



Université Claude Bernard Lyon 1



# Sympo BioTuesdays

## DisCoVeRy: enseignements, actualités et perspectives

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Infectiologue – CHU de Lyon

16/06/2020

Pression zoonotique → épidémie pandémie

Différences socio-anthropologiques intercontinentales

Globalisation

Interdépendances économiques (dominance/subordination)

Niveaux hétérogènes d'accès à la santé, "couverture" sanitaire universelle (?)

Niveau de développement et structuration de la recherche, connexion au réseau de santé ("plug in"), autorités réglementaires compétentes

# Concept 1

## World Health Organization Methodology to Prioritize Emerging Infectious Diseases in Need of Research and Development

Massinissa Si Mehand, Piers Millett, Farah Al-Shorbaji, Cathy Roth,  
Marie Paule Kieny, Bernadette Murgue

*Em Infect Dis 2017*



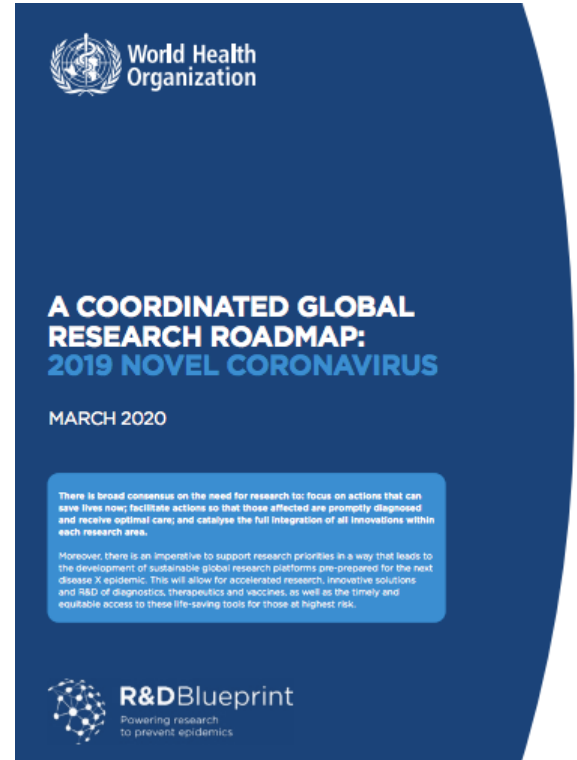
**R&DBlueprint**

Powering research  
to prevent epidemics

A global strategy and **preparedness plan** that allows the rapid activation of R&D activities during epidemics.

Its aim is to fast-track the availability of effective tests, vaccines and medicines

<https://www.who.int/teams/blueprint>



# First generation WHO therapeutic candidates against SARS-CoV-2

## Novel therapeutics

Remdesivir 100 mg IV

## Repurposing drugs

Lopinavir/ritonavir 400/100 mg (Marketing authorization HAART)  
Interferon (IFN)- $\beta$  1a 44  $\mu$ g SC (Marketing authorization MS)  
Hydroxychloroquine cp 200 mg

# Concept 2

*The NEW ENGLAND JOURNAL of MEDICINE*

REVIEW ARTICLE

**THE CHANGING FACE OF CLINICAL TRIALS**

Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D.,  
and Janet Woodcock, M.D., *Editors*

## Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both

Janet Woodcock, M.D., and Lisa M. LaVange, Ph.D.

*N Engl J Med* 2017;377:62-70. DOI: 10.1056/NEJMra1510062

Master protocol : a methodologic innovation responsive to this need involves coordinated efforts to evaluate more than one or two treatments in more than one patient type or disease within the same overall trial structure.

# The Platform Trial

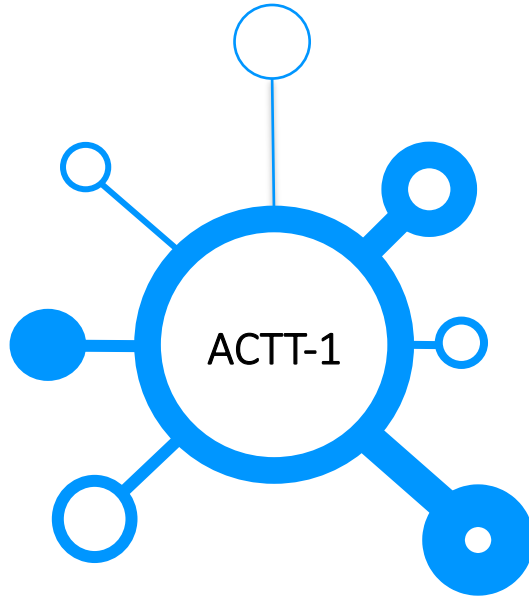
## An Efficient Strategy for Evaluating Multiple Treatments

