Christoph Licht: Hello, everybody. Good afternoon from Toronto. This is Christoph speaking. This is the beginning of the COVID-19 and aHUS live webinar. Within the next 60 minutes we'll go through some basic information on COVID-19 and answer questions that were either pre-submitted or can be posted throughout this webinar relating to the impact of COVID-19 on patients with atypical HUS. I'm joined by a panel of various experts from the medical field, who I'm asking to introduce themselves at this point. Gema?

Gema Ariceta: Yes. Good evening, good morning everyone. I am Gema Ariceta, pediatric nephrologist working in Barcelona at the Hospital Vall d' Hebron.

Christoph Licht: David?

David Cohen: Yes, hello, everyone. I'm David Cohen, I'm an adult nephrologist, and the medical director of the kidney transplant program at Columbia University in the US and state of New York. Welcome.

Christoph Licht: We were hoping to have Nicole Isbel on the call in the webinar, as well. She might join us slightly later.

Christoph Licht: I mentioned my name already, I'm Christoph Licht. I'm a pediatric nephrologist working at the Hospital for Sick Children in Toronto. Eric?

Eric Rondeau: Yes, Hi everybody. I'm Eric Rondeau, I'm working in hospital Tenon in Paris. I'm an adult nephrologist.

Christoph Licht: And Marie? So, we lost Marie at this point. Very sorry, but she will hopefully join soon. She is an adult hematologist from London, UK.

Christoph Licht: The purpose of this webinar is to bring a group of experts from the adult and pediatric nephrology and hematology areas together, who are either directly involved in the care for patients with aHUS or care for in other ways patients with complement-mediated TMAs. We are colleagues on the scientific advisory board of the global atypical HUS registry, which is an Alexion-sponsored international database. Like our colleagues, we have only limited specific knowledge about COVID-19 altogether, in particular its impact on patients with atypical HUS. However, we acknowledge that there's a very concerned community out there with whom we want to share our insights and experience. Also, as I mentioned already, we wanted to provide a platform for individual questions to be addressed.

Christoph Licht: There's a couple of disclaimers that we want to make again. The information and opinions expressed in this presentation and on the following slides are solely those of the presenters. If you have questions about your personal health, please speak with your physician. And we kindly acknowledge the technical assistance that Alexion provided in organizing the webinar, but we want to clearly state that Alexion had no and has no influence on its content.

Christoph Licht: A couple housekeeping pieces of information while you are seeing and hopefully hearing the panelists. As a webinar participant you can only see our faces, listen to us and see the slides, but we cannot hear you. Questions that you want to bring forward were either pre-submitted, or you

can submit them now in writing during the webinar by clicking on the Q&A button. The webinar is limited to 60 minutes, but it will be recorded and will become available online in the near future, in collaboration with patient advocacy groups.

Christoph Licht: A couple of basic facts about the COVID-19 pandemic. As you all know, by the end of December 2019 this new virus originated somewhere in mainland China in the Wuhan area and spread from there since then westwards, kind of covering by now almost all areas in the world. On the North American continent, as I said I'm talking from Toronto, we're still anxiously awaiting the tidal wave to hit here.

Christoph Licht: As you can see on this screenshot from the tracking site of patients with confirmed infections, deaths and so on that's from the Johns Hopkins University, this is taken from four hours ago today. There's today just short of 400,000 total confirmed infected cases and more than 17,000 patients who died from COVID-19 worldwide. As you have probably by now all learned the transmission of the COVID-19 causing virus happens from person to person through respiratory droplets from coughing and sneezing, but it can also be spread by airborne transmission when tiny droplets remain in the air, even after the person has left the area. The diagnosis can only be established in the laboratory. With an incubation time of up to 14 days, the main symptoms of COVID-19 are dry cough, fever and shortness of breath. Some and also point towards the loss of your smell and your taste buds' function for some time.

