# COVID-19

**China – Wuhan – 12/2019**

**Pneumonia**

**Insuficiência Respiratória Aguda Grave**

**Severe Acute Respiratory Syndrome Coronavirus 2**

**SARS-CoV-2**

# Plasma Hiperimune

**Administração passiva de Acs. policlonais**

**Doenças virais – (Respiratórias)**

**Gripe Espanhola (H1N1) - 1918**

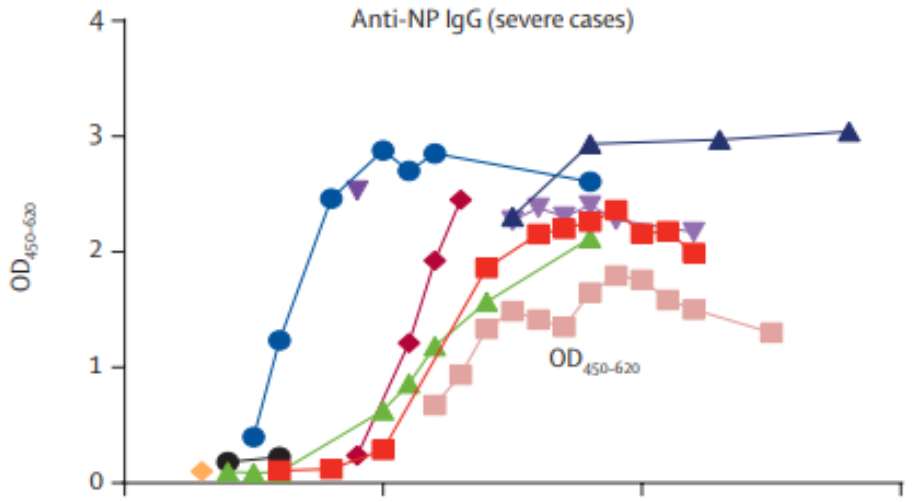
**Ebola - 1995**

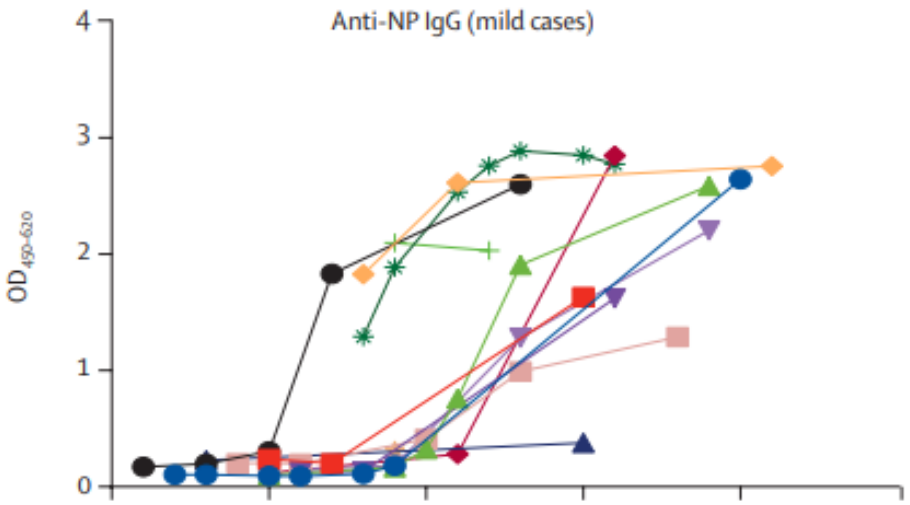
**SARS–Cov - 2003**

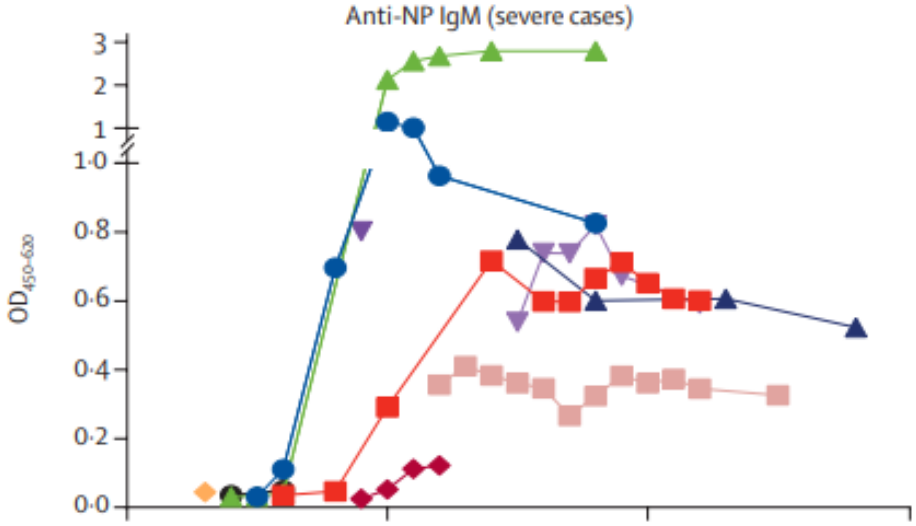
**H1N1 - 2009**

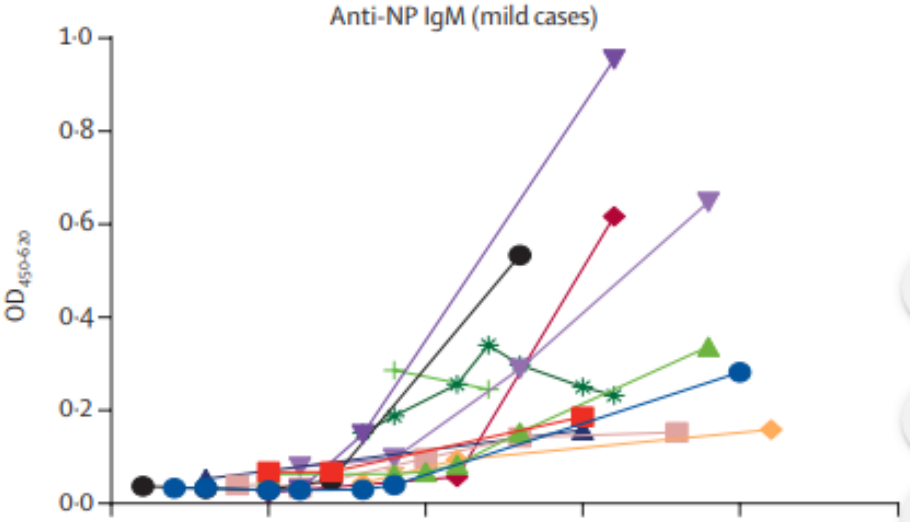
