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WHITE PAPER

Home based technology for rare disease patients: Aparito's approach for Late Onset GM2 gangliosidosis

August 2020

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Executive summary

Late Onset GM2 gangliosidosis (LOTS) is a rare and progressive neurological genetic disorder that has a devastating impact on those it affects. There is no cure and treatment for the disease currently focuses on managing symptoms.

Digital remote patient monitoring technology has been identified as having the potential to aid the drug development process. By developing new digital endpoints for clinical trials it will be possible to deliver healthcare and treatments tailored to the specific needs of patients. Innovative digital approaches for rare diseases can provide great opportunities for drug development, but they need to be suitable for the patients that will use them to ensure that sufficient data sets are generated.

In this white paper we summarise this innovative approach for a rare lysosomal storage disease (LSD) to show:

- The potential application of remote patient monitoring technology for an LSD in adults.
- The accessibility of the Aparito Atom5™ platform for patients with a neurodegenerative disease such as LOTS.
- The importance of collecting real world evidence for a rare disease to help develop a greater knowledge of the disease and its impact on the individual.
- That LOTS patients have many unmet clinical needs that need to be addressed with emerging therapies.

Challenges posed by LOTS

LOTS is a variant of Tay-Sachs and Sandhoff disease that presents in adults. As with the Infantile and Juvenile forms of the disease, it is a rare progressive neurological genetic disorder that is caused by the lack of the Hexosaminidase A (HEX-A) enzyme.

Pathophysiology

The HEX-A enzyme plays an important role in clearing away GM2 waste that is present in the neurons of the brain. The main issue for LOTS sufferers is that they don't have enough Hex-A enzyme, which results in them having too much GM2 waste present in their neurons. Hex-A is an enzyme that is created outside of a cell and absorbed into the cell. When the enzyme is mutated (like in LOTS), the cell does not recognize it and the quality control mechanism within the cell will not allow the mutated enzyme to be absorbed. Hex A's primary job is to break down waste inside a storage area in a cell. That storage area is called a lysosomal storage area and that is why LOTS is considered a Lysosomal Storage Disease (LSD).

Symptoms of LOTS differ greatly between patients and are dependent upon when they are first observed. These include ataxia, dyspraxia, dysarthria, seizures and as a neurodegenerative disease each individual follows a similar path where they will lose the ability to function independently and will eventually require palliative care.

Disease management & current treatments

LOTS is a disease for which there is no cure or approved therapeutics for the specific treatment of the disease. Current treatments focus on managing the symptoms seen in patients; for instance seizures, dystonia and mobility are all addressed with supportive therapies or medication. However, in the last five years there has been much progress in the development of potential treatments for LOTS, which includes approaches such as drug repurposing and substrate reduction therapy. Although not curative, they have the potential to improve the quality of life of those affected by LOTS and address the unmet clinical needs of patients.

Aparito's offering

Capturing real-world data

At Aparito the unmet clinical needs of LOTS patients has been acknowledged. Aparito's Atom5™ platform is capable of capturing continuous, patient-specific data measurements remotely, and in real time.

With the ability to capture RWD using our technology, a multidimensional profile for LOTS patients can be generated. This can play a key role in facilitating the drug d

evelopment process through developing disease specific and reliable digital endpoints.

Atom5™

Atom5™ is the technology platform which provides a framework that allows for the monitoring of the physical and emotional condition of patients.

This framework includes a mobile application which is available on Android and iOS operating systems and a web based clinician dashboard.

For the LOTS study, the mobile application was paired with a wrist worn wearable device that was connected via Bluetooth.

The device was then used to collect various disease specific physical measurements and through our clinician dashboard, healthcare professionals were able to monitor patients remotely.

LOTS specific real world evidence

LOTS specific configurations for Atom5™ included the addition of the following patient reported outcomes (PROs) and quality of life scales that each patient was asked to complete in intervals ranging from 8-60 days:

- *Tremor impact scale*
- *Impact of disease scale*
- *Impact on the family scale*
- *Wider impact scale*
- *Impact composite scale*
- *PedsQL Multidimensional Fatigue Scale*
- *Perceived stress scale*
- *Global Self Worth*
- *Rosenberg Self Esteem*
- *CHU9D*

A daily diary was also added to Atom5™ which allowed patients to plan, log and detail their visits to medical centres.

