Title: Evolution of Alzheimer's disease trial characteristics: 2000 - 2017

Authors: Smigorski K[1], Perez M[1], Hillsabeck R[1], Nations K[1]

[1] INC Research / inVentiv Health

The Methodological Question Being Addressed: How has Alzheimer's disease (AD) clinical trial design (including: study phase, key objectives, dementia severity, and complexity) evolved since year 2000?

Introduction: Research paradigms developed many decades ago have resulted in the FDA approval of only four cholinesterase inhibitors and memantine. Much current dialogue focuses on moving away from amyloid-targeting compounds and toward introducing more mechanistic diversity and at earlier stages of disease (1, 2). Cummings and colleagues (2017) recently reported that as of January 2017 there were 105 agents in the AD development pipeline, 25 agents in 29 trials in phase I, 52 agents in 68 trials in phase II, and 28 agents in 42 trials in phase III (1). This poster aims at providing insight into AD clinical trials methodology by approaching it from a different angle – analyzing the research activity in terms of study characteristics and complexity over time. A longitudinal analysis may provide a deeper understanding of clinical trial temporal dynamics and how trial landscape has changed in response to emerging research discovery.

Methods: Industry-sponsored, interventional AD trials were extracted from the database accessed at www.clinicaltrials.gov on 06Dec2017. Summary and inferential statistics were applied.

Results: A total of 565 selected trials posted since 2000, the year the NIH registry was created, have been reviewed. The number of trials significantly increased over time (r=0.64, 95% CI: 0.59-0.69; P<0.001). The year with the highest level of activity was 2009 (N=67), during which 95% of all trials initiated included patients in the mild/moderate or more severe disease stages. Since 2009, early stage disease has been the focus of significantly increased attention (mild cognitive impairment/prodromal AD/early AD), increasing from 5% of all activity in 2009 to 38% in 2017 ($\chi^2(1) = 13.01$, $p < 0.001$). While the proportion of pivotal trials initiated in the last three-year period (2015-2017) is the lowest it has been since the registry was created (21%), the total number of trials (N=123), the proportion of trials in early stage development (79%), and the number of unique interventions investigated in these trials (N=116) is not significantly different than the most active period of 2009-2011 (p = n.s.). Additional details, including distribution of type of intervention, key endpoints, and indicators of trial complexity will be presented.

Conclusions: Based on publicly available data accessed through clinicaltrials.gov, we provide a comprehensive look at the evolution of the AD clinical trial dynamics in phase I-III industry trials over the past 17years. Limitations based on data available in clincialtrials.gov will be summarized.

Disclosures: Disclosures: KS, MP, RH and KN are employees of INC Research/inVentiv Health.

References:

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