IPA Feedback Survey:
Response to Myozyme Supply Disruption

Results of an informal on-line and paper survey of the global community of sufferers of Pompe Disease, following a short interruption in the supply of their Enzyme Replacement Therapy, Myozyme.

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Background

Throughout the second half of 2008 board members of the International Pompe Association worked closely with the biotech company, Genzyme Corporation, and expert treating physicians to monitor the global Myozyme supply situation. Our main objective was to prepare a plan of action to modify patient demand should inventories become so tight as to jeopardise the treatment of the most vulnerable infants, children and adults within the Pompe community.

As it turned out, the disruption to supply was restricted to a single skipped infusion in early 2009 for most adults. However the IPA was aware that there were noticeable effects from this delay in treatment and so we decided to survey a sample of the patient community to make an assessment of the true impact.

Given the amount of time and effort required to prepare the Myozyme Stakeholders Working Group (MSWG) guidelines, and also the preparation of a global communication plan, we hoped to assess their quality through the same survey.

The questions presented grew from the original concept to 38 in number, very few questions were compulsory and respondents were at liberty to skip any questions that they were not comfortable answering, could not remember, or did not apply.

Response

The feedback survey attracted 130 returned forms from the Pompe community, the summarised answers below indicate an initial analysis of the data for each question, with further cross-referencing of the responses it may be possible to determine interesting trends for future consideration (e.g. response to missed infusion as a function of disease severity) but for the time being this preliminary report indicates a very simple view of the data.

There will undoubtedly be bias in the results of this survey as the patient groups who encouraged participation approached the same population who would have been sent the original guidance, but the responses show that those affected by the supply interruption received information from many other sources and a great deal of interesting information has been collected.

The following sections present a simple analysis of the responses to each question.

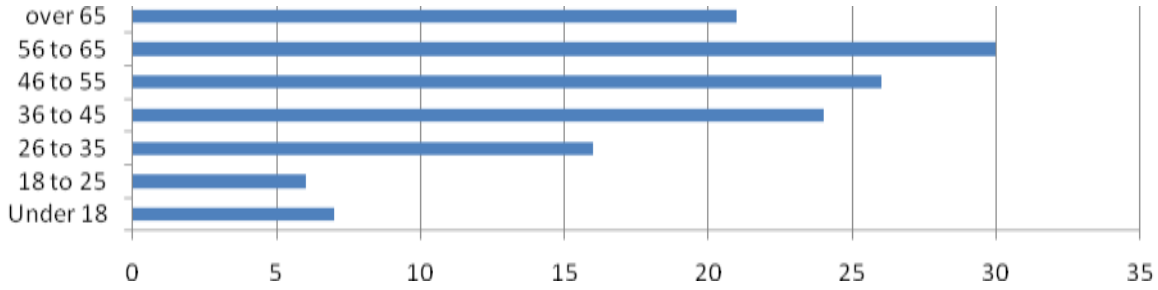
Personal Information

Gender

As expected the response was almost equally split between male and female (52 and 48% respectively).

