

Acute Respiratory Distress Syndrome (ARDS) in COVID-19

BC201 Combination therapy

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SARS-CoV-2

- Novel 2019 Corona virus -highly contagious
- Pandemic declared March 2020
- Severe COVID-19 disease in some patients
- >15M cases, 600k deaths (July 2020)
 - SARS-CoV - 8098 Cases, 774 deaths (2002)
 - MERS-CoV - 2495 Cases, 858 deaths (2012)

Complex disease requires a multifaceted approach:

1. Target SARS-CoV 2 cell entry AND reproduction (Val201)

- Src Kinase-Androgen Receptor Inhibitor (Src-ARi - ValiRx) (Phase 1/2 data in clinical trials for prostate cancer)
- Decapeptide selectively inhibits non genomic AR signalling
 - Block TMPRSS2 spike protein activator expression
 - Block Src mediated viral capsid and RNA synthesis

2. Mitigate host directed NETopathy and hyperinflammation

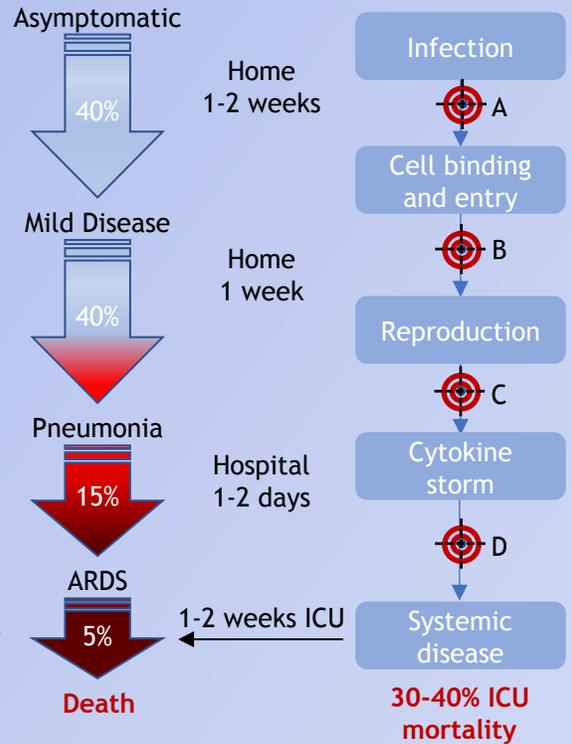
- Src-ARi inhibits kinase dependant transcription (in NETosis)
- Niacin - available as extended release formulation (AbbVie) (Clinically prescribed for hyperlipidemia - ↓ LDL and ↑ HDL)
- Vitamin B3 - Nicotine Adenine dinucleoside (NAD) substrate
 - Depletion increases NADPH level/activity, ROS* and NETosis
 - Protection against oxidative stress* (NET bystander effect)
 - Reduces neutrophil infiltration, edema, and cytokine levels
- Dornase Alfa (Recombinant DNase) (Genentech/Roche) (clinical NET digester used in cystic fibrosis patients)
- Pulmozyme® or generic Tigeraze® mucolytic agent
 - Improved lung function/oxygenation
 - Reduced cytokine production

BC201: Benefits of combined therapy

- *less severe disease - lower hospital admissions*
- *shorter disease time course - faster discharge*
- *less invasive treatment - lower ICU strain*
- *reduced long term damage - less ongoing support*

Broad applicability to viral and bacterial sepsis

BC 201 COVID-19 targets -



Neutrophil Extracellular Traps

