SARS-CoV2

Therapeutic challenges

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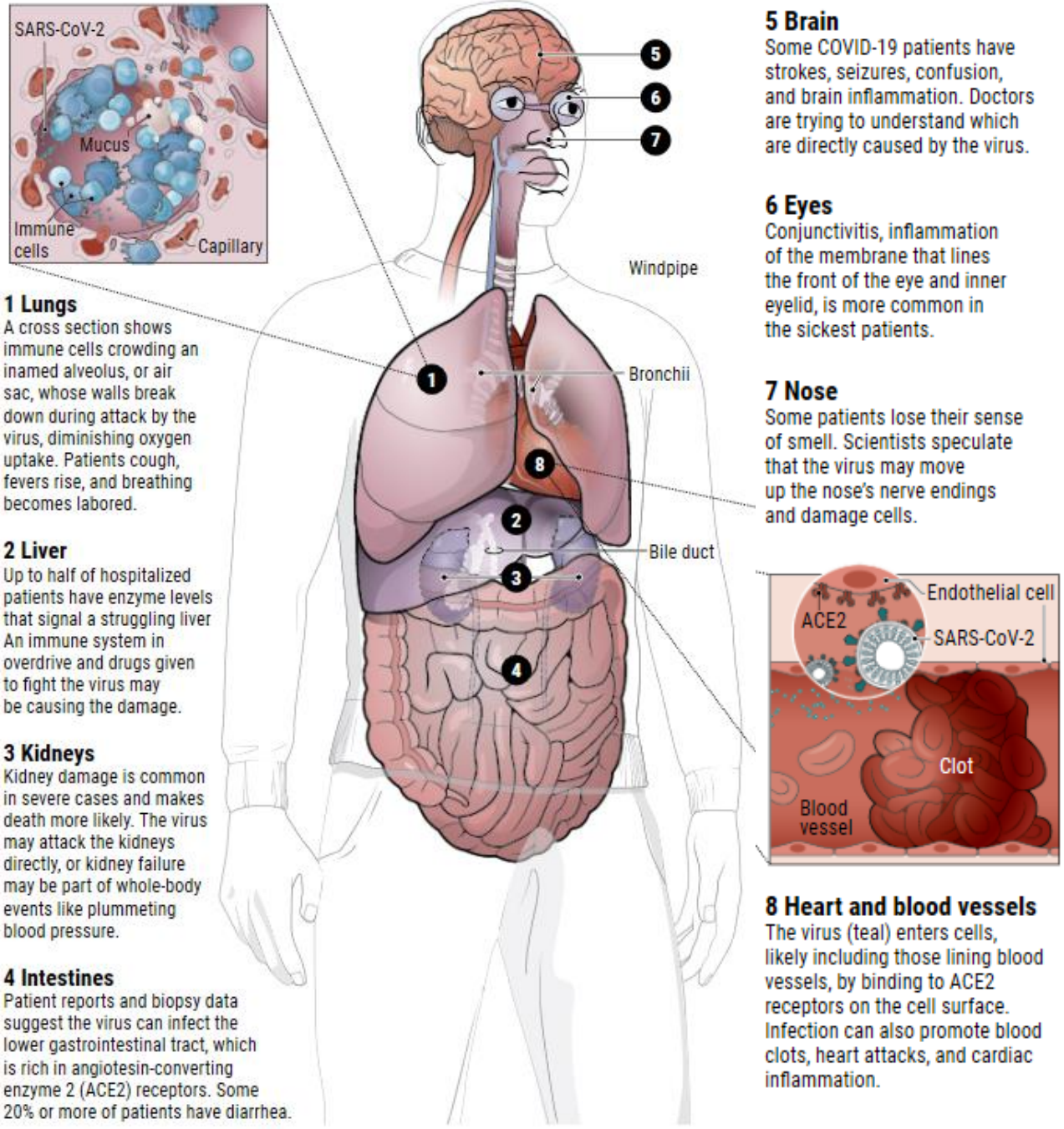
The invader's impact

As the number of confirmed cases of COVID-19 surges past 2.2 million globally and deaths surpass 150,000, clinicians and pathologists are struggling to understand the damage wrought by the coronavirus as it tears through the body.

