COVID CLINICAL UPDATE ROUNDS

OCT 8, 2020

COVID UPDATE ROUNDS

- Recurring
- Interactive
  - Slido/**#MedicalStaffCOVID**
- Choose your own adventure (send us requests for topics)
  - medstaffengagement@viha.ca, omar.ahmad@viha.ca
- Knowing local response is paramount

PREVIOUSLY ON RECURRING ROUNDS

- Cases remain low on the Island
  - 0 hospitalized, 0 in ICU, 11 active cases
- Canadian ICU Mortality:
  - ICU 26%
  - Ventilated 31%
  - Vancouver 15 (20)%
  - RJH 20%

PREVIOUSLY ON RECURRING ROUNDS

- Critical care management:
  - Look at the work of breathing and physiology
  - HFNC --> NIV → IMV
  - Standard fare ARDS mgt
    - Low TV, conservative/judicious fluids
    - Consider proning, higher PEEP trials in severe ARDS
    - Look at the driving pressure and maintain less than 15
      - DP = Plat – PEEP
    - L vs H phenotypes?

PREVIOUSLY ON RECURRING ROUNDS

- Critical care management:
  - Look at the work of breathing and physiology
  - HFNC → NIV → IMV → ECLS

PREVIOUSLY ON RECURRING ROUNDS

- Critical care management:
  - Standard fare ARDS mgt
    - Low TV, conservative/judicious fluids
    - Consider proning, higher PEEP trials in severe ARDS
    - Look at the driving pressure and maintain less than 15
      - DP = Plat – PEEP
    - L vs H phenotypes?
      - Measure the lung compliance

PREVIOUSLY ON RECURRING ROUNDS

- Critical Care Management:
  - Adam Thomas has seen a lot of COVID
  - Beware the PTX
  - Bronchs and Trach appear safe

OBJECTIVES, OCT 8TH

- Be aware of cohort protocols
- Be updated on epidemiology
- Review recent BC CDC Code blue 'draft' protocol
- Be aware of mask policy for patients and visitors
- Be aware of COVID research occurring at Island Health
- Review VTEp and VTE therapy
- Be updated on recent critical care literature

TODAY'S SPEAKERS AND SUPPORT STAFF

- Dr. Omar Ahmad
- Dr. Gordon Wood
- Dr. Shavaun MacDonald
- Dr. Adam Thomas
- Dr. Daniel Ovakim
- Matt Erickson
- Lisa Young
- Victoria Schmid
- Tara Holmes
- Kyja Levitt

