ASTRAZENECA UK LIMITED

Moderator: Thomas Larsen
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Good afternoon. Welcome, ladies and gentlemen to AstraZeneca's American College of Rheumatology Analyst Conference Call.

Before I hand over to AstraZeneca, I'd like to read the Safe Harbor statement. The company intends to utilize the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. Participants on this call may make forward-looking statements with respect to the operations and financial performance of AstraZeneca. Although we believe our expectations are based on reasonable assumptions by their very nature, forward-looking statements involved risks and uncertainties and may be influenced by factors that could cause actual results to differ materially from those expressed or implied by these forward-looking statements. Any forward-looking statements made on this call reflect the knowledge and information available at the time of this call. The company undertakes no obligation to update forward-looking statements.

I would now hand you over to Thomas Kudsk Larsen.

Thomas Kudsk Larsen: Thank you, operator. Thanks for the introduction. Good morning from San Francisco and good afternoon in Europe. I'm Thomas Kudsk Larsen from Investor Relations in AstraZeneca and I'm very pleased to welcome everyone to the Investor Science Conference Call today to talk about lupus and anifrolumab represented at the ACR conference yesterday.

For this conference call, we have made a presentation available on AstraZeneca.com under Investor Relations section. We have also e-mailed

many of you the presentation this morning. By the way, we hope that you like our new corporate website.

Before we start, just a kind reminder about the Safe Harbor statement on page 2 of the presentation. Please turn to slide number 4. During 2015, Investor Relations hosted a number of events for medical meetings and the highlights for each main AstraZeneca therapy area were; in March, we presented the PEGASUS data for Brilinta/Brilique at ACC in San Diego. Already in September, FDA approved the expanded label to take treatment beyond one year. The FDA also added the proven superiority over Clopidogrel for the first year of treatment.

In June, we presented a number of important data points from our oncology portfolio at the ASCO meeting in Chicago. These data points include immuno-oncology and the durvalumab and tremelimumab (IO-IO) combination data in lung cancer. I hope many of you saw the updated combination data from the SITC meeting last Friday. Further at ASCO, we also presented important data from the small molecule portfolio including Lynparza, Iressa, and AZD9291.

Today, we have the pleasure to present Phase II data on anifrolumab in lupus. As many of you know, lupus has been a difficult area for development of new medicines. And our ambition is that anifrolumab may soon be able to help patients.

Please turn into slide 5, please. And now for the agenda for today. Together with me in the room is Dr. Furie, who is the primary investigator of anifrolumab Phase II trial and we also have Bing Yao who is the MedImmune head of respiratory, inflammation, and autoimmunity, as well as David Chang who is the AstraZeneca head of late stage development for inflammation, autoimmunity and neuroscience. We also have Mitch Chan, Eugenia Litz and Mary Pericleous on the call from Investor Relations and many thanks to Eugenia and Mary for having been the project leads for our conference call today.

The plan is for Bing to introduce lupus interferon pathway and the science behind and then have Dr. Furie present and discuss the anifrolumab Phase II results and then hand over to David for the ongoing Phase III program and any future plans. After that, we'll take as many of your questions as we can and we'll spend about one hour on this conference call.

With that, I would like to thank Dr. Furie for his time this morning and the commitment to our conference call and hand over to Bing for his part.

Zhengbin Yao: Thank you, Thomas. It's a real pleasure to be here. Let's start with slide 7. Lupus is a chronic, severe autoimmune disease. The unmet needs are very, very high. Lupus can cause widespread organ and tissue damage and it can affect any part of the body unlike many other diseases.

So looking at the graphic on your top right, the disease activity in lupus can go up and down. However, as you can see below that, organ damage continues to accelerate regardless of the disease activity. Ninety percent of the sufferers of lupus are women, usually of childbearing age. The cornerstone of care are nonspecific in general. They have either limited efficacy or associated with significant toxicity. So there's a clear unmet medical need for more effective therapies and in particular targeted therapies to reduce disease activity and to spare steroidal use and also to reduce flares.

Now, slide number 8 looks at the population in seven major countries. So those are the U.S., five E.U. countries and Japan. So in total, the estimate of the population in those seven major markets are about 600,000. The vast majority of them or the 90 percent of those patients receives drug treatment. To further breakdown of the patient population, you can see on the bottom line – the bottom boxes, 40 percent has moderate and 20 percent has severe disease. Moderate to severe patients, those are 60 percent, are the biologics eligible patient population. It is also very important to note that at least 20 percent of the lupus patients may develop lupus nephritis during the course of the disease which tends to be more severe.

So slide 9, developing new therapies for lupus has been challenging. In fact, there's only one new approval in nearly 60 years, the many failures before and since that approval of the one drug.

So the barriers for drug development include the nature of the disease. I mentioned earlier disease activities can go up and down and that this complicates the trial assessment and also the disease assessment tools using clinical studies may not be sensitive sometimes – may not be as sensitive to changes and also understanding of the disease biology remains to be limited, and in the past, the select of biomarkers to select the right patient population.

To overcome these barriers, we focused on the understanding of the disease biology to target the critical pathways and identify the biomarkers using translational approach to select the right patient population and also you incorporate the learnings from the previous clinical studies, for example, using multiple outcome measures, not only the global activity but also organ-specific disease activity to ensure the data are robust and also consistent. So our approach has yielded two successful of these two clinical trials in lupus and anifrolumab will the focus for today's discussion.

So slide 10, anifrolumab is a first in class antibody targeting the central pathway in lupus. As you can see on the graph on your left, the antibody, previously we call MEDI-546, binds to interferon receptor alpha – interferon alpha receptor. So by binding to the receptor, so this antibody can broadly neutralize the activities of all types of interferon. It's not only alpha but also beta and omega.

Type 1 interferons can drive several pathways that are important for lupus. As you can see on your right side, this regulation of this pathway leads to activation of multiple cell types, effector T-cells, the B cells that could lead to autoantibody production and tissue damage. Those are the hallmarks for lupus.

The patients with overactivation or T-cell regulation of this pathway can be identified with a biomarker. The biomarker is an interferon gene signature. And anifrolumab has been shown to be able to completely normalize the gene

signature in three separate clinical studies. So I want to emphasize that this is our important distinction from the antibodies targeting interferon alpha. Those antibodies targeting alpha only partially reduce the gene signature. The gene signature has also been used in other clinical trials as a diagnostic biomarker. It has a potential to predict the patient responders.

So slide 11. So there's an increasing evidence for anifrolumab as a potential future therapy for lupus. At ACR this week, we presented six abstracts including three oral presentations relating to anifrolumab and interferon pathway. We highlighted how the molecule works. We shared that the PK and PD data the (inaudible) and shared the biomarker data. We presented the evidence linking interferon gene signature to higher disease activity and also increased oral corticosteroid use. We also shared new (inaudible) efficacy and safety data for anifrolumab.

