Pascal Soriot: "There are a lot of emotions on vaccines in EU. But it's complicated"

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(ansa)

An exclusive interview with AstraZeneca's CEO on the accusations from Europe after the delay of Oxford vaccine supplies, some revealing details of the vaccine contracts signed by Astrazeneca with Britain and EU ("no obligations, just best effort" for the latter), why Boris Johnson's government has taken some advantage and why the one-dose strategy is the "right one"

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LONDON. **Mr Pascal Soriot, CEO of AstraZeneca, why hasn't AstraZeneca been more specific on detailing the supply problem detected on its European plants? What exactly is the problem?**

“I think we have been relatively specific with the information. Of course, we are all very disappointed. We would like to produce more. I think we will deliver up to Europe in the month of February a reasonable quantity actually, very similar to what others have delivered on a monthly basis. But of course, it's less than expected and also because our vaccine is easy to use people expected more so we could scale up. Our team is working 24/7 to fix the very much issues of production of the vaccine itself. You have two steps in the production of a vaccine: one is you produce the vaccine itself. We call it a drug substance, the vaccine. Then, when we are finished with it, we move this into different plants where we put the vaccine into vials and we call that the drug product, the final product. For Europe the drugs substance is essentially produced in two plants, one in the Netherlands, one in Belgium. The drug product is actually produced in Italy and Germany. So from a drug product viewpoint, we have full capacity. We have zero problem. The current problems have to do with manufacturing the drugs substance”.

“So maybe I need to give you a little bit of explanation as to how we manufacture those vaccines. Essentially, we have cell cultures, big batches, 1000-litre or 2000-litre batches. We have cell cultures inside those batches and we inject them with the virus, the vaccine, if you will. Then those cells produce the vaccine, it’s a biotechnology protection. Now, some of those batches have very high yield and others have low yield. Particularly in Europe, we had one site with large capacity that experienced yield issues. So it's essentially a question of when you scale up to the level we are scaling up to - something like this that's never been done. We are scaling up to hundreds of millions, billions of doses of vaccines at a very high speed".

“A year ago, we didn't have a vaccine. When you do that, you have glitches, you have scale-up problems. Therefore, the yield varies from one to three, by the factor of three. The best site we have produces three times more vaccine out of a batch than the lowest producing site. We do this with a series of partners: in the US, those partners are actually approved by BARDA, the US administration, the group that manages those things and manages the capacity”.

"In the US, we also have issues of yield and essentially our engineers have worked with our partners to identify what the issues are. We believe we have sorted out the issues now. The issues are different, for instance, in Belgium: we believe it was more a question of downstream filtering because when you finish making the vaccine, you have to filter it. When you filter it, you put it into vials. Our partner in Australia for instance also had yield issues. And they have been in the vaccine business for 20 years. But it's complicated, especially in the early phase where you have to really kind of sort out all sorts of issues. We believe we've sorted out those issues, but we are basically two months behind where we wanted to be. We've had also teething issues like this in the UK supply chain. But the UK contract was signed three months before the European vaccine deal. So with the UK we have had an extra three months to fix all the glitches we experienced. As for Europe, we are three months behind in fixing those glitches. Would I like to do better? Of course. But, you know, if we deliver in February what we are planning to deliver, it's not a small volume. We are planning to deliver millions of doses to Europe, it is not small".

You say that EU is going to receive a reasonable quantity of doses by February. Could you please quantify this?
"First of all, as soon as we get an approval by EMA, in the next few days, we will be shipping at least three million doses immediately to Europe, then we'll have another shipment about a week later and then the third or fourth week of February. And the target is to deliver 17 million doses by February. So, I am just estimating roughly, that would mean like about 3 million doses for Germany, probably 2,5 million for Italy and something like 2 million for Spain. I don't know exactly what the precise allocation is, but it's based on the population of each country. If you're in Germany, you can vaccinate three million people in one month. It's actually not so bad especially for the people who are the most exposed and most at risk. That's not a small proportion. And if you apply the three month regimen, then in March, you can do the same again or more potentially because we are working hard to increase our goals. It's not as good as we would like to, but it's really it's not so bad".