DISCLOSURES/CONFLICTS OF INTEREST

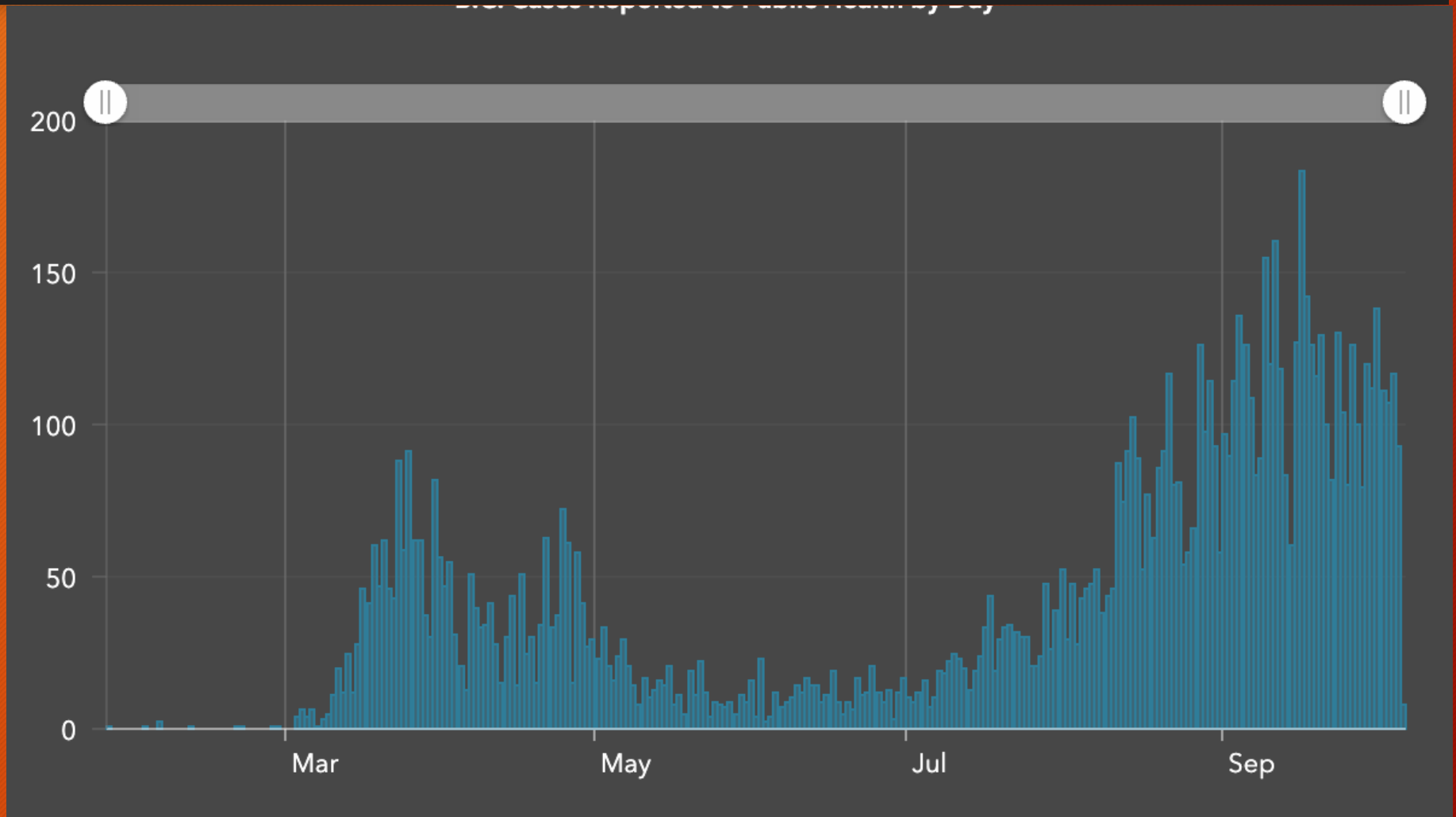
- None

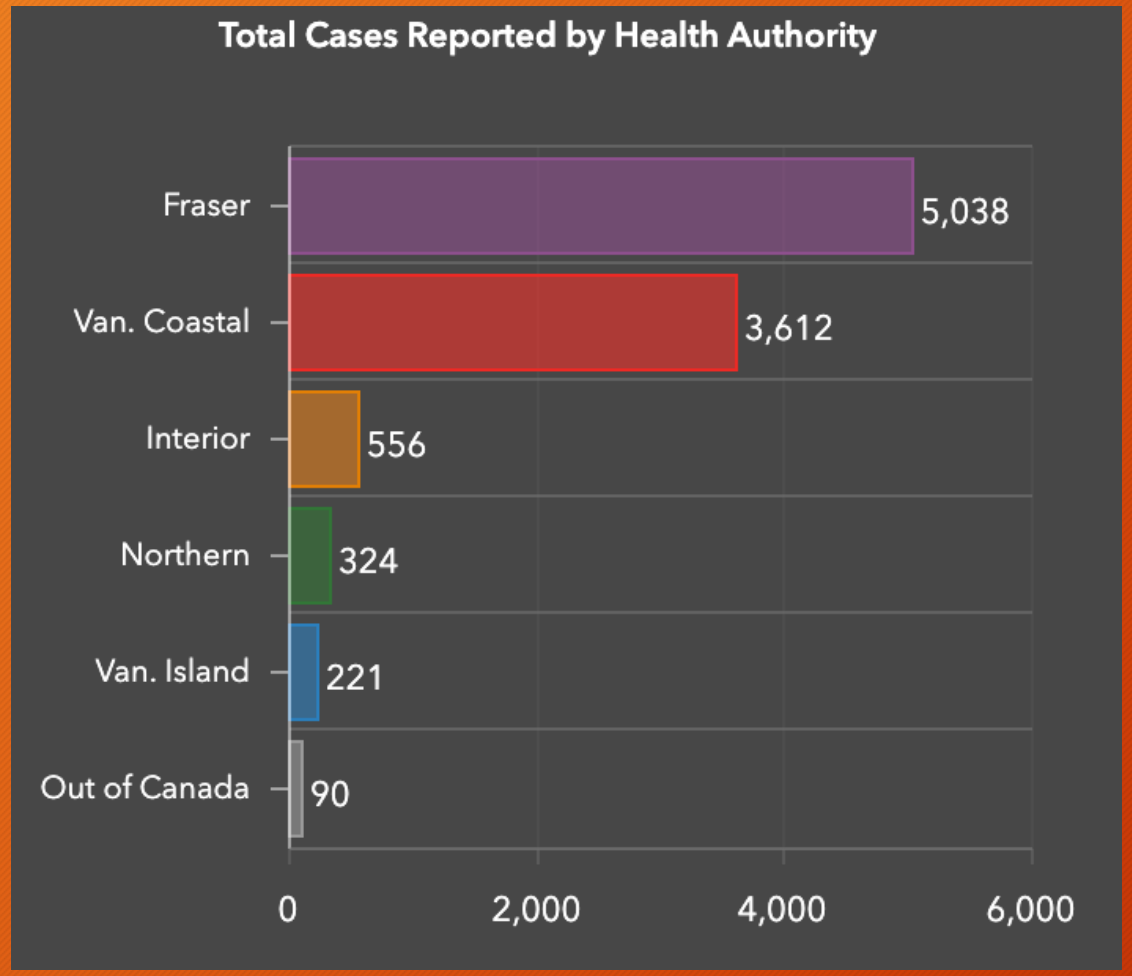
COVID 19 UPDATE

OCT. 7, 2020

EPIDEMIOLOGY

COVID CASES BC





Total Cases

9,841

Laboratory Diagnosed	Epi-Linked
9,665	176

Currently Hospitalized

71

Total to Date: 809

Currently Admitted to ICU

16

Confirmed Deaths

244

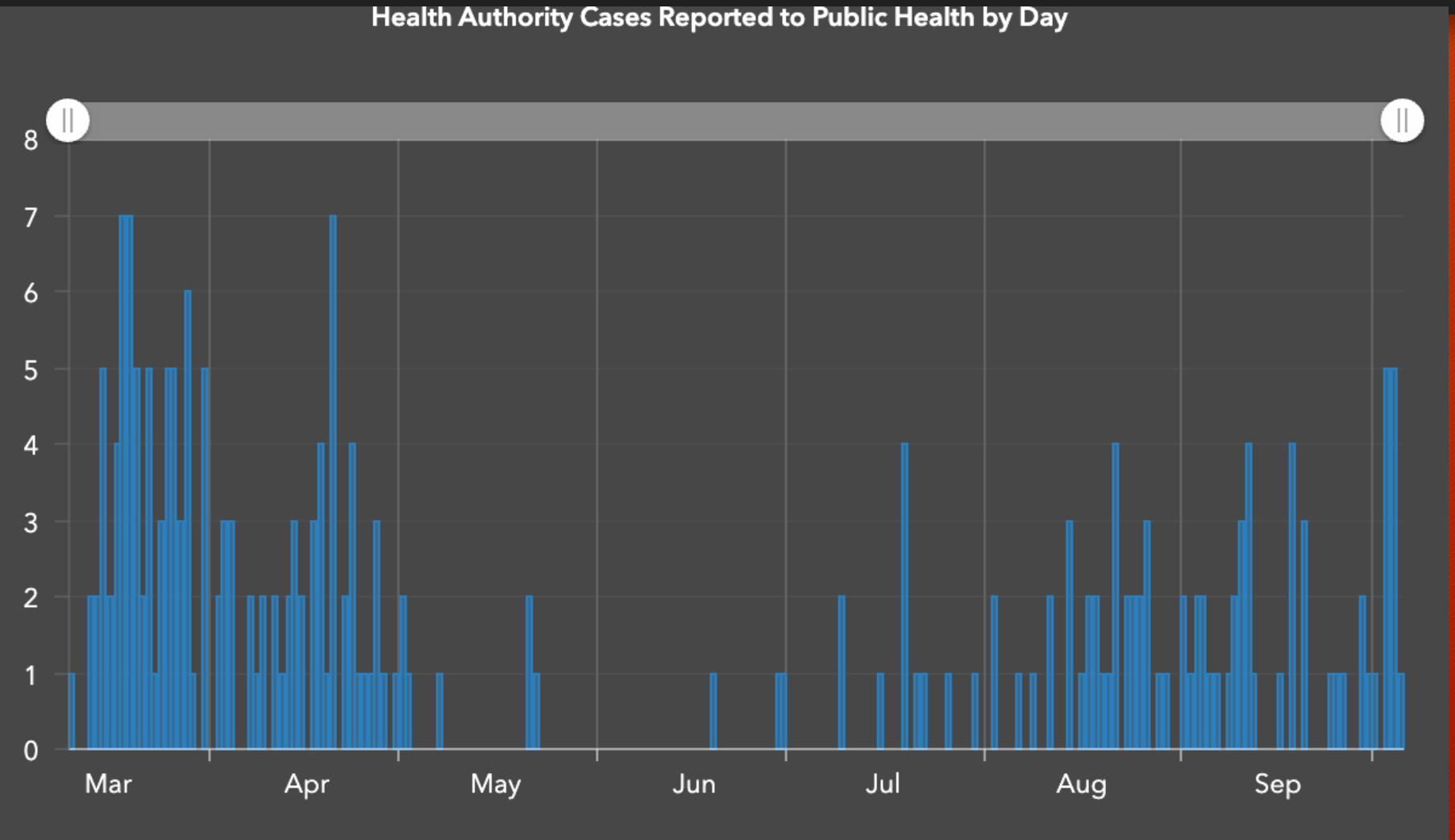
Recovered

8,184

Last Update

10/6/2020, 4:30 PM

COVID CASES VANCOUVER ISLAND



New Cases	Active Cases
1	11

Total Cases

221

Laboratory Diagnosed	Epi-Linked
217	4

Currently Hospitalized

0

Total to Date: 25

Currently Admitted to ICU

0

Confirmed Deaths

6

Recovered

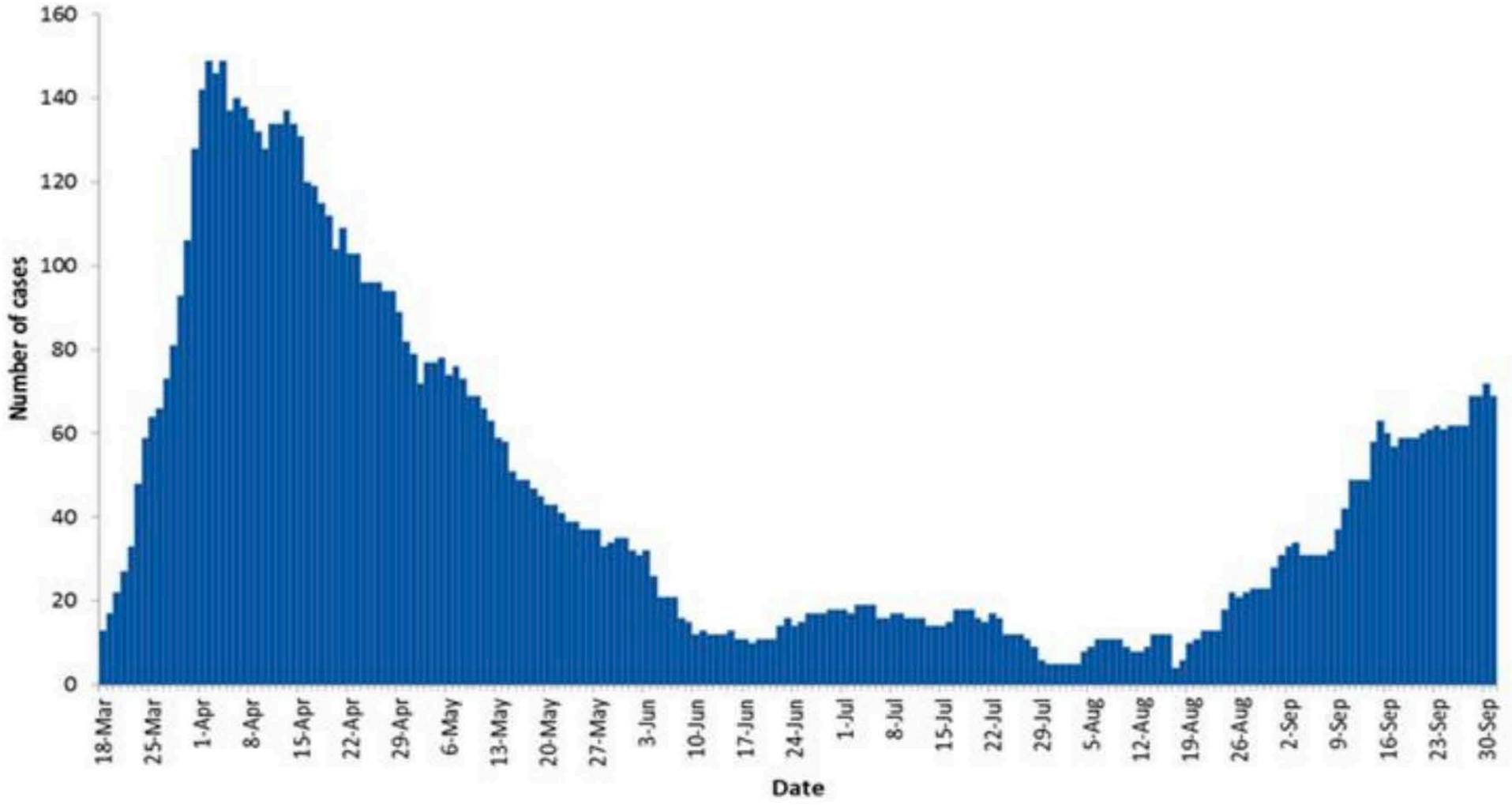
204

Last Update

10/6/2020, 4:30 PM

Number of COVID-19 Cases in Hospital by Day, BC, March 18 – October 1, 2020

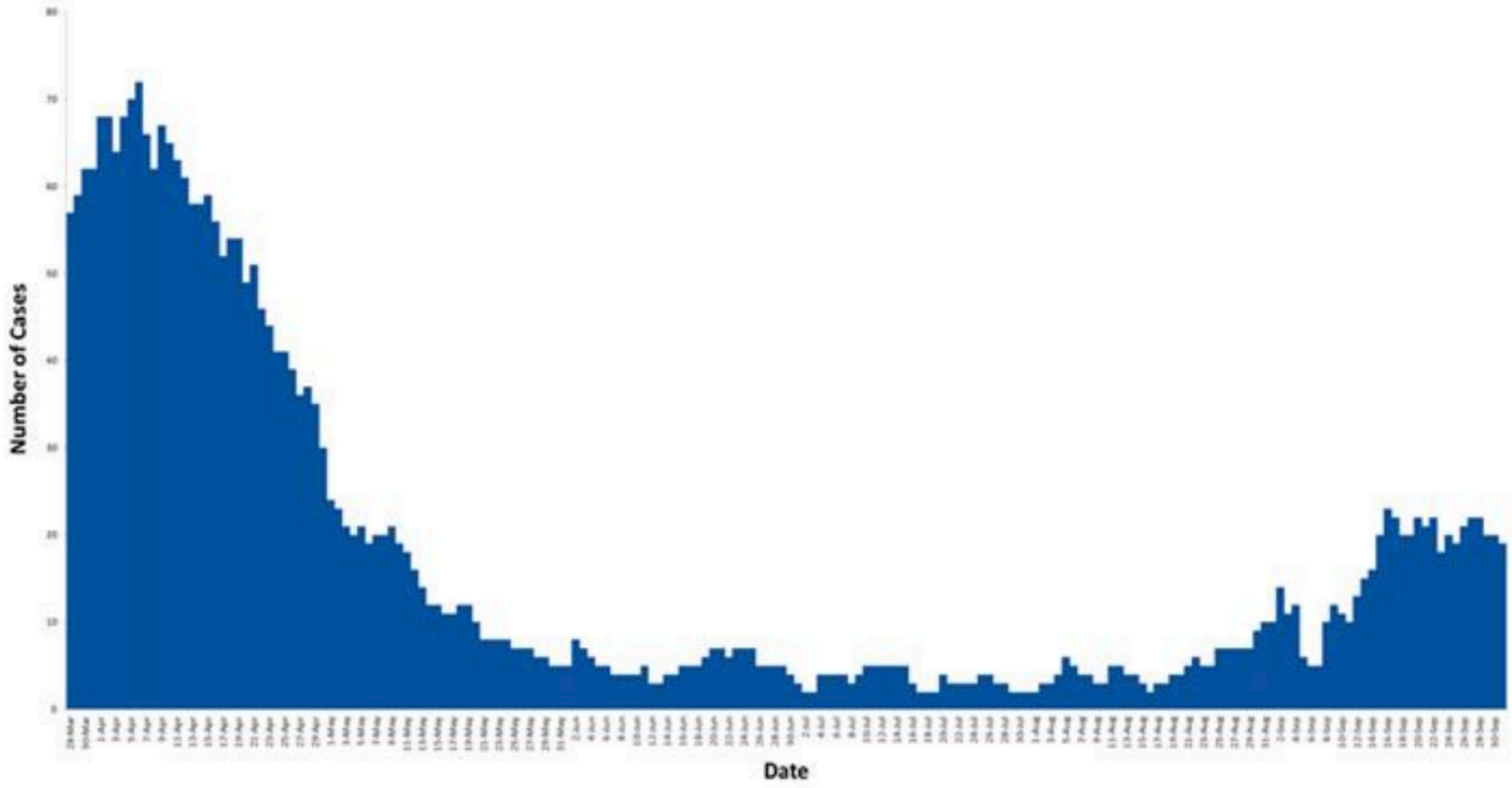
The number of cases currently in hospital is lower than in April.



Data available starting March 18. For dates with no data available (April 12; Sundays from May 10 onwards; and Saturdays from June 7 onwards).

Total COVID-19 Cases in Critical Care by Day, BC, March 25 – October 1, 2020

The number of cases currently in critical care is lower than in April.



Data source: PHSA October 1, 2020.
Note: critical care data may change over time due to small adjustments and improvements in data quality.

CODE BLUE RESPONSE

Coronavirus COVID-19

BC Centre for Disease Control | BC Ministry of Health

BRITISH COLUMBIA
Ministry of Health

Infection Prevention and Control (IPC) Protocol During Code Blue for Adult Patients at **Unknown** for COVID-19 in a Time of Low Community Covid-19 Prevalence

In patients with circulatory arrest, *early* bystander CPR improves survival and neurological outcomes. The likelihood of a patient having COVID-19 outside of designated COVID-19 units in acute care is low. Patients are risk-assessed on admission to health authority facilities for the possibility of COVID-19.

Time-motion studies by Alberta Health Services[2] suggest that it takes at least 3 minutes to don airborne PPE. Delay in commencing or stopping CPR may decrease the survival rate by at least 2%[3]. It is therefor advised to minimize any delay or interruptions to CPR.

A. Location/Environment

- Patients may experience a Code Blue/medical emergency in any part of the hospital. This includes the emergency department (ED), intensive care unit (ICU), ward, operating room, outpatient areas or common areas.
- Minimizing the amount of people present during a Code Blue enhances the safety and effectiveness of the care provided and limits the health care workers (HCWs) potential exposure to pathogens.
- As with any Code Blue, the environment should be optimized to provide adequate access to the patient and enhance safety. This may include moving the patient to a designated resuscitation area.
- When transporting patients during a cardiac arrest (e.g. from ambulance to resuscitation area) ensure CPR and assisted ventilations through a bag valve mask (BVM) and high efficiency hydrophobic filter, suproglottic airway or secured airway continues uninterrupted by HCWs wearing airborne and contact PPE (N95 respirator, gown, gloves and eye protection).
- CPR should not be interrupted to transport the patient.

B. Patient COVID-19 Risk Assessment

- All patients entering a hospital should be screened with an appropriate risk assessment tool, such as the PCRA tool, including all outpatient areas. Those screened as at risk (red) should be immediately isolated and referred for evaluation for COVID-19.
- All patients risk screen status should be displayed clearly on their chart and communicated with their treating team.
- All patients should be regularly re-evaluated on their COVID-19 risk status and the chart updated and transferred to an appropriate area if suspected or confirmed.
- The patient's COVID-19 risk screen status should be known at the point of commencing basic life support (BLS). However it is not always known, this should not delay the commencement of chest compressions.

C. Patient Assessment – Determining if a Code Blue Should be Activated

- Each facility should have a process for identifying the code status or advanced care directive of admitted patients. If there is uncertainty of the code status, a code blue should be activated inline with the patient assessment.
- Follow local guidelines, policies and training when activating a Code Blue.
- The HCW assessing the patient should wear standard PPE for the patient as outlined by local guidelines.

D. Initiating CPR

- Prior to commencing chest compressions a covering (surgical mask, cloth or oxygen mask) should be placed over the patients nose and mouth to minimize the risk of expose to droplets.
- For patients who are **not suspected or not known to be COVID-19 positive**, CPR should be commenced as per local CPR guidelines.
- When responding to a Code Blue:
    a. The first person on scene should commence chest compressions (after calling for assistance) wearing their current level of PPE (i.e. the first responder **should not** change/don PPE prior to commencing CPR).
    b. If there is uncertainty about the patients COVID-19 status the first person on scene should continue chest compressions until assistance arrives before donning additional PPE.

PATIENT RISK CATEGORY TABLE:

Does the patient have a risk factor for COVID-19 exposure?	*Does the patient have new onset COVID-19 like symptoms that cannot be explained otherwise?*	*COVID-19 test result (if applicable)*	Risk Category
NO	NO	NOT REQUIRED	GREEN
NO	YES	NEGATIVE	GREEN
YES	NO	NEGATIVE	GREEN
YES	YES	NEGATIVE	GREEN
YES	UNKNOWN	NEGATIVE	GREEN
UNKNOWN	UNKNOWN	PENDING/NOT DONE	YELLOW
YES	UNKNOWN	PENDING/NOT DONE	RED
NO	UNKNOWN	PENDING/NOT DONE	RED
YES	YES*	PENDING/NOT DONE	RED
NO	YES	PENDING/NOT DONE	RED
YES	YES	PENDING/NOT DONE	RED
-	-	**POSITIVE**	RED

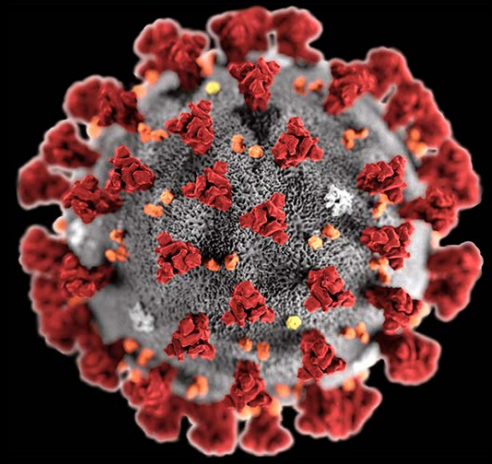
E. Airway Management During a Code Blue

- If intubation is required for:
  - Patients with low risk of COVID-19 (GREEN) the treating team should don droplet precaution PPE (surgical mask, eye protection, gown and gloves) prior to the procedure
  - Patients with unknown risk of COVID-19 (YELLOW) the treating team should don airborne and contact PPE (N95 respirator, gown, gloves and eye protection) prior to the procedure.
- If assisted ventilation via a BVM is required prior to intubation for:
  - Patients with low risk of COVID-19 (GREEN) the treating team should don droplet precaution PPE (surgical mask, eye protection, gown and gloves) prior to commencing breaths.
  - Patients with unknown risk of COVID-19 (YELLOW) the treating team should don airborne PPE (N95 respirator, gown, gloves and eye protection) prior to commencing breaths.

Critical Care Rounds

COVID-19: An Update

Therapeutics & Clinical Trials



island health

October 8, 2020

Conflict of Interests

- No relevant conflicts of interest

Outline

1. Review the current recommendations for Antimicrobial and Immunomodulatory Therapy for COVID-19
2. (Re)Introduce the Clinical Trials and research occurring at Island Health for inpatients with COVOD-19 (next session)
    - CATCO
    - CONCOR
    - ATTACC

1. COVID Therapeutics

Rita Panahi
@RitaPanahi

Professor of epidemiology at Yale School of Public Health Dr Harvey Risch said we'd slash COVID-19 death rate dramatically if we prescribed hydroxychloroquine & zinc to high risk patients early in the infection.

Interview on NOW @SkyNewsAust

The key to defeating COVID-19 alre
Contrary to what you hear, there is
efficacy of hydroxychloroquine.
newsweek.com

5:15 PM · Sep 5, 2020

2.5K See the latest COVID

Rep Andy Biggs
@RepAndyBiggsAZ

Arizona should embrace President
to give Americans the right to try hy

6:55 PM · Sep 5, 2020

AssocAmerPhys&Surg
@AAPSonline

Canadian doctor: Smear against Hydroxychloroquine drug in stopping COVID 'needs to stop' | News | LifeSite

Canadian doctor: Smear against Hydroxychloroquine drug in stopping ...
Ontario-based doctor Kulvinder Gill said bans on the drug have caused an 'unprecedented violation of the doctor-patient relationship.'
lifesitenews.com

7:54 PM · Sep 5, 2020

470 See the latest COVID-19 information on Twitter

WUWT
Watts Up With That?
The world's most viewed site on global warming and climate change

Daily Coronavirus Graph Page | Home | About | Climate FAIL Files | Climategate | Reference Pages

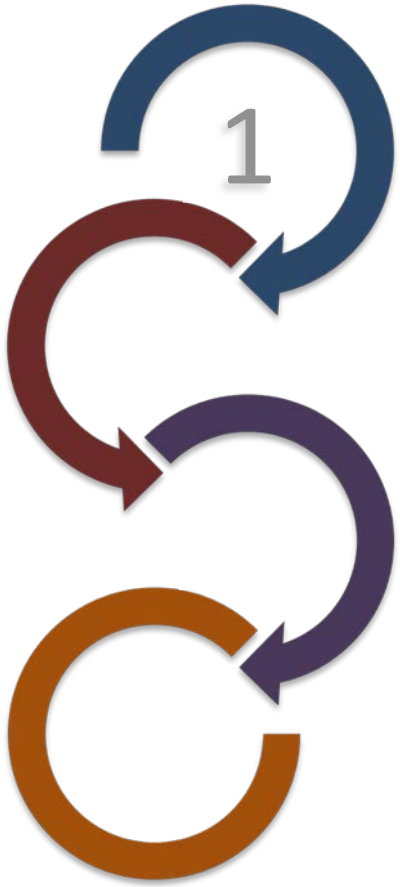
Hydroxychloroquine in COVID-19 Treatment, Actual Usage in the USA

Leo Goldstein / 2 weeks ago August 24, 2020

Preprint. August 23, 2020.

