Review Article

The role of patient advocacy organizations in shaping medical research: the Pompe model

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Abstract: The Pompe model is the term used by the Pompe community to describe the relationship that exists between the patient community, the medical/scientific community, and industry. The development of the Pompe model represented a new paradigm for the involvement of patients in new treatments—and also for scientists and pharmaceutical companies. It saw patients developing a sense of agency, of involvement in the process of treatment development rather than powerless recipients or (if lucky) occasional spectators. At the same time, as described below, it benefited the other partners in the process with the result that the different components of the model added up to more than the sum of their parts. However, in order for this to happen, each part had to undergo a transformation in mindset. The development of enzyme replacement therapy (ERT) for Pompe disease represented a unique set of circumstances and individuals that helped to bring about this change and, in doing so, created a model that has had far wider applications.

Keywords: Pompe disease; Pompe model; International Pompe Association (IPA)

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Introduction

The "classic" drug development model relegates the role of patients and patient advocacy groups to that of grateful recipients of new treatments that seem to fall from a clear blue sky. The process of development is opaque, and contact between research scientists and patients is relatively rare. Furthermore, contact between scientists and pharmaceutical companies might be characterized as transactional—a means to an end. There is little sense of a shared endeavor.

That all changed in the 1990s for the Pompe community. There are many factors that contributed to this change, and the resulting model that was created—the Pompe model, too many to give proper justice to here. Nevertheless, this review will seek to explore the creation of the Pompe model, why it is important, and how this new approach to drug development has had an enormous impact on the entire Pompe community. Ultimately, we believe that "the alliance between patient groups, researchers and industry should be a model for the development of treatments for other rare diseases" (1).

Creating the Pompe model

Patients

At every critical juncture, the Pompe patients/patient organizations have been a vital part in how events

transpired. And that is as it should be—the patient should be involved because at the end of the day it is the patient's life on the line. The question is: how did we get there? How did we evolve from a fragmented group affected by an untreatable condition, to a united, well-informed, and active group with a strong voice that was directly involved in the development of treatments? How did we create the Pompe model?

A number of factors contributed to this change. One was the development of the internet, which allowed patients to find patient groups and people in different countries to find each other and to share information. The clearest example of this can be seen in the creation of the GSDnet in 1996 (2). This was an email-based form or listserv that allowed emails from each member to be shared with all the others. While this listserv was for all glycogen storage diseases, the Pompe community became very active on it and the relationships and connections that were formed, as well as the information that was shared, were vital to the development of a strong international patient community. In fact, the benefit of previously isolated people to become part of an international community should not be underestimated; it led to not only the spread of information, but also the spread of hope. This was, in itself, an empowering experience. However, patients were not just "intelligent customers". Their developing sense of agency also led to them positively shaping events.

One example of this can be seen in the series of conferences that the Acid Maltase Deficiency Association (AMDA) hosted beginning in 1996 for scientists involved in Pompe research. In hosting the first conference in 1996, the AMDA brought together professionals in the Pompe field from all over the world for the first time. This far-sighted act created a sense of community amongst scientists, many of whom had never met before, similar to that sense of community growing amongst patients. It also helped change the relationship between patients and scientists.

However, this was just the first step in increasing the role of patients. The founding of the International Pompe Association (IPA) in 1999 was another critical step that really cemented the vital importance and value of the patient voice on the global stage. As the patient organization leaders around the world became more connected as a result of the internet, there emerged a recognition of the power and importance of the patient voice in the drug development process. What the individual organizations had each been doing on a national level, was something that they believed should be expanded to the international stage.

The first step towards creating the IPA was taken by a Dutch patient organization for neuromuscular disorders—the Vereniging Spierziekten Nederland (VSN). In 1998, the Dutch patients were the most organized patient group, with a long history of collaborating with the medical community. According to Kevin O'Donnell, one of the founding members of the IPA (through the AGSD-UK): "The VSN was a professional organization, well-funded, with a critical mass that allowed it to sustain full time employees and a national headquarters. They would bring those resources to bear on helping to organize the international Pompe community" (3). The VSN invited representatives from several of the national organizations to meet on March 21, 1998 to discuss the possibility of starting an international patient organization. Representatives from the Netherlands, Germany, the UK, and the USA met at the Tulip Inn in Naarden, the Netherlands and the seed that would be planted there grew into the IPA (3).

