PPMI Clinical Data Recap

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PARKINSON'S PROGRESSION MARKERS INITIATIVE
Play a Part in Parkinson's Research

OVERVIEW

Source of data for this presentation:

- Information comes from:
  - Tables produced for CSOC report
  - Tables produced for monthly review by steering committee
- All data comes from a data freeze based on data obtained from the LONI website on 04/02/12

ENROLLMENT

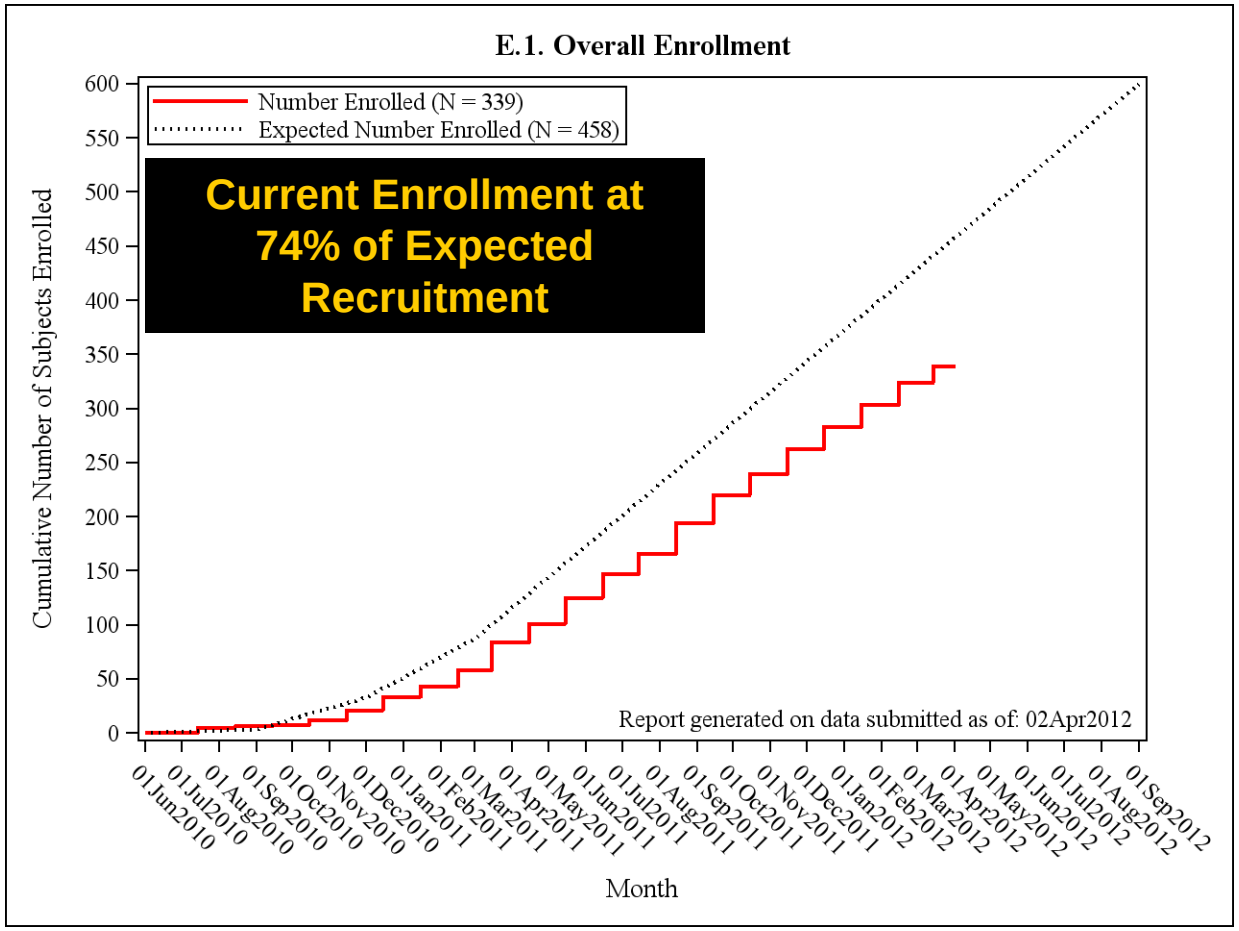
Group	Consented	Enrolled	Pending	Excluded/ Declined
PD Subjects	237	192	13	32
Healthy Controls	182	147	3	32
SWEDD Subjects	36	25	1	10

