Speaker: Kenneth Marek

Title: The Parkinson’s Progression Marker Initiative – Developing a Translational Toolbox for PD Progression

Brief Talk Description:
Authors: Parkinson’s Progression Marker Initiative
Objective: The goal of PPMI is to identify clinical, imaging and biospecimen biomarkers of Parkinson’s disease (PD) progression in subjects with manifest PD and those at risk due to genetic mutation, RBD, and/or hyposmia. The PPMI website provides rapid ongoing public access to PPMI data and biospecimen.

Background: Lack of progression biomarkers has been a major roadblock to studies investigating potential disease modifying PD drugs. Progression biomarkers may identify subsets of PD that define disease prognosis and response to therapy.

Design/Methods: Recently diagnosed PD, healthy volunteers (HV), SWEDD subjects, prodromal PD subjects and subjects with LRRK2 or synuclein mutations have been and continue to be enrolled at 32 international clinical sites and will be followed longitudinally with comprehensive clinical, imaging and biospecimen biomarkers assessments using standardized data acquisition protocols. All study data is integrated into the PPMI study database. Access to data and biospecimens is available at www.ppmi-info.org.

Results: The PD, HV and SWEDD cohorts have undergone baseline (n=683) and 1-year longitudinal follow-up (n= approx 400 as of Dec 31, 2013). PPMI has enrolled 423 PD (mean age 61.7, 65% Male), 196 HV (mean age 60.8, 64% Male) and 64 SWEDD (mean age 60.9, 63% Male). Duration of disease for PD was 6.6 mo and 8.0 mo for SWEDD. At baseline, the total MDS UPDRS for PD was 32.3 compared to 4.7 for HV and 29.0 for SWEDD. Baseline MoCA, GDS, and SCOPA-AUT were 27.1, 2.3, 9.5 for PD subjects, 28.2, 1.3, 5.9 for HV and 27.1, 3.3, 13.8 for SWEDD. CSF was acquired from > 97% of all subjects. Baseline CSF (pg/ml) Tau (44.7 vs 52.4), p-Tau (15.6 vs 18.3), and alpha synuclein (1847 vs 2197) were reduced in PD vs HV (p<0.01). Dopamine transporter (DAT) imaging, used as an inclusion criteria, excluded 12-15% from the PD cohort due to scans without dopaminergic deficit (SWEDD). DAT striatal SBR for PD is 1.41 vs. 2.57 for HV. Over 150,000 downloads and 35 biospecimen requests from the PPMI website have already occurred.

Conclusions: Baseline data from PPMI in untreated PD, HV and SWEDD cohorts demonstrate motor and non-motor deficits and reduction in CSF and imaging biomarkers in PD vs HV. Comprehensive longitudinal follow-up of the PPMI cohort is underway to characterize biomarker progression. Enrollment of prodromal PD subjects defined by hyposmia, REM behavior disorder and/or LRRK2 mutation or synuclein mutation is underway and these cohorts will be compared to the existing PPMI subjects undergoing longitudinal follow-up.

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Biographical Information:

Kenneth Marek is President and Senior Scientist at the Institute for Neurodegenerative Disorders. He was graduated from Princeton University (AB, biochemistry) and received his
medical degree from Yale University. Dr. Marek was trained in internal medicine and neurology at the Johns Hopkins School of Medicine and received further training as a post-doctoral fellow in neurochemistry at the Institute of Neurology, Queens Square, London. He has been a faculty member in the departments of neurology at Johns Hopkins University and Yale University. He has been the recipient of numerous grants and awards including those from the National Institutes of Health, Department of Defense, MJ FOX Foundation, Parkinson Disease Foundation, and National Parkinson's Foundation.

Dr. Marek's major research interests include identification of biomarkers for early detection, assessment of disease progression and development of new treatments for Parkinson's disease and Alzheimer's disease and related neurodegenerative disorders. His specific interest has been in in vivo neuroreceptor imaging biomarkers. Dr. Marek has and continues to be the principal investigator of several ongoing multi-center international studies (including the Parkinson Progression Marker Initiative (PPMI) and the Parkinson Associated Risk Syndrome (PARS)) study investigating the use of biomarkers to assess the onset, progression, and effect of treatment in Parkinson's disease, Alzheimer's disease and other neurodegenerative diseases.

Dr. Marek serves on the scientific advisory board of the Michael J Fox Foundation. He has served on the executive committee of the Parkinson's Study Group and in leadership roles in the Huntington Study group. He also was a co-founder and continues to lead Molecular NeuroImaging, LLC, a company providing clinical neuroimaging research services. Molecular Neuroimaging coordinates numerous Alzheimer disease imaging studies to assess AD radiotracers and potential AD therapies.