Are Clinical Trials of New Treatments for Alzheimer's Disease Early Enough and Long Enough-A Regulatory Perspective

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Are trials early enough and long enough?

- Results of purported "disease altering" treatments in patients with manifest AD have been disappointing (but not all data are in!)
- There is general agreement that starting early in the course of disease is preferable
- Primary problems:
  - Identifying patients
  - Assessing drug effects
  - How long?

Identifying patients

- Patients "with" AD can now be (more or less) reliably identified before frank dementia (MCI) or any clinical symptoms (familial AD)
- These patients can now be enrolled long before they reach a diagnosis of AD
- No good way yet to identify (with high probability) patients with sporadic AD

Identifying patients

- Some believe that patients with MCI may be too late in the disease process to be effectively treated
- From a regulatory point of view, there is no objection to studying patients as early as they can be reliably identified as "having" AD
- A drug that had a clear effect could be approved, even if "some" of those treated will never get AD, or if the clinical onset would be far in the future

Assessing drug effect

- Although this is a setting that is "ripe" for using a surrogate, we do not (yet) have a surrogate that is reasonably likely to predict a clinical benefit
- This means that we still need to rely on (at least one) clinical outcome (or time to diagnosis of AD)
- We are currently evaluating several clinical measures that may suffice
- A change on a sensitive cognitive measure in asymptomatic patients (with a biomarker) may be enough

How long?

- Of course, it appears that these studies might have to be very long (many years)
- Not necessarily; depending upon the population studied, they may not have to be “very” long
- If we can have an understanding of when a milestone may be reached (e.g., dx of AD), patients can be enrolled near that point
- If this is too late, very sensitive measures may be acceptable (see previous slide)
- Accelerated approval? (don’t think we’re there yet)

Summary

- Studies in very early patients (symptomatic or not) are likely to be done/necessary
- Some patients can be diagnosed early; many cannot (asymptomatic sporadic AD)
- Trials in those who can be diagnosed early are useful in themselves, and can inform decisions about even earlier patients