They are realizing that although the lungs are ground zero, its reach can extend to many organs including the heart and blood vessels, kidneys, gut, and brain



1 Lungs
A cross section shows immune cells crowding an inamed alveolus, or air sac, whose walls break down during attack by the virus, diminishing oxygen uptake. Patients cough, fevers rise, and breathing becomes labored.

2 Liver
Up to half of hospitalized patients have enzyme levels that signal a struggling liver An immune system in overdrive and drugs given to fight the virus may be causing the damage.

3 Kidneys
Kidney damage is common in severe cases and makes death more likely. The virus may attack the kidneys directly, or kidney failure may be part of whole-body events like plummeting blood pressure.

4 Intestines
Patient reports and biopsy data suggest the virus can infect the lower gastrointestinal tract, which is rich in angiotesin-converting enzyme 2 (ACE2) receptors. Some 20% or more of patients have diarrhea.

5 Brain
Some COVID-19 patients have strokes, seizures, confusion, and brain inflammation. Doctors are trying to understand which are directly caused by the virus.

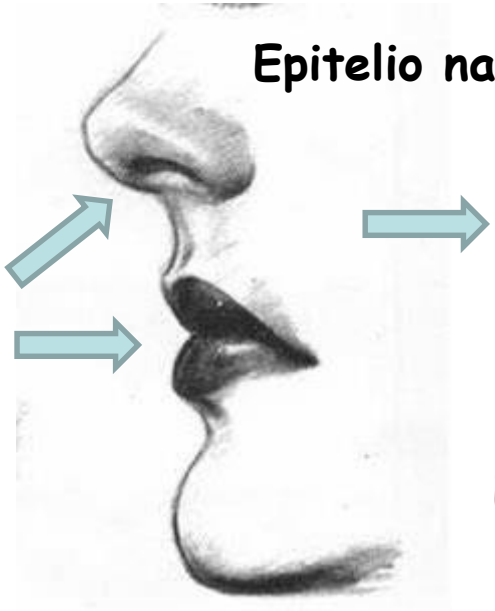
6 Eyes
Conjunctivitis, inflammation of the membrane that lines the front of the eye and inner eyelid, is more common in the sickest patients.

7 Nose
Some patients lose their sense of smell. Scientists speculate that the virus may move up the nose's nerve endings and damage cells.

8 Heart and blood vessels
The virus (teal) enters cells, likely including those lining blood vessels, by binding to ACE2 receptors on the cell surface. Infection can also promote blood clots, heart attacks, and cardiac inflammation.

pneumociti

Pericíti circolo coranarico



Epitelio nasale

Cellule ricche di enzima ACE2
angiotensin-converting enzyme 2

Cellule endoteliali sistema vascolare

Epitelio colon

Cellule renali

Corteccia cerebrale e tronco cerebrale

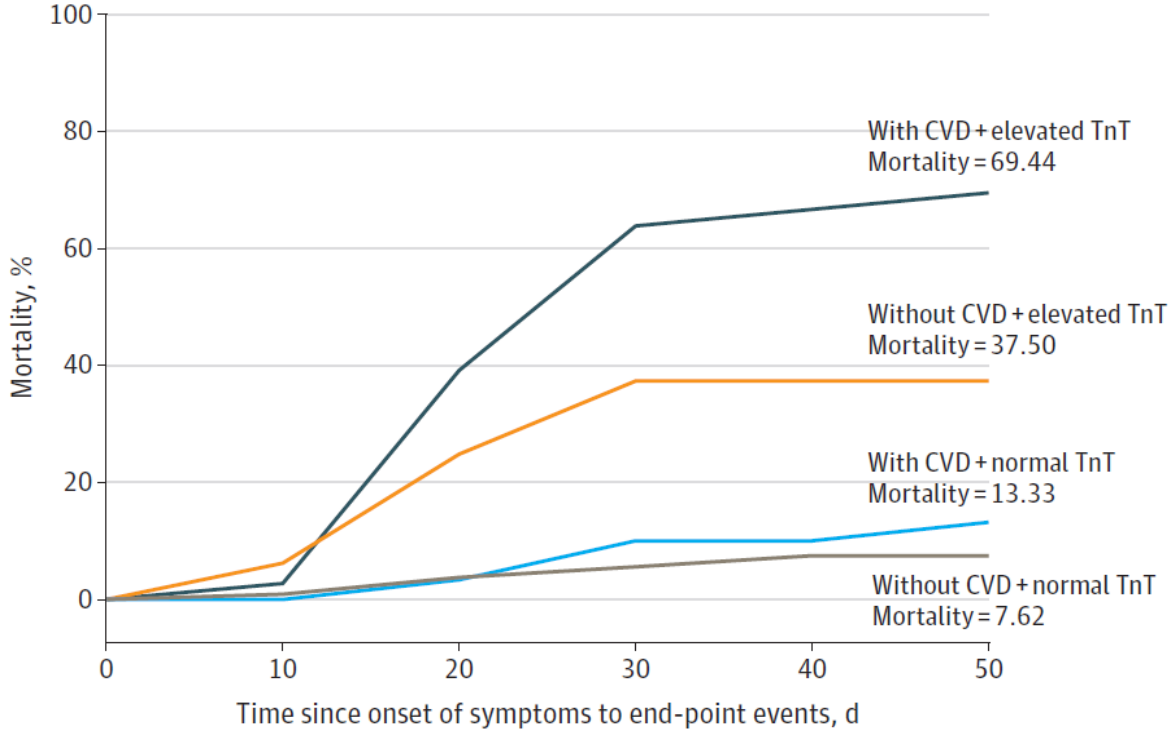
Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19).