Christoph Licht: The best way to protect yourself are those basic rules of hygiene and isolate social distancing: frequent and thorough handwashing; coughing or sneezing into your tissue or elbow; avoiding to touch, eyes, nose, mouth, any mucous membrane surfaces with unwashed hands; distancing from patients who are sick and social distancing by isolating yourself staying at home; and then measures of hygiene with cleaning and disinfection. Face masks are still debated and are recommended if they're available.

Christoph Licht: With that we're reaching the point where we start addressing questions that were submitted to be addressed in this webinar prior to the occasion. We organized a whole flurry of questions that came in in 18 overarching topics. The first 10 you see here on this slide. We'll start addressing amongst the panelists the first five of those, and then turn it over to you, and either address questions that come in live or continue addressing the questions you can see here on the slide. So, with that first question, I do want to address: am I more at risk to develop COVID-19 because I have aHUS? And that's in the background of being treated or not treated with Soliris/Ultomiris. Which of the panelists wants to address this question? Gema, do you want to start?

Gema Ariceta: Okay. Well honestly, we don't know. We don't know the specific risk. But as far as I know, in Spain there has not been cases reported of COVID-19 in aHUS patients, nor treated with Soliris or with Ultomiris, as well. You know that in Spain we are in a difficult situation with about 40 thousand diagnosed patients. And I can tell you that despite that, no patient with aHUS has developed the disease, as far as I know. So I think as any chronic condition, those who may have chronic kidney disease or cardiovascular disease, may be at some kind of higher risk, but our experience with children is not

that, and I see, please correct me if I'm not taking the correct information my adult colleagues, that cardiovascular disease and respiratory disease, AIDS, seniority and obesity are the major risk factors.

Eric Rondeau: A word for adult patients. So similarly, in France, we have quite a significant number of patients with the COVID-19 infection, and to date we have no cases of atypical HUS having COVID-19 infection. So, it doesn't seem that for this small population it's a significant risk, but I think we have to wait because there is a very small number of patients with atypical HUS in France. The cohort is maybe around two to three maybe 400, and it's difficult to compare but still we don't have a case today. I want to add that patients who are treated by Soliris or Ultomiris may be at risk for a specific bacterial infection, like meningococcal, but not specifically for viral infection, at least if we look at the registry during the last years.

Christoph Licht: Maybe I can add to that. Some of you might have visited the website of the central place in Newcastle for the NHS in the UK: the expert center for complement-mediated diseases, atypical HUS and C3G. They have on their website information on risk level and precautions for atypical HUS patients. They state that as we have just heard from both my colleagues that at the moment there's no data to identify patients on complement blocking treatment with eculizumab (Soliris) or Ultomiris to be at a higher risk, but they advise that neither are the identified patients with atypical HUS per se at a higher risk. But they advised to be extra alert. That's basically the summary of the message that they send out. David, do you want to comment?

David Cohen: Well, I would just second what Dr. Ariceta said that in the absence of any cardiac or renal disease or the other risk factors that as far as we know, atypical HUS is not going to add to the risk in terms of the treatment with complement blockade. The role of complement blockade in fighting viral diseases is not something there's a huge amount of data on, but I would say, what does exist, and certainly we don't know that much about anything specific for COVID-19, most of the data would suggest that does exist in the role of complement in viral disease does suggest other parts in the complement pathway may play a role. So that I think there's some level of reassurance. But again, we just don't have a lot of data to really give firm answers to these questions.

Christoph Licht: Right. Thank you. Can I just make sure that we have Marie Scully on the on the webinar for now?

Christoph Licht: We're looking forward to also seeing your face again. Maybe while we're awaiting that we can move to the second question. Which is one that is on many people's mind. What is the difference about the signs and symptoms of COVID-19 in children versus adults? Maybe also a pediatric and an adult's voice will be great.

Gema Ariceta: I can tell you our experience. We do not know the prevalence of the disease because we are not testing everyone, but in children it looks like a very mild disease if they have it, and less than 1% of admitted patients are children. Even those who are tested because of mild respiratory of fever symptoms, if they are being tested it's because of an underlying disease. We have a patient with a kidney transplant, and we could send the patient home because the patient was doing great. This is our experience. We only had three kids admitted and they have a milder disease.