**MERS-Cov - 2012**

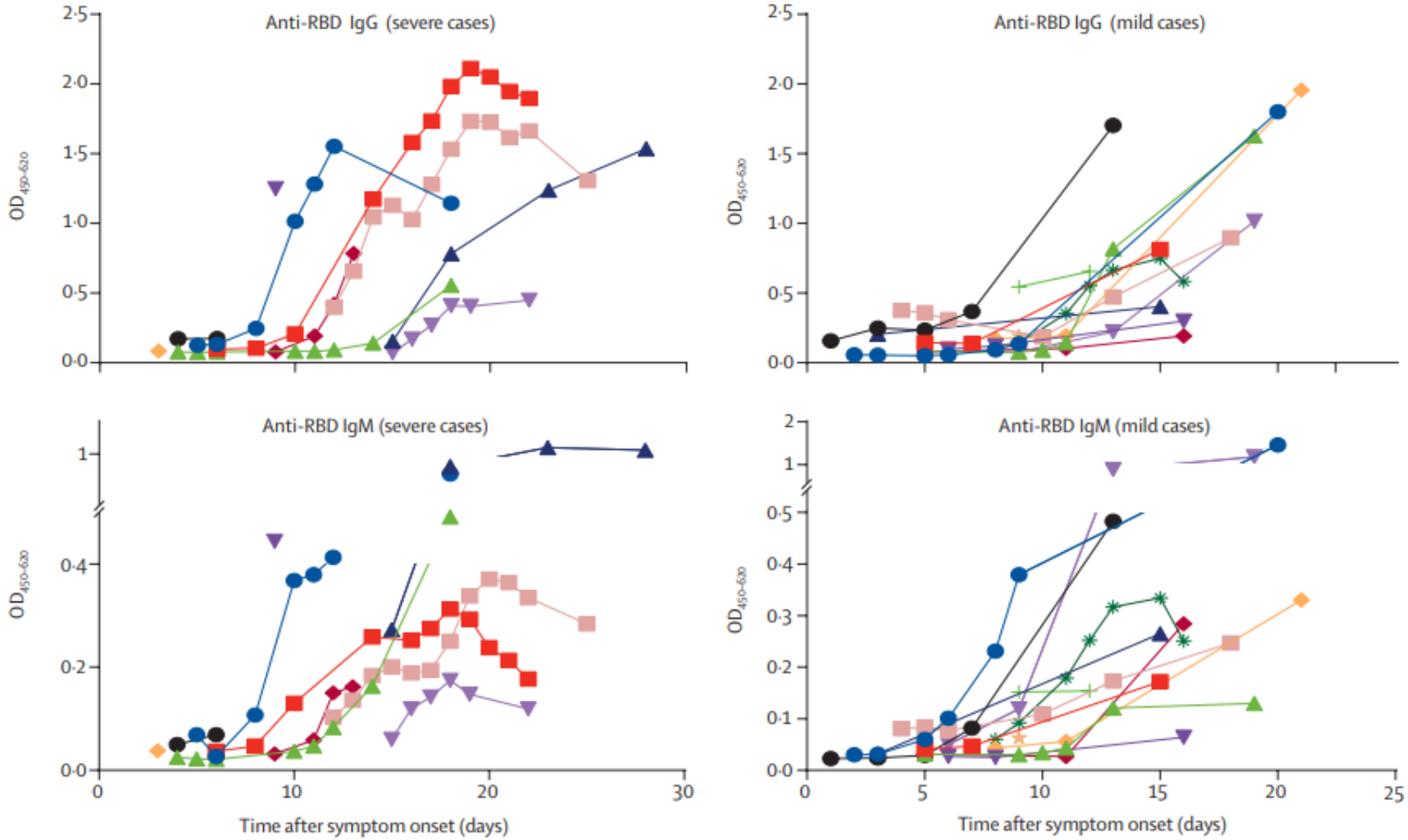
**O que ?**


Anti-NP IgG (severe cases)
$OD_{450-620}$
4
3
2
1
0
$OD_{450-620}$


Anti-NP IgG (mild cases)
$OD_{450-620}$
4
3
2
1
0


Anti-NP IgM (severe cases)
$OD_{450-620}$
3
2
1
1·0
0·8
0·6
0·4
0·2
0·0


Anti-NP IgM (mild cases)
$OD_{450-620}$
1·0
0·8
0·6
0·4
0·2
0·0


Anti-RBD IgG (severe cases)
Anti-RBD IgG (mild cases)
Anti-RBD IgM (severe cases)
Anti-RBD IgM (mild cases)
OD450-620
Time after symptom onset (days)
2·5
2·0
1·5
1·0
0·5
0·0
1
0·4
0·2
0·3
0·1
2
0
5
10
15
20
25
30

