Blood Cancer UK submission of 16 December 2022

PE1950/E: Ensure immunosuppressed people in Scotland can access the Evusheld antibody treatment

There are approximately 650,000 immunosuppressed people in the UK, of which over 80,000 are in Scotland. This group have medical conditions, or take certain treatments, that weaken their immune system and render them highly susceptible to infections, severe disease, and death. Due to their weakened immune systems, many also do not elicit a strong immune response from the Covid-19 vaccines, meaning they remain at very high risk from Covid, unlike most of the general population.

Evusheld

It is vital that this group has access to an effective preventative Covid treatment, because of their higher risk of severe illness and death. Evusheld is the only preventative Covid treatment approved by the MHRA (on 17 March) but it has yet to be procured. Real-world data from countries in which Evusheld is available show that immunocompromised people who took Evusheld had better outcomes. In one Israeli study, conducted during the BA.1 and BA.2 wave, patients who took Evusheld were half as likely to become infected with Covid, and 92% less likely to be hospitalised or die.[1]

Lab-based and real-world evidence show that Evusheld is effective against Omicron BA.1, BA.2, BA.4 and BA.5 (to varying degrees). However, it is uncertain whether it is effective against the currently dominant variants BQ.1 and BQ.1.1 (which are subvariants of BA.5) and other circulating variants such as CH.1.1 and XBB. In the week ending 30 November, BQ.1 and BQ.1.1 made up 52% of all sequenced Covid cases in the UK. CH.1.1 made up 12%, and XBB made up 4%.[2]

[1] https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac625/6651663
[2] GISAID data, accessed via covSPECTRUM: https://cov-spectrum.org/explore/United%20Kingdom/AllSamples/Past6M

Findings from a pre-print lab-based study using pseudovirus suggest that Evusheld does not neutralise the above variants of the virus.[3] A further pre-print using live virus also suggests that Evusheld does not neutralise BQ.1 (but did not test for other of the above variants).[4] Further studies have yet to be published, but it is expected that more will be made available in the coming weeks and months. While these results suggest that Evusheld is incapable of neutralising these variants, there is a lack of consensus among clinicians and researchers as to how closely lab results translate into real-world efficacy, due to a lack of pharmacokinetic and pharmacodynamic data. For more information on these studies, Blood Cancer UK's assessment of the available evidence, and what this might mean for people living with blood cancer, see our blog post on this topic.[5]

While some variants against which Evusheld has been proven to offer protection remain in circulation, the prevalence of these variants is relatively low. It is therefore unclear how much protection Evusheld offers in the current context. In the United States, clinical guidance recommends that Evusheld be used in regions where the above variants are not prevalent, while considering individual patients' risks and circumstances.[6]

Vaccine (in)efficacy

For immunocompromised people, their risk of death from Covid is higher than those with strong immune systems, even after vaccination. One study, published on 27 September, shows that, after a third vaccine dose, only 22% of patients with blood cancer had generated antibodies that could help neutralise the virus, and that of those only 58% had a T cell response. Of those without neutralising antibodies, only 45% had a T cell response.[7] This level of severe immunosuppression has clear consequences: among the unvaccinated, the immunocompromised make up 2.4% of Covid ICU admissions (in England, Wales, and Northern Ireland); among those with 3 vaccine doses, this is 27.7%. Further to this, vaccine uptake among this patient cohort is relatively low. In Scotland, only 60.4% of clinically vulnerable 5 – 64 year-olds have

[3] https://www.biorxiv.org/content/10.1101/2022.09.15.507787v4
[4] https://www.biorxiv.org/content/10.1101/2022.11.17.516888v2
[5] https://bloodcancer.org.uk/news/evusheld-does-it-work-against-omicron/
[6] https://www.covid19treatmentguidelines.nih.gov/overview/prevention-of-sars-cov-2/
[7] https://aacrjournals.org/bloodcancerdiscov/article/doi/10.1158/2643-3230.BCD-22-0077/709472/Anti-spike-T-cell-and-Antibody-Responses-to-SARS

had their autumn booster (as of 7 December, according to PHS). While severe outcomes in the general population have been mitigated by our vaccines programme, protections for the immunocompromised remain inadequate.

Post-exposure Covid treatment

While the protection mechanisms for the immunocompromised has relied upon post-exposure Covid treatments, these treatments are currently undergoing an appraisal by the National Institute for Health and Care Excellence (NICE), in collaboration with the Scottish Medicines Consortium (SMC). Their draft recommendations would withdraw all community treatments but one: Paxlovid. Paxlovid, however, has drug interactions with a significant number of cancer treatments used to treat and manage blood cancer. If these recommendations come into force in the spring, people with blood cancer for whom Paxlovid is contraindicated by their cancer treatments will either have to pause their cancer treatments to take Paxlovid (which can have long-ranging and devastating consequences), or wait until their Covid infection develops to such severity that they are hospitalised and placed on supplemental oxygen. Only at this clinical point is the next Covid treatment (tocilizumab) licensed for use.

Considering that the immunocompromised are protected only by vaccines (which, for many, do not adequately protect them) and by the post-exposure Covid treatments (which, in the spring, will become inaccessible to some of the blood cancer patients at highest risk), it is vital that a safe and effective preventative Covid treatment is made available for those at the highest risk.