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Transkript

„Diskussion neuer Daten zum AstraZeneca-Impfstoff AZD1222“

Expertin und Experten auf dem Podium

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Video-Mitschnitt

Einen Mitschnitt finden Sie auf der SMC-Website:
https://www.sciencemediacenter.de/alle-angebote/press-briefing/details/news/diskussion-neuer-daten-zum-astrazeneca-impfstoff-azd1222/

Transkript – das Press Briefing fand in englischer Sprache statt

Moderatorin: *[00:00:01]*
Last week, I was listening to a short news morning podcast where they talked about the updated recommendation by the German standing committee on vaccination, the STIKO - die Ständige Impfkommission, and they are now also recommending the vaccine for people above 65 years. The speakers of the podcast, they pointed out that probably for most people, this is quite confusing, that the vaccine was first recommended only for people below 65 years, even though the European Medicines Agency granted the authorization for all groups of ages. And now, only four weeks later, the STIKO suddenly updated the recommendation and agrees that the AstraZeneca vaccine should also be given to older people. Currently, almost on a daily level, there are plenty new data and information coming in concerning the vaccine: there are new results about continuously running clinical trials, there are real-world data coming in from the UK, where they have been vaccinating the population with AstraZeneca for two months now and there are news about how efficient the vaccine can fend off new virus variants and about putative side effects that are presumably associated with the immunization. So, we thought this press briefing today has just a very perfect timing to close all the gaps and answer the remaining questions about the vaccine and the science behind it. So please feel free to post your questions into the chat. You can do this either in English or German but we would be very happy if you do this directly in English so that we don't need to translate it. And then I will pass the questions to the experts. And I'm very happy to welcome the experts here whom I will introduce now. I want to start with Prof. Dr. Bernd Salzberger. He is the German expert here today and he is leading the Department for Infectious Diseases at the University Hospital in Regensburg and he is also the head of the German Society for Infectious Diseases. Mr Salzberger, the STIKO has updated their recommendation now for the AstraZeneca vaccine, and it can be now also applied to people above 65 years. The German Society for Infectious Diseases, where you are the head of, has recommended the steps already some days before. How do you evaluate now the decision by the STIKO and which aspects or which data actually convinced you and your colleagues to require the vaccinations also for people above 65 years?

Bernd Salzberger: *[00:02:43]*
I think the data coming from the UK, from the real-world data from Public Health England and also from Scotland demonstrate quite nicely that this vaccine works well in the elderly as well. And so we recommended to the STIKO to change their recommendation. I think STIKO based this on the same data we saw, they just looked a bit closer to that. What STIKO does, has more consequences and so they took a few days more. But I think it's really the real-world data which show that the vaccine prevents disease very well in the elderly.

Moderatorin: *[00:03:30]*
So how do you evaluate in this sense now the STIKO recommendation?

Bernd Salzberger: *[00:03:37]*
We are glad that the STIKO has made changes to the recommendation, which makes basically vaccination a lot simpler in all the centres all around Germany.

Moderatorin: *[00:03:49]*
All right, then I would like to continue with Sir Mene Pangalos. He is executive vice president of BioPharmaceuticals R&D at AstraZeneca in Cambridge. Sir Mene, could you tell us about the latest data coming from real-world vaccine effectiveness studies in the UK and how these data

are compared to the findings from global trial and are those data encouraging or how do you evaluate them?

Mene Pangalos: *[00:04:22]*
Thank you very much and thank you for having us to talk to the German media. Andy, I'm sure, will talk about the clinical data in the trials that have been run so far. I think what's very encouraging is that when we see the data that's coming out from the real-world use in the UK where the vaccine is being used in tens of millions of people and in many people over the age of 65 and over the age of 75, the efficacy is very high indeed. Over 90 percent efficacy in patients including patients over the age of 80 years old in terms of preventing them from becoming severely ill or hospitalized, which is obviously what you really want to do with this pandemic, is get people out of hospital, will stop them from getting into hospital and keeping them well and able to handle the virus. There's also very complementary data now from studies PHE-England *(public health england, nationaler Gesundheitsdienst in England; Anm. d. Red.)*, as Bernd said, which is showing over 80 percent effectiveness and again, people over the age of 80 in terms of severe disease and hospitalization. So overall, we're not just seeing a good effect on symptomatic disease across age groups, but we're also seeing, most importantly, the ability of this vaccine after one dose, just three weeks after one dose to keep people out of hospital and keep them from becoming severely ill, which is the ultimate goal of getting our societies back to normal, which is fantastic.

Moderatorin: *[00:05:48]*
So, may I ask, are those data all on the first dose or are there also already data for second doses?

