ATHERSYS, INC.

Moderator: Gil Van Bokkelen
April 29, 2015
2:00 p.m. ET

Operator: This is conference # 35326665.

Good afternoon. My name is Suzanne, and I will be conference operator today. At this time, I would like to welcome everyone to the Athersys Shareholder Conference Call.

All lines have been placed on mute to prevent any background noise. After the speakers' remarks, there will be a question and answer session. If you would like to ask a question during this time, simply press star, then the number one on your telephone keypad. If you would like to withdraw your question, press the pound key.

Thank you. Ms. Laura Campbell from Athersys, you may begin your conference.

Laura Campbell: Thank you, and good afternoon, everyone. I'm Laura Campbell, Vice President of Finance for Athersys. Thank you for joining today's call. Gil Van Bokkelen, Chairman and Chief Executive Officer; BJ Lehmann, President and Chief Operating Officer; and I will host today's call. We are also pleased to have two guests joining us on the call today, Dr. David Hess, Chairman of the Department of Neurology at the Medical College of Georgia at Georgia Regents University, and Dr. Lawrence Wechsler, Professor of Neurology and Chair of the Department of Neurology at the University of Pittsburgh Medical Center.

The call is expected to last approximately 30 to 45 minutes, and may also be accessed at athersys.com. A replay will be available two hours after the call's conclusion, and access information for the replay is included in the press release we issued last Friday announcing the call.

Any remarks that we may make about future expectations, plans and prospects constitute forward-looking statements for purposes of the Safe Harbor Provision under the Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by the forward-looking statements, as a result of various important factors, including those discussed in our Forms 10-Q, 10-K and other public SEC filings.

We anticipate that subsequent events and developments may cause our outlook to change. While we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so.

For the benefit of those who may be listening to the replay, this call was held and recorded on April 29, 2015. Since then, we may have made announcements related to the topics discussed, so please reference our most recent press releases and SEC filings.

With that, I would like to turn the call over to Gil. Gil?

Gil Van Bokkelen: Good afternoon, everyone. And thanks for joining the call today. As everyone listening in should know, several days ago, we announced a summary of the top-line results from our ongoing Phase 2 clinical trial evaluating the safety and efficacy of the administration of MultiStem to patients that have suffered an ischemic stroke.

However, since the majority of listeners participating on the call today did not have the opportunity to attend the presentation by Dr. David Hess in Glasgow at the recent European Stroke Organization Conference, during today's call, we felt it would appropriate to provide a summary of the initial results from the trial, as well as allow two key investigators from the study to provide some additional perspective.

To begin with however, I would first like to make a few comments regarding the procedure related to our initial assessment of the data, and the timing of the announcement of the initial results. As we had announced previously, the leadership team at the Company did not have access to the unblinded data from the trial until shortly before we announced the results.

Recognizing that the results of the trial were material and highly sensitive, we took steps to ensure that there would be no premature disclosure of the results. In advance of having access to the data, we implemented specific procedures designed to ensure and maintain the confidentiality of the results up until the time of the announcement.

Specifically, from the time we received the results until the time of their disclosure, the leadership team that was briefed on the results of the trial by the representative from our Contract Research Organization, or CRO, were sequestered at an undisclosed location, away from the Company. During that time, we refrained from external communication and strictly limited access to information related to the trial to a small group. To the best of our knowledge, there was no outside communication with anyone else regarding the trial results during that period.

We believe that the results from the trial are important for the field and provide substantial evidence for the potential of our cell therapy to treat ischemic stroke. We also believe that the results, and their importance to the Company, have been largely misunderstood by the market and the media, something we hope to help address during today's call.

As we have discussed in presentations in prior earnings calls, many people regard stroke as one of the greatest areas of unmet medical need in clinical medicine today. According to the World Health Organization, every year more than 15 million people suffer their first ischemic stroke. Of these, roughly 5 million people die shortly after having the stroke, either as a direct consequence of the stroke, or as a result of complications that occur in the wake of the stroke. Another 5 million people are left with substantial, permanent impairment and disability.

According to Datamonitor, each year there are approximately 2.2 million first-time ischemic stroke victims in the United States, European Union, and Japan combined. The current standard of care for patients that have suffered and ischemic stroke is the thrombolytic, or clot-dissolving agent, tPA, also known as Activase or alteplase.

However, administration of tPA must occur within several hours of the occurrence of the stroke (depending on regulatory jurisdiction, this time frame for administration ranges from 3 to 4.5 hours). As a result of this very narrow window, however, only a small percentage of patients are administered tPA, with most estimates suggesting that among the broader population of stroke victims, less than 10 percent of patients receive tPA.

Administration beyond that initial time frame is associated with a significantly higher risk of intracranial hemorrhage. And furthermore, even if tPA is administered within the recommended window, based on published data and the data contained in the labeling information for tPA, there is a meaningfully higher risk of intracranial hemorrhage among patients receiving tPA relative to those that received placebo.

So clearly there is a need for safer and more effective ways to treat stroke victims. Furthermore, there is a great need for novel treatment approaches that extend the window of intervention to a clinically practical time frame. Years of preclinical work with independent research teams gave us confidence that MultiStem could help us achieve both these goals.

As we set out to evaluate the safety and efficacy of MultiStem administration to patients that have suffered an ischemic stroke in this trial, we were focused on assessing a range of parameters. With regards to safety, we pre-specified a number of important events and categories that we were interested in evaluating, including monitoring for any evidence of infusion-related reactions, as well as examining mortality, life-threatening adverse events, infections, pulmonary events and complications, and a range of other events.

In prior clinical studies involving administration of MultiStem, we have consistently observed a favorable safety profile, and while we were confident

that we would also see a good safety profile on this trial, we did not presume to take that for granted.

In regards to efficacy, we utilized an approach patterned after other stroke clinical trials, in that we were focused on evaluating patient recovery using three clinical scales that are commonly utilized by stroke specialists. These include the NIH Stroke Scale or NIHSS, the Modified Rankin Scale, or MRS, and the Barthel Index.

The NIHSS is a 42-point scale that was used to evaluate patients for potential eligibility and enrollment in the trial. This scale evaluates cognitive and motor skill deficits, using a combination of tests that assess the patient's level of consciousness, visual acuity, facial paralysis, speech, cognition, motor skills and other parameters. Patients that exhibited a score of 8 to 20 at baseline were eligible for enrollment in the study, provided they exhibited stable deficits during the assessment period prior to treatment.

The Modified Rankin Scale is a 6-point scale that evaluates global or gross disability, with a score of zero reflecting no symptoms or deficit, 1 to 5 reflecting varying levels of disability, with 1 being the least disabled and 5 being the most disabled, and a score of 6 reflecting death. A level of zero, 1, or 2 on this scale is considered reflective of the patient's ability to live independently.

The Barthel Index is a 100-point scale that evaluates activities of daily living, including feeding, bathing, level of mobility, grooming, and other functions. A score of 95 or 100 is regarded as excellent outcome.

Each of these clinical scales evaluates patients in a different manner, and emphasizes distinct things. In accordance with the trial design, patients were to be evaluated at the time of screening using the NIHSS, again at baseline (to help assess patient stability), and then at 7, 30 and approximately 90 days post stroke. Patients will also be assessed at one year post enrollment.

