IGA neuronopathic Gaucher Disease (nGD)

Global Patient Registry

Phase 1 Final Community Report

Who are the International Gaucher Alliance (IGA)?

The IGA is an international umbrella group representing the interest of Gaucher patients and those of non-for-profit Gaucher patient groups as well as rare disease groups throughout the world.

Our Members;

Austria; Belgium; Bosnia & Herzegovina; Botswana; Bulgaria; Canada; China P.R. ; Croatia; Czech Republic; Denmark; Estonia; Finland; France; Germany; Greece; Guatemala; India; Israel; Italy; Japan; Jordan; Kazakhstan; Latvia; Lithuania; Luxembourg; Macedonia; Mexico x 2; Moldova; Morocco; Netherlands; Norway; Paraguay; Pakistan; Poland; Romania; Russia; Serbia; Slovakia; Slovenia; Spain; South Africa; Sweden; Switzerland; Turkey; Ukraine; UK; USA

Why do we need a Global Patient Registry?

The IGA is developing a global **disease** registry to support a better understanding of the natural history of neuronopathic Gaucher disease (nGD), to correlate global *phenotypes* (observable characteristics) and *genotypes* (the genetics), validate new *endpoints/ outcomes* (these are used in clinical trials to measure if a treatment has worked) and to generate a data source that can be used for both Regulatory and Health Technology Assessments evaluation of emerging drugs for nGD.

We also hope to be able to use the registry to assist in identifying patients for clinical trials and research projects.

What was the purpose of Phase 1?

Phase 1 lasted 24 weeks (January – May 2019) and was the planning phase, to engage with all the different parties that are important to have an input into the registry. Especially to understand what they think is important as this gives us the information on which to design and build the structure for the global registry.

They were:

- nGD volunteers, patient and their carers from around the world
- Key opinion leaders (doctors) in the field of Gaucher from different parts of the world
- Pharmaceutical companies interested in bringing new treatments to the nGD community

How did we go about it?

PATIENT ENGAGEMENT

Methodology

Led by the IGA, a global representative of patients and parents/carers were identified:

- On-line social media platforms (Facebook and Twitter) were used to distribute the opportunity to volunteer to take part.
- Volunteers were offered £80 Amazon vouchers for taking part in either the focus group and in-depth interviews.
- The Terms of Reference were emailed to the volunteers beforehand, along with the questions/topics to be discussed.
- Open-ended questions were drafted utilising the EQ5D-Y (a validated health related questionnaire) as a prompt to discuss both physical and psychological symptoms of the disease that had most disease impact on quality of life. These were shared with the volunteers ahead of time. Additional questions asked their opinions regarding sharing data and mobile health/wearables.
- The focus group and in-depth interviews were held on-line using Zoom video link, except for one which was held in person by volunteer request. One interview had to be stopped very early as the patient was having numerous seizures, and could not be rescheduled, therefore not included in the analysis.
- All interviews were recorded (with volunteers' consent) and then transcribed in order to support analysis.
- Thematic analysis was used to identify the symptoms and issues that were important to patients. Identified themes and topics in the focus group and in-depth interviews were then circulated in an on-line survey to gain the views of a wider group of patients.

1.1 Interview and focus group demographics

A total of ten volunteers took part in the interviews and focus group. Seven parents (two Dads, five Mums) and three patients (all females). The age range of the individual living with nGD ranged from 2.5 to 25 years of age.

Volunteers lived in the UK, Sweden, USA and Japan. Seven white Caucasian and four Asian. Only one of the volunteers (B) represented T2 disease specifically, while all the others represented the experiences of living with T3. It is noted that this older demographic may therefore cause a bias in the findings reported compared to the other disease presentations.

KEY OPINION LEADER (KOL) INPUT

1.2 Methodology

Key opinion leaders and experts in nGD were identified by the IGA.

- The Terms of Reference were emailed to the KOLs in advance of a face to face meeting in London.

- The agenda and a draft template of potential clinical data capture fields were emailed in advance of the meeting.

- Participants had their expenses covered but were not paid to take part in the meeting.

- Four participants representing UK, Germany and Israel joined the face to face meeting. Three other participants from Japan, USA and Egypt were also invited but could not attend in person but contributed to the process remotely.

- An additional thirteen KOL were invited to complete the on-line Delphi that had been agreed at the KOL meeting, from UK, Germany, Japan, USA, Egypt, Israel, Korea, Sweden, Poland, India, France, Spain, and Pakistan.

PHARMA PARTNER GROUP

Membership

Eight pharmaceutical companies currently working in the nGD space were contacted and four committed to be part of this Phase, including a payment of £12,500.

