Investor Webinar

ESC Congress 2024:

Results from Finerenone in Heart Failure

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Introduction

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Introduction

Good morning and good afternoon, everyone. My name is Thomas Kornek, and I'm part of Bayer's Investor Relations team. It's a pleasure having you all today and to welcome you to our next investor webinar of our Pharma division.

Agenda

Following yesterday's news flow on Kerendia at the ESC Congress, the goals of today's webinar are to provide a summary of the key data of Kerendia's Phase 3 study FINEARTS-HF in patients with heart failure and left ventricular ejection fraction of 40% or higher as well as from the pooled analysis FINE-HEART that includes the data from FINEARTS-HF plus the previously concluded Phase III trials FIGARO-DKD and FIDELIO-DKD in chronic kidney disease. We will put the data into the context of Kerendia's structural and clinical profile and the unmet medical need in heart failure and also outline Kerendia's further development program and next steps.

Moving to Slide 2, speakers today are Maria Borentain, Head of Cardiovascular and Renal Clinical Development of our Pharmaceuticals Division, who will present the key data of FINEARTS-HF and FINE-HEART. Before going into the results of the two studies, Christoph Koenen, Head of Clinical Development and Operations of our Pharmaceuticals division, is going to kick off the event with a quick overview of the unmet need and general characteristics and epidemiology data of heart failure as well as our rationale to develop Kerendia in this indication. Finally, Bernardo Kanahuati, integrated project team lead of Kerendia, will conclude how the new data add to Kerendia's overall clinical and commercial profile and our plans to broaden its use towards a true cardiorenal brand.

Today's webinar is scheduled for up to 1 hour. The presentations will take some 25 minutes and after that, you will have the chance to raise questions to the speakers. Instructions how to raise your questions are available in the Zoom chat, and I'll also remind you to those again later on.

Disclaimer

Before we begin, I would bring your attention to the forward looking statements included on Slide 3, currently on the screen. And with that, I'll hand the call over to Christoph.

Finerenone: Potential to make a difference in Heart Failure

Christoph Koenen

Head of Clinical Development and Operations, Bayer Pharmaceuticals

Thank you, Thomas. I'm excited to discuss with you today the results that we just presented regarding finerenone in patients with heart failure. However, before we go into results, I would like to take a minute to discuss the importance of providing an innovative treatment for patients with heart failure.

If you look at slide number five, I think you all know, but I want to highlight this again, how big the burden is that heart failure puts not only on the patient, but on healthcare professionals as well as the healthcare system as a whole. Heart failure is the number one reason for hospitalization in elderly patients worldwide. The mortality of heart failure is greater than in most common cancers. One in two person has the probability of dying within five years from heart failure. And the overall number of patients worldwide with an estimated 64 million is large. You can imagine that this huge burden that is represented here for each patient translates in an equally great burden when it comes to drawing resources from the health care system. The overall expenditure on the treatment of heart failure is extremely large. And the majority of this expenditure is actually used to treat heart failure patients in the hospital. And that, of course, highlights the importance in a clinical study to reduce hospitalization.

Let's now have a look at slide number six and talk a little bit about what is heart failure. We usually make a diagnosis of heart failure by measuring what we call left ventricular ejection fraction. It's essentially a measure of how much of the blood in the left ventricle is pumped out into the body. Normally left ventricular ejection fraction or LVEF is somewhere between 50% 70%. A reduced ejection fraction, meaning less than 40% of LVEF, we call heart failure with reduced ejection fraction or HFrEF. If the ejection fraction is somewhere between 41% or 49%, we call this heart failure with mildly reduced ejection fraction. And patients that have heart failure, however, a left ventricular ejection fraction of equal to or greater than 50%, we call heart failure with preserved ejection fraction or HFpEF. The larger number of patients with heart failure belong to the group of patients with HFmrEF or HFpEF. That is important because in these patient populations, so far, we have only one guideline recommended treatment option and that is SGLT2is, whereas in patients with reduced ejection fraction, we have four different guideline recommended treatment options. This again highlights the importance of presenting a new treatment options for patients with mildly reduced or preserved ejection fraction because it's the larger number of patients. And these patients have only one guideline recommended treatment option.

Let's now go to slide number six and have a look at how finerenone specifically works in patients in heart failure. When we talk about heart failure, it's important to recognize that not only the heart is impacted in the pathophysiology of heart failure, but it's the vasculature as well as the kidney that play a very important role in the development of heart failure. We call this the cardiorenal axis. Overactivation of the mineralocorticoid receptor plays an important role and leads to a vicious circle that leads to a deteriorating condition for the patient. Breaking that circle and blocking the mineralocorticoid receptor using, mineralocorticoid antagonist such as finerenone leads to an improvement in patient outcome because it specifically reduces fibrosis in the organs, it reduces oxidative stress and it reduces inflammation as well as it improves endothelial function. Finerenone is a highly selective inhibitor of the MR receptor. And I'm coming to the importance of that later in my next slide. It improves the function of the end organs, as you can see here in the heart. And it breaks this vicious circle that I described that is induced by overactivating of the mineralocorticoid receptor. And all of that leads to improved patient outcomes as well as then improved both cardio as well as kidney health.

