Letter to the Editor

Article to which the letter relates

Drug-drug interaction with oral antivirals for early treatment of COVID-19

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We read with interest the Danish population-based study estimating the risk of significant drug-drug interactions (DDIs) with the antiviral component nirmatrelvir of the drug combination nirmatrelvir/ritonavir (NMV/r) in the age groups ≥65 years and ≥ 80 years (Larsen, 2022). The study highlights the potentially detrimental effects of DDIs if this antiviral treatment is used as part of polypharmacy in this elderly population at high risk for the progression of SARS-CoV-2 infection to severe COVID-19.

Regarding statin treatment and NMV/r DDIs, it was found that 15.45% of the study population in the age group ≥ 65 years used simvastatin or lovastatin and that the respective percentage among ≥80 years was 17.70%. The percentages for atorvastatin in the age groups ≥65 and ≥80 years were 19.91% and 15.85%, respectively. As simvastatin and lovastatin are contraindicated during NMV/r treatment, Larsen (2022) recommends that “patients at low risk of atherosclerotic events could potentially pause the statin treatment during NMV/r administration”.

For several reasons, we are concerned about the potential risks for recommending discontinuation of statin treatment in the age group ≥65 years. Firstly, according to current guidelines, statins are not routinely prescribed for patients having a low risk for atherosclerotic cardiovascular disease (ASCVD) (Mach et al., 2020). Moreover, the decision to use statin in older individuals is not evidence-based and, therefore, must be made individually (Strandberg et al., 2014). Secondly, it is very difficult to estimate the true ASCVD risk in older patients, especially among those aged ≥75 years who are free of clinically overt ASCVD (Saeed and Mehta, 2020). Among patients aged <75 years, the efficacy of statins used for primary prevention is well-proven, and the relative risk reduction of major vascular events is about 20-30% for every 1 mmol/L reduction in LDL-cholesterol (Cholesterol Treatment Trialists' (CTT) Collaborators, 2012). Thirdly, in COVID-19 patients, several studies have shown that the use of statins is associated with an improved prognosis.
(Wu et al. 2021). Additionally, the main protease (M\textsuperscript{pro}) of the SARS-CoV-2 virus adversely affects microvascular endothelial cells in the brain, and statins may directly inhibit M\textsuperscript{pro} activity (Vuorio et al. 2022a). Fourthly, withdrawal from statin therapy may acutely worsen the prognosis of patients with non-ST-segment elevation myocardial infarction, even in patients without the additional cardiovascular burden caused by a viral infection (Spencer et al., 2004). In addition, statin withdrawal may easily remain permanent.

Based on the above considerations, we recommend that, rather than discontinuing simvastatin treatment, simvastatin should be substituted by either pravastatin or fluvastatin (Vuorio et al., 2022b). By taking into account the prognosis of both COVID-19 and ASCVD, the patient would then be at low risk of side effects from statin therapy and will be guaranteed the best possible benefits from statin treatment.

**Conflict of Interest**

AV has received consultancy fees from Amgen and Novartis.

PTK has received consultancy fees, lecture honoraria, and/or travel fees from Amgen, Novartis, Raisio Group, and Sanofi.

FR has received research grants, honoraria, or consulting fees for professional input and/or lectures from Sanofi, Regeneron, Amgen, and Novartis.

**Ethical Approval Statement**

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References


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