In addition to these individual component scores, we also pre-specified in an analysis of patients that achieved an excellent outcome by 90 days, which by definition requires that patients attain an excellent score in each of the three

clinical rating scales - meaning the patient must achieve an NIHSS score of zero or 1, an MRS score of zero or 1, and a Barthel Index score of 95 or 100 at the 90-day assessment.

In late 2013, we contracted with an independent consulting group to conduct an assessment of the types of information obtained from this study that would be most relevant to regulatory and reimbursement agencies, clinicians and hospital administrators. After we had obtained this feedback, we used it to finalize our statistical analysis plan for the study, and implemented the Global Statistic, or Global Stroke Recovery assessment, as the primary efficacy end point for the study.

We did this because it combines all three clinical rating scales into one metric. And along with the individual components and other metrics we were evaluating, provides a more complete picture of patient recovery, reflecting the specific feedback we had obtained from the interviews and analysis provided by the independent consulting group. We also pre-specified an assessment of hospitalization times, and time in the intensive care unit, or ICU.

Last week, the lead clinical investigator for the study, Dr. David Hess, presented a summary of the initial results at the European Stroke Organization Conference in Glasgow, Scotland. We were pleased to have Dr. Hess on the call with us today, along with one other participating investigator from the trial, Dr. Larry Wechsler. And in a few moments, I will formally introduce them and invite them to provide some additional perspective, context and commentary before we open it up for a brief Q&A.

First however, I would like to summarize some of the key findings from the trial regarding the safety and efficacy that was observed for patients that received either intravenous administration of placebo or a high dose of MultiStem, which were administered in a double-blind, randomized manner.

In terms of the overall demographics and patient profile for the study, the study was generally well-balanced. There were 67 patients that received administration of MultiStem and 62 patients that received placebo. In

particular, we note that mean patient age and age range were similar, gender distribution was balanced and medium NIHSS scores were identical.

Slightly more patients in the placebo group received tPA than in the MultiStem group, and there was a higher rate of tPA administration than we anticipated prior to the start of the trial. While lesion sizes were slightly smaller in the MultiStem group, this difference was not considered meaningful, especially given that the location of the infarct and the severity of the deficit are considered to be much more relevant indicators of disability and prognosis.

The observed safety profile among all patients that received administration of MultiStem versus placebo was favorable and was consistent with what we've seen in prior studies. In particular, there was no evidence of infusional or allergic reactions and no abnormal patterns in the safety labs, or in measurements of vital signs.

The adverse events that were observed were consistent with the type of events that would be expected for stroke patients of this type. We know, however, that through the 90-day evaluation period and beyond, there appeared to be a meaningful trend in the MultiStem treated group toward reduced mortality and a reduction in serious complications associated with the stroke.

Specifically, we observed a lower rate of life-threatening adverse events and deaths among the MultiStem treated patients, a difference that was statistically significant with a p-value of 0.04. In terms of cumulative mortality, in the placebo treatment group, there have been nine patient deaths that have died to date, whereas there have been only four deaths in the MultiStem treatment group. Four of the deaths that occurred in the placebo treatment group occurred within 30 days of the stroke, whereas only one patient in the MultiStem treatment group died within 30 days of the occurrence of the stroke.

We also observed lower infections among patients that received MultiStem, including meaningfully lower urinary tract infections and reduced pulmonary complications.

In terms of efficacy, initial inspection of the results was disappointing. We did not see any evidence of a meaningful difference between the patients receiving MultiStem versus placebo, and as a result, we did not meet the primary endpoint or the component secondary endpoints. However, we did see other signals that were encouraging, such as a higher percentage of patients that achieved an Excellent Outcome clinically, with 15.6% of MultiStem treated patients achieving an Excellent Outcome, versus 6.5% in the placebo treated group.

In addition, there was a favorable trend towards faster recovery among patients treated with MultiStem. When treated with the other observations of reduced mortality and life-threatening adverse events, lower rates of infections and reduced pulmonary complications, it suggested that we needed to look a bit deeper at the data. Furthermore, another piece of evidence strongly supported a key part of our therapeutic hypothesis related to the regulation of the immune system.

The pre-specified analysis of circulating levels of CD3 positive cells indicated that MultiStem treatment group had significantly lower levels than the patients that received placebo, with a p-value of less than 0.01. This suggested a meaningful reduction in the inflammatory response post stroke.

So given the positive signals in findings supporting our hypothesis, we asked a series of questions and conducted additional analysis that ultimately revealed some very important observations, and led us to some important conclusions.

When looking at the pre-specified efficacy population data, we notice two very interesting things. First, we observed that there appeared to be a trend in which earlier administration of MultiStem was associated with a better clinical outcome. Specifically, patients that received administration of MultiStem within 36 hours of the time of the stroke appeared to do meaningfully better than those patients that received treatment with MultiStem more than 36 hours after the occurrence of the stroke.

Second, this trend was not evident among the patients that received placebo. In fact, among those patients that received placebo, the exact opposite trend appeared to be occurring. Patients that received placebo at 36 hours or beyond appeared to be meaningfully better than patients receiving placebo at 36 hours or less. Since there is no evidence to suggest that administration of saline 36 hours or beyond provides a meaningful therapeutic benefit in stroke patients, we were skeptical that this was a real phenomenon, and we examined the data more carefully.

As we looked at the placebo patients more closely, we realized that there was evidence of a substantial imbalance. Specifically, there was a group of patients that received both tPA and mechanical reperfusion, that then subsequently received IV placebo at 36 hours or later.

All of these patients exhibited substantial recovery at 90 days, a recovery rate which is not in line with published data or normal clinical observation. It was clear that this imbalance was skewing the placebo data, and was responsible for the observed pattern that suggested that administration of saline more than 36 hours post stroke was somehow more beneficial than administration of saline less than 36 hours post stroke.

It's worth noting that patients receiving both tPA and mechanical reperfusion were originally excluded from the trial design, because given data available at the time, it was difficult to model the expected background results. Ultimately, we included them to increase enrollment at selected sites that were conducting this procedure.

Although it is now appreciated that the patients that received both tPA and mechanical reperfusion tend to experience better outcomes than patients that received tPA or mechanical reperfusion alone, only a small percentage of patients received tPA, and an even smaller percentage received both tPA and mechanical reperfusion. So while this approach is regarded as being promising, it will only be utilized in a small percentage of ischemic stroke patients.

To adjust for the imbalance and give us a clearer picture, we removed from consideration all of the patients that had received both tPA and mechanical reperfusion in both the placebo and MultiStem treated groups, regardless of when they received it. We retained all other patients in the subsequent analysis - including those that had not received either tPA or mechanical reperfusion, and patients that received either tPA or mechanical reperfusion.

As soon as we made this correction, the observed rates of recovery in the placebo groups normalized. There was essentially no difference between patients that received administration of placebo early versus patients that received administration of placebo late. This makes sense, if one believes that administration of saline has no meaningful therapeutic benefit, and that there should therefore be no difference in response rates, whether it is administered early or late.

Next we considered the MultiStem treatment group. Clinicians in the stroke field have long recognized that “time is brain” and that early intervention is key to saving as much brain tissue as possible. This is one of the main reasons why early intervention with tPA or mechanical reperfusion is regarded as critically important. The same observation is broadly relevant to patients that suffer acute ischemic injury, or acute neurological injury generally. Time matters.

When we examined the data further, we asked the straightforward question - is there any evidence that early administration of MultiStem is correlated with a better clinical outcome, and if so, how robust is the effect? Once we started examining the data, it quickly became apparent that there was evidence of a strong correlation between early administration of MultiStem and a better clinical outcome.