If we go to slide seven, you're all familiar probably with the fact that there have been drugs that address the mineralocorticoid receptor in the past. Those, however, are steroidal MRAs. Finerenone is a non-steroidal MRA that is highly potent as well as highly selective. And it has a

balanced tissue distribution specifically between the heart and the kidney. Only finerenone as a non-steroidal MRA was able to show benefit in the treatment of patients with heart failure with preserved ejection fraction. These fundamental differences between the two different classes of mineralocorticoid receptor antagonists are important because as I already pointed out, the highly selective activity for finerenone on the MR receptor and not other steroidal receptors explains the favorable side effect profile that we have observed with finerenone. We see, for example, less sexual side effects. In addition, the balanced distribution between the cardiac as well as the kidney tissue is important to address the cardiorenal axis appropriately. And then last but not least, the low incidence of hyperkalaemia that we have seen with finerenone is explained through the highly selective access that finerenone provides to the MR system. But even more important, of course, is now the clinical outcome that this specific mechanism of finerenone provides in patients with heart failure. And I'm now handing over to Maria to go into the data with us.

Finerenone: Key study results of FINEARTS-HF and FINE-HEART

Maria Borentain

Head of Cardiovascular and Renal Clinical Development, Bayer Pharmaceuticals

Well, thank you, Christoph. It is my great pleasure to share with you the most anticipated and highly positive results of FINEARTS-HF that was presented yesterday in hotline by Professor Scott Solomon from Harvard at the European Society of Cardiology Congress in London.

On slide ten, you could see the key elements of the design of FINEARTS-HF. That was a randomized, double-blind, placebo controlled, event-driven trial in patients with chronic heart failure and left ventricular ejection fraction of 40% or greater, also known as mildly reduced or preserved ejection fraction. The trial randomized 6,001 patients either to finerenone or placebo in addition to standard of care. The target dose of finerenone was 20 or 40 milligrams based on renal function. The primary endpoint of the study was cardiovascular death and total worsening heart failure events, which included hospitalizations for heart failure or urgent heart failure visits. Secondary endpoints included total heart failure events, a change in the Kansas City Cardiomyopathy Questionnaire or KCCQ, the total symptom score, a change in New York Heart Association, NYHA class, a renal composite endpoint and all-cause mortality. The appendix contains detailed information on patient population, including background therapy. And you might be wondering about SGLT2 inhibitors maybe. Of note, 13% to 14% of patients were on baseline SGLT2 inhibitors, reflecting the standard of care at the start of the study. Additional patients started taking SGLT2 inhibitors during the course of the trial with a bit more than a quarter of patients being on SGLT2s during the trial.

On slide eleven, you could see the primary objective. We are extremely excited that the FINEARTS trial achieved its primary objective. Finerenone significantly reduced the risk of the primary composite outcome of cardiovascular death and total heart failure events, but not only, reduced total heart failure events and improved patients reported health status in these patients with heart failure and mildly reduced and preserved ejection fraction. Importantly, it demonstrated consistency of effect across all pre-specified subgroups. Safety profile was in line with the well established safety of finerenone seen in previous trials.

So now let's go into more details, and on slide number twelve are the results of the primary endpoint. Finerenone significantly reduced the occurrence of the composite of cardiovascular death and heart failure events with a rate ratio of 0.84 corresponding to a 16% relative risk reduction with a highly statistically significant p-value of 0.007. *(*** Note: during the session, the additional comment "… and an absolute risk reduction of 3.3 per 100 patients-years." was made. The correct number is 2.8 instead of 3.3. This has been corrected on the slide and taken off the audio track. ***).* Of particular importance, when you look at the curves, you could see that the curves appear to separate very early and continue to separate over the course of the trial.

On the slide number 13, showed here are the components of the primary endpoint, the total first and recurrent heart failure events, which is also a key secondary endpoint, was reduced by 18% with a highly statistically significant p-value of 0.006. Cardiovascular death was numerically reduced by 7%. To put this into the context, the endpoint of cardiovascular death hasn't been powered for significance, and the reduction, it is in line with what has been seen with other effective therapies in this population, such as SGLT2 inhibitors.

On the next slide, on slide 14, the primary results were extremely consistent across the 17 pre-specified subgroups with no statistical evidence of heterogeneity, including in subgroups based on ejection fraction or whether patients were on background SGLT2 inhibitors. And you could find a totality of subgroup analysis in the appendix.