Table. General Characteristics of Traditional and Platform Trials<sup>a</sup>

Characteristic	Traditional Trial	Platform Trial	
Scope	Efficacy of a single agent in a homogeneous population	Evaluating efficacy of multiple agents in a heterogeneous population; explicitly assumes treatment effects may be heterogeneous	→ Stratification
Duration	Finite, based on time required to answer the single primary question	Potentially long-term, as long as there are suitable treatments requiring evaluation	→ Expensive
No. of treatment groups	Prespecified and generally limited	Multiple treatment groups; the number of treatment groups and the specific treatments may change over time	} Flexibility
Stopping rules	The entire trial may be stopped early for success or futility or harm, based on the apparent efficacy of the single experimental treatment	Individual treatment groups may be removed from the trial, based on demonstrated efficacy or futility or harm, but the trial continues, perhaps with the addition of new experimental treatment(s)	
Allocation strategy	Fixed randomization	Response-adaptive randomization	
Sponsor support	Supported by a single federal or industrial sponsor	The trial infrastructure may be supported by multiple federal or industrial sponsors or a combination	→ International

<sup>a</sup> Platform trials and similar trials may also be called basket, bucket, umbrella, or standing trials.

# Adaptive Covid-19 Treatment Trial (ACTT-1)



Adaptive platform to rapidly conduct a series of phase III, randomized, double-blind, placebo-controlled trials



Stage 1

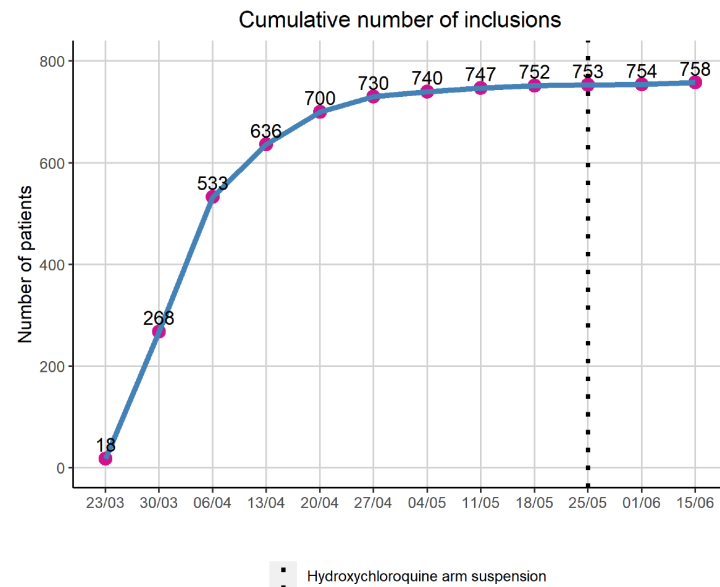
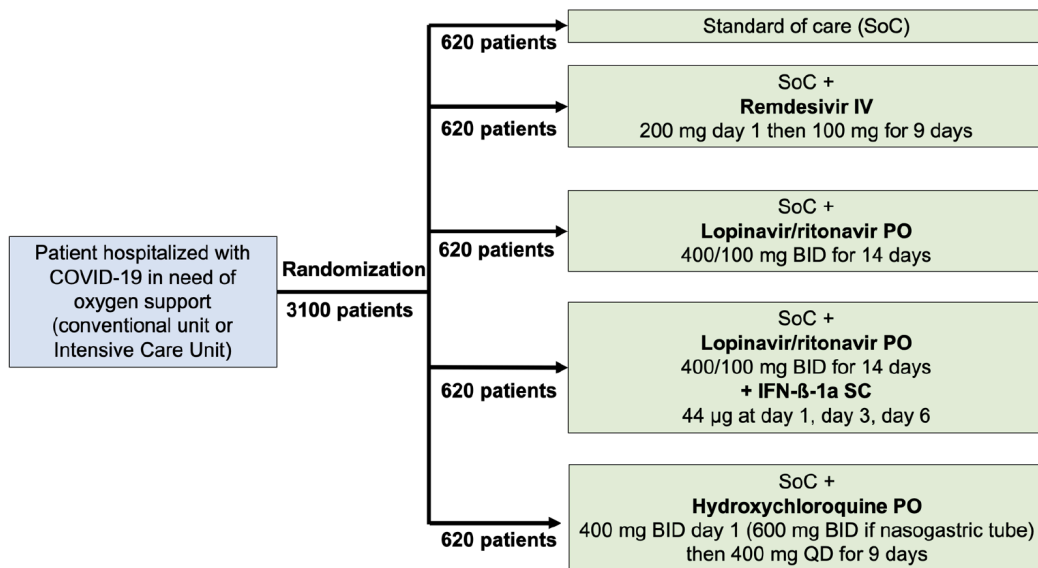
Remdesivir (GS-5734) vs. placebo  
T0 February 21, 2020