Christoph Licht: Eric or David?

Eric Rondeau: Yeah, in adult patients, the disease can be very severe and now in the intensive care unit in my hospital there are around 30 patients who need to be ventilated and are in a very dangerous situation. So, in adults, it can be severe, and at the beginning we believed that it was for the eldest, but actually now it's in patients who are around 50 years of age, for example. They have a very big fever and inflammatory syndrome. They have, of course, pulmonary signs. But at the beginning, they may have some diarrhea without any fever or pulmonary signs and it's very unusual or strange, and they have, as you said, the possible anosmia where they lose their smell and also their taste and we have to listen to the patient talking about this. So, I'm talking about patients who are not so old and not so much with associated cardiopathy or nephropathy and so on. So, I think the picture in adults can be severe even in the absence of co-morbidities.

Christoph Licht: David, do you want to add anything?

David Cohen: No, I think that the general evidence is that the diseases generally, as Dr Ariceta said, is milder in children and young adults, not exclusively in terms of the signs and symptoms. I think we're still learning about what the full range of signs and symptoms of the disease are. The loss of a sense of smell and loss of sense of taste are something we all only learned about it within the last several days, and the sense that diarrhea may be a presenting illness is also relatively new. So, there may be more things to come that might differentiate children or adults.

Christoph Licht: Yeah.

Eric Rondeau: What I can say, also is that we, to the best of my knowledge, don't have evidence of even mild thrombotic microangiopathy in these patients. They have fever. They have inflammatory syndrome. But we don't have evidence to date of TMA.

Christoph Licht: Maybe I can just take the first shot at the third question: what do you advise if a child with aHUS show signs of infection during this pandemic? So, in principle, nothing has changed compared to what you were advised in the past. We have no firm evidence that this particular infection would increase the risk or come without risk to trigger an atypical HUS flare. So, any infection should be monitored closely and should be addressed in the appropriate ways. So if there's any suspicion it could be COVID-19 or SARS-CoV-2 infection, then appropriate measures and according measures should be put in place, but nothing extra other than monitoring for signs of atypical HUS activity as you would have done with other infectious intercurrent illnesses or events as well. Maybe my colleagues wanted to add to that? Any additional comments from my colleagues or can we leave it at that?

Gema Ariceta: I think as usual, if you have symptoms or you have a fever: talk to your doctor. It's also very important before arriving to the hospital in case that you may have COVID-19, try to, in advance, communicate with the hospital, or at least when you arrive, to prevent spreading the virus. It's very important. So, if your healthcare professional is saying that you may have COVID-19 symptoms it is also important to keep the place safe for the other patients as well.

Christoph Licht: Okay, and related to that, what additional preventative measures, the fourth question for COVID-19, should I take because I have aHUS compared to the general population? Again, in the background of being treated or possibly treated with Soliris or Ultomiris.

Eric Rondeau: I can try to answer this. In our center we carry on the treatment, we do not stop the treatment during the epidemic. And it seems very important not to stop the treatment because of a risk of a potential infection, and as we said before, probably even with a viral infection there is no specific risk due to the eculizumab in this context. So, all the patients with atypical HUS should follow the preventive measures for COVID-19, of course. But this is like in the general population, and they have to carry on their treatment and I've no other advice to give.

Christoph Licht: Right.

Gema Ariceta: Yes, we are also keeping the patients on treatment. The only general measures that we have adopted, and it's not only for at the hospital, we are very strict with distance between patients and also try to avoid healthcare professionals. We are tracking who is exposed. So, all these things are very important. Also trying to protect one patient from the other. We are more strict than usual, but otherwise we are we are giving the same treatment to everyone.

Christoph Licht: Perfect. This kind of leads to a next question that, at least in the medical fields made a lot of noise, which was the role of treatment with angiotensin converting enzyme inhibitors, ACE inhibitors, or the angiotensin receptor blockers, ARBs, in patients, and whether treatment with that or not, would create or define an extra risk to be susceptible for COVID-19? Does anybody want to comment on that?

