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Interview with Alfred W. Sandrock, Jr., M.D., Ph.D., Executive Vice President & Chief Medical Officer of Biogen

## an the Antibody Aducanumab, an Investigational Treatment, Lead to a Potential Treatment for Alzheimer's Disease?

By Japan SPOTLIGHT

Volume 537 of *Nature* magazine, published on Sept. 1, 2016, highlighted an academic article on "the antibody aducanumab" which reduces beta amyloid plaques in the brain. Could this become a potential treatment for Alzheimer's disease? It may be premature to ask, but we highlight this investigational treatment as a notable scientific development that might possibly help us overcome the disease in the long run.

The following is an interview with Dr. Alfred W. Sandrock, Jr., executive vice president and chief medical officer of Biogen, the US-based biotechnology company. He kindly responded to our questions by e-mail in spite of his extremely busy schedule in early March 2017.

### Introduction

### JS: Could you briefly introduce yourself and explain the various positions you've held at Biogen?

Sandrock: I was trained as a neurologist and neurobiologist, and after working as an academic neurologist at Massachusetts General Hospital and Harvard Medical School for almost 10 years, I moved to Biogen where I am currently the executive vice president and chief medical officer. Previously I served as executive vice president of neurology discovery and development, in the neurodegeneration therapeutic area. I have served as chief medical officer since February 2012.

(Japan SPOTLIGHT adds: In addition to the roles detailed above, since joining Biogen in 1998 Dr. Sandrock has held several senior executive positions, including senior vice president of



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### Aducanumab, an Investigational Treatment

### JS: Could you please tell us about the development of aducanumab?

**Sandrock:** Aducanumab is an investigational compound being developed for the treatment of early AD. Aducanumab is a human recombinant monoclonal antibody (mAb) derived from a de-identified library of B cells collected from healthy elderly subjects with no signs of cognitive impairment or cognitively impaired elderly subjects with unusually slow cognitive decline using Neurimmune's technology platform called Reverse Translational Medicine (RTM). Biogen licensed aducanumab from Neurimmune under a collaborative development and license agreement.

Aducanumab is thought to target aggregated forms of beta amyloid

development sciences, senior vice president of neurology research and development, and vice president of clinical development in neurology. Dr. Sandrock holds a B.A. in human biology from Stanford University, an M.D. from Harvard Medical School, and a Ph.D. in neurobiology from Harvard University. He has also completed an internship in medicine, a residency and chief residency in neurology, and a clinical fellowship in neuromuscular disease and clinical neurophysiology (electromyography) at Massachusetts General Hospital.) including soluble oligomers and insoluble fibrils which can form into amyloid plaque in the brain of AD patients. Based on pre-clinical and Phase 1b data to date, treatment with aducanumab has been shown to reduce amyloid plaque levels.

#### JS: What is aducanumab being developed to treat?

Sandrock: Aducanumab is currently being studied in early

Alzheimer's disease.

# JS: Based on the results published in *Nature* (volume 537), how might aducanumab contribute to treating Alzheimer's disease?

**Sandrock:** The presence of amyloid plaques is a pathological hallmark of Alzheimer's disease. The amyloid hypothesis posits that beta amyloid causes the impairment in cognition and neurodegeneration in Alzheimer's disease. Our therapeutic hypothesis is that removing toxic forms of beta amyloid from the brain may slow the clinical decline of people who have Alzheimer's disease. Aducanumab targets the soluble and insoluble aggregates of the beta amyloid protein that we believe are responsible for causing Alzheimer's disease.

The Phase 1b placebo-controlled study of aducanumab in prodromal and mild AD patients published in *Nature* demonstrated that it reduced amyloid plaques in the brain as seen through PET imaging, and that this reduction was dose- and time-dependent (*Images 1, 2 & 3*). Exploratory results from the Phase 1b study also demonstrated dose- and time-dependent slowing of clinical decline.

We hope that the ongoing Phase 3 studies of aducanumab will result in a benefit on cognitive decline for people taking aducanumab. We also expect our Phase 3 studies to further characterize aducanumab's benefit-risk profile.

#### **Future Milestones**

### JS: Following the publication of Phase Ib data from the PRIME study in *Nature*, what are the upcoming milestones Biogen is looking forward to in the development of aducanumab?

Sandrock: The completion of our Phase 3 studies is a milestone we look forward to achieving. We are currently recruiting two global Phase 3 studies, ENGAGE and EMERGE, which are designed to evaluate the safety of aducanumab and its efficacy in slowing cognitive impairment and the progression of disability in people with early Alzheimer's disease.

We can't speculate on when the studies will be completed, they are difficult to enroll because many people who qualify for the study are not aware of early AD symptoms, which are often dismissed as part of aging.

The studies, which are being conducted in more than 20 countries in North America, Europe and Asia, including Japan, will enroll approximately 2,700 people with early Alzheimer's disease.

# JS: Would a clinical test to prove aducanumab's safety be sufficient, or would it be necessary to reform public policy related to health and welfare regulations?

Sandrock: The first step is to demonstrate the safety and efficacy profile of aducanumab for regulators and importantly for patients. We also recognize the importance of working with the entire community involved in ensuring that people have access to the treatment they need, including those who develop public policy and the healthcare providers and caregivers of Alzheimer's disease patients.

JS: I think dementia is a disease unique to elderly people and becoming more serious with the aging of societies. Do you think aducanumab would be useful in treating dementia? Or in treating Lewy body dementia or frontotemporal dementia?

**Sandrock:** While Alzheimer's disease is a leading cause of dementia, at this time aducanumab is only being studied in people with early Alzheimer's disease. If our Phase 3 studies of aducanumab are successful we hope that it will be a potential treatment for people with dementia due to early Alzheimer's disease.

If aducanumab is successful in benefitting patients with Alzheimer's disease, we may one day also become interested in understanding if aducanumab might be an option in other diseases where amyloid plaque could play a role in the development of neurodegenerative disease — like Lewy body dementia — but clinical studies would be needed to answer that question.

### JS: Could you explain briefly what these diseases are and how they differ from Alzheimer's disease?

**Sandrock:** Neurodegenerative disease is complex and can have multiple causes; amyloid beta is only one cause. Biogen remains committed to advancing the scientific understanding of these complicated diseases and we are investigating several approaches for potentially treating Alzheimer's disease, including BACE and antitau treatments in addition to anti-amyloid.



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