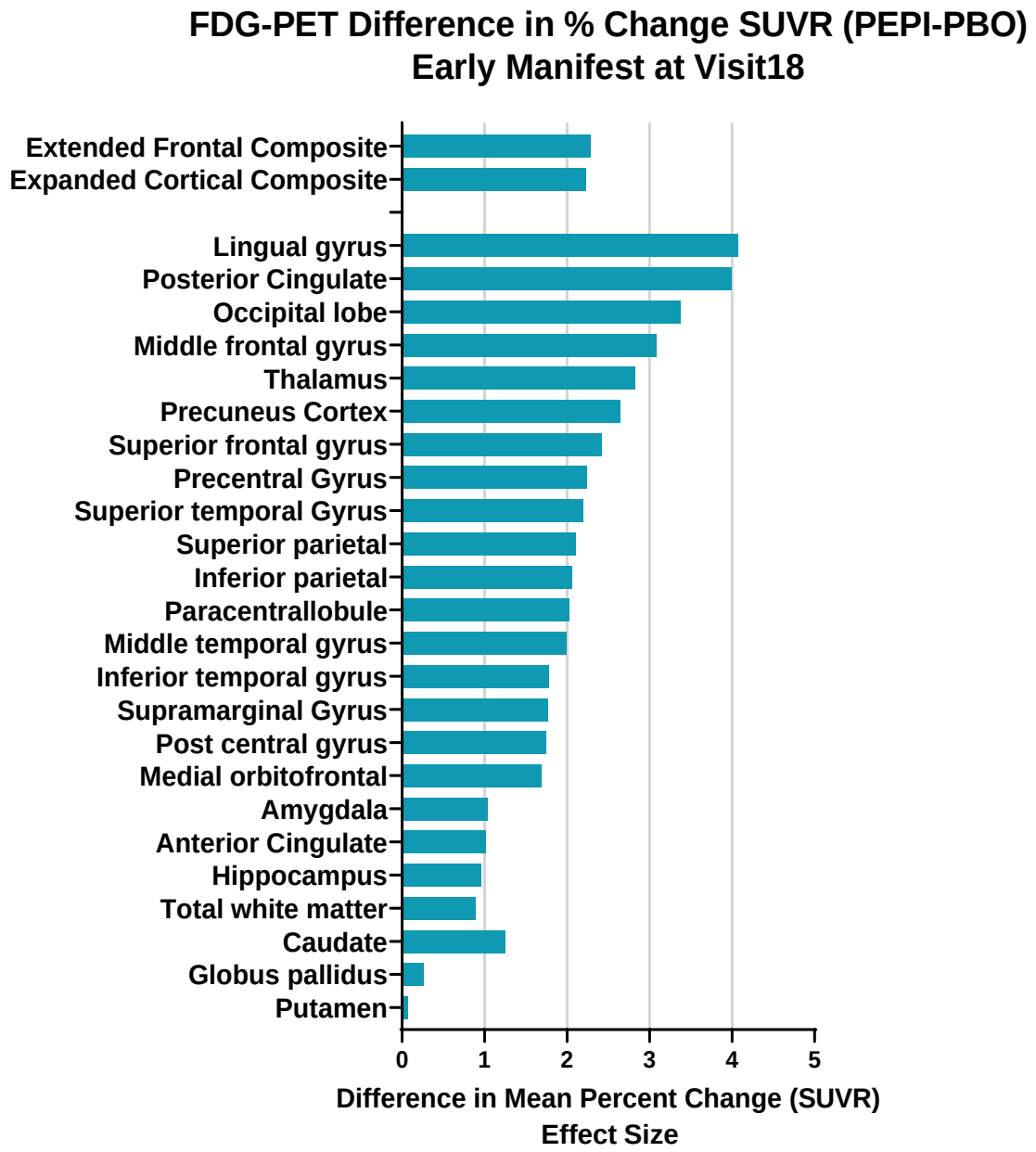


vMRI Extended Frontal Composite Region – Early Manifest

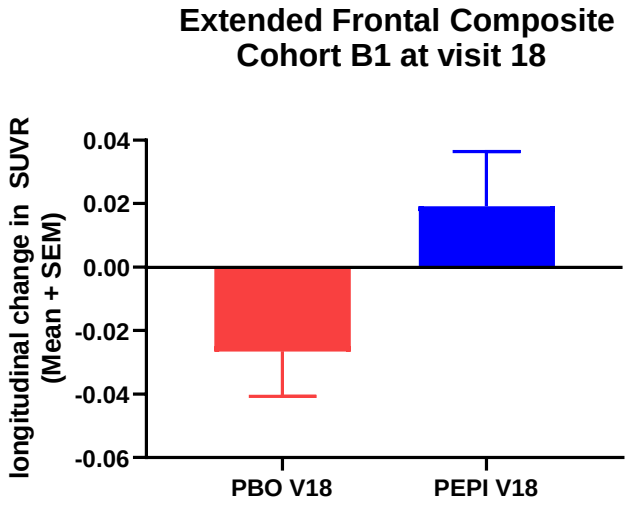


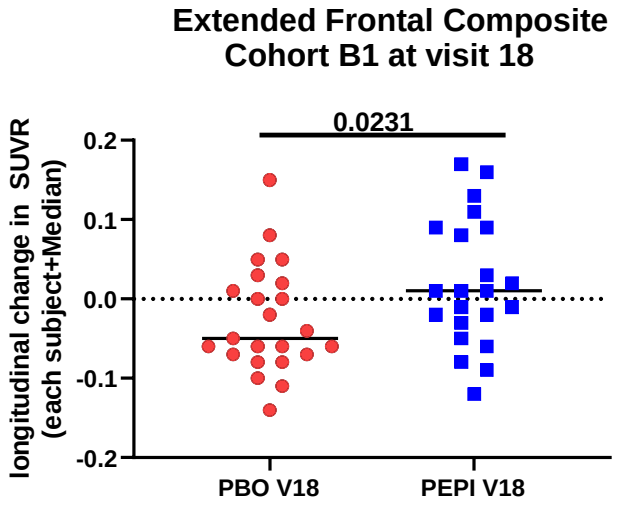
FDG-PET, Change in SUVR at 18 Months – Early Manifest

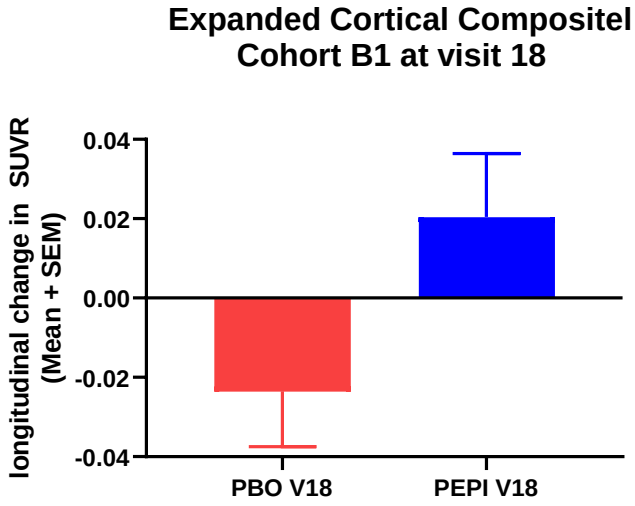


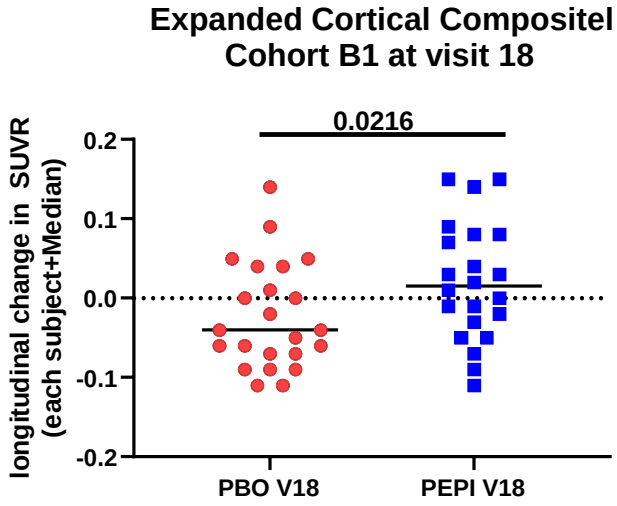


