Welcome to the 1st edition of the Biogen SPARK 228PD201 Study Newsletter!

We want this newsletter to be valuable for you so please share your feedback and suggestions.

STUDY PROGRESS

We are now actively enrolling for Cohort A. Our goal for this cohort is 24 subjects randomized. As of 07Feb2018, our study status is as follows:

<table>
<thead>
<tr>
<th>Sites Initiated</th>
<th>Sites Activated</th>
<th>Total Screened</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>6</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total in Screening</th>
<th>Total Screen Failed</th>
<th>Total Randomized</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

We encourage you to consider continuing with pre-screening efforts so that you may begin screening immediately after initiation. For sites that have been initiated, please remember to complete the pre-screening log and send on the 1st and 3rd Monday of each month.

The pre-screening logs should be sent to SPARKBIogen@quintiles.com with your assigned CRA in copy.

CONGRATULATIONS!

Dr. Jason Aldred’s site for randomizing our first SPARK subject!

Dr. Robert Hauser’s site, currently with two subjects in screening!
PARKINSON STUDY GROUP

The Parkinson Study Group (PSG) is a non-profit group of physicians and other health care providers in the United States, Canada and Puerto Rico. PSG is experienced in the care of Parkinson patients and is dedicated to clinical research of Parkinson’s disease (PD). PSG provides valuable input for the SPARK study and provides the opportunity for investigators to become PSG credentialed. We extend our gratitude to PSG for collaborating with us to make this important study a success!

INFORMED CONSENTS

Study Subjects

Subjects will be presented with three ICFs at the time of screening (one required main ICF and two optional).

<table>
<thead>
<tr>
<th>ICF Type</th>
<th>Cohort</th>
<th>Required</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main ICF</td>
<td>A+B</td>
<td>Yes</td>
<td>Required – separate ICF for each cohort</td>
</tr>
<tr>
<td>Pharmacogenetic ICF</td>
<td>A+B</td>
<td>Optional</td>
<td>Retention of residual DNA samples for exploratory research related to diseases and traits of interest</td>
</tr>
<tr>
<td>Future Scientific Research ICF</td>
<td>A+B</td>
<td>Optional</td>
<td>Retention of residual whole blood, plasma, urine, serum and CSF samples for exploratory biomarker research</td>
</tr>
</tbody>
</table>

Study Subjects and Healthy Non-Study Subjects for First MRI Scan

1. Bioclinica provides training and qualification for MRI facilities.
2. Bioclinica provides authorization to scan the first subject.
3. Site identifies either a healthy volunteer or a SPARK study subject to undergo the qualification MRI scan.
   
   *Only if a healthy non-study subject is used for this process, they should sign a Healthy Subject Volunteer ICF. It is optional if you use a healthy volunteer for this purpose.*
4. The first subject scan is acquired, transmitted and reviewed for quality checks to confirm that additional subjects may be scanned for the trial.
5. A passing QC report is provided to the site after this scan is complete and deemed acceptable.
SUBJECT VISIT TIPS & TRICKS

The site staff at Dr. Aldred’s site in Spokane, Washington shared some very valuable tips and suggestions to make the subject visits go more smoothly:

• Encourage subjects to eat a good breakfast and stay hydrated to help with blood draws and to make IV insertion easier and less painful.

• Have them bring a book/kindle and have a nice, quiet, spot for them to relax.

• Remember that this might be a little overwhelming, especially for new PD patients.

• Provide lunch. Nothing cheers people up more than good food, especially if the day is really wearing on.

• This is an intense trial for a neurodegenerative disease and this population has only been dealing with PD for 3 years or less. Talk them through it and explain what is going on and what their expectations should be to make them feel at ease.

BBK RECRUITMENT AND RETENTION PROGRAMS

BBK is the provider of recruitment and retention tools for the SPARK study. Please contact your assigned CRA for any questions and/or if you require access to Trial Central Net (TCN). The website can be accessed at [https://tcnconnect.com](https://tcnconnect.com)

Use for any subject travel arrangements and accommodation.

• Site staff can make requests for travel by accessing the Trial Central Network (TCN) website.

• Subjects will need to provide consent to the IRB approved travel policy located on TCN and an itinerary will be provided to the site for travel arrangements.

• This program eliminates the need for site invoicing for subject travel.

Use for subject reimbursements.

• Assigned to subjects

• Once the card is assigned, the site will manage the subjects account through TCN, which involves entering reimbursements on a category-by-category basis, with the site referencing subject receipts.

• This ensures immediate reimbursement with subjects being able to literally walk away from their first study visit with a loaded card in hand.

• The cards can be utilized anywhere where VISA is accepted and subjects may also visit an ATM to withdraw funds without incurring any costs.

DATSCAN DOSE ORDERING

• Use the site-specific dose order form

• Doses must be ordered according to the instructions on the form

• Submit the order form before 11am EST at least 3 business days prior to the scan

• Doses are available for delivery Tues-Thurs

• Cancellations must be made at least 3 business days prior to delivery date

• Dose order forms must be faxed to the number on the form

• Communication between the site staff and SPECT facility is key in this process.

SAFETY INFORMATION

AEs and SAEs

Per protocol section 15.2.3, severity of all adverse events should be graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. Please confirm that grading is clearly documented in the source.
**FREQUENTLY ASKED QUESTIONS**

**Q:** Should sites obtain the frequent PK sampling by repeated venipuncture or is a peripheral IV (PIV) line acceptable?

**A:** Sites must do repeated venipuncture from the arm opposite of the infusion or perhaps a PIV placed in the opposite arm for repeated sampling. For example, infusion in left arm and butterfly in right arm.

**Q:** Can you confirm/clarify the frequency and extent of physical exams (PE)/Neurological exams (NE)?

**A:** A full PE and NE will be performed at the specified time points. At all other visits, a targeted PE and NE examination will be performed if the investigator determines it is warranted by adverse events or clinical picture.

**Q:** What is required for Bioclinica imaging qualification prior to SIV?

**A:** Pre-Trial Questionnaire (PTQ) completion followed by remote web training and submission of phantom scans for MRI; For SPECT, PTQ completion followed by onsite training and acquisition of striatal phantom followed by protocol validation test phantom by facility. Authorization letters will be sent to the site for each facility once all is complete.

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**Tip of the Month**

Did you know that the Firecrest Investigator Web Portal is not just for site staff training? Explore all the useful tools available under the Navigation tab:

- Trial Drive: Investigator Meeting slides, vendor manuals, and the vendor contact information tool
- My VBVG tab: a visit guide and visit planner/calculator

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**GLOBAL STUDY TEAM CONTACT INFORMATION**

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