Stage 2

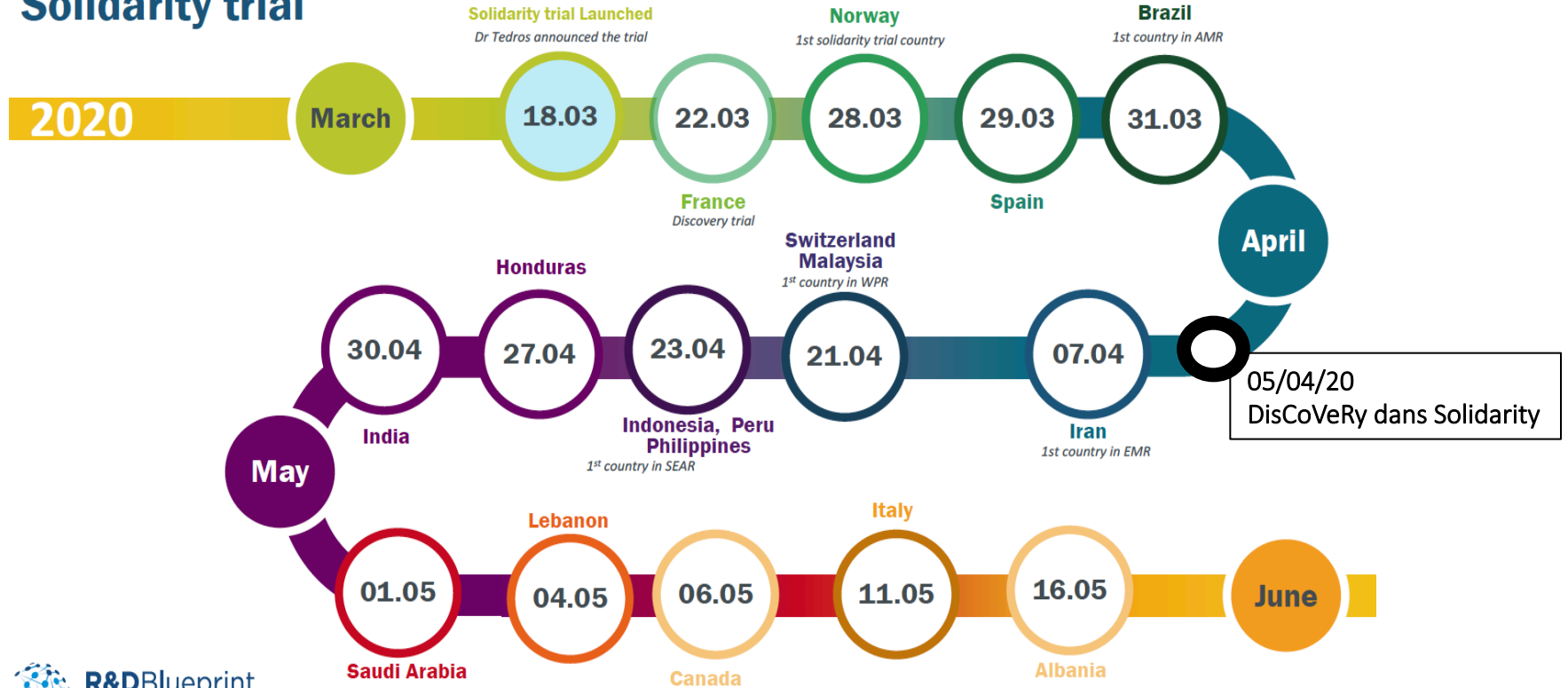
Remdesivir vs. Remdesivir + baricitinib  
Remdesivir vs. Remdesivir + tocilizumab