The wearable device functioned to capture the walking abilities of LOTS patients, providing continuous real time data on the:

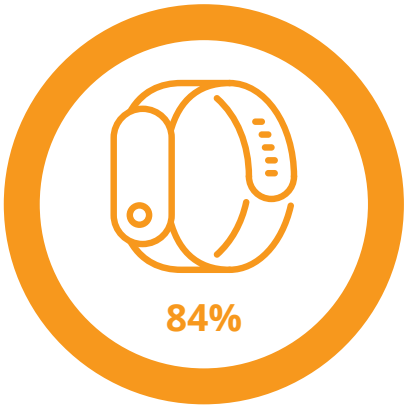
- *Average daily maximum number of steps taken in a 30 minute epoch (ADM)*
- *Average number of steps taken daily in a month (ADS)*
- *Average number of steps taken per 30 minute epoch (ASE)*

Aparito's natural history study

Aparito's technology was deployed as part of a six month natural history study. The study was carried out in partnership with the patient advocacy group, National Tay-Sachs & Allied Diseases Association (NTSAD) alongside the National Institute of Health (NIH) in America.

The study aimed to identify clinical markers of importance, and to shed light on possible outcomes that might convey disease burden. This is particularly important as there is still a lot to be learned about LOTS; tracking the disease over time could provide insights previously unknown which could support drug development and patient treatment.

A key part of this study was not to only generate RWD but to develop technology that was capable of being understood and used by both healthcare professionals and LOTS patients.



Demographics

Eight patients were recruited through the NIH. This cohort consisted of patients aged between 28 and 61 years of age on the day of consenting to the study, with the median age being 42.5. Three of the participants were male, and five were female.

Adherence to technology

Adherence rates for use of the wearable device and PROs within Atom5™ were recorded over the course of the study. Adherence to the technology was high throughout the study, with the median adherence rate being 84% for the wearable device and 91% for the PROs, which suggests that the LOTS patients were highly engaged.

PERSONALISED & ACCESSIBLE CARE

The Atom5™ platform, together with the use of the wearable device was shown to be a viable tool for providing real world evidence. The technology deployed in this natural history study for LOTS disease successfully captured various patient measurements that showed the physical and emotional state of patients, and was achieved over a six month period.

It is the continuous collection of health related patient measurements that will allow for the adjustment of treatments as needed, and the monitoring of disease progression that may detail the specific effects that the disease has on an individual. Furthermore, the personalised nature of the Atom5™ platform places the patient in charge of reporting symptoms that are important to them; this can empower patients to inform clinicians.

Whilst remote monitoring platforms such as Atom5™ have great potential for in-depth remote patient assessment, adherence to such platforms may be an issue due to the complex nature of modern technology, and as a result crucial data may not be captured. Difficulties with using digital technology may be more common in older adults or those with limited physical abilities or brain function. A survey carried out in the United States showed that the older an adult was, the less likely they were to own a smartphone.[1] Additionally individuals who were categorised as having a disability were shown to engage with digital technology at a lower rate.[2] For LOTS disease the weakening impact on brain function and mobility may mean that patients are more likely to struggle with using the technology. However, the high adherence rates observed over the course of this study are suggestive of the acceptability of Aparito's technology for LOTS patients.

The proof of concept for the technological function of Aparito's platform is well defined, and with high levels of engagement also being observed, this shows that the platform can potentially provide drug development and patient support solutions that are readily accessible and enjoyed by the wider LOTS population. Clinical insight from the study can be found in the paper published in the Orphanet Journal of Rare Diseases.

Acknowledgements

We would like to thank all patients who participated in the study. We would also like to thank NTSAD and NIH for helping organise and deliver this study, and the Buryk Foundation for providing funding.

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aparito

+44 (0) 1978 896 191

info@aparito.com

Unit 11 Gwenfro Technology Park
Croesnewydd Rd
Wrexham LL13 7YP