After the first meeting in 1998, the representatives who were present at the meeting at the Tulip Inn went to work. They started reaching out to the people they knew in different countries, working with the existing organizations and encouraging the formation of new national organizations, and they organized the first International Pompe Association Conference in Naarden, the Netherlands in July 1999. All of their hard work paid off and the first Conference was attended by representatives from Spain, Belgium, the Netherlands, India, USA, UK, Germany, France, Australia, Italy, the Philippines, and Japan, as well as scientists from all across the world. There were also representatives of three pharmaceutical companies, each of whom was developing an enzyme replacement therapy (ERT) for Pompe disease. After this Conference, the IPA would be the acknowledged voice of all patients around the world—a "group of people who were joining together to take charge of their own destiny" (4).

Scientists

For scientists, there was a change too. Previously remote from patients, and to a certain extent from each other, the AMDA conferences helped bring about a productive alliance. The fact that Pompe was an untreatable and invariably fatal condition had led to an understandable wariness from researchers to have too much contact with patients. They were concerned about giving false hope

to people in a desperate position, who were often not in a position to understand the science involved. It was a significant burden for academic researchers—even though their life's work, in many cases, was aimed at helping those very patients. Dealing with organized patient groups helped to square that circle. This allowed researchers to engage with patients in a way that was removed from the often-desperate circumstances of individual cases. Moreover, dealing with patient groups who were aware of and understood their work, was a motivating and morale-boosting experience for scientists working in what was a pretty obscure field. This led to a virtuous cycle where patient groups were able to come to an informed view on where they could best put their funds to help advance treatment. In this way, the "proof of principle" funding of ERT took place. Furthermore, in order for change to occur, scientific evidence must be collected to ensure that the change is safe and efficacious, but it must also be communicated effectively among all stakeholders. This is where the Pompe model played a vital role in the development and approval of a treatment for Pompe.

Industry

The growing alliance between patients and scientists needed a third partner to translate the research into commercial treatments. It is probably fair to say that for industry, being lobbied by patients to develop a specific new treatment was a novel experience. However, the fact that the science was sound and that they were being presented with an organized, identifiable customer base probably helped. When companies realized that there was the basis of a new product there, they found that the relationship between the scientists and the patient groups was such that they came as a packaged deal. Companies would have to deal with them both—and they did. And so, with the final stakeholder in place, the Pompe model was born.

Results

The Pompe model depends on one thing: all three stakeholders (patients, scientists/doctors, and industry) having an equal voice.

Since the Pompe model was firmly established, the national patient organizations, and the IPA itself, have continued to play an active role in improving the lives of patients around the world. One clear example of the importance of the patient voice can be seen in the IPA/Erasmus Medical Center (MC) Pompe Survey.

The IPA/Erasmus MC Pompe Survey was started in 2002, and it is an ongoing international study in which data is collected from children and adults with Pompe disease by means of self-reported questionnaires. The goal of this survey is to gather as much information as possible on the natural course of the disease, the severity of the disease in the patient population, and the impact on the daily lives of patients. The continuous data collection from over 400 patients has allowed researchers to describe the natural course of non-classical Pompe disease, as well as the alterations brought about by ERT. The international character of the survey allows access to a large cohort of patients which makes it possible to draw conclusions on a group level.

This survey is unique in that the patient is able to directly report on his or her current condition. The IPA is a solid partner in this important scientific research—research that gives Pompe patients a direct voice in how Pompe affects them. The longevity of the survey is also unique and important. With the Survey now in its 17th year, it is the longest running survey or registry on Pompe patients.

The national organizations play a vital role in the IPA/Erasmus Survey as well. They help to recruit patients to participate, help to distribute the surveys as needed, and serve as points of contact for any questions that arise. Unlike other surveys and registries, by including the patient organizations in the process, there is an opportunity to provide explanations for why patients have stopped participating. For instance, if a patient passes away there is an ability for the patient organization to reach out to the family to see if the death was related to Pompe disease or something else (i.e., cancer, car accident, etc.). In addition, patient organizations can increase patient participation and retention by encouraging patients to continue to participate on a yearly basis, as well as to help recruit new participants. The survey would not be the success it is without the IPA, the national patient organizations, but most importantly, the patients themselves.