The slide number 15 shows the secondary endpoints. The total worsening heart failure events were reduced by 18% of relative risk reduction, highly statistical significant result, and a significant improvement in total symptoms score of KCCQ, a well validated patient reported outcome of feel and function and quality of life in patients with heart failure. We didn't see a difference versus placebo on top of standard of care in the improvement of the NYHA class, a more crude and maybe less sensitive physician assessed functional scale. There also was no difference in the renal endpoint. There was a numerically better all-cause mortality relative to this reduction, but it didn't reach statistically significance as the trial was not powered for mortality as we have discussed before.

On slide number 16, we could see the safety of finerenone. Overall, finerenone was well tolerated. There were similar number of serious adverse events in the finerenone and placebo groups. We saw more hyperkalaemia but the majority were without clinical consequence. Very few events of hyperkalaemia led to hospitalization and there were no fatal events due to hyperkalaemia, in line with the well established safety profile of finerenone from previous trials. In the same time, we saw less hypokalaemia with finerenone. And hypokalaemia, it's also related to increased risk of cardiovascular events, particularly due to its potential proarrhythmogenic effects.

Now in conclusion on slide 17, finerenone reduced the risk of primary composite outcome of cardiovascular death and total heart failure events, reduced the total heart failure events and improved overall health status in patients with heart failure with mildly reduced and preserved ejection fraction. The benefit appears early and the curves continue to separate over time. Findings were consistent across pre-specified subgroups, including across left ventricular ejection fraction and in those on SGLT2 inhibitors. Hyperkalaemia was more common, but hypokalaemia was less common in those receiving finerenone. And we are very confident that

these data support the use of finerenone in patients with heart failure with mildly reduced or preserved ejection fraction. The results were published simultaneously in the New England Journal of Medicine yesterday. We are planning a series of secondary presentation and publication at the upcoming medical conferences starting next week with the diabetes EASD Conference, then the Heart Failure Society of America, HFSA, and American Heart, AHA, later this year.

And now on slide 18, let me switch gears a little bit and talk about another exciting analysis we presented at this Congress together with our academic partners, the FINE-HEART analysis presented in hotline yesterday as well by Dr Muthiah Vaduganathan from Harvard. FINE-HEART is a participant-level pooled analysis of our three major Phase III trials with finerenone in patients with chronic kidney disease, FIGARO and FIDELIO, and heart failure with left ventricular ejection fraction of 40% or above, the FINEARTS, totalling about 19,000 patients. Pooling data in the FINE-HEART program increased the robustness to show the efficacy and safety of our non-steroidal MRA finerenone on important cardio-kidney outcomes in a patient population that sits at very high burden of cardio-kidney metabolic multimorbidity.

On the next slide on slide number 19, you could see the results of this pooled analysis. Firstly, what we could see again is a very consistent positive treatment effect across a wide range of clinically important cardio-kidney metabolic endpoints. While this pooled analysis didn't reach the pre-determined level of significance for cardiovascular death, and it actually barely missed the significance with a p-value of 0.076, this result was sensitive to the definition of cardiovascular death, as the pre-specified sensitivity analysis that consider deaths of undetermined causes to be cardiovascular death showed a significant reduction in cardiovascular mortality. Finerenone was associated with significantly lower all-cause mortality, a significant reduction in a range of cardiovascular events such as hospitalizations for heart failure, major adverse cardiovascular events, all cause hospitalization, significant reduction in kidney outcomes as well in an endpoint that has a big importance for physician, of new onset atrial fibrillation. Again, finerenone was well tolerated in line with its known safety profile. The results of FINE-HEART analysis were published simultaneously online in Nature Medicine yesterday.

On slide 20 now, in conclusion, FINE-HEART with its 19,000 patients represents the largest analysis of efficacy and safety of the non-steroidal MR finerenone across the cardio-kidney metabolic spectrum. Finerenone consistently showed benefits across a range of highly patient-relevant cardio-kidney outcomes, including all-cause mortality. Taken together, these results support the disease modifying potential of finerenone in a broad, high risk patient population encompassing cardiovascular, kidney and metabolic diseases. We would like to take the opportunity to thank all our investigators, the participants in the studies as well as our academic partner for these results.

And let me finish up on slide 21 by highlighting the ongoing MOONRAKER program of which FINEARTS was part of that will further strengthen the existing body of evidence by generating new data in patients with heart failure. Very briefly, REDEFINE-HF in patients hospitalized or recently discharged with a diagnosis of decompensated heart failure with an ejection fraction of 40% or greater, CONFIRMATION-HF in patients hospitalized with heart failure or recently discharged in combination with an SGLT2 inhibitor independent of the ejection fraction. And FINALITY-HF in patients with heart failure with an ejection fraction lower than 40%, so heart

failure with reduced ejection fraction, who are intolerant or not eligible for treatment with a steroidal MRA such as spironolactone or eplerenone. These three studies are currently open and enrolling patients, and we are looking forward to sharing the results with you as they become available. With that, I finish my presentation and handing over to Bernardo.