Key Words: hydroxychloroquine, COVID-19, SARS-CoV-2, Wuhan

https://en.wikipedia.org/wiki/Ipse_dixit



Therapeutic Recommendations

- Antiviral therapy
- Antibacterial therapy
- Immunomodulatory therapy
- Other therapies

British Columbia COVID-19 Therapeutics Committee (CTC) Clinical Practice Guidance for

Antimicrobial and Immunomodulatory Therapy in Adult Patients with COVID-19

SUMMARY
last updated August 24th, 2020

Recommendations in this document apply to patients > 18 years of age. For details including special populations, refer to the complete summary document.

There is limited clinical evidence to guide antiviral therapy for patients with COVID-19.

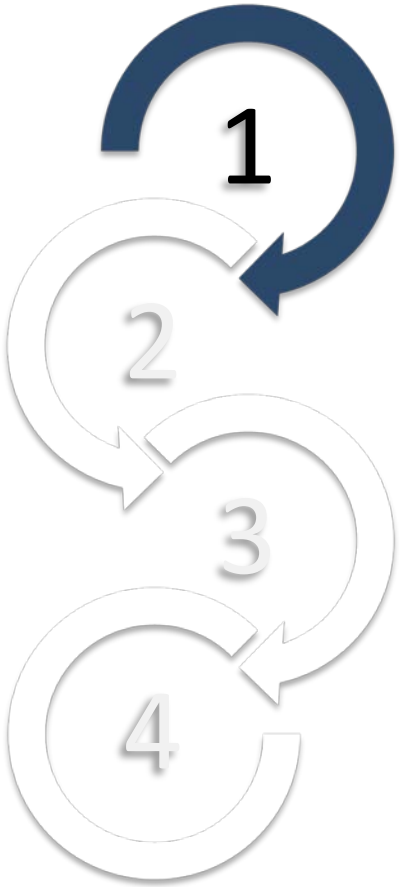
Specialist consultation (e.g., Critical Care, Infectious Disease, Hematology, or Rheumatology) is recommended if any investigational treatment is offered to a patient with COVID-19 outside of approved clinical trials. Informed consent should be obtained from the patient or the substitute decision maker.

SEVERITY OF ILLNESS	ANTIVIRAL THERAPY Unless otherwise specified, recommendations include antivirals alone or in combination	ANTIBACTERIAL THERAPY	IMMUNOMODULATORY THERAPY	OTHER THERAPEUTICS
Critically Ill COVID-19 Patients *Hospitalized, ICU-based* Patients requiring mechanical ventilatory and/or vasopressor/inotropic support	**Chloroquine** or **Hydroxychloroquine** is **not** recommended for the treatment of COVID-19 **Lopinavir/ritonavir** is **not** recommended outside of approved clinical trials **Remdesivir*** has received conditional approval by Health Canada for the treatment of COVID-19. Remdesivir shortened time to clinical recovery but failed to show any survival benefit in the ACTT-1 trial. In British Columbia availability of remdesivir remains limited to clinical trails at this time. **Ribavirin/Interferon** is **not** recommended outside of approved clinical trials	**Ceftriaxone 1-2 g IV q24h x 5 days** is recommended if there is concern for bacterial co-infection (alternative for severe beta-lactam allergy: moxifloxacin 400 mg IV q24h x 5 days) **Azithromycin 500 mg IV q24h x 3 days** is recommended if atypical bacterial infection is suspected (not required if on moxifloxacin) De-escalate on the basis of microbiology results and clinical judgment	**Dexamethasone 6 mg IV/PO q24h for up to 10 days** is **strongly recommended** (RECOVERY trial), unless higher doses are indicated**. If Dexamethasone is not available, methylprednisolone 30 mg IV q24h is the preferred alternative. **Tocilizumab** or **sarilumab** is **not** recommended outside of approved clinical trials; where clinical trials are not available, expert consultation is recommended (Infectious Diseases, Hematology, Rheumatology)	**Enoxaparin 30 mg SC q12h** is **suggested** for VTE prophylaxis **ACE inhibitors** and **ARBs** should not be discontinued solely on the basis of COVID-19 **NSAIDs** should not be discontinued solely on the basis of COVID-19
Severely Ill COVID-19 Patients *Hospitalized, ward-based, long-term care* Patients requiring supplemental oxygen therapy	**Chloroquine** or **Hydroxychloroquine** is **not** recommended for the treatment of COVID-19 **Lopinavir/ritonavir** is **not** recommended outside of approved clinical trials **Remdesivir*** has received conditional approval by Health Canada for the treatment of COVID-19. Remdesivir shortened time to clinical recovery but failed to show any survival benefit in the ACTT-1 trial. In British Columbia availability of remdesivir remains limited to clinical trails at this time. **Ribavirin/Interferon** is **not** recommended outside of approved clinical trials	Antibacterial therapy is **not** routinely recommended outside of approved clinical trials unless other indications justify its use (e.g., suspected bacterial co-infection in COVID-19 positive patients)	**Dexamethasone 6 mg IV/PO q24h for up to 10 days** is **recommended** (RECOVERY trial), unless higher doses are indicated**. If Dexamethasone is not available, methylprednisolone 30 mg IV q24h or prednisone 40 mg PO q24h are the preferred alternatives. If dexamethasone supplies are limited, they should be reserved for critically ill patients. **Tocilizumab** or **sarilumab** is **not** recommended outside of approved clinical trials	**Enoxaparin 30 mg SC q12h** should be **considered** for VTE prophylaxis in severely ill hospitalized patients **ACE inhibitors** and **ARBs** should not be discontinued solely on the basis of COVID-19 **NSAIDs** should not be discontinued solely on the basis of COVID-19
Mildly Ill COVID-19 Patients *Ambulatory, outpatient, long-term care* Patients who do not require supplemental oxygen, intravenous fluids, or other physiological support	**Chloroquine** or **Hydroxychloroquine** is **not** recommended for the treatment of COVID-19 **Lopinavir/ritonavir** is **not** recommended outside of approved clinical trials **Remdesivir*** is **not** recommended outside of approved clinical trials **Ribavirin/Interferon** is **not** recommended outside of approved clinical trials	Antibacterial therapy is **not** routinely recommended outside of approved clinical trials unless other indications justify its use (e.g., suspected bacterial co-infection in COVID-19 positive patients)	**Corticosteroids** are **not** recommended outside of approved clinical trials unless otherwise indicated** **Tocilizumab** or **sarilumab** is **not** recommended outside of approved clinical trials	**ACE inhibitors** and **ARBs** should not be discontinued solely on the basis of COVID-19 **NSAIDs** should not be discontinued solely on the basis of COVID-19
Prophylaxis Patients with known COVID-19 exposure	**Chloroquine** or **hydroxychloroquine** is **not** recommended for prophylaxis in patients with known COVID-19 exposure			

** Currently unavailable in Canada*
*** e.g., asthma exacerbation, refractory septic shock, history of chronic steroid use, obstetric use for fetal lung maturation*

This document is dynamic and addresses key therapeutic areas of concern for clinicians. The complete and most up-to-date version of the guidelines is available at http://www.bccdc.ca/health-professionals/clinical-resources/covid-19-care/clinical-care/treatments

Vancouver Coastal Health · fraserhealth · Provincial Health Services Authority · Providence Health Care · island health · Interior Health · northern health · British Columbia Ministry of Health · BC Patient Safety & Quality Council · First Nations Health Authority



Antiviral Therapy

- Chloroquine and Hydroxychloroquine
- Lopinovir/Ritonovir (Kaletra®)
- Ribavirin/Interferon
- Remdesivir

ANTIVIRAL THERAPY
Unless otherwise specified, recommendations include antivirals alone or in combination

Chloroquine or **Hydroxychloroquine** is **not** recommended for the treatment of COVID-19

Lopinavir/ritonavir is **not** recommended outside of approved clinical trials

Remdesivir* has received conditional approval by Health Canada for the treatment of COVID-19. Remdesivir shortened time to clinical recovery but failed to show any survival benefit in the ACTT-1 trial. In British Columbia availability of remdesivir remains limited to clinical trails at this time.

Ribavirin/Interferon is **not** recommended outside of approved clinical trials

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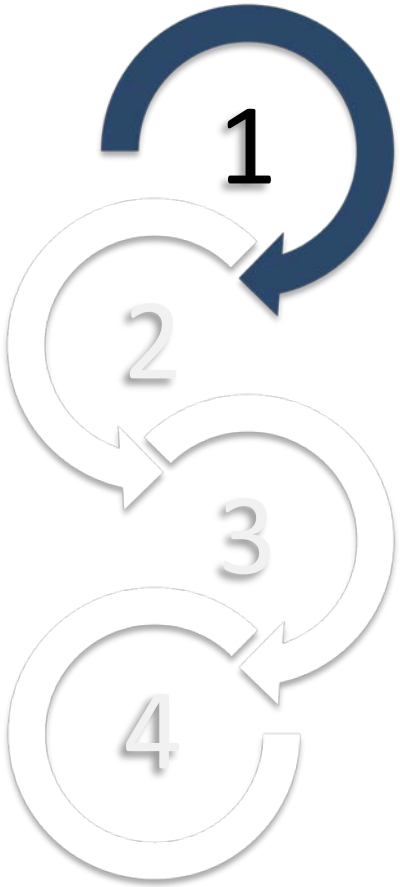
Lopinavir/ritonavir is **not** recommended outside of approved clinical trials

Remdesivir* is **not** recommended outside of approved clinical trials

Ribavirin/Interferon is **not** recommended outside of approved clinical trials

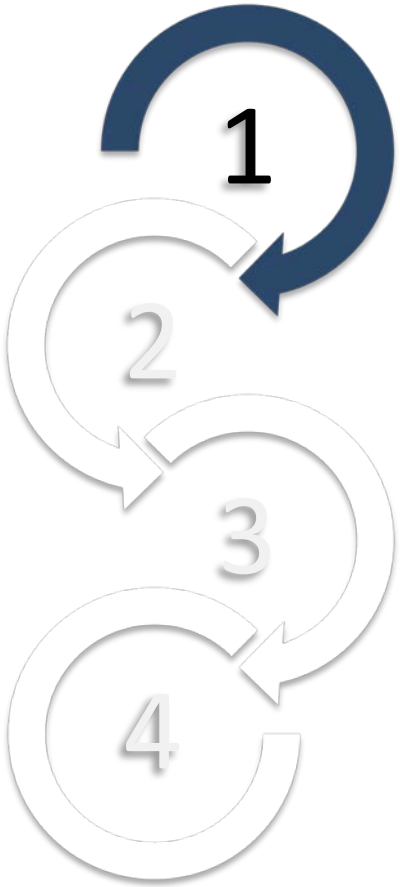


Antiviral Therapy

Chloroquine and Hydroxychloroquine

- Antimalarial agent
- Primarily used in rheumatologic disease
- NOT recommended
  - Treatment of all forms of disease
  - Prophylaxis after known COVID-19 exposure

Critically Ill COVID-19 Patients *Hospitalized, ICU-based*	**Chloroquine** or **Hydroxychloroquine** is **not** recommended for the treatment of COVID-19
Severely Ill COVID-19 Patients *Hospitalized, ward-based, long-term care*	**Chloroquine** or **Hydroxychloroquine** is **not** recommended for the treatment of COVID-19
Mildly Ill COVID-19 Patients *Ambulatory, outpatient, long-term care*	**Chloroquine** or **Hydroxychloroquine** is **not** recommended for the treatment of COVID-19



Antiviral Therapy

Chloroquine and Hydroxychloroquine

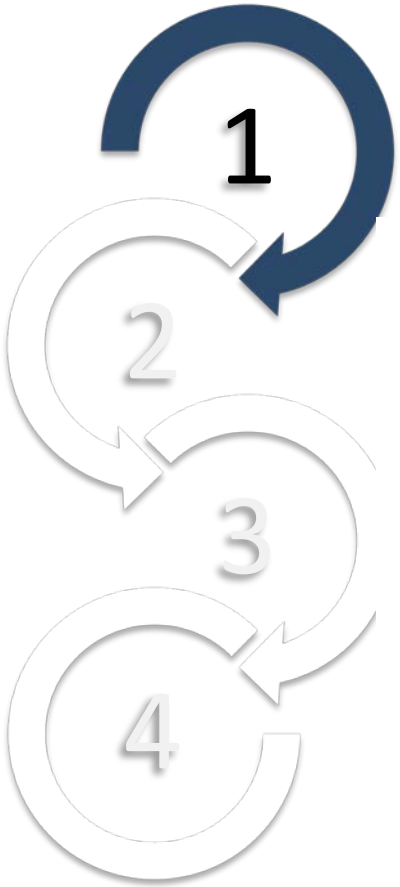
Conclusion: Despite its small sample size, our survey shows that hydroxychloroquine treatment is significantly associated with viral load reduction/disappearance in COVID-19 patients and its effect is reinforced by azithromycin.

EXPRESSION OF CONCERN

Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial ☆

Philippe Gautret[a,b,$], Jean-Christophe Lagier[a,c,$], Philippe Parola[a,b], Van Thuan Hoang[a,b,d], Line Meddeb[a], Morgane Mailhe[a], Barbara Doudier[a], Johan Courjon[e,f,g], Valérie Giordanengo[h], Vera Esteves Vieira[a], Hervé Tissot Dupont[a,c], Stéphane Honoré[i,j], Philippe Colson[a,c], Eric Chabrière[a,c], Bernard La Scola[a,c], Jean-Marc Rolain[a,c], Philippe Brouqui[a,c], Didier Raoult[a,c,*]

International Journal of Antimicrobial Agents 56 (2020) 105949



Antiviral Therapy

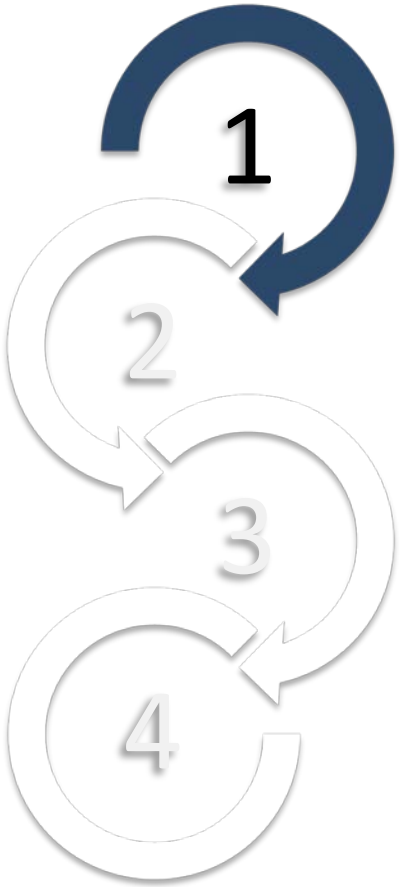
Chloroquine and Hydroxychloroquine

CONCLUSIONS

In this observational study involving patients with Covid-19 who had been admitted to the hospital, hydroxychloroquine administration was not associated with either a greatly lowered or an increased risk of the composite end point of intubation or death. Randomized, controlled trials of hydroxychloroquine in patients with Covid-19 are needed. (Funded by the National Institutes of Health.)

Joshua Geleris, M.D., Yifei Sun, Ph.D., Jonathan Platt, Ph.D., Jason Zucker, M.D., Matthew Baldwin, M.D., George Hripcsak, M.D., Angelena Labella, M.D., Daniel Manson, M.D., Christine Kubin, Pharm.D., R. Graham Barr, M.D., Dr.P.H., Magdalena E. Sobieszczyk, M.D., M.P.H., and Neil W. Schluger, M.D.