A review of the articles published as a result of the IPA/Erasmus MC Pompe Survey shows how important this work is. From revealing how Pompe disease affects patients' quality of life, to recording the effect of ERT on a patient's life, the Survey has enabled the patient voice to be heard. Below is a list of the papers that have been published to date based on the data from the IPA/Erasmus MC Pompe Survey:

- Hagemans ML, Winkel LP, Hop WC, et al. Disease severity in children and adults with Pompe disease related to age and disease duration. Neurology 2005;64:2139-41.
- Hagemans ML, Hop WJ, Van Doorn PA, et al. Course of disability and respiratory function in untreated late-onset Pompe disease. Neurology 2006;66:581-3.
- Hagemans ML, van Schie SP, Janssens AC, et al. Fatigue: an important feature of late-onset Pompe disease. J Neurol 2007;254:941-5.
- Hagemans ML, Laforêt P, Hop WJ, et al. Impact of late-onset Pompe disease on participation in daily life activities: evaluation of the Rotterdam Handicap Scale. Neuromuscul Disord 2007;17:537-43.
- Hagemans ML, Janssens AC, Winkel LP, et al. Late-onset Pompe disease primarily affects quality of life in physical health domains. Neurology 2004;63:1688-92.
- Hagemans ML, Winkel LP, Van Doorn PA, et al. Clinical manifestation and natural course of late-onset Pompe's disease in 54 Dutch patients. Brain 2005;128:671-7.
- Rigter T, Weinreich SS, van El CG, et al. Severely impaired health status at diagnosis of Pompe disease: a cross-sectional analysis to explore the potential utility of neonatal screening. Mol Genet Metab 2012;107:448-55.
- Güngör D, de Vries JM, Hop WC, et al. Survival and associated factors in 268 adults with Pompe disease prior to treatment with enzyme replacement therapy. Orphanet J Rare Dis 2011;6:34.
- Güngör D, Kruijshaar ME, Plug I, et al. Impact of enzyme replacement therapy on survival in adults with Pompe disease: results from a prospective international observational study. Orphanet J Rare Dis 2013;8:49.
- Güngör D, de Vries JM, Brusse E, et al. Enzyme replacement therapy and fatigue in adults with Pompe disease. Mol Genet Metab 2013;109:174-8.
- Güngör D, Kruijshaar ME, Plug I, et al. Quality of life and participation in daily life of adults with Pompe disease receiving enzyme replacement therapy: 10 years of international follow-up. J Inherit Metab Dis 2016;39:253-60.
- van der Meijden J, Güngör D, Kruijshaar M, et al. Ten Years of The International Pompe Survey: Patient Reported Outcomes As A Reliable Tool for Studying Treated and Untreated Children and Adults With Non-Classic Pompe Disease. Value Health 2015;18:A673.
- van der Meijden JC, Kruijshaar ME, Rizopoulos D, et al. Enzyme replacement therapy reduces the risk for wheelchair dependency in adult Pompe patients. Orphanet J Rare Dis 2018;13:82.
- Kanters TA, Redekop WK, Rutten-Van Mölken MP, et al. A conceptual disease model for adult Pompe disease. Orphanet J Rare Dis 2015;10:112.
- Kanters TA, van der Ploeg AT, Kruijshaar ME, et al. Cost-effectiveness of enzyme replacement therapy with alglucosidase alfa in adult patients with Pompe disease. Orphanet J Rare Dis 2017;12:179.

Beyond the IPA/Erasmus Survey, the patient voice has been a critical factor in the commercial approvals of Myozyme/Lumizyme (the first commercial treatment for Pompe disease) around the world. At meetings in Australia, Canada, Europe, and the United States, the patient voice was a strong and unified call for approval—and it succeeded. Ultimately, it was the combined voices of the scientists, patients, and the data from the industry sponsored trials that led to the approvals—every voice was important. If there had been an absence of any one voice, it is very possible the approvals would not have occurred.

Unfortunately, even after the commercial approval of a treatment, there were bumps in the road. One such obstacle that had to be overcome was the shortage of the commercially approved Myozyme. This shortage took place from 2007–2010. The causes of the shortage are not the subject of this paper. Instead, we would like to explore how the Pompe model contributed to the successful management of the shortage.

In 2007 and 2008 the shortage affected only the US population (5-14). However, it was clear at the end of 2008 that supply from the commercially approved manufacturing process was not going to be sufficient and that our global community would face more severe shortages in early 2009 until a larger manufacturing process was approved around the world.

It was at this point that the Myozyme Stakeholders Working Group (MSWG) was formed at the request of the IPA. This working group was comprised of all three stakeholders in the Pompe model: (I) leading physicians and experts from around the world; (II) members of the International Pompe Association Board; (III) and Genzyme (the manufacturer of Myozyme/Lumizyme) representatives.