Kerendia: Building a true cardiorenal brand

Bernardo Kanahuati

Product Team Lead Kerendia, Bayer Pharmaceuticals

Thank you, Maria, and a warm welcome from my side as well. It is my pleasure to wrap up the previous presentations and provide an update on how we look at the great study results we've seen today from a patients, physicians and overall product perspective.

If we go to slide 23, I would like to start by highlighting that the successful completion of our Phase 3 study FINEARTS-HF represents a key moment for the patients suffering from heart failure with ejection fraction equal or about 40%, offering them new hope. And it's also a very special moment for the treaters that until now had only one option with proven evidence for this patient population. As mentioned before, multiple attempts took place to provide a new therapeutic option for these underserved patients, and failed. That is why we are very proud that Finerenone has shown significant evidence and becomes the first and only MRA to demonstrate proven clinical benefit in all patients with heart failure with left ventricular ejection fraction equal or above 40%. With heart failure, we'll now enter a market with substantial opportunities and significant unmet needs. We are talking about 50% of the 64 million patients across the world that live with this condition. The results of FINEARTS-HF position Kerendia in a unique way to become a foundational pillar of a multi-treatment strategy, finally unlocking the MRA pathway in left ventricular ejection fraction equal above 40%. This based on proven efficacy in a study with over 6,000 patients. In addition, the results of FINE-HEART presented by Maria consistently show benefit across a range of highly relevant cardio-kidney outcomes, including all-cause mortality, and confirm the well-established safety profile of finerenone.

If you go to the next slide, I think we can clearly say that Bayer is ready to continue maximizing the growth and potential of Kerendia. In our current indication for CKD in patients with type 2 diabetes, we've launched in 75 countries and hundreds of thousands of patients are already benefiting from this innovative therapy. Since launch, Kerendia has secured multiple international guideline recommendations across heart and kidney from prestigious organizations such as the American Diabetes Association, European Society of Cardiology and Kidney Disease Improving Global Outcomes, better known as KDIGO. All of them positioning Kerendia as a foundational pillar in the treatment of CKD with patients of type 2 diabetes. Entering the heart failure space marks an inflection point, for patients as it offers opportunities to improve highly relevant health outcomes, for cardiologists as it empowers them in their decision making based on proven outcomes, and for the franchise, as it not only provides a very significant standalone potential for Kerendia in this indication, but also offers the opportunity to unlock its full cardiorenal potential. We are working diligently to submit the regulatory dossiers to health authorities across the world, aiming to obtain the heart failure indication for this patient population studied in FINEARTS-HF as soon as possible. We are

determined to continue our growth trajectory with Kerendia and believe that for each indication Kerendia has blockbuster potential.

If we go to the next slide, I think it's a busy slide, but it shows us Bayer's commitment to fully maximize the value of Kerendia is well reflected in our ambitious development program FINEOVATE. This program is designed to continue expanding evidence on efficacy and safety of finerenone across CKD and heart failure. FINEOVATE is composed by two major programs, one in heart failure, MOONRAKER, that has been nicely explained by Maria, and another one in CKD, THUNDERBALL, that with six Phase III trials and one Phase II trial aims to consolidate the efficacy and safety of finenerone across a broader spectrum of patients suffering from CKD, including type 1 diabetes CKD, non-diabetic CKD and paediatric indication. Our development program will involve more than 35,000 patients across both diseases. And together with our real-world evidence studies, we'll guide clinical usage and we'll consolidate Kerendia as the leading non-steroidal MRA across heart and kidney diseases. Let us not forget that over 900 million people worldwide are living with CKD and heart failure. Many are underdiagnosed or poorly treated, facing them at significant risk or increased morbidity and mortality.

If we go to the last slide, in summary, the positive results of FINEARTS-HF is a major milestone for Kerendia and provides a strong evidence to enable a new foundational treatment option and brings new hope for more than 32 million patients suffering from heart failure with left ventricular ejection fraction equal or above 40% that for decades had very limited options with proven clinical efficacy to treat their condition. FINEARTS-HF and the pre-specified pool analysis FINE-HEART offer the next level of evidence in cardiovascular and renal protection and confirm the proven safety profile of finerenone. As we've seen, we have an ambitious development program in place to fully unlock the potential of Kerendia as the leading non-steroidal MRA to treat heart and kidney diseases. We are very excited about entering the heart failure space where Kerendia is poised to become the next foundational treatment pillar addressing an underserved patient population. We hope you share our excitement and follow closely the development of this innovative medicine. With this, I conclude my part of prepared remarks. And now I hand the call back to Thomas to kick-off the Q and A session. Thank you.