Mene Pangalos: *[00:05:55]*
This is all after the first, the whole data are after the first dose. Andrew Pollard can talk about data after the second dose as well. We're convinced, I'm sure, that after we've had a good into dose interval of 12 weeks for those to see very good efficacy and better efficacy after two doses as well, that will be important in maintaining efficacy, thus improving the numbers because the numbers are very good now in the real-world in terms of protection.

Moderatorin: *[00:06:20]*
All right, I want to continue with Professor Andrew Pollard. He is director of the Oxford Vaccine Group at the University of Oxford, and he has been leading the Oxford vaccine trials in the U.K., Brazil and South Africa. Mr. Pollard, could you please summarize the latest data from clinical trials and how effective is the vaccine and all groups that you have tested?

Andrew Pollard: *[00:06:50]*
Well, I was on mute, so thank you very much. First of all, just sort of echo the comments that many made, which is that the real-world effectiveness data shows very clearly that even in the oldest adults who we know with vaccines are the hardest to protect, that even after the first dose, we're seeing very high levels of protection against hospitalization and severe disease. And I think the other thing that's important is come out of those studies is that level of protection is very similar to the other vaccine that we're deploying in the U.K., which is from Pfizer and the RNA vaccine. So that's the first observation. And the reason why that's so critical is that for the reason why this is a pandemic is because our hospitals have been filling up with severely ill people and people have been dying. And so that end point that is captured in those studies is the most important one that we need to look at. Now, we do know when we go back to the trials that at that end point, we have no cases of hospitalization or death in those who were vaccinated in the trials once you get to three weeks after the first dose, and that's across

all ages. The problem with trials is that you need enormous studies of hundreds of thousands of people to have a large number of cases in the control group, those who didn't get the vaccine, going into hospital. That's why the real-world data is so important. That allows us to get granularity about that critical bit which matters to our health systems. But what we can do in the trials is look at the less severe infections and so we have very large numbers of people in the trials that we've run from Oxford, in the UK, in Brazil and South Africa with over 24 000 people included. And that shows very high efficacy against a milder disease. As you may know, there's another trial running in the US run by AstraZeneca, which has another 30 000 people in it, so there will be more data coming soon from that. What we learnt from the trials is that protection that we see in younger adults is similar in older adults. We just have less information in older adults for two reasons. One is we enrolled them a bit later last year. So there's been less time to capture the data and also because older adults are a bit more cautious than younger adults and so they've actually had less infections so that the database is a bit smaller to answer the question. But what data we do have from the trials isn't exactly the same direction as younger adults. We see a protection, it's just statistically it's not as large a number to give absolute confidence. I think the decisions the regulators have made is based on the strong immune responses across all ages and the evidence that there is around effective efficacy from the trials is that it's appropriate to authorize the vaccines for use of all ages. That scientific bodies then need to look at that, like STIKO, and make a decision based on the population supply and their rules about the level of evidence required about whether to recommend vaccines or not. I think that was the reason for the previous STIKO decision. And of course, as more data emerged, that could then be reversed as there's more information to build further confidence from the real-world evidence. I think there has been a problem in communications around this, and it's really important that people understand the scientific process, which is about weighing up levels of evidence, and that there's never been a situation where people thought the vaccine didn't work in older adults. It's just there wasn't enough evidence for STIKO to be competent. And that has changed now that there's plenty of evidence across all ages to show very high protection and from the vaccine. And the critical thing in Europe is that over the last few days, around four thousand people died every day across the whole of our continent. And we absolutely have to get vaccines into people's arms as quickly as possible. And to get beyond that, and I think this current position that STIKO has taken is critical to help us move along and get all of our citizens across Europe protected.

Moderatorin: *[00:11:14]*
Thank you, Mr. Pollard. I have directly a follow up question for you concerning the clinical trials in the US and South America. When do you expect the publication of the data and what kind of findings do you expect from the trial? What kind of dose intervals were studied?

Andrew Pollard: *[00:11:35]*
Those trials are being run by AstraZeneca, so perhaps Mene would be best to answer that question, but I mean, those trials are using a four-week dosing interval and includes all ages, including around a quarter of those enrolled are older adults. So, Mene Pangalos if you want to answer?

Mene Pangalos: *[00:11:53]*
The slight challenge we have with the US study, although we're very hopeful it will be a positive study because it is a four-week interval. It will be at the lower end of the vaccine efficacy range. We know that as you increase the interval between doses from four weeks to eight weeks to twelve weeks, the vaccine efficacy increases as well. That's not unusual for vaccines. And so, I think the real-world evidence data, again, becomes very important, both

after one dose and two doses. And as we say, the hospitalization rates come down very dramatically in the U.K.. It shows us that the vaccines having an effect in the population, that ultimately is the data that should be determining and giving people confidence to use the vaccine.

