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The advantages of frontotemporal degeneration drug development (part 2 of frontotemporal degeneration: The next therapeutic frontier)

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Abstract Frontotemporal degeneration (FTD) encompasses a spectrum of related neurodegenerative disorders with behavioral, language, and motor phenotypes for which there are currently no effective therapies. This is the second of two articles that summarize the presentations and discussions that occurred at two symposia in 2011 sponsored by the Frontotemporal Degeneration Treatment Study Group, a collaborative group of academic and industry researchers that is devoted to developing treatments for FTD. This article discusses the current status of FTD clinical research that is relevant to the conduct of clinical trials, and why FTD research may be an attractive pathway for developing therapies for neurodegenerative disorders. The clinical and molecular features of FTD, including rapid disease progression and relatively pure molecular pathology, suggest that there are advantages to developing drugs for FTD as compared with other dementias. FTD qualifies as orphan indication, providing additional advantages for drug development. Two recent sets of consensus diagnostic criteria will facilitate the identification of patients with FTD, and a variety of neuropsychological, functional, and behavioral scales have been shown to be sensitive to disease progression. Moreover, quantitative neuroimaging measurements demonstrate progressive brain atrophy in FTD at rates that may surpass Alzheimer's disease. Finally, the similarities between FTD and other neurodegenerative diseases with drug development efforts already underway suggest that FTD researchers will be able to draw on this experience to create a road map for FTD drug development. We conclude that FTD research has reached sufficient maturity to pursue clinical development of specific FTD therapies.

Keywords: Frontotemporal degeneration; FTD; Alzheimer's disease; AD; Progressive supranuclear palsy; Corticobasal degeneration; Treatment; Clinical trial; Biomarker; Drug development

1. Introduction

This is the second of two articles on FTD drug development that summarize the discussions that took place at two meetings in 2011 sponsored by the Frontotemporal Degeneration Treatment Study Group (FTSG), an organization dedicated to promoting therapeutic development for FTD. The previous article discusses the clinical and neuropathological subtypes and molecular biology of FTD, as well as animal models that have been developed to study this group of diseases.

This article summarizes the advantages of pursuing drug development in FTD as compared with Alzheimer's disease (AD), as well as clinical research literature on FTD that is relevant to drug development. These topics were discussed at an FTSG meeting in March 2011 at the Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Nevada, and at a symposium on FTD drug development that was held as part of the Clinical Trials in Alzheimer's Disease meeting in San Diego, California, in November 2011. This second symposium focused on clinical aspects of FTD drug development, including the epidemiology, current experience with clinical trials, and potential outcome measures for clinical trials.

2. Attracting the pharmaceutical industry to FTD drug development

Although the majority of FTD research to date has been done in academic laboratories and clinical research centers, rapid development of successful therapies will require the involvement of the pharmaceutical industry, with its large therapeutic compound libraries, translational medicine and clinical trials experience, and funds to help support such large-scale endeavors in FTD. The following sections outline the arguments for increased industry involvement in FTD drug development research.

2.1. FTD and related disorders have no US Food and Drug Administration–approved therapies and few interventions with any symptomatic benefit

There is great unmet medical need to develop effective therapies for FTD. Although antidementia and psychiatric drugs are often used off-label for symptomatic treatment of FTD, there is little evidence to suggest that these medications are efficacious (refer to section 4) [1,2]. Although particularly difficult for patients and their families, the lack of effective therapies is advantageous for the conduct of clinical trials in FTD because FTD patients and their families are highly motivated to participate in clinical trials. Moreover, because few drugs are beneficial for these patients, concomitant medications seldom exclude patients from participating in clinical trials, and experimental medications can be tested in the treatment of naive patients. Finally, the absence of approved FTD therapies allows a new product (or the first of several products) to be strongly positioned in the market.