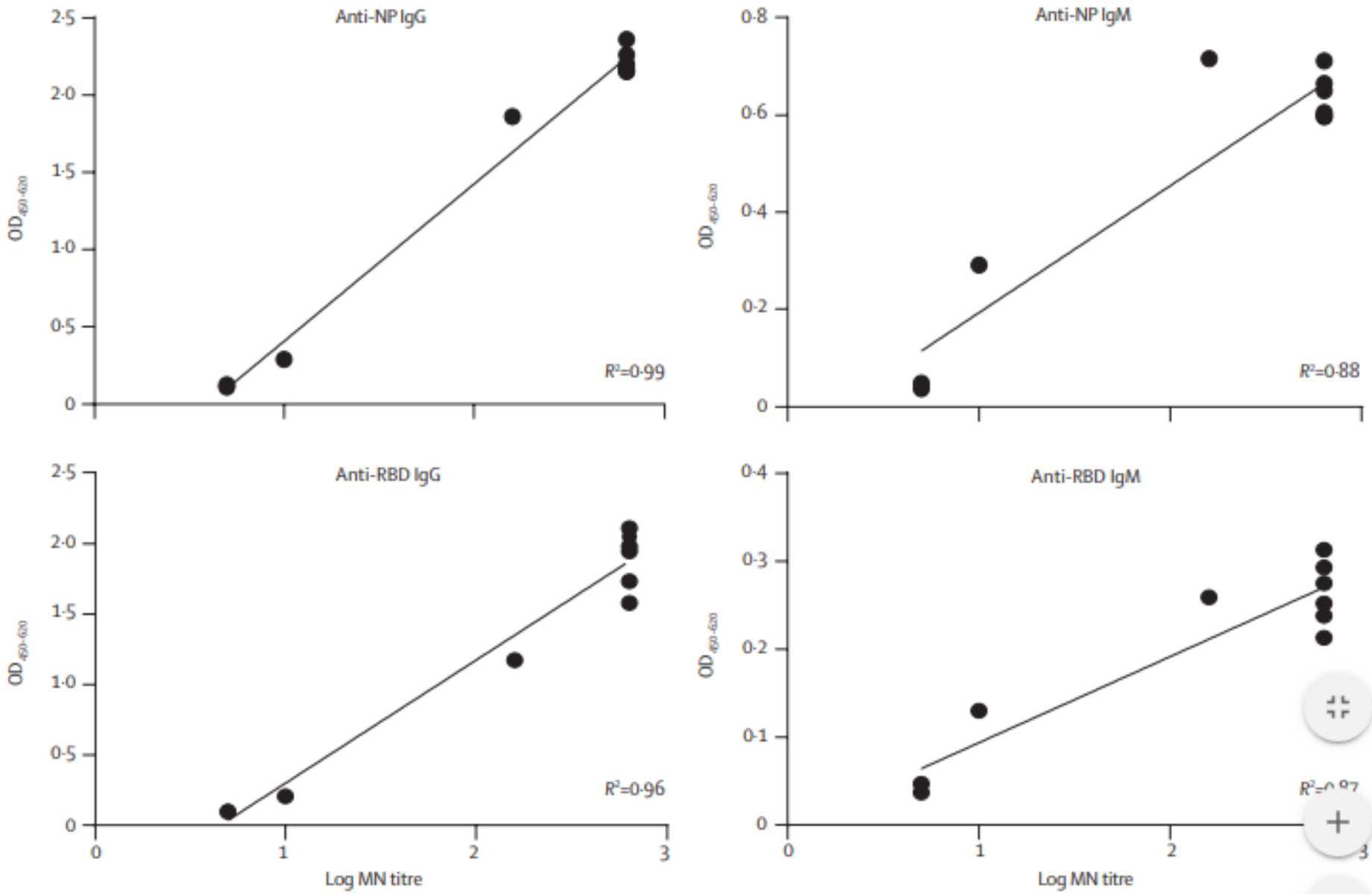



*Figure 5*: **Correlation between MN antibody titres and anti-NP or anti-RBD IgG or IgM**

# Por que ?

# Mecanismos

- Ligação ao patógeno – Neutralização
- Ativação do complemento
- Citotoxicidade Ac. Dependente
- Fagocitose - facilitação

**Oferecer imunidade imediata a Indivíduos susceptíveis**

# Como ?

# Como

- Pacientes convalescentes
- 14 dias assintomáticos – PCR negativo
- Coleta por aférese – 600 mL – 3/4 coletas
- Titulação de anticorpos (neutralizantes)

