ConnectMPS Registry Project and Natural History Studies: An Example of Patients, Parents and Researchers Collaborating for a Treatment

Jill Wood[1,2] , Vanessa Miller[3] Paul Levy[4], Raquel Marques[5].

[1]Jonah's Just Begun, P.O. Box 150057, Brooklyn, NY 11215, USA, [2]Phoenix Nest, P.O. BOX 150057, Brooklyn NY 11215, USA, [3]Patient Crossroads, 4 West 4th Avenue, Penthouse C, San Mateo, CA 94402 [4] The Children's Hospital at Montefiore, MMC CHAM, 3415 Bainbridge Avenue, Bronx, NY 10467, [5] Associação Sanfilippo Portugal, Apartado 544, 2821-901 Lisboa, Portugal

Abstract

In the past five years, six clinical trials have begun for Sanfilippo type A and B. These recent scientific advancements towards treatments for Sanfilippo Syndrome indicate that it is time for us to collect and analyze information on Sanfilippo patients in a single centralized registry as part of the Patient Crossroads CONNECT registry. In addition it is important we understand how the disease progresses and what differences and similarities there may be between the different types. This requires natural history studies (NHS) which can help us in determining the clinical outcome measures, identify potential surrogate endpoints via defined assessments including standardized clinical, biochemical, neurocognitive, behavioral, developmental, and imaging measures. **From our experiences such data collected from NHS studies are not shared between researchers except when published as papers at a much later date**. Sanfilippo Syndrome has a very small patient population and the participation in multiple NHS (which may be occurring simultaneously) places an unrealistic burden on patients and families. Sanfilippo Syndrome is ultra-rare and patients are geographically diverse. Providing patients and families with an outlet to find pertinent information pertaining to Sanfilippo, such as where Natural History Studies and clinical trials are taking place, or making themselves known by participating in a centralized registry, is essential.

We will describe how the data collected from the NHS studies for Types A and B performed at Nationwide Children's Hospital and for Type C and D at The Children's Hospital at Montefiore will be available to other qualified institutions to prevent repetition. Such NHS studies and registries can also help in identifying participants for clinical trials. We will illustrate how close collaborations between parent/patient led disease organizations and clinical and company researchers, is essential to ensure our limited funding and time is well spent as we try to identify treatments.

What is Sanfilippo Syndrome?

Sanfilippo Syndrome IS A PROGRESSIVE AND FATAL NEURO-DEGENERATIVE DISORDER that belongs to a group of diseases called mucopolysaccharidoses, specifically known as type III (MPS III). Sanfilippo children are missing a lysosomal enzyme. This enzyme is supposed to breakdown complex sugar molecules or 'substrate' – heparan sulfate. The substrate builds up in the body, stored in the lysosome of the cells, causing catastrophic health problems. The central nervous system is severely affected, causing profound brain damage. Bone deformation may occur; spleen, heart and liver damage may also develop as well.

There are 4 subtypes of MPSIII designated: A, B, C, and D corresponding to 4 different enzymes responsible for breaking down Heparan Sulfate. One of these 4 enzymes is lacking in the disease. Combined the prevalence is estimated at 1: 70 000 births.

There is currently no treatment but there are research efforts to find one. Breaking headlines of MPSIII A and B clinical trials have sent shockwaves of hope through the Sanfilippo Community. In the past five years, six clinical treatment trials have begun for MPS III A and B for either gene therapies, enzyme replacement therapies (ERT) or substrate reduction therapies (SRT). Seed funding for most of these treatments came from patient organizations.

Lysogene	SAF-301 gene therapy MPSIIIA	Start Date **August 2011**
UniQure	A gene therapy for MPSIIIB	Start Date: **October 2013**
Shire	SHP-610 an ERT for MPSIIIA	Start Date **February 2014**
Synegeva/Alexion	SBC-103 an ERTfor MPSIIIB	Start Date **August 2015**
Biomarin	BMN-250 an ERT for MPSIIIB	Start Date: **April 2016**
Abeona	ABO-102 A Gene Therapy for MPSIIIA	Start Date: **May 2016**
Manchester Univ	Genistein a SRT for all MPS subtypes	Start Date: **August 2014**

Other groups have also announced their intensions to develop treatments:

Esteve	March 2014 - to develop gene therapy MPSIIIA
Orchard Therapeutics	May 2016 - to develop stem cell / gene therapy for MPSIIIA
Phoenix Nest/LABioMed	June 2016 STTR to develop stem cell / gene therapy for MPSIIIB
Phoenix Nest/LABioMed	2014 and 2016 STTRs to develop ERT for MPSIIID

What about MPSIII C and D?

HANDS - Helping Advance Neurodegenerative Disease Science

HANDS came together to identify and fund science in academic groups focused on MPSIII C & D.
- Funding: gene therapy, chaperone, and other exploratory science in Canada and Europe.
- Created KO mouse model for MPSIIID
- Natural History Study for MPSIIIC and MPSIIID
- Created Sanfilippo Registry Project
- Expanded registry to include all MPS's

Phoenix Nest, Inc.

Founded in 2012 by HANDS co-founders and Dr. Sean Ekins (CEO)
Won ~$2M STTR grants with LABioMed
Started ERT for MPSIIID. Also working on MPSIIIB and MPSIIIC
Goal to be the complete Sanfilippo syndrome company

Natural History Studies

Natural history studies are an important tool for understanding the untreated course and progression of the disorder, determining clinical outcome measures and identifying potential participants for clinical trials. Data collected from these types of studies are not typically shared between researchers other than through published papers, which often delay studies. Since rare diseases like Sanfilippo Syndrome have small patient populations, participating in multiple studies places a burden on affected children and their families. Patient organizations understand this burden and are committed to sponsoring trials that require data to be openly shared.

Patient Driven NHS

The Sanfilippo Research Foundation & The Children's Medical Research Foundation are sponsoring the NHS for Sanfilippo type's A & B, led by Dr. Kevin Flanigan, Center for Gene Therapy at Nationwide Children's Hospital. Jonah's Just Begun & H.A.N.D.S. are sponsoring the NHS for Sanfilippo type's C & D, led by Dr. Paul Levy, at The Children's Hospital at Montefiore.

Industry Led NHS for Sanfilippo type A & B

The following companies have already initiated their own NHS : **Shire** types A & B, **Biomarin** type B, **Synageva/Alexion** Type B, **Lysogene** Type A.

ConnectMPS

Our Sanfilippo Patient Registry has now expanded to included all MPS diseases!

This registry is a collaboration between leading MPS organizations around the globe. Launched in 2014 with just two Sanfilippo (MPS III) advocacy organizations, this registry expanded to 22 international advocacy groups by early 2016. In the summer of 2016, through the partnership with the National MPS Society, the ConnectMPS registry has rebranded itself to become a centralized comprehensive global database of individuals with MPS related diseases. By coming together, we not only demonstrate our UNITY and efforts toward cures for these diseases but offer researchers and industry the most efficient, and uniform source for patient data to advance treatments for all subtypes of mucopolysaccharidosis.

ConnectMPS

PatientCrossroads™

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