Autoimmune kidney disease (includes vasculitis, lupus, glomerulonephritis and nephrotic syndrome) unshielding group (GN group) – summary of evidence review (up to 19.7.2020)

We have reviewed medical literature (110 studies, case series & case reports) published up to 19th July 2020 in populations taking immunosuppression medication across a broad range of medical conditions including kidney diseases, rheumatological and auto-immune diseases, inflammatory bowel, neurological and skin diseases. From these data on 6439 patients, we estimate that the overall risk of death in patients receiving immunosuppression who are infected with SARS-CoV-2 (coronavirus, COVID-19) is around 5.9%. However, it is hard to state whether the risk of death from COVID-19 in the autoimmune kidney disease population is higher or lower than the mortality risk for the general population infected with Covid-19 as very significant uncertainty exists about such mortality estimates due to differing reporting practices for SARS-CoV-2 cases and deaths within and between countries. As of 6.8.2020, the global reported mortality from COVID-19 is 3.75% (https://coronavirus.jhu.edu). In the UK, 15% of all people with proven or suspected COVID-19 have died (https://coronavirus.jhu.edu/region/united-kingdom).

Establishing the excess risk of death from COVID-19 due to immunosuppression for autoimmune kidney disease is challenging and there is definitely not a "one size fits all" answer. Different autoimmune kidney diseases predominantly affect different genders (e.g. lupus is 8 x more common in women than men), age groups (e.g patients with FSGS tend to be much younger than those with vasculitis) and ethnicities (e.g. patients with FSGS or lupus nephritis are much more likely to be from the BAME communities whilst vasculitis patients are most commonly Caucasian). This is important as the risk of death from COVID-19 varies depending on gender (higher risk if male), age (higher risk if ≥60yr), ethnicity (higher risk if from the BAME communities) and the coexistence of other illnesses /conditions (comorbidities) such as diabetes, chronic kidney disease (impaired kidney function), lung or heart disease. Having autoimmune kidney disease, or the treatment for it, may predispose to these comorbidities and it may be that the presence of these may account for at least some of the possible additional risk of death from COVID-19 rather than their underlying kidney disease or its treatment.

There are sparse country specific data on autoimmune kidney disease. The OPENSAFELY study[1] extracted data on 40% of the population of England from NHS primary care records. The data of 17,278,392 adults were linked to 10,296 COVID-19 related deaths and the key associations with COVID-19 related death were being male, older age, deprivation, diabetes, and being Black or South Asian. Looking more specifically at populations relevant to autoimmune kidney disease, the fully adjusted hazard ratio (HR) for death in those with rheumatoid arthritis, or lupus, or psoriasis (lupus would have been the minority group in the 800,000 patients with these diagnoses) was 1.19 (95% CI 1.11-1.27) – this compares, for example, with a HR of 1.7 (95% CI 1.34-2.16) for other immunosuppressive conditions (non cancer) and 1.33 (1.28-1.40) for those with CKD 3 and 2.52 (2.33-2.72). Simply being aged 60 to 69 is associated with a HR of 2.4 (2.16-2.66) and this goes up steeply such that for those aged 70-79 the HR is 6.08 and for those over 80+ 20.61. It is not clear whether the risks of having e.g. immunosuppression and CKD 3 are additive or synergistic but it is reasonable to assume that the more comorbidities present, the higher the risk of a poor outcome from COVID-19 infection. It also reasonable to assume that being old and having

an autoimmune condition requiring immunosuppression will confer a high risk of death if they develop COVID-19. This is borne out by the UKIVAS registry data which to 16th June 2020 had reported 64 patients (mean age 66.1yrs) with vasculitis infected with COVID-19 of whom 17 had sadly died – a mortality rate of 26.5%.

At present there is very little information about which specific immunosuppressive medications may lead to poorer outcomes following SARS-CoV-2 infection, other than taking *pre-existing* higher dose (≥10 to 15 mg predisolone/day) glucocorticoids (steroids). For this reason, with the caveat that our risk stratification is largely an expert opinion based statement, we consider patients with newly diagnosed or recently relapsed disease who are receiving *induction* immunosuppression are likely to be at higher risk that patients whose autoimmune kidney disease is in remission, and who are on stable maintenance immunosuppression.

The major caveat to all our advice is that the overall rates of COVID-19 infection in all reports of patients with autoimmune conditions (registries and cases series) are remarkably low.   There is now a global registry of cases of COVID-19 infections in patients with autoimmune kidney disease – International registry of Covid infection in Glomerulonephritis (I-RocGN)   https://redcapsurvey.niddk.nih.gov/surveys/?s=FPM87NK7T4   (into which we encourage everyone to enter their patients – fully anonymised and does not require local ethical approval) and although established a little after peak (launched on April 20th), allowed entry of prior cases. 14 centres from the USA, UK and EU participated initially and 4 centres reported 0 cases and the other 10 only had 43 patients in total, of whom 16% died (Meryl Waldman, personal communication). This is clearly a tiny proportion of total patients with autoimmune kidney disease. It is highly likely that the very low rates of infection seen reflect strict shielding and social isolation practiced by these patients around the world – as has been reported in Italy and certainly is the case in the UK. It will be very important to document rates of infection as social restrictions ease and particularly as people return to work and children to school.

It is our intention to periodically re-review the literature relevant to this section, and update the information provided accordingly. In due course we will provide a link to our full data search.

1. Williamson, E.J., Walker, A.J., Bhaskaran, K. *et al.* Factors associated with COVID-19-related death using OpenSAFELY. *Nature* (2020). https://doi.org/10.1038/s41586-020-2521-4