O+

**Quanto ?**

# Quanto

## Dose variável

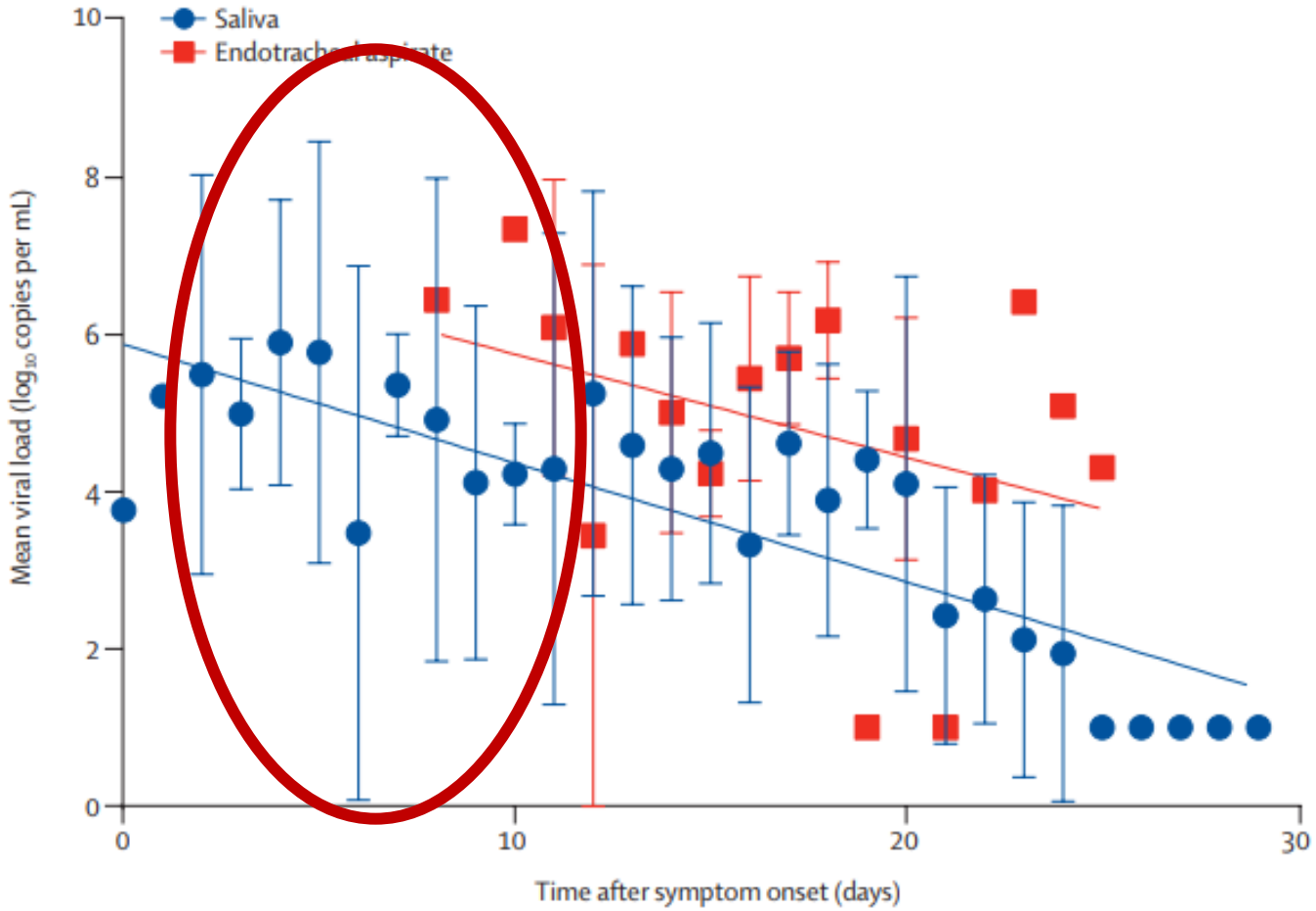
- 200 mL – dose – 2x ?
- 5 mL/Kg – título 1:160 ?
- 10 mL/Kg – 3 dias ?

# Quando ?

- **Pacientes com doença moderada ou grave**
- **$SaO_2 \leq 93\%$ em ar ambiente**
- **Entubado**

**Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study**

Lancet Infect Dis 2020




| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| D | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 |
| S | 1 | 1 | 3 | 3 | 5 | 5 | 5 | 4 | 7 | 10 | 5 | 8 | 7 | 7 | 6 | 7 | 8 | 5 | 6 | 5 | 6 | 6 | 5 | 6 | 4 | 3 | 3 | 2 | 2 | 1 |
| E | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |

# Effect of Convalescent Plasma Therapy on Viral Shedding and Survival in COVID-19 Patients

| | Plasma n = 6 | Controle n = 16 | |
|---|---|---|---|
| Fatality | 5 (83.3) | 14 (93.3) | 0.500 |
| SARS-CoV-2 clearance in all patients | | | |
| Yes | 6 (100) | 4 (26.7) | 0.004 |
| No | 0 (0) | 11 (73.3) | - |
| SARS-CoV-2 clearance before death in fatal patients | | | |
| Yes | 5/5 (100) | 3/14 (21.4) | 0.005 |
| No | 0/5 (0) | 11/14 (78.6) | - |

## SARS-Cov

- < 14 dias de infecção
- PCR + / Ac. –

**Melhor evolução**

**Uso precoce**
**< 5 dias sintomas**

# Riscos

# Mesmos transfusão de plasma

- Triagem clínica
  - Mulheres nulíparas
- Triagem laboratorial
  - Exames de rotina doação de sangue
- Reações transfusionais
  - Alérgica
  - TRALI
  - TACO

**E daí ?**

# The Effectiveness of Convalescent Plasma and Hyperimmune Immunoglobulin for the Treatment of Severe Acute Respiratory Infections of Viral Etiology: A Systematic Review and Exploratory Meta-analysis