So Dr. Richard Furie, the lead investigator, will highlight those data for you. So Dr. Furie?

Richard Alan Furie: OK. Thank you. For those of you who followed the lupus space, you know that we have been battered. The lupus community has been battered with a series of negative trial results and the termination of many programs. We needed to break the string and I think you'll find these data are incredibly uplifting.

Let's go to the next slide. We just heard a review of this. And I think the burning issue is whether broader suppression of the type 1 interferon system with anifrolumab will translate into greater clinical efficacy than what was seen with rontalizumab or sifalimumab.

We'll go to the next slide. This study, the gist of the study was to take active patients and make them active – less active. And this is really no different than a typical Phase II or Phase III design. What is a little bit different in the inclusion criteria is that we were really selecting pretty severely active patients. So in order to get into the study, one had to be serologically active. And the clinical requirements were as follows – the SLEDAI-2K had to be 6 or greater. In addition, the patient had to have a BILAG 1A or 2B scores at

least and the Physician Global Assessment had to be 1 or greater. And then on top of that, at baseline, patients had to be clinically active with a SLEDAI score of 4 or greater.

They all had to be on a background medication. It could be prednisone, an anti-malarial, or an immunosuppressive or any combination thereof. We did, as in most studies, exclude severely active patients in the neuropsychiatric domains and in the renal domain. There are three stratification factors, the interferon signature, high versus low; the dose of prednisone with 10 milligrams as the cut point; and the SLEDAI score with 10 as the cut point.

We'll move to the next slide. This shows the study design. There were two doses of anifrolumab, 300 milligrams and 1,000 milligrams. They were given intravenously every four weeks. You can see the sample size of roughly about 100 in each group. And this is all administered on background therapy, so standard of care, SOC, and SOC was a combination of the medicines that I just mentioned.

As you go to the bottom of the slide, the primary endpoint is there. And it was not only the SRI-4 but it was the requirement to get the prednisone dose to less than 10 by day 85 and that dose could be no higher than the day 1 dose. So this is a pretty strict endpoint. I mean SRI, a lot of different studies are using, but the addition of the requirement to get prednisone dose down is somewhat – is very unique.

Now, not only that, but they had to maintain that reduction of steroid from day 85 through day 169. Now, if you go to the middle – oops – if you go to the middle of the slide here, the schematic shows a few symbols. There's a rectangle, a clear rectangle, and that's when steroids could actually be reduced. You'll see there's a little break for eight weeks prior to the primary endpoint. The steroid dose could not be changed at all. The purple triangle is when the target was for the steroid reduction and then the stars represent the primary endpoint at day 169 and then there was a secondary endpoint at day 365.

We'll move to the next slide. Demographics are probably no different than any international study, more females than males. I can see the numbers of Hispanic versus non-Hispanic. The predominant group was the white group, relatively few black patients and then other represents patients of mix races.

Next slide. And as I mentioned earlier, this population was a sick population. And you can see on the top row, the SLEDAI score was about 11, a lot of data here. We'll jump down to – I just want to point out the Farr assay for anti-DNA antibodies and you can see that's roughly about 80 percent of the patients had anti-DNA antibodies. And jump down to the bottom, the interferon gene signature was high in three quarters of the population. So in summary, a sick population not only clinically but also serologically.

Let's move to the next slide. This looks at the background medications. And you can see about 80 to 90 percent of patients were on prednisone. And for those on prednisone greater than 10, it amounted to the majority about 50 to 60 percent. It's gratifying to see that three-quarters of the patients were on antimalarials. The dogma in these days that every lupus patient be on hydroxychloroquine. And immunosuppressive use is listed below and you can see that about 50 percent of the patients were on background immunosuppressives.

Go to the next slide. Somewhere between 12 and 30 percent of the patients did not complete the study and the reasons for not completing are listed in the slide. You can take a quick look at that.

All right. We'll move on to the next slide. All right. Here are the results. On the left is the primary endpoint and on the right is the secondary endpoint. Remember that the primary endpoint required not only an SRI-4 to be met but the patients had to reduce their prednisone per the rules for response. These slides are pretty much set up all the same and that the color codes are gray is placebo, red is the 300-milligram group, blue is the 1,000 milligram group. And then you see tables below. We've given you the effect size, the odds ratio, the 90 percent confidence intervals for the odds ratio and then the P values for the odds ratio. And you can see on the left-hand side of the slide that almost twice as many patients receiving 300 milligrams responded

compared to placebo slightly less for the higher dose. And then move over to the right-hand side of the slide and you'll see that the magnitude is even higher at day 365.

I'm not sure how your slides are set up, but I want to show you some interferon high versus low responses and we'll move to this. What's happens with the interferon high – and remember that 75 percent of the patients were interferon high of baseline. You see similar response rates with the drug, but what you see is a reduced placebo response, not only at day 169 but also at day 365 and the odds ratio grow. And we haven't seen odds ratios like these kinds of numbers in our lupus trials.

And then I'll show you interferon low. What happens here is that with treatment with anifrolumab the response rates are roughly about the same, but the placebo response goes up. And we need to better understand that, but it may be that the interferon low patients represent, you know, different level of activity and different requirements for treatment response.

All right. Let's move to the next slide. This slide – and there's a series of slides – show the kinetics of response at different levels of responsiveness. This is the SRI-4 but it's excluding the requirement for the steroid taper. The histogram on the right shows the effect sizes of 22 and 14 percent for 300 milligrams and 1,000 milligrams respectively.

Looking at the next slide, SRI-5, and this is a higher threshold response. So instead of a four-point reduction including the SLEDAI, a five-point reduction is required. And you see nice separation between treatment and placebo. And the next slide shows SRI-6 and the next one SRI-7. So the take home message here is consistency.

Let's move to the next slide. The BICLA is another type of responder index that was made popular with the Epratuzumab program and what you see here is clear separation between treatment with either dose versus placebo. And you'll notice that the separation actually occurs earlier than what was seen with the SRI. The bottom part of this slide or the next slide shows the kinetics for interferon high and the next one interferon low.

Now, there's sort of mix messages here looking at the table versus looking at the graphs. To me, the graphs look superimposable except for two time points and that's day 169 and day 365. At day 169, for whatever reason, the placebo response dips down and that's why you see a nice delta in the table. And then at the end of study, the 300-milligram group goes up for unknown reasons and that's why you'll see an effect size of 26 percent.

But we're talking about small numbers with the interferon lows and I think we should focus on some of the neighboring time-point to day 169 and day 365. Next slide.