May 7, 2020
Observational
1446 Patients



Antiviral Therapy

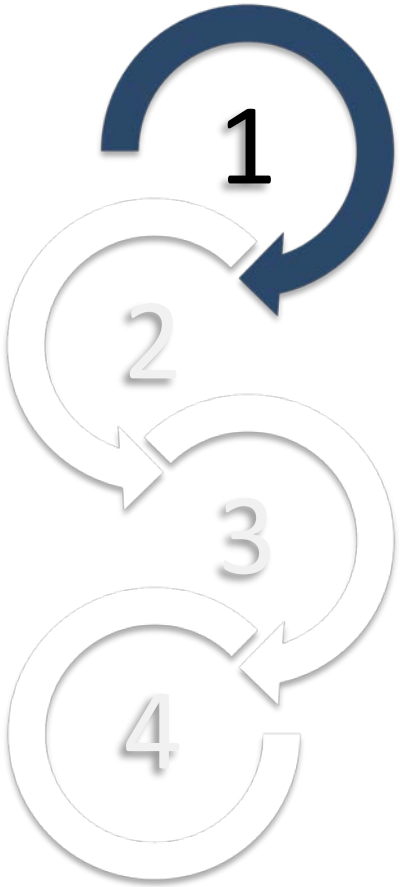
Chloroquine and Hydroxychloroquine

CONCLUSIONS AND RELEVANCE Among patients hospitalized in metropolitan New York with COVID-19, treatment with hydroxychloroquine, azithromycin, or both, compared with neither treatment, was not significantly associated with differences in in-hospital mortality. However, the interpretation of these findings may be limited by the observational design.

Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State

Eli S. Rosenberg, PhD; Elizabeth M. Dufort, MD; Tomoko Udo, PhD; Larissa A. Wilberschied, MS; Jessica Kumar, DO; James Tesoriero, PhD; Patti Weinberg, PA; James Kirkwood, MPH; Alison Muse, MPH; Jack DeHovitz, MD; Debra S. Blog, MD; Brad Hutton, MPH; David R. Holtgrave, PhD; Howard A. Zucker, MD

May 11, 2020
Observational
1428 Patients



Antiviral Therapy

Chloroquine and Hydroxychloroquine

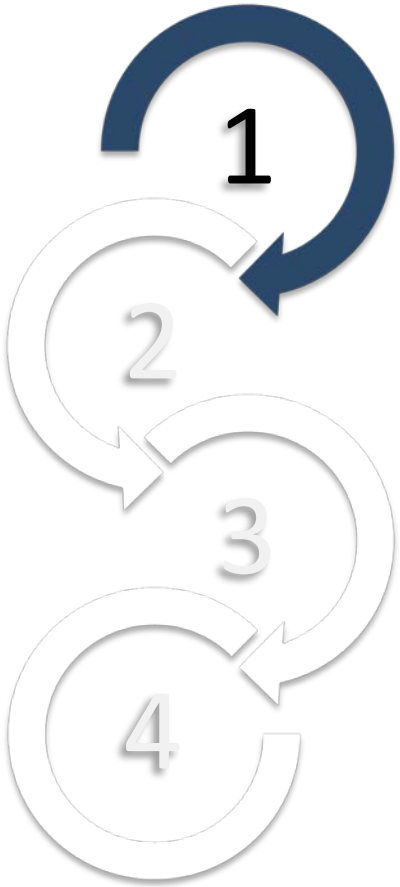
CONCLUSIONS

Among patients hospitalized with mild-to-moderate Covid-19, the use of hydroxychloroquine, alone or with azithromycin, did not improve clinical status at 15 days as compared with standard care. (Funded by the Coalition Covid-19 Brazil and EMS Pharma; ClinicalTrials.gov number, NCT04322123.)

Azithromycin in Mild-to-Moderate Covid-19

A.B. Cavalcanti, F.G. Zampieri, R.G. Rosa, L.C.P. Azevedo, V.C. Veiga, A. Avezum, L.P. Damiani, A. Marcadenti, L. Kawano-Dourado, T. Lisboa, D.L.M. Junqueira, P.G.M. de Barros e Silva, L. Tramujas, E.O. Abreu-Silva, L.N. Laranjeira, A.T. Soares, L.S. Echenique, A.J. Pereira, F.G.R. Freitas, O.C.E. Gebara, V.C.S. Dantas, R.H.M. Furtado, E.P. Milan, N.A. Golin, F.F. Cardoso, I.S. Maia, C.R. Hoffmann Filho, A.P.M. Kormann, R.B. Amazonas, M.F. Bocchi de Oliveira, A. Serpa-Neto, M. Falavigna, R.D. Lopes, F.R. Machado, and O. Berwanger, for the Coalition Covid-19 Brazil I Investigators*

July 23, 2020
Randomized
Open label
Max 4L O_2



Antiviral Therapy

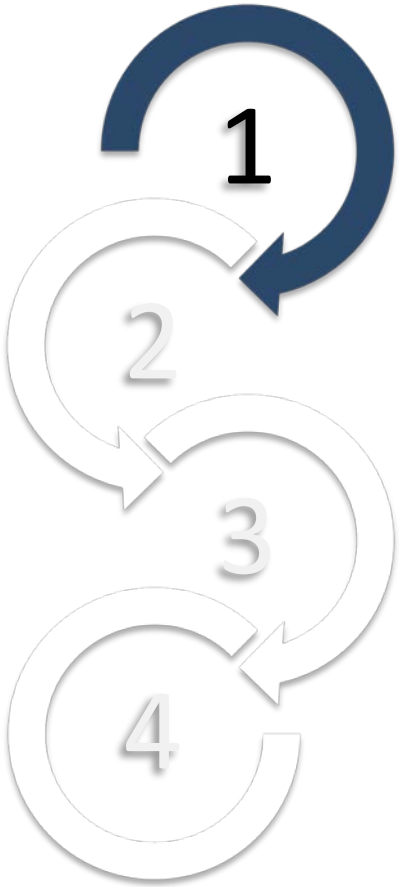
Chloroquine and Hydroxychloroquine

CONCLUSIONS AND RELEVANCE In this cohort study, patients who received hydroxychloroquine for the treatment of pneumonia associated with COVID-19 were at high risk of QTc prolongation, and concurrent treatment with azithromycin was associated with greater changes in QTc. Clinicians should carefully weigh risks and benefits if considering hydroxychloroquine and azithromycin, with close monitoring of QTc and concomitant medication usage.

for Coronavirus Disease 2019 (COVID-19)

Nicholas J. Mercuro, PharmD, BCIDP; Christina F. Yen, MD; David J. Shim, MD, PhD; Timothy R. Maher, MD; Christopher M. McCoy, PharmD, BCPS(AQ-ID), BCIDP; Peter J. Zimetbaum, MD; Howard S. Gold, MD

May 1, 2020
Observational
Boston

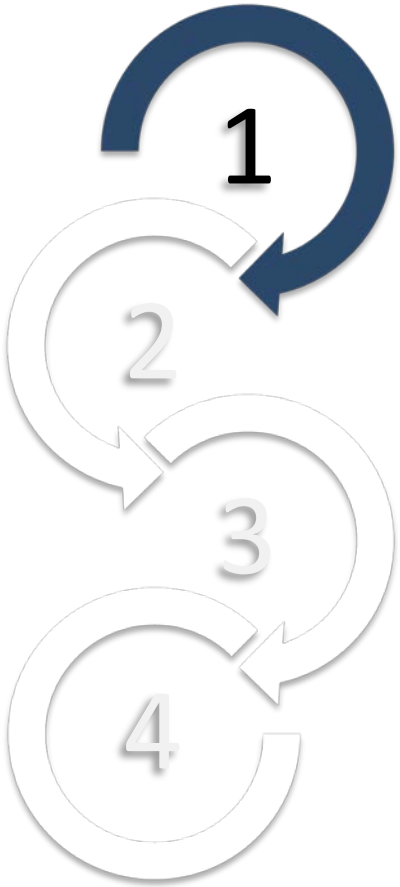


Antiviral Therapy

Lopinavir/Ritonavir

- Antiretroviral combination used in HIV
- Previously shown to have *in vitro* activity against SARS-CoV (2003)

Critically Ill COVID-19 Patients *Hospitalized, ICU-based* Patients requiring mechanical ventilation	**Lopinavir/ritonavir** is **not** recommended outside of approved clinical trials
Severely Ill COVID-19 Patients *Hospitalized, ward-based, long-term care* Patients requiring supplemental oxygen therapy	**Lopinavir/ritonavir** is **not** recommended outside of approved clinical trials
Mildly Ill COVID-19 Patients *Ambulatory, outpatient, long-term care* Patients who do not require oxygen	**Lopinavir/ritonavir** is **not** recommended outside of approved clinical trials



Antiviral Therapy

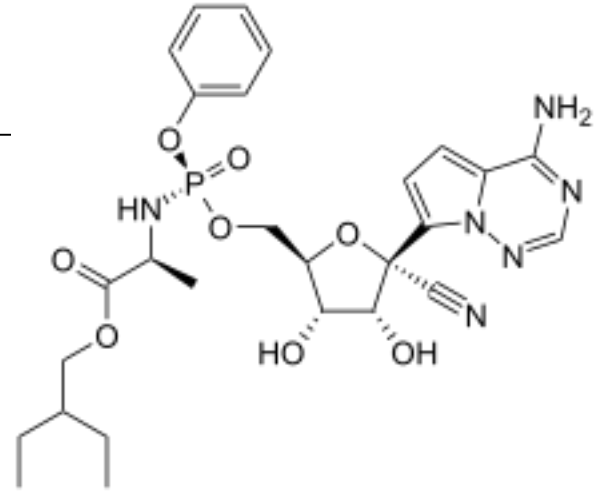
Lopinavir/Ritonavir

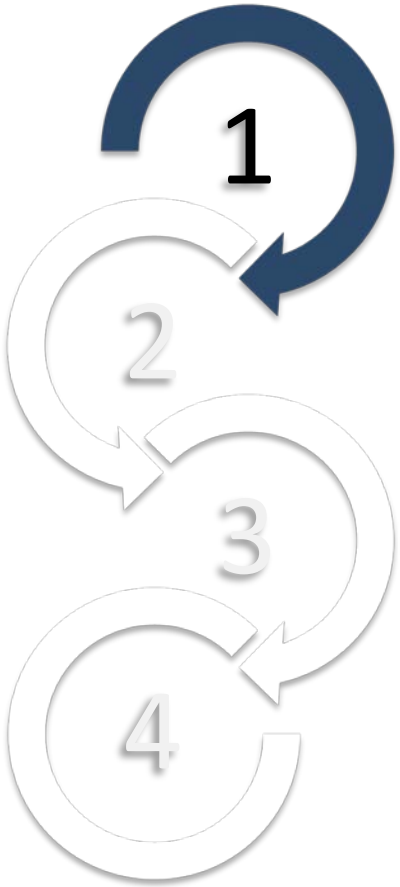
CONCLUSIONS

In hospitalized adult patients with severe Covid-19, no benefit was observed with lopinavir–ritonavir treatment beyond standard care. Future trials in patients with severe illness may help to confirm or exclude the possibility of a treatment benefit. (Funded by Major Projects of National Science and Technology on New Drug Creation and Development and others; Chinese Clinical Trial Register number, ChiCTR2000029308.)

B. Cao, Y. Wang, D. Wen, W. Liu, Jingli Wang, G. Fan, L. Ruan, B. Song, Y. Cai, M. Wei, X. Li, J. Xia, N. Chen, J. Xiang, T. Yu, T. Bai, X. Xie, L. Zhang, C. Li, Y. Yuan, H. Chen, Huadong Li, H. Huang, S. Tu, F. Gong, Y. Liu, Y. Wei, C. Dong, F. Zhou, X. Gu, J. Xu, Z. Liu, Y. Zhang, Hui Li, L. Shang, K. Wang, K. Li, X. Zhou, X. Dong, Z. Qu, S. Lu, X. Hu, S. Ruan, S. Luo, J. Wu, L. Peng, F. Cheng, L. Pan, J. Zou, C. Jia, Juan Wang, X. Liu, S. Wang, X. Wu, Q. Ge, J. He, H. Zhan, F. Qiu, L. Guo, C. Huang, T. Jaki, F.G. Hayden, P.W. Horby, D. Zhang, and C. Wang

March 18, 2020
Randomized
China



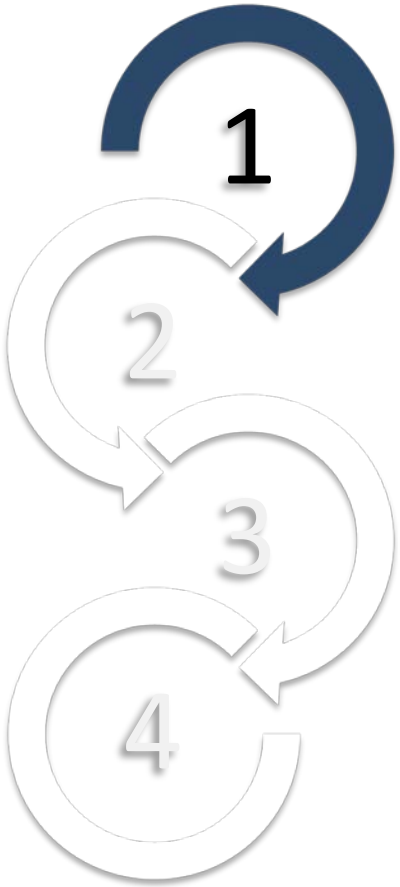


Antiviral Therapy

Remdesivir (AKA Tamiflu 2020)

Remdesivir* has received conditional approval by Health Canada for the treatment of COVID-19. Remdesivir shortened time to clinical recovery but failed to show any survival benefit in the ACTT-1 trial. In British Columbia availability of remdesivir remains limited to clinical trails at this time.

Conditional approval by Health Canada (July 23)



Antiviral Therapy

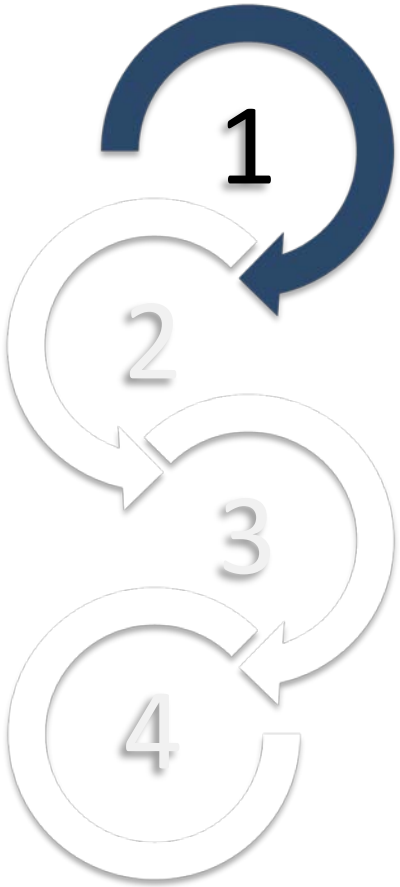
Remdesivir (AKA Tamiflu 2020)

CONCLUSIONS

Remdesivir was superior to placebo in shortening the time to recovery in adults hospitalized with Covid-19 and evidence of lower respiratory tract infection. (Funded by the National Institute of Allergy and Infectious Diseases and others; ACCT-1 ClinicalTrials.gov number, NCT04280705.)

