

# Gaucher Disease: Alternative Treatment Options Town Hall *Transcript*

## Introductions

### ***Stuart Berman, Co-chair of NYU Patient Support Group and Moderator***

Good afternoon everyone.

My name is Stuart Berman and I'm here with Kevin Kline to moderate this town hall meeting, featuring Dr. Gregory Pastores, Associate Professor at the NYU Medical Center, and Director of the Neurogenetics Laboratory at NYU.

As some of you may know, Kevin and I are Gaucher patients, and are also Co-Chairs of the NYU Gaucher Patient Support Group. Kevin and I are pleased to welcome you to this town hall meeting on Gaucher disease alternative treatment options.

And I want to also thank Dr. Pastores for making the presentation that you're going to hear shortly, and Rhonda Buyers, head of NGF Association, for being with us as well.

Before we start, let me say that Kevin, Dr. Pastores, and I are volunteering our time here today in order to assist the Gaucher patient community and are receiving no payment or fees for participating here today.

I'd like to turn the meeting over to Kevin now, so that he can say a few words.

### ***Kevin Kline, Co-chair of NYU Patient Support Group and Moderator***

Thanks, Stu. I'd like to start off by thanking you all for taking the time to call in today and I want to preface our discussion by saying that the purpose of this call is not to go over how we got here, but discuss what we as patients and caregivers can do moving forward.

Furthermore, as you heard, at any time during the call, feel free to ask any questions you may have and the operator will take your name and question and we here will attempt to answer any and all of the questions that we get.

With that being said, I'd like to turn it over to Dr. Pastores to say a few words before we get started.

### ***Dr. Gregory Pastores, Associate Professor at the NYU Medical Center, Director of the Neurogenetics Laboratory at NYU***

Thank you, Stuart and Kevin. And thank you again to everyone for joining us on today's call.

Please note that this conference is being hosted for informational purposes only, and in many ways you probably should think of it as a virtual patient conference or support group, meaning like we've had on an annual basis through the years at NYU and at Mount Sinai when I directed the Gaucher Clinic at that institution.

Please note that our discussions today are not intended to provide specific medical advice or recommendations. And the views that I personally express on this call don't necessarily represent

the views of the national Gaucher Foundation or any of the pharmaceutical companies who manufacture therapies or drugs for Gaucher's disease or that are mentioned during this call.

I will be speaking in general terms about the situation and my own understanding, based on my own experience, my own assessment of the literature, and discussions about the concerns that patients have called to my attention, and focus primarily on the issue that has come up with imiglucerase, which I will subsequently only refer to now as Cerezyme. That has been essentially the standard of care for a significant number of Gaucher patients on therapy.

If you have any questions regarding the course of your own treatment, I strongly advise you seek recommendations or advice from your personal physician.

In order for us to be able to make this event accessible to patients around the country, we are grateful to Actelion for providing funding for the cost of hosting this conference call and the transcript that will be made available following the call on the National Gaucher Foundation Web site.

As Stu has pointed out earlier, Mr. Berman, Kevin Kline, and I are not being paid for our time today. In the interest of full disclosure, most of you are probably aware that I have been a long-term investigator for Genzyme Corporation, and have also been engaged with practically all pharmaceutical companies that either have approved products for the treatment of Gaucher Disease or have drugs in trial or will seek regulatory approval. I don't personally own any stocks or a beneficiary financially of any therapies that patients are on.

With that said, I'd like to reintroduce Rhonda Buyers, CEO and Executive Director for the National Gaucher Foundation, who is also on the line with us today. And I thank Rhonda for calling attention to this program on the National Gaucher Web site, so that she can also inform us of the stuff that NGF itself has undertaken to ensure that the patient's concerns are adequately addressed during the period when Cerezyme is not available for patients.

***Rhonda Buyers, CEO and Executive Director, National Gaucher Foundation***

Thank you very much, Dr. Pastores. And let me also thank Stu Berman and Kevin Kline and Actelion for their support of this meeting. What I also want to do is tell you that I also am not being paid for this.