Low disease activity is defined as the percentage of patients whose SLEDAI dropped to 2 or below and you see marked differences between treatment and placebo, basically about twofold difference between the 300 milligram and placebo and another similar analysis showed the major clinical response on day 365 and that's on your next slide.

A major clinical response is defined as a BILAG C score in all domains, achieved by day 169 and it had to be maintained for the next half year. And again, you see a significant differences between treatment without anifrolumab versus placebo. Move to the next slide.

CLASI is an instrument that we used to define disease activity in the skin and about 25 percent of the patient had a very high skin score, a CLASI of 10 or greater at baseline. And you can see significant separation between treatment and placebo and what's quite remarkable, it occurred very early on within the first eight weeks or maybe even slightly before that. And here we have odds ratio of 7, I think that's unheard of in lupus. Next slide.

Steroids are very important in the treatment of lupus but they also create a lot of toxicity for a patient. It's very important to try to get patients down to lower doses of steroids. Now I should emphasize that steroid reduction was part of the primary endpoint but it was not a requirement that patients reduce steroids, that it wasn't mandated. It was heavily suggested however.

And in this analysis, we took patients who are greater than 10 milligrams of prednisone at baseline and looked at what percentage we're able to reduce to

7.5 milligrams per day or less. And you see statistical significance with the 300-milligram group and just numerical superiority with the 1000-milligram group. Next slide.

Flares are important to control because flares can be associated with more damage and here we show the percentage of patients with flares. There were 17 in the placebo group and 12 in each of the treatment groups. And flare here is defined as the new development of the BILAG A or 2 Bs. If you look at the total number of flares, you also see significant differences. Next slide.

This is analysis of patient reported outcomes, the fatigue, using the FACIT Fatigue Scale and then the SF-36 and these are fairly standard for a lupus trial. And we looked at thresholds of 3 points for the FACIT Fatigue, 3.1 and 3.8 for the physical component and mental component scores. And you see numerical superiority; however, you don't see statistical superiority in any of these analyses. Next slide.

And similar for serologic changes, we see numerical improvement in C3 but not reaching statistical significance and we see reductions in anti-DNA antibodies, numerical but not statistically significant. Next slide.

This is a very nice slide demonstrating the kinetics of the neutralization of the gene signature. And it occurs quite rapidly and it sustained throughout the study and you see a bit of rebound with the 1000-milligram group and you see within about eight weeks or to 12 weeks total return to normal versus placebo as a flat line with no changes. All right, we'll move onto the next slide.

This is a busy but I don't think there's anything that stands out as far as adverse events in the safety population. And so we'll move unto the next slide.

Now a lot of interest in – well what happens with viral infections when you neutralize the type 1 pathway. And we did see a dose-dependent increased in herpes zoster, two patients in the placebo group versus 5 and 10 in the 300 and 1000 milligram groups respectively.

And also a higher frequency of influenza, though I should caution you that there was no confirmation of true influenza. This is just reported as the flu. I don't think there's anything else on the slide is terribly striking. Infusion reactions were very limited. All right, we'll move to the next slide.

So, this was the conclusion and the farthest one on the right was not really there to test your eyesight but to just kind of give you the broad view, to emphasize the magnitude and breadth and the consistency of the response. I believe we've never seen data, Phase II data. You can even extend that to Phase III data like this.

The Phase III study is underway with the 300-milligram dose of the maximum dose. So that was a summary, that was what I was – what I reported yesterday and it was very well-received. A lot of excitement and I must say sorely needed.

David Chang: Great, thank you, Dr. Furie. So, let's go to next slide, slide 43. So, the potential differentiators of anifrolumab in lupus are listed here. First of all, it could be the first-in-class mechanism of actions. It is the most advanced molecule that targets an interferon receptor and it does block all Type 1 interferons, not just the interferon alpha.

In addition, there's opportunity to be the potential best-in-disease efficacy. As Dr. Furie presented, we saw that SRI-4 with sustained reduction of oral corticosteroids at year one was 26 percent difference versus placebo. In addition for corticosteroid dose reduction, almost 30 percent of patients versus placebo we're able to reduce the dose of steroids less than or equal to 7.5 milligram per day of prednisone at day 365.

And finally there's an opportunity for anifrolumab to come up with a personalized healthcare approach by utilizing a complementary interferon test to help identify patients who are most likely to respond to therapy. Next slide, 44.

So what we've initiated is the TULIP study and that's the treatment of uncontrolled lupus by the interferon pathway and the trial objectives are listed here. So, the primary objective for the study for anifrolumab is to evaluate the

effect of anifrolumab compared to placebo on disease activity as measured by the lupus responder index with improvement of greater than or equal to 4 or the SRI-4 at week 52.

There are several secondary objectives and the key ones are listed here. And this again is the comparative the effect of anifrolumab compared to placebo on first of all SRI-4 at week 52 in the interferon test-high sub-group. The second key secondary objective is to look at the percent of subjects who actually achieved steroid dose reduction to less than or equal to 7.5-milligram per day at week 40 but sustained and maintained to week 52.

Next one is to look at the patients who actually have a skin disease as noted by the CLASI or the Cutaneous Lupus Activity and Severity Index and that the patients showed at least a 50 percent reduction in the skin score at week 12. We're also looking at the SRI-4 at week 24, not just at week 52 but also at an earlier time point. And finally, the secondary objective, we'll also look at the annualized flare rate through the 52-week treatment period. Next slide 45.

So, here's the trial design. As I mentioned, this is the Phase III study. They will be multi-center, randomized, double-blind and placebo controlled. There are two studies nearly replicate with a minor difference and that's TULIP SLE I study and the TULIP SLE II study. You have difference in sample size 450 for the first study ad 360 for the second study because the first study will have an extra dose to look at the anifrolumab 150-milligram dosing regimen.

As noted on the left hand side on the bottom, the dosing of anifrolumab will be given intravenously at every four-week. And as you can see here, we still look at the very same patient population at the Phase II study which are adult patients with active moderate to severe lupus with auto-antibody positive receiving standard of care. Next slide, 46.

And here's the trial schema, if you can look at this, you can see that there's a screening period. Patients get randomized, they received 13 doses of anifrolumab or placebo over the 40-week period and the week 52 is the primary endpoint where we will look at the SRI-4. In addition, there's a follow-up period for eight weeks after the primary endpoint. Patients will be

eligible, who complete the study, to continue on in the long-term extension trial. Next slide, 47.

So, this is where we stand today with anifrolumab, the Phase III lupus program had been initiated and we anticipate that the final data will be available in the 2018 with the regulatory submission to follow the year after. In addition for the life-cycle management program, we're looking at a Phase II lupus nephritis trial which is expected to start before the end of the year as well as the Phase I subcutaneous study that will be starting before the end of the year as well.