The group attempted to come up with a framework and program to minimize impact on the patient community. The MSWG met frequently over the course of several months to discuss options for clinical management of patients who would be affected by a period of intermittent delay in supply. The goal of the MSWG was to develop practical guidance (i.e., the MSWG guidelines) for clinicians and patients to ensure that the most vulnerable patients were protected from the tight supply (15-16). Over the course of multiple teleconferences and email discussions, the group endeavored to discuss all possible outcomes and to make preparations for each.

Each stakeholder had a different perspective to bring to the table—and all were equally important. It was Genzyme's job to fully explain the extent of the shortage and their plans to remedy it. In order to make appropriate plans, we all had to fully understand the situation. It was the role of the physicians and experts to provide input on the physical effect that missed infusions could have on patients and to provide guidance on how different proposed solutions might affect different populations. Finally, it was the role of the IPA representatives to speak for the patients.

During the Working Group's discussions, ensuring that the patients would be given a clear understanding of what was going to happen was of supreme importance. It was the responsibility of the IPA representatives to ensure that the communications that were put together were sufficient (17-21). It was a difficult task as the shortage had different effects on different sections of our community. By working together, abiding by a strict confidentiality that allowed open conversation, and ensuring that there was a clear and unified message from all stakeholders, as a united community we were able to get through those shortages. With the IPA having been a vital member of both the Working Group and the Pompe model in general, it is clear to us that the shortage would not have been handled as successfully as it was without all of the stakeholders having an equal seat at the table to develop a solution.

The future of the Pompe model

In 2019 the Pompe patient community is in a completely different place than it was in the 1990s or even in the early 2000s. There is a commercial therapy on the market, multiple next generation enzyme replacement therapies in trial, and multiple groups and companies working on gene therapies. The future for Pompe patients has never looked brighter. But with all of the activity, comes great responsibility. As we move forward in this next phase, the patient voice, as represented through the national and international patient organizations has never been more important. It is up to the patient leaders of these organizations to be neutral observers of ongoing activities. To provide information on new developments, to be the voice for patients throughout the drug development process, and to continue to fight for equal access to treatment and care for all Pompe patients around the world.

Over the last ten years, social media has had an increasing presence within the global patient community and the role of the national and international patient organizations within the realm of social media is continuing to evolve. Social media is a vast tool for patient organizations to use to spread information at a rapid pace. It also helps the national organizations to stay in tune with the day-to-day needs and concerns of a large and diverse patient community. Prior to the wide-spread use of social media, patients and their families generally relied on patient organization websites, one-on-one contact via phone or email, or the GSDnet to stay connected and up-to-date on all things Pompe related. Patient organizations were able to connect directly with patients through these media, and, where necessary, to step in to correct misinformation or misunderstandings that occurred. As the patient community's use of social media has increased, the patient organizations have had to adapt their presence on these forums accordingly. Beyond using it as a tool to provide information, it is also necessary, particularly at the national level, to try and monitor the different forums so that in the event incorrect information is being shared it can be addressed. This is increasingly difficult, yet incredibly important. It can extend beyond patients sharing incorrect medical advice, to sharing information about trials that may be misleading or incorrect. To that end, the patient organizations rely on their partners within the Pompe model—industry and the medical/scientific community—to help provide accurate and helpful information on their respective social media platforms. In addition, there is an attempt to comment and correct information on other platforms as possible. However, with the near-instant ability to share information it is admittedly impossible to catch everything. This will be an area of continuing discussion and debate within the community in the years to come. How do we harness the great potential good of social media, while minimizing the harm that it can cause with misinformation? We believe that it will take the entire community, working together—the very definition of the Pompe model.

Newborn screening is another area that needs the full attention of all stakeholders in the Pompe model in the coming years. There will likely be thousands of Pompe babies born in the next year, and as things stand today, it is likely that many will pass away without being diagnosed. This is especially true of those born with infantile-onset Pompe, where life expectancy of untreated children is approximately one year of age. Even for those fortunate enough to be diagnosed and have access to treatment, they are usually diagnosed due to their symptoms. This is problematic because many patients have irreversible damage to their muscles by the time they are diagnosed and able to access treatment. In addition, it has become clear that early diagnosis and access to therapy is key to the best outcomes (22-23). However, things are starting to change.