Moderatorin: *[00:12:38]*
All right, there is another follow up question, that I quickly want to put in before I come to you, Professor Gilbert: Is there a way to explain why AstraZeneca seems to be more efficient if the time between the first and second dose is longer?

Andrew Pollard: *[00:12:53]*
Yes, well, I mean, I think this is not unexpected in that we know with most vaccines that if you have a longer interval between the doses, you get better immune response. And that's why, for example, in teenage girls, the HPV vaccine, the cervical cancer vaccine is given with a six- or 12-month interval between the two doses because the immune response is a much better with the longer interval. It's just to do with, after the first dose, giving some time for the immune response to mature and give the better response to the second dose. And we've seen that very clearly in our studies, where the longer interval gives a much better immune response to the second dose.

Moderatorin: *[00:13:37]*
All right, thank you. So, Professor Dr. Sara Gilbert. She is a Said professor for vaccinology at the University of Oxford, and she is a scientific head behind AstraZeneca and her group has developed this vector vaccine before the pandemic. She has already worked on a MERS-coronavirus vaccine and used her experience directly to apply to generating a vaccine to get SARS-CoV-2. Professor Gilbert, so far, the vaccine seems to be very effective against the circulating variants in the UK. Do you already know if the variant P1, which was first identified in Brazil, can overcome the vaccine induced immunity? And if yes, how do you prepare for this kind of future challenges?

Sarah Gilbert: *[00:14:25]*
Thank you. So, as you said, we already have real-world effectiveness data against the B.1.1.7 variant that was first identified in the U.K. and that is very highly transmissible and has been spreading. So the effectiveness data that came from the first couple of months of this year were at a time when that was the major virus strain that was circulating in this country. So the numbers we've been hearing this morning with the 80 percent effectiveness in over eighties of keeping them out of hospital, 70 percent effectiveness in over seventies from symptomatic disease. Those are against a mix of viruses, which is mainly to be B.1.1.7 variant. So we don't have any concerns about that. But the Brazil and South Africa variant, the situation is somewhat less clear. And we are still in a situation of needing to piece together different pieces of information from different sources to have a full understanding of the situation. And this will develop as time goes on and we will develop a better understanding of it. What we saw in Brazil when we reported on our phase-III-trial results back in November, we saw exactly the same level of efficacy in Brazil using the same dose interval as we saw in the UK. But at that time in Brazil, the P1 and P2 variants were not very common. So that doesn't really help us interpret anything about those variants. And since that time, there have been more cases accumulated in the trials and we need to go back and work out whether those cases are occurring in the trials were the new variants or whether they're with the original variant. And that work isn't finished yet. There is some work that's being done on antibodies generated to the vaccine, all of the vaccines that are now being used, particularly the neutralizing antibodies. And there was actually a paper in the New England Journal of Medicine yesterday

about the Pfizer vaccine, showing the antibodies raised by vaccination are little affected by the Brazil variant. The neutralizing antibody responses are nearly as good against the Brazil variant as they were against the original variant. And we can expect to see something similar, I think, for other vaccines. But we still need to get all of that information collated and the data published. So, we're waiting for that to happen. For the South African variant, we did have a trial in South Africa when the new variant virus there was circulating, but it was a small trial. It was 2.000 people, and they were young population. The median age of the population was 31 years. And in the control group in that population, there was no severe disease. So that means we can't report on the efficacy of the vaccine against severe disease. We can only report on mild disease. And that was definitely much lowered from the efficacy that we saw in the UK. But other vaccine trials being run in South Africa that were larger trials with more older people among them were able to report on efficacy against severe disease. And although it's slightly reduced from what they saw in other countries, it was still very strong. So, we know that preventing severe disease is more likely to be possible with a vaccine than preventing mild disease or asymptomatic disease. At the moment, the picture looks like the vaccines in general may be less effective against mild disease for the South African variant, but still do a very good job of protecting against severe disease, hospitalizations and death. So, we should still, for the moment, be seeking to use the existing vaccines even when the South African variant is the dominant strain. But of course, we are working on the development of new versions of the vaccine, updating the spike protein in the vaccine so that we can have a new version. And we're doing that in Oxford working with AstraZeneca. We've been planning our pipeline and our process to go from the idea of updating the vaccine all the way through to license of the new vaccine, including manufacturing and clinical testing that needs to happen. That process is going well. We have a number of variants in that pipeline, and we expect to be doing the clinical testing of some of those during the summer months.