FDG-PET, Change in SUVR composites at 18 Months





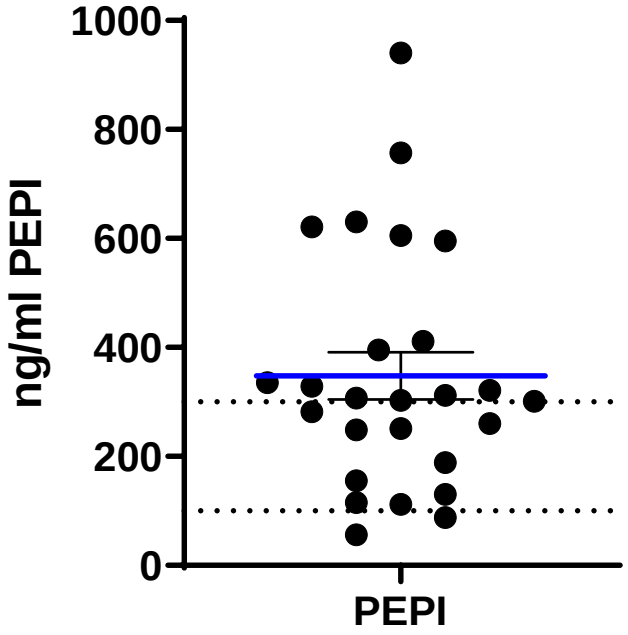




Simple one-sided t-test to compare values at mo18 only

Pepinemab and sSEMA4D levels in CSF
Exploratory - PD

Most subjects dosed with pepinemab have ≥ saturating levels (100-300 ng/ml) in CSF



sSEMA4D increases in subjects dosed with pepinemab – suggesting target engagement