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

May 22, 2020
ACTT-1 study
DBRCT
NIAID-sponsored



Antiviral Therapy

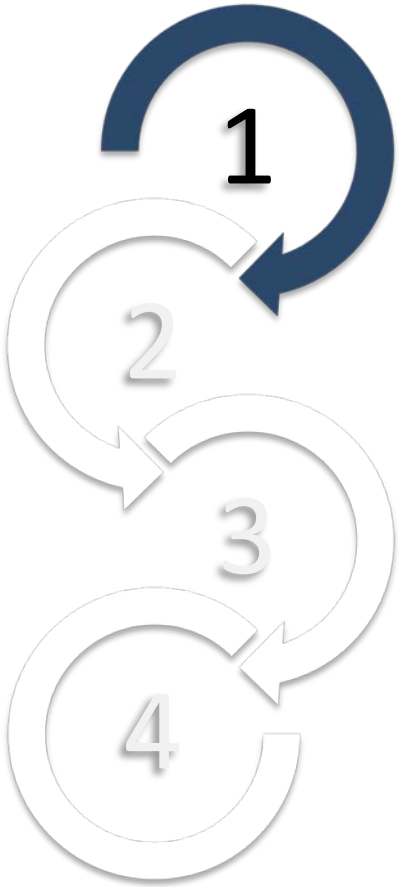
Remdesivir (NIAID Study)

- Randomized, double-blinded, placebo-controlled
- Multiple centres/countries
- COVID-19 positive requiring oxygen (NP to ECMO)
- Primary outcome = recovery (discharge)
- Median time to recovery shorter (11 vs. 15d)
- More benefit in those not yet critically ill

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*



Antiviral Therapy

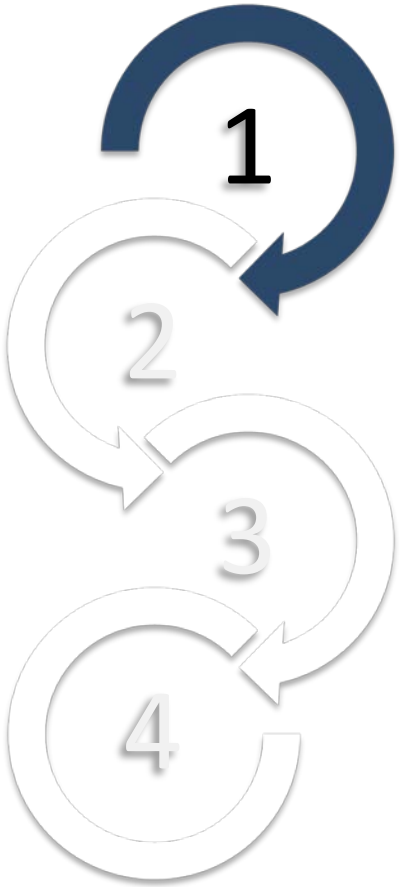
Remdesivir (Goldman et al.,)

CONCLUSIONS

In patients with severe Covid-19 not requiring mechanical ventilation, our trial did not show a significant difference between a 5-day course and a 10-day course of remdesivir. With no placebo control, however, the magnitude of benefit cannot be determined. (Funded by Gilead Sciences; GS-US-540-5773 ClinicalTrials.gov number, NCT04292899.)

Jason D. Goldman, M.D., M.P.H., David C.B. Lye, M.B., B.S., David S. Hui, M.D., Kristen M. Marks, M.D., Raffaele Bruno, M.D., Rocio Montejano, M.D., Christoph D. Spinner, M.D., Massimo Galli, M.D., Mi-Young Ahn, M.D., Ronald G. Nahass, M.D., Yao-Shen Chen, M.D., Devi SenGupta, M.D., Robert H. Hyland, D.Phil., Anu O. Osinusi, M.D., Huyen Cao, M.D., Christiana Blair, M.S., Xuelian Wei, Ph.D., Anuj Gaggar, M.D., Ph.D., Diana M. Brainard, M.D., William J. Towner, M.D., Jose Muñoz, M.D., Kathleen M. Mullane, D.O., Pharm.D., Francisco M. Marty, M.D., Karen T. Tashima, M.D., George Diaz, M.D., and Aruna Subramanian, M.D., for the GS-US-540-5773 Investigators*

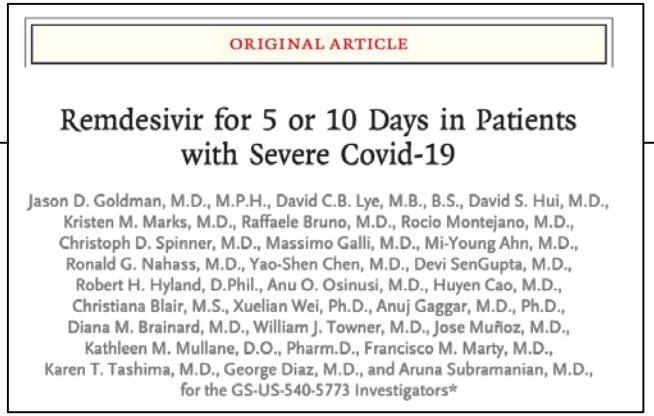
May 27, 2020
Open-label
No placebo
Gilead-sponsored



Antiviral Therapy

Remdesivir (Goldman et al.,)

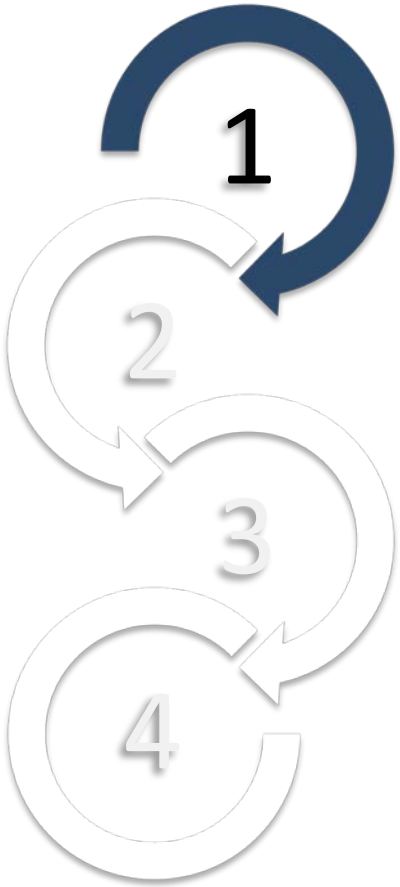
- Randomized, open label study
- Severely ill patients (MV, ECMO) excluded
- No difference in 5 vs. 10d course
  (may guide future clinical treatment course)
- Mortality lower in 5 vs. 10d course (NSS)
  Patients allocated to 10d were sicker at baseline



ORIGINAL ARTICLE

Remdesivir for 5 or 10 Days in Patients with Severe Covid-19

Jason D. Goldman, M.D., M.P.H., David C.B. Lye, M.B., B.S., David S. Hui, M.D., Kristen M. Marks, M.D., Raffaele Bruno, M.D., Rocio Montejano, M.D., Christoph D. Spinner, M.D., Massimo Galli, M.D., Mi-Young Ahn, M.D., Ronald G. Nahass, M.D., Yao-Shen Chen, M.D., Devi SenGupta, M.D., Robert H. Hyland, D.Phil., Anu O. Osinusi, M.D., Huyen Cao, M.D., Christiana Blair, M.S., Xuelian Wei, Ph.D., Anuj Gaggar, M.D., Ph.D., Diana M. Brainard, M.D., William J. Towner, M.D., Jose Muñoz, M.D., Kathleen M. Mullane, D.O., Pharm.D., Francisco M. Marty, M.D., Karen T. Tashima, M.D., George Diaz, M.D., and Aruna Subramanian, M.D., for the GS-US-540-5773 Investigators*



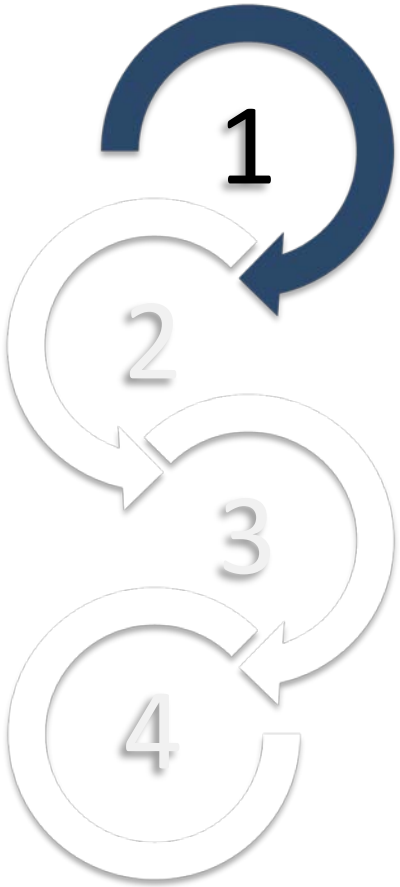
Antiviral Therapy

Remdesivir (Spinner et al.,)

CONCLUSIONS AND RELEVANCE Among patients with moderate COVID-19, those randomized to a 10-day course of remdesivir did not have a statistically significant difference in clinical status compared with standard care at 11 days after initiation of treatment. Patients randomized to a 5-day course of remdesivir had a statistically significant difference in clinical status compared with standard care, but the difference was of uncertain clinical importance.

Louis Yi Ann Chai, MD; Meta Roestenberg, MD; Owen Tak Yin Tsang, MD; Enos Bernasconi, MD; Paul Le Turnier, MD; Shan-Chwen Chang, MD; Devi SenGupta, MD; Robert H. Hyland, DPhil; Anu O. Osinusi, MD; Huyen Cao, MD; Christiana Blair, MS; Hongyuan Wang, PhD; Anuj Gaggar, MD, PhD; Diana M. Brainard, MD; Mark J. McPhail, MD; Sanjay Bhagani, MD; Mi Young Ahn, MD; Arun J. Sanyal, MD; Gregory Huhn, MD; Francisco M. Marty, MD; for the GS-US-540-5774 Investigators

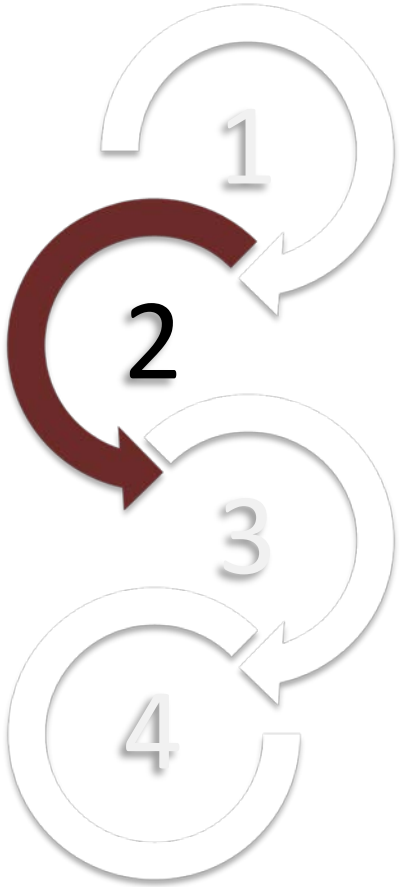
August 21, 2020
Open-label
No placebo
Gilead-sponsored



Antiviral Therapy

Remdesivir: Issues

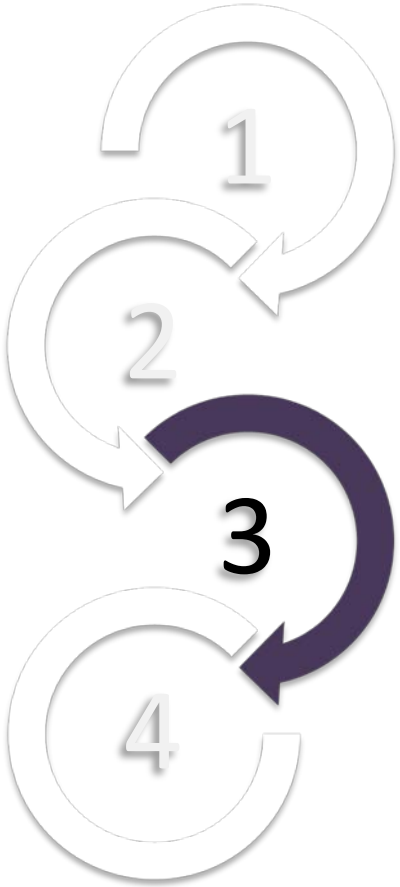
- Allocation (only 78 vials in BC)
- Which patients benefit?
  - Unknown who will do better (or worse)
- Cost: $3000/5 day course (vs. fewer days in hospital)
- Reserve for Clinical Trials (CATCO) only (next week)
- Which hospitals get it?
- Transfers/patient demands etc…



Antibacterial therapy

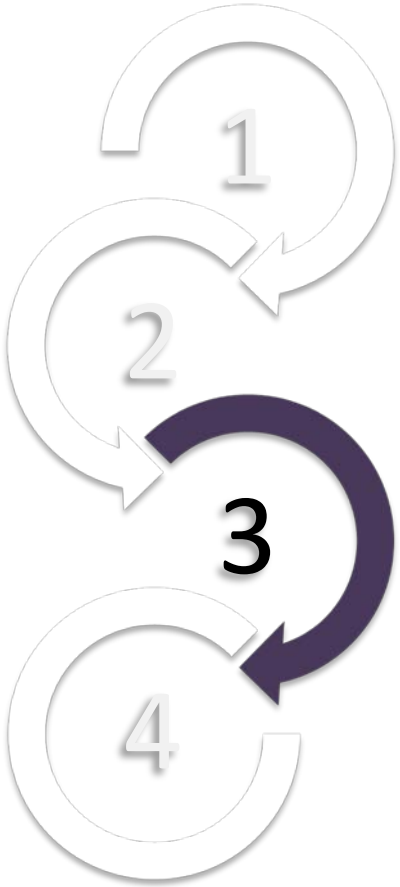
- Empiric antibiotics depending on disease severity

Critically Ill COVID-19 Patients *Hospitalized, ICU-based* Patients requiring mechanical ventilation	**Severely Ill COVID-19 Patients** *Hospitalized, ward-based, long-term care* Patients requiring supplemental oxygen therapy	**Mildly Ill COVID-19 Patients** *Ambulatory, outpatient, long-term care* Patients who do not require oxygen
Ceftriaxone 1-2 g IV q24h x 5 days is recommended if there is concern for bacterial co-infection (alternative moxifloxacin 400 mg IV q24h x 5 days) **Azithromycin 500 mg IV q24h x 3 days** is recommended if atypical bacterial infection is suspected	Antibacterial therapy is **not** routinely recommended outside of approved clinical trials unless other indications justify its use	Antibacterial therapy is **not** routinely recommended outside of approved clinical trials unless other indications justify its use



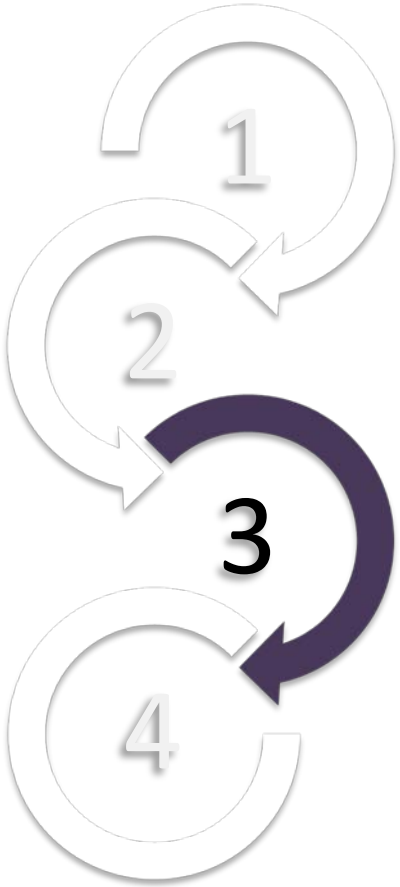
Immunomodulatory therapy

- Corticosteroids
  - Dexamethasone
  - Hydrocortisone
- Biologic agents
  - Tocilizumab
  - Sarilumab