But what I thought would be helpful would be for you all to understand what the NGF has been doing and will continue to do throughout this period. It's certainly a time that we learn everyday and we are trying to deal with situations as they arise and also anticipate situations.

And I just want everybody to understand that if you do have questions, if you need assistance in any way, whether it is to locate physicians, specific treatment sites, help with financial situations, please give the NGF a call.

And also you can go on our Web site. I do want to mention our Web site is being worked on to provide better information to all of you. We will have separate pages for the companies involved and the most up-to-date information that we can provide.

Clinicaltrials.gov is about four to five days behind, as far as lead time and getting the information up. And we are trying to get it to you more quickly. And we've pretty much worked out how we'll do that. So if you'll check our Web site, whenever you have questions or you just want to get the most up-to-date information, we are hoping to provide that to you.

And I don't want to take up any more time, but I just wanted to reiterate: please call us if you have any questions. We have been taking many, many calls and many emails in trying to help the people involved to get them the best care that we can.

***Dr. Pastores***

Thank you, Rhonda. So let's get started and hopefully we can make the most of our time this afternoon.

Stuart and Kevin have prepared a list of questions to guide today's call. And hopefully we'll also be taking some questions from folks on the line.

Kevin, would you please ask the first question.

**Q&A**

***Kevin Kline***

Once again, thanks everybody for being on the line.

First off, I want to ask what the latest on the Cerezyme shortage is and how the shortage is impacting your treatment strategy for patients?

***Gregory Pastores***

So I'd like to preface that question by giving a people a feeling for who I am, in terms of my own practice and the kind of patients I deal with.

I have been dedicated to the care of patients with Gaucher disease and research in this field since 1990, and now actively follow 300 patients, more or less, including treated and untreated individuals, including children and adults -- so essentially all comers.

I was one of the principal investigators for Cerezyme and was involved as a principal or co-investigator for Shire's velaglucerase and Protalix, prGCD. I was also the initial investigator in the United States for Actelion's Zavesca, or miglustat. And also I've been engaged in the clinical trials for Amicus Plicera.

And as of yesterday I can confidently say that I probably am the only physician in the world, if you would allow me to brag, who's used all of the therapeutic options- and obviously with some of the options that have been introduced, for probably the longest period of time- in the most number of patients.

So I will speak of my own experience, but obviously any statements I make may not necessarily be infallible statements. And I would be happy to be corrected and anything I say regarding other products, if there are representatives from the other pharmaceutical companies that may be a part of this discussion, could please call those matters to my attention.

And I have asked each of the companies to provide me a brief statement that may be the basis for some of my answers to date.

So having given you that long introduction, with respect to Kevin's first two questions, my understanding is the following.

Genzyme, as you know, ran into manufacturing problems a couple of months ago, but have started production. And we expect Cerezyme, again, to be available sometime in November or December. However, we are awaiting information of when supply will be back for particular patients in terms of what it was before the shortage, or whether patients will still need to be enrolled into the treatment gradually based on a prioritization schedule.

As you probably realize, people talk about prioritization, but in my eyes, this probably equates to rationing. And that really is the situation that we are in, but people, I guess, are not comfortable referring to it as such.

With respect to the second part of Kevin's question, in terms of how this has impacted our treatment strategy for patients, as with all of my patients, whether treated or untreated, I recommend that they be seen on a regular basis for monitoring.

And if you are a patient that has been on treatment, but have now had your treatment disrupted and have not seen your primary physician recently for a reassessment of your status, I strongly recommend that. Because at the end of the day, the decision for what alternatives are available is really influenced by several factors, including age, the presence or absence of a spleen, the presence of other medical problems besides Gaucher disease, or other medications that you may be on for Gaucher or other non-Gaucher medical problems.

So once your current medical status is clarified and I will address later some of the things we've undertaken to monitor our patients, there can then be a basis for assessing what I'd like to refer to as the risk benefit ratio, deciding which of the available or anticipated options are appropriate for you in your particular case.

And I'm sure everybody has some level of frustration because the situation we're in has obviously not been anticipated. Why there has been no contingency plan to address such a possibility, is beyond my ability at this point to clarify. But, the precipitous nature or the fact that all of this happened abruptly, I believe, to some extent, is what made people very anxious about the situation we're in.