364 Total Subjects Enrolled

PARKINSON'S PROGRESSION MARKERS INITIATIVE

Play a Part in Parkinson's Research

ENROLLMENT



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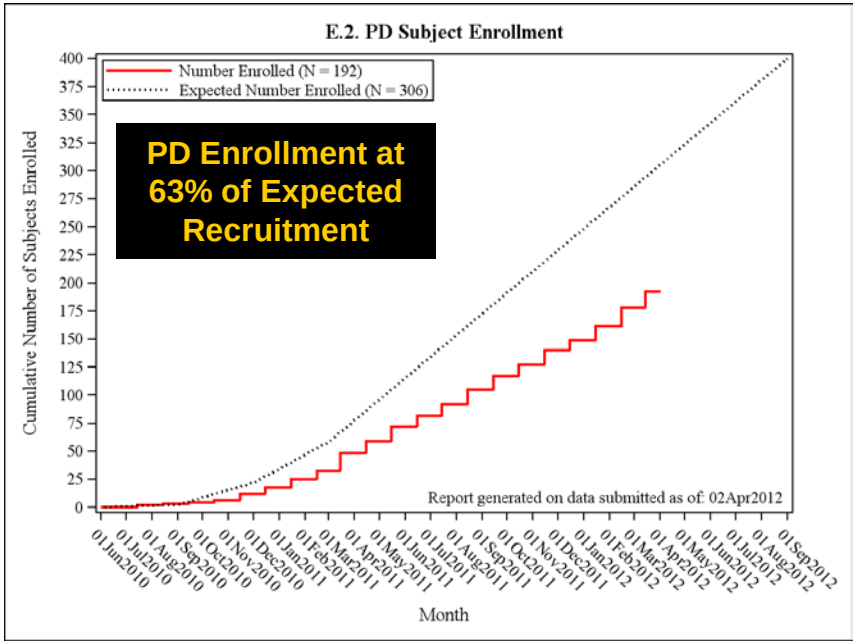
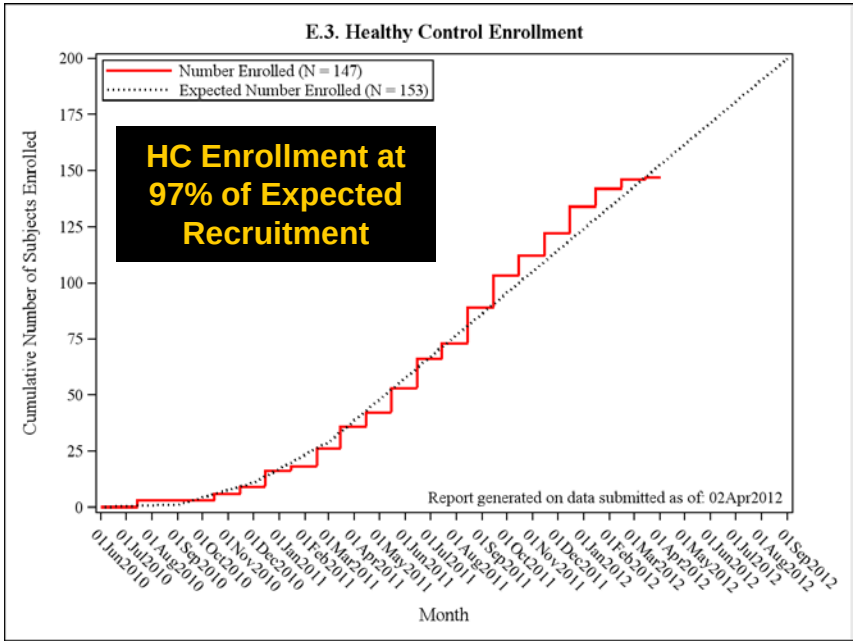
ENROLLMENT