Moderatorin: *[00:18:28]*
So, you change the spike protein in a way that it's adapted to the major mutations that we know now from the occurring variants or how do you design that*?*

Sarah Gilbert*: [00:18:39]*
Yes, that's right. Instead of using the original spike protein sequence that came out of China on the 11th of January of 2020, we now have spike protein sequences from Brazil and South Africa. And actually, many of the mutations in these different variants are the same. And I think one thing that makes the whole situation somewhat less concerning is that we're not seeing very many different types of mutations occurring all over the world. We're seeing the same mutations occurring in the same places. And it looks like there's a reason for a virus evolving in a certain way. But that means there's potentially less diversity that we have to cope with. And that makes it more certain that when we update the vaccine, we will have a version that will protect against multiple different variants because actually, they're very similar.

Moderatorin: *[00:19:27]*
About the data or observations you made in South Africa, which role could antivector immunity play as a cause of the lower efficacy in South Africa?

Sarah Gilbert: *[00:19:38]* We see very low anti-vector immunity to the ChAdOx1 vector. It's not an adenovirus that normally circulates among humans, and that's why we use it. And we've previously looked in the UK and Africa, at the level of pre-existing antibodies to the vector and they're very low. We also know that giving a single dose of the vaccine results in some anti-vector antibodies, but a very low level. And this doesn't interfere with the ability of the vector

to boost the immune response when we give the second dose, even when that's given at four weeks. The anti-vector immunity doesn't affect the ability of the vaccine to boost, but there is better boosting if we wait for the immune system memory to develop and then boost at a later time point.

Moderatorin: *[00:20:26]*
All right, I got another question about the efficacy. In the clinical trials, the efficacy was lower than for the RNA vaccines in the clinical trial. Now, the observations from the field data seem to be a bit different. But how do you explain those differences between the two types of vaccines?

Andrew Pollard: *[00:20:54]*
Perhaps I can take that, I mean, it's very difficult to compare trials that are run in different populations with different endpoints for deciding whether someone's a case or not. And as I said in my introductory comments, if you were to use hospitalization and death as your endpoint, then all of the vaccines look pretty much the same with very, very high levels of protection from the trials. But once you come to milder disease, the way that's defined is very different between the different developers. And so, it doesn't exclude the possibility that there are some real differences between the vaccines. But at this moment, I think it's very difficult from the trials to address that question. And I think the real-world evidence is going to be important, because what we really want to do is to stop people getting sick, going into hospital. And I think we're going to see huge impacts of the vaccines; whichever one is used against those really important end points.

Mene Pangalos: *[00:21:52]*
The other piece I would add – I completely agree with Andrew Pollard – is that because we have different interdose intervals in our studies, you get a range of vaccine efficacy, as Sarah and Andy have said, and as I've said as well. The longer you leave that interval, the higher the vaccine efficacy number. And actually, when you look at the patients that have been dosed, the 12-week interval, the vaccine efficacy even against symptomatic disease is over 80 percent. That starts to become very similar to the mRNA vaccine data that's been published as well. So, first and foremost, we should be worrying about the severe diseases and hospitalizations. And then, as Andrew Pollard said, it becomes very difficult to compare vaccines. But when you're up in the 70s, 80s, 90s, you have highly, highly effective vaccines, even against symptomatic disease for all the vaccines.

Moderatorin: *[00:22:39]* Do you actually have already any information about sterile immunity or if the vaccine can induce sterile immunity and also reduce the transmission of the virus?

Andrew Pollard: *[00:22:49]*
We've got, I think, quite a lot of emerging data on this, some of which we've just recently published, showing that if you take the whole population, who have been vaccinated, so that includes people with mild disease, severe disease and asymptomatic infection. And you remember that any one of those people could transmit the virus to someone else. And you look at the overall impact and the only way you can do that is in trials where you're taking swabs regularly from people to see who's got infection, even asymptomatic infection. And from our trials in the UK, you see around about a two thirds reduction in the number of people who are positive over the course of the trial after they've had two doses and – sorry after they've had one dose. So that means that there will be two thirds fewer people able to transmit any virus. And although we haven't formally shown that there's no transmission,

clearly if you have no virus, you can't transmit. So that two thirds reduction is really important. We then also look to the other people who are still PCR positive, and we find that they have much less virus than those who are unvaccinated. They're less likely to transmit, but also that they shed the virus for a shorter period of time. So, taken all of that together, I think as long as we are not dealing with new variants that can evade an immunity, if we're dealing with the variants we have in Europe at the moment, then I think our vaccine, in fact, no, I suspect: all the vaccines will have a big impact on the transmission of the virus.