David Cohen: I could comment on that. So, I think certainly the statements by the CDC and others have been quite clear that the evidence is really lacking to make any firm recommendation about the use or changing from ACEs or ARBs as antihypertensive therapy. And at the moment, I think there is no reason that people should be switching. Obviously, if they are switching to other antihypertensive medications because there are problems in terms of kidney function or other reasons why one of those medicines should be discontinued, of course, they should be discontinued, but the data that they actually worsen the course or have any impact one way or the other on the course of COVID-19 disease is really lacking at this point.

Christoph Licht: Alright. Any other comments?

Marie Scully: So, we've had statements from the British Society of Heart Failure and the British Renal Association regarding not stopping ACE inhibitors, because there is a lack of evidence.

Christoph Licht: And I can echo that, for at least pediatric nephrology side. Various overarching national and international organizations basically stated exactly the same for the pediatric age group as well.

Christoph Licht: Alright. Maybe at this point, we should, as promised, take a look at questions that came in from our listening audience, and I just pick one that is extending the scope of topics to include kidney transplantation. So, I just read as it stands here: I have aHUS. I had a kidney transplant in 2016 I have a

child who I had when I was on dialysis. My current doctor is very adamant that I cannot have any further children due to the fact that I take mycophenolate. Spoken to the National Kidney Foundation and done my own research and have found that to not be true in men, but in women who take that medication. Do you have any advice on this topic? Obviously I didn't read through, this is not a COVID-19 specific question, but maybe we can address this anyways?

David Cohen: Yes, well, sounds like it falls into my area. So, it's very clear that there's a risk of congenital malformation for a woman who's taking mycophenolate during pregnancy. There has not been great data on mycophenolate use for men fathering children. It is recommended that they be off mycophenolate, if possible. I think we have to stick with that recommendation even knowing that the data is weak to support it, but it's a precaution that sounds prudent for people to take.

Christoph Licht: Alright. Any other comments?

Marie Scully: But there are other immunosuppressives for which there is some data and mycophenolate definitely not through pregnancy in any condition that requires immunosuppression, but tacrolimus, I believe there is some data. I'm not suggesting that patients should change their therapy because it's not without risk, but there may be alternatives, but that is very much dependent on the transplant physician.

David Cohen: Yeah, I should add, in this situation, I would consult with your physician about the safety and advisability of a change in the immunosuppression. There may very well be alternatives. Thank you, Marie.

Christoph Licht: Alright. Maybe we move on for now with question number six. Again, if I get COVID-19, what should I do differently, compared to the general population? Background treatment with Soliris or Ultomiris. I think Eric, you have addressed this already, in a way, and Gema, but maybe you just want to restate?

Eric Rondeau: Yeah. To date we don't have evidence that a patient with atypical HUS represents an at-risk population for COVID-19 infection, and also, we don't have much evidence that the complement system is important to kill the virus or to predispose the patient to viral infection. So, my guess would be that patients, if they are infected, would have the same kind of disease. Just to mention this, but it's very recent, it appears on the clinicaltrials.gov that there is a proposal for trial of eculizumab in patients with the COVID-19, suggesting that blocking the complement would decrease the inflammatory response I was talking before, especially in the lungs. So, I don't think, first that the signs of the COVID-19 infection would be different as compared to the general population. And second, I say again that the patient should not stop eculizumab treatment during the epidemic.

Christoph Licht: Yeah, maybe I can just footnote what you just said. Touching on this trial. Since there seems to be some interest amongst the audience, whether that means this trial, the fact that the trial is ongoing means that we should consider eculizumab being basically a prophylactic treatment or something that puts us into a safer place towards infection. And to the best of my knowledge, and I'm happy for you to add your point, this is way premature. This is a trial, it's ongoing, there is no evidence

and we cannot state anything to that effect that eculizumab would be a prophylactic treatment if you want.

Eric Rondeau: Absolutely, absolutely agree with you.