Taiwan has been screening for Pompe disease at birth since 2005 (24), and it is becoming more common in the United States as more states add Pompe disease to their state's newborn screening panels (25-26). The patient community is passionate about newborn screening because we have seen, first-hand, the dramatic difference it can make in patient's lives. Patients diagnosed at birth have the best chance possible to avoid irreparable muscle damage because as soon as the first signs of Pompe are detected, treatment can be commenced. The basic idea behind newborn screening for Pompe is quite simple. With an available treatment, and the knowledge that early access to treatment is the key to the best outcomes, it is clear that newborn screening is in the best interest of patients. However, despite this knowledge, and despite the fact that newborn screening can be cost-saving and life-saving, it is not yet a widespread reality and practice. A collective effort among the stakeholders within the Pompe model is essential to address remaining questions regarding best practices of newborn screening and appropriate guidelines for follow-up when it is implemented. To that end, the IPA has been working with the other stakeholders in the Pompe model (the medical community and industry) to advance newborn screening around the world, and we look forward to continuing this important work.

Another topic that is a focus of the IPA and the other stakeholders is how to ensure that treating physicians have the necessary flexibility to administer the best possible treatments to their patients. Today, there is only one commercially approved treatment for Pompe; however, treatment administration varies around the world. While the majority of patients receive the standard dose of 20 mg/kg/bi-weekly, this is no longer the only dose administered (27-30). After nearly 13 years of experience with commercial therapy (even more experience if you consider the seven years of clinical trials before that), it is becoming increasingly clear that a single dose structure for all patients is clearly not the ideal. With the onset and rate of progression of Pompe varying significantly from patient to patient, it is increasingly likely that different doses are necessary to be beneficial. However, because of these factors there is not yet a consensus on the ideal dose for every patient. With that said, as we are moving more and more towards the paradigm of personalized medicine throughout the medical field, we must ensure that the Pompe community is able to take part in this growing movement. In fact, the IPA, working with the other stakeholders, is making this a priority. If a physician believes that his or her patient will benefit from a dose that is different than the currently approved dose, they must have the flexibility to try it.

Finally, in terms of future treatments and therapies, it is vital that all stakeholders work together from the very beginning of the development process in order to develop necessary, effective, and affordable new therapies. When the patients have a voice to say "This is what I need," and the scientists/doctors and industry hear that voice, they are better able to focus their research and funding to answer the questions and unmet needs that most need to be addressed. This is how the Pompe model was able to successfully bring one treatment to the commercial market—and how it will bring future therapies to the market as well.

Conclusions

The Pompe community has evolved over the last 20 years. When the IPA was founded in 1999, the first clinical trials for ERT had just started, and we did not yet know if they would be successful. Now, 20 years later, we have had a commercial therapy on the market for almost 13 years, and there are numerous next-generation enzyme replacement therapies and gene therapies in the pipeline.

Despite these changes, one thing has remained the same—the absolute commitment to the patient community from the Pompe patient organizations, the scientific/medical community, and industry. The Pompe model has resulted in a very close community that is committed to continuing to work for the best interests of patients around the world. It is clear that we each have an important role that must be fulfilled, and, over the last twenty years, we have repeatedly shown the world that when all stakeholders

have an equal seat at the table, great things can happen.

As we move forward, the IPA remains committed to ensuring that the patient voice is always heard. Just as the effects of Pompe vary from patient to patient, so, too, do a patient's needs. The IPA will continue to speak for all patients and to serve as a bridge between patients and the other stakeholders in the Pompe model (the medical/scientific community and industry). The Pompe model links the strong and unified voice of the patients to the enthusiasm, energy and dedication of the scientists and doctors. It also links the increasing interest of industry in our very rare disease. The Pompe model will continue to set the standard as it is only when we all work together, that great things are achieved. Together we are strong!