Terms of references were drafted and shared with all.

Face to face meeting

Two representatives from each of the Pharma partners were invited and met in March 2019, two joined via teleconferencing. The purpose was to undertake a scoping exercise to gain the pharmaceutical perspective of the requirements (commercial and regulatory) for a global disease registry.

Utilising MENTI as a tool for scoring, participants were asked to score on a scale of 0-10 on the priority, as they see, of the following:

- Convey patient/carer disease impact
- Improve disease understanding/define natural history
- Provide Real World Data for regulatory
- Provide real world data for reimbursement submissions
- Pharmacovigilance requirements post MA for each new drug on the market
- Support the identification of patients for clinical trials
- Validate new outcomes/endpoints
- Anything else (free text)

What were the findings?

Key highlights identified are:

- ✔ All the partners and stakeholders that took part in this project expressed great enthusiasm for a global disease registry. The community as a whole considered it to be a valuable initiative to support patient needs.

- ✔ Patient input was extremely informative, via both the qualitative interviews and focus group but also via the on-line Delphi. Reaching a broad group of patients covering wide global reach and disease type/ severity. This highlighted key areas that need to be addressed in order to address outcomes important to patients and to provide on-going care and support.

- ✔ Today, is the right time to instigate this. As an increasing number of pharmaceutical companies bring hope to patients with new treatments, but against a backdrop of increasing challenges in ensuring rapid and affordable drug access to patients with high unmet needs.

PATIENT ENGAGEMENT RESULTS

The overarching recurring themes identified from this analysis include pain and physical symptoms, psychological experiences, unmet needs, and impact on quality of life. The word clouds below under each theme express the outcomes of the nGD volunteer feedback:

Experiences of pain and physical symptoms

Psychological experiences

Unmet needs (lack of adequate support)

Quality of life (QoL)

Tell my story (improving awareness)

KEY OPINION LEADER (KOL) RESULTS

During the face-to-face meetings participants identified the various data capture fields that would be important and the overall function of a global registry in terms of frequency of repeated data capture.

A total of 138 data captures were identified and included for the follow up on-line Delphi with the additional KOLs.

Based on the findings of the Delphi results, data fields that were scored as Disagree/Strongly Disagree by three or more KOLs were deleted from the list. A total of eleven initially proposed data points were subsequently removed. The pharmaceutical representatives were in overall agreement with the KOLs in all but one data capture fields.

New insight gathered via the Delphi suggested the following points:

Clarification in definitions for the signs and symptoms associated with diagnosis, and a few more options of nGD (T2 and T3), developmental delay, etc.

Some of the new data captured fields proposed were date of death, longitudinal height and weight, respiratory infection history, Tanner stage/infertility, defined developmental delay.

All of the proposed data capture fields will need to be classified into standardised in terms as part of Phase 2. Variables will also need to be ranked in order of importance, ease of collection and meaningful analysis based on unambiguous definitions.

- Define a minimum dataset of required fields. Make these fields all drop down/radio boxes to enable quick data entry and maximum interoperability
- Make the minimum data set as small as possible so data collection task is quick and easy. Only collect data that will be used.
- Pedigree trees are important in many rare diseases. These can be effectively support by defining a Proband patient, a family ID and then family members relationship to the Proband.
- Genotype data is highly specific and will need to be updated as further genetic variants are identified. These should be selected from an approved drop-down list and support type ahead text selection e.g. typing “508” will select the variant “deltaF508”
- Disease burden (child, family and society) and measuring the economics part is fundamentally important to understand and defend for reimbursement agencies later in the drug life cycle.