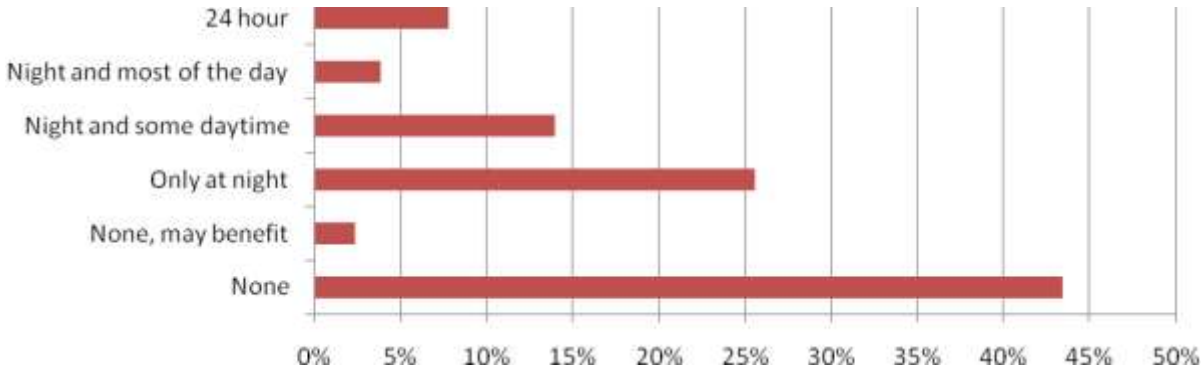
Age

The age of respondents was evenly spread between the ages of 25 to 65, although the dip at the higher age range may indicate a lack of IT availability/familiarity. It was disappointing to see reports for under 18 year-olds as this survey was not intended for them; perhaps this indicates that the survey introduction should have been more clearly worded. The response from younger adults seems to be low, whether this is due to under diagnosis or motivation cannot be determined from this survey alone.



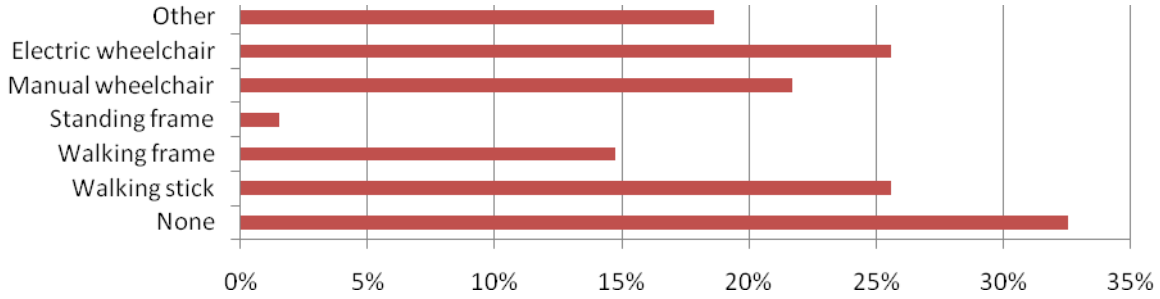
Ventilator Support

43% of respondents are ventilator free although a small number (3 or 2%) felt that they would benefit from night time use. 53% use some form of ventilator with half of them needing assistance nocturnally. The remaining half was divided equally between occasional day-use and most/all of the day use.



Mobility Aids

One third of respondents use no mobility aids at all. One quarter of respondents use a walking stick and at the other end of the scale 25% require electric wheelchairs.

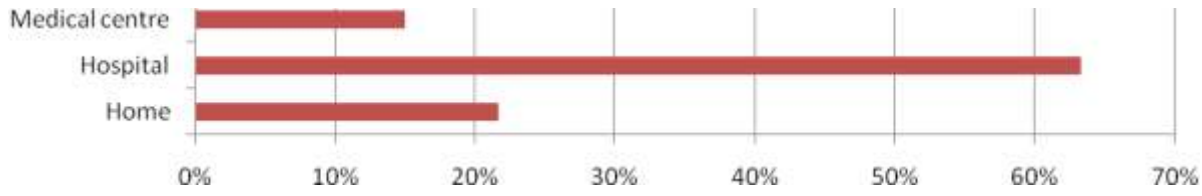


Myozyme Infusions

Six respondents are not currently prescribed Myozyme and so the responses to questions on the effects of supply interruption have been ignored, although their awareness of the communication process and any anxieties are of interest.

Of those who knew their Myozyme dosage, 90% receive the recommended dose of 20mg/kg every two weeks. 10% receive double this dose every fortnight. This is a large number considering that all these respondents are adults.

The majority of infusions still take place in the hospital setting or local medical centre, although the number of home infusions is significant (22%).