Q&A Session

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Thomas Kornek: Yes. Thanks so much, Bernardo and Maria and Christoph, for your great presentations. Before we start the Q and A session, some quick housekeeping items. As always, if you have a question, please click on the raise your hand icon. If your question has been answered or you wish to cancel your request, please click on the lower your hand icon. When you will be called to ask your question, you first have to unmute yourself by confirming the corresponding prompt that will appear on your screen. If you have joined the conference via telephone, the procedure is slightly different. Please press the star followed by the 9 on your telephone to queue for asking a question, and when you are being prompted to ask your question, please press the star followed by the 6 to unmute yourself. While there was also newsflow at ESC around other of our development programs yesterday, this webinar today is intended to focus on Kerendia. And as we have a total of three speakers in the session today, please indicate at the beginning whom you like to address your question to. Maria is obviously

happy to comment on our study related inquiries of FINEARTS-HF and FINE-HEART, Christoph is ready for your questions on the clinical programs, and of course Bernardo will cover commercial aspects. Lastly, I would like to ask you to limit your contribution to two questions so that we can accommodate more participants in this session.

That's it. And I see already the first question coming from Richard Vosser from JPMorgan. Richard, go ahead.

Richard Vosser (JP Morgan): Thanks, Thomas. Good morning, everyone. Two questions, please. First question, there was some discussion at the ESC yesterday about the combination use of finerenone and SGLT2s. So do you think physicians will accept the combination use prior to the CONFIRMATION trial? How do you think guidelines might change? Or do you think you need this trial to fully unlock the benefit of finerenone in heart failure? And then second question, a commercial question just on the DKD indication that's already there. Where is finerenone being used today? So is it being used in combination with SGLT2s? Or is it being used post SGLT2s? Or how is it being used in that indication? And what are the growth prospects there like in the markets? Thanks very much.

Christoph Koenen: Thanks for your question, Richard. Let me start with the first question. I think there's two aspects, in my opinion, that are very important. The first aspect is that heart failure, like for example kidney disease as well as hypertension, is most likely going to evolve in a field where combination therapy and our desire to have a maximum effect for patients' benefit will play a very important role. And that's why it's so important for us that when we talk about the FINEARTS-HF study results, we do stress the fact that a large number of patients in this study have been treated in combination with SGLT2 inhibitors. And we have in this study clearly been able to show that the effect that has been seen in the overall population has been preserved in the combination with SGLT2 as well. That is important because we do anticipate that the use of SGLT2s as well as Kerendia is going to emerge as an important cornerstone in the treatment of heart failure. And we do expect this to be appropriately reflected in the guidelines as well. Regarding your DKD question, I will refer to Bernardo.

Bernardo Kanahuati: Thank you, Christoph, and thank you, Richard, for the question. I mean, to a great extent our current indication, CKD Type 2 diabetes, now it's being used mainly by primary care physicians and nephrologists. And it's clearly showing a very nice growth. We believe that now with entry in heart failure, we will be expanding our broad population. Cardiologists will be much more interested. And I do see that the cardiovascular benefits that have been shown in FIGARO will be even strengthened by this new study. So clearly, to your question, it's nephrologists and primary care physicians, the ones that are using these in their CKD patients with Type 2 diabetes.

Richard Vosser (JP Morgan): Thanks.

Thomas Kornek: Okay. I see the next question coming in from James Quigley from Goldman Sachs. James, go ahead please.

James Quigley (Goldman Sachs): Great. Thank you for taking my questions. Hopefully, you can hear me okay. I have two, please. So firstly on the subgroup analysis by ejection fraction that you showed earlier, so the greater than 60% ejection fraction, the confidence intervals cross 1. But the point estimate was slightly below 1. So, how do you think this could impact use in this population? I mean, we saw in the Entresto label that there's a comment that says

that it works better in patients who have lower or slightly reduced ejection fraction. Is that a risk here that you can get a similar type of labeling? And the second question sort of related to that is on the guidelines. How quickly do you think the guidelines could be updated? Is there a risk the heart failure with preserved ejection fraction, i. e. greater than 60% or greater than 50%, could maybe not be included for Kerendia? How are you thinking about that given the data you've seen? Thanks.

Christoph Koenen: Let me start with your guideline question, James, before I hand over to Maria. I mean, when we talk about guidelines, I think it's always important for us to stress the fact that, of course, guidelines are done by scientific societies based on scientific evidence, yes? With finerenone, we have now been able to produce a significant body of evidence that supports the use of patients in mildly reduced as well as in preserved ejection fractions, and as I stated before, we do think that the evidence we have produced will be sufficient to be represented in a prominent way in the guidelines. And I do think that it's not only based on the evidence, that is of course based on the unmet need that we have in this specific patient population as well and that's why these results are so important. And Maria, could you maybe comment on the distinguishing between the 60% and above and below?

