

**Protocol Title: Pilot, single center, open, trial of rifaximin in
probable Alzheimer's Disease**

NCT Number: NCT03856359

Date: September 6, 2019

Scientific Rationale for Study Design

This is an open label pilot study designed to provide preliminary evidence on the clinical efficacy of rifaximin in improving cognition in AD patients. We will be looking for improvement in test scores, changes in serum levels of neuronal markers and cytokines and changes in gut microbiota following treatment. We will also be collecting data regarding the safety of long-term use of this non-absorbed antibiotic for this disease. This pilot may form the basis for a future larger randomized, double blind controlled study to further test this hypothesis.

Summary statistics will be compiled for mean/SD change from baseline to endpoint on all cognitive, biomarker and microbiome variables. Statistics for cognitive and plasma biomarker tests will be based on nominal p-value of 0.05 given this is a pilot study. We will also examine multiplicity adjusted p-values for correlations between change in cognitive and biomarker/microbiome variables.

Statistical analyses will combined subjects on QD and BID for analyses as this is a pilot study and both doses may impact gut flora. In posthoc analyses we will put dosing as a covariate to examine dose effects.

As such any improvement in cognitive test score and/or significant correlations between cognition and microbiota changes will be viewed as a positive outcome to inform the design of a future larger study.