***Kevin Kline***

So I heard you mention other options available. Could you go through what those other options are for Gaucher disease Type 1, besides Cerezyme?

***Gregory Pastores***

So for this question, at the moment, I will only focus on those who are already or have been on Cerezyme. I'm sure most are aware, working with several stake holders, primarily the Medical Advisory Board of the NGF, which represents physicians with probably the greatest and longest experience in caring for patients with Gaucher disease. They have defined some basis for determining, based on what's available, in terms of Cerezyme, who should have, if possible, no treatment interruption.

And with respect to those who had their treatment interruption, we've approached it along the following lines. If the patients identified do not meet part of the most vulnerable group, what we've decided to do is screen for particular patients.

I have, for instance, two cases who have had liver transplants who we've just been able to stabilize. And I was really just too concerned about those patients having a setback or a Gaucher related complication in the midst of other medical concerns.

In a similar way, two other patients have a malignancy for which they are on high-dose chemotherapy and because Gaucher disease can impact the bone marrow, we want those patients to obviously get the maximum benefit from the treatment by not having their therapy interrupted.

Now for the rest of the group, what that really leaves them to, I believe, are the options of either waiting it out, until Cerezyme becomes available, although obviously, I'm sure the problem with that, at least in my own situation, relates to the fact that we have not systematically evaluated a large cohort of patients who had a drug holiday.

Because, in many ways, that is what we are in today, but as some of the healthcare providers have told me, it's not really a drug holiday in the sense that people have chosen to be off drug. And obviously in situations in the past where people have elected to not go on drugs, if and when they felt they wanted to restart, we knew we could make Cerezyme available for them in that particular situation.

So obviously, for everybody again, as a reminder, come see your physician and get evaluated so that your situation can be put in its proper context. If patients are not comfortable waiting it out or the physicians and the patients are concerned of a relapse, and I'm sure you can understand most individuals who've never had the experience of treatment as children, have had their spleen removed or maybe have undergone a hip replacement, don't want to relive such experiences, particularly after most of them have been stabilized by Cerezyme for decades.

And that leaves those group of patients at least two options that I refer to as viable options because patients can get to that today, if they so desire and if their physicians feel it is appropriate for their particular situation.

So up to the day that Cerezyme was available, most of you are probably away that there was only one other FDA approved drug, which was Zavesca or miglustat, an oral agent, and that clinical trials have been undertaken or are ongoing with respect to other options.

And perhaps the best way to put this into context, as I discuss it with most patients, is in terms of trying to explain the mechanism of action for the different options with the following.

If you think of a sink as your liver and one of the sites in the body where the Gaucher cells accumulate because you're deficient for the enzyme, in many ways it is analogous to having a sink that has a plug in its drain. And really the whole idea behind enzyme replacement therapy is to clear that clog in the drain and let the storage buildup clear out.

And really in the 1990s when Cerezyme was introduced, because it essentially was replacing or replenishing patients who did not have sufficient amounts of the enzyme, it was a relatively straightforward of treating patients, and as most of you know, has been very safe and effective.

And essentially right now, there are alternative enzymes that are available, but not commercially. And what I am referring to is velaglucerase, which is a form of the human enzyme generated from human cells. And because you are talking about human cells, all you need to do essentially to produced velaglucerase, and I'm talking here in a shorthanded fashion, as it were, is to turn the switch on.

Because I'm sure most of you are aware Cerezyme is produced in Chinese hamster ovary or rodent cells. And unfortunately, a contamination by a rodent virus of the Chinese hamster ovary cell line has affected its production.

Now the other alternative enzyme formulation is the human enzyme produced by Protalix, using carrot cells.

So in essence, as common to all of these drugs, is that they are based or incorporate the human sequence, but because there are differences in the source of production, there may be subtle differences in patient's tolerability of this drug or in terms of how it would work in their particular situation.