We first examined the dataset looking at patients that received treatment with MultiStem within the time frame of 24 to 36 hours post stroke, versus patients that received treatment in the 36 to 48 hour portion of the treatment window. As we described previously, we originally designed the trial to allow for treatment of patients 24 to 36 hours post stroke, but subsequently modified the window, extending it to 48 hours in order to accommodate the limited hours

of operation at the cell-processing facilities that were participating in the study.

When we examined patients that received administration of MultiStem beyond the 36 hour window, we observed that there was no meaningful difference in recovery rates among those patients, either compared with subjects receiving placebo overall, or those receiving placebo that was administered in the window from 36 to 48 hours post stroke.

However, when we examined the clinical outcomes for patients that received MultiStem within 36 hours of the time of the stroke and compared it to the broader group of patients that received placebo, we saw a dramatically different picture. Among the patients that received treatment with MultiStem early, we observed that there was a very robust response, either when compared with subjects receiving placebo overall, or when compared with those receiving placebo early.

Specifically, among patients that received administration of MultiStem within 36 hours or less, we observed there was a consistent pattern of robust improvement relative to the placebo group across each of the key clinical parameters we had pre-specified. Relative to the placebo group at the 90-day (or final) clinical assessment, we observed the following:

- 48.1 percent of the MultiStem treated patients achieved a Modified Rankin Score of zero, 1 or 2, whereas only 32.7% of placebo patients achieved this score, a difference of 15.4%;

- In terms of the NIHSS improvement, we observed that 51.9% of the MultiStem treated patients improved by 75% or more, whereas only 30.8%of patients that received placebo exhibited this magnitude of improvement, a difference of 21.1%;

- In terms of the Barthel Index, we observed that 55.5% of MultiStem treated patients achieved a score of 95 or higher, whereas only 38.5% of patients that received placebo attained this score, a difference of 17%;

- In terms of the Global Statistic, or Global Stroke Recovery score, the odds ratio was very strong at 2.21 with a p-value of 0.065, just missing statistical significance;

- In the MultiStem treated group, 18.5% of patients achieved an Excellent Outcome, whereas only one patient out of 52 (or 1.9%) in the placebo treated group achieved an Excellent Outcome, with a p-value = 0.03.

- The pre-specified shift analysis, which examines the relative improvement of the aggregate patient population using the MRS metric, was also strongly in favor of MultiStem, with a p-value = 0.03.

It's worth noting that this pattern of improvement was evident regardless of whether we considered the broader group of placebo patients, or only the subset of patients that received placebo within 36 hours or less, discounting the possibility of a placebo effect among patients that received an IV infusion early.

It should also be noted that in terms of demographics and patient profile, these groups were very comparable: for example, the mean and median stroke severity scores for these groups were equivalent, (an NHISS equal to 13 for both groups); the average lesion sizes were also equivalent at 45.4 and 46.6 mls; the age and gender distributions were almost identical; and the populations were very similar in other key respects.

Furthermore, and another interesting point we did not convey in the press release (because we had not completed the analysis at that point), was that hospitalization times were also meaningfully shorter in the MultiStem treated patients compared to those that received placebo. Specifically, among the patients that received MultiStem treatment within 36 hours or less, there was a 35% reduction in hospitalization times relative to the placebo group (which corresponds to a mean reduction of 3.6 days per patient), which had a p-value of less than 0.01, and 37.5% reduction in Intensive Care Unit hospitalization (which corresponds to a mean reduction of 1.8 days per patient), which had a p-value of 0.09.

So, in summary, with regard to almost every key parameter we examined, there was a consistently superior pattern for the patients that received MultiStem within 36 hours or less, relative to patients that received placebo, or those patients that had received treatment with MultiStem at 36 hours or beyond.

However, in order to challenge the assumption of whether earlier treatment with MultiStem is better, we went one step further, and analyzed the response rates among patients treated in the first 8 hours of our treatment window (meaning patients that received treatment in the 24 to 32 hour window post stroke), versus the second 8 hours (meaning 32 to 40 hours post stroke), and the last 8 hours (meaning 40 - 48 hours post stroke).

If our hypothesis was correct, we predicted that the strongest responses would be seen in patients that received earlier treatment - and this is exactly what we observed. The largest responses occurred in the earliest treatment group, and the smallest responses occurred in the latest group.

As I mentioned earlier, we initially designed the trial to accommodate treatment of patients in the 24 to 36 hour window post stroke. We believed then, and believe even more strongly now, that this is a highly relevant and clinically practical window, and it appears to be a critical period involving the hyperinflammatory response emanating from the spleen and peripheral immune system that exacerbates much of the damage that occurs in the wake of the initial ischemic event.

Recent data from research conducted by independent experts in the field supports the concept that this hyperinflammatory response occurs faster in humans than in the preclinical models that are typically used.

So, in summary, we believe the data from this trial is providing important evidence of the consistent safety profile for MultiStem when administered to ischemic stroke patients, and also provide promising evidence of meaningful therapeutic benefit. The response among clinical experts has been very positive, and we have already received many requests from clinicians that would like to be part of a future study.

To provide additional perspective on the trial, we are pleased to have two esteemed clinicians with us here on the call today: Dr. David Hess, Chairman of the Department of Neurology at the Medical College of Georgia at Georgia Regents University. Dr. Hess is a specialist in stroke care and lead clinical investigator for the trial.

Joining Dr. Hess is Dr. Lawrence Wechsler, Professor of Neurology and Chair of the Department of Neurology at the University of Pittsburgh Medical Center. Both Drs. Hess and Wechsler are clinical investigators for the study and are recognized as independent experts and key opinion leaders in the field of stroke treatment.

Neither Dr. Hess nor Dr. Wechsler has received compensation from the Company for their participation in this study, or for their participation in this call, nor do they own equity in the Company. Both have volunteered to participate in this call because they believe that this trial represents an important step forward for the field.

I would first like to invite Dr. Hess to provide some introductory comments on the trial. Then in response to questions that we have received from shareholders, interested observers and the media, we've asked both Dr. Hess and Dr. Wechsler to comment on several specific questions regarding the safety and efficacy data from the trial, current standard of care, the concept of a “time window” for administration of MultiStem, and the clinical and commercial practicality of treating stroke patients within a 36-hour window.

With that, I would now like to turn it over to Dr. Hess. David?

David Hess: Thanks a lot, Gil. It's a pleasure to be on the call today. And I thank you for having me. As Gil noted, currently we have very few effective treatments for stroke. Ischemic strokes make up approximately 80% of all strokes. And unfortunately, we only have two effective treatments - IV tissue plasminogen activator, which I'll just call tPA, and mechanical clot-retrieval devices. However, tPA has to be started in less than 4.5 hours from when the stroke begins, and the clot-retrieval devices must be used in general within 6 hours.

Moreover, clot-retrieval devices will only treat probably less than 3% to 4% of the total sum of stroke patients.

So we need treatments that can be used later in the first 24 to 36 hours. By that time, the vast majority of stroke patients have come to the hospital. Early trials of tPA that enrolled patients in the first six hours such as the European Cooperative Acute Stroke Trial I, that's called ECASS1, or in a three to five hour window, a trial called the ATLANTIS trial done in the United States, were negative.

