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Risks and Impact of Angiotensin-Converting Enzyme Inhibitors or Angiotensin-Receptor Blockers on SARS-CoV-2 Infection: A Template for Sustaining RAASI Therapy.

The spread of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has already taken on pandemic proportions. As of August 6, 2020, the COVID-19 pandemic has exerted an unprecedented impact across the globe. More than 19.46 million cases have been reported worldwide, including 722,285 deaths. The recommendations of the World Health Organization (WHO) have led to a “lockdown” of more than one-third of the world’s population and many countries have closed their borders, affecting both the industry supply-chain and global travel. Although the major current focus of public health authorities is to develop a coordinated global response to prepare health systems to meet this unprecedented challenge, a corollary concern has been identified that is of particular interest to clinicians and investigators with a major focus on cardiovascular disease, hypertension, and diabetes mellitus. Because the ACE2 (angiotensin-converting enzyme 2) is the receptor that facilitates coronavirus entry into cells, some clinicians have postulated that preexisting use of renin-angiotensin system (RAS) blockers may increase the risk of developing a severe and fatal SARSCoV-2 infection. In my lecture I will discuss this concern and conclude that based on current evidence, there is NO reason to abandon RAS blockers in patients receiving this important class of cardiovascular and antihypertensive agents because of any putative concerns of either increased risk of contracting SARS-CoV-2, or of worsening its clinical course. I will document that there are no data to support the notion that ACE inhibitor or angiotensin II type 1 receptor blocker administration facilitates coronavirus entry by increasing ACE2 expression in either animals or humans. Indeed, animal data support elevated ACE2 expression as possibly conferring potential protective pulmonary and cardiovascular effects. Soluble ACE2 (sACE2) in which the transmembrane domain has been removed is sufficient for binding S and neutralizing infection. Several laboratories are focusing on engineering human ACE2 to optimize binding to the spike protein of SARS coronavirus. Consequently as will be discussed at this symposium, randomized clinical trials have been initiated to test the hypothesis that a) RAS blockers and b) humanized ACE2 fragments may be beneficial in the treatment of SARS-CoV-2 Infection.