PARKINSON'S PROGRESSION MARKERS INITIATIVE

Play a Part in Parkinson's Research

DaTSCAN AVAILABILITY ISSUES

For some subjects, a DaTSCAN was not performed at the same time as the baseline clinical assessments.

Reasons:

- DaTSCAN was unavailable in the United States from 01/27/2011 to 06/23/2011
- German sites did not obtain Radiation safety approval to proceed with scans for healthy controls until March 2012.

DaTSCAN AVAILABILITY ISSUES

To differentiate concerns beyond control of sites, the PPMI investigators produced two versions of CSOC tables.

A modified version counted forms as complete, and did not count deviations, once the scan was completed.

The CSOC agreed that the scan could be counted as complete ***if conducted within 4 months of baseline***.

DaTSCAN AVAILABILITY ISSUES

PD Subjects:

- 46 enrolled without baseline DaTSCAN
  - 43 (94%) had DaTSCAN completed within 4 months
  - 2 (4%) had DaTSCAN completed after 4 months
  - 1 (2%) did not have DaTSCAN completed (termination)

Healthy Controls

- 49 enrolled without baseline DaTSCAN
  - 23 (47%) had DaTSCAN completed within 4 months
  - 8 (16%) had DaTSCAN completed after 4 months
  - 18 (37%) have not yet had a DaTSCAN (German sites)
    - 14 (29%) have already passed 4 month window

DaTSCAN AVAILABILITY ISSUES

SWEDD Subjects:

- 6 enrolled without baseline DaTSCAN
  - 4 (67%) had DaTSCAN completed within 4 months
  - 2 (33%) had DaTSCAN completed after 4 months

BASELINE DATA COMPLETENESS

Including forms with DaTSCAN performed within 4 months of baseline:

- 290 (80%) have all baseline information entered into the publicly-accessible database
  - 359 (99%) have cognitive testing
  - 357 (98%) have a blood sample
  - 355 (98%) have a urine sample
  - 354 (97%) have all clinical forms entered
  - 349 (96%) have a lumbar puncture
  - 338 (93%) have an MRI
  - 326 (90%) have a DaTSCAN

GENDER/AGE DISTRIBUTION

- PD Subjects:

Group	Enrolled
Male / <56	30
Male / 56-65	54
Male / >65	51
Female / <56	17
Female / 56-65	21
Female / >65	19

GENDER/AGE DISTRIBUTION

- Healthy Controls:

Group	Enrolled	Expected Based on PD Enrollment	p-value
Male / <56	29	23.0	< 0.001
Male / 56-65	27	41.3	
Male / >65	29	39.0	
Female / <56	24	13.0	
Female / 56-65	25	16.1	
Female / >65	13	14.5	

Controls are more likely to be:

• Young / Female

GENDER/AGE DISTRIBUTION

- SWEDD Subjects:

Group	Enrolled	Expected Based on PD Enrollment	p-value
Male / <56	4	3.9	0.14
Male / 56-65	4	7.0	
Male / >65	5	6.6	
Female / <56	6	2.2	
Female / 56-65	3	2.7	
Female / >65	3	2.5	

DEMOGRAPHIC CHARACTERISTICS

	PD Subjects (N = 192)	Healthy Controls (N = 147)	SWEDD Subjects (N = 25)
Males	135 (70%)	85 (58%)	13 (52%)
Age (mean)	62	59	58
• <56 years	47 (24%)	53 (36%)	10 (40%)
• 56-65 years	75 (39%)	52 (35%)	7 (28%)
• >65 years	70 (36%)	42 (29%)	8 (32%)
Hispanic/Latino	3 (2%)	3 (2%)	1 (4%)
Race			
• Caucasian	180 (94%)	136 (93%)	23 (92%)
• African-American	1 (1%)	9 (6%)	0 (0%)
• Asian	3 (2%)	0 (0%)	1 (4%)
• Other	8 (4%)	1 (1%)	1 (4%)