Infusions missed during the period of supply disruption

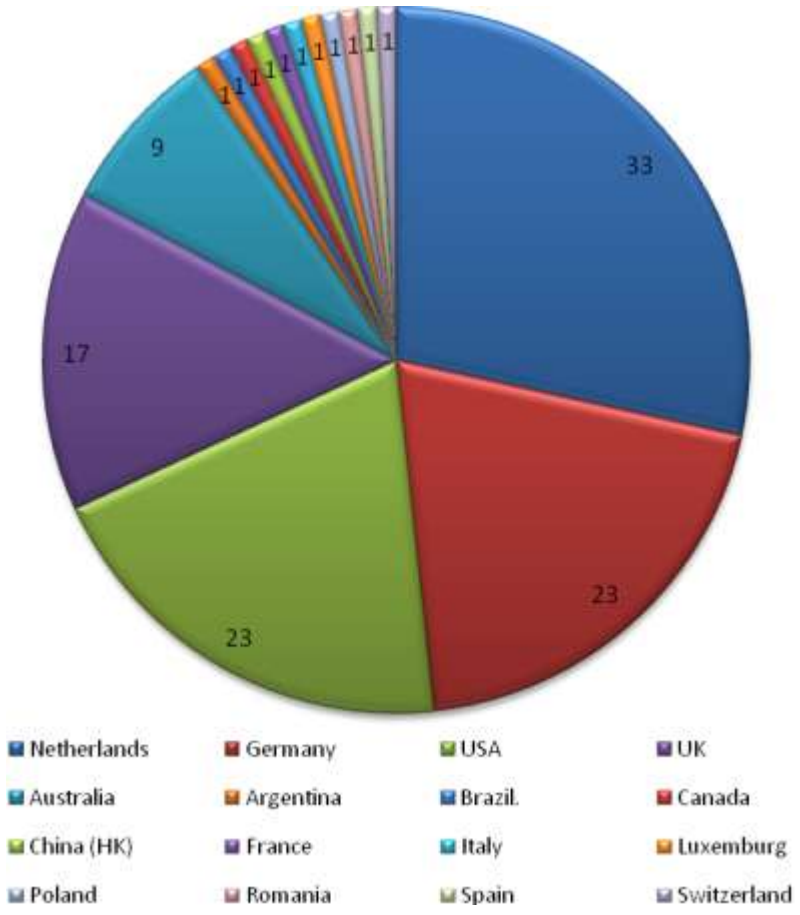
It was expected that each adult would need to miss one infusion only, so it was surprising that over one fifth of the population did not miss any infusions; it is believed that this can be explained by a number of separate situations:

1. A small number of patients were too severely affected to tolerate a missed infusion,
2. Some hospitals had sufficient inventory of Myozyme to allow them to continue infusions despite a shortfall in subsequent deliveries from Genzyme, and
3. Some treating physicians were either unaware of the supply interruption or chose to ignore it. It is not clear to the IPA how they managed their own hospital inventories during this period.

It is also surprising that a small number had to tolerate three or four missed infusions.

Country of Residence

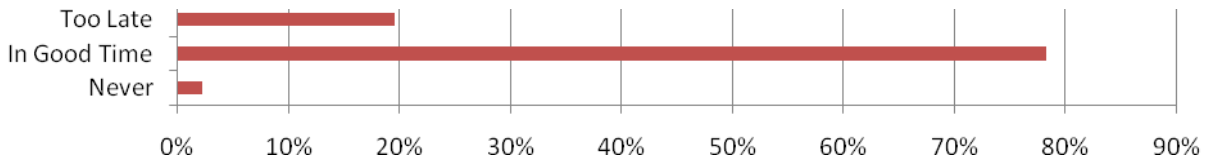
Good responses came from countries where the patient groups are well represented by the IPA Board members and through GSDNet (GSD email network) contact. It was reassuring to see a global response but we would like future surveys to reach many more families in countries outside the five dominant nations.



