International Pompe Association
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IPA Community Advisory Board Meeting

Summary by IPA Board

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Holiday Inn-Riverwalk, San Antonio, Texas (USA)

Introduction

The IPA established a **Community Advisory Board (CAB)** for Pompe disease in 2019. A CAB is a group of volunteer patients/advocates who offer their expertise to public or private sponsors of clinical research on overall program development, single clinical trials and other aspects beyond the research program. A CAB may advise several sponsors in the same field and, by doing so, it ensures that research studies are designed to take into account the real needs of patients, resulting in higher quality research.

The IPA's CAB consists of 24 individuals from the patient community. They include patients, family members of patients, and patient organization leaders, and they are from different countries and continents around the world, representing the range of varieties of Pompe disease, from infantile to late-onset Pompe disease. The mission of the IPA's CAB is to inform research and development through to market approval and reimbursement by providing its accumulated experience and knowledge to accelerate access to effective treatments for Pompe Disease.

The inaugural meeting of the IPA's CAB included five companies actively involved in Pompe treatment development. Therefore, the agenda for this first meeting necessarily focused on more general topics. Over the course of the meeting there were four main topics covered: the diagnostic journey, daily living with Pompe, unmet needs within the Pompe community, and desires for future therapies.

The meeting was moderated by James Valentine—an independent third-party moderator, and each member of the CAB that was present was open with their own personal stories and their hopes for future therapies. Mr. Valentine kept conversations flowing, and every member was able to offer their perspective on each topic. It was an extremely productive meeting and certainly set a high standard for future meetings.

Key Take-Aways from the Meeting

Session 1: Diagnostic Journey

Most members reported first symptoms related to movement/muscle problems, and many described lack of athleticism as children in school. In addition, most adult respondents described lengthy diagnostic odysseys, some lasting decades.

When asked whether they had received a misdiagnosis prior to being diagnosed with Pompe, thirteen members reported a misdiagnosis. These included: congenital myopathy, myotonic dystrophy, hepatitis,

Becker muscular dystrophy, Limb Girdle muscular dystrophy, and unspecified glycogen storage disease. Some reported additional misdiagnoses during their diagnostic odysseys including: SMA, asthma; irritable bowel syndrome, psychiatric issues, myositis, hypertonia, polymyositis, myopathy, diabetes mellitus. Overarching themes underlying these misdiagnoses indicated a lack of knowledge about Pompe among physicians.

Following their diagnosis, nearly all of the CAB members indicated that they received their first "real" Pompe information from the internet.

The final topic in the diagnosis session related to the CAB member's thoughts on newborn screening for Pompe (NBS). While a third of the CAB members identified as passionate or firm believers in NBS, and there was general agreement regarding the benefits of early diagnosis (ie vastly improves outcomes, etc), there were also an in-depth conversation related to the challenges of diagnosing late-onset Pompe at birth. Despite these challenges, the consensus was that any potential challenge was outweighed by the benefit.

Session 2: Living with Pompe disease

This session started with the CAB Members discussing what they viewed as the most debilitating symptom that they, or their child, suffered from. While some reported pulmonary insufficiency, the majority reported muscle weakness as the most significant symptom in their lives. CAB members were also asked to explain why it was viewed as the most debilitating. The reasons ranged from their effects on their independence, to mental health effects. Interestingly, half of the CAB members reported that the symptom they currently identify as the most debilitating has changed over time.

When asked to identify the activity that was most important to them that was impacted by Pompe, responses included: the ability to work, ability to visit the bathroom alone, the ability to participate in recreational activities that were source of social/ohysical activity, the ability to drive a car, and other activities of daily living.

The final question of the session related to concerns for the future and the overarching theme for these responses revolved around fears of the unknown and inability to predict or control what the future holds.

Session 3: Unmet Needs in Treatment and Management of Pompe

This session began with CAB members sharing their experiences with supportive therapies (ie not treatment with enzyme replacement therapy). The two primary types of supportive therapy reportered were diet and exercise. While all diets were described as high protein/low carbohydrate, the types of exercise varied. In general, exercise approaches were focused on strength and endurance training. Stretching and massage were also discussed.

Another take-away from this discussion was that information related to supportive therapies varied depending on where the patient lived, and as a result the majority relied on other patients and patient organizations for best practices.

While almost all of the CAB members indicated that they are currently receiving ERT (they were asked not to say whether it was commericially approved or in a clinical trial), experiences on treatment varied.

When asked about the burdens/impact of ERT (including psychosocial effects), answers ranged from the difficulty of scheduling work/school and infusions to unfulfilled expectations of ERT to immune reactions that had to be overcome.

The final topic covered in this session related to specific symptoms that are not currently being adequately addressed. The consensus was that there needs to be: greater knowledge within the physician community outside of the expert centers; a greater focus on, and support of, mental health needs; and a treatment that repairs damage, instead of just slowing or stabilizing patients.

Session 4a: Desire and Preferences for Future Therapies

CAB members started this session by discussing what the term “cure” meant for them or their child. While answers varied, they could be clustered into four broad categories: fixing the genetic defect; regenerative medicine that would restore lost abilities; stability in condition; a treatment that would end all uncertainty (as caused by Pompe) from their future.

It was also implied that a cure could mean a combination of one or multiple therapies. But the consensus was that the current standard of care is not specific enough given the individual differences of people with Pompe disease. Short of a cure, CAB members were interested in the following: a decrease in infusion duration, an oral drug, certainty of no further progression and a less frequent infusions.

An important key takeway was that the was agreement that there should be consistent treatment guidelines across countries. There is a concern that guidelines are dictated by reimbursers, and not best clinical practices. There was also an expressed desire for access to more personalized medicine, especially in light of the heterogenicity of Pompe disease. Finally there was a concern that access to future therapies (and current) may be limited in the future due to the cost.

The final portion of this session related to clinical trial assessments currently being used. The common theme of the responses from the CAB on this topic reflected frustration over the lack of scientific rigor and crude measures of mobility and effort through the 6MWT, FVC, and manual measures of muscle strength. There were comments about the pain, embarrassment, and fatigue experienced by people with Pompe when undergoing tests. A number of suggestions for improvement which would make trials more open to people in different disease states. Better psychological assessment tools; use of activity monitors and development of new tools, such as the smartphone app for the 6MWT under review by the FDA.

Session 4b: Desires and Preferences for Clinical Trials

The first question in this session asked CAB members to discuss the information they would need to make an informed decision on whether to participate in a clinical trial. Comments clustered in six themes:

1. Evidence: Being fully informed with strong pre-clinical and clinical evidence.
2. Dose: How is dose determined? Strategies for antibody suppression. Want highest safe dose.
3. Phase of trial: Concern about timing of participation in the early stages of new trial.
4. Burdens: reimbursement; number of site visits and tests; travel; loss of home infusion nurse; needle biopsies; side effects; drugs to counteract side effects; risk of organ failure.
5. Standard of Care: Several people commented on not wanting placebo unless placebo meant the current standard of care treatment.
6. Post-trial: Assurances to stay on a new therapy or ability to return to former treatment.

In discussing prior (or on-going) clinical trial experiences, several issues were raised, including:

- Need for a travel companion to navigate travel and for other support.
- Restrictive inclusion/exclusion criteria that do not take into consideration individual abilities.
- Reimbursement issues: out-of-pocket expenses; travel arrangements; and flexibility in payment methods.

End of Meeting