With that, I'm going to turn it back over and …

Thomas Kudsk Larsen: Thanks to Bing and Dr. Furie and David for their presentations. We're now ready to take questions. If we can limit perhaps, one, two questions to each person, then we can always do another around later.

Please press star one on your phone to indicate that you wish to ask a question, so back over to you operator.

Operator: Thank you very much. If you would now like to ask a question, please press star one on your telephone keypad. To cancel your request, please press the hash key.

OK, your first question today comes from Seamus Fernandez from Leerink. Please ask your question.

Seamus Fernandez: Oh thanks very much, so looks like a really good data, you know, obviously, exciting. Maybe just a first question for Dr. Furie, can you maybe compare and contrast these data to some of the data that we've seen with belimumab and you know how you're utilizing Benlysta today? I just want to know a little bit of the clinical utility of the Benlysta relative to the data that you're seeing here and your direct experience in treating patients.

And then separately, can you maybe talk – if the team could talk a little bit about what it was that, you know, had you choose anifrolumab over and above

sifalimumab specifically, where did that – where did that product fall short on a relative basis and I think the – I believe it might be the interferon signature.

And then just as a final question, the interferon signature data, is the expectation that, you know, given today's cost conscious environment that the focus will be much more to the interferon high-signature patient population. The reason that I asked – and maybe if you could just characterize, was the 75 percent of patients with the interferon high-signature reflective of what we would see in the overall patient population? So would 75 percent of lupus patients typically have an interferon high-signature anyway? Thanks a lot.

Thomas Kudsk Larsen: Thanks, Seamus, for your questions. So, we have two for Dr. Furie about the comparison to belimumab. We have also the clinical use of belimumab today and then we have essentially, let's say maybe for Bing, a question about anifrolumab versus sifalimumab. And then lastly on the kind of use of the biomarkers, so I'll hand over to Dr. Furie for the first two questions.

Richard Alan Furie: OK so comparison, well we can compare Phase II to Phase II and there – there really is no comparison. These data are very robust, they're very consistent. But you have to keep in mind we're going back I guess about 8 to 10 years for Phase II belimumab and there was a learning curve.

We learned the hard way that we had to include patients with serologic activity and you can go down the list. So, it maybe a little unfair but the Phase II belimumab study was a failure. The post (hoc) analyses kind of resurrected the interest in pursuing Phase III, looking at the serologically active patients. So, 72 percent of patients are serologically active.

So head to head Phase II versus Phase II, there's no comparison. These data are far superior. You could get into a Phase II versus belimumab Phase III comparison, I'm not sure that's fair but as I mentioned I have never seen odds ratio like we're seeing with anifrolumab.

How do I use belimumab? Well I'm a big supporter of belimumab. We had about 70 patients in all the different studies and we probably have about 40 or 45 patients who received it as part of their care outside the studies. And I

view as a very safe medicine, it works, it's hard to identify. We don't know how to identify those who eventually respond but we certainly could use a more robust medicine with, you know, greater and quicker response.

Thomas Kudsk Larsen: Thank you, Dr. Furie, and then we'll move over to Bing for the question regarding the choice of anifrolumab versus sifalimumab.

Zhengbin Yao: Sure, yes. As you are aware, we have two molecules, one sifalimumab which are targeting the interferon alpha – interferon alpha is a subset of the (type 4) interferons. So, anifrolumab targeting the receptor, I mentioned earlier, targeting the receptor, we you can block all the activities of (type 4) interferons. In fact, that's been confirmed in the clinical studies.

If you block a (Inaudible), you block 40 percent of the gene signature. If you block and use anifrolumab, so you can get a normalization of 89 percent to 90 percent. So, it's more complete inhibition. Interestingly, I think not surprisingly in clinical studies you saw more robust efficacy with anifrolumab.

What we have seen when we compare, you know, the two datasets is that with anifrolumab, we have more consistent efficacy, more broader efficacy based on that, based on the – our strategy from the first study to take one forward to for SLE in Phase III. So based on the data, so we select anifrolumab for Phase III in lupus and also for Phase II clinical study in lupus nephritis, so we're committed to anifrolumab moving forward.

Thomas Kudsk Larsen: And then there was a question about the potential use of the biomarker if approved.

David Chang: So David Chang here, so I think one of the – one of the questions also was related to the 75 percent of patients reflect on lupus patient population and from our studies, that does seem to be the correct number, about 70 to 80 percent have the interferon-high signature.

And in terms of the future study, we will be utilizing the same interferon signature test to find – to identify patients who are high versus low. But we intend to actually study the full population because as Dr. Furie mentioned

earlier, we need to further characterize the patients who are interferon-low. So, we will be looking for patient populations.

Thomas Kudsk Larsen: Thank you, David, thanks for the insightful answers. We're ready for the next question please.

Operator: Thank you and your next question comes from Simon Baker from Exane. Please ask your question.

Simon Baker: Thank you for taking my questions, two if I may, please. Firstly on the dose selection, it's pretty clear that within this study, 300-miligram is superior to a 1000-milligram but I wonder if you have any gauge on doses between 300 and a 1000. I'm just trying to understand why the other dosing going forward into the Phase III is 150 rather than somewhere between 300 and 1000. And secondly, I just wondered if you could give us some color on the death in the anifrolumab 1000-milligram arm please? Thank you.

Thomas Kudsk Larsen: Thanks, Simon, for your question. So, I think on dose selection if we have any data between 200-milligram and 1000, I'll hand it over to Bing and then maybe Dr. Furie can cover the safety presented from the Phase II.

Zhengbin Yao: Yes, so in terms of dosing, we have studied several doses in Phase I clinical study, different indications, scleroderma, and based on those data and also because this one binds in the receptor, we did an extensive dose modeling, so select the two dosage. So based on the predictions, 300 milligram actually is a maximum dose.

And it can – it can occupy essentially all the receptors and have the maximum biological effect, that's based on the modeling data. So based on those data, we have taken two dosage into Phase III study, so 300 and 1000. We did not study any dose in between in the Phase II study. But I have to say that the data here are pretty confirmed that, you know, with the 300-milligram, you can give the maximum efficacy.

Thomas Kudsk Larsen: Thank you, Bing, for that answer and maybe to Dr. Furie first on the safety-related question.

Richard Alan Furie: Yes and I just want to come back to the 300 …

Thomas Kudsk Larsen: OK.

Richard Alan Furie: … and 1000 milligram issue. So as far as safety, you specifically asked about the death. The death occurred in the 1000-milligram dose and I don't know all the specifics but it was a patient who early on developed colitis. I think she just received one, maybe two doses of anifrolumab and then died of a sepsis and a perforation. I think the investigator at the site felt that the experimental drug was not responsible for the patient's death.

