Is the Clinical Trial a Potential Barrier to Alzheimer’s Disease Pharmacotherapy Development?

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Background

Alzheimer’s disease (AD), a complex, chronic neurodegenerative disease, is the leading cause of dementia in the United States. AD symptoms are devastating and range from difficulty remembering recent events to a complete loss of bodily functions, which may lead to death. AD prevalence is projected to increase from 5.8 million to 16 million Americans by 2050. Despite the severity and social, psychological, physical, and economic impact of AD, only five FDA approved drugs are available on the market to provide symptomatic relief for AD patients. The urgent need for an AD pharmacotherapy to stop or reverse the disease progression has been ongoing for decades; however, no therapeutic drugs have been developed or approved by the FDA.

Objective

This project examined five years (2015-2020) of clinical trial results of AD drug development failures to explore how clinical trial design attributed to development failure and elucidate whether modifying the design/procedure (e.g., disease diagnosis, outcome measures, test populations, etc.) improves clinical development.

Methodology

Clinical Trial Site and Patient Population Analysis

- **Results:**
  - **Clinical Trial Site and Patient Population Analysis**
    - **Pre-Trial AD Diagnosis Method Analysis**
      - Method of AD Diagnosis in Phase II and III Trials with Fully Disclosed Results (n=28)
      - Method of AD Diagnosis in Successful vs Unsuccessful Phase II Trials (n=28)
    - **Clinical Trial Outcome Measure Analysis**
      - Number of Outcome Categories Used in Successful vs Unsuccessful Phase II and III AD Trials (n=48)
      - Success of Phase II and III AD Trials Relying on Clinical Measurements as an Outcome Measure (n=18)
    - **Success Rate Comparison**

**Exclusion Criteria #1 (n=58)**
- Futility method meeting or evaluable efficacy via clinical effect...
- Agitated (well)-condition of AD...
- Adverse events are not enogenous to the study.
- Any patient diagnosed with Alzheimer’s disease during the study.
- Other.

**Exclusion Criteria #2 (n=27)**
- Trials in which enrolment and enrollment data were not published or publicly disclosed (n=27).

**Exclusion Criteria #3 (n=37)**
- Phase 2a Trials (n=37)
- Phase 2b Trials (n=37)

**Exclusion Criteria #4 (n=41)**
- Includes: All trials involving novel AD pharmacotherapy OR existing pharmacotherapy for a new indication of AD...
- Outcomes: Determine comprehensive representative AD Phase 2 and 3 clinical trial failures and how clinical development can be improved.

Discussion

There are significant differences in clinical trial design of successful versus unsuccessful AD drug clinical trials.

- **Future Research:**
  - I will expand this research by continuing to add new AD drug clinical trial data to my data pool. Additionally, I will look into the re-evaluation and re-standardization of the cognitive and behavior assessment tools used in AD drug clinical trials.

Contact Information

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References

Tyler Fukunaga, PharmD ’23 is currently a dual degree student in the Doctorate of Pharmacy and MS Regulatory Science programs at USC. He received his bachelor’s degree at the University of California, Santa Barbara, majoring in Pharmacology and was a former research associate at the University of California, San Francisco, studying lung cancer. His current research focuses on evaluating Alzheimer’s Disease pharmacotherapy clinical development failure from the perspective of clinical trial design. Specifically, he will research the evolution of Alzheimer’s Disease drug clinical trials and elucidate whether modifying the design, procedures, outcome measures, or test populations of these studies improves and advances clinical development in a more promising direction. Tyler hopes to pursue a career in the pharmaceutical industry where he can apply his future clinical and regulatory expertise. tfukunag@usc.edu