ABSTRACT

The present invention relates to the early treatment, including pre-diagnosis treatment, of sepsis and acute inflammatory syndromes such as systemic inflammatory response syndrome (SIRS) by PLA2 and metalloprotease inhibitors to improve the performance of antibiotics and outcomes prior to and after confirmation of the diagnosis of sepsis and/or SIRS in a patient or subject. Additional embodiments include methods of treating sepsis, anthrax and severe acute respiratory syndrome coronavirus (SARS and SARS-CoV2) and related inflammatory syndromes and compositions, including pharmaceutical compositions and blood sample compositions. In further embodiments, the present invention is directed to embodiments which evidence that LY315920, LY333013 and related sPLA2 inhibitors are particularly effective COVID-19/cytokine release syndrome therapeutics-prophylactics. In embodiments, the PLA2 inhibitor is varespladib (LY3l5920), methyl varespladib (LY3330I3), AZD27l6--(R)-3-(5'-benzyl-2'-carbamoyl-[1,1'-biphenyl]-3-yl)-2-methylpropanoic acid- as a racemic mixture or separately, as the "R" enantiomer AZD Compound 4 (3-(5'-Benzyl-2'-carbamoylbiphenyl-3-yl)propanoic acid) and LY433771 ((9-[(phenyl)methyl]-5-carbamoylcarbazol-4-yl) oxyacetic acid), a pharmaceutically acceptable salt thereof or a mixture thereof. In embodiments, the metalloprotease inhibitor is Prinomastat, Batimastat, marimastat or vorinostat dosed alone or in combination with preferred sPLA2 inhibitors for the treatment of infection, inflammatory and wound conditions arising from various causes. Methods and compositions for achieving accelerated treatment of wounds and burns, anthrax metalloprotease toxin (lethal factor) driven complications, ARDS, neo-natal and pediatric acute respiratory distress syndrome (neo-natal/pediatric ARDS), including meconium aspiration syndrome are also disclosed.