Back to the 300 versus 1000-milligram issue, if you look back at the slides, you'll see that there were about 11 patients more in the higher dosing group, in the 1000 group versus the 300 group who did not complete the study and if you do use different methods of imputation like LOCF or mixed model or in fact do a complete analysis the 300 milligram and 1000 milligram dose actually have very similar results but going forward it was felt that the 300 milligram dose was the one to use because it's probably a ceiling effect, there's probably a plateau effect and not an inverse dose relationship effect.

Simon Baker: Great, thanks so much.

Thomas Kudsk Larsen: Thank you, Simon, for the question. So, I think we are ready for the third question.

Operator: Thank you. Your next question comes from Eric Keisman from Capital World Investors. Please ask you question.

Eric Keisman: Hi, so my question is, you know, we've seen data for instance the epratuzumab Phase II data that was, you know, looked a little bit questionable in terms of the non-linear dose response and – but the point is we've seen data kind of go away, you know, good data in Phase II that kind of regress to the mean that somehow didn't work in Phase III. Can you talk a little bit about why for instance the epratuzumab trial failed and why we might expect this data to be more robust in terms of its likely success in Phase III?

Richard Alan Furie: OK, so to review the epratuzumab Phase 2B study known as EMBLEM, the 2400 milligram group outperforms the other doses and it was statistically significant compared to placebo. Now, that was very remarkable first of all to see a positive response but to see it at 12 weeks with a very rigorous endpoint so there was a lot of excitement but I always get nervous when the next higher dose does not do as well.

And again, that study had, I think it was about 40 patients per group, so it's a relatively small study and then superimposed on that the mechanism of the action was not really well understood with the anti-CD22. And so I think to contrast that here we have strong biology, you have consistency across multiple metrics and I just think this – I mean I understand your concern about Phase II studies are relatively small but this was not such a small study this is 300 patients. I think the breadth, the magnitude and most importantly the consistency across multiple metrics makes me a believer. And then you can also contrast interferon high versus interferon low responses and that supports the pathobiology as well.

Thomas Kudsk Larsen: Thanks, (Eric). I think also Bing has a comment on this question.

Zhengbin Yao: Yes, (Eric), I just want to add a one point here. So if you look at, we have also shown the doses – the responses over time. So if you look at that two doses responses over time, multiple time points, you know, SRI-4, 5, 6, 7, CLASI and also look at flares too), so the two doses are actually – efficacy overlapping.

Thomas Kudsk Larsen: Thanks for that, Bing. I think we have …

Eric Keisman: Can I have a quick follow-up, Thomas?

Thomas Kudsk Larsen: … of course, yes please.

Eric Keisman: For those of us who are a little slow, could you again Dr. Furie sort of compare the endpoints that we've seen in the Benlysta studies in the epratuzumab study and these endpoints for any differences that might be meaningful in terms of whether this was an easier endpoint to hit or harder

endpoint to hit and whether it's more robust in terms of again likely read through in the Phase III.

Richard Alan Furie: OK, so belimumab-epratuzumab and these studies. Belimumab use the SRI. In fact, the SRI was developed post-hoc from the Phase II belimumab data and in order to be a responder, one had to have a 4 point reduction in SELENA SLEDAI. There could be no worsening and worsening was defined using BILAG, there could be no worsening more than a 1A, you couldn't have a 1A or 2B or worse that should be considered a non-responder.

And the third component was the physician global assessment and there could be no worsening there. There was a little wiggle room, about 10 percent wiggle room. So all three components have to be met.

Epratuzumab is kind of the – we'll call it the inverse of that, that was the BICLA and the BICLA came out of the epratuzumab program where the driver of efficacy was not the SELENA SLEDAI but the BILAG and there had to be domain reductions from A to B and B to C and so forth but anyway the driver of efficacy was the BILAG.

But no worsening was defined as the SLEDAI couldn't get worse and the BILAG couldn't get worse and then there could not be increases in steroids. Anyway, in some ways, I think the BICLA is a little bit more rigorous but it also uses BILAG where there are graded responses, so the BILAG actually might be a little more sensitive to change than the SLEDAI.

And then we come here to the anifrolumab endpoint and it use the SRI but in addition required for the primary endpoint, so you see analysis that the secondary analysis without that steroid requirement.

So, the primary endpoint required an SRI-4 and when we say 4, it's the 4 point reduction and that the steroid dose be less than 10 at day 85 and no higher than the day 1 dose and that had to be sustained until to the primary endpoint which was day 169, so that I would consider a far more rigorous endpoint than SRI alone. How to compare that to BICLA and I think it's very tough but you saw BICLA data in your slide set and you actually you saw a nice separation

maybe even greater separation with BICLA and earlier responses by a couple of months as I recall.

Thomas Kudsk Larsen: Thank you that's very helpful.

Thomas Kudsk Larsen: Dr. Furie, I think we have all become experts now in lupus endpoint, so I hand it over to …

Richard Alan Furie: No one is ever an expert.

Thomas Kudsk Larsen: … I hand it over to David for a follow-up …

(Crosstalk)

David Chang: I could add on to what Dr. Furie stated, if you reference back to slide 24. I know we don't like to compare our study versus another study, different study population, you know, there may be some differences. But, you know, to make an indirect comparison that endpoint that was used by Benlysta, the closest one you can get is slide 24 which is SRI-4 that excludes oral corticosteroid taper and you can see the responses there and you can look up and (list it) and see how that compares. But again it's hard to make this comparison across studies but that's how the closest way you can do that comparison. And same thing with BICLA, you can reference the slide and reference epratuzumab data.

Thomas Kudsk Larsen: Thanks, David, for that follow-up. Eric, do you have anything more?

Eric Keisman: No, I'm all set. thank you.

Thomas Kudsk Larsen: Good. Thank you. Then we are on to the next question, please?

Operator: Thank you very much. Your next question comes from the line of Richard Parks from Deutsche Bank, please ask your question.

Richard Parks: Hi, thanks for taking the question, very interesting data. It is quite exciting. I wondered if you could talk a little bit about the significance of – in context the herpes zoster infections and I just wondered whether the 10 percent dropout, I

think that was at the top dose whether that was related to herpes zoster infections, I'm just wondering whether this is – what we should think about this is just being simply viral reactivation or maybe you could talk about the severity of those infections, I'm just wondering whether we should expect any other type of viral reactivations with extended use.

Then the second question I think I'm just so intrigued by the difference in the placebo response between the interferon low and interferon high subpopulation because I wonder if you could maybe speculate about that a little more if that signature also associated with prognosis or severity in anyway, thank you.