Having said that, obviously there's nothing published about the clinical trials for both Shire's velaglucerase and Protalix's prGCD (a carrot derived enzyme), because those trials have really just come to conclusion are ongoing. But, my understanding is, with respect to the data that investigators who've worked with Shire will be in a meeting next month to be informed about the

details of trial results and similarly Protalix will have their meeting in December for the investigators.

In the meantime, if people would like to consider an alternative enzyme formulation there are no clinical trials of velaglucerase that I am aware of. Fortunately, velaglucerase has been made available by the FDA and Shire, in an expanded access program. But, because it's an expanded access program and that's something that any doctor anywhere can just prescribe, that restricts its availability to centers that have institutional approval and contractual arrangements with Shire to make this drug available to their patients.

And with Protalix, there is an ongoing clinical trial, for which in fact we have five patients that have committed, including one that started therapy, uneventfully, yesterday. And for people interested in Protalix, they may want to seek information on where those clinical trials are being conducted.

I understand from Rhonda that additional information will be available on the National Gaucher Foundation Web site, about the different therapeutic alternatives. And the patients can obviously, or any interested parties, access on the Web or Internet, the companies that have invested in the Gaucher community to make treatment available while Cerezyme is not available.

So hopefully the subsequent questions will allow us to expand on the other issues. In the next few minutes, I'd like now to just focus briefly on the other options outside enzyme replacement therapy.

So if you think back to the analogy of the liver as a sink that is clogged because of the enzyme deficiency and how replenishing and affected person's body can effectively clear that clog in the drain, with oral therapies, what you essentially are doing is not clearing the clog in the drain but turning the tap down.

So basically, this type of drugs slows down the production of the lipid that is not completely digested in the cells of a person with Gaucher disease. And in many ways, although this is an idea that people have had since the early 80s, because the problems with breaking down and not making the lipid people were initially hesitant to do even introduce this option.

But, as you know, studies done in animal models prior to the introduction of miglustat or Zavesca into clinical trials, essentially provided the groundwork that led to the subsequent development of that product, which was initially tested clinically outside of the United States.

And because there were issues regarding its tolerability, the company at the time, OGS, or Oxford GlycoSciences, before Actelion even got involved had approached several investigators and really I understand I was the only one willing to work with them to clarify some of the issues back then.

And those issues are what is on the product label such as the diarrhea, flatulence, or bloating that some people have reported; some of the tingling or numbness, and some of the problems with memory or recall that some people have reported.

And because the number of patients in the trial was small obviously and these problems had not been addressed upfront, it was not certain how much of what patients reported while on miglustat in the clinical trial weren't necessarily due to the drug. And in fact that was how I got involved to clarify really what the basis is for some of the problems that patients have talked about.

And perhaps I'm going beyond what we've tried to cover in the first few questions, but on that point what I can tell you is that we had in the trial seven patients who ultimately were on miglustat for two years. And three of those patients continued on miglustat following regulatory approvals and about six patients prior to the lack of Cerezyme availability had already asked to be switched from Cerezyme to miglustat or Zavesca for various reasons really.

In some cases, out of concern about the weight gain that they had experienced on Cerezyme, in other cases because their job or study required their travel abroad. And in fact in the third instance really, because they essentially as they put it, sick and tired of committing to IV therapy.

Now since the period of no Cerezyme becoming available, we've had several more patients inquire about the use of Zavesca are in essence monitoring a new subset of patients who have opted for Zavesca as choice.

There is another oral alternative, which is Genzyme's Genz-112638 drug, but that product, as you know, is still in clinical trials and not really available outside of the clinical trials.

Perhaps I'll stop here for a second to just make sure I don't miss any points that Kevin or Stu want me to address.

***Kevin Kline***

Thanks. Going a little bit off the topic where you just were, what patients are most at risk as a result of the shortage? And with that being said, what monitoring do you recommend if patients decide to take a wait and see approach? And furthermore, as far as the Chito (Chitotriosidase) test is concerned, how would a patient go about scheduling it with their doctor?

***Gregory Pastores***

Right. So as I pointed out, I recommend all patients see their primary physician, and in my case, obviously in some cases we may have seen the patient a month or two ago, more recently than doctors who we may not have seen for about a year or more. And basically we are using the visit as an opportunity for patients to inform me of how they've done over the last few weeks or month, and whether there may be ongoing or acute medical problems that require medical attention.