BASELINE CHARACTERISTICS

	PD Subjects (N = 192)	Healthy Controls (N = 147)	SWEDD Subjects (N = 25)
UPDRS Part III	20.4	1.2	15.4
MOCA Total	27.2	28.3	27.7
GDS Total	2.3	1.3	3.0
SCOPA AUT	9.5	6.0	12.3

PD CHARACTERISTICS

	PD Subjects (N = 192)	SWEDD Subjects (N = 25)
Family Hx of PD	50 (26%)	4 (16%)
Mn duration of disease	8 months	10 months
Mn MDS-UPDRS score		
• Total score	33.5	29.8
• Part I	5.7	7.8
• Part II	6.1	5.8
• Part III (Motor Exam)	21.7	16.2
Mn Modified Schwab	93	95
Hoehn & Yahr		
• Stage 1	73 (38%)	12 (48%)
• Stage 2	113 (59%)	13 (52%)
• Stage 3-5	2 (1%)	0 (0%)

VISIT COMPLIANCE

Group	Month 6 # Expected (% Seen)	Month 12 #Expected (% Seen)
PD Subjects	105 (97%)	32 (100%)
Healthy Controls	89 (97%)	26 (88%)
SWEDD Subjects	6 (83%)	N/A

There are 3 sites with 100% in-window accuracy for in-person visits:

023 (5 total follow-up visits)
028 (9 total follow-up visits)
291 (26 total follow-up visits.)

LUMBAR PUNCTURE COMPLETENESS

Group	Baseline # Expected (% Complete)	Month 6 # Expected (% Complete)	Month 12 #Expected (% Complete)
PD Subjects	192 (95%)	105 (92%)	32 (91%)
Healthy Controls	147 (97%)	89 (83%)	26 (69%)
SWEDD Subjects	25 (96%)	6 (83%)	N/A

PROTOCOL DEVIATIONS

PD Subjects: 38 protocol deviations (in 34 subjects)

- 18 due to eligibility criteria
  - 1 due to baseline DaTSCAN not performed
  - 1 due to baseline DaTSCAN performed beyond 4 months
- 10 due to DaTSCAN (dosage)
- 3 due to Lumbar Puncture
- 3 due to research specimen(s)
- 2 due to clinical labs
- 1 due to 'Other' (CSF testing for hemoglobin)

PROTOCOL DEVIATIONS

Healthy Controls: 53 protocol deviations (in 45 subjects)

- 30 due to eligibility criteria
  - 7 due to baseline DaTSCAN performed beyond 4 months
  - 18 due to missing baseline DaTSCAN
- 11 due to DaTSCAN (dosage)
- 3 due to research specimen(s)
- 2 due to lumbar puncture (CSF testing for hemoglobin)
- 2 due to clinical labs
- 1 due to MRI not done

Controls are significantly more likely to have a deviation – mostly due to German DaTSCAN issue.

PROTOCOL DEVIATIONS

SWEDD Subjects: 5 protocol deviations (in 5 subjects)

- 3 due to DaTSCAN (dosage)
- 2 due to eligibility criteria
  - Both due to baseline DaTSCAN performed beyond 4 months

EARLY STUDY TERMINATIONS

PD Subjects: 3 early study terminations

- 2 due to adverse event (headache, exasperation of PD symptoms)
- 1 due to 'other' ("patient decided to take anti-parkinsonian medication today")

Healthy Controls: 3 early study terminations

- 2 withdrew consent
- 1 due to 'other' (unwilling to comply with lumbar puncture)

REPORTABLE EVENTS

PD Subjects: 52 reportable events (in 50 subjects)

