Poster #91713: Neflamapimod treatment reduces plasma glial fibrillary acidic protein GFAP levels in patients with dementia with Lewy bodies (DLB) who do not have co-existing AD co-pathology

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BACKGROUND

In a 16-week, 91-patient placebo-controlled study in DLB, named AscenD-LB, neflamapimod significantly improved cognition and function, and gait (Jiang et al, 2022), with the effect being most prominent in patients without Alzheimer's disease-related co-pathology, assessed by plasma ptau181 (Alam et al, 2023).

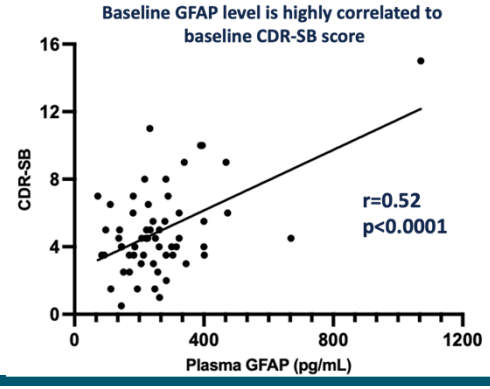
Plasma GFAP discriminates MCI-DLB from health controls (Hamilton et al, 2023; Diaz-Galvan et al, 2024). In DLB (Bolsewig et al, 2024), plasma GFAP is associated with rate of cognitive decline, but not with CSF Aβ42 status, suggesting that GFAP has potential as a marker of DLB-specific disease processes.

METHODS

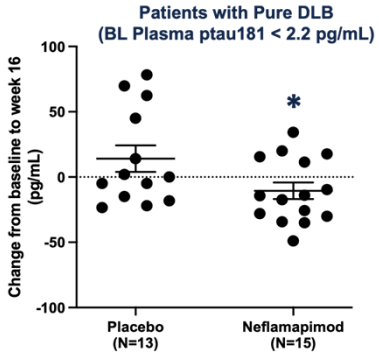
GFAP levels (pg/mL) in stored plasma samples from AscenD-LB determined using Simoa® platform. Plasma ptau181 of ≥ 2.2 pg/mL in the pre-treatment sample was prospectively defined for determining the presence of AD co-pathology

BASELINE RESULTS

At baseline, GFAP was higher (p=0.02) in DLB with AD co-pathology [282(SD=120, n=29] versus in pure DLB [215(SD=91), n=28].

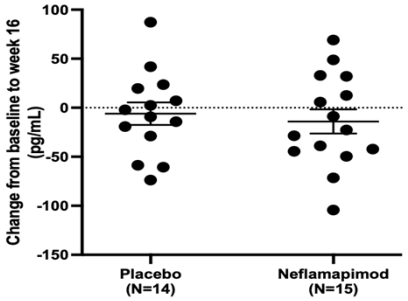


Neflamapimod Reduces Plasma GFAP Levels in Patients without AD co-pathology (plasma ptau181< cut-off)



Difference between neflamapimod and placebo: -24.7 pg/mL (95% CI: -0.7, -48.7), *p=0.04 vs. placebo

Neflamapimod Does Not Reduce GFAP Levels in Patients with AD co-pathology (plasma ptau181 ≥ cut-off)

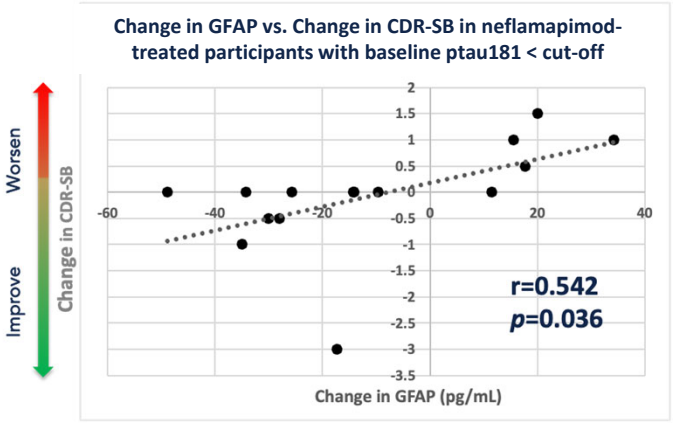


CONCLUSIONS

The effects on GFAP, particularly the association between GFAP response and clinical outcomes, further support that neflamapimod beneficially impacts the underlying disease process in DLB.

Combined with the recent literature, the results, including the baseline correlation to CDR-SB, also demonstrate the potential of plasma GFAP as biomarker to monitor DLB-specific disease processes

Change on-treatment in plasma GFAP is Correlated to the Clinical Outcome (Change in CDR-SB from Baseline to Week 16)



Increased GFAP associated with worsening CDR-SB, reduction in GFAP associated with improvement on CDR-SB among neflamapimod recipients (r=0.542, p=0.036). The correlation was not seen in placebo-recipients (r=0.31, p=NS)