Communications preceding the supply disruption

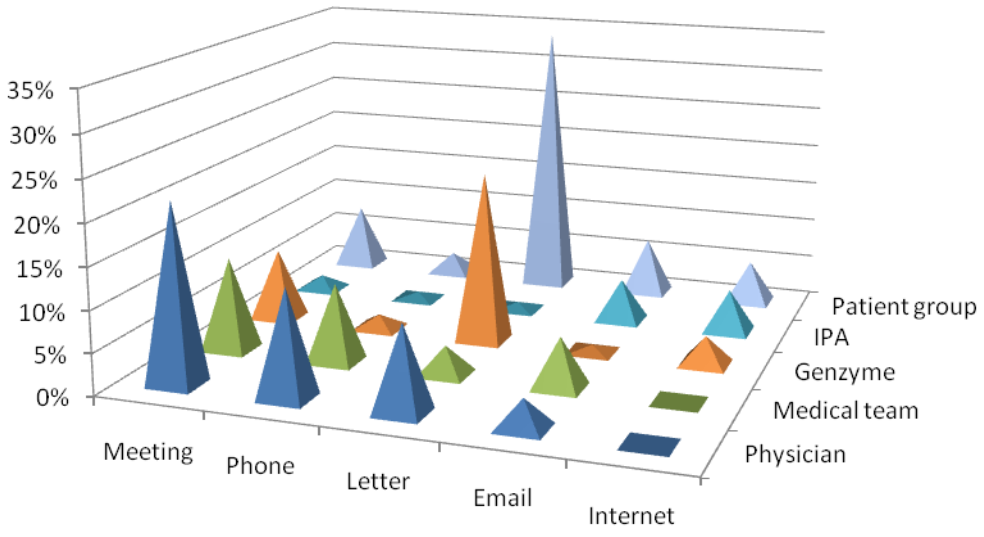
Notification about the disruption to your supply of Myozyme

One fifth of respondents felt that they did not receive information about the supply interruption in good time; they would have preferred notice much earlier. Two respondents did not hear anything.



Communication Methods

It seems that the plan to approach communication from “top-down” and “bottom-up” worked extremely well. The message was passed down from Genzyme through physicians and medical teams to reach the vast majority of patients. Equally impressive was the reach of patient associations whose message, originated by the IPA, was received largely by surface mail. It is also clear that Genzyme was able to reach a large number of (US) patients directly by letter.



Message Clarity

90% of respondents thought that the message about supply interruption was clear. Although only 43% confirmed that they had seen the guidance documents from the Myozyme Supply Working Group. This is a little surprising since, although the European authorities would not permit EU physicians to distribute the guidance, it was sent to many affected families through the patient organisations.

Message Content

76% of respondents were happy with the guidance they were given, of the remaining 24% it would seem that many were satisfied after further discussion, though further analysis of the detailed response is required.

Exemptions from the recommendations

A very high number (46 or 40%) of respondents were informed that they may apply for continued treatment due to their exceptional circumstances. Of those, 6 chose to apply and all seemed to be successful. Genzyme representatives were involved in all of these applications so that it would seem that physicians were not simply choosing to treat despite EMEA or MSWG recommendations.

It was noted that in some regions (notably Germany) that the exemption procedures were not clearly communicated to the hospitals. There were severely affected patients who weren't told that they could apply for exemption.

> *"I was told too late – after having trouble with missed infusions for 4 weeks."*

Psychological wellbeing

Prospect of missing infusions

The prospect of missing an infusion did cause additional anxiety for about half of all respondents.

"It was of some concern if the tight supply situation went on too long"
"To miss a step means a fall - continuation is essential"
"I had missed treatment before and felt the effects"
"Not worry but concern and disappointment"
"Somewhat, especially if it was going to be prolonged. I was actually curious to see whether or not I would notice a difference"
"Since I knew it was temporary, I was not worried"
"Concerned but not worried"
"The prospect of missed infusions made me anxious of life-threatening consequences"
"My physician was surprised when I told him that I could have been exempt from missing infusions"

Discussion of the recommendations with others

Most (75%) respondents felt that they had someone with whom they could discuss their worrying situation although a significant number (15%) felt that they were alone with their predicament.

