Alzheimer's Drug Discovery Foundation

ADDF ACCESS

Animal Study Design Checklist

One of the major challenges in bringing new drugs to market for neurodegenerative diseases has been the failure to demonstrate clinical efficacy for compounds that showed great promise in animal studies. This is due, in part, to the lack of models that accurately recapitulate the human disease and the poor reproducibility of preclinical data. The following questions, adapted from ADDF's Preclinical Animal Study Worksheet, should be considered when planning preclinical animal studies. Answering these questions should improve the rigor of your study design and the reproducibility and predictive value of the preclinical results.

- ☑ Is your study an exploratory or therapeutic animal study? Exploratory studies are early proof-of concept or pilot studies to show that modulating your target with a test compound can influence the disease process, and should include initial target engagement and pharmacokinetic (PK) outcomes. Therapeutic studies are comprehensive efficacy studies that should be designed and executed with similar rigor to human clinical trials (see Snyder, et al and Shineman, et al for more details).

- ☑ What is your justification for the animal model selected? Has it been extensively characterized? Genotype and phenotype should be confirmed throughout the duration of the study.

- ☑ Do you have PK data showing that your therapeutic agent reaches its intended target at a sufficient concentration to ensure that your hypothesis is being tested? PK experiments should inform your dose selection and should be performed with the same route of administration and formulation intended for use in your efficacy study.

- ☑ What are your primary and secondary outcome measures? Disease-relevant outcomes should always be pre-specified and relevant to your hypothesis.

- ☑ What is your pharmacodynamic readout of target engagement?

- ☑ How do you expect efficacy readouts in your animal study to translate into human clinical outcomes? Is a translatable biomarker for your target or mechanism of interest available?

- ☑ What are your inclusion and exclusion criteria? (i.e. excluding sick animals, only including animals of a specific phenotype, etc.)

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- ☑ What is your statistical analysis plan, and have you performed a power analysis to justify your sample size? Has your power analysis accounted for previously observed variability in your outcome measures?

- ☑ How will cohorts be randomized and what methods will be used to ensure experimenter blinding?

- ☑ Do you plan to use both males and females? Will the results be analyzed separately?

- ☑ How will dropouts or premature deaths be reported and dealt with in the statistical analysis?

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