PPMI Status Update

Ken Marek

PPMI Investigators Meeting
May 2, 2012
New York, NY
PD patient vignette

- 67 yo right headed WF in excellent general health
- History
  - 6 month history of poor tennis play
  - Note 1-2 years – mild constipation
  - 2 months intermittent R UE tremor while reading the newspaper, or if in stressful situation
- Exam
  - Mild R UE resting tremor
  - Reduced R arm swing
- PD DIAGNOSIS – 1 MONTH AGO

- “IF THE SYMPTOMS REMAIN AS THEY ARE NOW – I COULD DEAL WITH THIS”
PPMI-PD patient vignette

- 62 yo right headed WM lawyer in excellent general health
- History
  9 month history of slowly worsening R UE tremor
  6 month history of R shoulder pain
  3 months voice less reliable in public speaking
- Exam
  Mild R UE resting tremor
  Mild R bradykinesia
- PD DIAGNOSIS – 3 MONTH AGO

- “PPMI is attractive because no meds and I can do something that will help research”
PPMI-Control vignette

• 62 yo right headed WF school principal in excellent general health
• History
  Husband has PD for 17 years
  No previous participation in clinical research
• Exam
  Normal

• “PPMI is something I can do for my husband even if he can’t join the study”
PPMI- Prodromal vignette

- 64 yo right headed WM painter in excellent general health
- Noticed no longer bothered by smell of paint x 2-3 years
- Wife reports episodic jumping out of bed during sleep
- Maybe balance not quite as good on ladders

Exam
Normal

- Can PPMI track prodromal period in individuals at high risk for PD – P-PPMI
**Parkinson’s Progression Markers Initiative**

**Requirements for Biomarker Infrastructure**

**Specific Data Set**
- Appropriate population (early stage PD and controls)
- Clinical (motor/non-motor) and imaging data
- Corresponding biologic samples (DNA, blood, CSF)

**Standardization**
- Uniform collection of data and samples
- Uniform storage of data and samples
- Strict quality control/quality assurance

**Access/Sharing**
- Data available to research community → data mining, hypothesis generation & testing
- Samples available for studies
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Establish a Specific Data Set

- **Enrollment** – 204 PD 149 HS 25 SWEDD - 378 subjects

- **Retention** – 202 PD 146 HS 24 SWEDD - 372 subjects

- Study governance - weekly meetings of the executive steering committee and monthly meetings of the full steering committee consisting of all study cores

- Data flow from sites to Study Cores to LONI. Outstanding success in collection of study data (98% LP at baseline and about 90% overall at 6 months and 12 months)

- Data presentation at major scientific meetings
ENROLLMENT

E.2. PD Subject Enrollment

PD Enrollment at 63% of Expected Recruitment

E.3. Healthy Control Enrollment

HC Enrollment at 97% of Expected Recruitment
Recruitment – Early lessons learned

- It is do-able, but challenging to recruit at planned rate – 1 PD/month, 1 control/2 months

- Multiple strategies to enhance recruitment are necessary – Fox Trial Finder

- Control recruitment on hold

- Recruitment challenge 400 subjects by July 4.
Recruitment – Retention - moving forward

- Ongoing recruitment will require continued efforts

- Retention strategies are crucial
  - Continued participation in all assessments
  - Need for PD medications

- PPMI Longitudinal data
  - Subject assessments
  - Subject data

- PPMI as an iterative study
  - Additional assessments/studies/cohorts
  - D/C assessments
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# Subject Enrollment & Sample Collection

## Collected Samples

(Enrolled patients)

<table>
<thead>
<tr>
<th>Specimen</th>
<th>BL</th>
<th>V01</th>
<th>V02</th>
<th>V03</th>
<th>V04</th>
<th>V05</th>
<th>ST</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma</strong></td>
<td>370 (372)</td>
<td>280 (284)</td>
<td>178 (182)</td>
<td>114 (116)</td>
<td>79 (79)</td>
<td>5 (5)</td>
<td>37 (37)</td>
<td>1063 (1075)</td>
</tr>
<tr>
<td><strong>Serum</strong></td>
<td>370 (372)</td>
<td>281 (284)</td>
<td>182 (182)</td>
<td>114 (116)</td>
<td>79 (79)</td>
<td>5 (5)</td>
<td>37 (37)</td>
<td>1068 (1075)</td>
</tr>
<tr>
<td><strong>CSF</strong></td>
<td>358 (372)</td>
<td>6 (6)</td>
<td>161 (179)</td>
<td>-</td>
<td>68 (78)</td>
<td>-</td>
<td>32 (36)</td>
<td>625 (671)</td>
</tr>
</tbody>
</table>

*Including 6 CSFs at V01 visit, 93% of CSF were collected
BL 98% of CSF were collected
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Play a Part in Parkinson's Research
Standardization of data acquisition/analysis

- Manuals/SOPs for all data acquisition

- Training for biosample collection and shipping, UPDRS, neuropsych, imaging acquisition and data transfer, clinical data entry.