In almost all cases we are obtaining blood to check on blood counts, liver function, and other indicators of general health, depending on when their last MRI, x-ray, ultrasound, or bone density was. Based on the ICGG guidelines or my own clinical experience, I may recommend that those be updated as well. And obviously, depending on what acute concerns the patient may have, we recommend a dedicated assessment.

And we sort of use that as a basis for deciding where this patient stands. Has the patient really achieved a normal state of good health or does the patient have residual disease or does the patient have ongoing medical problems for whom the risk may be great to not be without treatment during this period of Cerezyme's unavailability.

And I must admit, one of the challenges is really not knowing for certain for each of the individual patients that I have when they can be guaranteed to have their drug, because that could have been another consideration I could weigh while trying to address how we deal with what's going on.

A lot people look to Chitotriosidase, I must tell you that I've begun drawing Chitotriosidase in all of my patients and I've never really used it in the past in decision-making processes for patients on therapy because I felt that the single marker cannot reliably express the multifaceted aspects of this disease, and even though early on they had shown a relationship with Chitotriosidase in terms of the dose that people are on, I firmly believe that the dose people are on should really be determined based on medical need and where they are in terms of their status and whether things have been stabilize.

But, as it turns out, and most of you may know about this, when people discontinue therapy or consider other therapies that may not be as potent, that Chitotriosidase begins to rise. So it may be one of the early signals that things are headed in the wrong direction.

Obviously, what we don't know is whether there is a threshold, a point beyond which it goes from calm to the perfect storm, right? And also we don't know if the precipice, so to speak, is a month from now or six months from, you know?

So that is why I encourage patients really to communicate with their primary care provider or with a center that they feel may have the information that can help them understand what their options are.

In terms of Kevin's second part question about who I feel may be at highest risk, this is an interesting question, because I treat children, but as it happens some of the children I treated in the 90s are teenagers now or even young adults, including young and not so young adults with families of their own.

And in fact when the guidelines were initially written, the feedback I subsequently got from my patients, particularly those who are 30 and above and have had their spleens taken out as children or have had a hip replacement, is: while I am not necessarily at vulnerable risk, I grew up without the benefit of treatment and have this complication now, and I think my risk is higher than a child with Type 1 disease who was picked up very early and never experienced a disease-related complication.

You know, obviously I'm not here to adjudicate the wisdom of those decision-making processes and to insure that such a patient who is frustrated about this situation is not disenfranchised or left in the cold as it were, we are rapidly looking at all the options. And now if I said as of yesterday, every option is available to me and what we do is we discuss with patients an assessment of their risk-benefit ratio and what I feel may be appropriate in their particular circumstances.

I think another basis for decision-making is your past medical history. Like I said, if you are a patient who's running into serious trouble related to your Gaucher disease in the past, I can understand why you can be very anxious to be without treatment.

The second instance are those cases that I pointed to earlier about patients who may have ongoing medical problems.

For instance, in my practice right now I have three patients with Parkinson's disease. I've pleaded for these people to go on Cerezyme, but have been denied because the stock as I understand is very limited and I can appreciate that. Gaucher disease may not kill these patients in the next three months or so, until Cerezyme can be available and I don't think Cerezyme is going to cure them of their Parkinson.

But, really the rationale behind all of that is I cannot have a patient with Parkinson that already has an impaired quality of life, developed during this period of no treatment, experience a relapse, fracture of bone, or go into a medical crisis and really have that patient's life, which is not great as it is, go down the drain, you know? So those are the kinds of situations that we are dealing with.

And in fact, one of the other situations that Rhonda has called to my attention is how do people access the drug if it's not available locally, because it's not like you can go to your local pharmacy with a prescription from me or your primary doctor to just pickup these drugs.

And one of the classic examples about this is a sibling of one of the patients I care for in New York who happens to be living in Guam. Well Guam does not have a site that is contracted with Protalix or Shire to dispense the alternative enzyme formulation. And that patient had asked, in this case, what else is available, and essentially, for every patient really, miglustat is available because it is an FDA approved product.