So Europe signed the contract too late, instead of the UK?
"I will not pass judgment on this. But I can only tell you the facts and the facts are that we basically signed an agreement with the UK three months before we did have it with Europe. Now, part of this can be easily explained. When we entered

the agreement with Oxford, they had already been working with the UK government on this. So they had a head start. We were able to quite quickly take the UK supply chain and improve it. We had to modify the formula in the process, because Oxford gave us a process that needed to be modified to enable manufacturing at scale. Just think about, we've done all of this in months. Usually, it takes years. We got a manufacturing process that Oxford gave us, which was producing a good vaccine, but not at an industrial scale. It was just able to produce quantities for clinical trials. So then we had to modify the process to turn it into a process that could manufacture billions of doses. At a cost that is reasonable and at a speed that is reasonable".

"We had to change all of these. Then we had to do what we call technology transfer. So we go to each partner and we train them on the process. We train them on how to manufacture. And then, you know, some people are new to this process. It's like they learn the process. They don't know how to make the vaccine and they're not as efficient as others".

"So you may have lower productivity. That's why we have a productivity going from one to three. And so, unfortunately, it's really bad luck. Actually, there's nothing mysterious about it. But look, the sites that have the lowest productivity in the network are the sites that are supplying Europe. And quite honestly, I mean, we're not doing it on purpose. I'm European, I have Europe at heart. Our chairman is Swedish, is European. Our CFO is European. Many people in the management are European. So we want to treat Europe as best we can. You know, we do this at no profit, remember? We didn't go into this to try and make money or whatever. We would like to treat Europe as good as possible. I actually do believe we treated Europe fairly".

"Now, let me give you another number. Our total capacity globally now is about 100 million doses a month. From February onwards we are able to make 100 million doses a month, that's not small. Most vaccines have 100 million doses a year, that already takes us on a 1,2 billion pace per year. We are going to keep growing. Of course, we are ramping up production and Europe is getting 17 percent of this global production in February for a population that is 5 percent of the world population. Now, from the beginning we took very seriously the approach that Europe took, which we thought was fair and we all took. In fact, the US didn't say that Europe said that. Europe said the vaccine is common good

and everybody needs to get access at the same time globally. That's what we are doing. Europe is getting 17 percent of our global supply for a month for 5 percent of the world population. The problem is: 100 million doses is a lot, but we have 7,5 billion people in the world".

"We are in the ramp-up phase and basically it will improve, but it takes time. Having said all of this, I'm not looking for excuses, honestly. We take accountability. We want to do better and we're working day and night. Our people in manufacturing, we have hundreds of people, thousands of people now. Many of them didn't take any Christmas vacation. I'm not asking you feel sorry for us but you know, we're doing our very best. But it's a very complicated process and a big scale".

After the explanation you just gave at the same time it is striking the aggressive way which the EU has responded, even threatning to impose a new control on exports of activity out of Europe. Some are suggesting that you're selling your product to some other countries.

"The suggestion we sell to other countries to make more money is not right because we make no profit everywhere.That's the approach we took and we agreed on that. That's the agreement we have with Oxford University. It's actually even written in a contract we have with Oxford University: that we will be at no profit. We have slightly different prices from one geographic to the other because the cost of goods may be different. We have a supply chain in Brazil, we have another one in Latin America, another one in South Asia. We have one in Japan. Of course, you know, local costs are different. So you've got slight variations, but more or less, it's about three to four dollars, more or less everywhere. It makes no difference. Zero difference. I understand we all want to be vaccinated. I think the populations of Europe, like everywhere else in the world, have been under so much stress with this pandemic for so long now, for a year or so, that people are tired. And I think the people who didn't want to be vaccinated maybe six months ago are now saying: "I want to be vaccinated". You have a lot of people who want to be vaccinated".

"So, governments are under pressure. Everybody is getting kind of a bit, you know, aggravated or emotional about those things. But I understand because the Commission is managing the process for the whole of Europe. We're certainly not taking vaccines away from the Europeans to sell it somewhere else at the profit. It

would not make sense, honestly, if you think about it: we engaged in this process a year ago and we're going to make zero profit. It would not make sense for us to then say "we're going to make a profit somewhere else and destroy the whole spirit of the agreement". First of all, we would be in breach of the agreement we have with Oxford. Secondly, we've done it because we want to do it for the good of humankind".

You said that the UK signed the AZ vaccine contract three months before EU, so you had more time to tweak and fix the potential disruptions of the supply. Why then did you commit to similar contracts with the EU, if you knew that in a very short time there could be problems like the one the EU supply chain is experiencing right now?

