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

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OBJECTIVE

To evaluate clinical trial design as a factor in clinical development failures for Alzheimer’s Disease (AD) drugs to better understand how modification of the clinical trial design can push AD drug development in a more promising and patient-inclusive direction.

BACKGROUND

❖ AD is the leading cause of dementia in the US.\(^1\)
❖ AD prevalence is projected to increase from 5.8 million to 14 million Americans by 2050.\(^1\)
❖ Only five FDA approved drugs are available on the market to provide symptomatic relief for AD patients.\(^2\)

METHODOLOGY

Initial clinicaltrials.gov search criteria:
- Completed or terminated AD trials
- Timeframe: 2015-2020

Inclusion Criteria:
- Drug therapy
- Published results
- Phase II and III trials

163 AD Clinical Trials

41 AD Clinical Trials Were Analyzed

FINDINGS

❖ Only 23.9% of 41 AD drug clinical trials met endpoints, none of which were Phase III trials!
❖ AD diagnosis criteria through the use of both a biomarker AND a cognitive diagnosis method (rather than a cognitive diagnosis alone) did not trend toward higher trial success rates.

<table>
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<tr>
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<th>Clinical Outcomes Only (n=18)</th>
<th>Clinical Outcomes with Biomarker OR Pharmacokinetic Outcomes (n=21)</th>
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<tbody>
<tr>
<td>Success Rate</td>
<td>16.7%</td>
<td>38.1%</td>
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Table 1. Effect of Combining Clinical Outcomes with Biomarker or Pharmacokinetic Outcomes on Trial Success Rate

<table>
<thead>
<tr>
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<th>Trials That Met Endpoints (n=12)</th>
<th>Trials That Did Not Meet Endpoints (n=17)</th>
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<tr>
<td>Average # of Participants (SD)</td>
<td>63.4 (60.5)</td>
<td>348.8 (366.8)</td>
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<tr>
<td>Average # of Investigator Sites (SD)</td>
<td>8.7 (12.3)</td>
<td>78.8 (84.7)</td>
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Table 2. Average Number of Participants and Investigator Sites in Successful Versus Unsuccessful Phase II Trials

❖ Clinical outcome measures such as cognitive measures are not viable as standalone outcome measures.
❖ AD diagnosis by a cognitive test AND a biomarker measurement is a generally good medical practice, but this does not guarantee higher trial success rates.

CONCLUSIONS

❖ Using fewer investigator sites may limit variance in cognitive rating by clinicians as successful studies had less than 10 sites on average.
❖ Limiting AD patient enrollment to those who can truly benefit from the scope of the drug’s mechanism of action should be considered.

REFERENCES


CONTACT

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