READOUT – TELEVISED PRESS CONFERENCE ON THE OXFORD/ASTRAZENECA VACCINE [1520 – 1620]

Panel

- Professor Jonathan Van-Tam, Deputy Chief Medical Officer for England, DHSC (**JVT**);
- Dr June Raine, Chief Executive of the MHRA (**JR**);
- Sir Munir Pirmohamed, Chair of the Committee of Human Medicines (**MP**); and
- Professor Wei Shen Lim, chair of the JCVI (**WSL**).

Intros

JVT - I'm JVT DCMO, and this is a clinical and scientific briefing. I'm joined today on my right by professor Wei Shen Lim - chair of JCVI, Professor June Raine, MHRA, and Professor Munir Pirmohamed, chair of CHM. Today's briefing is about the Oxford/AZ vaccine, and we will explain as we go through about a change of course, a course correction to programme. If you could have said to me in March 2020 how successful we would have been in 2021, wouldn't have thought we'd get as far as we have. Enormous success - if you had told me by March 2021 we wouldn't need a course correction, that also would have amazed me. Need to keep in context of huge achievement so far.

JR - Vaccine saved 6,000 lives, no effective medicine or vaccine without risks. Benefits can be to people or other people not taking vaccine. Clinical trial - common side effects, very rare side effects identified at scale. Why UK had careful monitoring systems in place. AZ in extremely small number of people - evidence firming up and review concluded more work is needed to establish beyond all doubt the vaccine has caused these side effects. Our role is to continually monitor safety, to ensure performing as expected, to ensure benefits outweigh risks. Public safety at forefront of minds. Epidemiologists reviewed all safety reports and safety reviews carried out in tandem of vaccination programme. Safety data, rigorous scientific review of all available data with suspected blood clots with low platelet count. CHM also met frequently and assessed all the data. This is also including lay representatives and advice from haematologists. Benefits of covid-19 vaccine and associated risks. Hospitalisation and death continues to outweigh the risks. Our review has reinforced risk remains extremely small. 20 million doses - 79 case reports up to and including 31 March. All 79 cases occurred after first dose. 19 people have sadly died. Occurred in 51 women and 28 men, from reports, risk of rare blood clot 1 in 4 million. 3 in the 19 were under 30 years. 14 were of cerebral venous. Balance of benefits and risk very favourable for older people, fairly balanced for younger. Evolving evidence should be taken into account when considering how vaccine used. Communicating advice on how to minimise risks, including how to report any suspected cases. Info will be updated and info for the public as we continue to monitor issue. Anyone who has symptoms should seek prompt medical advice, shortness of breath etc. I'd like to reiterate this is extremely rare. With proven effectiveness against disease, balance of benefit and known risks of the vaccine still very favourable for vast majority of people.

MP - I worked with CHM and expert working groups to thoroughly review all the cases, taken into account wide range of cases, and updated incidents rates for different populations be age and gender. Two committees spent two weeks reviewing reports, carefully scrutinised by MHRA and further info obtained where necessary to develop case definition of events, and reported via yellow card scheme. CHM advising the following - pregnant women should continue to discuss whether benefits outweigh risks. People with history of blood disorders should only have the Oxford vaccine where benefits outweigh risks. Anyone who experiences cerebral or major blood clots with low platelets after first vaccine of Ox should not have the second dose. We will be continuing monitoring further reports as they come in, identifying risk factors so we can refine advice we give. Data on

people with two doses are limited, and comparatively small number of doses have been given. Unclear to draw a conclusion on second dose - will be reviewed. Pulmonary embolisms occur in 7% of COVID-19, clots in leg in 11% of COVID-19, 23% have some sort of clot if end up in ICU with COVID-19. Causes strokes in 1.6%, that was into context that risks of clots much higher.

JVT - slide 1- this slide shows you in blue to left the potential benefits from covid-19 vaccination, and the orange part the potential harms. You can see as you go down slide those benefits and potential harms are arrayed by age bands from young adults to older adults. Arrayed in terms of intensive care admissions, and serious harms potentially due to vaccine on right. First slide set from title in scenario of low exposure, and rates of disease assumed in this scenario are lower than those we currently have in UK at the moment. If you look at 20 - 29 age band, 0.6 ICU admissions compared to serious harms of 1.1. As you go up through age groups, amount of serious harm declines, averted ICU admissions becomes much more pronounced. Arrayed over 16 week period - don't expect vaccine to last for 16 weeks. Expect it's going to be many many months, reason for using 16 weeks is typical pandemic wave, duration of it. At a very low exposure risk, lower than in the UK at the moment, the risk benefit finely balanced.