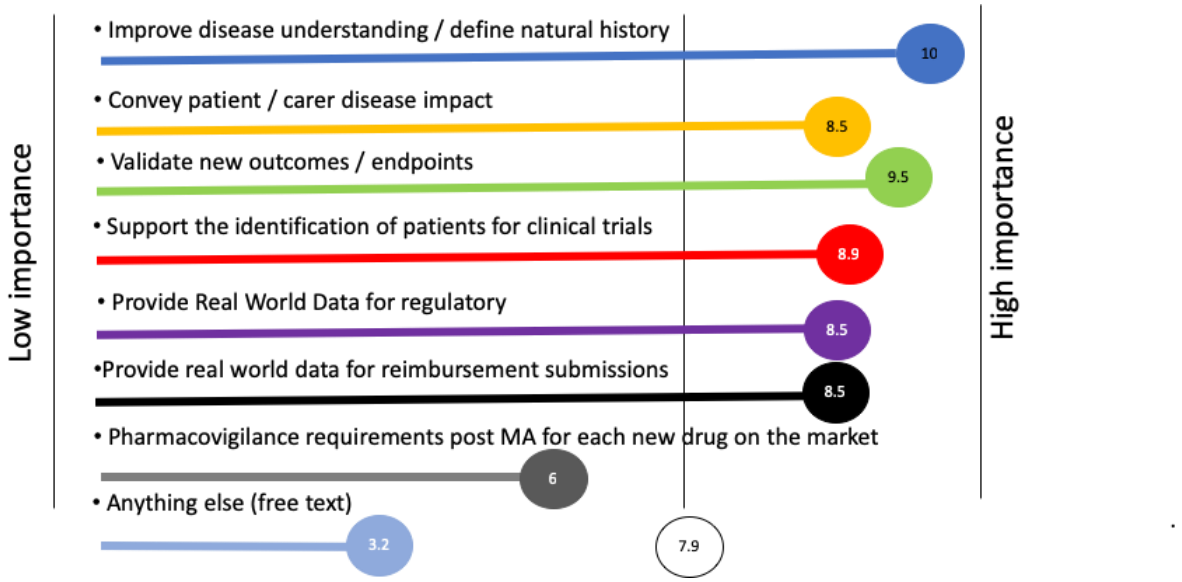
One of the key messages that emerged from both the KOL meeting and the follow up Delphi is the important, but crucial distinction between data capture requirements for an observational disease registry vs a more active research study. Keeping it as lean and simple as possible will ensure better compliance in data input long term.

A priority that did emerge during the KOL meeting and follow up Delphi is of an urgent requirement to develop a new severity scoring scale – keeping both the visceral and neurological manifestations of nGD. In Phase 2 it is therefore proposed that a dedicated workstream looks at developing this, either from modifying the currently available tools (e.g. mSST) or creating a new one.

The same priority emerged for validated disease specific Patient Reported Outcomes (PROs)s.

PHARMA PARTNER GROUP RESULTS

Scoring was not for ranking them from the most important to the least important, but for scoring the individual level of importance for each one. These were not considered mutually exclusive, as all are considered part of the same ambition which will also evolve over the times as all the companies move forward in their development. Having said that, the priority that scored the highest today was “improving disease understanding and defining natural history”, while validating new outcomes and endpoints also had a high priority score.



Summary of requirements

Results from the meeting highlighted the following:

- The top priority for the pharma partners is disease understanding and natural history and validating new outcomes and endpoints. This is also a topic highlighted by the key opinion leaders.
- Identify the outcomes and the endpoints will be selected as an outcome of talking to patients and families in the focus group and in-depth interview to ensure they are relevant and important to them
- Possible use of biomarkers for stratification across GD2 and GD3 and within GD3, subtypes.
- The challenge that the data fields we want to collect are not globally assessed and globally accessible in a way that will lead to meaningful results.
- Developing a standard set of assessments is likely to be required with annual review to monitor quality and content to ensure and maintain data quality and value.
- A long-term priority to remember is that of pharmacovigilance (PV), and that a company’s requirement is sometimes mandated to create a registry. With early input with regulators, a disease registry that can meet the requirement of Pharmacovigilance, rather than a new drug registry could be used.

- Sub-studies (e.g. from regulators) could utilise the registry if technically designed to add additional data capture field, which would be funded by the individual sponsor.
- Disease burden (child, family and society) and the economics part is absolutely a fundamentally important one to understand and defend for reimbursement agencies later in the drug life cycle.
- To involve regulators and to see what other health authorities mainly in the EU and the US would like to see from this type of natural history data.

What happens now?

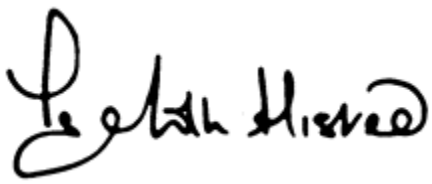
Next steps for Phase 2 of the project are:

- ✔ Create a legal, governance, compliance and reporting structure that assures trust and quality for all.
- ✔ Seek regulatory buy-in (EMA/FDA) to the planned registry (technically and compliance).
- ✔ To create a sustainable business model through a partnership agreement with Kantar.
- ✔ Create a technical platform today that can expand to meet the needs of the future, promoting FAIR data principles, and putting the patient at the centre.

How you can support this initiative?

The Global registry will not only collect clinical information via the patients treating clinician, it will also be a portal to communicate with patients and their carers and collect quality of life data directly from patients and families. If you would like to be included onto the Global Registry please let us know by emailing: tanya@gaucheralliance.org

Please note the role out of the Registry to collect clinical data will be over several years, however the patient communication portal will be available to all patients from the beginning.



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