However, when they subsequently conducted a post hoc analysis on patients treated in the first three hours post stoke in the ECASS1 trial, they saw a benefit. So this highlights the critical importance of the “time window” in acute stroke trials. It also reinforces the idea that we learn important things from initial studies with novel treatments, even from a post hoc analysis. We can then apply that knowledge in subsequent studies.

Most strokes patients do arrive at the hospital within 24 hours, especially the moderate and moderate-severe strokes that are the target strokes for MultiStem. By 12 to 18 hours after stroke, the improvement from tPA and mechanical reperfusion will likely be evident, so MultiStem could be given to these patients who have not responded well and others who arrive too late to be treated with either tPA or mechanical reperfusion.

Cell therapy is a promising avenue of treatment. I have been working with MultiStem for about a decade from the preclinical phase of research to the clinical side. During that time, we’ve developed a pretty good understanding of how these cells help promote recovery in the neurological injury area.

One of the ways MultiStem works is by targeting the immune system. It's clear these cells are immunomodulatory, allowing them to work in the first days after stroke. The MultiStem clinical trials show them to be safe and very well-tolerated in ischemic stroke patients. That is important, as tPA has not been used as much as we would all like because of the risk of bleeding in the brain.

As Gil mentioned, while MultiStem did not, at first blush, appear to provide a meaningful benefit in the 24 to 48 hour time window, when we looked at patients who received the cells at less than 36 hours, that is in the 24 to 36 hour window, they seemed to provide a meaningful benefit. This time-related benefit is in keeping with biological plausibility - they are targeting the spleen and immune responses that are activated and operating within the first couple of days post stroke. So we need to administer them in this window.

With this trial, we have learned a lot more about the potential window for effective intervention. Another advantage of MultiStem is that they can be administered as an “off-the-shelf” agent. This is very important because it means we could administer the treatment in almost any hospital setting. This is unlike mechanical thrombectomies; they require an enormous infrastructure, and will only be used in a few centers in each state.

It should be pointed out that this clinical trial was originally designed for treating patients under 36 hours. However, issues related to the lack of cell processing availability after hours, for example after 5:00 PM and on some weekends, and getting all the measurements and labs drawn for a clinical trial resulted in an extension of the time window to 48 hours.

This won't really be an issue in future clinical trials, because the Company has already developed thaw-and-administer formulations that don't require specialized cell processing facilities or personnel, which will greatly simplify things and make enrollment a lot easier in the future.

In the stroke, in the neuroprotective window, and what I mean by that, where the aim is to protect neurons and other cells from dying, the earlier the treatment, the better. We have no examples where treating later is better than earlier, and all neuro-protective treatments are time dependent.

MultiStem likely works both by “neuroprotection” and also in the “remodeling/reparative” phase, where the goal is to help the brain recover by inducing the brain to recover. Since a primary mechanism of action is likely immunomodulatory - through effects on the spleen and lymphoid organs - it's likely that earlier treatment is better.

The preclinical data in stroke, traumatic brain injury and spinal cord injury models all suggest that early IV administration of MultiStem is important, but this window appears to extend well beyond the window for tPA - perhaps to up to 24 hours or a little longer.

Recent data suggests the spleen appears to shrink fast in humans; and, therefore, the inflammatory splenocytes are leaving the spleen early. This suggests that we need to administer the cells early, such as within the 36 hour window we observed in this trial.

In terms of safety, MultiStem appeared to be very safe. There were no infusion reactions and all the trends were in favor of MultiStem - less mortality, infections. In fact, MultiStem appears to be safer than tPA, because tPA has a 3% to 6% rate of intracerebral hemorrhage, so physicians would not be worried about the "harming" the patient. As we say in medicine, *primum non nocere*, "first do no harm."

The evidence suggests that a time window for administration under 36 hours is effective. As an early phase clinical trial, the MultiStem trial gives us the opportunity to learn. The data from the trial suggests that treatment under 36 hours appears to be effective. This will require confirmation in another clinical trial, as is typically the case. But I'm very encouraged by these initial results, and the response from other investigators in the field has been very positive.

Gil Van Bokkelen: Thanks, David. With that, I'd like to invite Dr. Wechsler to make a few comments and share his perspective.

Lawrence Wechsler: Thanks, Gil. And good afternoon, everyone. Thanks for asking me to participate in this call. David has nicely summarized the important issues relating to stroke treatment and the implications of the MultiStem results.

I would like to briefly expand on a few key points and give you my perspective on the results of the MultiStem study. As David pointed out, our current treatments for acute stroke are limited to IV tPA and mechanical thrombectomy. Both treatments are applicable to only a small percent of all stroke patients.

In addition, although more patients recover with these treatments than without them, not everybody responds. In fact, 40% to 50% of patients who receive these treatments do not return to independent functioning. So we desperately need additional effective treatments for stroke patients to supplement these therapies.

IV tPA and thrombectomy are also not without risk. Serious bleeding occurs in 6% to 7% of patients who receive this treatment. A new therapy with a better safety profile would be a very welcome addition to our armamentarium.

My involvement with cell therapy for stroke dates back 15 years to the earliest human trials of cell therapy in chronic stroke. Thanks to the work of investigators such as David Hess and others, we've learned a great deal in these 15 years about how cell therapy works, the optimal cell type, timing and route of administration.

An off-the-shelf intravenous product such as MultiStem represents an ideal therapeutic approach. The MultiStem study shows us that this product is remarkably safe. In fact, not only is there no demonstrated harm, but there's evidence of an advantage over placebo in reduced infection rates and reduced mortality. These are very important findings from a clinical perspective.

While it would have been great to achieve the efficacy endpoints, we cannot be discouraged by non-significant trends in an early phase study such as this one. Despite all our progress, there's still more things to learn, and more detailed time analysis from this study shows us that our time window was probably not optimal and that earlier treatment results in better outcomes and treatment effect.

This is consistent with all that we know about stroke and stroke treatment; that the earlier treatment is started, the better the chances of altering the outcome from stroke. There is a strong time-to-treatment interaction with IV tPA and mechanical thrombectomy, so it's certainly no surprise that the same relationship would be seen for cell therapy.

In summary, the results of this trial are very encouraging, not discouraging. In a relatively small number of patients, we've demonstrated safety and found that with early treatment there is a strong indication of efficacy compared to placebo. To see the positive treatment effect and sizeable absolute difference in multiple efficacy endpoints as well as the expected change in biomarkers of inflammation, all point to a promising therapeutic effect.

We would be very excited to take this to the next step of confirming these initial findings in additional clinical trials with protocol changes that are informed by these results.

Gil Van Bokkelen: Thanks Larry. So in summary, we and the investigators participating in the trial are very encouraged by these results, and we have received positive feedback from many experts in the field. We believe that there are a lot reasons to be excited about moving this program ahead.

With that, we'd like to open it up for a few questions.

Operator: At this time I'd like to remind everyone in order to ask questions simply press star and the number one on your telephone keypad. We'll pause for just a moment to compile the Q&A roster. Again, that is star, then the number one on your telephone keypad.

Jason Kolbert.

Jason Kolbert: Dr. Wechsler, we really appreciate the review. I guess a couple of -- where we're getting the most questions -- is on the post hoc analysis, what the differences were between the treated patients in terms of their infarct size and their disability. And I know, Gil, you mentioned that on the call. Could you take a couple of minutes and just walk us through exactly what were the differences in the compared groups from time 24 to time 36. In other words, did the active group -- I understand that the lesion size of the stroke was similar. Walk us through those numbers again, the locations, how are they variable; and would the expected recoveries, given this mix, be different between the control and the treated arms?