Moderatorin: *[00:24:26]*
There are actually several questions coming in concerning side effects, so there are strong reactions in response to the vaccine, including fever, limb-pain, even partial paralysis are among them, and the Paul Ehrlich institute, it's an institute in Germany who collects also this kind of side effects, reported last week: a higher rate for those effects, side effects with the AstraZeneca vaccine compared to those of BioNTech and Moderna. What do the real-world data in England and Scotland show, especially for people above 65 years?

Andrew Pollard: *[00:25:04]*
Well, I think we have the best data from trials where the information is very carefully collected from every individual, and we know in the trials that after vaccination, some people will feel shivery, they may have a fever although that's not very common, and they may have a headache, develop muscle aches and joint pain. And that spectrum of symptoms is very similar with the RNA-vaccines from Pfizer and Moderna, as well as with the viral vectors. The interesting thing about the two different types of vaccines is that the most severe side effects are seen with the first dose, with the Oxford AstraZeneca vaccine, but they're seen with the second dose, with the RNA vaccines. And what we find with the second dose of the Oxford AstraZeneca vaccine is that those side effects are very mild. And so they're sort of the other way around from from the Pfizer and the Moderna vaccines. So, I mean, it's absolutely true that people do get side effects from the vaccines. If they take paracetamol, these side effects can be reduced. But it is well documented, both from the trials, and we are seeing it in the real-world data as well. If you ask a question about age, it's very much less likely for side effects to occur in the oldest adults. It's much more common in those who are under 35 years of age.

Mene Pangalos: *[00:26:25]*
Kind of that's something because I think it becomes quite difficult to compare this piece around age is hugely important. If you think about the implementation in Europe versus the implementation in the U.K.. In the U.K., we have prioritized immunizing people with the AstraZeneca Oxford vaccine over the age of sixty-five, where tolerability is a little bit better because the reactogenicity is less intense. Whereas in Europe, because of some of the age restrictions to begin with, which are now changing, they've been immunizing people under the age of 65. And as Andrew Pollard said, you react more if you're younger, particularly on the first dose. And so, if you think the mRNA vaccines in Germany, for example, will be used in the over sixty-fives and AstraZeneca is being used in the under sixty-fives, you would expect to see more reactionicity in a younger population.

Andrew Pollard: *[00:27:16]*
I think just one thing, to add to that. For people who have had reactions to the first dose and are wondering about having the second dose, we can be very reassuring the second dose is much less likely to cause reactions.

Moderatorin: *[00:27:31]*
So there was a question today about side effects which are quite severe and even could result into dizziness. Mr. Salzberger, do you think that the STIKO considered those aspects when recommending the vaccine to older people? Because maybe that could result also in tripping and falling if people get dizzy and have even higher complications. Is this an aspect that they put into the recommendation?

Bernd Salzberger: *[00:28:04]*
I'm certain that STIKO considered all the side effects, and I think STIKO made the decisions on really looking at the side effects, and I don't think there's a signal that side effects to the AstraZeneca vaccine are more severe in the elderly than was mRNA vaccine, as xxx said. All the side effects are really, really centered in the younger population, and that may be also the reason why PEI has reported this higher rate of vaccine adverse events in Germany until now.

Mene Pangalos: *[00:28:49]*
Just one more thing to add, again, in the tens of millions of people that have been vaccinated in the U.K. across age groups, because we're getting now down into people in their 50s and below the age of 65. The adverse event profile, which we're obviously looking at on a daily and weekly basis, is very much in line with everything that Andrew Pollard has talked about in terms of what we saw in the clinical trials. So it's very consistent.

Moderatorin: *[00:29:19]*
So there have been news about some really severe putative adverse events reported now in Austria after one person died after having a coagulation disorder and also about people in Korea, even though there is no evidence yet that this is really a direct correlation. How do you evaluate these findings?

Andrew Pollard: *[00:29:44]*
I mean, I think it's very important that as new vaccines are rolled out, whatever the vaccine is, that the public health authorities do take note of any events that happen. And, of course, in the real-world, lots of things happen to people anyway. And we don't know whether or not they're caused by the vaccine. But it's important that there's good data collected so that if there are some unexpected effects that can be thoroughly evaluated. To our understanding there haven't been any signals here in the UK with many millions of doses used in very close surveillance. But I think it's absolutely right. And I think reassuring to me that public health authorities in these various countries are investigating every event that happens to make sure we've got really good safety data that's collected around all of the vaccines being deployed.

Moderatorin: *[00:30:31]*
Professor Gilbert, but are there any information about if the vaccine can have an influence of blood clotting?

Sarah Gilbert: *[00:30:40]*
No, I'm not aware of any evidence that the vaccine would influence blood clotting, this would be this is a unique finding, as far as I'm aware.

Moderatorin: [00:30:50]
All right. We also received several questions concerning the possibility if the ChAdOx1-genome could be integrated into the human genome, is there any indication that this could happen?