Maria Borentain: Right. So thank you very much for the question. There is, subgroup analysis is a tricky question because we are always tempted to look in details and see whether there are differences in different subgroups. Now there is a statistical method that tests exactly for that aspect. And that's the consistency of effect, it’s the heterogeneity of subgroups, and we are testing it with the interaction method, so a p-value for interaction. And we haven't seen any p-value for interaction that would hint towards a heterogeneity. So when looking into subgroups, you'll obviously, because there are, you know numerous subgroups that are tested, you will see a little bit of variation of the point estimate around what the primary endpoint has shown. But what we see in this trial is a remarkable consistency of effect between the subgroups with no interaction whatsoever. So the statistical analysis is a p-value that usually you want to be, in this case, non-significant compared to the results in the endpoints. And we haven't seen any significant interaction. And that is in stark contrast with what Entresto actually showed, that because you mentioned it, they have seen an interaction between ejection fraction lower than normal and preserved ejection fraction. So we don't think that regulators would look at it as different in these two types of ejection fraction, and we consider it to be extremely consistent.

James Quigley (Goldman Sachs): Great, thank you very much.

Maria Borentain: Thank you.

Thomas Kornek: Okay. I guess that brings us to Pete Verdult from Citigroup.

Pete Verdult (Citi): Yes, morning. Pete here from Citi. Thanks for the presentation and the great data. Just one question, maybe to Bernardo or the whole panel. Just if we think about how heart failure is going to develop over the next 1 to 2 years, high likelihood we'll see the GLP-1 class come through with heart failure on the label. Now, I know IRA probably limits out of pocket costs, but I would be interested in your thoughts about are we really going to see a situation where the standard of care becomes GLP-1, SGLT2 and MRA or do you see docs going to one or two of those drug classes, just looking at about the commercial outlook when you bring GLP-1 into the equation as well? That's an open ended question, but thanks, would be interested in your thoughts.

Bernardo Kanahuati: Yes, thank you for the question. You were breaking up, so I hope I got the question right. And I would like to start by, you know, reminding the potential of finerenone in both indications we have, in the current indication we have in CKD type 2 diabetes and in the potential heart failure field indication. We're talking about almost 900 million that are suffering from comorbidities. You've alluded to different alternatives to treat them. And today, Kerendia has proven in FINEART-HF the clinical benefit for these patient populations of patients who have HF with a preserved ejection fraction equal or above 40, which it's a substantial number of patients, it's 32 million patients across the world. Many of these patients, as we saw also in FINEARTS and also in the pooled analysis of FINE-HEART, have comorbidities. And again, finerenone has shown that independently of background therapy has the same level of efficacy. And I think that's really important to remember. So we do see that Kerendia as a clear foundational treatment pillar, both in CKD and in heart failure with preserved ejection fraction. Now clearly, there's a very dynamic market, and we talk more and more about the cardio-kidney metabolic syndrome, and I personally believe that Kerendia should become a key pillar in the treatment of these two diseases. So I hope that answers your question. And I don't know if Maria or Christoph want to add something on top of it.

Christoph Koenen: Yes. Maybe let's just make one more comment, of course, where we see the treatment landscape in heart failure evolve, yes? I mean, it is a large patient population. It's a large diverse patient population. And that, again, stresses the importance of combination therapy. And of course, because of its unique mechanism of action, finerenone is really a great combination partner for other treatment interventions as well.

Pete Verdult (Citi): Thank you.

Thomas Kornek: Thank you, Pete, and thanks, everyone, for answering the question. That gets us to Kritika Kalia from Berenberg. Kritika?

Kritika Kalia (Berenberg): Hi, there. Thank you for taking my questions, two, if I may. My first question is about the arrival of two generics of Entresto. Do you think that this could impact the adoption of Kerendia in some countries? And the second question was looking at the primary outcome in patients with eGFR below 60. Given that Kerendia is approved in CKD patients with type 2 diabetes, do you have any kind of explanation for why the primary outcome confidence interval crossed 1 for these patients? What could explain this discrepancy? Thank you.

Christoph Koenen: If I may, Kritika, you broke up at the beginning of your question, so I missed that part, what class of drugs you're talking about. I think you're referring to SGLT2, but I'm not sure.

Kritika Kalia (Berenberg): It was Entresto, sorry.

Christoph Koenen: Entresto, okay.

Kritika Kalia (Berenberg): Yes.

Christoph Koenen: So let's maybe start with the second question regarding the confidence interval, Maria, and then go to the Entresto question.