# DisCoVeRy



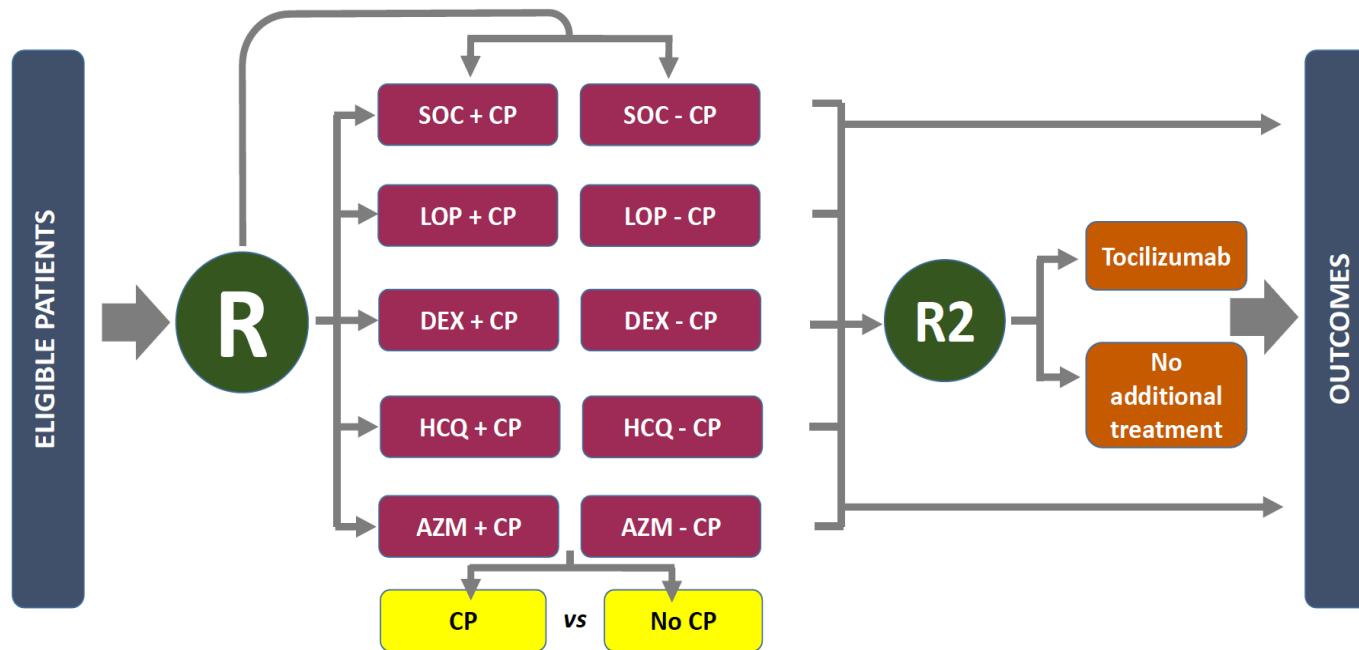


# Solidarity trial



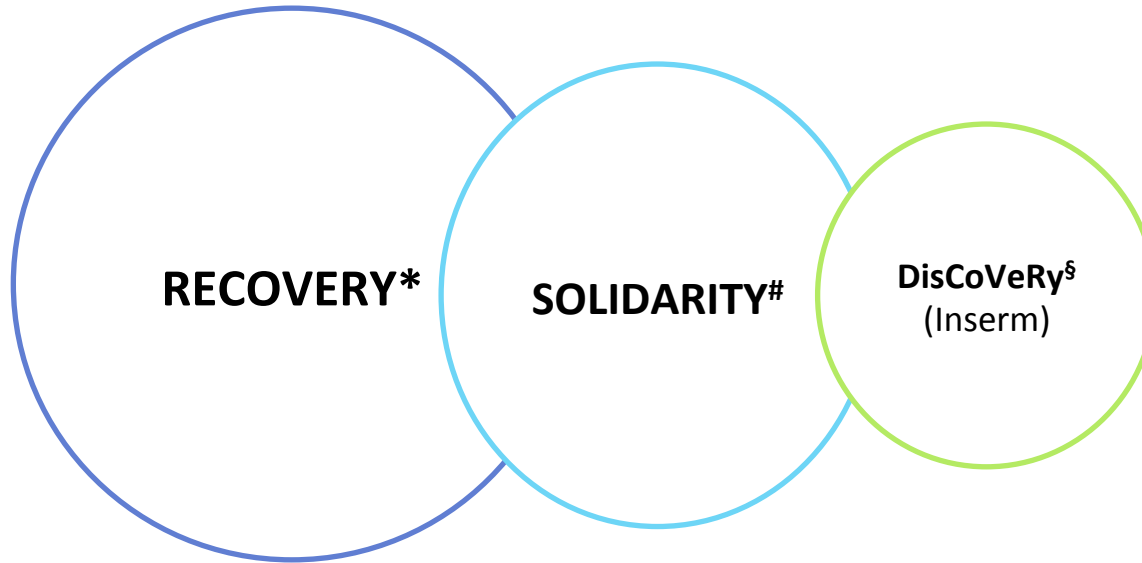
# Recovery

Factorial design  
176 active sites  
11 539



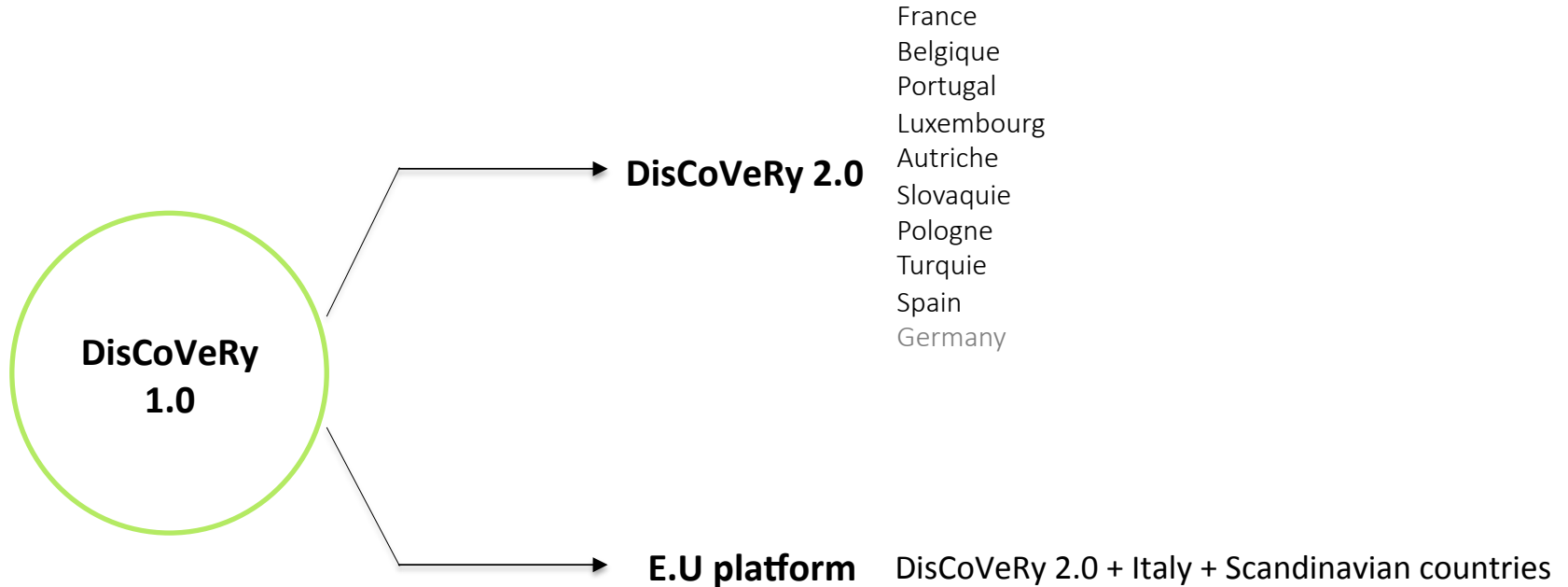
Perspectives

# Court terme

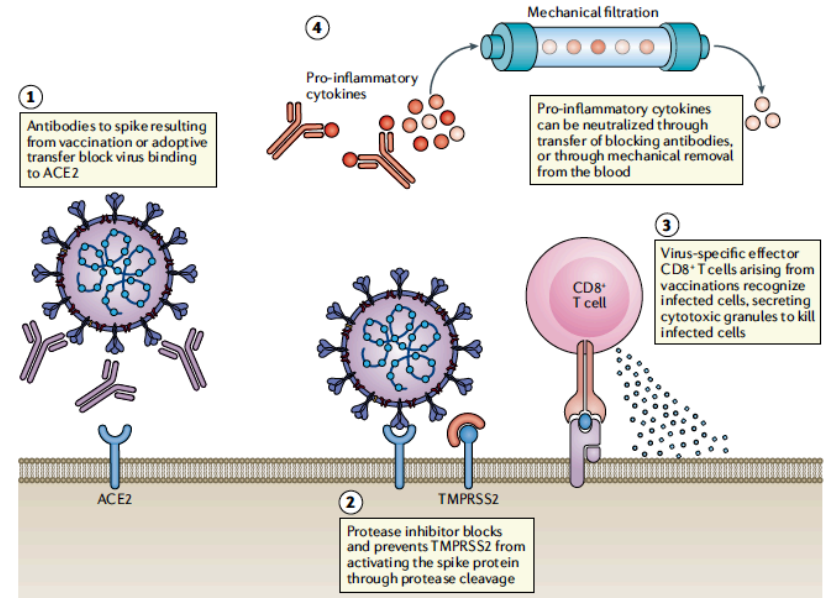
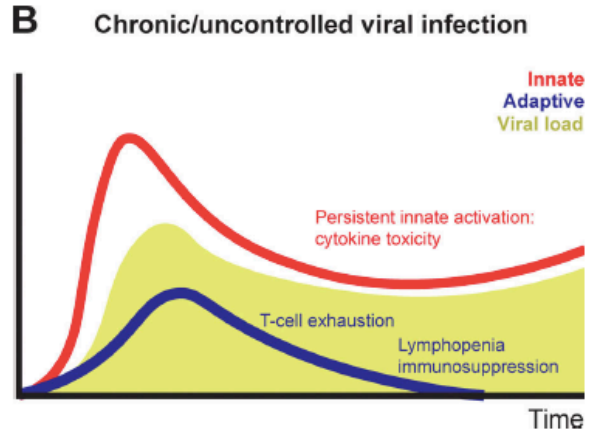