Sarah Gilbert: *[00:31:05]*
OK, so it's based on an adenovirus, but an adenovirus, that can't replicate, it can't spread through the body. We all get multiple infections without adenoviruses throughout our lives. They cause respiratory tract infections, they cause sometimes gut infections, and we have a mild disease, we have a cold. Our immune system responds and fights off the adenovirus and we recover. And we're not particularly aware of what it was we were infected with. This is something that happens all the time. And adenoviruses, as a result of those infections, don't integrate into the genome. They're not a virus like HIV that does integrate. They're a virus that causes a brief infection, which is then overcome by the immune system unlost. And so it's considered safe to start to use adenoviruses as a vaccine vector because of this repeated safe exposure. Other than the short-lived disease, we don't have any lasting effects from Adenovirus infections. And Adenoviral vectors have been in development for a good 20 years now. This isn't something that we started on last year and prior to doing the initial clinical studies with human adenoviruses. So AD5 is sometimes users of vaccine vector. AD26 is another human adenovirus used as a vaccine vector and then moving on to the simian adenoviruses *(Adenovirus, das ursprünglich Affen infiziert; Anm. d. Red.)* on which we started to work with in partnership with other people. The regulators wanted us to look at these questions and bio distribution studies to see where the vaccine goes in the body. So, all of these questions were answered many years ago. There's no reason you would expect it to integrate when we looked, we don't find that it does integrate.

Moderatorin: *[00:32:42]*
All right. Which further clinical studies are actually on your list? Do you plan to include pregnant women and children in the future or is it already running?

Andrew Pollard: *[00:32:58]*
Yes. We're already running the first trials in children and we've enrolled already children between 12 and 17 years of age and hope to be starting soon. The trials in younger age groups to six years of age next. And then there are plans being put in place to do much larger scale trials in children to meet the requirements the regulators will have for those studies. And AstraZeneca is currently planning some studies for evaluation and pregnancy and but those aren't underway yet.

Mene Pangalos: *[00:33:35]*
Then the other studies that we're doing, which we're very interested in, are heterologous boosting studies where we want to see what happens when you dose somebody initially with an mRNA vaccine and then follow up with ChAdOx1 or vice versa. You start with ChAdOx1 and follow up with an mRNA vaccine. Those studies are actually running in the U.K. We also have an heterologous boosting experiments running with the Gamaleya Center vaccine, which is another adenovirus based vaccine from the Russian group, which would also give us information on how you can mix and match Adeno-based vaccines as well. But this will become very important as we get into the normal world where people will, you know, one year maybe have an mRNA vaccine another year, have an Adeno-based vaccine. Understanding how they interact with Sarah and her group, where we demonstrated frequently that you can heterodoxy *(mit alternativen Vakzinen, Anm. d. Red.)* boost these vaccines and get a very robust immune response when you do one funded by the other, which I think is very encouraging again.

Moderatorin: *[00:34:37]*
Because there has been the question asking that there were some evidences that the immune

response increases with each vaccination so the side effects could become stronger. Could this be problematic if regular vaccination is required?

Andrew Pollard: *[00:34:52]*
We're not saying that with the Oxford AstraZeneca vaccine, the reactions are lower with future doses rather than higher. And we've seen that with the second dose of the vaccine. There's much lower reactionicity.

Sarah Gilbert: *[00:35:08]*
And I think the other thing to say is that the idea of hetrologous boosting is not new either. It's something that's been in development for many years, for decades now with lots of different types of vaccines. And it's well understood that giving one type of vaccine and then another type, two different viral vectors or DNA and a viral vector, DNA and protein, lots of different combinations, can result in very strong immune responses. And this may be a very good way to use the vaccines, but it's also a question of practicality. If somebody comes for their second vaccination and the clinic on that day doesn't have the same vaccine that they were given the first time around, is it safe to give them a different vaccine and will that be effective? So we need to gather the data for that reason. But it's really not a novel idea to be mixing and matching the vaccines.

Moderatorin: *[00:35:58]*
Mr. Salzberger, do you know if the mixing and matching is actually a topic which is discussed in Germany?

Bernd Salzberger: *[00:36:05]*
It is discussed, but I don't think anybody will do this before the studies are out. I think there's still some hesitancy to do this before there's real data from good planned and good done studies.

Moderatorin: *[00:36:22]*
How about immunosuppressed people, for example, those that are suffering from HIV? Did you get already any data for this kind of smaller groups?

