Antiviral treatments for COVID-19
s47F

12 February, 2020

There are no registered treatments for coronaviruses.

Potential treatments

A 2017 UK evidence summary listed potential treatments for SARS and MERS-CoV. It was suggested that the following treatments may be considered for use

- Convalescent plasma
- Interferons (esp IFN- β)
- Lopinavir
- Monoclonal and polyclonal neutralising antibodies

The following treatments were considered to be of uncertain risk benefit

- Interferon + ribavirin combination
- Remdesivir
- Galidesivir
- Nitazoxanide
- Chloroquine

Current clinical trials activity for MERS and COVID-19

Current clinical trials for MERS-CoV (from WHO International Clinical Trials Registry and Clinicatrials.gov)

- MERS-CoV Vaccines: ChAdOx1, BVRS-GamVac, MVA-MERS-S_DF-1, MVA-MERS-S
- Lopinavir/ritonavir and IFN- β1b
- SAB-301
- Lopinavir/ritonavir and Arbidol (umifenovir)
- Umifenovir
- Methylprednisolone (40mg) vs no treatment
- Remdesivir

Current clinical trials for COVID-19

- Novaferon, Lopinavir/ritonavir, combination
- Steroids
- Ribavirin + Interferon alpha-1b; lopinavir / ritonavir + interferon alpha-1b;Ribavirin + LPV/r+Interferon alpha-1b;
- Umifenovir (antiviral)
- Lopinavir-ritonavir and interferon-alpha 2b

Other drugs with limited evidence of activity include

- Chloroquine
- Favipiravir
- Nafamostat

This document was released under the Freedom of Information Act 1982 by the Department of Health

Trial platforms

The development of WHO Master Global Trial Protocol was announced on 5 Feb, 2020; a priority list of treatments to be tested is being developed. A distinction should be made between patients with nCoV with critical illness (where a dysregulated immune response dominates the clinical picture) and less severe illness.

The REMAP-CAP trial has submitted a pandemic appendix to test treatments for new pathogens in critically ill patients. Potential interventions that could be tested in a treatment domain include standard of care vs lopinavir/ritonavir vs lopinavir/ritonavir+IFN- β vs IFN-β. A domain testing anakinra (IL1RA inhibitor) vs no treatment is also being considered for viral pneumonia. This trial is running in Australia, New Zealand and Europe/UK and has recently commenced enrolment in Canada. A design feature is response adaptive randomisation, where more patients are allocated to the better performing arm (ie a self-learning system).

Other clinical research needs include

- Other ICU strategies, including ECMO
- Infection prevention interventions
- Clinical characterisation and surveillance
- Vaccines and preventative strategies

This document was released under the Freedom of Information Act 1982 by the Department of Health

Table: Potential treatments for coronavirus infections (abstracted from UK Guidelines for MERS-CoV)

Treatment	Evidence in SARS and MERS	Safety	Availability
Benefit likely to exceed risks of harm			
Convalescent plasma (or high neutralizing antibody titre products)	SARS: No RCT; Observational data suggests benefit MERS One RCT ongoing (NCT02190799) In vitro and mouse model supportive Antibody levels may vary – Yaseen Arabi commented that MERS Ab low post infection.	Risks of transmission of coronavirus Usual risks of blood products	s47F (Lifeblood) – indicates generic process established but TGA and NBA approval required.
Interferons	SARS: In vitro and animal models suggest activity of Type I (α, β), type II (γ), and type III (λ) IFNs MERS In vitro, IFN-β most effective, IFN-β1b effective in primate model Concern that primate model differs from human model Current trial of lopinavir/ritonavir and IFNβ-1b is recruiting in Saudi Arabia (NCT 02845843).	Well established agent for MS and previously used in HCV, known safety profile	Available
Lopinavir	SARS In vitro inhibition Observational data suggests reduced mortality MERS In vitro inhibition at clinically relevant concentrations Improved outcomes in non-human primate model Current trial of lopinavir/ritonavir and IFNβ-1b is recruiting in Saudi Arabia (NCT 02845843).	Well established agent for HIV. Good safety profile	Available
Monoclonal and polyclonal neutralising antibodies (mAbs) SAB-301 LCA60	SARS In vitro studies mAb against SARS-CoV spike protein found neutralising effect MERS In vitro studies mAb against MERS-CoV spike protein found neutralising effect Human mAbs suggest benefit in murine models	Little data – phase 1 studies in progress (NCT 02788188)	Research only

This document was released under the Freedom of Information Act 1982 by the Department of Health

REGN3051 & REGN3048	Evidence of efficacy as prophylaxis when in primate model		
Uncertain risk benefit			
Interferon + ribavirin combination	SARS: In vitro evidence of synergy between R+ IFN-β Combination used in patients but no comparison with individual agents MERS In vitro evidence of synergy between R+ IFN-α2b Some evidence of activity in primate model No apparent benefit of IFN-α2a/R in cohort study	High incidence of haemolysis	Available
Remdesivir (GS-5734)	SARS: Potent inhibitor in vitro Mouse model – improved outcomes if used early but not late MERS Potent inhibitor in vitro Some benefit in primate model Activity in mouse model	Trial in Ebola – not effective but no safety signals	Gilead – not registered
Galidesivir (BCX4430)	SARS: In vitro activity MERS: In vitro activity	Phase 1 trial in progress (NCT02319772)	BioCryst - not registered
Nitazoxanide	SARS: no data MERS: in vitro activity Viral pneumonia: no reduction in LOS in clinical trial in viral pneumonia (Gamino Arroyo CID 2019)	Well established agent	Available
Chloroquine	SARS: no data MERS: in vitro activity	Well established agent	Available
Likely harmful			
Steroids			

This document was released under the Freedom of Information Act 1982 by the Department of Health

Ribavirin
IVIG
Mycophenolate

This document was released under the Freedom of Information Act 1982 by the Department of Health