Gil Van Bokkelen: Thanks, Jason. So, I'm just referring back - I want to make sure that I have the numbers right. So in terms of the balance between the study, again, that's one of the very first things we looked at because we wanted to make sure that there were no glaring imbalances in terms of the analysis that we conducted that might confound or complicate the assessment, in terms of the patients that got MultiStem at less than 36 hours versus the broader placebo group.

So just to walk through those numbers again, in terms of the stroke severity, the NIHSS median scores were 13 for both groups. The average scores were virtually identical. I think it was 12.9 and 13.2. So they were just spot on one another.

The average lesion sizes were also virtually identical. It was 45.4 and 46.6 mm. So within about a 1 mm difference, which David and Larry can certainly comment on this, but that certainly wouldn't be regarded as being anything that would be meaningful.

So when we looked across a whole range of different parameters, we saw, fortunately, that it was very, very balanced between these two groups.

Jason Kolbert: And that includes location also of the stroke itself?

Gil Van Bokkelen: I don't have the location data in front of me. But I can tell you that the types of strokes that we included in the study were cortical strokes. And again, the balance, because we did look at that. And I think -- I'm not sure if, David, if you summarized that in your presentation or not, in terms of left versus right, and general area. But again, it appeared to be very balanced.

Jason Kolbert: OK, good. That's very helpful. And one of the things that we've been talking a lot about is mechanism of action and how we change the inflammatory response, and specifically the migration of immune cells through the spleen, theoretically into the brain. Dr. Wechsler or Dr. Hess, can you help us understand what you think is happening in these patients and relate that to the time course? That would be helpful.

David Hess: This is Dr. Hess. I'll take the first pass at that question. So of course everything we know about the spleen is pretty much from rodents. But what

appears to happen in rodents is that the spleen shrinks after a stroke in rodents. And the reason that is important, it shrinks for two reasons.

One is some of the cells die. They undergo a process called apoptosis. They undergo program cell death. But the other probably important reason is that the cells, the splenocytes, the activated -- and these are mostly B lymphocytes and some macrophages, leave the spleen and are targeted to the brain.

Of course this is worked out very well in rodents. But of course you can't really do these studies in humans. And so in humans, it's hard to know the time course of that. Although there is some recent data from Sean Savitz at the University of Texas Houston, who did serial ultrasounds showing that the spleen is smaller a day after stroke and then gets bigger at 90 days. Now in people, we don't know when they're going to have a stroke, so we can't get a pre-stroke ultrasound. So you have to kind of extrapolate backward.

But his data would suggest that in humans the spleen does shrink, and the same thing is happening, and actually maybe happening a little bit earlier than in rodents. And so if you give MultiStem to a rodent with a stroke or even a traumatic brain injury, the cells target to the spleen and the spleen doesn't shrink. And it's probably not shrinking for two reasons. One is the cells are not dying. And that's probably good. Because if they die, they may not be available later on to fight infections. And secondly, it seems to prevent the cells from leaving the spleen.

So we think MultiStem, certainly in rodents, targets the spleen. And we suspect that happens in humans. And since that spleen shrinkage is pretty fast and maybe even faster in humans, this study is more evidence that we probably have to get the cells in there earlier, maybe closer to 24 hours -- certainly under 36.

So that's what we know. And not just the spleen, but there's other lymphoid organs involved. They're much more difficult to measure. And in rats the thymus shrinks. So other lymphoid tissue is probably having the same process. So we think the cells are going to the spleen, migrating to these lymphoid organs, and preventing the splenocytes from being activated and

then leaving the spleen, migrating to the brain, where acute inflammation is generally harmful.

Inflammation is a double-edged sword. There's good inflammation and bad inflammation. But this early inflammation appears to be harmful.

Lawrence Wechsler: This is Larry Wechsler. I would just add, I mean David has a great deal of expertise in this, and more than I do, but I would emphasize that last point, which is that inflammation in the setting of stroke is a two-edged sword, and that there is clearly a harmful part and a phase where it could be helpful.

But the earlier phase of it seems to be the harmful part. So that I think makes sense, when we look at this information that earlier administration does better. Because I think biologically we would expect that earlier suppression of inflammation would be the most beneficial in terms of stroke, and it may be that even giving it later could be harmful because of suppression of a positive effect of inflammation. So it's always good when the data that's coming from a study like this fits with what we think biologically should happen. And I think that's what we're seeing here.

Jason Kolbert: That's very helpful. And can we just kind of change gears a little bit? Because I know part of the design of this trial was to begin treating patients at time 24, with the idea that there is some percentage of patients that spontaneously recover. Have the results of this trial modified that thinking at all versus having a trial that goes 24 to 48 hours?

Gil Van Bokkelen: I'll address that Jason. I mean I think we still, first off, we still have a lot of analysis that we're conducting. I mean we've got a lot of biomarker analysis that's ongoing that will take a few weeks to complete, and then additional analysis just based on the pretty extensive data set that we already have. So it's going to take us a little while to go through that, and go through it with David and Larry and the other people involved in the study.

I think it's too early for us to say exactly what type of window we would use in the next study. I mean we believe that the evidence tells us pretty clearly that we need to administer MultiStem within that 36 hour window in order achieve maximum therapeutic benefit.

We are cognizant of the fact that it's very useful to have a window of initial evaluation for the patient so that we can determine whether or not they're spontaneously recovering. And as David mentioned in his comments, you generally get a pretty good sense based on feedback from David, Dr. Wechsler and a number of other clinicians that we've interacted with that you get a pretty good sense within that 18 hour to 24 hour time frame of whether or not patients are recovering spontaneously.

And so we think that it might make sense to perhaps focus on a window with administration, perhaps something in the 18 to 36 hour window. But again, we haven't made any definitive conclusions about that. And we still have a fair amount of work that we want to do and kind of think through strategically and tactically how we want to approach that next study.

Jason Kolbert: Thanks, Gil. And let me just, I don't want to take the whole call, so let me ask just one more question. I know one of the things that I'm being asked by investors a lot is where is Chugai? Have you had a chance to discuss the data findings with them? And do you have any sense for what they're thinking? I know it's early. But people are interested.

Gil Van Bokkelen: Yes, it is early. I mean we have had some initial conversation with Chugai, and they've been very constructive. I think Chugai has a very experienced team. They've run lots and lots of clinical trials. It's common knowledge in the landscape of sponsors and companies that are developing experimental therapies that Phase 2 studies like the one we've just run tend to be the place where you learn the most information.

And sometimes you learn some slightly unexpected things, as we believe that we did here in this study. But I'd say that the discussions with Chugai have been very, very constructive. We're actually going out there next week to spend time with the team in Japan. I suspect it's going to take a little bit of time for them. We've already done a pretty substantial data download to them, which their team is going through. It's going to take them some time to continue to go through that, and we intend to work with them and actively support them in that regard.

I think they'll probably, as we will, also want to get some feedback from the clinical KOLs, and as we've said, we've seen a pretty enthusiastic response in terms of people that have said that they want to participate in the next study. And in fact, we'll be meeting with a meaningful number of clinical KOLs in Japan that we've had discussions with over the past 16 months or so that are very enthusiastic about the program.