Maria Borentain: Okay. So well, thank you very much for the question. Again, you know, looking in subgroup analyses, we did see that many of the subgroups cross the unity line and that's usual in subgroup analyses because subgroup analyses are not powered to be statistically

significant. When we look at subgroup analyses, again, we look at the consistency of effect. We do this interaction analysis, a statistical method that will give us a hint whether we have a completely different, unexpected result in one of the subgroups. So we are looking, of course, because Kerendia is indicated in CKD, we are looking at patients with lower eGFR and those with normal eGFR and we'll be publishing these results very soon. It's one of the pre-specified analysis that we will do, and you will see more data coming very soon about the efficacy of Kerendia in these two subgroups, more details. But so far, what we could say from the subgroup analysis is very consistent in both subgroups, both below 60 or above 60 of eGFR.

Christoph Koenen: And maybe regarding your Entresto question, I think, again, it's important because I think Maria already highlighted that in one of her previous answer, yes, that of course what we have presented here with Kerendia is a robust outcome in a pre-specified, that's the majority of the heart failure population, patients with mildly reduced and preserved ejection fraction, yes? The evidence base for the use of Entresto in these patients is shaky. And therefore, we do think that the role that Kerendia will play in the treatment of in this patient population will be significant.

Kritika Kalia (Berenberg): Thank you very much. Thank you.

Thomas Kornek: Okay. I think we have currently no further people in the queue to raise questions. I got some upfront from Harry Sephton from UBS, actually pointing to the subgroup analysis, whilst underpowered, showed weaker efficacy in patients older than 73 than those younger. Do you think this warrants further investigation? Or could this be an issue with regulators? And another one, and pointing to the same direction, do you think the limited data in some regional subgroups could be an issue in getting approval in some markets?

Christoph Koenen: Maria, why don't you take one?

Maria Borentain: Yes. So again, coming to the subgroup analyses. So I would like to remind again the importance of the consistency of the effect, the remarkable effects that we see across all pre-specified subgroups that we didn't have any subgroup, actually, in usual clinical trials, you would see subgroups that will go completely in the wrong direction, we don't see that. So everything is on the right direction. And again, because of the number of analyses, the point estimate will vary a little bit across subgroups. It doesn't mean that they don't have the benefit, it's only an artifact of the statistical analysis due to multiplicity of analysis. So of course, we will look in all subgroups and we'll try to understand better. And many of the subgroup analyses actually are in the planning, and you will see more coming. As I said, we have a number of publications and presentation that will be coming at upcoming congresses this year, starting next week with the diabetes conference in Europe and following with HFSA and AHA, we have quite a number of publication. And some of them are taking into account these questions that you have about the subgroups.

Christoph Koenen: And if I may, of course, it's like almost always in these large trials, that we see slight differences between some subgroups, yes? And obviously, we're used to present these kind of data to regulators and we're confident that they, of course, will interpret the consistency of effect that we see across these subgroups, such as different age subgroups, the same way we do. And we are therefore confident that we will get an appropriate label for the treatment in patients with mildly reduced and preserved ejection fraction.

Thomas Kornek: Okay. Thank you. I think we got another question from one of our live participants, Sachin Jain from Bank of America. Sachin?

Sachin Jain (Bank of America): Hi, there. Sorry, good day. Sachin Jain here from Bank of America. Just a big picture commercial question, if I could. So I think in recent calls, Stefan's talked about the CKD launch potentially plateauing earlier than expected. And it's not clear that you've got the share that you previously aimed for. So my question is basically what learnings can you take from the CKD commercialization you can apply to heart failure? So is there anything on price, positioning versus SGLT2, size of sales force? Or any other factors that you can point to that can impact launch beyond the quality of the data, which is also strong for CKD? Thank you.

Bernardo Kanahuati: Thank you, Sachin. So let me start probably by saying that we do see heart failure as a new launch. Entering the heart failure space is going to be really exciting for us. It's a population that until today has been underserved. There is a really high interest from the cardiologist community to learn more about this. There was a lot of excitement at ESC when the data was presented. So we see really the high potential to become a foundational treatment pillar in heart failure with preserved ejection fraction. Now in regards to CKD, I think it's important to underline that we're so highly confident in the product profile and value proposition and, you know, the uptake of the launch and the trajectory of the growth makes us confident that this product in this indication will become a blockbuster as well. So more than anything, the fact that now that we're entering the heart failure space will even strengthen our already proved cardiovascular benefit in FIGARO and will have a, to my point of view, a higher degree of adoption in those prescribers that today will start getting more acquainted with our product. So clearly really excited and for both CKD Type 2 and for our potential future indication heart failure.

Sachin Jain (Bank of America): Thank you.

Thomas Kornek: Okay. The next question comes from James Quigley again from Goldman Sachs. James, go ahead please.

James Quigley (Goldman Sachs): Hello. Thank you for taking my follow-up. It's along with similar lines to Sachin's question in terms of the commercial outlook for finerenone or for Kerendia. So in terms of the heart failure of preserved and minimally reduced ejection fraction markets, is there any off-label use of MRAs as it is today? And do you have an estimate of what that is? And could that then be a sort of quicker route, I suppose, for switching patients on to MRA and the commercial opportunity there? And then secondly, in terms of the SGLT2 penetration, do you have any sort of estimates or best guesses as where we are with SGLT2 penetration in heart failure, the ejection fraction market or the markets you're looking to penetrate as again that might make the CONFIRMATION heart failure trial a bit more important as well on that side?

