Developing recommendations for expanding the TREAT-NMD SMA Registries Core Dataset. An initial guidance document

Informed by the TREAT-NMD SMA Data-item Workshop Meeting

8-9 May 2017, Amsterdam, Netherlands

June 29 2017

Workshop Description:

The SMA Dataset Workshop brought together interdisciplinary SMA experts in Amsterdam and was supported by Biogen, a pharmaceutical company with a recently approved therapy for spinal muscular atrophy (SMA). This is the initial guidance from the work completed at that meeting and has been prepared by members of the TREAT-NMD secretariat; Jo Bullivant and Becca Leary, employees of Newcastle University in the UK, with review and input from the workshop planning committee, worksship participants and the wider SMA National Registries.

The workshop planning committee comprised the TGDOC Chairs and support from TREAT-NMD Secretariat:

- Nathalie Goemans
- Craig Campbell
- Hugh Dawkins
- Rebecca Leary
- Jo Bullivant

With input from Biogen employees: Sue Hall, Sarah Clark, Cynthia Jones

Recognizing that many SMA Registries are looking for immediate guidance about suggested data items the purpose of this report is to provide an overview of the meeting's discussions and resulting recommendations, in a timely manner, while ongoing development of specific data item definitions take place. It does not necessarily represent the full perspectives of any individual attendees, Biogen, or TREAT-NMD.

Purpose:

The purpose of this TREAT -NMD initiative was to coordinate a global approach to producing a set of recommendations for collecting an updated set of additional items (beyond the existing SMA mandatory and highly encouraged items- in an era of novel specific therapies for SMA. These items would be used to inform the understanding of the natural history of SMA, provide context to understand the safety and effectiveness of new treatments, and to potentially support post marketing surveillance (PMS).

There is an existing worldwide network of SMA patient registries affiliated to and coordinated by the TREAT-NMD Neuromuscular Network, and there is an existing core data set collected by these registries, made up of mandatory and highly encouraged data items. There also exists a number of SMA registries or information repositories that are not part of the TREAT NMD Network. The following recommendations are meant to be helpful to all of these entities and is meant to be a guidance based on expert consensus.

Key messages:

1. The purpose of expanding the core dataset of the TREAT-NMD SMA registries should be "to collect robust longitudinal data that (a) captures natural history, (b) measures the effectiveness of interventions and (c) informs standards of care for patients"
2. A total of 38 data items across 9 different categories are recommended for consideration for inclusion in the revised core dataset. It is not proposed that all 38 items are included. The data items within each category are ranked in order of priority/preference according to multiple factors
3. The existing core dataset remains important for many stakeholders, and will continue to be highly valued.

4. It is recognized that registries have varied methodologies and resources and so there may be solutions for data item inclusion that varies between registries. At this point the items are present in general terms and should be used as guidance.
5. It is important to consider upcoming regulatory changes, ensure appropriate training and IT infrastructures are available, and coincide timings with other key developments such as standards of care. However, it is also important that a 'first draft' version is compiled as a matter of urgency, so that registries with patients already taking nusinersen can start implementing straight away if they are able.

Next Steps:

1. A small working group is meeting to construct the wording of the data items and develop a data dictionary.
2. The implementation will take place over the coming months with a plan for final implementation by the next TGDOC meeting in November 2017.
3. A small number of registries are identified as a pilot group for the implementation of the first draft of the updated dataset in the immediate future.

It is to the credit of all the stakeholders that have been involved in the process that consensus was reached, nevertheless, TREAT NMD acknowledges that no solution is perfect for everyone, and there is much work still to do to develop these recommendations into a realistic and implementable plan.

The following Figure shows the final list of prioritised data items in each category. With the understanding that new therapy availability for SMA is now a reality in the US, EU and Canada and that these consensus elements were urgently requested to inform clinician data collection to be implemented at patient visits.

Figure 8: Prioritised data items recommended for consideration for inclusion in the core dataset

Motor measures in infantile onset SMA 1. HINE Section 2 only, with SMA-specific training 2. WHO Gross Motor Milestones 3. CHOP-INTEND 4. Hammersmith Functional Motor Scale	**Motor measures in later onset SMA** 1. WHO and BROOKE 2. HFMSE (Hammersmith Functional Motor Scale – Expanded) 3. RULM (Upper Limb Module) 4. 6-minute walk test	**SMA-specific drug treatment** 1. Disease modifying drug ** 2. Compliance: a. Dose b. Frequency c. Route 3. Adverse events (related to route administration only) 4. Reason to stop treatment
Diagnostics 1. Age at diagnosis via genetic test** 2. SMN2 copy number * 3. Age of onset of symptoms**	**Medical history** 1. Hospitalisations 2. Co-morbidities 3. Therapy interventions 4. Medications (other meds not related to disease modification)**	**Physical assessment** 1. Physical assessment 2. Pulmonary function measures* 3. Ventilation (Y/N, IV/NIV)* 4. Bulbar function 5. Scoliosis (Y/N, Severity, Surgery)* 6. Highest and current motor function achieved* 7. Cognition 8. Fatigue
Demographics 1. GUID / PPRL 2. Date of death** 3. Sibling / Family* 4. Ethnicity: cultural / racial background**	**Patient-reported outcome measures (PROMS)** 5. Overall visual analogue scale for wellness 6. PedsQL (Pediatric Quality of Life Inventory - HRQOL measure with generic and NM scales) 7. PEDICAT or equivalent (SMA FRS) 8. PedsQL Fatigue Scale 9. ACEND (Assessment of Caregiver Experience of NMD)	**Electrophysiology and biomarkers** 1. CMAP (Compound Muscle Action Potential) 2. DEXA (whole body and spine): training must promote consistency in collection

*already in core dataset **ranked as easy to include