Marie Scully: And furthermore, there's over 300 drugs that have suddenly become interesting in the COVID-19 short era which are going through very quick clinical trials. So, it's not just, you know they're looking anything that could impact on the immune system.

Christoph Licht: Right. I think my knowledge is that there is repurposing of some drugs that are used for specific infection. For example, the anti-malaria medication, that's something people are talking about. There are antiviral drugs that people are using, and then there's obviously a combination with antibiotic treatments that are used. And then, of course, other organ involvements need to be addressed if the lungs are affected by ARDS, then steroid treatments. So, this is kind of a list of medications. Maybe with, in principle, modern antiviral treatments being the lead of what people hope to develop in terms of being successful. But again, please add to what I just said.

Eric Rondeau: Yeah. Can I add something about the recommendation for the general population? And I think it's also for the patient with atypical HUS. We do not recommend to use high-dose steroid and anti-inflammatory drugs in patients suspected with COVID-19 infection. It seems to be a risk factor for severe lung disease.

Christoph Licht: Yes, and I forgot, obviously, this group, which is the suppressed inflammatory reaction group of drugs. That's the other one, the IL-6 blockers, for example. Any other comments at this point, please?

Gema Ariceta: Yes. Can I add one comment? Of course, in the case of very severe disease in a treated patient, it's case by case. We recommend when you may be very sick that the patient's physician should consider the underlying treatment, but not if the patient is not very sick. But of course, if an aHUS patient got really very sick, I think you should consider adjusting the underlying treatment, but we don't know because so far, we haven't had any case.

Christoph Licht: Well, and that kind of leads then naturally to the next question, which is basically the other side of the same coin, and we touched on it already earlier: is COVID-19 theoretically a trigger for TMA relapse? And is the risk for that different being on Soliris or Ultomiris or not?

Christoph Licht: So, I'm on record already having said we don't have evidence for that, but maybe my colleagues want to comment on that?

Marie Scully: I think that we need to be mindful that any infection potentially can either instigate or trigger a TMA relapse. But it doesn't mean every infection will do that. So last year, in particular, influenza A was within our group more prevalent in aHUS patients in causing maybe a mild reduction in counts but less so in patients on treatment or precipitating acute disease. I think given the number of cases with COVID-19 and many countries have not seen cases it doesn't mean that there's so far, thankfully, an association with severe TMA relapses and it may well be that having a milder version of

the infection, particularly as many patients are not high-risk, will not result in a frank TMA relapse. It is a very unpredictable science in aHUS, and infections causing acute episodes or sub-acute episodes.

Christoph Licht: Alright. Any other comments? I think the next couple of questions are also really of high interest to our audience referring to the risk of meningococcal infections. Do I need to get re-vaccinated from meningococcal infection because of COVID-19 or in the context of COVID-19? And the other question, which is also really touching on a very interesting aspect, the vaccination against pneumococcal infection in the background of COVID-19? Who wants to comment? Maybe the second one is more for David? But, you know, whoever wants to take.

David Cohen: Well, I think we don't know that there's a higher risk of meningococcal infection in the setting of COVID-19. I don't think it's; I haven't seen any data that would suggest that, that one specifically get revaccinated because of this. I think all patients on a complement blockade treatment need to attend carefully to their prophylaxis against meningococcal infection and make sure their vaccinations are up to date, or if they're on oral antibiotics, to continue that. But I don't know of any data that would suggest that specifically a re-vaccination is needed at this time.

Christoph Licht: Any other comments?

Eric Rondeau: I agree with David where we don't have evidence that we need to perform a new meningococcal infection vaccination. It's important that the patients on eculizumab treatment are vaccinated just before to start the treatment, and then in France, we recommend to perform again the vaccination every three years. I don't know if it's the same everywhere, but that's our recommendation for meningococcal against different serotypes and including the B serotype, which is more frequent in France. And also, we recommend the patient take oral penicillin every day during this treatment.