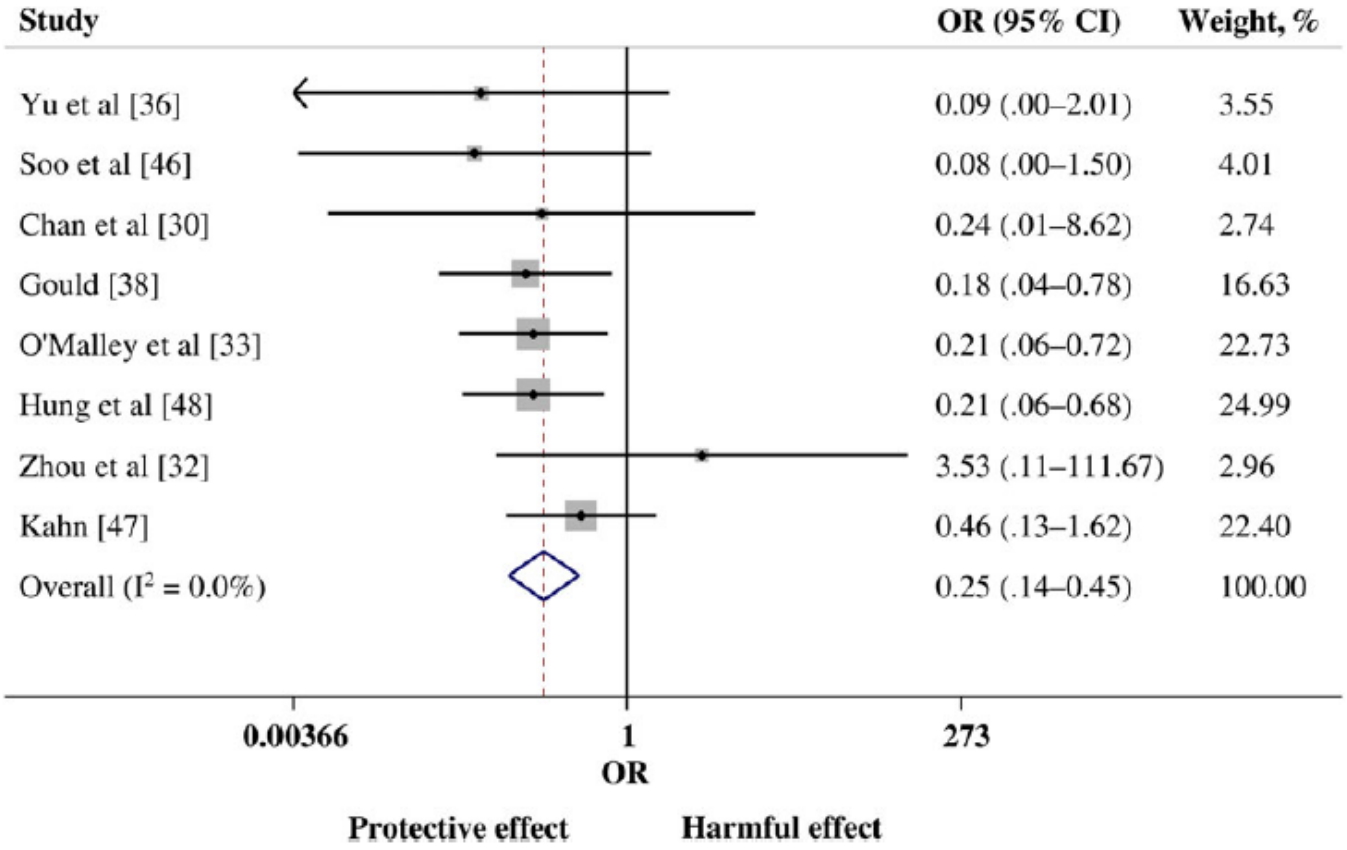


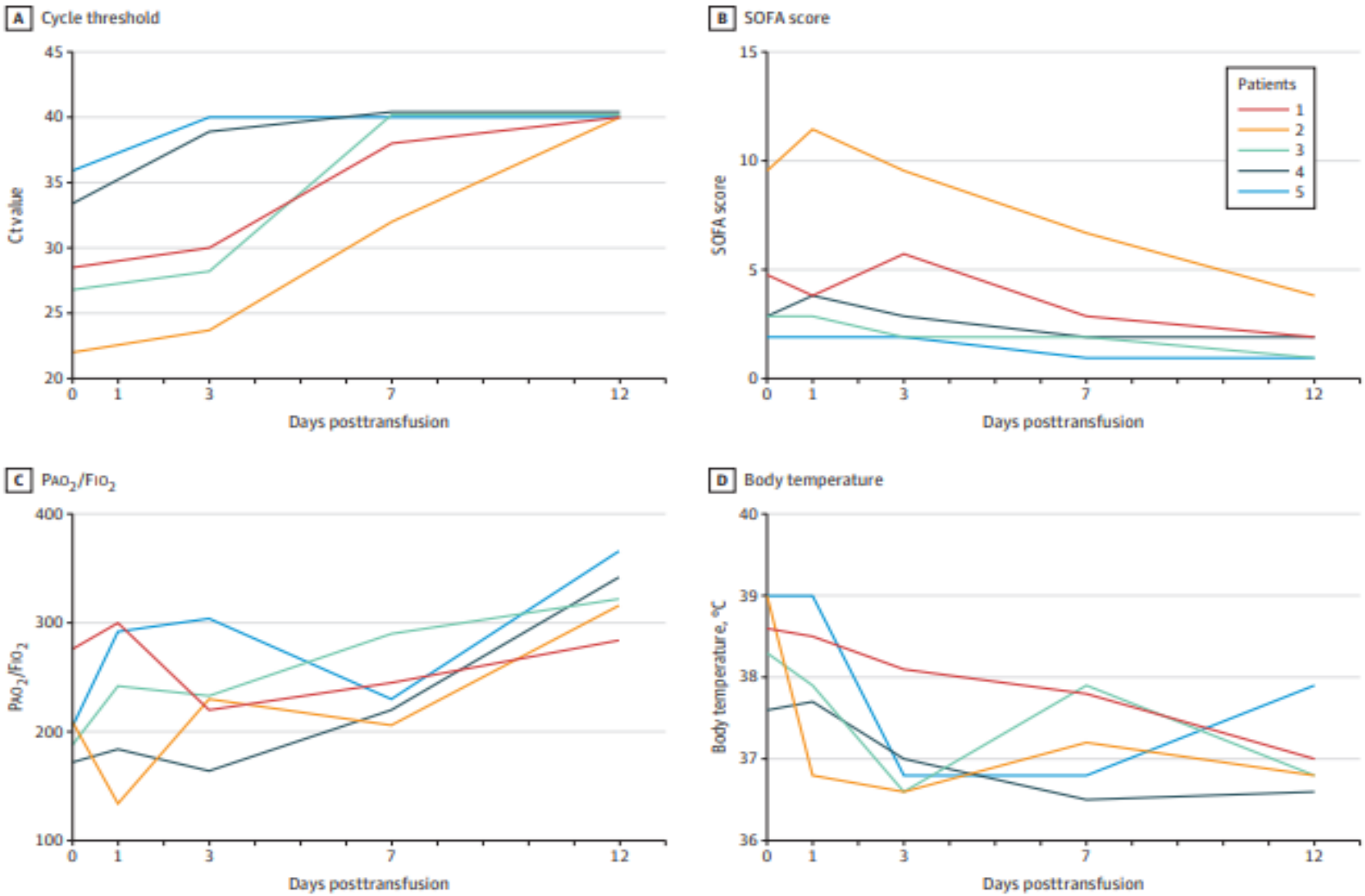

**Figure 3.** Forest plot of pooled odds ratios (ORs) of mortality following treatment with convalescent plasma or convalescent serum (n = 8 studies). Weights are from random-effects analysis. Abbreviation: CI, confidence interval.

JAMA | Preliminary Communication

# Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma

Chenguang Shen, PhD; Zhaoqin Wang, PhD; Fang Zhao, PhD; Yang Yang, MD; Jinxiu Li, MD; Jing Yuan, MD; Fuxiang Wang, MD;