Previous experience of missed infusions

59% of respondents reported that they had never missed an infusion before, although 39% had done so. It may be appropriate in future circumstances of this kind to recommend exemption for patients who have recently missed infusions for other reasons:

"I have had infusions delayed by a week or more, due to scheduling problems"
"Once when I was hospitalized with pneumonia and once during bad weather"
"One missed during transition from clinical trial to MTAP"
"I missed two infusions during the US shortage in 2007, when Genzyme recommended all adults miss one in August and one in October"
"I missed the infusion immediately before the shortage, due to an ice storm, resulting in 3 instead of two misses"
"Hospital cancelled because there was a problem with the pharmacy and the infusion could not be made up"
"After pneumonia and missed infusions, I was much weaker, less coordinated, had a lot more difficulty with breathing, and had less stamina"
"After missing the 2 infusions -- one during the ice storm, then a month later because of the shortage of Myozyme, I had less stamina, my breathing has deteriorated, and my strength in arms had deteriorated"
"Was in hospital for severe torn muscle in back for three weeks and they did not want to give me the medications with all my other medications"
"When I was in the clinical trials, I missed two or three infusions because Genzyme could not import Myozyme on time"
"Because I was unwell I spent about ten days mostly on my bed"
"The whole unit closed over the Christmas break meaning that one infusion was 3 weeks after the previous one"
"Vacations, conflicts with work, unable to find parking at the hospital"

"When trying to get on MTAP I missed two infusions. Noticed decline from having missed two in a row"
"The nurse who does the infusion was on leave and I had to miss an infusion"

Missing infusions in the future

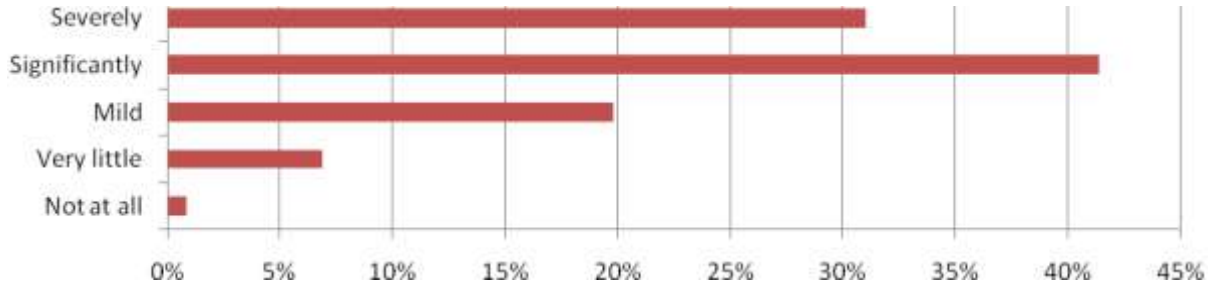
After this experience it was interesting to see that 31% of respondents would voluntarily miss an infusion in the future, should the need arise:

"Only if totally unavoidable"
"I would only consider missing an infusion for illness"
"Only one; I started having problems with more than one missed infusion during the shortage"
"I am still going backwards despite the Myozyme treatment. I know that Myozyme does help me so I would not go without willingly"
"Only if it would only be a single skip, and I knew that I would receive several on schedule both before and after the skip"
"I would do everything I could to not miss an infusion"
I'd rather just reschedule due to a holiday rather than completely skip a treatment - but if there were a shortage, skipping would be fine"
"I am currently missing two infusions due to being abroad for a month. Have missed infusions in the past for the same reason"
"Not if I can help it"