Thomas Kudsk Larsen: Thank you, Richard, for the questions. We can say that we share your excitement about this data point. So, on the significance – there was one question on the significance of the herpes infection and then the second question was about the difference in placebo response between the two biomarker populations. So I'll give Dr. Furie a chance to cover the herpes question.

Richard Alan Furie: Hi, well shingles, plaques are – not only at lupus patients, all our patients who are on (immunosuppressors) and you saw a dose dependent increase in herpes zoster. Now, all of these patients were easily treated with antiviral. There was no dissemination and as far as – you asked about the dropout in the highest dose where they because of herpes zoster and the answer is no.

Richard Parks: Thank you.

Richard Alan Furie: Oh, OK. Any other questions about viral infection? I also – we showed data about influenza, but I have to caution you interpreting that, those were not confirmed cases of influenza, they were, you know, "flu."

Richard Parks: Yes, I'm just – I'm wondering just from the mechanism whether I mean is this just an immunosuppressive effect or is it potentially specific viral reactivation and is there any of, you know, theoretical concerns around other viral reactivations that might be associated with this mechanism?

Richard Alan Furie: Well, I think that's on all of our minds but, you know, what we have is what we showed you.

As far as the interferon high versus low, so with the interferon low population, again, I caution you, it only represented 25 percent of the population, but it seemed that the placebo response was much higher so maybe it represents a slightly different population. I mean traditionally the interferon low are less serologically active, they might be a little clinically less active and maybe just easier to treat but, you know, that was very striking.

Thomas Kudsk Larsen: Thanks for that answer. Also Bing has a follow-up answer (inaudible)?

Zhengbin Yao: Yes, so just a follow-up on your question whether for example interferon signature associated with the increased disease activity. This area, we continue the study, we continue to look at the data but we did present our abstract with this meeting. We found that the high interferon signature is associated with the increased disease activity and also reduced the (serological set), complemented the Phase III and also patients with high signature have the increased oral corticosteroid use. So then it points to, there are more severe patient population with the higher signature.

Richard Parks: OK, thank you.

Richard Alan Furie: Thank you.

Thomas Kudsk Larsen: Thanks, Richard, for the question. Let's get the next one please.

Operator: Thank you. The next question comes from Alexandra Hauber from UBS, please ask your question.

Alexandra Hauber: Thank you. Both questions has been answered, but I still would like to go back to the endpoint topic and since especially since you mentioned the learning curve, we have been – had in lupus trial design, can you just tell us how that was actually then incorporated in TULIP? From what you said, it seems that the steroids dose reduction incorporated but that doesn't seem to be

in the primary endpoints so is it sufficient in the – to capture that in the secondary endpoint.

And then the second question is back to the biomarker, I understand that this is incredibly interesting mechanistically, but in real practice, I mean in other areas I've heard if the biomarker finds 75 or 80 percent of the population, you may not need it, can you just give us your view what that will mean for the clinical practice later on?

Thomas Kudsk Larsen: Thank you, Alexandra. I think I'll hand it over to David for the questions and they were around the endpoints in Phase III primary and secondary endpoints as well as whether that biomarker is available, (covers) 80 to 85 percent in the patient population.

David Chang: Right. I think the first question is related to the primary endpoint and what kind of learnings we've taken into coming up with that primary endpoint. So obviously we've looked at our Phase II data and looked very carefully at how that endpoint was constructed, but also looked at other clinical trials that have worked into lupus space and essentially we've mostly replicated what we've done in the Phase II study and we kept a fairly strict criteria of trying to find patients who have active lupus (mild) to severe disease, who also have autoantibody positivity and patients on a standard of care.

So, it is a very similar patient population to Phase II, so we have a lot of confidence that we will replicate the patient population and hopefully replicate results.

You had the second question regarding the secondary endpoint, could you clarify that one again please?

Alexandra Hauber: Sorry, I'm just looking at the slide 44 which describes the endpoint, my understanding from the explanation about the validity of those endpoints in the Phase II was that you included – you included the steroid dose reduction as a requirement but looks like to me that the primary objective doesn't capture that, so A, is that correct; and B, is it therefore sufficient to capture the secondary endpoint?

David Chang: Right, right. So there is a difference there and thank you for repeating that. But the primary objective and the endpoint, we are looking at this endpoint was also looked at in the Phase II study, so the endpoint is a little bit different because did now exclude the oral corticosteroid dose reduction, so now it's focused primarily on the SRI-4. Again, that's consistent with how belimumab did their study as well and we thought that it's actually a cleaner endpoint to utilize just the SRI. However, we continue to include oral corticosteroid dose reduction as a key secondary endpoint.

Alexandra Hauber: OK.

Thomas Kudsk Larsen: Then there was the question on the biomarker and development of 80-85 percent …

David Chang: You know, I think the question was related to in fact they are fairly high percentage of patients with lupus, who have 80 percent interferon high signature, do we really need that test. Obviously right now to this point, we've identified probably 70 to 80 percent, there could be potential variability in other populations, but so far it's been fairly consistent to have that number but we believe that this still provides an opportunity to identify patient who are most likely to respond and the ones that would respond best to anifrolumab therapy, so I think there would be a clinical utility of having this complementary test.

Thomas Kudsk Larsen: Thank you, David, for that. And so I think it's also a point about that it gives flexibility also for physicians going forward, if there is a biomarker available.

                 Now, with that I think we have Steve Scala with a question.

Steve Scala: I have two questions. First, what percent of lupus patients would qualify for the strict inclusion criteria used in the study, so that's the first question. The second question is sifalimumab data showed some geographic variability with patients from North America and Western Europe not responding as effectively as patients from Asia, South America and Eastern Europe was the same geographic variability observed in anifrolumab study? Thank you.

Thomas Kudsk Larsen: Thank you, Steve.   So, the question were about if you use the same inclusion criteria, does that cover how many percent of let's say are traditional in a normal lupus population. And then also if there are any geographical differences in the Phase II, will you try Dr. Furie to answer these questions?

Richard Alan Furie: Yes, the first one is – I'm not sure, I can give you specific numbers but you asked about the percentage of, you know, a typical cohort that might qualify for this study and I'd say it's very low, but I think the more important question is what percentage of patients in need that is the patient who's refractory to their standard of care would qualify for this study.

So, for the first part it's obviously very low. I see a lot of lupus patients and we're talking about single digits who are either interested or qualified for our studies but the patient who's refractory to conventional therapy is looking for this study. So, you know, I will be very happy to put 5 to 8 patients in this particular study, and I would say we have about or maybe 4 to 500 patients a year that we see with lupus, but then you have to divide that into lupus nephritis and extra-renal lupus, so it's really hard to do those calculations.