The patient has reviewed his particular circumstance, the inability, both financially and in time to travel to New York or to any center that participates with the other company, and would like to

give miglustat a shot. And that patient is now going to be monitored to see how he is doing on miglustat and has indicated that if, in fact, he remains stable, may choose, after years of enzyme therapy to stay with miglustat.

But, obviously in our situation, for instance, we're not going to look back. I mean I would now like to see this situation, tragic or unfortunate as it is, as an opportunity, really to address where we should be moving forward. And in terms of the options that are available or will become available to patients.

**Kevin Kline**

What is required if a patient would like to switch drugs during the shortage? What are the risks? And furthermore, what is required if the patient at the end of the shortage, would like to switch back to Cerezyme and what are the risks in doing so as far as that is concerned?

**Dr. Pastores**

Right, so my own investigation into the situation and my interactions with the patients have led me to following opinions. And obviously, all of this is a moving target, and may change depending on what trials are going on when and when the drug is going to be available and what patients have access to.

And like I said, I want to look at the situation as an opportunity to really understand what happens to particular patients during the period of time they choose to be on no drug. Do those patients remain stable or not? And what are the factors that influence that?

If you are without a spleen, which usually functions as the warehouse for your Gaucher cells, are you at greater risk now of those Gaucher cells that will reaccumulate infiltrating your other organs? And second, obviously for the patients who choose other options, with respect to miglustat or Zavesca, that is commercially available, there is information on the efficacy and safety of that product and individual patients. And physicians can decide, whether for any given patient that is their best option.

With respect to the other options, you can really only access them through either an expanded access program like with velaglucerase from Shire or in clinical trial or ultimately in expanded access like the carrot derived enzyme from Protalix.

I failed to mention that there is actually a hypothetical third option, which is Plicera (which is a pharmacologic chaperone) that Amicus, in collaboration with Shire, are hoping to develop. As I understand it, there were 18 patients in a trial that lasted for six months and the data so far seems to indicate that of these 18 patients on Plicera or AT2101, although all of them showed an increase in enzyme activity, only one had a relevant change. And that leads me to believe at this point in time, that this is not a viable option for patients.

So moving forward, the question is should people look at the current options as a stopgap measure or as a bridging agent?

And my answer to that is I don't think necessarily so, because the situation we're in is such that -- and these are what patients have called to my attention -- they don't understand why we're in this situation and they don't want to relive it. And definitely they don't want to have a relapse. And in fact, most patients are considering other options.

Having said that, what it boils down to is we don't want all our eggs in one basket anymore. If there's going to be more than one company that can make this drug, then I think that best serves our greater future and, you know, to some extent I can understand that situation.

So I think moving forward, if you choose an alternative option for your situation, you tolerate that product and the monitoring is saying that you are stable or doing well, then that tells me that

we've just generated a lot of information that was not available before that will now guide us for particular patients, particularly those who have never been on any treatment, what may be the best option.

The truth of the matter is when there becomes more than one option, it may eventually be out of our hands because it may be dependent on the price that these other drugs are sold in relation to the value that you get out of it and whether if every drug becomes available on the formulary, patient's co-payments may be different.

I hope people realize that some of what I said this afternoon are speculative on my part and to some extent reflects my opinion and feeling about the whole matter at this time. And I hope that when speaking of other drugs I've been accurate and would be happy to be corrected on those points.

**Kevin Kline**

So which of those following drugs that you mentioned are available today and if you could give a little indication of how they work and how they're administered, that would be great?

**Dr. Pastores**

So we'll start off with the only other FDA approved product outside of Cerezyme, which is miglustat or Zavesca. And people can access this drug through CuraScript and I believe the information about how to access that product will be on the NGF Web site and the Actelion Web site. Or if one does a Google or Netscape or whatever else is out there, to access information on a drug like Zavesca.

I recommend people read information about Zavesca, call it to their physician's attention, and then review whether in their particular situation this is appropriate as one of the options to consider.

