Measuring Dyskinesia in Parkinson's Clinical Trials

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Webinar Series
Question 1:

1. How are PD motor complications evaluated in clinical trials?

2. What are the challenges with clinical trial dyskinesia endpoints, and how can they be improved?

3. How can home-based motion sensor dyskinesia assessment improve your clinical trials?
Motor Complications of Chronic Levodopa Therapy

1. Motor fluctuations
   - Alternate between therapy “off” and “on” states over dose cycles

2. Levodopa-induced dyskinesia (LID)
   - Involuntary, episodic, and irregular movements
   - Peak-dose most common

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### Clinical Trials for Parkinson's Disease and Dyskinesia

<table>
<thead>
<tr>
<th>Rank</th>
<th>Status</th>
<th>Study</th>
<th>Conditions</th>
<th>Interventions</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Not yet recruiting</td>
<td>Safety and Efficacy of AVP-923 in the Treatment of Levodopa-induced Dyskinesia in Parkinson's Disease Patients</td>
<td>Dyskinesia; Parkinson's Disease</td>
<td>Drug AVP-923-46; Drug Placebo</td>
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<td>2</td>
<td>Recruiting</td>
<td>Open-label, Long-term Safety Extension Study of AFQ056 in Parkinson's Patients With L-dopa Induced Dyskinesias</td>
<td>Dyskinesias; Parkinson Disease; Movement Disorders; Parkinsonian Disorders; Anti-Dyskinesia Agents</td>
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Clinical Trial Endpoints

- Clinical Assessments
  - UPDRS, UDysRS, mAIMS, PDYS-26
  - Patient retrospective recall

- Patient diaries
  - Self assessment at home
  - 0.5-1 hr interval diary entries

- Body-worn motion sensors
  - Shift in research
  - Unconstrained continuous assessment at home
    - Transition to clinical trial use not trivial
    - Importance of quality assurance (e.g. FDA, ISO, CE, TGA)
Challenges with Clinical Trial Endpoints

- Resolution of clinical rating scales
  - Severity: 0-4 integer scoring
  - Temporal: snapshot of dyskinesia response

- Compliance of home diaries
  - Correlation between reported and actual compliance
  - Patient awareness of, understanding, and recognizing therapy states

- Costs
  - Clinician and patient time in clinic
  - Accuracy may affect statistical power
Motion Sensor LID Assessment: Clinical Validation Study

- Collaborators
  - Michelle Burack, MD, PhD
  - NIH-funded SBIR Phase I

- Goals
  1. Capture peak-dose dyskinesia over a levodopa dose using hand-worn motion sensors
  2. Develop a scoring model to automatically rate dyskinesia
  3. Determine whether a single motion sensor unit could accurately assess global dyskinesia
Methods: Study Preparation

- Off levodopa from previous night or end of dose
- A wireless motion sensor unit positioned on each hand
- Two discrete motor tasks:
  1. Arms resting
  2. Arms Extended
- Serial subtractions as distraction
Methods: Data Collection

- Two motor tasks at hours 0, 1, 2, and 3 after levodopa dose
- Motion sensor data were wirelessly streamed to a computer
- Video of task performance was recorded and later scored by two expert raters
  - modified-Abnormal Involuntary Movement Scale (m-AIMS)
    - 0 (none) to 4 (severe) global dyskinesia ratings
- Severity scoring models developed using sensor data and clinician global m-AIMS scores
Clinical Assessment

The time to reach peak-dose dyskinesia varied by subject.
Symptom Feature Extraction

Time Signal

Power Spectrum

Clinician Scores

Dyskinesia  Tremor

0  2

2  0

0  1
Dyskinesia Severity Scoring Model

![Graph showing correlation coefficient and root mean squared error for Clinician Agreement and Model Performance.](Image)

![Scatter plot showing correlation between Mean Clinician Global m-AIMS and Model Score.](Image)
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Clinical Trial Drug Comparison

Drug A:
Medication State Distribution

- ON: 11%
- OFF: 36%
- ON+DYS: 53%

Drug B:
Medication State Distribution

- ON: 24%
- OFF: 24%
- ON+DYS: 52%
Advantages For Your Clinical Trials

Motion sensor assessment during discrete tasks

- Clinical validation and quality assurance
- Home assessment kit
- Single motion sensor to assess global dyskinesia fluctuations
- Electronic formatting
  - Instant access, reports
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References

Questions?

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