Guo T et al, JAMA Cardiol. 2020 Mar 27

Retrospective study aimed to evaluate the association of underlying cardiovascular disease and myocardial injury with fatal outcomes in patients with COVID-19.

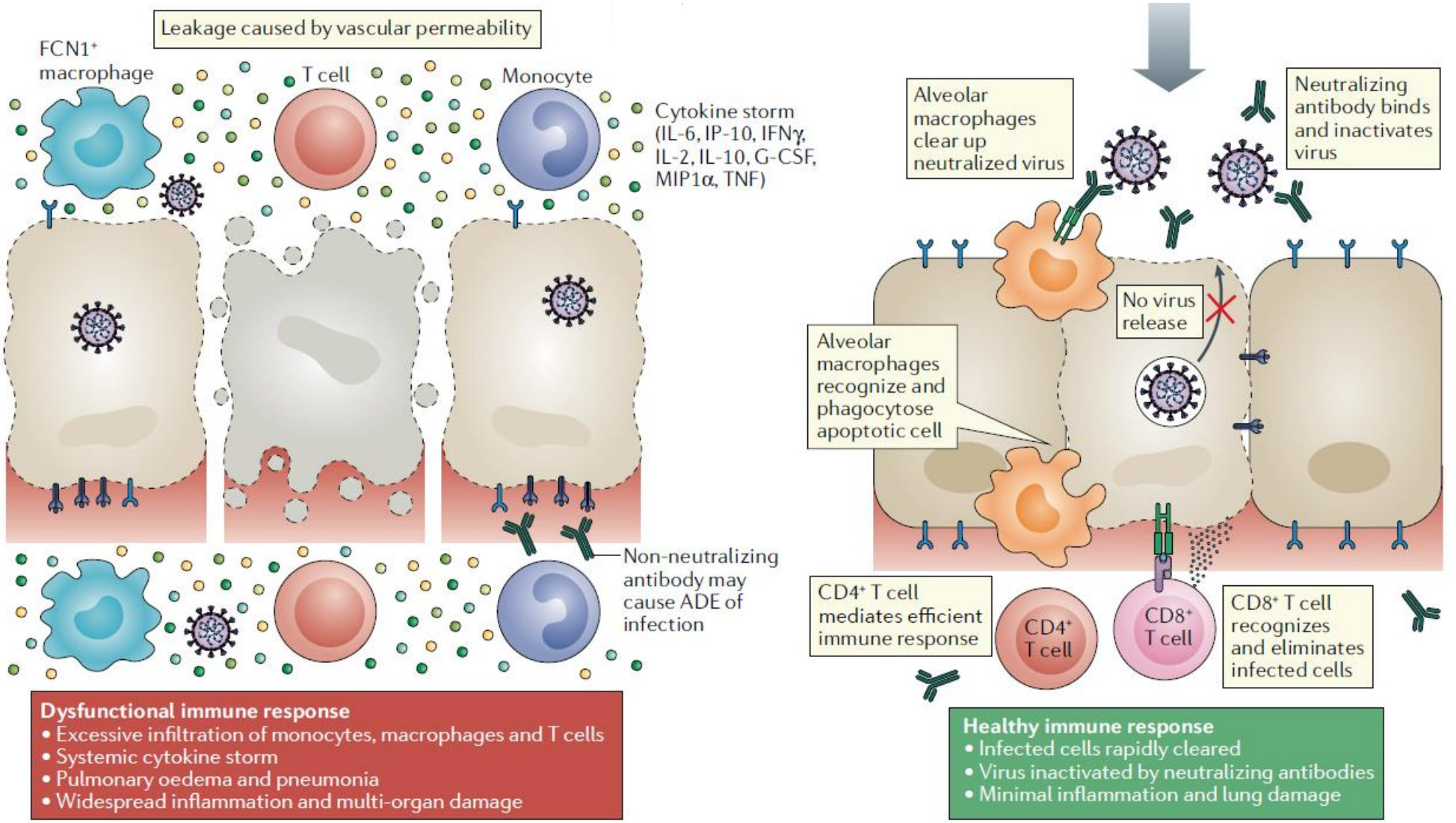
Mortality of Patients With COVID-19 With/Without Cardiovascular Disease and With/Without Elevated Troponin T Levels