"First of all, we have different plants and they have different yields and different productivity. One of the plans with the highest yield is in the UK because it started earlier. It also had its own issues, but we solved all, it has a good productivity, but it's the UK plant because it started earlier. Anyway, we didn't commit with the EU, by the way. It's not a commitment we have to Europe: it's a best effort, we said we are going to make our best effort. The reason why we said that is because Europe at the time wanted to be supplied more or less at the same time as the UK, even though the contract was signed three months later. So we said, "ok, we're going to do our best, we're going to try, but we cannot commit contractually because we are three months behind UK". We knew it was a super stretch goal and we know it's a big issue, this pandemic. But our contract is not a contractual commitment. It's a best effort. Basically we said we're going to try our best, but we can't guarantee we're going to succeed. In fact, getting there, we are a little bit delayed".

So is this the contract that the EU signed?

"Yes, certainly. Now we have a vaccine and everybody thinks it's easy. But in April last year, everybody was saying "it's impossible to do a vaccine by the end of the 2020", or "you're going too fast" or "you're cutting corners", "you can't do it", eccetera. Now everybody is saying "you're too slow", while before we were "too fast". At that time, when we talked about those things, first of all we didn't know whether we would have a vaccine or not. We didn't know what the yield would be. When you develop a vaccine, usually you do that over five, six years. We did this in a few months, so we thought, you know, if we are successful, we can get through this yield. Unfortunately, some manufacturing sites got to the yield and others didn't. We knew that it was going to be very challenging. But if we had not

stretched the process like this, maybe we would not even be able to produce vaccines now".

Italy is one of the countries that have explicitly threatened legal action against AstraZeneca. However, from what you have been saying, there is no feasible basis for a potential legal action against AstraZeneca.
"I don't want to give judgment on anything that has been said. I can only tell you what's in their contract. And the contract is very clear. Our commitment is, I am quoting, "our best effort". There are a lot of emotions running in this process right now, and I can understand it: people want vaccine. I want the vaccine too, I want it today. But, at the end of the day, it's a complicated process. We are getting there, in two or three months we will be at scale. We have a 17-million-dose production per month right now, it is actually not small at all. But of course, it's less than people want and understandably so".

Is there any chance that the contracts could be reconsidered in the sense that you may distribute the vaccines in some other way? For instance, would it be possible to take some of the vaccines destined for UK and move them to the EU or some other countries? Or is this such a fixed contract that you cannot change it?
"The UK agreement was reached in June, three months before the European one. As you could imagine, the UK government said the supply coming out of the UK supply chain would go to the UK first. Basically, that's how it is. In the EU agreement it is mentioned that the manufacturing sites in the UK were an option for Europe, but only later. But we're moving very quickly, the supply in the UK is very rapid. The government is vaccinating 2.5 million people a week, about 500,000 a day, our vaccine supply is growing quickly. As soon as we have reached a sufficient number of vaccinations in the UK, we will be able to use that site to help Europe as well. But the contract with the UK was signed first and the UK, of course, said "you supply us first", and this is fair enough. This vaccine was developed with the UK government, Oxford and with us as well. As soon as we can, we'll help the EU. I mean, as a company we are half Swedish and half British. In fact, we're global, of course, but we are European as much as we are British".

About the allegation on the "8% efficiency of AZ vaccine among the elderly" yesterday quoted in the German paper Handelsblatt last night: official authorities in Germany have already strongly denied this story. Do you think this is kind of an exercise of political scapegoating? And what is the risk of

this?

“What can I say? I don't have any idea where this number is coming. It’s incorrect. Several regulators of many countries have approved this vaccine for people 18 years old and above. How can one think that all these people, all these regulators around the world would have approved our vaccine if its efficiency was eight percent? I mean, of course not. Lots of very smart people are working for regulators, we must have approval now in 10 or 12 countries, including the UK, of course, which is a very strong, very tough regulator. I don't know where these numbers come from. Now, why do people come up with this? I don't know. Again, the emotions are raw. I would really like to call on people to really focus on the details and focus on the regulators. There is a lot of silly talk going on right now about all sorts of things. Some people making up stories, for what reason? I'm not sure. There may also be local political considerations sometimes? I can't say. Like testing and masks in the past, vaccines have become a political tool. It's unfortunate because you would like to tell people this is a moment to come together, really work together and try and resolve this issue. It's not a moment to use the testing of vaccines as a political tool”.

So, you can assure that this vaccine is efficient for the elderly?