Slide 2 - medium risk scenario, 60 cases per 100,000, marginally higher than UK average at the moment, but lower than some remaining hotspots in UK. When more exposure, benefits start to stack up.

Slide 3 - pandemic wave, height of second wave. Reflective of kind of scenario we want to avoid in forthcoming autumn and winter, here a lot of covid-19 circulating, even in 20-29 group, potential benefits in terms of intensive care, very much higher than serious harms due to vaccine - that's why regulators have concluded as they have about risk benefit for AZ vaccine. Hope that's placed it all into bit of context, detailed scientific discussion, hopefully figures bring it to life.

WSL - JCVI been meeting, reviewed safety evidence, kinds of data seen earlier on slide. Well aware of high level of protection, particularly against serious disease, dying from covid. Must be balanced, uncertain occurrence of extremely rare events. Acting really in interest of safety, JCVI feels there are three points of advice put across. First is info given to individuals and health professionals should be updated to reflect the latest considerations by MHRA and JCVI. Those who receive first doses of Oxford should get second dose of Oxford. Adults who are aged 18 - 29 who do not have underlying health condition that puts them at higher risk should be offered alternative covid-19 vaccine in preference to AZ vaccine where available. What is not advised - a stop to any vaccination for any individual in any age group. We are describing a preference for one vaccine over another for one age group, out of utmost caution rather than because serious safety concerns. Implications for operations and deployment of vaccines.

JVT - what does this mean for me, what shall i now do? Change in clinical advice for under 30s, will require changes in way national health service operationalises programme. I am assured that actually because of supply situation, effect on timing should be zero or negligible. Contingent on getting supplies we expect to get of alternative vaccines, which are Pfizer vaccine and Moderna vaccine that we hope to bring into deployment. That's the what does it mean for me. On the what should I do? Please be reassured that two sets of independent experts on regulatory side and clinical advice side are all over this and I can testify to many hours of work to get advice to you in last week or so, working without a break. Thanks to members of various committees to get to this point. This is a course correction, no question about that, but in medicine quite normal for physicians to alter preferences for how patients treated over time. Happened with vaccines only a few years ago. Advice to elderly and flu was get your vaccine, JCVI changed advice is for adjuvanted vaccine for elderly. Changes in preference for vaccines are business as usual. Massive beast that we are driving

along at enormous pace with enormous success, if you sail a massive liner across the Atlantic, it's not reasonable you aren't going to have to make a course correction during the voyage. NHS has a message that we will get the right vaccine to you in right time according to new JCVI advice. Might be small delay, might be smaller distance asked to travel, but NHS is all over this and understands challenge to make truly operational. To sum up - course change, based on clinical preference, based on newly emerging data, careful review, please remember benefits accrue over very long period of time, fairly confident months and months, whereas event of vaccination is brief moment, way for lives to get back to normal again.

Q&A

Fergus Walsh, BBC - worried change of course will damage vaccine confidence in young. Are risks for those in vaccine and under 30s significantly higher than older age groups?

JVT - on first point, and say that clearly this is a course change. We don't want it to result in loss of vaccine confidence, I hope I have reassured carefully considered decisions, remains vitally important those who come back for second dose come back for it - important all those come back for vaccination.

WSL - importance not just risk, younger people compared to older people. Benefit risk balance, benefit from vaccination is as we know very high in older people and decreases as age goes down as risk goes down with age, but still a benefit to younger people and overall benefit still in favour of being vaccinated. Where we have alternative vaccine, it would be preferable to offer youngest people who have no health conditions, alternative vaccine, really just on the side of safety rather than specific concern from vaccine itself.

JVT - slides were based on ICU admissions and didn't take into account additional benefits in preventing long covid, costs of the illness itself and potentially passing on infection to family and friends.

Tom Clarke, ITV News - vaccine confidence, what advise someone who is under 30 years of age?

WSL - very good question, discussing earlier. Know someone whose daughter is around 30/31, important question. One of fundamental things is should be fair and transparent, which is why doing briefing now to set out risks and benefits, so people are informed before vaccination. For someone who is 31/32, have to make own decision about what they want to do, still say balance in favour of benefits.

Tom Clarke - risk of someone below 29, 5 and a half times higher than someone 60 to 69 - what seen in data, definite trend in higher risk of blood clots in young age groups, questions raised for paediatrics?

WSL - risk signal from ages in terms of the clots, paediatric vaccination, JCVI not made firm decision yet, clinical trials still ongoing on safety in children. No decision made on that yet.

JVT - JCVI's decision to give advice for under 30s was taken fully cognisant of advice applying above age of 30, and that was part of consideration. Talking here in context if extremely small numbers. Makes difficult to interpret.