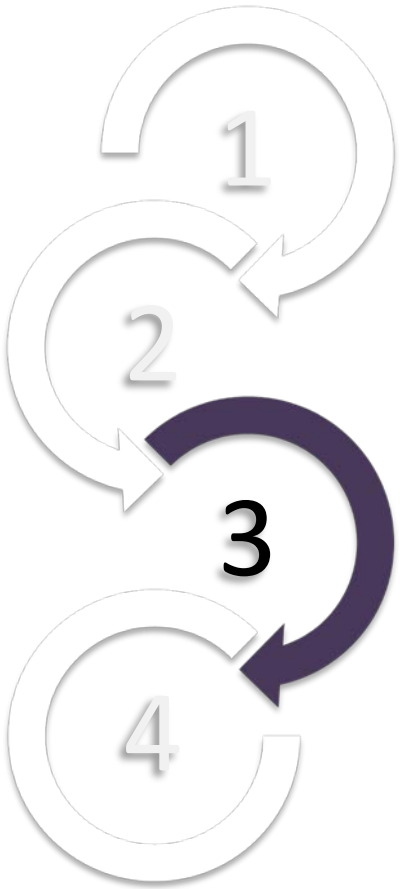
The saga of steroids in the ICU

- Decades of research in using steroids:
  - Pneumonia
  - Septic shock
  - ARDS
- Inconclusive data due to study limitations
- Recent data suggest benefit in septic shock (APROCCHSS and ADRENAL)
- DEXA-ARDS (2019): Improved mortality in patients with moderate to severe ARDS



The saga of steroids in the ICU

- Previous studies of other viral pneumonias (SARS/MERS) suggested poor viral clearance
- Associated with increased mortality in influenza related pneumonia



Steroids and COVID-19

Mixed guidance regarding steroids

January 2020 — **March 2020**

RECOVERY
Randomised Evaluation of COVID-19 Therapy

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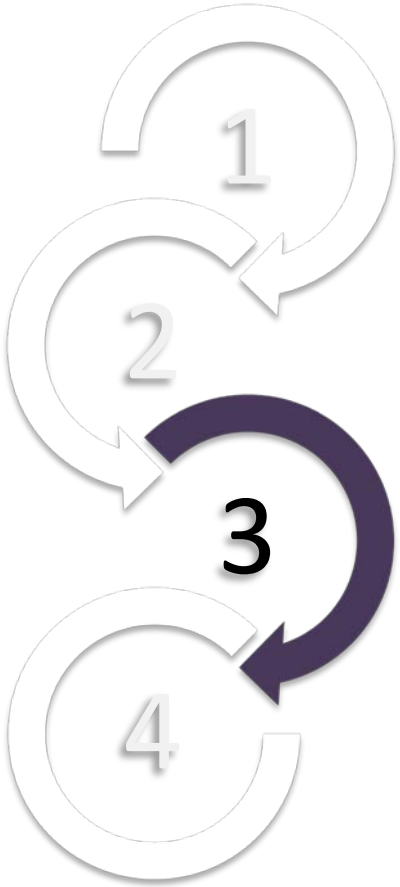
News / Low-cost dexamethasone reduces death by up to one third in hospitalised patients with severe respiratory complications of COVID-19

Low-cost dexamethasone reduces death by up to one third in hospitalised patients with severe respiratory complications of COVID-19

16 June 2020

Statement from the Chief Investigators of the Randomised Evaluation of COVid-19 thERapY (RECOVERY) Trial on dexamethasone, 16 June 2020

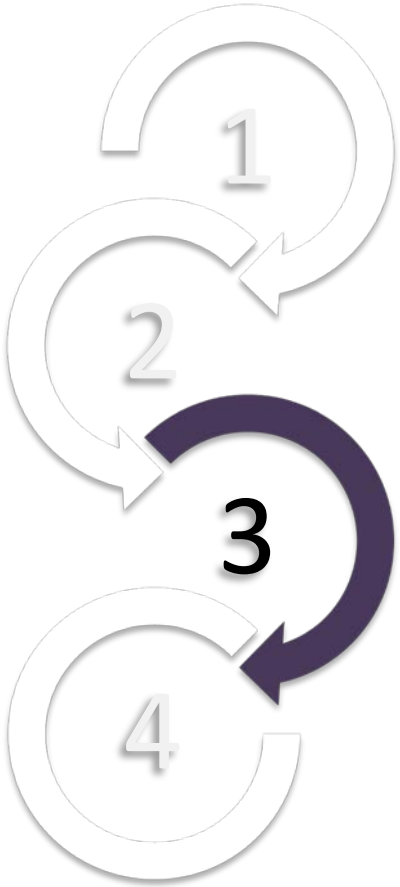
June 2020



Steroids and COVID-19

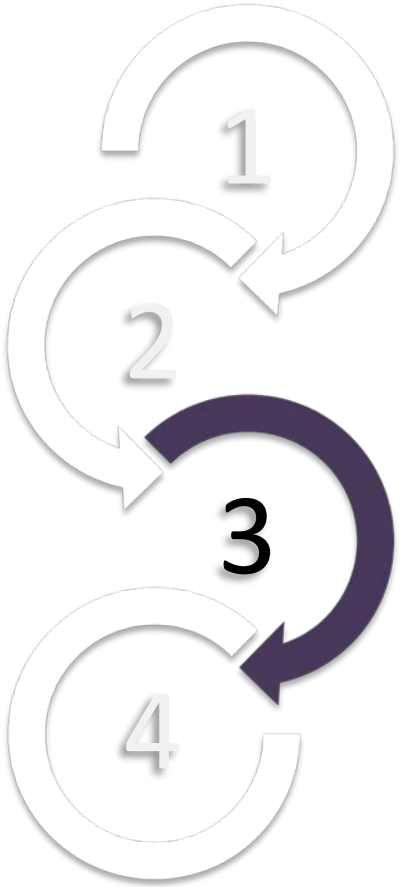
June 16, 2020
RECOVERY trial
press release
Change of clinical
practice

June 2020 **September 2020**



Corticosteroids for COVID-19

Critically Ill COVID-19 Patients *Hospitalized, ICU-based* Patients requiring mechanical ventilation	**Severely Ill COVID-19 Patients** *Hospitalized, ward-based, long-term care* Patients requiring supplemental oxygen therapy	**Mildly Ill COVID-19 Patients** *Ambulatory, outpatient, long-term care* Patients who do not require oxygen
Dexamethasone 6 mg IV/PO q24h for up to 10 days is **strongly recommended** (RECOVERY trial), unless higher doses are indicated**. If Dexamethasone is not available, methylprednisolone 30 mg IV q24h is the preferred alternative.	**Dexamethasone 6 mg IV/PO q24h for up to 10 days** is **recommended** (RECOVERY trial), unless higher doses are indicated**. If Dexamethasone is not available, methylprednisolone 30 mg IV q24h or prednisone 40 mg PO q24h are the preferred alternatives. If dexamethasone supplies are limited, they should be reserved for critically ill patients.	**Corticosteroids** are **not** recommended outside of approved clinical trials unless otherwise indicated**



Corticosteroids for COVID-19

Dexamethasone: RECOVERY

ORIGINAL ARTICLE

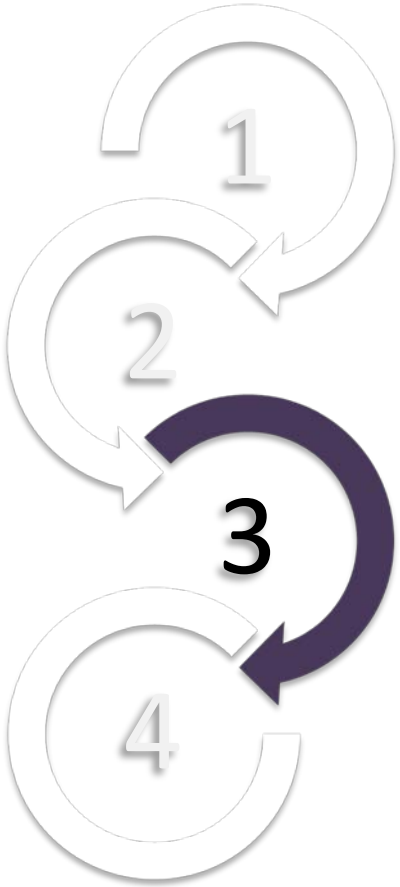
Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

The RECOVERY Collaborative Group*

ORIGINAL ARTICLE

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

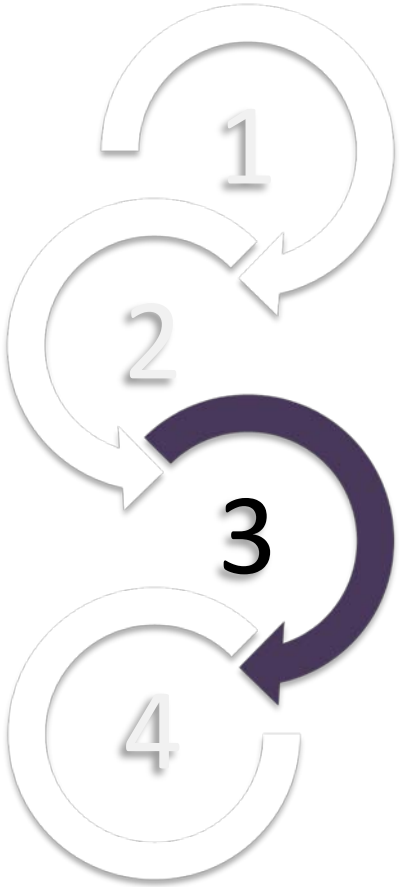
The RECOVERY Collaborative Group*



Corticosteroids for COVID-19

Dexamethasone: RECOVERY

- Largest trial to date to show improved survival for *any* intervention in COVID-19
- High quality study and considered indisputable
- All other steroid trials were subsequently halted
- Mortality results:
  - Mechanical ventilation: 29.3% vs. 41.4%
  - Oxygen alone: 23.3 vs. 26.2%
  - No oxygen: 17.8% vs. 14% (NS)



Corticosteroids for COVID-19

Dexamethasone: CoDEX (Brazil)

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients With Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19
The CoDEX Randomized Clinical Trial

Bruno M. Tomazini, MD; Israel S. Maia, MD, MSc; Alexandre B. Cavalcanti, MD, PhD; Otavio Berwanger, MD, PhD; Regis G. Rosa, MD, PhD; Viviane C. Veiga, MD, PhD; Alvaro Avezum, MD, PhD; Renato D. Lopes, MD, PhD; Flavia R. Bueno, MSc; Maria Vitoria A. O. Silva; Franca P. Baldassare; Eduardo L. V. Costa, MD, PhD; Ricardo A. B. Moura, MD; Michele O. Honorato, MD; Andre N. Costa, MD, PhD; Lucas P. Damiani, MSc; Thiago Lisboa, MD, PhD; Letícia Kawano-Dourado, MD, PhD; Fernando G. Zampieri, MD, PhD; Guilherme B. Olivato, MD; Cassia Righy, MD, PhD; Cristina P. Amendola, MD; Roberta M. L. Roepke, MD; Daniela H. M. Freitas, MD; Daniel N. Forte, MD, PhD; Flávio G. R. Freitas, MD, PhD; Caio C. F. Fernandes, MD; Livia M. G. Melro, MD; Gedealvares F. S. Junior, MD; Douglas Costa Morais; Stevin Zung, MD, PhD; Flávia R. Machado, MD, PhD; Luciano C. P. Azevedo, MD, PhD; for the COALITION COVID-19 Brazil III Investigators

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

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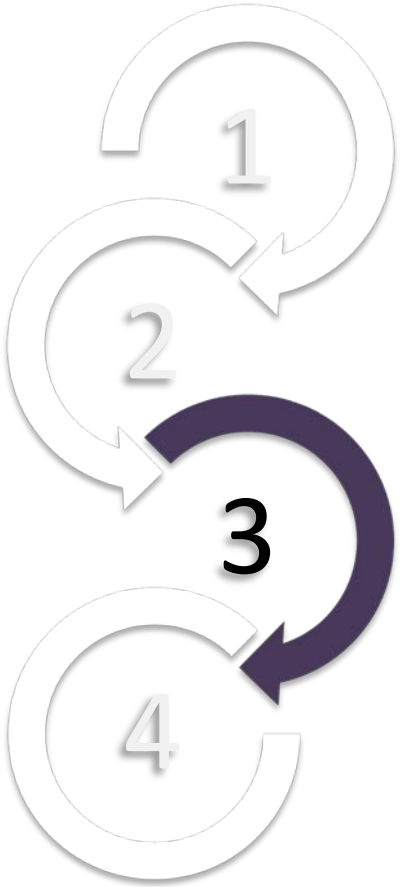
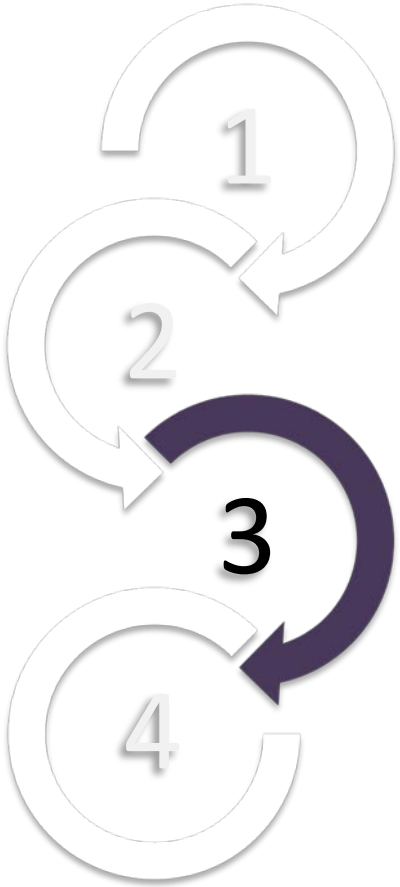


Corticosteroids for COVID-19

Dexamethasone: CoDEX (Brazil)

- High dose Dexamethasone
  - 20 mg x 5d; 10 mg x 5 days
- No mortality difference
- Ventilator free days
  - 6.6d dexamethasone vs. 4.0d standard care



Corticosteroids for COVID-19

Hydrocortisone: REMAP-CAP

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Hydrocortisone on Mortality and Organ Support in Patients With Severe COVID-19

The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial

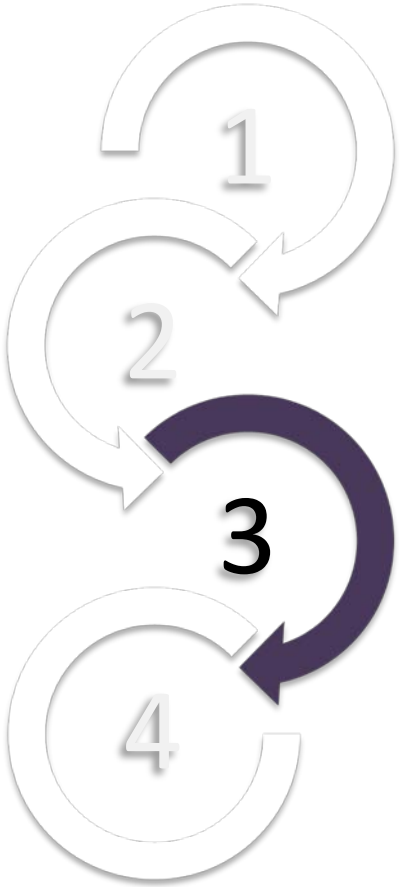
The Writing Committee for the REMAP-CAP Investigators

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Hydrocortisone on Mortality and Organ Support in Patients With Severe COVID-19