“The issue with the elderly data is not so much whether it works or not. It´s that we have today a limited amount of data in the older population. You have to think that the program we have today was run by Oxford, it was the Oxford program. And Oxford is an academy group. They´re very ethical, and very academic. So they didn´t want to vaccinate older people until they had accumulated a lot of safety data in the 18 to 55 group. They said it was not ethical to vaccinate old people until they had enough safety data in younger people. Other companies took this risk, went ahead and vaccinated older people faster or earlier. If you start earlier, you have more data. Essentially, because Oxford started vaccinating older people later, we don´t have a huge number of older people who have been vaccinated. So that's what the debate is. But we have strong data showing very strong antibody production against the virus in the elderly, similar to what we see in younger people. It's possible that some countries, out of caution, will use our vaccine for the younger group. But honestly, it is fine. There's no enough vaccines for everybody. So if they want to use another vaccine for older people and our vaccine for younger people, what´s the problem? It’s not a problem. We're trying to deal with this crisis together. If you add up our capacity, plus the Pfizer capacity, plus the Moderna capacity,

there’s not enough in the world. There's not enough for the entire world. I personally think that the group of people who are between 50 and 70 are an important group to protect. If you are 50, 60, you need to be protected. Many people may have hypertension, overweight, you need to protect them. And the younger people, at some point, we need to protect them also. So, even though no country has done so so far, it’s possible that some countries will say: we will not use the AZ vaccine in older people until we have the US data confirming that it is indeed to be used in older people. Different groups or countries will take different approaches. The UK said: we believe it works in older people, we’re going to use it in older people”.

But how efficient is the AZ vaccine for people over 65? Can you give us a number?

"I don’t have the number in mind, to be honest with you, because the team has been finalizing the analysis. We had an interim analysis based on the November analysis of the data. What you do when you run a big trial like this is you do interim analysis. Pfizer did an interim analysis, so did Moderna. So we had an interim analysis with the data as they were in November, with a number of elder people, and then we had a final analysis in December, with more than 200 cases of infections, so a very high number of infections. And so the efficacy in that group, I don't remember precisely the number, it´s comparable to what you had in younger people".

"The problem is that it is a statistics debate, in a way. When you run a trial, you then say, the result es X%. And then you say, there is a confidence interval around this result. You may have heard this expression, we have 95% confidence interval, which is around this estimate of X%, what could be the lowest and what could be the highest. And if you have a lower number of people in the trial, then the confidence interval is very wide. So you have a point estimate, but the reality is that it could be higher or it could be lower. And that´s why people say, we don´t know, we can´t be sure, because we don´t have enough patients and therefore you have a large confidence interval".

"So the answer to this is that the data is showing good level of antibodies in elderly as you see in younger people, so we believe other regulators concluded the point estimate is real, even though the confidence is large. So it´s comparable to what we had in younger people. The point is that what´s important as far as the efficacy...at the end of the day, what is really important is the protection against severe disease and hospitalization. Because if you can stop people from

being severely sick, and importantly, if you stop them from going to the hospital, the whole thing becomes completely manageable. The hospitals are not overwhelmed, and people may cough a bit, or maybe run a little bit of fever, but they get on with their lives, as with the flu. That´s what you really want to do. Eliminate severe disease and hospitalization. Get rid of it. And, in our study, we have 100% protection against severe disease and hospitalization".

Is there any risk that this may embolden the anti-vaccine movement in Germany and elsewhere?

“The anti-vax are quiet powerful in Germany. They are powerful in the Netherlands, they’re powerful in France. I’m sure they are powerful in Italy and Spain, everywhere. They spread all sorts of stories..like that the mRNA vaccine is going to modify your DNA, you´'e going to die of an allergy... by the way, the safety profile of the Oxford vaccine is very good. The reactions you might get like fever, pain in the arm or headache after vaccination were really quiet low. And in the second dose are lower than in the first dose, while with other vaccines you have more reactions. So the safety is good".

"So the anti-vax, yes, anybody who makes statements on the vaccines that have to do with its efficacy or safety, if they do for scientific reasons, they should debate it in scientific circles. But if they do this for political reasons, it´s shameful, because basically what it does is that reduces people´s confidence in vaccines. People will start thinking about it, maybe this vaccines don’t work...everything is confused, I don´t want to be vaccinated. That´s why I say to the media, that sometimes get attracted by this, that you have to be very careful with what you write. Because, of course, you want to attract attention to issues, etc, but you also should also remember that people listen to you, and people can be impacted and lose trust in vaccines. Ultimately, these vaccines are approved by regulators. And those are experts. And it´s not just one. It´s not like you only have one regulator. You have one in Europe, one in the US, one in the UK, one in Japan...in Australia, in Canada, in India. Everyone has its regulator. There’s a whole series of very smart people who are experienced, looking at this data. You really would have to be a big conspiracy theorist to believe they conspire together on a global basis to approve vaccines that are risky or not effective. Fundamentally, people should trust those experts. And, on top of it, in the medicines and the drug world, when the regulators approve the medicine then it gets used. In the vaccine world, when the regulators approve the vaccine, it then goes -in most countries, not all countries but most countries- it then goes to an expert group of vaccinologists.