187 enrolled patients. Overall, 35.3% had underlying CVD including hypertension, coronary heart disease, and cardiomyopathy, and 52 (27.8%) exhibited myocardial injury as indicated by elevated TnT levels.

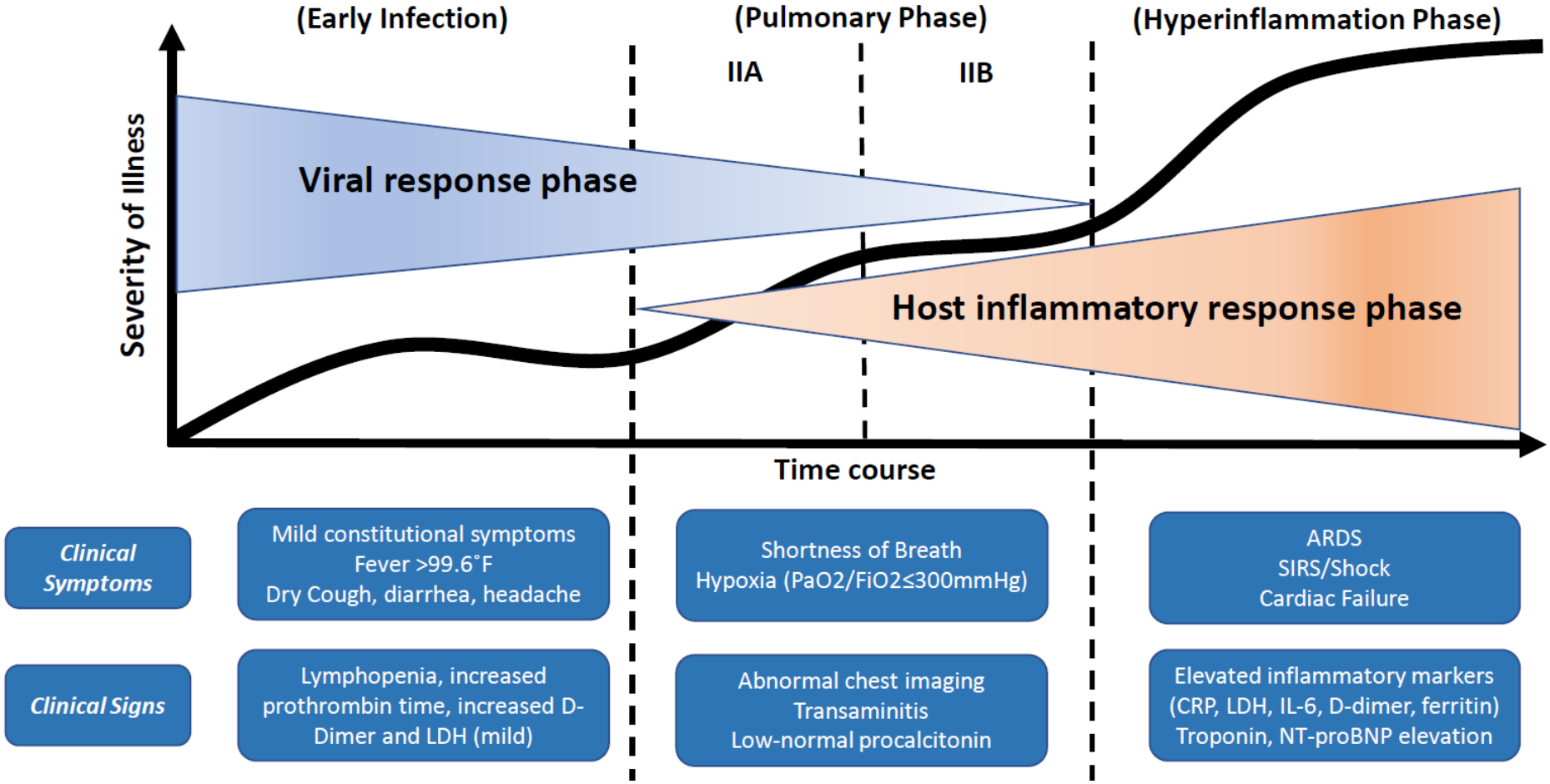