Christoph Licht: The vaccination protocol for patients in Canada would be almost exactly identical, except for the fact that we would re-vaccinate only every five years, but we would cover the same serotypes and we would also combine immunization and antibiotic prophylaxis. And we would not, just to add this, at this point we don't see either a need to re-vaccinate patients in this particular situation. But the next question maybe might be some interest as well. The vaccination against pneumococci. So my limited knowledge here is that some countries, and my home country, Germany, included, recommend this vaccination for patients or for individuals older than 60 years, and as a little bit of a nuance, the German Chancellor is currently in quarantine since she, as you know, an individual qualifying for this age group, received this pneumococcal vaccination, but from a positive view, testing physician. So, she's well testing negative, but she's in quarantine at the moment, but that basically exemplifies that that is practiced in some countries for some age groups. I have not seen this in action here in Canada, and I would not be aware of any recommendation for other risk groups, in particular for children, but maybe my colleagues can comment on that as well. Please.

Marie Scully: Well the children get pneumococcal vaccine now standardly in the UK.

Christoph Licht: Sure, but in addition to their standard vaccination protocol. That's what I mean.

Marie Scully: Other than other areas where they've got hypersplenic features, such as aHUS, but otherwise, no, we wouldn't use it.

Gema Ariceta: I think we all have treated patients with updated vaccinations, but any situation is a good time to recheck that everything is updated. All of them are vaccinated against pneumococcal.

Christoph Licht: Right. Any other comments? Right, and then I think we have touched on the last point already. The last question on this page. Has anyone with atypical HUS contracted COVID-19 to date? Any of my colleagues aware, would any of my colleagues, be aware of one of those cases?

Marie Scully: No.

Christoph Licht: I'm not either, but, you know, here we have to disclaim we could be wrong; this could just be a lack of information so that the audience is clear on that. There is one aspect.

Eric Rondeau: Sorry, Christoph, just a comment. Is it because we don't have the information or because of the still low incidence of the disease? Because if, for example, it's 60,000 patients in France who have the COVID-19 that is one out 1000 of the population. And I told you that we have in France around 400 patients with known atypical HUS. So, one out of 1000, it's difficult to have a conclusion about the statistics. They don't seem to be at risk. We don't have a single case, but we have to wait, I think.

Christoph Licht: Yeah. I think that's a very, very important point. And again, this adds to the disclaimer of our limited knowledge. It's just, even though it has turned our life upside down, it's still very early days in terms of learning about this disease.

Christoph Licht: There's a very practical question that came in from the audience, which refers to access to eculizumab. And there's, to my understanding, two aspects to that. One aspect would be the company's capability to provide drug and to the best of my, to our, knowledge. This is a given that there's no foreseeable or current issue in terms of providing patients with drug. However, neither of us would be in a position to predict what impact this pandemic will have on delivery of goods across borders, and that is out of our control and out of our knowledge. So, we can't comment on that. But we were told, since we were preparing for this question, by Alexion, that there is no current or foreseeable shortage of drug to be provided to patients from the company side.

Gema Ariceta: Yes, also a reminder that there is a closing for free movement of people, but deliveries and supplies are still being transferred and transported. So just to make clear it is a limitation for the general population.

Christoph Licht: Right. Excellent. I'll move on to the next set of questions. Well we addressed without having remembered the first one already. Next one. What do you say to someone with aHUS who is working the front lines? Doctor, nurse, social worker, pharmacist.

Marie Scully: I was asked this today. I'm not sure that we have the answer to it. One of our patients is a senior nurse in the emergency department. All we can say is we have the information that inherently he's low risk as we've discussed, but if he gets COVID-19 he could develop an episode of HUS. I'm not

sure what the answer is about saying that all patients who work as front line, in front line jobs, should self-isolate. So, I'd be interested to hear your opinions, actually.

Christoph Licht: Anybody wants to comment?

Marie Scully: Very difficult, isn't it?

Eric Rondeau: I have one patient. She's a medical doctor. She's working in a hospital, and she asked me this question. So, I told her that she had to take care of her, of course, and everybody around her, and also that she can work, but in case there are too many cases around she should stop working and stay at home. I don't know if it's reasonable or not? Maybe I should say, "you stop working now"? But I don't know why. But she also wanted to work. So, I just recommended that she doesn't go to work if there are one or several cases in people working in the hospital with her.