Physical effects of missing an infusion

Disease Severity

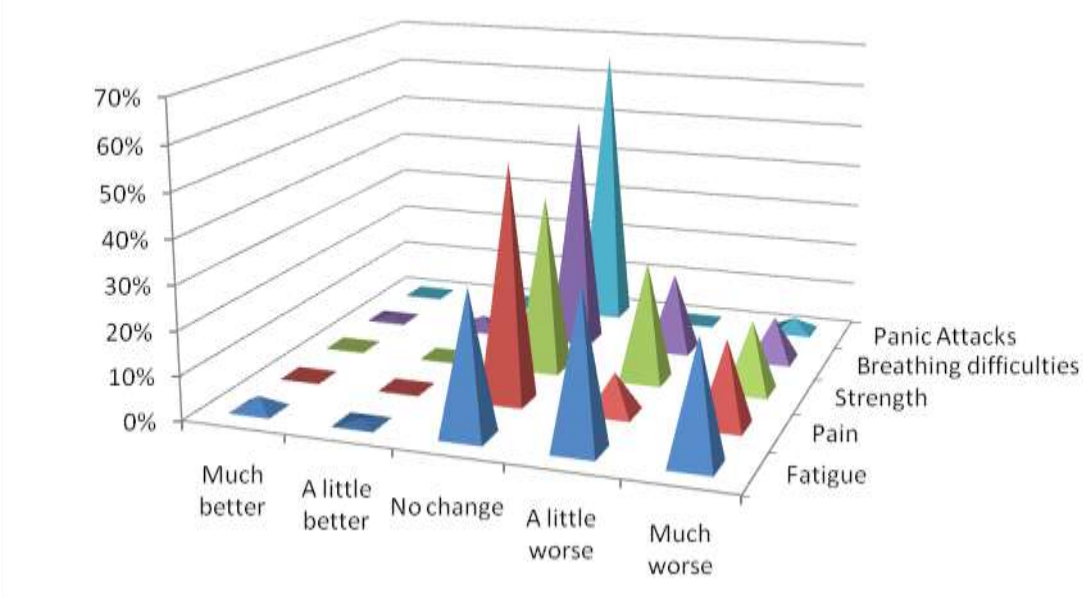
A significant number of respondents (72%) felt that they were severely or significantly affected by Pompe Disease. One patient reported that they were not affected at all by the disease.



Physical effect of missing infusions

It is apparent from the response to this question that fatigue was a major consequence of missed infusions affecting 63% of respondents.

It may have been the case that parts of this question were worded badly or that translations did not express the true sense of the options available, but the result was that several respondents reported muscle strength improvement, much improvement in some cases. It has been assumed, however, that this data was entered incorrectly and those scores have been reassigned as signs of increasing muscle weakness rather than strength. With that assumption made it is estimated that muscle strength deteriorated for 43% of respondents.



Respiratory function was also affected with 28% reporting a decline and muscle pain increased for the same proportion. Panic attacks only increased for a very small number (3%).

Resolution of physical effects since restarting regular infusions

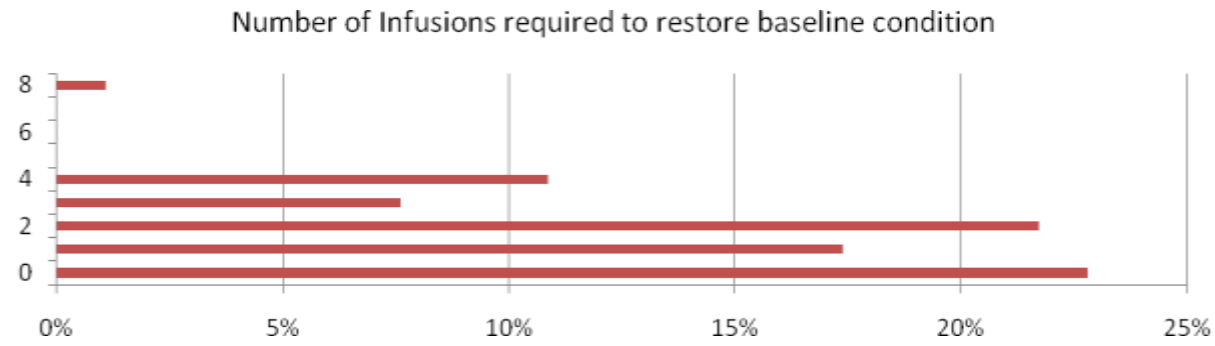
Fatigue does seem to have become a pronounced feature of Pompe disease; the prevalence of which seems to have become more evident since Myozyme became available:

"I'm slowly gaining back some of the strength that was lost"
"Everything has gone back to normal, as it was before the break"
"Almost back to ""normal"". Still have increased fatigue and pain, but not as bad as during missed infusions"
"Since restarting infusions every 2 weeks my legs don't feel as heavy as they did on monthly infusions"
"Very slow progress in getting to the level I was at before missing two infusions. At this rate I think it will take six months to recover"
"Yes, Muscle pain, cramping, restlessness and fatigue levels have returned to the pre-shortage range"
"No fatigue and less breathing difficulties."
"I have less fatigue. I have less pain and I am grateful for that"
"Don't feel so tired"
"I feel like I am now back to my "normal" self again"
"I still seem to be deteriorating, though I do notice an improvement in the week following an infusion."
"I am not back to pre-missed infusion"
"Back to how I was before missing, but it took two infusions to get back there"
"Lack of fatigue seems to be the first thing I notice"
"Has all gone back to normal"
"Almost back to where I was before missing infusions energy wise"
"Less fatigued"
"Yes I m back to my condition before the supply difficulties"
"Back to 'normal'"

Infusions required before your condition stabilised

Whilst 23% of respondents felt that missing one infusion had not adversely affected their condition, it took others up to four infusions before they felt fully restored to their condition before the supply interruption. In one atypical case it took eight infusions. Comments suggest that others may also be taking longer to recover from the interruption of supply:

"Have not yet fully recovered"
"Has not stabilized yet"
"I am still declining"



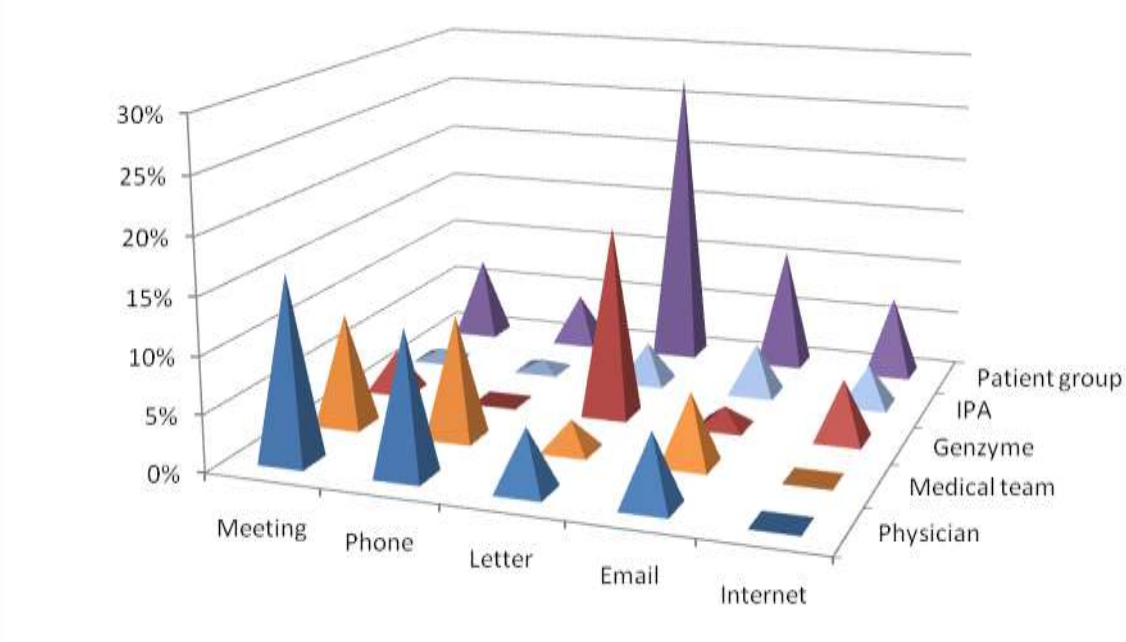
New capabilities since restarting infusions

No new capabilities were recorded.

Communications at the end of supply disruption

Communication method

The pattern of communication about the ending of the supply interruption seems to have been very similar to its initial announcement with the medical teams, patient groups and Genzyme (in the USA) all playing important and complimentary roles.



Message Clarity

Only 5% felt that the message was not clear:

> *"Clear to me yes, but not to the hospital. The pharmacist never received the message"*

8% asked for further clarification. Of those only about one third were satisfied with the response they received.

