Sacubitril/Valsartan and SARS-CoV-2

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Dear Editor,

SARS-CoV-2 (COVID-19) is responsible for the current global pandemic. At the date, no antivirals directed against the virus or effective vaccines are available. (1) It is essential to recognise the risk factors and components that may play a protective role. There is no clear evidence on the correlation between changes in the Renin-angiotensin system (RAS) by ACE-is, ARB or DRis and COVID-19 infection.(2) (3) (4) Randomised controlled trials are needed to verify the involvement of COVID-19 viral infection and chronic treatment with these drugs. A possible scientific hypothesis to investigate is the role of the neprilisin inhibitor Sacubitril in association with valsartan in the more severe stages of COVID-19 infection. The challenge to defeat the current pandemic poses several objectives, among them try to give added values to therapeutic solutions, in this direction the association sacubitril/valsartan has already demonstrated the therapeutic efficacy in the treatment of chronic symptomatic heart failure with reduced ejection fraction in several studies (5), indirectly the therapeutic benefits of cardiovascular type are also directed to a decrease in the risk of infection and complications from COVID-19. Furthermore, there is evidence of a significant increase in NT-proBNP in COVID-19 patients. (6) Studies show that higher NT-proBNP was an independent risk factor for death in patients with severe COVID-19, (7) moreover, NT-proBNP is associated with proinflammatory effects. (8) (9) Sacubitril through its mechanism of action increases neprylisin-degraded peptides, such as natriuretic peptides (NP), ANP and BNP, (10) evidence associates these peptides with anti antiflammatory, antihypertrophic and antifibrotic effects, recent evidence shows that IL-1? secretion is strongly inhibited by the BNP/NPR-1/cGMP axis to all molecular mechanisms closely controlling its production and release, NF-kB, ERK 1/2, and all elements of the NALP3/ASC/Caspase-1 inflammasomic cascade, and that NALP3 inflammatory inhibition is directly related to the deregulatory effect of BNP on the activation of NF-kB/ERK $\frac{1}{2}$,(11) also the decrease of NT-proBNP by Sacubitril is known. Valsartan in association, by blocking the AT-1r receptor of ang II, decreases profibrotic and proinflammatory activity mediated by AT-1r, and indirectly increases the action of ang II on AT-2r with antifibrotic, antifibrotic effects. Based on the evidence and in relation to our generated hypothesis, we believe that a use of sacubitril/valsartan in the most severe stages of COVID-19 infection could have therapeutic efficacy, with anti-inflammatory and antifibrotic effects mediated by natriuretic peptides. Clinical studies are required to confirm this hypothesis.

Main Statement

I, the undersigned, Antonio Vitiello and any other author, declare that:

The manuscript was written entirely by the authors; All authors made an equal contribution in the development of the paper; We have no conflict of interest; We have not received funding/source; There are no sensitive data and no patients were recruited for this study; The document does not conflict with ethical legislation. The authors accept the full TRANSFER OF COPYRIGHT to the journal.

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