Letter from the Jain Foundation

WOW!!! Can you believe it has been almost 4 years since the first COS participant enrolled in the study? As of Oct 2016, all participants have completed their 1 year visit, 90% have completed their 2 year visit, and 40% have completed their 3 year visit. In addition, we still have 193 individuals participating in the study. That is a 92% retention rate!! This shows what a wonderful, motivated, and committed community we have for dysferlinopathy. We truly appreciate your commitment to this pivotal study and we are extremely hopeful that with all of us working together we will beat this disease.

We are learning so much about dysferlinopathy from this study. The data analyzed so far has been presented at numerous conferences, the first paper has been published and a number of additional publications will likely be submitted for publication before the end of 2016. The information gained from the study already has generated interest in dysferlinopathy from several drug companies and we are hopeful this will lead to clinical trials with at least some of them.

Because the current study is going so well, we are extending the study for up to 2 more visits (year 4 and 5) per COS participant at as many sites as possible. Having more information on progression over multiple years will help us better evaluate the reliability of tests to measure changes in the disease and determine which tests will work best in the evaluation of possible treatments. See the next page for more detailed information about the extension and how to sign up.

Please be sure to read the entire newsletter and ask us your questions!!

The Jain Foundation Team

Oversight and funding for COS is provided by the Jain Foundation. Email us at contact@dysferlinoutcomestudy.org or go to our website at www.jain-foundation.org

What we are already learning...

- Despite the differences in initial clinical presentation, individuals with a diagnosis of LGMD2B or Miyoshi Myopathy are proving to be very similar and therefore can be considered as the same disease. This increases the pool of patients which is an extremely important factor in such a rare disease.

- Analysis of the 1 year progression data is showing small but significant changes over a 1 year period. This is important as most clinical trials run for around 1 year and require tests that show a difference in that time period.

- MRI analysis is showing what muscles are the most and least affected over the course of the disease. This information will help us choose tests that evaluate the most relevant affected muscles which will increase the sensitivity of our analysis.

- We are beginning to better understand the relevant clinical features of dysferlinopathy and how it progresses. This will help your physicians take better care of you.

Check out the first COS publication

Included with this newsletter is a paper which describes the findings of our analysis of the baseline COS visit (visit 2). We couldn’t have done this without your participation. Thanks!!!
COS EXTENSION—YEAR 4 AND 5 VISITS

It is extremely valuable to have as much personal data as possible for each and every person participating in COS. Since this is the first long term study for LGMD2B/Miyoshi Myopathy, it is also the first time anyone has had such a large amount of data on the progression of this disease. Having information from additional visits will not only give us a greater understanding of dysferlinopathy in general, but the longer you participate in COS the better we will understand your individual progression rate.

Drug companies have told us that having individual historical progression data is highly beneficial. Therefore, participating in more COS visits could possibly increase your chances of getting recruited into various trials and could help make the trials more successful.

For these reasons, the Jain Foundation is extending COS until at least March 2018. This will allow many participants to complete a year 4 visit and for some a year 5 visit will also be possible.

We hope that you will seriously consider participating in the additional visits.

- All extension visits must be completed by March 31, 2018. If your year 4 or 5 visits would be later than that these additional visits would not occur as part of this extension.
- Not all COS locations are able to participate. Please talk directly with your study coordinator to see if they are participating and discuss date estimates for additional visits.
- Participation in additional visits is optional and requires the signing of an additional consent.
- Assessments done at the additional visits will be the same as the 3 year visit.

Without an informative; long term study of your rare disease, the chances of treatments making it into the clinics is lower. Please remain involved.

Participant Quote about participating in additional visits:

“If the opportunity arises, I will absolutely continue participating in COS for a fourth or fifth year visit. Understanding the progression of dysferlinopathy cannot be done in three years. If there is any insight I can help provide to better understand this disease’s progression and help lead to a cure or treatment, I will gladly participate for 100 years!”

CureDriven—2B Cured

The Jain Foundation has developed a new patient registry called 2B Cured. Our former patient registry, which as a COS participant you were a member, was one sided where an individual would enter their information once and that was the end. The new registry, 2B Cured, is designed to be an open conversation between patients and the foundation. 2B Cured is an interactive site that allows individuals with dysferlinopathy to communicate directly with one another and the members of the Jain Foundation. You will be receiving an email invitation from the new site (called CureDriven). Once you receive your invitation, you need to set up your profile to be activated. If you don’t become activated, the Jain Foundation and others with dysferlinopathy will not be able to communicate with you through the 2B Cured site. We cannot wait to connect with you through this new site!!!

2B Cured features:

- Forums for the discussion of relevant topics
- Posts of all updates on the progress toward discovering treatments and therapeutic strategies
- Ability to connect with others with dysferlinopathy (LGMD2B/Miyoshi Myopathy)
- Educational and clinical trial information
- Surveys to collect information important to our understanding of the disease and the development of possible therapies
Patient reported muscular/physical symptoms:

**How do your symptoms compare?**

Look at the data below to see how you compare to other COS participants

**Laboratory tests:**

- **Blood tests**

  - % low
  - % high

Blood tests evaluated during COS show changes typically seen in individuals with a muscular dystrophy such as high liver enzymes (ALT/AST), high CK, and low creatinine values. Patients with dysferlinopathy need to make sure their physician understands that these abnormal values can be from their muscle disease as this could affect the interpretation of renal and liver function investigations.

**Patient reported muscular/physical symptoms:**

- **Dizziness 12%**
- **Snoring 34%**
- **Breathlessness 20%**
- **FVC <60% predicted 9%**
- **Requiring ventilation 2%**
- **Palpitations 12%**
- **Hypertension 13%**
- **Abnormal ECG 5%**
- **Abnormal echocardiogram 5%**
- **Constipation 15%**
- **Leg swelling 24%**
- **Joint contractures 36%**

Symptoms were chosen from a range of options presented in the baseline questionnaire and patients were given the option to list ‘other’ symptoms. The percentage of participants reporting a specific symptom is indicated next to the symptom in the figure above. Only the most common symptoms are listed.

It isn’t too late to provide blood and skin samples!!!!!

Thank you to those of you who have already donated blood and skin to the biobank. We have already used a few samples to diagnose patients that did not have a complete diagnosis and are currently using other samples to identify blood biomarkers that can be used to easily track disease progression using blood. Numerous other experiments are being planned that will provide us with important information about dysferlinopathy.

If you haven’t already consented to give blood or skin samples please considering donating at your next visit. If you have already consented please continue to give samples at all your visits including the year 4 and 5 visits in the extension.

These samples help us to fully understand this disease and test possible therapies in the following ways:

- Find new dysferlin mutations in people with only 1 identified mutation (requires blood and skin samples) – **this directly helps the participant who donated** and helps other people who have not yet been diagnosed!
- Test whether particular treatments are beneficial (requires skin)
- Understand why the disease progresses differently in different people (requires blood)
- Look for disease markers to use for non-invasive monitoring during clinical trials (requires blood) - this will allow us to do clinical trials without needing muscle biopsies!