The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial

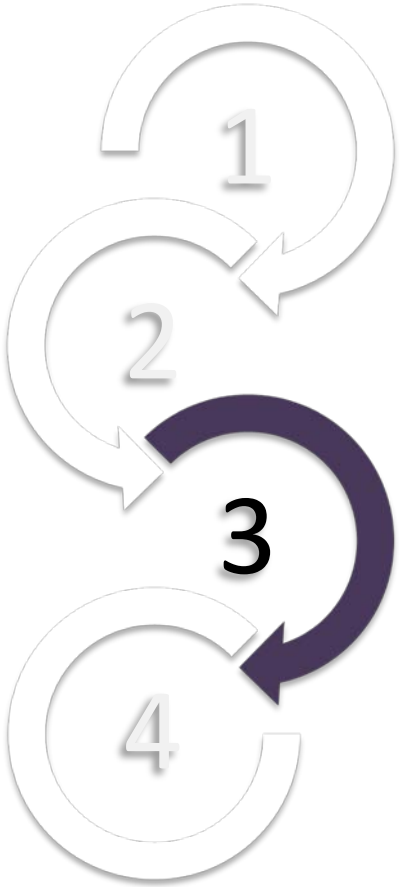
The Writing Committee for the REMAP-CAP Investigators



Corticosteroids for COVID-19

Hydrocortisone: REMAP-CAP

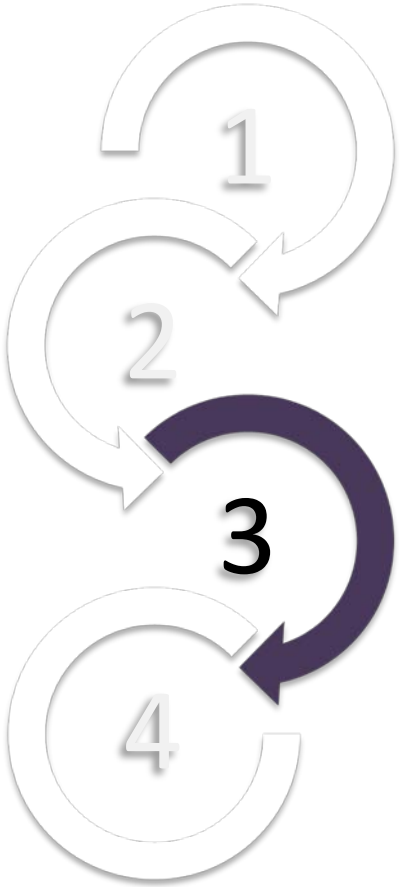
- Fixed dose (50 mg or 100 mg IV q6h) vs. shock-dependent (50 mg IV q6h) with shock vs. none
- Primary outcome: organ support-free days
- Results
  - 93% vs. 80% probability of superiority with regards to improvement in primary outcome



Corticosteroids for COVID-19

Summary

- Solid evidence for both dexamethasone and hydrocortisone for COVID-19 patients requiring oxygen
- CTC Recommendations will be updated to include hydrocortisone

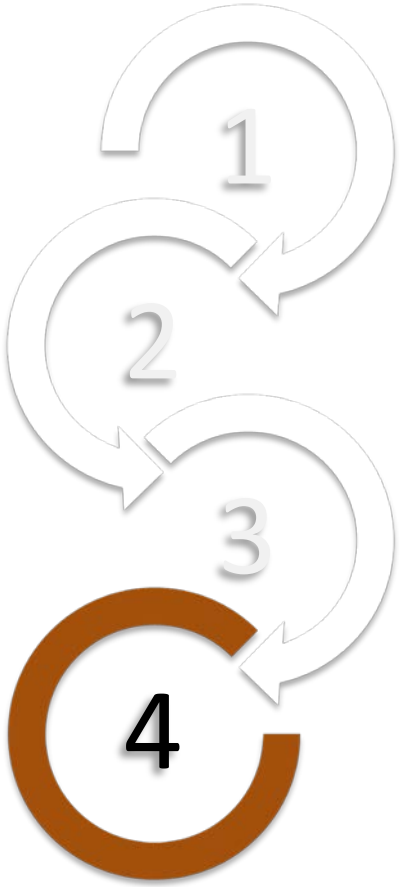


Biologics/IL-6 inhibitors

- "Indicated" in cases of COVID-related Cytokine Storm
- Controversial
- Currently NOT recommended outside of clinical trials
- If being considered, expert consultation recommended

Critically Ill COVID-19 Patients
Hospitalized, ICU-based
Patients requiring mechanical ventilation

Tocilizumab or **sarilumab** is **not** recommended outside of approved clinical trials; where clinical trials are not available, expert consultation is recommended (Infectious Diseases, Hematology, Rheumatology)



Other therapies

- DVT Prophylaxis
- NSAIDS
- ACE-I/ARBs

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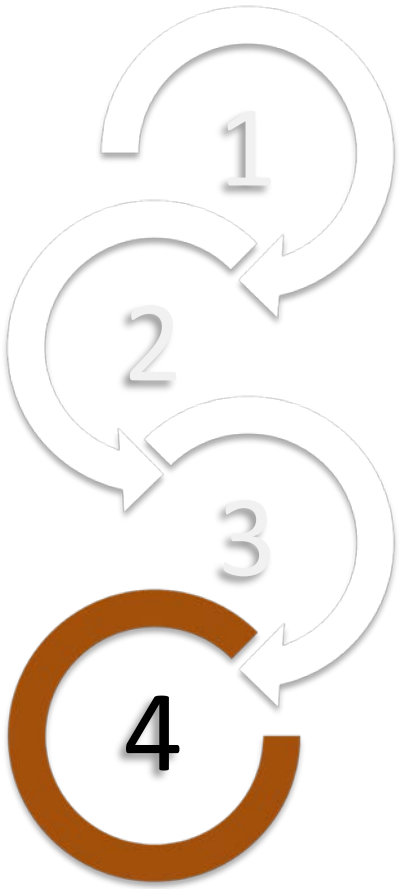
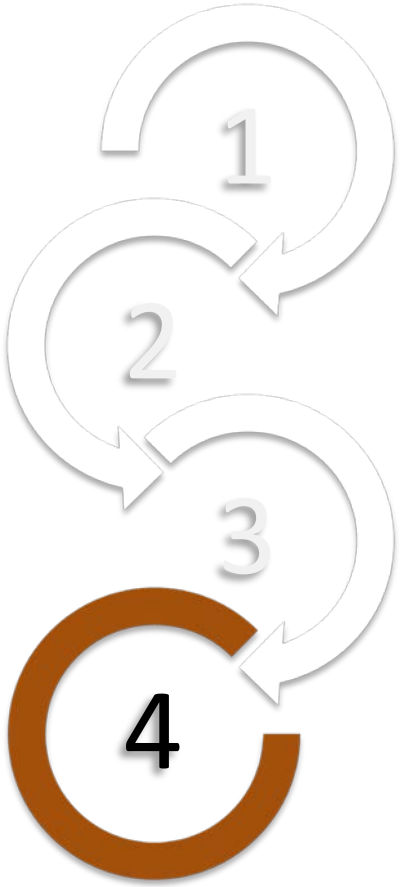


Other therapies

DVT Prophylaxis

- Controversial
- Living SBAR document available on Island Health intranet

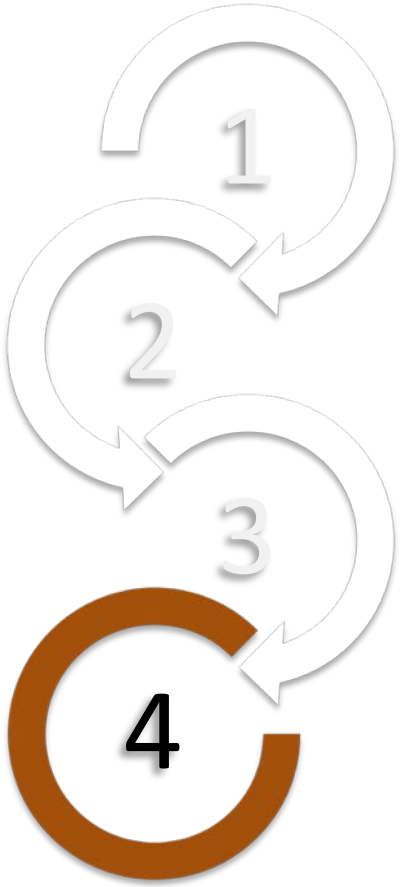
Critically Ill COVID-19 Patients *Hospitalized, ICU-based* Patients requiring mechanical ventilation	**Severely Ill COVID-19 Patients** *Hospitalized, ward-based, long-term care* Patients requiring supplemental oxygen therapy
Enoxaparin 30 mg SC q12h is **suggested** for VTE prophylaxis	**Enoxaparin 30 mg SC q12h** is **suggested** for VTE prophylaxis



Other therapies

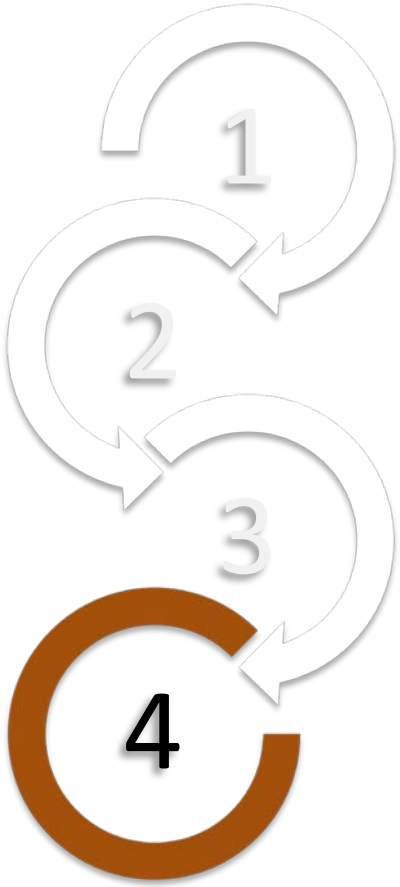
DVT Prophylaxis

- Severe COVID-19 infection is likely a hypercoagulable state
- Increased risk of DVT/PE
- Studies of alternate DVT prophylaxis dosing or empiric therapeutic anticoagulation are in progress.



Other therapies

	Dose based on estimated glomerular filtration rate (eGFR)		
Weight (kg)	eGFR greater than or equal to 30mL/min	eGFR 20 to 29mL/min	eGFR less than 20mL/min
40-100	Enoxaparin 30mg SUBCUT q12h	Enoxaparin 40 mg SUBCUT q24h	Heparin 5000 units SUBCUT q8h OR Consider clinical pharmacy consult for consideration of non-formulary Tinzaparin
Greater than 100	Enoxaparin 40mg SUBCUT q12h	Enoxaparin 60 mg SUBCUT q24h	Heparin 7500 units SUBCUT q8h OR Consider clinical pharmacy consult for consideration of non-formulary Tinzaparin

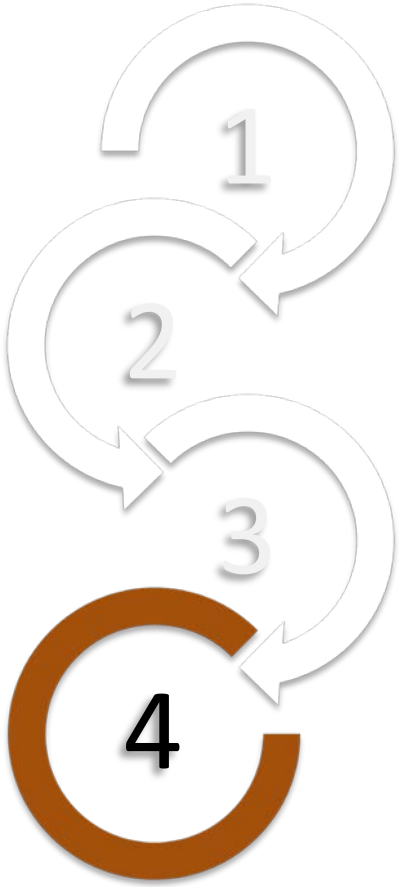


Other therapies

NSAIDS and ACE-I/ARB

ACE inhibitors and **ARBs** should not be discontinued solely on the basis of COVID-19

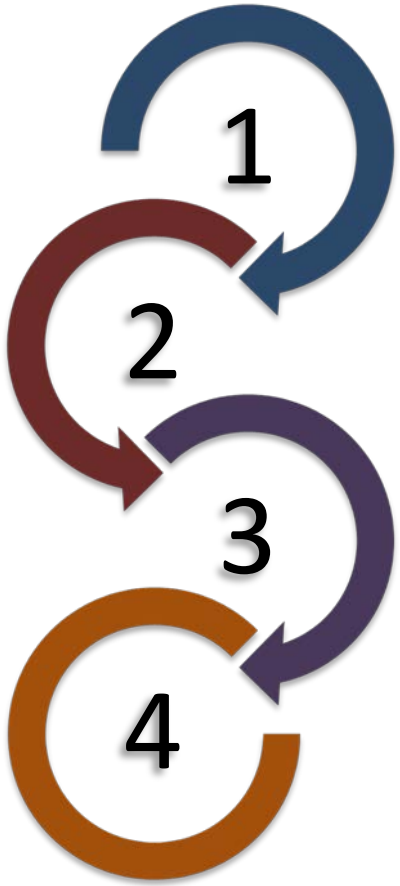
NSAIDs should not be discontinued solely on the basis of COVID-19



Other therapies

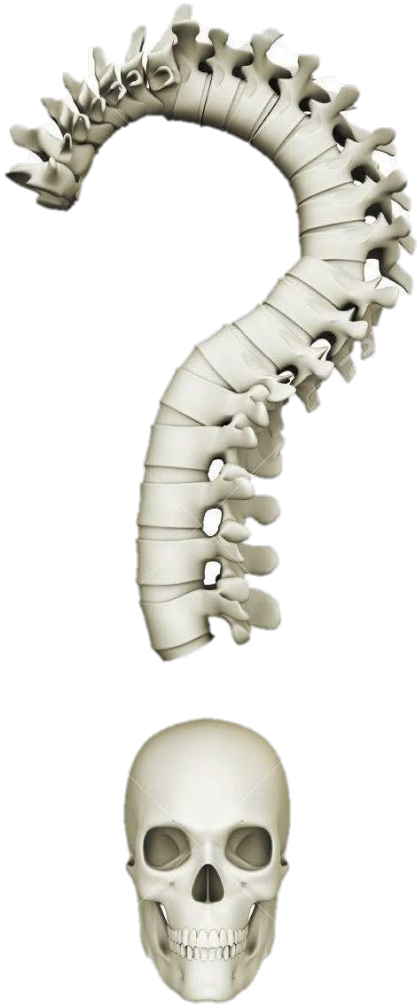
Other other therapies

- Colchicine
- Zinc
- Vitamin D
- Oleander
- Bleach
- Unicorn tears



Therapeutic Recommendations

- Antiviral therapy
- Antibacterial therapy
- Immunomodulatory therapy
- Other therapies