Christoph Licht: So, you identify disease burden and exposure as one of the possibly, you know, changing factors in the approach here. What about if this patient was on immunosuppressive treatment?

Marie Scully: That would be different, I think.

Eric Rondeau. Yeah. For our transplanted patients, whatever the initial disease, we recommend that they stay at home, at the present time.

Christoph Licht: Yeah. And that that leads to, thank you, a complex that is obviously also of high interest we touched on it already. And there were questions coming in from the audience in that regard. So, we should focus for the next little while on this particularly vulnerable population of the transplanted patients on immunosuppression. So, I just read those couple of questions and then maybe we can just address them together? What are the special considerations for aHUS patients waiting for a transplant? And then what are the special considerations for patients with a transplant on immunosuppression plus eculizumab?

Christoph Licht: I can just add from this UK website. There was a strict recommendation for those patients, as Eric just alluded to, to stay at home, self-isolate for 12 weeks. That was the recommendation on that website.

David Cohen: So, there are two separate questions. One was special considerations for anyone waiting for a transplant. I think they're, basically what you said, Christoph, that patients need to take care of themselves and obey all the recommendations that are in place for everybody. I think in my many, many places, anyone waiting for a transplant would have to anticipate a significant delay in getting a transplant for a variety of reasons. One is the risk of receiving intense immunosuppression at the time of the transplant. And the other is the risk, or the competing need, for resources at the hospital. So certainly, if someone's waiting for a live donor transplant the vast majority of centers have stopped doing live donor transplants, except in the exceptional circumstances. The issue of testing donors and recipients prior to transplant to make sure no one is infected with a virus prior to the transplant is certainly, for anyone considering a live donor transplant, should definitely be done. For deceased donor

transplants, I think, I can't answer for other countries, but the vast majority of potential deceased donors are being tested for COVID-19. And some transplants are going forward if the donor is determined to be negative. Again, there are risks being in the hospital where there may be exposure to COVID-19. And then the risk of returning to the community following transplant, where one may be exposed. And I think there's a lot of concern about patients in the immediate post-operative period with intense immunosuppression potentially having a worse outcome with the virus. I don't think there's a lot of data on this, but it certainly makes sense. And so, anyone waiting, I think we'll have to, again, anticipate a significant delay, and others have more to add about that, about what's happening in other parts of the world.

Christoph Licht: If I can just share from Canada's point. The LRD program, living related donor program, has been discontinued temporarily, and in fact, also the deceased donor program, except with some exceptions, to the best of my knowledge, is still also changing, with respect to the highly sensitized patients, the ones with antibodies levels of 99%, and this is not due to a specific concern, as you said, you know, testing of donors and so on, will probably allow for, moving forward, maybe with specific information or shared with the recipient, but the concern is to not overload, to not consume resources that might be needed in different contexts. So, it's more resource management issue here than anything else.

Eric Rondeau: In France we also stop the living related donation and the deceased donor transplantation for the kidney, not for the heart and liver, for both reasons you explained before: that is, the risk of infection and also the resources in the hospital that are very much concerned with the COVID-19 infection.

David Cohen: I think on the second question about special considerations with someone who already has a transplant we addressed that somewhat. I think anyone on long term immunosuppression needs to be particularly careful and we have strongly recommended, really, self-isolation for these patients and all the other recommendations. We're delaying routine laboratory tests and routine monitoring of immunosuppressive drug levels and the allograft function. If it's absolutely necessary, of course, we have to do it, but we want patients to stay home and avoid community exposure to the extent that that’s possible

Christoph Licht: Right.