Andrew Pollard: *[00:36:35]*
I mean, I think the first thing to say is on safety, that none of the vaccines that we have in Europe should have any concerns about safety in the immuno-suppressed individuals because they are not able to cause infections or to cause a problem, whether it's the Oxford-vaccine or the Pfizer- or Moderna-vaccines, they're all perfectly safe in the immunosuppressed. The difficulty in answering the second question is: it depends what you mean by immunosuppressed. And it's a huge population of people from those whose immune systems work perfectly normally but are on some treatments that prevent some types of inflammation and to those whose immune systems don't work at all. And if your immune system doesn't work, no vaccines will work in those individuals. So, there are some studies going on in the UK at the moment to look at various different and clinical conditions where the immune system is suppressed. But I think the answer is really going to have to be for the individual patient with their clinician because it depends exactly what treatments they're on and how badly affected their immune system is. But the important thing is there's no harm in being vaccinated and many individuals with immunosuppressive treatments will still benefit from being vaccinated.

Moderatorin: *[00:37:46]*
So, there was another follow-up-question on the combination with other vector vaccines added the booster study was Sputnik V, the Russian vector vaccine. Did it already start.

Mene Pangalos: *[00:38:02]*
It has started but it hasn't read out yet? So, yes. Is ongoing. That still is ongoing.

Moderatorin: *[00:38:08]*
Thank you. How long can the AstraZeneca vaccine be stored? Have you looked at what happens if kind of old vaccines are injected or do they lose some of its effects? Are there any more adverse events then popping up or other studies on this planned?

Andrew Pollard: *[00:38:28]*
It is very careful work done with regulators to look at the shelf-life of vaccines and from a manufacturing perspective that has to be approved each time you develop new data showing how long the product survives at the same potency, the regulators review that and allow changes to the label. So that's where shelf-life comes from. It's from a very careful scrutiny of what happens. And of course, the other thing is that with all vaccines at the moment, they can be stored as bulk in very low temperatures, which very much extends the time which they can be stored for. And then at once you've got it out and it's at fridge temperatures. And there's also very good data about that. And these viral vector vaccines like the AstraZeneca vaccine, a very, very robust and even at fridge temperatures for prolonged storage.

Mene Pangalos: *[00:39:23]*
And I think that is clearly one of the big benefits of this vaccine. It easy of storage and of stability, and as you know, it's given an ten-dose bar, which means, you can just keep it in the fridge and it becomes very easy to use in the community, in places where you don't have minus eight to a minus 20 refrigeration, it becomes much easier. Which, of course, is why it's so important to the low- and middle-income countries as well as a vaccine, because with it comes a very easy vaccine to administer and implement.

Moderatorin: *[00:39:57]*
I would like to come to the next question, it's a different topic, and I think this question refers to the situation in Germany at the moment. There are reports of doses not being vaccinated because of reservations amongst the population. And Professor Pollard, you touched on this question before. What is your view on the debate about the vaccine yet, Germany?

Andrew Pollard: *[00:40:20]*
You mean about the hesitancy? Which bit of the debate you mean specifically?

Moderatorin: *[00:40:25]*
Yes, about the hesitancy that developed because of the communication. Like, how do you evaluate how did that happen?

Andrew Pollard: *[00:40:38]*
Well, I think we've all got to be very careful to make sure we communicate very clear messages about the vaccines to the public. Because public confidence is critical. If we're going to get ahead of the pandemic and be able to protect people from this virus. We are very short of vaccine doses for the world. And I mean, that's very apparent across Europe at the moment. And we absolutely have to make sure that every dose that there is gets into people's arms,

because the vaccines have no impact if they're sitting in a vial on a shelf. And we know that they have very high levels of protection. And so, we don't need to think about which vaccine. We just need to have people vaccinated as soon as possible to protect them. And particularly the vulnerable, the oldest adults and certainly those over 65, but indeed, we do see much higher rates of severe disease in the over 50s. So, everyone over 50, as soon as possible, needs to be vaccinated.

Mene Pangalos: *[00:41:35]*
And I just reflect, Andrew, on what you said earlier, you know: four thousand people dying a day in Europe. You know, I'm a Greek European living in Britain, very proud of being British, but, you know, I want everyone to be well, we all need everyone to be vaccinated and to be protected. And I remind people, the real-world data in the UK, where the two vaccines that have been predominantly used, are the Pfizer-vaccine, the one that everyone in Germany is very familiar with, and the AstraZeneca vaccine: the efficacy in the real-world looks identical to each other. Very, very high levels of protection from serious disease and hospitalizations across all age groups. It's paramount that the vaccine gets used because it's the best way of protecting our populations around the world.

Andrew Pollard: *[00:42:28]*
I think it's worth just adding to that, that there are three separate U.K. studies which have been done independently that provide confidence in this, all of which showed the same thing. There is a study from Scotland, a study from Public Health England and from academics at the University of Bristol. And they've all shown very high levels of protection even in the over seventies or the over eighties.