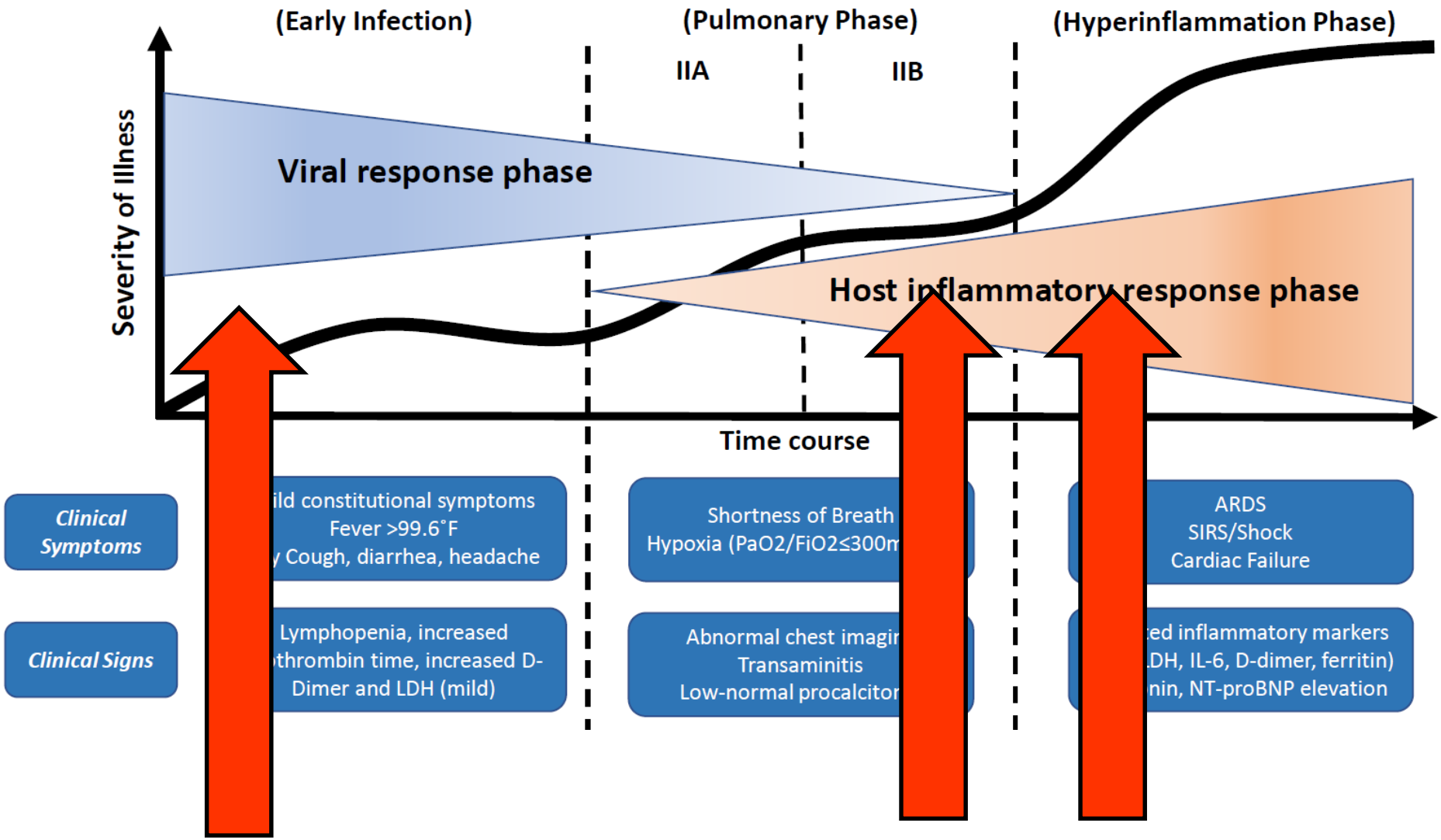
No. at risk					
Without CVD + normal TnT (n = 105)	102	86	41	10	0
Without CVD + elevated TnT (n = 16)	15	12	7	1	0
With CVD + normal TnT (n = 30)	29	25	10	4	0
With CVD + elevated TnT (n = 36)	34	20	8	2	0