- Quality control of biosamples, imaging data
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Data/Biosample Access/Sharing

[www.ppmi-info.org]

• Biologic samples available via website

• Data available via website

• Ancillary study application through website
Visual Interrogation System
PPMI Study

PPMI Steering Committee

Clinical Core

Imaging Core

Bioinformatics Core

Statistics Core

Bioanalytics Core

Genetics Core

Biospecimen access

Data access

PPMI Sites

MJFF - Michael J. Fox Foundation for PD Research

ISAB - Industry Scientific Advisory Board

EAC - External Advisory Committee

CSOC - Clinical Study Oversight Committee

PPMI Sites

PPMI Sites
## PPMI SC and Study Cores

<table>
<thead>
<tr>
<th>Steering Committee</th>
<th>PI-K Marek, A Siderowf, C Tanner, D Jennings, K Kieburtz, W Poewe, B Mollenhauer, T Simuni, (core leaders, MJFF, ISAB), S Lasch</th>
</tr>
</thead>
</table>
| Clinical Coordination Core | University of Rochester’s Clinical Trials Coordination Center  
  • PI: Karl Kieburtz, Emily Flagg, Alice Rudolph, Cindy Casaceli |
| Imaging Core             | Institute for Neurodegenerative Disorders  
  • PI: John Seibyl, Norbert Schuff, Susan Mendick |
| Statistics Core          | University of Iowa  
  • PI: Chris Coffey, Qing Yang |
| Bioinformatics Core      | Laboratory of Neuroimaging (LONI) at UCLA  
  • PI: Arthur Toga, Karen Crawford |
| BioRepository            | Coriell/BioRep  
  • PI: Alison Ansbach,  
  • Paola Casalin, Giulia Malferrari |
| Bioanalytics Core        | University of Pennsylvania  
  • PI: John Trojanowski, Les Shaw |
| Genetics Core            | National Institute on Aging/NIH  
  • PI: Andy Singleton |
PPMI Committees

- **Biologics**
  - John Trojanowski
  - Les Shaw

- **Imaging**
  - John Seibyl

- **Neuropsych / Neurobehavior**
  - Andrew Siderowf

- **Sleep**
  - Wolfgang Oertel

- **Genetics**
  - Andrew Singleton

- **Statistical**
  - Chris Coffey

- **Biospecimen review**
  - Gene Johnson

- **Data and publication**
  - David Standaert

- **Ancillary study**
  - Carlie Tanner

- **Recruitment/Retention**
  - Danna Jennings

- **Website**
  - Carlie Tanner

- **CSOC**
  - Ron Pfeiffer
PPMI MJFF team

- Sohini Chowdhury, PPMI Overall Project Manager
- Mark Frasier, PhD, Biologics (Biorepository selection; biologic collection SOPs, assay identification and optimization)
- Claire Meunier, Recruitment/Retention Strategies
- Jamie Eberling, PhD, Imaging Core and imaging SOPs
- Debi Brooks, Industry partnership development, Recruitment/Retention Strategies
- Todd Sherer, PhD, MJFF CEO
Industry Scientific Advisory Board (ISAB) Membership

Abbott
Michelle Collins
Katherine Widnell

Avid Radiopharmaceuticals
Mark Mintun

Biogen Idec
Bernard Ravina, Chair-elect

Covance
Peggy Taylor

Elan
Ted Yednock

Genentech
Marcel van der Brug

GlaxoSmithKline
Alastair Reith

GE Healthcare
Igor Grachev

Pfizer
Thomas Comery, Chair

Roche
Susanne Ostrowitzki
Paulo Fontoura

MERCK
Johan Luthman
David Michelson
Meeting Goals

• Review study success
  • Develop and implement PPMI infrastructure, enrollment, retention.
  • Highlights – CSF, DTI, DAT, UPDRS

• Meet study challenges
  • Recruitment of PD. Retention.
  • Continue rigorous efforts to acquire high quality data.