- 45 due to starting PD meds
  - 5 within 3 months from baseline
  - 24 within 4-6 months from baseline
  - 9 within 7-9 months from baseline
  - 4 within 10-12 months from baseline
  - 3 greater than 12 months from baseline
- 3 started another study
- 2 due to early withdrawal
- 1 due to an SAE

REPORTABLE EVENTS

Healthy Controls: 4 reportable events (in 4 subjects)

- 2 due to early withdrawal
- 1 due to change of diagnosis
- 1 started another study

SWEDD Subjects: No reportable events

ADVERSE EVENTS

PD Subjects: 79 adverse events (in 41 subjects)

- 55 LP-related AE's
  - 23 occurrences of "Headache"
  - 6 occurrences of "Injection Site Pain"
  - 6 occurrences of "Myalgia"
  - 5 occurrences of "Back Pain"
  - 2 occurrences each of "Musculoskeletal Discomfort", "Dizziness", & "Post Lumbar Puncture Syndrome"
  - 1 occurrence each of "Nausea", "Pain", "Tenderness", "Pain in Extremity", "Loss of Consciousness", "Parkinson's Disease", and "Presyncope"
- 2 DaTSCAN-related AE's

ADVERSE EVENTS

Healthy Controls: 92 adverse events (in 52 subjects)

- 76 LP-related AE's
  - 34 occurrences of "Headache"
  - 12 occurrences of "Back Pain"
  - 7 occurrences of "Injection Site Pain"
  - 4 occurrences of "Myalgia"
  - 4 occurrences of "Dizziness"
- 5 DaTSCAN-related AE's
  - 1 occurrence each of "Sensation of Pressure", "Myalgia", "Dysgeusia", "Headache", & "Pruritus"

ADVERSE EVENTS

SWEDD Subjects: 11 adverse events (in 6 subjects)

- 6 LP-related AE's
  - 3 occurrences of "Headache"
  - 1 occurrence each of "Back Pain", "Muscle Spasms", & "Myalgia"
- 2 DaTSCAN-related AE's
  - 1 occurrence each of "Dysgeusia" & "Headache"

ADVERSE EVENTS

- Subjects with an AE:
  - PD Subjects – 41/192 (21%)
  - Healthy Controls – 52/147 (35%)
  - RR = 0.60, 95% CI: (0.42, 0.85)
- Subjects with an LP-related AE:
  - PD Subjects – 34/192 (18%)
  - Healthy Controls – 48/147 (33%)
  - RR = 0.54, 95% CI: (0.37, 0.79)
- Subjects with a DaTSCAN-related AE:
  - PD Subjects – 2/192 (1%)
  - Healthy Controls – 4/147 (3%)
  - RR = 0.37, 95% CI: (0.07, 1.99)

ADVERSE EVENTS

- Subjects with an AE:
  - PD Subjects – 41/192 (21%)
  - SWEDD Subjects – 6/25 (24%)
  - RR = 0.89, 95% CI: (0.42, 1.88)
- Subjects with an LP-related AE:
  - PD Subjects – 34/192 (18%)
  - SWEDD Subjects – 4/25 (16%)
  - RR = 1.11, 95% CI: (0.43, 2.87)
- Subjects with a DaTSCAN-related AE:
  - PD Subjects – 2/192 (1%)
  - SWEDD Subjects – 2/25 (8%)
  - RR = 0.13, 95% CI: (0.02, 0.88)