SARS-CoV-2 : events chronology



The trinity of COVID-19: immunity, inflammation and intervention.
Tay MZ et al, Nat Rev Immunol 2020 Apr 28


(Early Infection)
(Pulmonary Phase)
IIA
IIB
(Hyperinflammation Phase)
Severity of Illness
Viral response phase
Host inflammatory response phase
Time course
Clinical Symptoms
Mild constitutional symptoms
Fever >99.6˚F
Dry Cough, diarrhea, headache
Shortness of Breath
Hypoxia (PaO2/FiO2≤300mmHg)
ARDS
SIRS/Shock
Cardiac Failure
Clinical Signs
Lymphopenia, increased prothrombin time, increased D-Dimer and LDH (mild)
Abnormal chest imaging
Transaminitis
Low-normal procalcitonin
Elevated inflammatory markers
(CRP, LDH, IL-6, D-dimer, ferritin)
Troponin, NT-proBNP elevation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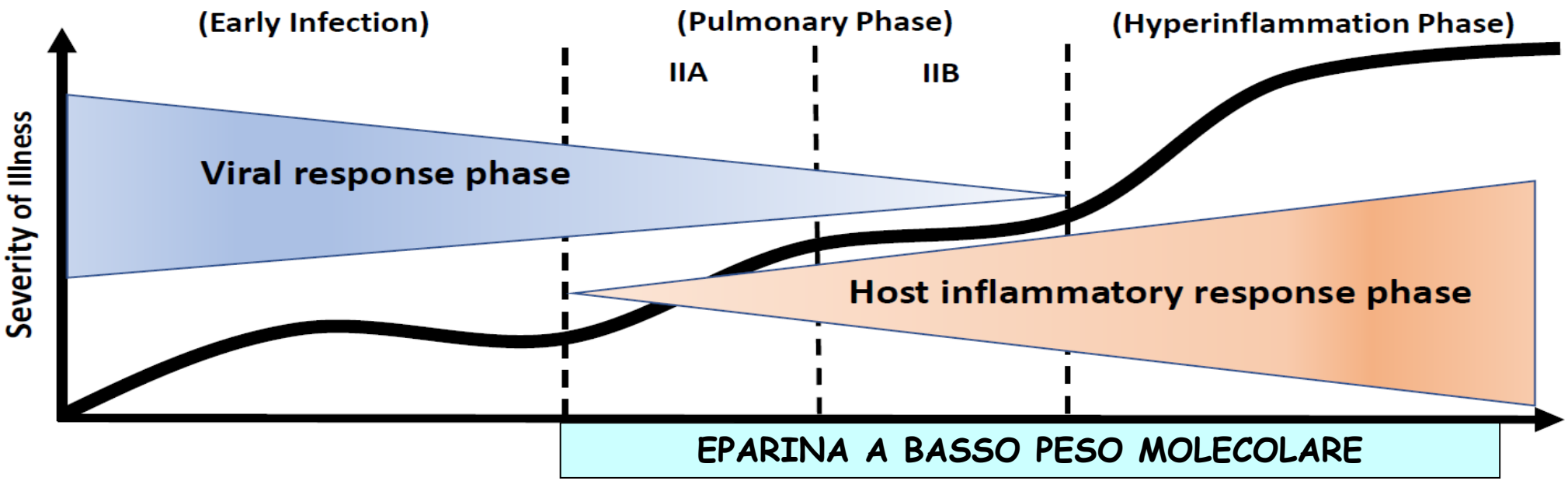

CLOROCHINA

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REMDESIVIR

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Anti-CBS (ABX464)

TERAPIA ANTI-INFIAMMATORIA