So I think that getting feedback from the clinical KOLs and also getting feedback from the regulatory agency, the PMDA in Japan, and getting feedback from the FDA and the EMA - those are all going to be very important in terms of refining our thinking and helping us decide what type of a study we intend to run next.

But I think that the take-home message, and one of the things that we wanted to stress to people on the call today is, when you take a look at the totality of the evidence that we've obtained from this trial, it actually creates a very, very exciting picture. And yes, we understand people are very disappointed at the fact that we didn't hit the primary and the component secondary endpoints.

But -- and we empathize. I mean obviously we feel that way as well, but I think that the things that we've learned in terms of the consistency of the very positive findings that we've gotten from study across the board actually are very encouraging and give us a lot of reason for optimism and excitement.

Jason Kolbert: Gil, thank you. And my thoughts echo exactly that. And I wanted to thank Doctors Hess and Wechsler, particularly for highlighting some of the issues that tPA faced and the initial results of the ECASS and ATLANTIS trial. I know that I was not aware of that. And we all know that Phase 2 trials are exploratory. So my message to people is look at the data. So thanks very much for holding this call.

Gil Van Bokkelen: Yes. Thank you. And just one further comment while we're waiting for the next questioner. I mean, I personally think it's a bit disingenuous for people to say that you shouldn't conduct a post hoc analysis of the data. I mean, that's kind of ridiculous. The reality of it is, is that we're learning a lot. And people frequently do learn a lot when they see the data set and it allows them to ask

important questions that ultimately enables them to understand the data set more completely, and then it helps guide their thinking towards the next type of study that they want to run.

I mean, there are three general reasons why Phase 2 studies don't work out the way people plan. One is because there is a serious safety problem. Well, we clearly don't see that here. And you've heard that directly. The second reason is that there is no evidence that suggests that there's meaningful therapeutic benefit. And again, we clearly don't think that's the situation here. We think there is very clear evidence that there's a therapeutic benefit. We just have to administer MultiStem within 36 hours or less.

The third category is the kind of category where I think we are. Which is, you learn some unexpected things about dosing, timing of administration, route of administration or your therapeutic window. And I think that's exactly where we are. But in the cases where companies or sponsors make those types of observations, their success rate tends to be very high when they go on and run other studies that inform them as to how to design a more effective study and power it appropriately.

And so I think for all those reasons, we're actually pretty optimistic about where we're at.

Operator: Steve Brozak

Steve Brozak: Yes. Hi. Good afternoon. I'd like to jump right into a question and one follow up. That way I'll give as many other questioners the opportunity to have questions asked and answered. For Doctors Hess and Wechsler, you had mentioned both earlier on about how tPA -- didn't really see the results that people were looking for initially, based on time constraints and considerations.

Can you clarify in whatever shape you think is relevant as to how the tPA advantages were brought to light and what people eventually looked at, saw? And then I'll have one follow-up question after that, please.

Lawrence Wechsler: If you want David, I'll start with that.

David Hess: Go ahead, Larry.

Lawrence Wechsler: So I think what happened was that the earliest tPA trials tried to -- or used a time window that was a bit longer than what we ended up with. So the time window was out to six hours, and there were some other design flaws such as inclusion of patients with two big strokes and that sort of thing. That was changed by the pivotal NINDS trial where the time limit was limited to three hours. And in fact, many of their patients were treated within 90 minutes. So again, they emphasized this time issue, as opposed to the ECASS trial and the ATLANTIS trial, which extended the window to six hours. And many of those patients were treated in the later part of the time frame. So five to six hours.

And as David had pointed out, in the ECASS study in particular, when they later parsed the study by looking at only patients under three hours, they found the same benefit that the NINDS pivotal trial found, by only treating patients under three hours, and making sure the patients were treated earlier. So the main difference was the time window, which was much shorter in the NINDS tPA trial. But in addition, there were some design differences. In the ECASS trial in particular, there were a lot of patients who we call protocol violators. Because in fact, they had very large strokes on their CT. They probably shouldn't have been included in the trial. And the NINDS trial not only had fewer of those patients because of the shorter time window, but also were better at making sure that those patients weren't entered into the trial. And so they had a more accurate sample of patients who could benefit from this kind of treatment.

So I think, in my view, those are the main differences.

David Hess: Yes. I think Larry covered that question perfectly.

Steve Brozak: OK. On tPA, there is one thing that I've looked at. And that's specifically that there's still some resistance in the Emergency Room setting, and it's still a function of trying to convince people on how to use it, when to use it, and you're obviously always fighting a battle as to what standard of care is. Although tPA is considered to be standard of care.

How do you see MultiStem going out there and being able to supplant tPA into the future, given what you're seeing right now. And of course the study results do have to be repeated and you do have to fine-tune it, but what would obviously, other than the time constraints, be the significant advantages of MultiStem over tPA? And what kind of -- how much easier will it be to convince the Emergency Room settings of its value? And I'll jump back in the queue. Thank you.

David Hess: Well, I'll start with that. So Larry and I are both believers in tPA. And MultiStem wouldn't supplant or replace tPA. It would be in addition to tPA, so it would not be in place of. That's very important. When patients would come in, we'd all want to give them tPA.

You're absolutely right on your observation. There's still some groups of ER physicians that are resistant to tPA because of the risk of hemorrhage and Larry and I have kind of made a career of doing telemedicine and supplying neurologists to ERs to help give the drug and so, telemedicine has really helped give the drug, as it overcomes this resistance that many ED physicians have.

Stroke is harder to diagnose than a heart attack. It requires clinical decision-making and a clinical -- some clinical acumen. And reading a CT scan, there's no EKG change like you have in cardiology. So it's a little bit more difficult.

So I think the advantage of MultiStem, and what always attracted me to it, was -- I was interested in other types of stem cells initially, and then I met Athersys in around 2004 or 2005. And they had this allogeneic therapy, which to me made a lot of sense. You can never harvest somebody's own bone marrow cells - it would be very difficult, and try to give them back in within 36 to 48 hours. I mean it's possible, but it's heroic, and it would never be scalable.

So the beauty of MultiStem is since they can sit in a blood bank or a pharmacy and you thaw them and give them, there's really no hospital which couldn't do this. Maybe a small critical access hospital, and I'll pick on my state of Georgia, couldn't do it, but those patients are generally coming to a larger

stroke center like University of Pittsburgh where Larry is or where I am. So we bring those people in. We'd be able to easily give them the cells within an 18 to 36 hour window.

So I think the cells would reach a lot more people since there are virtually no side effects and maybe a late benefit of reducing infections. That remains to be demonstrated. But the signal is in favor of reducing infections. That would be another reason people would give them. So there would be really no downside for a doctor, an ER doctor or neurologist. And these would mostly be given by neurologists in primary stroke centers, I think.

But literally, no hospital would be left behind, if you will, for this therapy.

Lawrence Wechsler: If I could add to that, I think the two concerns that the ED docs have is number one, the hemorrhage rate, and number two, the fact that if they don't act quickly, they can miss a patient who could have potentially benefitted; and then by the time they get there, they're beyond the window.

MultiStem doesn't have the hemorrhages. It doesn't have the downside in terms of complications. So you don't have to worry about that and we're talking about 24 to 36 hours potentially, a much longer window and a later window, so you're not likely to miss your opportunity to treat that patient, and potentially end up in a lawsuit. So I think this is going to be much more easily accepted by EDs for acute stroke treatment.

