Welcome to the Biogen SPARK 228PD201 Study Newsletter!

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

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STUDY STATUS

<table>
<thead>
<tr>
<th>Total Screened</th>
<th>482</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Randomized</td>
<td>357</td>
</tr>
<tr>
<td>Active Randomized</td>
<td>348</td>
</tr>
<tr>
<td>Early Terminations</td>
<td>9</td>
</tr>
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As announced previously in the July newsletter (Issue 11), protocol amendment version 6 is now finalized and IRB/EC submissions are in progress!

The amendment adds a dosing extension phase that will allow eligible subjects to continue dosing in the double-blind active treatment period until the last subject completes Year 2. The maximum duration of participation will be 178 weeks. Subjects will need to be reconsented at the Week 96 visit before moving into the extended phase.

To allow for uninterrupted dosing from the Week 96 visit for each subject, sites with a local IRBs/ECs are encouraged to expedite revision of the draft consents so that approval of the amendment is not delayed. In addition, for those sites that have patient stipend information in the consents, we ask that you expedite contract amendment negotiations so that IRB/EC submission can occur as quickly as possible.
Now that enrollment for SPARK is complete, we have noted some delays with submission of imaging scans. In order to ensure study compliance, it is essential that MRI and SPECT scans are submitted to Bioclinica within 24 hours.

**LUMBAR PUNCTURES**

Lumbar punctures (LP) are an essential part of the SPARK study for measuring the effect of BIIB054 on potential biomarkers in the CSF. For this reason, it is very important that the procedure is completed for all three timepoints (baseline, Week 24 and Week 52) for all subjects enrolled into the CSF subset.

Fluoroscopy may be used for LPs to help minimize discomfort. Sites will be reimbursed for the procedure. Please discuss with your IQVIA Site Manager if your informed consents must be revised to include fluoroscopy per site policy.

**FROZEN SAMPLE STORAGE AND SHIPPING**

All lab samples should be stored and shipped to Q² Solutions according to the guidelines in the central lab flowchart. Sites are encouraged to use the logs provided in the Study Reference Manual (frozen sample storage/shipping log and temperature log; site specific logs may also be used as long as all information is documented. Min/max/actual temperatures must be recorded on working days min/max/actual temperatures for lab sample freezers.

- Freeze all vials immediately at -70/-80 °C
- If stored at -70/-80 °C, original samples must be shipped frozen on dry ice to Q² Solutions monthly;
- Back-up (BU) samples must be shipped frozen on dry ice to Q² Solutions with the next available shipment
- If a -70/-80 °C freezer is unavailable, samples may be stored at -20 °C until shipment and original samples MUST be shipped DAILY to Q² Solutions; Back-up (BU) samples must be shipped within 5 days

**PD MEDS AND DISEASE PROGRESSION**

Per protocol section 11.3.1.1, symptomatic PD treatment may be initiated at the discretion of the Investigator, although subjects should refrain from taking symptomatic PD medications for as long as possible (for at least 6 months following Day 1). Investigators are asked to contact the medical advisor to discuss if you are contemplating starting symptomatic PD medications prior to the 6-month time point.

Worsening of PD or PD symptoms should only be reported as adverse events if there is an unexpected worsening beyond the natural disease progression of PD. Starting medications for symptomatic PD should not trigger an adverse event to be reported, unless there is also unexpected worsening of PD symptoms beyond what is expected. In cases where the investigator feels that there is a worsening outside of the normal progression of PD, these details should be clearly documented in the source chart and an adverse event should be reported.

**SUBMISSION OF SCANS**

Now that enrollment for SPARK is complete, we have noted some delays with submission of imaging scans. In order to ensure study compliance, it is essential that MRI and SPECT scans are submitted to Bioclinica within 24 hours.

**SPARK WEBINAR**

11:30 am EST / 1730 CST
Please make plans to attend.
DATA ENTRY REMINDERS

Please see below for helpful reminders regarding data entry and query resolution timelines:

➢ Please check Rave on a **weekly basis** to close all queries
  - All open queries must be answered within **5 days** of issue
  - Answer all CRA queries during monitoring visits, if possible

➢ Data should be entered within **3 calendar days** of the subject visit

➢ Complete all required fields for the Screen Failure subjects:
  - Screening Visit: Date of Visit, Informed Consent, Demographics, PD History, PD Treatment History
  - Day 1: Inclusion/Exclusion Criteria
  - Study Status regarding 228HV101 (US only)
  - End of Study

➢ Ensure there is no missing data and if a data is unknown or not collected leave field blank and provide an explanation in the query response.

➢ Local Lab Reference Ranges
  - Should be entered on the site level per CRF Completion Guidelines
  - Ranges must be entered for entire age range and female/male
  - Dates of ranges must be current in the “To Date” and “From Date” fields
  - Once entered, should show beside local lab results in CRF

➢ Protocol Amendment Page
  - Should be added once a subject is reconsented for a protocol amendment
  - Allows for the date of reconsent to be entered and applicable forms to populate

Your IQVIA Site Manager can be contacted for any questions/concerns.

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QMA SENSOR STICKERS

All sites have received or will receive 10 stickers with a white arrow on a transparent background. Per the instructions provided, please ensure that 1 sticker is placed on each QMA sensor with the arrow that covers the word ‘Opal’ on the sensor face and pointing toward the blinking LED light but does not cover the light.

The aim of the stickers is to reduce the number of the errors deriving from incorrect sensor placement.

Your Site Manager will confirm that the stickers have been correctly placed at the next onsite visit.

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FIRECREST V6 TRAINING

Firecrest protocol version 6 training module is now available for site staff! Protocol version 5 changes are included in the training as well. The training module is required for all subject-facing site staff and unblinded staff prior to performing study related tasks. Site staff are encouraged to complete the training now so that all is in place well in advance for protocol version 6 approvals!

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PROTOCOL DEVIATION TRENDS

We have noted a steadily increasing trend of protocol deviations, with the majority being related to missed study procedures or not done correctly, lab samples not collected or processed per protocol and out of window visits. As we strive to have the highest quality data for SPARK we encourage sites to implement measures to prevent the same deviations going forward.

The Firecrest visit calendar and Visit-by-Visit guide are very helpful tools that can help site staff prepare for subject visits well in advance to minimize protocol deviations. Sites are also encouraged to discuss recurring issues with their assigned Site Managers.
FREQUENTLY ASKED QUESTIONS

Q: How can sites make corrections to scale dates in Virgil?

A: Sites should refer to page 101 in the Virgil Portal User Guide for instructions on how to perform this task. The current version of the user guide can be found via the following link:


Q: How is the protocol amendment CRF page added for a subject in Rave?

A: This page can be added by using the Add Event drop down box on the home page for each subject. (ref: ages 96-97 of the CRF Completion Guidelines version 5).

Going forward, we will highlight one site in each newsletter as recognition for your hard work on the SPARK trial!

This month’s award goes to...

Prof. Pavese and his staff from the Clinical Ageing Research Unit (Newcastle University) in Newcastle upon Tyne, United Kingdom. Prof Pavese’s site responded to the highest number of queries in the least number of days.

Congratulations and many thanks to Prof Pavese and his team!!

Did you know that...

An easy way to confirm that IP is administered within 6 hours of IP preparation is for the unblinded staff to include the time of preparation on the IV bag sticker along with the volume prepared.

The infusion staff can then quickly confirm just prior IP administration that the infusion is being conducted according to the DHA. A photocopy of the sticker can be included in the subject’s chart or the infusion staff can clearly document the time and volume in the source chart.

Tip of the Month

GLOBAL STUDY TEAM CONTACT INFORMATION

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