**Figure 1. Temporal Changes of Cycle Threshold Value, $PaO_2/FiO_2$, SOFA Score, and Body Temperature in Patients Receiving Convalescent Plasma Transfusion**



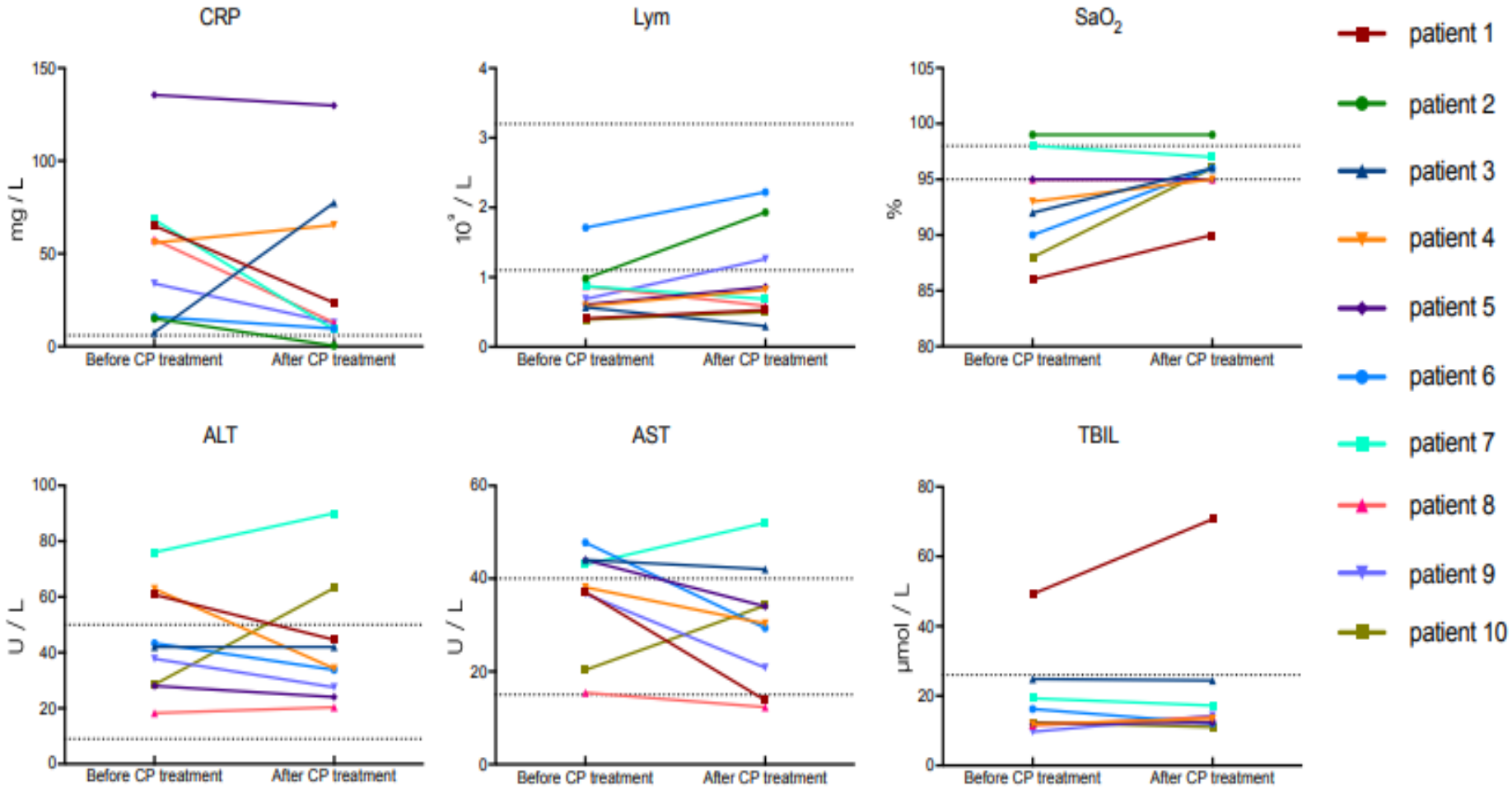



**Fig. 2.** Dynamic changes of laboratory parameters in all patients. The dotted horizontal line represents the reference value range. $SaO_2$, oxyhemoglobin saturation; TBIL, total bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Lym, lymphocyte.