Steve Brozak: Great. Thank you, gentlemen, for all the feedback and obviously all the work that you've done.

Operator: Ted Tenthoff

Ted Tenthoff: Great. Thank you. Can you hear me OK?

Gil Van Bokkelen: Yes. Hey Ted, how are you doing?

Ted Tenthoff: Good. So I appreciate you guys taking time to review through this. A lot of questions have been answered. I guess my question has to go back to this

exclusion of tPA and mechanical reperfused patients, and I want to make sure I understand that.

Is that for these patients, is it -- were they excluded just because the benefit of tPA and mechanical reperfusion occurs beyond the 24 hour end point, so that really a longer term benefit from both either tPA or mechanical wasn't being included. I'm still not sure why--

Gil Van Bokkelen: Yes. So let me provide a little bit of additional clarity. There was a larger cluster of patients actually in the placebo group that were administered placebo post 36 hours that got both tPA and mechanical reperfusion, so that was a larger cluster, relative to the other kind of three quadrants, if you will. And the response rate among that larger group was across the board, 100 percent of the patients got better.

So it created, when we looked at that, it created this obvious imbalance in terms of the placebo patients in particular, but really with respect to the entire balance of the study. And it created the appearance again that if you gave placebo late, or saline late that that was somehow substantially better than if you get saline early. And of course that's just not plausible. It's not in line with anything we know about the administration of saline and stroke patients or anything else.

So to correct the imbalance and try and get a clearer picture of what was going on, we said well, let's just remove all of the patients in each of the quadrants that got tPA and mechanical reperfusion. And when we did that, then everything became extremely well-balanced.

Ted Tenthoff: OK. That's helpful to understand that a little bit more clearly. And I guess it has been asked a couple of different ways, so I apologize for asking it again of the doctors. But since we have you on the call, let me just try to ask it in my own way. What patient population would you see MultiStem working in?

So let me kind of characterize that and see if I've getting this right. So because of that exclusion, would this be used most likely in patients who missed the tPA window? Would this be used in patients who already got tPA and then they'd still get MultiStem on top of it? Or even mechanical reperfusion on top

of it? Because I know that's growing in utilization, but it's still not widely utilized, just because of how many facility have actually the wherewithal to do that.

So what kind of patients would you see getting this ultimately within that 36 hour window? Would there be any exclusions on who would actually get a MultiStem?

David Hess: No. This is David Hess. I'll start. So I think it's similar to the population. I think we would maintain a focus on moderate to moderate-severe strokes, because they have the most to benefit from -- and those patients, we think, from animal models, etc., the immune system is playing a proportionally larger role.

So I think there would be three types of patients. In this trial, about over 40% of the patients got tPA. So I think-- and going ahead in the next trial and then in general use, you would certainly include tPA patients, and you would also include people that get tPA and thrombectomies. That would be group two. And the third group would be the patients that we sometimes call sort of "wake-up" strokes. Strokes often occur when people are sleeping and so they wake up and so we don't know the time of onset, and they don't get to a place in time. And even though we have the imaging modalities now to still give tPA and do thrombectomies to some of them, still they're not going to get to the hospital on time.

So really I see three groups, the tPA patients who for whatever reason don't respond, the tPA and mechanical thrombectomies who still have a substantial deficit, and the patients who just get to the hospital too late for either of those. And that's still a substantial number of patients, unfortunately, in this country and throughout the world.

Lawrence Wechsler: Yes. I think we have to go back to the basic principle here that tPA and thrombectomy are doing something entirely different here. They're opening up arteries and restoring flow before damage occurs. The MultiStem is probably doing multiple things. But it's the inflammatory response, which is involved with the propagation of the damage, and potentially the neural protection

effect, which both of these things would be complementary to what we think tPA and mechanical thrombectomy are doing.

So this would be additional, and still be given to patients who get these other treatments, but as David pointed out, also be available to patients who arrive beyond that time window or the wake-up stroke, so that they can't get those treatments. So it's a whole other group of patients who could potentially benefit here.

Ted Tenthoff: Great. That's really helpful. Thank you.

Gil Van Bokkelen: Yes. And just based on the numbers, Ted, I mean I think that last category of patients is likely to be the largest group. Because it's a fairly small percentage of patients that actually get tPA. It's a fairly small percentage of patients that get thrombectomy, and an even smaller percentage that get both.

So I think what it illustrates, and I think all three of us are saying the same thing, there's a lot of unmet medical need out there among patients that have more meaningful strokes. And a lot of these, as David and Larry both mentioned, are wake-up stroke patients that they don't know when exactly they had the stroke, and they show up at the hospital and they've got a meaningful disability. And, frankly, for the vast majority of those people, there's not much you can do for them other than keep your fingers crossed and hope that they'll progress on their own. And eventually they can go on to physical therapy or rehabilitative therapy.

So we think it's a pretty big landscape of clinical need, and we think that this technology could actually help address it in a pretty powerful way.

Ted Tenthoff: Thank you all very much.

Operator: Christian Glennie

Christian Glennie: Good afternoon, gentlemen. Just if I could still further explore the potential even earlier treatment potential with this, mostly given the disease course in these patients, the information; the proposed mechanism of action of these cells. What's to stop going even much earlier and effectively either just

alongside tPA at a much earlier point to get that information down and so forth? Even considering the fact that obviously one of the issues with running studies in those areas is that you have this natural respond to phenomenon. Just some thoughts on that.

Gil Van Bokkelen: Yes. I mean, I'll answer that first, and then David and Larry, if you wouldn't mind kind of adding color as well. But just from our perspective, there might be nothing that prevents us from going very early on in the administration.

I think we have to distinguish though between running a clinical trial that's designed to minimize the background that is caused by patients that might be spontaneously recovering on their own because they had a TIA, or a transient ischemic attack, or because the body is up regulating compensatory blood flow, in the case of a small focal stroke that actually happens in an important region in the brain.

So in the case of running a clinical trial, we think it's very useful and this is one of the reasons why we designed the trial that we just are running now, in the way that we did, to provide a reasonable window for clinicians to assess the patients to determine which individuals were getting spontaneously better on their own, or were highly unstable, so that they were not included in the analysis.

But in terms of the clinical practice of this, it may very well be that as we extend through the development cycle and through the clinical phases of development that we're actually looking at earlier and earlier administration of MultiStem for certain types of stroke victims. And from a safety perspective, as David and Larry have both commented, there doesn't seem to be any reasons why we wouldn't do that.

Because it appears to be a very, very clean and consistent safety profile, so it's something we would intend to explore clinically. In terms of running the next clinical study, I tend to think that we would have a defined window so that we can kind of minimize the background noise while we're also fully exploring this earlier time of administration.

David, Larry?

David Hess: This is David. I mean I agree with what Gil said. I think certainly the clinical trial, the sample size would be very, very large if you were enrolling an earlier time point. Because there is a lot of spontaneous improvement. And so I think we would probably still go a little bit later, and of course then after the first study was done and hopefully positive, then you can go back and even look at earlier time points.

The other reason, just to maybe to avoid that early-- those first few hours that there's so much going on with tPA and making the decision of mechanical thrombectomy, and there's just a lot going on in that space. So that's why we always thought a little later space, since the cells seem to work later, would provide a greater opportunity to meet this unmet need.