MP - risk in younger age group, as already said, need to look at relevant benefits vs risks, reason why higher risk in younger age group is not clear, need to undertake further evidence. Trial paused by

data safety monitoring board for children. Much lower risk of clots for children, accumulate more data over next few weeks, be able to determine whether trial can start again.

JVT - on children, multiple manufacturers with different types of vaccines all working to do trials on children. Not the only show in town to see if vaccines for children.

Tom Moore, Sky - presented as choice between AZ and having COVID, young could be given alternative vaccine then why not middle aged too? Europe/Canada decided not to give anyone under 55/60 vaccine, too cautious?

WSL - Every country has different values, programmes, risks, every country has to make own decision regarding risk and benefit. Just as example - in some countries life expectancy not as good as the UK, and people live to mean age of 50, their life expectancy means risk benefit when to draw a line after particular vaccine will be different from another country where life expectancy may be different. Given our vaccine availability, supply, kind of pandemic we're having, variant, the correct judgement is around 30 year threshold where young people with no health conditions where we would offer alternative vaccine. Extremely rare adverse event - do not know for sure related to one vaccine or not, may not be related to vaccine, may be related to covid itself, unsure and advice based on protecting population and working on principle that safety is biggest concern.

JVT - reinforce point about context - low income country where life expectancy not the same, risk and benefit different in every population. JCVI entirely free to make advice and recommendation - always independent and they can say and do as they wish. Idea of vaccine in 40-49. Noting you would clip a vaccine at that point is absurd, independent decision, I think it's been taken in an extremely rational way.

[question cut out on broadcast]

JVT - absolutely wasn't and programme shouldn't be delayed because of this course.

Nick McDermott, The Sun - link between Az and blood clots, language vague and unsure, link is firming up, avoidance of doubt. There is a link between this jab and rare blood clots? Second question, Janssen one shot jab in summer - saying under 30s prioritised for alternative jabs, potentially a story Janssen for under 30s as don't need to wait for second jab?

JR - important question on how firm is the evidence, pattern of those cases, much more solid base in regulatory world to put in side effect into product information, reasonably plausible link. Needs to be much more work on scientific understanding to give us understanding of proof.

MP - early evidence suggests consolation of symptoms caused by immune response by platelets, leading to clotting in different parts of body, don't have link between vaccine and immune response, where work needs to go on to identify link to develop strategies for future.

JVT - Janssen, in terms of immediate available alternatives right now is Pfizer, do expect to have Moderna beginning to be deployed from mid-April and those will be two for next two weeks - common knowledge, UK has placed ordered with Janssen, don't yet have certainty on timings of delivery, one dose schedule, must be in frame for solutions for vaccine requirements going forwards, and for young people referred to. Always been part of the UK strategy to have multiple horses in race to be in good position to exercise it. Final cautionary point for you - this is vanishingly rare but serious adverse reaction, but vanishingly rare. Cannot pick these up until tens of millions of doses of

vaccine. Have to wait and see if going to see or not see similar signals. Reinforces message that it's important to have many horses in race.

<u>Tom Whipple, The Times</u> - mechanism, great to explain theories about how triggered, several other vector vaccines, presumably the mechanism that causes likely to be in there too. If know possible side effect, are there ways to mitigate it?

MP - early evidence suggesting immune response occurring into relation to whatever event is and vaccine, way that that immune response then targets platelets and why targets in small number of individuals, not clear on that final work at the moment, really important to understand mechanisms at the moment, if you were able to identify mechanisms, refine advice given so risk factors. Then think about modified vaccines that don't cause event in future. Viral vector - several vaccines, don't know whether related to viral vector or something else.

<u>Hanna Geisler, The Express</u> - majority of cases were in women, smaller number in men, not a lot of data yet, are there any biological reasons why women higher risk than men? And yellow card scheme collects data on effects, any hint of increased risk?

MP - 79 cases, 51 women, 28 men. Numbers are small. May reflect who is getting vaccine as many healthcare workers are women. Incidence rate, no difference between men and women. Continue to monitor and see if gender prediction. Do not have evidence to say men or women more likely to get this.

JR - every week, publish report. Encourage people to read it, and encourage people to report to us - every report matters and every report carefully looked at.

<u>Conclusion</u>

JVT - I would like to conclude by thanking colleagues for time and more importantly for immense amount of time and effort they have put in behind the scenes to get us to this point. Covid19 remains serious illness that CMO has said, something to live with in long term. Vaccine is likely to be and continue to be extremely important in getting life back to normal;. Managing very carefully. Real evidence of authentic experts looking after your interests. Course correction, but full speed ahead