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Footnote

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References

1. O'Donnell K. Pompe Disease—the real story. Introduction: where to begin? Cited 10 March 2019. Available online: http://pompestory.blogspot.com/2009/03/introduction.html
2. O'Donnell K. Pompe Disease—the real story. GSDNet. Cited 10 March 2019. Available online: http://pompestory.blogspot.com/2009/12/gsdnet.html
3. O'Donnell K. Pompe Disease—the real story. The birth of the International Pompe Association. Cited 10 March 2019. Available online: http://pompestory.blogspot.com/2009/12/birth-of-international-pompe.html
4. O'Donnell K. Pompe Disease—the real story. IPA Founding Conference part 2. Cited 10 March 2019. Available online: https://pompestory.blogspot.com/2009/12/ipa-founding-conference-part-2.html
5. Genzyme Pompe Program Update April 2007. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/PompeProgramUpdateApril2007.pdf
6. MTAP Fact Sheet. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/MTAPFactSheetMay.pdf
7. Pompe Program Update May 2007. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/Pompe_Update_May_2007.pdf
8. MTAP Fact Sheet June 2007. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/JuneFactSheetFinal.pdf
9. Genzyme Pompe Program Update June 2007. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/JuneProgramUpdateFINAL.pdf
10. October Update on the US Myozyme® Supply. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/OctoberSupplyUpdateFinal.pdf
11. January 2008 US Myozyme Supply Update. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/January2008USSupplyUpdateFinal.pdf
12. US Myozyme Manufacturing Update-April 2008. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/APRIL2008ProgramUpdate.pdf
13. Genzyme Program Update November 10th, 2008. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/november_10_2008_pompe_program_update.pdf
14. Genzyme Pompe Program Update-November 17, 2008. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/november_17_2008_pompe_program_update.pdf
15. International Pompe Association. Important Myozyme Supply Information Has Been Released (global version). 2008. Cited 10 March 2019. Available online: https://worldpompe.org/index.php/news/106-important-myozyme-supply-information-has-been-released-global-version
16. International Pompe Association. Important Myozyme Supply Information Has Been Released (EU version). 2008. Cited 10 March 2019. Available online: https://worldpompe.org/index.php/news/105-important-myozyme-supply-information-has-been-released-eu-version
17. International Pompe Association. Important Myozyme Supply Information Has Been Released (Global Version). 2009. Cited 10 March 2019. Available online: https://worldpompe.org/index.php/news/106-important-myozyme-supply-information-has-been-released-global-version

18. International Pompe Association. Important Myozyme Supply Information Has Been Released (EU version). 2009. Cited 10 March 2019. Available online: https://worldpompe.org/index.php/news/105-important-myozyme-supply-information-has-been-released-eu-version
19. IPA Statement: The End of Myozyme Supply Restrictions. 2009. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/IPA_4K_Approval.pdf
20. Pompe Program Update–May 22, 2009. Cited 10 March 2019. Available online: https://worldpompe.org/images/pdfs/Program_Update_5_21_09_FINAL.pdf
21. International Pompe Association. Statement from IPA concerning Lumizyme Approval. 2010. Cited 10 March 2019. Available online: https://worldpompe.org/index.php/news/53-statement-from-ipa-concerning-lumizyme-approval
22. Chien YH, Hwu WL, Lee NC. Pompe disease: early diagnosis and early treatment make a difference. Pediatr Neonatol 2013;54:219-27.
23. Yang CF, Yang CC, Liao HC, et al. Very Early Treatment for Infantile-Onset Pompe Disease Contributes to Better Outcomes. J Pediatr 2016;169:174-80.e1.
24. Chien YH, Chiang SC, Zhang XK, et al. Early detection of Pompe disease by newborn screening is feasible: results from the Taiwan screening program. Pediatrics 2008;122:e39-45.
25. Yang CF, Liu HC, Hsu TR, et al. A large-scale nationwide newborn screening program for Pompe disease in Taiwan: towards effective diagnosis and treatment. Am J Med Genet A 2014;164A:54-61.
26. NewSTEPs. Newborn Screening Status for All Disorders. Cited 10 Mar 2019. Available online: https://www.newsteps.org/resources/newborn-screening-status-all-disorders
27. van Gelder CM, Poelman E, Plug I, et al. Effects of a higher dose of alglucosidase alfa on ventilator-free survival and motor outcome in classic infantile Pompe disease: an open-label single-center study. J Inherit Metab Dis 2016;39:383-90.
28. Yanovitch TL, Casey R, Banugaria SG, et al. Improvement of bilateral ptosis on higher dose enzyme replacement therapy in Pompe disease. J Neuroophthalmol. 2010;30:165-6.
29. Case LE, Bjartmar C, Morgan C, et al. Safety and efficacy of alternative alglucosidase alfa regimens in Pompe disease. Neuromuscul Disord 2015;25:321-32.
30. Chen wM, Zhang L, Quan S. Enzyme replacement therapy for infantile-onset Pompe disease. Accessed 30 Mar 2019. Available online: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011539.pub2/information#CD011539-sec1-0015a

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