Lawrence Wechsler: Yes. I think that's the point. I think the first 24 hours is not necessarily a biologic phenomenon. It just makes things messier. And most of the complications that we see from thrombectomy and tPA for example, bleeding complications and so on, are going to occur within the first 24 hours. After that, things are kind of stabilized.

And I think the other reason for kind of arbitrarily picking 24 hours was that all the information we have about whether you're going to do well after tPA or a thrombectomy is we kind of traditionally look at that 24 hour time interval and say, well. If you've had substantial improvement by 24 hours, you're probably going to do well.

But we could have looked at 18 hours, too. It's just that 24 hours is kind of a nice round number. So I think those are the main reasons. And I think probably the biggest one is that it's just going to make things a lot messier from a study point of view to try to go earlier, but there may be no reason why it wouldn't work earlier.

Christian Glennie: Sure. Thank you very much and then just on the use of tPA that was observed in this study. Now obviously there will be typically it obviously would be a higher rate to adoption of sort of standard of care in a clinical trial versus a real world, but just the level sort of 43% to 48% in both groups, was that

higher than you possibly expected versus what I understand to be the sort of real world, more in the sort of 5% to 10% region. I may be wrong on that.

David Hess: This is David, Dr. Hess. So yes, you're exactly right. I think we did this at leading centers in the UK and the United States ad so these centers, the tPA rates are generally going to be much higher than they are in the community. So that's one of the reasons-- whenever you do trials now, one of the issues with trials, you generally do them in centers with better care and there tends to be a ceiling effect. Because everything is done that can be done. And even the rehab is better and the clinical care is better. So it's always more difficult to show an effect.

So I think that's largely the reason. Plus we're enrolling moderate to severe strokes. And those patients are just more likely to get-- a lot of those people are just more likely to get tPA because they're being routed. The bigger strokes are being routed to larger centers.

Christian Glennie: OK. Thank you. And then finally, I mean, I know this is obviously a -- or it had initial phases of dosing lead in, but then it was a single dose, I just wondered whether there's any comments at this stage. I mean just in the data (there didn't actually tease something out) -- but whether there's any comments around appropriate dosing of cells, and whether that's a consideration for further studies.

David Hess: I'll just address that. Of course we used doses based on kind of extrapolating from rodent data. We saw what worked in rodents, and we basically multiplied that almost by the size of the human compared to the rodent. So we got out with 400 million cells, which is actually a large number of cells, and then 1.2 billion.

And I probably should have mentioned that on my comments. 1.2 billion cells is a large, large number of cells. I mean MultiStem are about the only cells you can expand to get that number. We obviously had only six MultiStem patients in each group as we dosed escalated, and two controls. They were certainly safe. So we know now going through this trial that the 1.2 billion is safe. So you're asking a very perceptive question.

Could a lower dose or a higher dose be even more effective? Well, we don't think a lower dose would be, at least extrapolating from the animal data. Because 1.2 billion was from allometrically scaling, where the optimal dose was in rodent. So we tend to believe that. That that's probably the dose.

And could you go higher? Well, you're just getting to an astronomical number of cells and so a good question, but we probably covered the doses I think pretty well. Could there be a U-shaped dose response where there's even a lower dose that's better? Possibly, but unlikely, so I think we found a dose that's certainly safe, and achievable.

And you infuse these cells in just in hour. It's quite amazing. An hour, and this is all done. tPA takes an hour, and these cells take an hour to infuse. And the 1.2 billion cells is probably higher than you'll get with any other cellular therapy IV in a short period of time like this.

Lawrence Wechsler: Hey, Gil and David and all, unfortunately I'm going to have to sign off. But thank you all for your attention to this.

David Hess: He's going to treat a patient with tPA probably. [Laughter]

Lawrence Wechsler: A telemedicine case.

Gil Van Bokkelen: Larry, thank you very much. We appreciate you making time for the call today.

Lawrence Wechsler: OK. Thanks. Alright.

Gil Van Bokkelen: And I think we have time for maybe one more question, actually.

Operator: Jack Fraser

Jack Fraser: Thank you and thanks for taking the question. Given that Dr. Wechsler has jumped off, Dr. Hess, this may be more directed at you. It's a two-part question and first is, I'm wondering if you believe that in your clinical experience that doctors, assuming that another trial was pursued and we reached statistical significance and was able to be approved and used, I'm wondering if in that trial you feel that centers would be more likely and more

rapid enrolling patients giving the data that we've now seen, A. And then B, the second part of the question is, in the event that that were to happen and that approval would actually occur in Western countries, what comments or opinions would you share with us regarding the likelihood of doctors using MultiStem and adopting it as a therapy for all stroke patients, given that it is sort of a second stage, if you will, or later stage treatment paradigm?

David Hess: Yes. Well, that's a very good question. First of all to get to the first part is, if we did another trial would it be easier to enroll? And I think that it would be, for a variety of reasons. I think there would be excitement, number one. And number two, one of the major problems with the study was that we had to thaw the cells in a cell processing facility. And unfortunately those people tend to go home at 5:00 and so that made it more difficult to enroll patients. So there was that logistical block which is no longer there. So I think it would enroll much, much faster than this one did.

And I think the second question is a good one, if doctors -- you know doctors are concerned about two things. Is it easy to administer? Which this is an IV infusion. And then secondly, what are the side effects? Because I said before, what doctors fear the most is a complication. And one of the reasons the ED is so concerned about this is many ED physicians, Emergency Department physicians, back in the days when they were treating heart attacks were giving tPA for a heart attack. And the most feared complication was intracerebral hemorrhage. So then you tell these ED doctors, we're going to use tPA for stroke, which is the most feared complication of heart attacks.

And so if you see, and I've had the experience myself. I gave tPA a couple months ago and I had a hemorrhage in a young lady who I felt terrible for. I had trouble giving tPA for a week. But I looked at the data. I said it works. You never forget that. I mean when you harm a patient, there's no worse feeling in medicine.

I think with MultiStem, you're never going to be concerned about harming a patient, right? I mean there are no infusion reactions in any of the studies. If anything, it's going reduce infections, so you're not going to have that fear. So it would then-- it may come down to a reimbursement issue.

But doctors, when you're working in the trenches, you're not really looking at reimbursement. You're going to give the drug or the treatment that you think that works and you're going to let the smoke clear. Because that patient is your responsibility.

So let's say it works and the label changes. I don't know. Say it works after 36 hours. An NIHSS score of 8 to 20. Well, I mean if a doctor sees an NIHSS score of 5, at that period of 6, you're going to give the treatment in all probability. You're not going to withhold it, because it's two points off.

If it's really mild you may not give it, because they're destined to do well anyway. So I think the big advantage is for a doctor is ease of use and lack of side effects. Then things get to be used. We all use aspirin and statins in stroke, because there's virtually no side effect and it's easy to administer. So that's a big advantage for a drug, when it's safe and easy to use.

Jack Fraser: I really appreciate the input. Thank you.

Gil Van Bokkelen: Well with that, I think we've used up enough time, and we've tried to be very patient and cover as much information as possible. I hope this has provided additional context and information that give people room for optimism, enthusiasm and excitement about the program. That's certainly how we feel about it. And again, I'd like to thank Dr. Hess and Dr. Wechsler for participating in the call today. And you'll be hearing from us all again in a couple of weeks when we have our earnings call in early May.

So with that, I'd like to wrap the call today, and thank you all for your time and for your continued support.

Operator: This concludes today's conference call. You may now disconnect.

END