With respect to velaglucerase, in clinical trials, and I believe shortly on the NGF Web site and on the Shire Web site and also through One Path, people can know of the sites through which they may receive (velaglucerase) because it is another enzyme therapy, as with any protein drugs, and can only be administered intravenously and in that situation obviously we want to make sure that there are no ((inaudible)) or allergic type reactions during the infusion, and the same is true as well for Protalix carrot derived enzyme. And that is why people who choose those other options must realize they cannot these drugs at home.

Shire has made the velaglucerase available to different centers and I understand a whole lot of other centers have begun the process to make velaglucerase available also through their sites, not only in the United States but in all countries that want their patients to be on this drug and the same situation is true as well with Protalix drugs. And Shire ultimately indicated that after three infusions in a clinic setting without any incidents, patients who have received their infusions at home may be able to access those options.

Incidentally because Shire and Protalix drugs are not FDA approved, there are inclusion/exclusion criteria in terms of access to those products. And the best thing about it at the end of the day is that they are made available without cost to the patient or their prescribing physician.

But obviously, we don't have the length and number of patients on this type of drugs the way we've had it with Cerezyme where, you know, a significant level of comfort has been in place for several years now.

**Kevin Kline**

Speaking of that, and as far as the aforementioned options available, can you discuss a little bit about the adverse events that may occur associated with those options?

**Dr. Pastores**

So my own experience with velaglucerase by Shire and with the carrot derived enzyme by Protalix, or prGCD, have really not been any different from what we have witnessed through the decades with Cerezyme. Fortunately, none of my patients have had any serious or major adverse events, and in fact, none of the patients have premedication.

I understand that other sites have witnessed other problems, the details of which hopefully will become available, but I understand that none of this has necessarily led to the interruption of therapy, except for idiosyncratic or exceptional cases.

With miglustat, as you know, there are tolerability concerns. But, I must tell you in my own experience, that important problems have been seen in 100% of patients. Yes, there are a proportion of patients who initially have bloating, gas, and diarrhea and to some extent, that appears to be related to the inhibition of other enzymes responsible for the digestion of carbohydrates in the intestine. And obviously, (about) concern are the tingling and numbness, but some of that is obscured by the fact that other patients who've experienced this problem, may be B12 deficient or have diabetes or some other medical problems that can give rise to this type of issues.

But, in any case, one has to be vigilant and if you do try Zavesca, there are things that may need to be monitored that was not a part of your routine Gaucher monitoring.

**Kevin Kline**

You had also mentioned that some of these options were still in the trial phase. Are the guidelines for the admission to these trials for patients going to be relaxed a little bit in order to allow patients who may not qualify as they stand to be allowed in to these trials?

**Dr. Pastores**

So essentially, the way I feel, at least for my patients, because I am engaged with all of the products, basically, where there is a perceived medical need, all such patients will have therapy and not be without therapy. And obviously, some patients go without therapy and we have a better understanding of how well they do. And if some do well, it raises the other question of whether on a year-to-year basis people may choose to be on some sort of a break a drug holiday from whatever therapies they are on.

So I think all of what's happened is going to create different paradigms for how we treat patients moving forward, and obviously how the insurance will be looking at this in terms of reimbursement.

**Kevin Kline**

I think that pretty much covers my questions.

**Stuart Berman**

Before we wrap-up, does Rhonda or Dr. Pastores have anything they'd like to add beyond what's been said so far?

**Rhonda Buyers**

I feel like Dr. Pastores has covered everything quite thoroughly.

**Stuart Berman**

Doctor, do you want to add anything?

**Dr. Pastores**

Well I'd like to use this opportunity, again, to thank everyone who has taken the time this afternoon. I hope I've not misspoken -- I'm not the Pope; I'm not infallible. And, you know, I speak

from the heart, hopefully, most of the time from the mind. And if you I've misspoken or you feel strongly about some of the things I've said or have disagreement, don't hesitate to call me, send me an email, or write me a letter. And my hope is that people have found there time with us this afternoon to useful and informative.

***Stuart Berman***

I want to thank you, Dr. Pastores, for a very informative discussion; Kevin, for being so helpful to everybody; Rhonda, for all the hard work the NGF does; and Actelion for helping us provide this hour.