H.Hemo

# Use of Convalescent Plasma Therapy in Two COVID-19 Patients with Acute Respiratory Distress Syndrome in Korea

N = 2

> 18 anos

Pneumonia

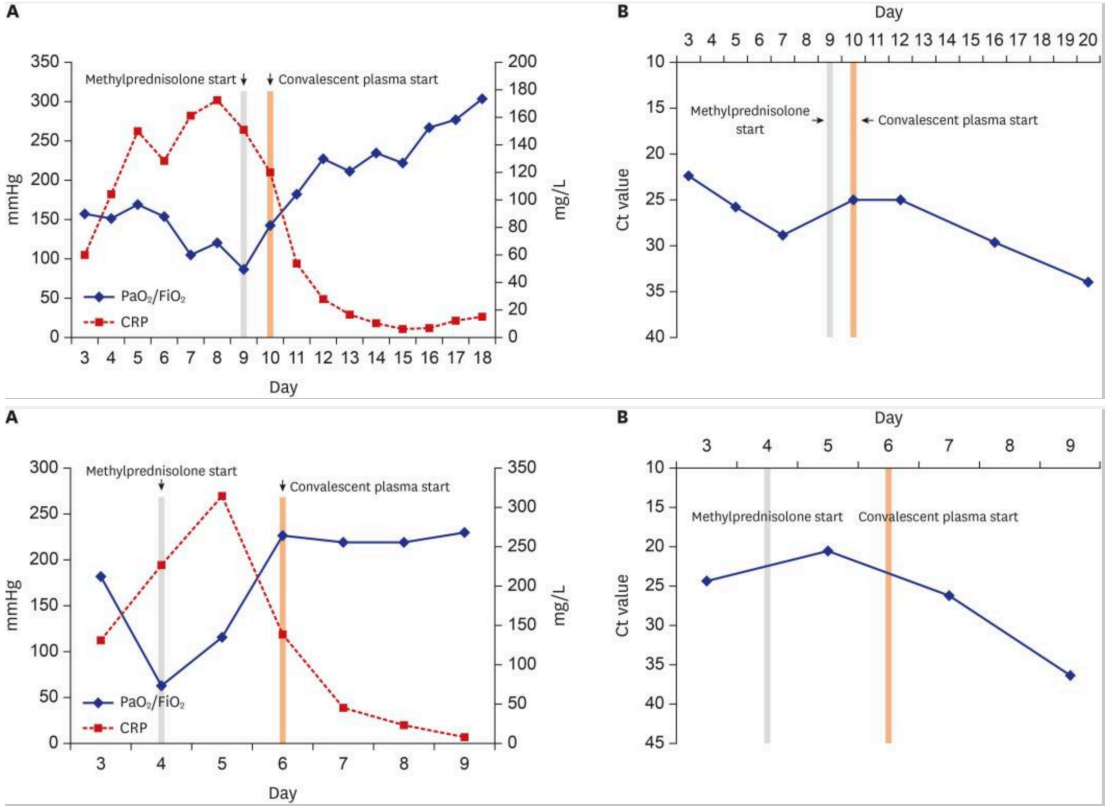
Insuf Respiratória

Lopinavir/Ritonavir

Cloroquina

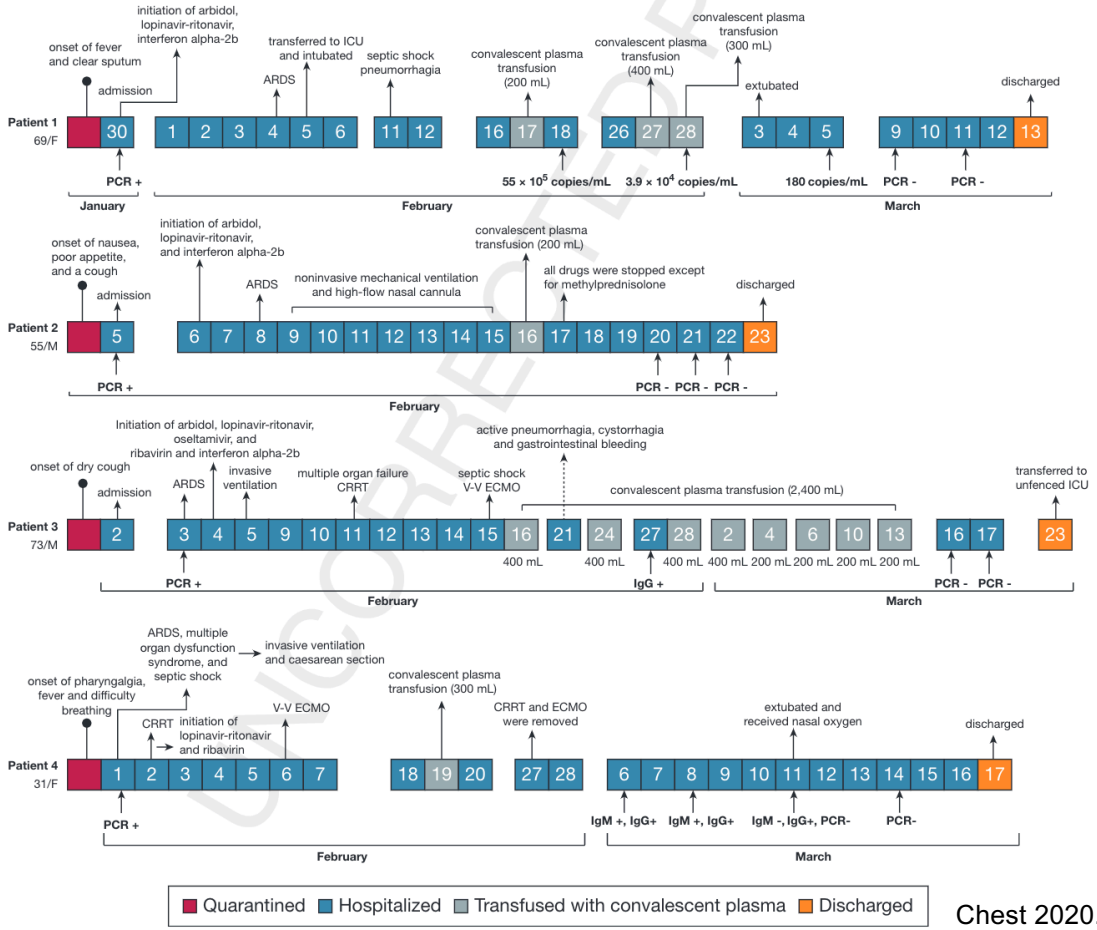
Corticóide

500ml PFC (1x)




