

Statin Needs to be Continued During Paxlovid Therapy in COVID-19

TO THE EDITOR—We read with interest the study published by Najjar-Debbiny and co-authors [1]. This recent large population-based study was carried out in Israel among patients who were at high risk for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and who had no contraindications for the use of Paxlovid. Very interestingly, those patients who benefited the most from Paxlovid were those who had a preexisting cardiovascular ($P = .028$) or neurological disease ($P = .016$).

The authors emphasized that several drugs have been suggested as treatments of SARS-CoV-2 infection, but most of these measures have not effectively reduced the risk of progression to severe disease or are too expensive or logistically difficult to be used widely. As pointed out above, Paxlovid treatment was most beneficial among patients having a preexisting cardiovascular or neurological disease, and therefore being at high cardiovascular risk. The majority of these patients should have been treated with a statin to reduce their cardiovascular risk [2]. Simvastatin is a very frequently used statin as it is cheap and worldwide available. In the protocol of the study, the use of simvastatin was a contraindication for the use of Paxlovid, which accords with the information provided by the manufacturer of Paxlovid [3]. However, there are other statins like fluvastatin and pravastatin which can be safely used with Paxlovid to substitute for simvastatin during the critical early phase of severe SARS-CoV-2 infection [3].

Statins have been shown to improve the prognosis of severe SARS-CoV-2 infection [4]. So we argue that the ongoing use or introduction of statins needs to be taken into account when trying to prevent severe clinical consequences associated with a serious SARS-CoV-2 infection. For the physicians

managing such patients, what needs to be emphasized is that statin therapy should not be discontinued and, in many cases, may need to be even intensified. This particularly applies to patients with severe hypercholesterolemia, such as those with familial hypercholesterolemia, who are at highly increased risk of coronavirus disease 2019 (COVID-19)-related vascular incidents including acute myocardial infarction and ischemic stroke [5, 6].

An additional very interesting view derives from the observation in animal models demonstrating that the SARS-CoV-2 main protease (M^{Pro}) adversely affects microvascular endothelial cells in the brain [7]. While Paxlovid is an inhibitor of the SARS-CoV-2 M^{Pro} [8] it has also been suggested that, at least in silico, statins could directly interact with the M^{Pro} , fluvastatin being one such example [9]. So from a theoretical point of view, dual inhibition of M^{Pro} could be accomplished by using Paxlovid together with fluvastatin. However, any added clinical benefit of such combination therapy needs to be confirmed in human studies. The other advantage of long-lasting statin therapy is that the inhibition of M^{Pro} would also last longer compared to the short period of Paxlovid therapy. This aspect is important to consider, especially because in some COVID-19 patients, the infection rebounds after stopping Paxlovid treatment [10].

Note

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