Bernardo Kanahuati: So I hope I understood your question. You broke up a little bit, can you repeat your first question, James, please?

James Quigley (Goldman Sachs): So it's just to what extent is there any off label use of any of the other MRAs today in these indications? And could that be a potential easy switch for some physicians that are using those drugs off-label, if at all?

Bernardo Kanahuati: I mean, if you're talking about reduced ejection fraction, I think there's data that points that there's some degree of use of MRAs, of steroidal MRAs in this indication. And the preserved ejection fraction, the only MRA that has shown improvement in clinical efficacy today in FINEARTS, it's finerenone. So I think I cannot speculate how the treaters will look at these, and of course, we do not promote off-label use. So clearly, the robustness of our cardiovascular profile will make much more adoption in cardiologists that want to prescribe for patients that have also type 2 diabetes CKD. So that's what we expect now to see a greater level of adoption in our CKD Type 2 diabetes 2 indication. And you had a question about the SGLT2s penetration, which also I didn't fully get.

James Quigley (Goldman Sachs): Yes. So just do you have an estimate of where we are in terms of the SGLT2s currently? What percentage of patients or what's the penetration so far for the SGLT2 class in heart failure with preserved ejection fraction? Again, just sort of thinking about the combination use and how important CONFIRMATION-HF trial could be? Or is there still a number of patients who are just not very well treated at all with anything and that could be the sort of the key initial market that you could target?

Bernardo Kanahuati: Yes. I don't have the data about penetration, but I think what we can clearly say is that in the data we've seen, it was clear that regardless of the use or not of SGLT2s, finerenone showed a very consistent level of efficacy. So clearly, as I think already mentioned by Christoph, finerenone, it's a drug that can be securely and safely combined with one of the other pillars in treatment therapies. So I guess that's a benefit that was clearly established in FINEARTS.

James Quigley (Goldman Sachs): Got it. Thank you.

Thomas Kornek: Okay. And I think we have some more time also for a follow-up from Richard, Richard Vosser from JPMorgan.

Richard Vosser (JP Morgan): Thanks, Thomas. It's just one question on hyperkalaemia. So …

Christoph Koenen: You're breaking up, Richard.

Richard Vosser (JP Morgan): Okay. Hang on a second. I think I just got out. Can you hear me now? Apologies.

Christoph Koenen: We do. Yes.

Richard Vosser (JP Morgan): Okay. Perfect. Sorry about that. It was on hyperkalaemia. So the first part of it is, to what extent has hyperkalaemia been a barrier for use in DKD? And then some of the data, I mean, there was still hyperkalaemia in FINEARTS, but part of the discussion was on hypokalemia actually at ESC. And I wanted to understand from your side how much of a benefit that is and how much a marketable benefit that's going to be for you in heart failure and how receptive the doctors were to that risk and the reduced risk that you showed?

Christoph Koenen: Maybe I'll start and then I will ask you, Maria, to maybe talk about it a little bit as well. So I think what you're referring to was a discussion that one of the discussants raised about an increase in mortality both for hyper- but specifically for hypokalaemia, yes? And that is, of course, something that is discussed in the scientific community and that treating physicians are aware of. So we do consider the benefit when it comes to seeing less

hypokalaemia than placebo in our clinical trial, we do consider this clinically relevant and as something that will influence a treatment decision of a health care professional. Maria, do you want to elaborate a little bit?

Maria Borentain: Well, I think what I would add to that is that indeed physicians are sensitive to both ends, hyperkalaemia and also hypokalaemia. What we see, it's a slight increase in hyperkalaemia, as you've seen. So usually, we, in all our trials, we have shown that finerenone actually doubles the rate of hyperkalaemia, but the majority are without clinical significance. But the good result actually from this trial is to see how much we decrease the risk of hypokalaemia, and that will warrant further investigation and further publications, for sure, to understand both ends of the spectrum. But we see the slight increase in hyperkalaemia, which is manageable. Hypokalaemia is manageable as well, but it's very much a risk for further cardiovascular events. So for sure, something that we'll dig into, and I'm sure you will see some publications coming up.

Richard Vosser (JP Morgan): Thanks.

Thomas Kornek: Okay. I guess we are reaching the end of today's webinar, and I'm also seeing no further inquiries in the queue. So I guess with that, that concludes our program for today. I'd like to thank all of you for your participation. We hope you enjoyed this event and found it useful. Have a great day and goodbye.

Maria Borentain: Thank you.

[END OF TRANSCRIPT]