Moderatorin: *[00:42:50]*
Do you have any idea or a recommendation how the communication about this topic could have been improved or could be improved?

Andrew Pollard: *[00:43:02]*
Well, I think it's really important that that the the scientific bodies and the politicians across Europe really get behind the vaccine programmes don't distinguish between products because we know that they're only authorised in Europe if they are highly effective and to recommend that people get vaccinated as soon as possible. I think that we've got to change the tone of the story around this one, which is about saving lives across the continent.

Moderatorin: *[00:43:33]*
Mr. Salzberger, maybe can I also have or listen to hear your view on this emotionalized debate about the role in Germany?

Bernd Salzberger: [*00:43:41]*
I think that a pandemic is a is a hotspot for breeding concerns. And I think about the different percentages of protection that were discussed and that made a lot of discussion. And what Professor Pollard pointed out before has not been recognised in this debate, that it's not about preventing symptomatic disease, that it's about preventing severe disease. Preventing symptomatic disease was kind of a surrogate marker in the efficacy studies. And so I think the whole debate about comparing these rates was kind of not very scientific and not very rational. And I think the real-world data changed this view now, and everyone can see that the protection against severe disease is really good with all the vaccines now used in these large real-world situations. So I think I hope this concern fades very rapidly in Germany and vaccine

hesitancy goes away. We have seen very encouraging rates of vaccine acceptance in health care workers in our hospital, where we have very high rate of severely ill patients. And I hope this spills over to the community as well. And hesitancy goes away. Otherwise, the pandemic will not go away.

Moderatorin: *[00:45:21]*
All right, so we are almost at the end and I would like to ask you if you have anything that you want to add or make you make sure that this has been said, and maybe I would like you to tell us one sentence that fit for you to be most important for the next few weeks.

Sarah Gilbert: *[00:45:48]*
In Oxford, with my colleagues and a large team, which Andy joined very early on and a lot of other people, we worked really hard last year to develop this vaccine with the technology that we had a lot of confidence in. And we now have a vaccine that's licensed in Europe and we have to complete the process of using the vaccine because it's using the vaccine, getting people vaccinated that actually saves lives. We will try to do our part to make this possible. And now we need to see that last part of the process to be completed.

Moderatorin: *[00:46:19]*
Sir Mene, do you want to continue?

Mene Pangalos: *[00:46:22]*
Just like that, I would say I would like to focus on fighting the virus in the pandemic, not politicians and preconceived biases and other companies. I think we're all actually doing this, as Sarah said, to save lives, to tackle this virus and to get all of our societies as closely back to normal as we can as quickly as possible. And the best way of doing that is by vaccinating all populations of any of these vaccines.

Moderatorin: *[00:46:52]*
Thank you, Professor Pollard, what do you what do you want to ad?

Andrew Pollard: *[00:46:57]*
Well, I think the last two weeks have been incredibly important with the restarting of rollouts of vaccine through COVAX to the many low-income countries around the world, and I think that, to me, refocuses the importance of getting the right messages here in Europe, because the people do look to what's being said in Germany or in France or in other countries about their confidence. And we do hear people from many other countries around the world asking questions based on the communications happening here in Europe. We have a huge responsibility to get this right and to make sure that we've explained to people about the importance of vaccination that this is important here in Europe. But it's also what we say and do has an impact everywhere in the world. We've got to make sure that those doses get into people's arms and people are protected everywhere.

Moderatorin: *[00:47:52]*
Mr. Salzberger, I started with you. You have now the chance to finish the press briefing.

Bernd Salzberger: *[00:48:00]*
Looking back on the last year, we have made some but not much progress on treating this severe disease caused by this new virus. We have made tremendous progress in making several vaccines and some will come out in the next weeks and next months. And I hope we or

I think we must do everything to get these vaccines out as fast as possible. And we have to look not only at our nations, we have to look at the world. Otherwise, we will not be able to stop this pandemic. So not only focus on our small countries but focus on the bigger picture and vaccinate as fast as possible.

Moderatorin: *[00:48:45]*
Thank you so much for your statements and all the information you shared with us today here. I also want to thank the journalists who attended this press briefing and ask all the questions. I hope we could solve most of your questions. As usual, you will find the video to the press briefing on our Web page in several hours. And also, we will prepare the transcript for you and hopefully have it online by tomorrow. So, I wish you all a pleasant afternoon. Thank you very, very much for taking the time here with us. Be there for the German speaking journalists. And I wish you a very well. A nice afternoon. Thank you so much.

Andrew Pollard: *[00:49:30]*
And thank you to the Science Media Centre in Germany for hosting us.

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