Medical Director

COVID-19 BULLETIN

12 January 2021

Update on concerns over second dose delay

Dear colleagues

I am very aware that there has been a high degree of concern regarding COVID vaccination, much specifically related to the UK-wide decision to defer the second vaccine dose until 12 weeks after the first dose has been received. I have spoken with a number of our clinical leaders in the organisation to hear the concerns being expressed, and had the opportunity to feed this back directly to the Chief Medical Officer of Wales, along with the MDs from every other Health Board, on Friday. Reassuringly we are all working to the same guidance interpretation.

The key messages that we discussed and I would like to share with you are:

1. The decision to convert the 2nd dose timing from <4 to <12 weeks was made by the expert group, the JCVI, taking into account the current pandemic status, the supply/delivery chain for vaccination UK and world-wide, and the available scientific evidence regarding the efficacy of the Pfizer, AZ and Moderna vaccination programmes, with the 2nd dose given in a delayed, 12-week, fashion.
2. Their assessment is given in the attached document: *12-week JCVI*. The message is very transparent. Converting to a 12-week strategy will save lives. I understand that their modelling actually suggests that if we used half the extra million doses that this policy will generate for staff, and half for the most vulnerable, it would save more than 2,000 lives directly and indirectly.
3. It is also clear though that there is a differing amount of evidence to support the scientific validity of their recommended approach with each specific vaccine, with the AZ vaccine having the strongest evidence base in this regard. Indeed the Oxford-AZ vaccine trial *did* include different dose intervals and found that a longer gap of 8 to 12 weeks led to a greater immune response compared to second dose at 4 weeks
4. In that regard the NEJM has published the full data from the original research study on the Pfizer-BioNTech vaccine and made it freely available NEJM 2020;383:2603, similarly the Oxford-AZ vaccine study is available Lancet Dec 2020. I would stress though that the JCVI also had access to unpublished data that they used to make their decision.
5. Netherthless it is clear that all the vaccines are highly effective at preventing COVID illness after 10-21 days post 1st dose, and that any additional short-term benefit from a 2nd dose is at best minimal. For example, the Pfizer vaccine, once an immune response has been initiated, is ~89-90% effective at preventing COVID infection. After a 2nd dose that may rise to 95% (based on a sub-set of data with small numbers and with wide confidence intervals (95% CI 52% to 97%)). It is very likely that this is a very small benefit compared with the 89-90% benefit seen by giving a 2nd individual a 1st dose in our currently constrained system.

6. Therefore the 12-week approach has been recommended by JCVI, but crucially it has also been supported by the MHRA, The Royal College of Physicians, all four Chief Medical Officers of the United Kingdom, the Chair of the Academy of Medical Royal Colleges, plus by the British Society of Immunology. The BSI statement in this regard is attached.
7. Support for a delay, '*until adequate stocks of vaccine are available*' to both treat all our high-risk population groups and all health and care staff, has additionally been given by The Association of Anaesthetists, the Intensive Care Society, the Faculty of Intensive Care Medicine and the Royal College of Anaesthetists. Their statement is also attached.
8. Just to reiterate that the 2nd dose is utilised to give a subsequent sustained, long-term, protection against COVID illness. It is reported that it does so by re-activating memory cells, to boost their immediate and future immunological potential. There is good evidence in other vaccination programmes that delaying this 2nd dose is in fact beneficial in giving better sustainability to the immune response (as there are more memory cells available to be boosted). The mechanism of the current COVID vaccines may not be directly comparable with prior vaccine programmes of course, so we do understand this is a potential for actual benefit, rather than one that is yet fully proven, but it should not be dismissed, especially considering the AZ evidence above.
9. Furthermore, there is a clear additional benefit of rapid population vaccination related to the potential for emergence of immune resistant strains. Suppression of the virus, both through vaccination and our ongoing efforts of social/non-pharmacological interventions and isolation of contacts, is the best way to prevent the emergence of potentially resistant strains. With lower levels of virus circulating, natural variation of the viral genome is reduced, and therefore the potential for emergence and selection of strains with reduced response to the vaccine is much lower.
10. It is estimated that we could immunise, with a 12-week policy, the highest risk groups within 6 weeks - in which over 90% of all COVID deaths occur. Clearly it would take at least double that time with a 4-week policy
11. No one is suggesting that vaccine mixing is appropriate - and should be discounted in all but the most unusual cases. That is UK policy reassuringly.

As such I believe that it is morally, and scientifically the right thing to do to delay the 2nd dose until 12 weeks, and we should support it. I know that some will be concerned by the decision, and I do understand that, and as such I will continue to keep you updated if the policy changes or any new evidence emerges from the Chief Medical Officer.

You can view more documents here

COVID-19 vaccination for intensivists and anaesthetists

JCVI 12 week guidance

British Society for Immunology statement on COVID-19 vaccine dosing schedules

Many thanks for all you are doing

Stuart Walker

PS - may I also just point out that full compliance with current PPE standards is still required post-vaccination! Just for the avoidance of doubt...