General comments regarding experiences throughout this period

"I had heard via a listserv email that there may have been some manufacturing issues which contributed to the supply problems."

"Two brothers and I did not miss an infusion, we were not informed why. I am very grateful for having this treatment."

"I was worried about how long the shortage would last. Missing only one infusion was Ok but if continued might have been a problem"

"I've been on Myozyme for 2 years. Very helpful improvement during the first two months and little to none thereafter. I believe I came to take Myozyme for granted, though I never missed an infusion. Became very, very stiff (I'm most affected in my legs and back) with some 'pain' after about a month. Couldn't wait to get back on the twice-a month routine. It in fact scares me as to finding out the degree to which I rely on Myozyme."

The missed infusion was something tolerable for one occasion and I knew it would be difficult given that I have felt so much benefit from Myozyme. I was surprised however at how marked the change for the worse was especially in the 4th week of the missed infusion.

"Considering the possibility of infants not getting their treatments, I was ok with missing one treatment a month. However, I did not expect to have this much trouble regaining strength, and have my breathing continues to be worse than usual"

"I know the medication works to stop the progression of the disease but missing two infusions really set me back. I know missing many more would be devastating to me"

"Before the shortage I had talked to my Doctors about the possibility of going to a once monthly infusion instead of every other week. Since the shortage gave us 3 months experience with this treatment plan, we now realize that this option would make a significant difference in my treatment and would not be a good option for me"

"Some members of our [patient] association did not miss a treatment; I found that to be unfair on members who went without a treatment"

"I got much more tired after missing the infusion, I noticed the difference after week 3 from the previous infusion, and by week 4 I was exhausted. If this ever happens again, I would much prefer to be able to go to a 3-week infusion rather than 4-week"

"I was very afraid that the supply shortage would continue"

"I did not like the interruption of infusions"

"I was pleased to hear that the children still had their supply! We as adults can still go on!"

"It happens - It was handled well. I used the time for missed infusions to do extra exercise to help make up for missing ERT"

"I would like to thank all at the IPA for their excellent work during the supply difficulties. The time and effort you give to support and care for all Pompe's patients is very much appreciated"

" I was shocked and discouraged to see how quickly the positive effects of the infusions disappear when infusions are skipped. I don't want to imagine what happened if I had to stop therapy."

" I never imagined that skipping two infusions would show consequences that quickly and fiercely."

Conclusion

Overall the survey has revealed some interesting indications of how the supply interruption was received by the global Pompe community. The survey was intentionally informal, took advantage of a free Internet application and was prepared in a very short period of time (we wanted to collect the data before memories faded). So it does not have the scientific rigour associated with medical surveys and registries of patient populations.

However the analysis presented is based on a collection of 130 individual responses representing over 10% of the global patient population receiving Myozyme infusions, and so has value both as feedback for the IPA, the Myozyme Stakeholders Working Group (MSWG) and the Pompe population as a whole. It may also be useful to other groups facing similar difficulties in the future. We would hope that lessons have been learnt from this experience and that protections can be put in place not only for the most vulnerable patients but for the whole patient community.

The survey has shown that on the whole the communications plan was well designed and had the intended effect of informing the majority of patients worldwide, to prepare them for the supply interruption and to provide them with the information they needed to prepare for the event. We do feel, however, that an unacceptable number of patients, severely affected by Pompe disease, were not exempted from the recommendations. Improved exemptions (to include those who recently missed infusions) and better communication of the exemptions would be highly desirable. It is also unacceptable that patients in relatively stable condition were able to avoid missed infusions whilst others, more severely affected, missed one or more treatment.

It is apparent that a large number of respondents were affected both psychologically and physically by the event and that it took several weeks for them to recover from its effects; some still feel damaged by the episode several months later.

We also learnt the importance of structure and wording of even simple surveys and how easy it is for simple questions to be misinterpreted.

Finally I would like to thank all those who responded to the survey to provide us with these highly valued insights into their experiences.

Allan Muir
Chairman
International Pompe Association