J Korean Med Sci. 2020 Apr 13;35(14):e149

# Treatment With Convalescent Plasma for Critically Ill Patients With SARS-CoV-2 Infection

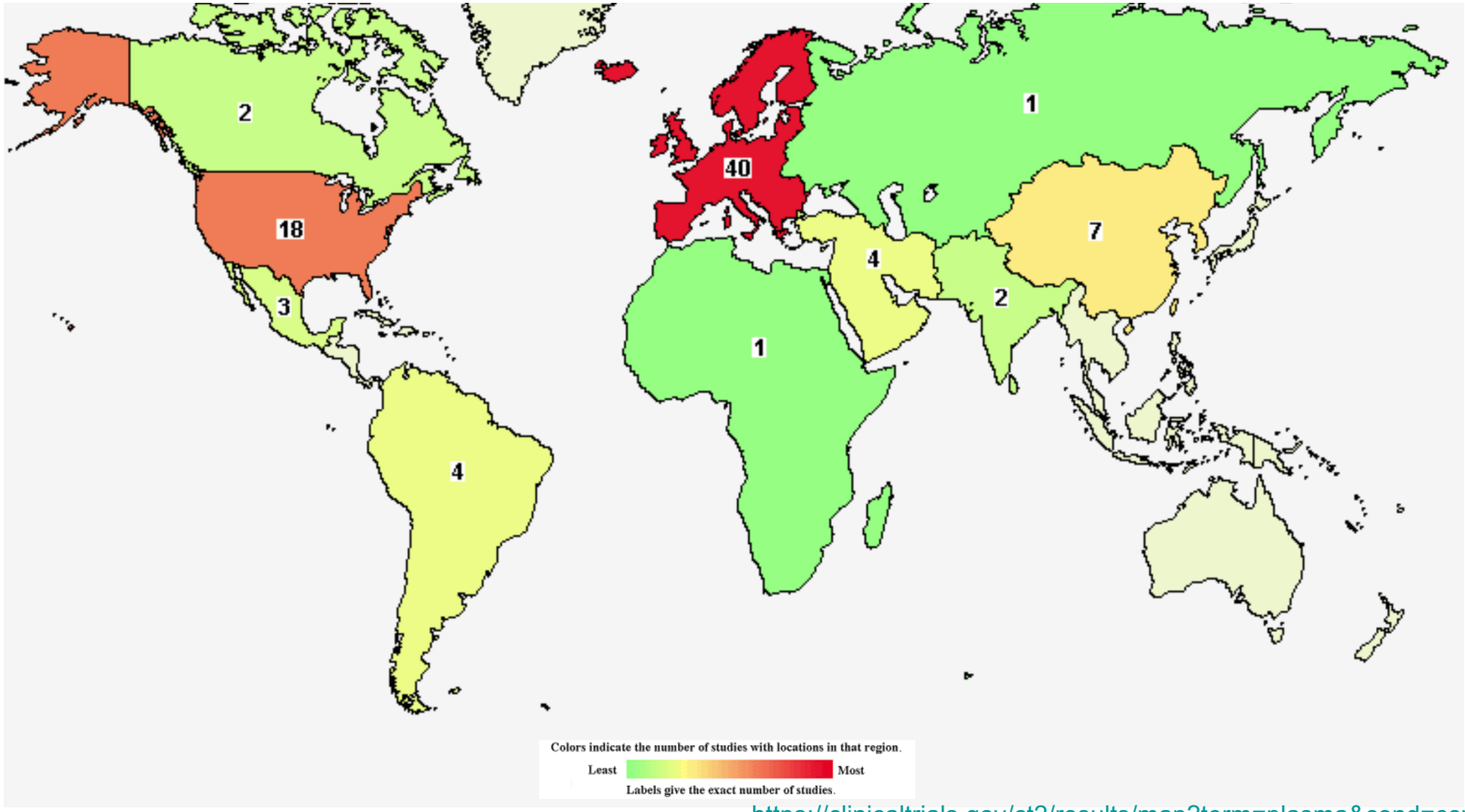



Chest 2020. https://doi.org/10.1016/j.chest.2020.03.0

ClinicalTrials.gov

H.Hemo

# 95 estudos Plasma Convalescente




https://clinicaltrials.gov/ct2/results/map?term=plasma&cond=covid-19&map=

# Conclusões

**Table 1:** Advantages and disadvantages of the use of immunoglobulins or convalescent plasma to treat COVID-19.

| PROs | CONs |
|---|---|
| High-titre specific antibodies to bind to SARS-CoV-2 and neutralise the viral particles | High costs |
| Possible application in critically ill patients | Burdensome logistics |
| Few significant secondary effects | Lack of high-quality studies, i.e., randomised controlled trials |
| Proved efficacy in past viral outbreaks | Lack of knowledge of the basic biology of SARS-CoV-2, including virus variability and mutations |
| Large pool of plasma donors due to the large number of patients recovered from COVID-19 | Passive immunisation, thus a short duration of the effect |