

Summary for patients  
**NDF's 5<sup>th</sup> Annual Symposium on GNE myopathy**  
**August 30-31, 2018 at UCLA, California, USA**

I am summarizing some of the important points raised in this symposium.

**Regarding Therapy for GNE myopathy**

**ManNAc trial by NIH-**

**Dr. Marjan Huizing** (NIH) described their work so far, and their plans for phase 3 with ManNAc.

2012-13: phase 1

2015-18: phase 2

Starting 2019: phase 3

In the phase 1 and 2 studies with ManNAc they did not see any adverse side effects (except GI complaints). It is generally well tolerated.

They had tried 3g, 6g, and 10g single dose, twice daily. 6g showed better result than 3g, but 10g was not better than 6g.

Taking a single high dose of ManNAc is not beneficial. Better to take smaller doses at more frequency. They recommend 4g, thrice daily rather than 6g, twice.

Phase 2 trial was open label, no placebo, ManNAc 6g, twice daily, 30 mth trial. Its statistically analyzed results will be available by Dec 2018. MRI-guided muscle biopsies were taken in phase 2. These were examined and showed improvement in patients taking ManNAc.

They measured disease progression by MRI, functional tests, patient-reported outcomes. Their detailed results will be available by end of 2018.

Leadient Biosciences is now their Company collaborator

They have a large number of CROs listed as collaborators.

**Nancy Parsons (representative from Leadient Biosciences)**

They have experience in drugs for genetic disorders. NIH approached them for ManNAc to bring it to patients. They have looked into manufacturing process of ManNAc, and how to optimize it. They will also design the trial to meet FDA guidelines.

They are concerned about pricing, and that drug should be available to each patient. Will look at reimbursement policy (This would be relevant for US patients).

**Kennan Bradley (NIH)**

She is handling the phase 3 clinical trial and gave update on it.

Objectives of phase 3 trial-

- To measure slowing of progression compared to placebo
- Long term safety
- Evaluate effect on physical function and activities of daily living compared to placebo

4gm ManNAc x thrice daily will be given.

Multicenter trial will be implemented through NeuroNEXT. Co-PIs are Dr. Amato (Harvard) and Dr. Carillo (NIH). Company partner- Leadient

It will be Randomized, double-blind, placebo-controlled, for 24 months.

51 patients, randomized. One-third of the patients will be on placebo.

End point- Quantitative muscle strength (QMA)

Analysis- slowing in rate of progression

Multicentric- Trial will be conducted at NIH, Brigham's (Harvard), UCLA, Columbia, Utah, Rochester, Kansas, Ohio

Inclusion criteria- Both GNE mutations known. Genetic test should be certified (CLIA)

International patients can also register. Write to Kennan Bradley for details (kennan.bradley@nih.gov).

Patient screening will start early 2019.

### **Gene Therapy-**

The consensus in the meeting was that Gene therapy is the most promising mode of treatment for GNEM and deserves to be pursued urgently. We need robust funding to develop the technology, test it and obtain FDA approval. One can expect a minimum of seven years for FDA approval for drug use, after we start the work.

**Lale Welsh (CEO, NDF)** informed that they have commitment of \$2.5 million from anonymous donor as matching grant to be used only for gene therapy. They need to raise 2.5 mn of their own to get this grant. This money will be used for gene therapy studies by academia- phase1. After that will be taken up by biotech. They are in touch with companies like Sarepta.

The study has to be carefully designed with the help of experts so that it meets the requirements of FDA. Otherwise approval will not be granted for clinical trials. It is not clear to me exactly who will be conducting this study.

### **Other Studies-**

**Dr. Madhuri Hegde** (Emory Univ., USA and Perkin-Elmer)

She will be doing whole genome sequencing (WGS) of 100 GNEM patients. The idea is to understand whether any other genes (other than GNE) are important in giving the symptoms of GNE myopathy. This is because patients differ a lot in disease progression and symptoms.

**Dr. Monkol Lek and Dr. Angela Lek** (Yale Univ., USA)

They will be doing RNA sequencing from patient skin cells to see any differences in RNA from GNE myopathy patients versus controls. If robust differences are found, these will be very good biomarkers to look at disease progression, and to monitor future therapies.

They will also do WGS (DNA sequencing) from patient blood samples.

### **Rehabilitation strategies and advice for patients-**

**Dr. Galen Joe and Mr. Joseph Shrader from NIH** demonstrated (through video) some of the exercises for patients. They advised that patients should do optimum exercise so as to maintain their core strength but not to stress out the weak muscles. Regular exercise is recommended at the level suitable to each individual.

**Amy Curran (GNEM patient) and Jonathan Pizzi** (Program Managers, NDF)

They gave useful tips for patients. A scanned copy of their presentation is already circulated by Rushabh. They gave suggestions about nutrition, and about gadgets that can help patients to negotiate daily tasks.