SavaDx, a Novel Plasma Biomarker to Detect Alzheimer's Disease, Confirms Mechanism of Action of Simufilam

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INTRODUCTION

SavaDx is an investigational plasma diagnostic/biomarker for Alzheimer's disease (AD) funded by a research grant award from NIH. SavaDx is under development to detect altered filamin A, a proteopathy in AD brain. SavaDx complements simufilam, a drug candidate that targets and reverses the filamin A proteopathy. Here we evaluate **SavaDx in a randomized, double-blind, placebo-controlled, multi-center Phase 2 trial of simufilam in patients with mild-to-moderate AD**.

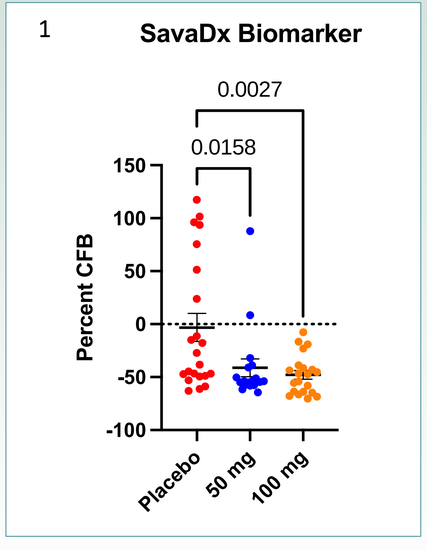
METHODS

SavaDx was used to measure changes in levels of altered filamin A and to evaluate treatment effects of simufilam in a randomized, double-blind, placebo-controlled, multi-center Phase 2 study of simufilam in patients with mild-to-moderate AD. In this study, 64 patients with MMSE 16 to 26 and CSF total tau/$A\beta_{42}$ ≥ 0.28 were randomized to placebo, 50 or 100 mg b.i.d. oral simufilam for 28 days. CSF and blood samples were collected pre-dose and on Day 28. Plasma P-tau181 was measured in duplicate by SIMOA®, a digital ELISA platform. Data with CVs >11% were repeated and excluded if >15% on repeat. Biomarker analyses were conducted blind to treatment, with Day 1 and 28 samples for each patient analyzed together. Prior to this study, SavaDx candidate antibodies were assessed in small sample sets of plasma from confirmed AD, MCI and healthy controls.

SAVADX RESULTS

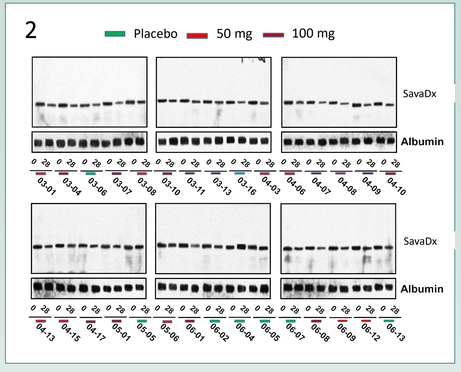
Comparing Day 28 to Day 1 plasma samples, SavaDx values (i.e., altered filamin A levels) decreased 44% and 48% in the 50 and 100 mg arms, respectively (p=0.02 and p=0.003 versus placebo), versus a 3% mean decrease in the placebo arm (**Fig. 1**).

1



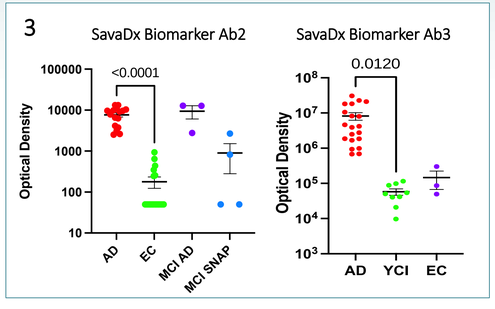
Immunoblots of the SavaDx assay show changes from Day 1 to Day 28 in plasma samples from 30 study subjects in placebo, 50 mg and 100 mg treatment arms (**Fig. 2**).

2



Prior to the Phase 2 study, SavaDx candidate antibodies distinguished between AD and Elderly Control (EC), with intermediate values for Mild Cognitive Impairment due to AD (MCI AD) and MCI Suspected Non-Amyloid Pathology (MCI SNAP). Another study distinguished AD from Young Cognitively Intact (YCI) and AD samples (**Fig. 3**). AD was confirmed by PET.

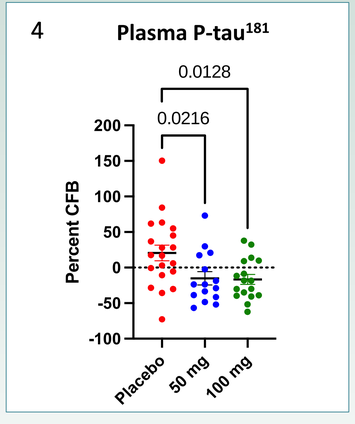
3



PLASMA P-TAU^{181} RESULTS

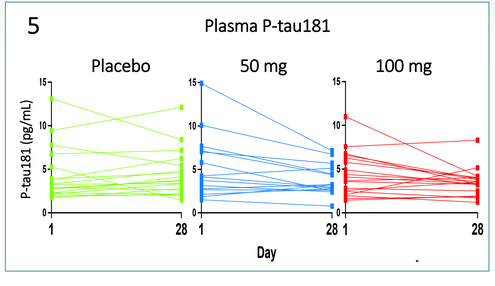
In this Phase 2 study, 28-day oral treatment with 50 and 100 mg simufilam significantly reduced plasma P-tau181 levels by 15% and 17%, respectively, versus a mean 20% increase (driven by an outlier) in the placebo arm (**Fig. 4**).

4



Spaghetti plots show individual changes in plasma P-tau181 in pg/ml (**Fig. 5**).

5



CONCLUSIONS

SavaDx and plasma P-tau181 both detected treatment effects in a Phase 2 clinical trial of simufilam in subjects with mild-to-moderate AD, confirming simufilam's mechanism of action and target engagement. Treatment effects in a panel of CSF biomarkers in this study were previously reported. SavaDx also distinguished AD from healthy controls.

These data highlight the possibility of a new plasma biomarker for AD. Larger studies are needed to provide additional insight on SavaDx outcomes.

KEY TAKEAWAY

SavaDx is a plasma assay to detect altered filamin A, a proteopathy in AD. SavaDx detected treatment effects of simufilam in a Phase 2 clinical trial, suggesting potential as a plasma biomarker for Alzheimer's disease.

ACKNOWLEDGEMENT

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