• PPMI must continue to be innovative
  • Novel analytes, imaging tools, clinical assessments, analyses
  • P-PPMI implementation
## Annual Investigators Meeting
### May 2/3, 2011

**AGENDA**

<table>
<thead>
<tr>
<th>Wednesday May 2, 2012</th>
<th>Thursday May 3, 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2:30-2:45 pm</strong> Welcome and Introductions</td>
<td><strong>8:00-8:30 am</strong> Breakfast</td>
</tr>
<tr>
<td>Marek, Sherer</td>
<td><strong>All</strong></td>
</tr>
<tr>
<td><strong>2:45-3:00 pm</strong> PPMI Status Update</td>
<td><strong>8:30-9:30 am</strong> Recruitment and retention</td>
</tr>
<tr>
<td>Marek</td>
<td>Jennings, Meunier</td>
</tr>
<tr>
<td><strong>3:00-3:30 pm</strong> Clinical Data Recap</td>
<td><strong>9:30-10:00 am</strong> Using PPMI Data</td>
</tr>
<tr>
<td>Coffey, Kleiburtz</td>
<td>Lasch, Toga</td>
</tr>
<tr>
<td>• Demographic Information</td>
<td></td>
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<tr>
<td>• Collected data (motor, non-motor, neuropysch and neurobehavioral)</td>
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<tr>
<td>• Data entry and future training</td>
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<tr>
<td><strong>3:30-4:00 pm</strong> Imaging Recap</td>
<td><strong>10:00-10:15 am</strong> Break</td>
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<tr>
<td>Selby, Schuff</td>
<td></td>
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<tr>
<td>• Update and data on DaTSCAN, DTI and MRI</td>
<td></td>
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<tr>
<td>• Future training</td>
<td></td>
</tr>
<tr>
<td><strong>4:00-4:15 pm</strong> Biologics Recap</td>
<td><strong>10:15-11:15 am</strong> Ancillary/Sub-Studies</td>
</tr>
<tr>
<td>Scutti, Frasier</td>
<td>Siderowf, Tanner</td>
</tr>
<tr>
<td>• Update on inventory/process</td>
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<tr>
<td>• Data on received samples</td>
<td></td>
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<tr>
<td>• Biospecimen request process/Biospecimen Review Committee (BRC)</td>
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<tr>
<td><strong>4:15-5:15 am</strong> Report from Industry Scientific Advisory Board</td>
<td><strong>11:15-11:45 am</strong> Strategies for PPMI analysis</td>
</tr>
<tr>
<td>Comery</td>
<td>Marek, Kleiburtz</td>
</tr>
<tr>
<td><strong>5:15-5:30 pm</strong> Closing Remarks – Preparation for Tomorrow</td>
<td><strong>11:45-12:45 pm</strong> Lunch – With Working Groups</td>
</tr>
<tr>
<td>Marek</td>
<td></td>
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<tr>
<td><strong>6:00 pm</strong> Dinner (Venue TBD)</td>
<td><strong>12:45-1:45 pm</strong> Future PPMI Studies – Recommendations from Working Groups (WG)</td>
</tr>
<tr>
<td>All</td>
<td></td>
</tr>
<tr>
<td><strong>1:45-2:45 pm</strong> PPMI Data Analyses</td>
<td></td>
</tr>
<tr>
<td>• Description of planned analyses</td>
<td>Siderowf, Frasier, Shaw, Selby</td>
</tr>
<tr>
<td>• Input on future analyses</td>
<td></td>
</tr>
<tr>
<td><strong>2:45-3:45 pm</strong> P-PPMI: Pre-Motor-PPMI Proposal</td>
<td>Marek</td>
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<tr>
<td><strong>3:45-4:00 pm</strong> Sharing PPMI Data and Activities</td>
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<tr>
<td>• Publications, Talks, Abstracts</td>
<td></td>
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<tr>
<td>• Upcoming meetings and activities at meetings</td>
<td></td>
</tr>
<tr>
<td><strong>4:00-4:15 pm</strong> Closing</td>
<td><strong>2013 Annual Meeting dates</strong></td>
</tr>
<tr>
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<td>Marek</td>
</tr>
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