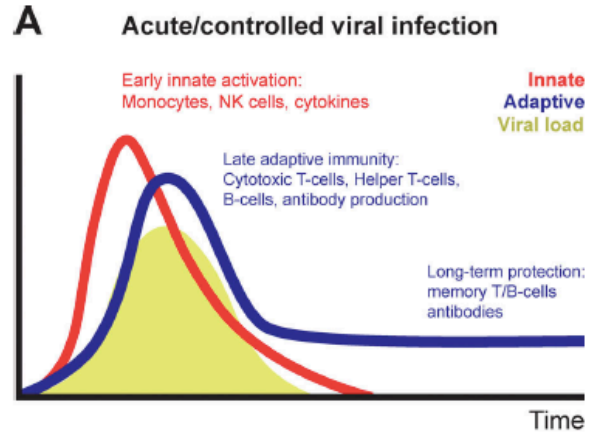


1. Lopinavir/rotonavir<sup>\*,#,\$</sup>
2. Lopinavir/rotonavir/ifn- $\beta$ -1a<sup>#, \$</sup>
3. OHchloroquine<sup>\*,#,\$</sup> (dose)
4. Remdesivir<sup>#, \$</sup>
5. Azithromycine<sup>\*</sup>
6. Low dose CC<sup>\*</sup>
7. Convalescent plasma<sup>\*</sup>
8. Tocilizumab<sup>\*</sup>

## H2020 03/06/20 “E.U. RESPONSE”



Nouveaux anti-viraux ?



**Nouveaux anti-  
viraux ?**

**Immunothérapie  
?**

Immunomodulation  
Immunothérapie passive  
Thérapie cellulaire/  
transfert adoptif

**Approches  
combinées ?**

**Immuno-  
prophylaxie  
Vaccinale ?**