You asked about geographic differences, I know we've represented a poster, I don't know that I've seen the result yet with the anifrolumab data broken down by geography and I don't know maybe someone else can comment on that.

Thomas Kudsk Larsen: Is there anything from Bing maybe on the – of any difference in geographical data?

Zhengbin Yao: Yes, we do see a higher for example response rate in South America. However when we look at anifrolumab, so the differences, you can still see a trend, but much less. So in our clinical studies, the C3, we definitely are looking into to account for this.

Thomas Kudsk Larsen: Thank you, Bing, for the question. I think we have a couple of more people on the line please.

Operator: Thank you. The next question comes from Marietta Miemietz from Prim Avenue, please ask your question.

Marietta Miemietz: Yes, good evening. Thanks for taking my questions. The first one is on the renal manifestation, so you have a lupus nephritis trial starting in a few weeks, can you just summarize for us what we know to date about the compound activity on renal symptoms and is there any concern that the exclusion of patients with severe renal disease in Phase III, (Phase III) trials now ongoing is actually going to decrease utility in clinical practice because I thought then a lot of the really treatment refractory patients actually had severe renal manifestations and I thought the lack of renal efficacy was actually the main (rock) on Benlysta.

And then a couple other much simpler questions one is just on the one neoplasm, can you tell us roughly when that occurred does that occur early in the study or is there any chance at all it could be drug-related?

And my final question is on the dose response, I didn't quite get your answer earlier, so what is your level of confidence that 150 is really the load effective dose because I think the FDA is going to ask for the lowest effective dose and I mean if it turns out that 150 gives you the exact same activity as the 300 in the Phase III, would you then be able to file on the 150? Thank you very much.

Thomas Kudsk Larsen: Thank you, Marietta.   Can I please kindly ask to repeat question number two, we didn't get this question in the room here?

Marietta Miemietz: Oh, I apologize. It was the lung cancer that occurred in the study, I was just wondering when it occurred was it early on the study or is there any chance that it could be drug-related?

Thomas Kudsk Larsen: Thank you. So let me just summarize the questions here before we hand them out so there is a question about renal and I think that may be one for Dr. Furie. There is the safety question on lung cancer and I could tell you we're trying to find the details, but we may not have them, so we may have to get back to you on that one.

And then there is a question again about dose response and the dose – efficacious dose, so I think with that, I'll hand the first question over to Dr. Furie on the renal.

Richard Alan Furie: Yes, you had a few sub-questions within the renal, so let me see if I can remember them.

Just talking about lupus populations in general, I kind of think of patients is either having renal disease or extrarenal disease and certainly they can have both, but we're talking about two different types of therapies.

The patients who have active or severe renal disease, proliferative nephritis for example, we're talking about different types of therapy. They are getting induction therapy with high doses of steroids. They'll get mycophenolate mofetil or cyclophosphamide, the refractory ones, rituximab, so that's one group and that group may comprise anywhere from a low of 20 percent of the population to at some centers a bit higher.

The extrarenal group is really what we're talking about here and it's fairly typical in a study of extrarenal lupus to not include patients with severe renal disease, the patients who actually need the induction therapy that I just described.

That doesn't mean if you have renal disease you can't get into these extrarenal studies. There's usually caps on how much proteinuria or creatinines and so it's possible to glean some information about the kidney from these extrarenal studies and I don't know that those analyses have been done with this Phase II study, but they can easily be done.

What percentage of patients have proteinuria, hematuria, et cetera and look at whether there is any hints, but you have to remember we're talking about 300 patients to begin with and I can quote the belimumab experience is about I think one-seventh or one-eighth of their population had renal domains checked off on SLEDAI, so if you take one-eighth of your 300, you're dealing with a very small sample size to look at renal parameters.

Where there any other questions about renal?

Marietta Miemietz: No, that was very helpful. Thank you very much.

Richard Alan Furie: OK. You asked about lung cancer, so actually it turns out that the lung cancer pre-existed entry into this or receipt of drug on x-ray that was found, so that was ...

(Crosstalk)

Marietta Miemietz: OK, great.

Thomas Kudsk Larsen: And then we have the question again on the dose response. Do you want to cover that Bing?

Zhengbin Yao: Yes, sure, yes. We did add 150-milligram dose into the Phase III – into the Phase III in one of the studies. So based on our modeling, so that would have been suboptimal dose because of the receptor occupancy. We added it because we want to fully characterize the dose response. And I would also would like to mention that we did have, you know, had our Phase II meetings with the – with the agency.

Thomas Kudsk Larsen: Thanks, Bing, for giving some more background on the biology as well. Marietta, does that answer all of your questions?

Marietta Miemietz: So how do you know that 300 milligram is probably the lowest effective dose, so what if the FDA comes back and says "OK, the 150 milligram wasn't effective, but maybe 200 could have worked" or is there any sort of like, you know, did you have any (feel at all) what the lowest effective dose is?

Zhengbin Yao: I think that dose was selected based on the modeling. I mentioned that we did a Phase I study in scleroderma, as you can see because the antibody targets to the receptor. Receptor generally are pretty – the number is pretty consistent, so that would have predict, you know, 300 milligram would have been the maximum dose and also this confirmed our gene signature suppression.

If you look at the 300 and the 1000 that, you know, the level of suppression are very similar. The answer to your question would be it's really going to be,

you know, based on (us), it's going to be really hard to distinguish for example 150 and a 200, but if we pick a 100 milligram – a 150 milligram this just characterized another dose. I mentioned that we did – we did have – in our Phase II meeting with the – with the FDA. Thank you.

Marietta Miemietz: That is very helpful. Thank you very much.

Thomas Kudsk Larsen: Thanks, Marietta, for the questions. So we have I think a couple more minutes. We have had an e-mail question in for Dr. Furie.

So the question is that if you compare these data to Benlysta, how much more or less do you think that you will use this drug, if the Phase II replicate in Phase III, so that would be the first question and that's given your daily clinical practice. And then the question is on the herpes safety finding, is that if immunization can eliminate the zoster herpes.

Richard Alan Furie: All right, you're really putting me on the spot with that first question. Yes so we need to replicate this data for sure. I'm very impressed with the Phase II anifrolumab effect sizes and consistency that were seen. So I think it's just, you know, when any new drug comes out, we just have to develop our own opinions and I would be very tempted to use this drug and we'll just have to wait a few years and see how I compare it to belimumab.

You asked about vaccination. So I don't know what the policies are or the guidelines are in other countries. In United States, it sort of taboo to give a live vaccine to a lupus patient, so I have not been giving shingles vaccine to my patients and that really needs to be studied. Now I know in development is an attenuated vaccine and we really need that because shingles can be severe in some patients.