They further review the data and further decide how to use the vaccine. So, I mean, you have two layers of expert reviews. If you can´t trust this, what will you trust? But people who actually spread those rumours, unfortunately, they impact the people's trust".

Given the fact that a lot of countries have high hopes on the Oxford AstraZeneca vaccine but now there are supply problems, does it makes sense for EU countries to give a second thought to one-dose strategy that the UK is using?

"I think the UK one-dose strategy is absolutely the right way to go, at least for our vaccine. I cannot comment about the Pfizer vaccine, whose studies are for a three-week interval. In our case, the trial we're talking about was conducted by Oxford University. We AZ are conducting the US trial, which we think is going to be ready very soon. Oxford University conducted the so-called Oxford trial in UK and Brazil, and we have data for patients who received the vaccine in one-month interval, 2 or 3 months interval. First of all, we believe that the efficacy of one dose is sufficient: 100 percent protection against severe disease and hospitalisation, and 71-73 percent of efficacy overall. The second dose is needed for long term protection. But you get a better efficiency if you get the 2nd dose later than earlier. We are going to do a study in the US and globally to use two-month dose interval to confirm that this is indeed the case, there are many reasons to believe it is the case with our vaccine. We have a different technology. First of all, when you look at level of antibody production, this is higher if you give the second dose three months or two months later than one month later. Also, if you look at Ebola, its vaccine, which is also using the Adenoviral vector like the Covid one, the second dose needs to be given eight weeks later. Finally, the J&J vaccine with Adenoviral vector also are performing studies on a two-month interval. And J&J has the same technology as ours. Therefore, for our vaccine, there is no doubt in my mind that the way the UK is going is the best way, because right now you have a limited amount of vaccine, but also you have a limited number of doctors and nurses able to inject people. So you maximize the number of people who get one dose. You give them enough protection for two or three months, then you give them the second dose after 3 months. By March, the UK will have vaccinated maybe 28 or 30 million people. The Prime Minister has a goal to vaccinate 15 million people by mid-February, and they're already at 6,5 million. So they will get there".

Will you get an Oxford vaccine jab?
“Yeah, of course, as soon as possible. My mother lives in France, she is 92 and she was offered the Pfizer vaccine. I told her to take it and be protected quickly but she said, “No, I want to take the AZ vaccine”. So I would take it myself, of course. It’s a good vaccine”.

And what about the new variants?
"You probably have seen that Moderna published data on the South African variant. Essentially, what they said is that...what you call neutralization...in which you take the blood of people who have been vaccinated, you take the antibodies and you apply then to the virus, to see if these antibodies neutralize the virus. And the neutralization effect against the south African variant is 6 fold lower. But still, they believe it is high enough to control the disease. And it's still higher than what people who had the disease have. They say that they are developing a new vaccine for the new variant. In our case, we don´t have the results yet. Public Health England, which is the UK health system, is doing the analysis and we should have it very soon. I believe it's logical to think we'll have the same effect as seen with the Moderna vaccine but we do not know yet. The neutralization may be reduced. But I also think that there is a good chance patients will still be protected. At least, if they get infected, they will not get seriously ill, because the t-cells, the cellular immunity, will also be protecting. Having said that, we’re also working on a vaccine with Oxford University that will target the variant. In the meantime, I don’t think people should worry so much, because this variant is not that common in Europe and elsewhere. The vaccination will protect people, even if not completely to some extent. And it may be like flu, we´ll have to produce a new vaccine every couple of years or something".

"But I think an important point is...and in some extent this sort of takes us back to Europe: this virus mutates and perfects itself. We need to vaccinate as many people as possible around the world, because if you let the virus multiply in other parts of the world, it will mutate among these populations. Because it moves around people, and it mutates as it moves. So we need to vaccinate a sufficient number of people around the world. And that's why it’s so important to say, as Europe said, that we should get access to vaccines to everyone around the world in a fair and quick manner. For Europe to say they are going to control exports is the contrary to what they said a few months ago, that they were going

to give access to everybody. We have supply chains that are dedicated to regions, but we also manage our supply chain globally."

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