SERIOUS ADVERSE EVENTS

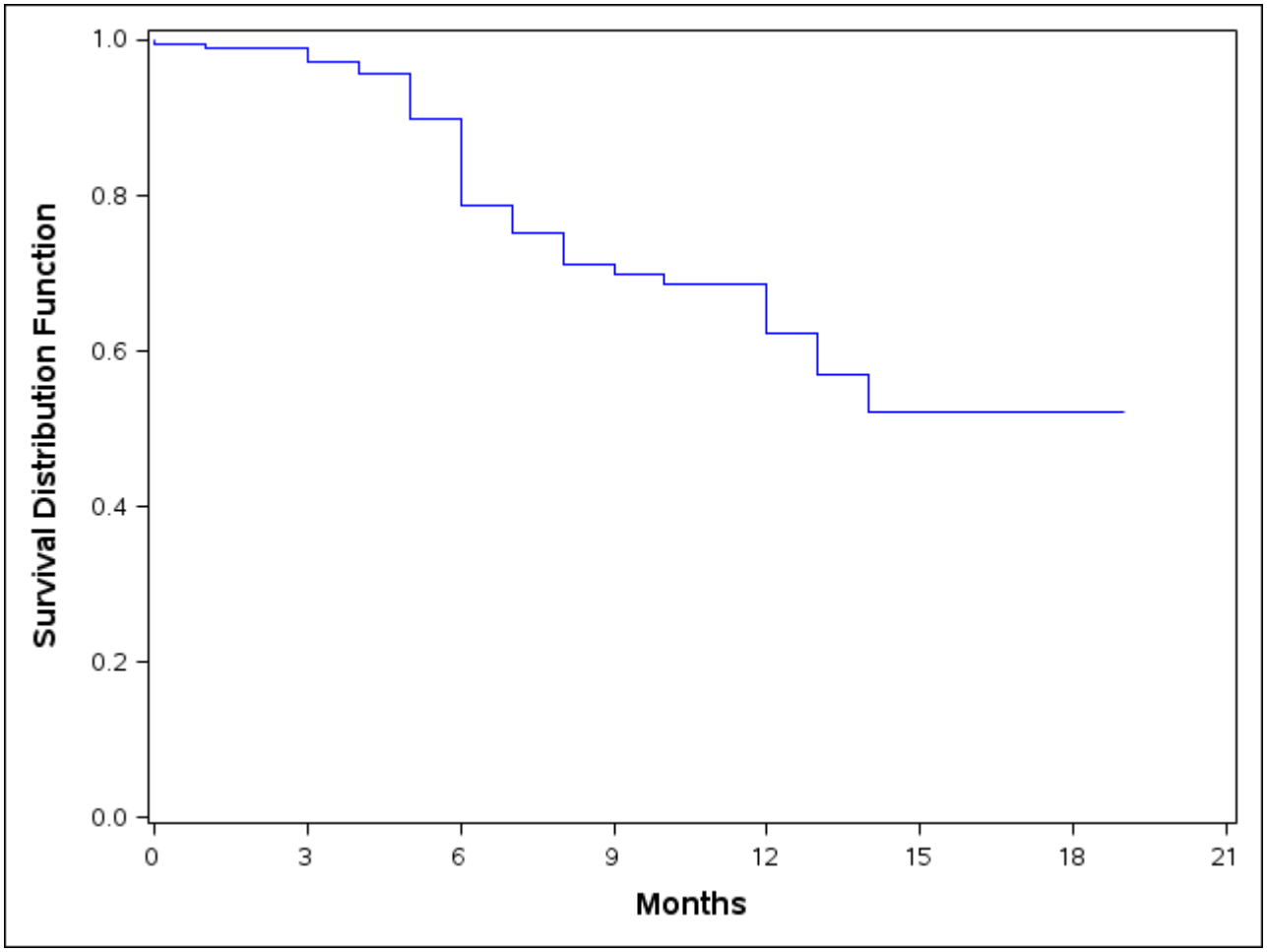
PD Subjects: 2 serious adverse events (in 1 subject)

- 1 ‘Colitis’ and 1 ‘Pancreatitis’
- None related to LP or DaTSCAN

Healthy Controls: No serious adverse events to date

SWEDD Subjects: No serious adverse events to date

TIME TO START PD MEDICATIONS



Time	Percentage Starting PD Meds
3 Months	3%
6 Months	21%
9 Months	30%
12 Months	38%

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