Thomas Kudsk Larsen: Thanks for that. I think we have a couple more people in line. Let's extend for another few minutes to cover all our questions here.

Eric Le Berrigaud, I think is next on the line.

Eric Le Berrigaud:Yes, thank you. Two questions please. First on the duration of the study, just to get the understanding whether it's some kind of conservatism from your

side based on the strengths of the Phase II data, it looks to me that more than three years to complete, the Phase III trials may look a little bit pessimistic, is there any way for AstraZeneca now based on this result to speed up the development like (having) new centers or anything that could make the data before late 18.

And the second question would be for Dr. Furie perhaps, just to understand we had been also very excited about Benlysta at the time of the Phase III data also because it was all the very first drug since decades and the ramp up has been very low and even years after launch it has been disappointing, just to understand why that be and second sub-question would be do you expect the shift from IV to subcu to play a significant role in terms of adoption for that drug. Thank you.

Thomas Kudsk Larsen: Thank you, Eric, for the two questions. So the first one to David on the development timelines for the Phase III and then Dr. Furie on let's say the promise and maybe disappointment of previous medicines and also the use of the subcutaneous version.

David Chang: Yes, so I would agree with you that this is a very exciting results that we're seeing today and we would also like to speed up the development program as much as possible and get the drug into the hands of patients and Dr. Furie identified, you know, how robust that data is and this would be a great drug for patients who do need it.

I think that we hope that the results of the Phase IIb study will further create that interest in the community and that we would be able to enroll faster, but we would like to take a very conservative timeline at this point and leave the data as they are, but if we do get better enrollment, we will update as needed, but appreciate your support.

Thomas Kudsk Larsen: Thank you.

Richard Alan Furie: Yes, I just want to give you the perspective from an investigator. There's a lot of competition out there. There is an amazing number of studies in extrarenal lupus and lupus nephritis right now despite, you know, a lot of negative trial results so the question is what studies do you sign on to when

you're at site because there's just a finite number of patients eligible for studies and I think these compelling data have certainly affected me which study I'm going to do for the Phase III and how you're going to funnel patients into a study. So the Phase II data I think clearly will get out there amongst the lupus community and I'm hoping to see a quick enrollment.

All right. You asked about belimumab and the slow or low ramp up. Well I guess it starts before the drug was even approved and there, I think, was a lot of hype. You know we don't have any drugs for lupus. Nothing has been approved, but that didn't mean we weren't treating our lupus patients. We were using unapproved drugs and so that I think the expectations were super high. I mean all the calculations using a figure of 1.5 million patients in the United States with lupus and looking at the percentage of moderate and severe totaling, you know, maybe 60, 80 percent and everybody doing the math and I think the expectations were really high and probably not realistic before the drug even got approved.

The other problem is I honestly don't think people truly understand the SRI, so they saw a low effect size and the mindset has been rheumatoid arthritis effect sizes of 40 percent, 45 percent and then to see an effect size of, you know, 10, 12 percent, I think disappointed a lot of doctors.

But the SRI is a very high threshold to me and if you meet it, you're truly a responder and we published an article, I guess about last year, looking at the Phase III belimumab data combining the two studies and doing the analysis irrespective of treatment assignment and the analysis was to compare laboratory and clinical correlates of SRI response versus not being an SRI responder.

And if you were an SRI responder, your prednisone got reduced, you didn't need extra high doses of prednisone. You didn't have severe flares. I think the severe flare rate was reduced by about five or six-fold and it goes on and on and on, so it's very important to be an SRI responder.

So the low ramp up, I just think the community, not the lupus community, but the rheumatology community is kind of polarized on the effectiveness of

belimumab for those, at least those couple of reasons. But again, you have to try a drug. I think the safety is there and there are a lot of doctors who are convinced that it's effective and I think when you see subcu available, maybe there'll be more used and we happen to have an infusion center. We have an 8-bed infusion center, so giving IV drugs is not an issue for us.

Thomas Kudsk Larsen: Thanks for that additional perspective. I think it's also important to add from AstraZeneca that we try to underpromise and overdeliver.

So with that, I'll hand over to the last person asking question. I believe it's Seamus. Go ahead, Seamus.

Seamus Fernandez: Oh thanks. So just most of my questions have been asked, but just as a follow-up in terms of steroid-dose reduction that appears to have been more required in the Phase II. This is a follow-up on Alexandra's question.

Did you break out the response rates in terms of the patients who achieve those corticosteroid dose reductions? I'm just wondering if those who did not have corticosteroid dose reduction, you know, ended up having overall lower disease activity. Really the reason that I asked the question is as we look at the Phase III, it doesn't appear that corticosteroid dose reduction is mandated in the same way and I would just a minor concern, but that – that that could impact the placebo response at a higher, you know, basically driving up the placebo response so just looking for a little bit of comfort in that regard. Thanks.

Richard Alan Furie: Yes, that's an excellent point. I don't have the answer to your first question, but as far as mandated or not, so I should emphasize for the Phase II in order – it figured into the endpoint, but there was not a mandated taper. It was heavily suggested especially if patients were doing well to taper steroids, but it was not a requirement as we've had in some of the other studies like the EXPLORER or LUNAR study.

Thomas Kudsk Larsen: Thank you, Dr. Furie. Does that answer your question, Seamus?

Seamus Fernandez: Yes, I think that's – that helped, so if it's not mandated, it sounds like it would be something that would be likely to occur as well in the Phase – in the Phase III is that – would that be your expectation, Dr. Furie?

Richard Alan Furie: Yes, so sort of the same rules in Phase III as Phase II, it's just the steroid taper requirement was excluded from the endpoint in Phase III.

Seamus Fernandez: OK, great. Thank you.

Thomas Kudsk Larsen: Thank you. Operator, are there any last questions?

Operator: We have no final questions.

Thomas Kudsk Larsen: That's perfect. Thanks very much. So with that, I'll just give a quick, you know, summary before we close the call.

So in summary, we are very pleased with the Phase II data of anifrolumab and the potential that this medicine has to in the future hopefully help patients with lupus. We have outlined the Phase III plans that are ongoing the TULIP trials plus lifecycle management including the Phase II in lupus nephritis as well as the Phase I that we're doing for the subcutaneous formulation and these studies are starting up very quickly. And this is of course documenting AstraZeneca's commitment to patients with lupus.

So with this, I'll thank all presenters and speakers for their time today in particular Dr. Furie for his very insightful presentation and the answers. I hope that we have educated everyone here on the excitement that we see for this molecule and for the difference we can make to patients with lupus and of course also thanks for the interest in AstraZeneca. Have a nice day.

Operator: Thank you. That does conclude our conference for today. Thank you all for your participation. You may now disconnect.

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