David Cohen: More complicated issues have come when a household member is diagnosed or has an exposure and there are few good guidelines if a household member is exposed if it's possible for the transplant recipient to move to another location or isolate in the home. That's a recommendation. That's obviously not always very practical. And so, we asked them to do the best they can, take their temperature twice a day and report if they develop any symptoms. There isn't really any clear evidence for any prophylaxis that we might give for an exposure. Obviously that's a topic of great concern to people with a lot of, you know, information about potential drugs that might help prevent the disease or ameliorate the course of the disease if taken early, but that evidence is still very, very preliminary and

it's very difficult to recommend to anyone to take any of these anti-malarials or azithromycin or anything else at this point.

Christoph Licht: Yeah. Any other comments?

Eric Rondeau: Yeah, maybe just want to say that this is not specific for a patient with atypical HUS having a transplant, but in transplanted patient we have already eight patients in my hospital who are transplanted and got the COVID-19 infection. And when they have fever and pulmonary signs we usually decrease or stop the MMF treatment and just remain with CNI and low-dose steroids. Whether it's appropriate or not, it's the usual way we choose to do it, and we share this condition with the other centers in France, and they use to do this.

Christoph Licht: Eric, that is a good segue to address a question that came in from the audience. Did you experience that your patients being transplanted under immunosuppression experienced more severe symptoms of the COVID-19 disease?

David Cohen: I can, I can start to address that, I think. We've seen the entire spectrum of disease in our transplanted patients. Again, the numbers are not big, but we've seen people with very mild disease, and we've seen people who are in intensive care units. So, I think it's not predictable what the course would be like. It may have to do with other co-morbid factors, other disease conditions that patients may have that determine the course, in addition to just the transplant.

Christoph Licht: Right. But if I correctly understood from Eric, you basically decreased as much as reasonable and possible the standard immunosuppression, being at least concerned that there could be a more severe presentation, with the combination of immunosuppression and COVID-19?

David Cohen: Yes, for anyone documented to be infected, we would follow essentially what Eric said. For people who are home and fine and feeling well, we have not recommend any preventive change in immunosuppression, and I think that would be a mistake to just start lowering immunosuppression in people who are totally asymptomatic with no known exposure and are feeling fine.

Christoph Licht: For the remaining couple minutes that we have, I would like to address quickly two questions that are possibly of interest. One is here on the slide, which is the role of genetic mutations possibly defining a higher risk for patient with atypical HUS in the COVID-19 context. Any comments?

Marie Scully: We have no evidence. We have no evidence that somebody with an MCP, or no mutation, or factor H have variability in disease presentation.

Christoph Licht: I would echo this very loudly. I think this is very important to state that we just don't know. Typically, we follow some sort of common sense of a risk profile defined by genetic findings. Presence of antibodies, antibody titers and so on, and apply that in various risk situations, including the transplant allocation and management, and discontinuation of treatment, but in this situation, we just don't know. I think that this is just the truth. We just don't know. Does anybody else want to comment on that question?

Christoph Licht: And the other question goes back to the front-line patient situation, were the question is, basically, I'll just read it: I'm a nurse with aHUS and I'm at home at the moment. There are studies to defend that we are not at higher risk, but, as you said, if we get COVID-19 we can develop an episode again, like a relapse. My question is, if this is possible under Soliris?

Eric Rondeau: To the best of my knowledge, the risk of recurrence on Soliris is very, very low and even with the infection. So, I don't think so.

Christoph Licht: Any other comments?

Marie Scully: I agree.

Christoph Licht: Alright. We're just past the hour, and I think we are with that coming to the end of this webinar. I thank my colleagues. This was with very short notice, and I am deeply grateful that we could organize this panel and have this webinar. I also want to acknowledge again the technical support by Alexion to allow us to have this and to host this this webinar. As I said this was recorded and will relatively shortly be available online and we will find ways to distribute that information within the community. And with that, I obviously thank in the first place, our audience, all the patients all the relatives, everybody who put forward questions, pre-session or during the session. We will try to find a way to address the ones that have not been addressed yet. We hope this was somewhat helpful. Again, we professionally have to apologize for ignorance, but that's just the way it is, but we try to put forward our best foot. With that, thank you very much. Best wishes to the world and stay safe. Take care.