Questions:
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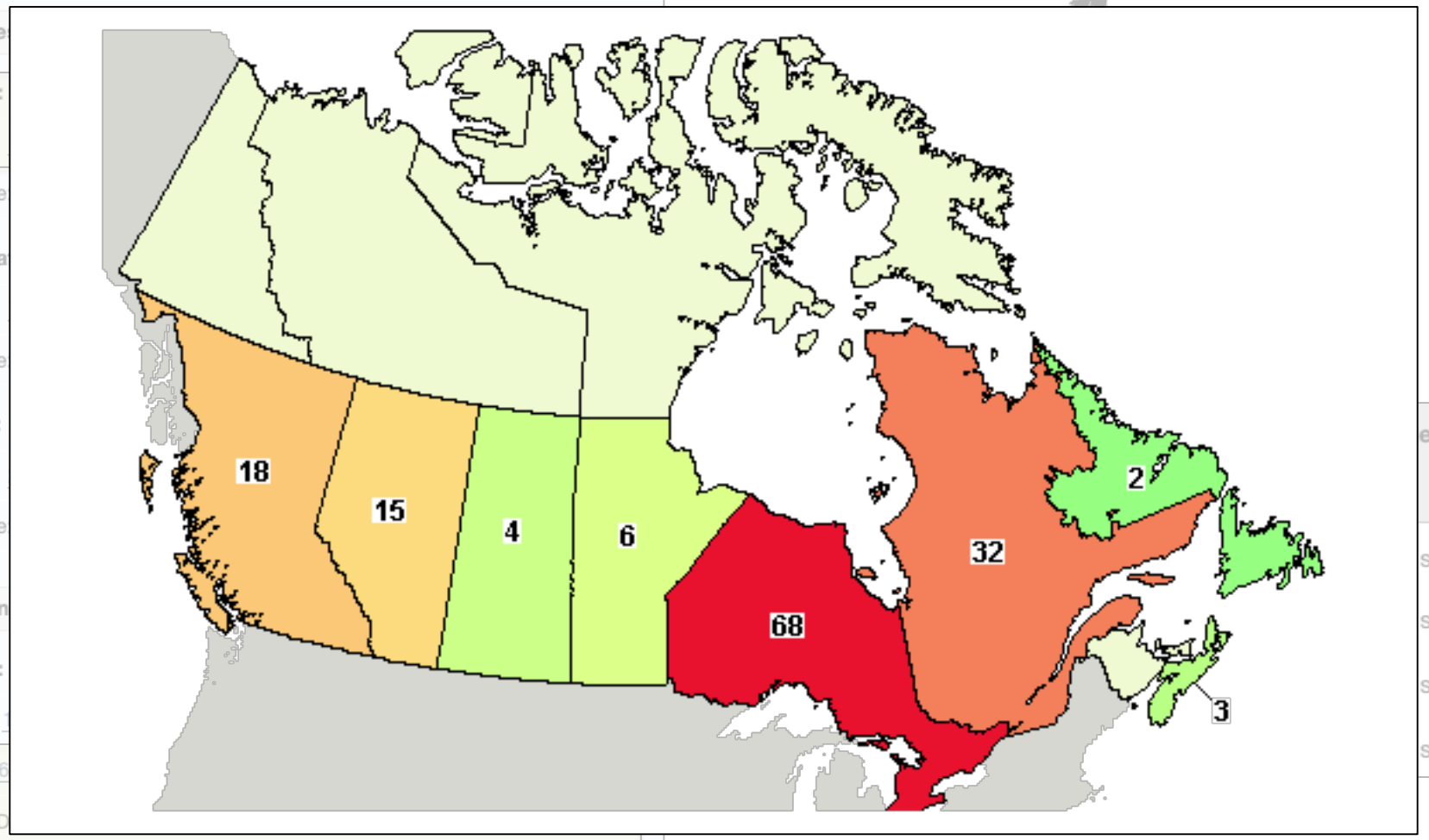
NIH U.S. National Library of Medicine

ClinicalTrials.gov

Clinical Trials



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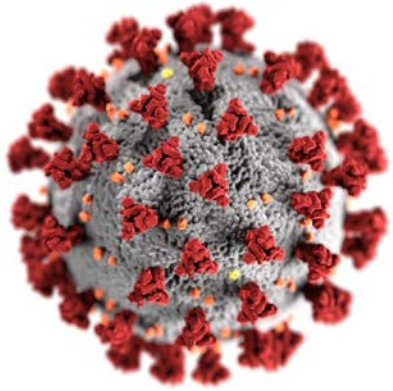
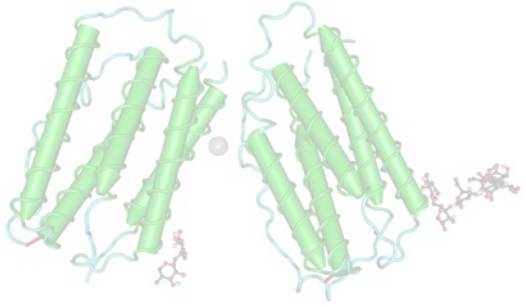
Clinical Trials



CATCO



ATTACC

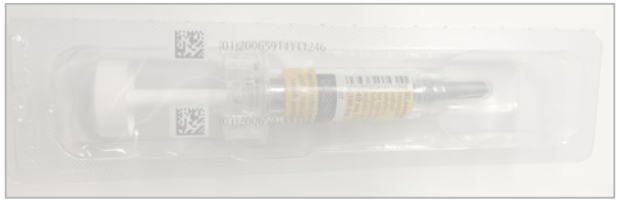
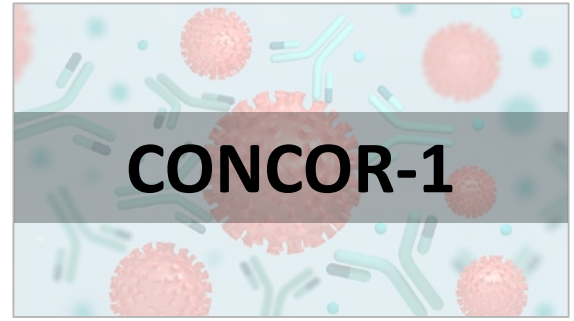
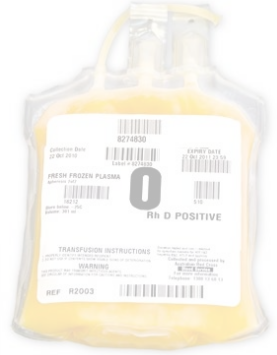
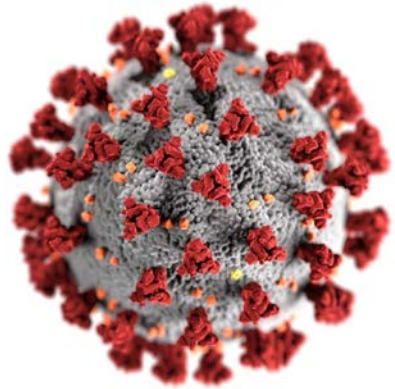


Photo credit: Dr. Anna Maruyama



CONCOR-1





Commonalities

- Confirmed SARS-CoV-2 via PCR
- Randomized, open-label studies
- Hospitalized
- Co-enrollment permitted (with other ICU trials too)
- Optimized supportive care
  - Supplementary oxygen
  - Dexamethasone 6 mg IV daily (for patients on O_2)
  - Routine ward vs. ICU care (ARDS management)

CATCO

CAnadian Treatments for COVID-19

- Run in conjunction with the global WHO SOLIDARITY trial
- Adaptive, open-label, controlled trial
- Hospitalized patients with COVID-19
- Randomized to one of the following groups:
  1. Remdesivir 200 mg IV Day 1, 100 mg IV daily x 9 days
  2. Interferon-beta-1a 44 mcg SC on days 1, 3, 6
  3. Optimized supportive care only

CATCO: Rationale

Remdesivir

- Broad-spectrum nucleotide prodrug that inhibits RNA-dependent RNA polymerase
- Thought to slow down viral replication

CATCO

Inclusion criteria

- Adults ≥ 18 years of age
- Laboratory confirmed SARS-CoV-2 infection
- Hospitalized

Exclusion criteria

- Will be transferred to non study site
- Moribund state

CATCO: Outcomes

Primary

- All cause mortality

Exploratory

- Viral clearance

Secondary

- Clinical severity
  - Ordinal scales: Time to improvement
  - Oxygenation: Oxygen free days, new oxygen use
  - Mechanical ventilation: Ventilator free days, new MW
- Duration of hospitalization
- Safety

CATCO: Outcomes

Primary

- All cause mortality

Secondary

- Clinical sev
  - Ordinal s
  - Oxygenat
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  - Mechani
    days, nev
- Duration of
- Safety

Patient State	Descriptor	Score
Uninfected	Uninfected; no viral RNA detected	0
Ambulatory	Asymptomatic; viral RNA detected	1
	Symptomatic; Independent	2
	Symptomatic; Assistance needed	3
Hospitalized: Mild disease	Hospitalized; no oxygen therapy	4
	Hospitalized; oxygen by mask or nasal prongs	5
Hospitalized: Severe disease	Hospitalized; Oxygen by NIV or High flow	6
	Intubation & Mechanical ventilation, pO_2/FIO_2 ≥150 or SpO_2/FIO_2≥200	7
	Mechanical ventilation pO_2/FIO_2<150 (SpO_2/FIO_2 <200) **or** vasopressors	8
	Mechanical ventilation pO_2/FIO_2<150 **and** vasopressors, dialysis, or ECMO	9
Death	Dead	10

Ordinal Scale for evaluating clinical status

CATCO

Status

- Ready to enroll
- Remdesivir on site (2 patients)
- Interferon not ready

ATTACC

Anththrombotic Therapy To Ameliorate Complications of COVID-19

- Prospective, open-label, randomized, adaptive clinical trial
- Establish whether therapeutic anticoagulation improves outcomes in patient with COVID-19

ATTACC: Rationale

COVID & Hypercoaguability

- COVID-19 is associated with a hypercoagulable state
- Many patients experience significant cardiac and pulmonary thrombotic complications
- Heparin induces a confirmational change in the SARS-CoV-2 receptor spike protein limiting invasion
- Heparin has anti-inflammatory effects
- D-dimer levels could potentially be used to risk stratify patients

ATTACC

Inclusion criteria

- Adults ≥ 18 years of age
- Laboratory confirmed SARS-CoV-2 requiring hospital admission
- Anticipated to be in hospital ≥ 72h
- Enrolled < 72h of hospital admission

ATTACC

Exclusion criteria

- Invasive mechanical ventilation
- Active bleeding
- Risk factors for bleeding
- Thrombocytopenia/DIC
- Hg < 80
- DAPT
- Independent indication for therapeutic anticoagulation
- Pregnancy

Risk factors for bleeding

- intracranial surgery or stroke within 3 months
- history of intracerebral AVM
- cerebral aneurysm or mass lesions of CNS
- intracranial malignancy
- history of intracranial bleeding
- history of bleeding diatheses
- GIB within previous 3 months
- thrombolysis within the previous 7 days
- presence of an epidural or spinal catheter
- recent major surgery <14 days
- uncontrolled hypertension
- physician-perceived contraindications

ATTACC: Study Protocol

Intervention

- Therapeutic-dose parenteral anticoagulation
  - Up until 14 days, or recovery (discharge or liberation from oxygen)
- Preference is for LMWH
  - Enoxaparin is the preferred LMWH (viral inhibitory properties)
- IV UFH can be used if LMWH contraindicated
- Control group to receive standard prophylactic dosing based on institutional practices

ATTACC: Outcomes

Primary

- Outcome at 30 days
  - No IMV
  - IMV
  - Death

Secondary

- Safety of therapeutic anticoagulation
  - Laboratory confirmed HIT
  - Major bleeding
- Efficacy of therapeutic anticoagulation
  - Mortality/Intubation/ICU-free days
  - NIV or HFNC
  - Symptomatic VTE at 30 and 90 days
  - MI at 30 and 90 days

ATTACC

Status

- Ready to go
- Eligible patients from ward, HAU, ICU

CONCOR-1

CONvalescent plasma for COVID-19 Respiratory Illness

- Randomized, open label trail using plasma from patients known to have recovered from COVID-19
- To establish whether COVID-19 Convalescent Plasma (CCP) can reduce poor outcomes from COVID-19

CONCOR-1: Rationale

Immunologic response to COVID-19

- Recovered patients have been shown to have high levels of neutralizing antibodies (compared to those that died)
- Insufficient viral clearance may lead to a hyperimmune response to virus (“cytokine storm”)
- Antibody response may determine outcome
- Passive immunization may facilitate viral neutralization and prevent a disproportional immune response

CONCOR-1

Inclusion criteria

- Adults ≥ 16 years of age
- Laboratory confirmed SARS-CoV-2 requiring hospital admission
- *Receiving supplemental oxygen*
- 500 mL of ABO compatible Convalescent Plasma is available

CONCOR-1

Exclusion criteria

- Onset of symptoms >12 days prior
- Intubated or to be intubated imminently
- Contraindication to plasma

CONCOR-1: Study Protocol

Intervention

- 2:1 randomization (CCP:standard care)
- Stratified by centre and age
- COVID-19 Convalescent plasma (CCP)
  - One unit of 500 mL (singe donor) or
  - Two units of 250 mL each (from one or two donors)
- Control patients to receive standard of care

CONCOR-1: Outcomes

Primary

- Intubation or death at Day 30

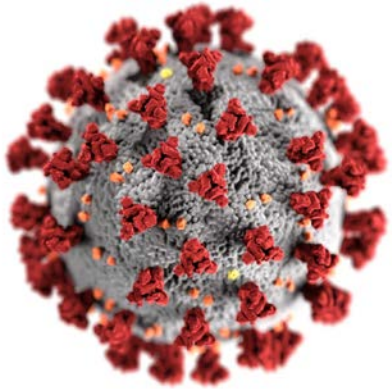
Secondary

- Intubation before Day 30
- Time to intubation
- Death at Day 30
- Length of ICU/hospital stay
- Need for ECMO
- Need for RRT
- Myocarditis
- Serious adverse events (SAE)

CONCOR-1

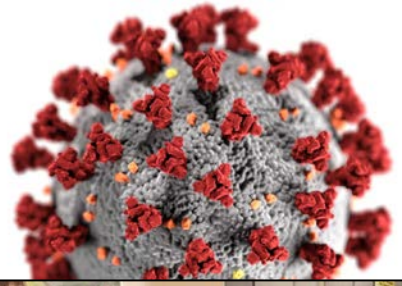
Status

- Ready to go, CCP on site
- Eligible patients from ward, HAU, ICU



Summary

Study	Population (SARS-CoV-2 PCR positive)	Intervention	Comparator	Outcome	Status
CATCO	Hospitalized	Remdesivir or Interferon	Optimized supportive care	All cause mortality Clinical severity	Remdesivir on site Ready to enroll
ATTACC	Hospitalized *Not intubated*	Therapeutic anticoagulation		Outcome at 30d (IMV/death)	Ready to enroll
CONCOR-1	Hospitalized *Receiving oxygen*	Convalescent Plasma			CCP on site Ready to enroll



Who to contact?

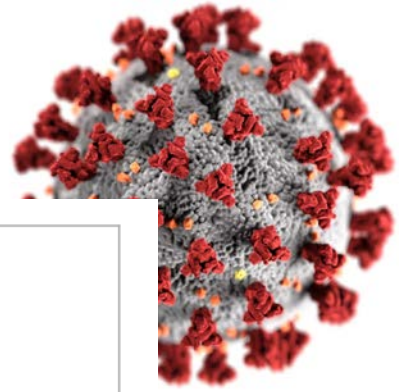
Research Team

- Fiona Auld
- Deb Parfett
- Gayle Carney

Investigators

- Daniel Ovakim
- Gordon ()Wood
- Eric Partlow
- Matt Moher
- David Forrest (NRGH)

COVID-19: Clinical Trials at VIHA



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Clinical Order Set

Demographics

COVID-19 Treatment Adult Suspected or Confirmed (Module)

Page 1 of 4

Key: **Req** – Requisition **MAR** – Medication Administration Record **K** – Kardex **Dis** – Discontinued

Key	Phase
	lt (Module)

Instructions for completing this order set:

- ☑ Indicates a pre-selected order. To delete a pre-selected order, draw a line through it
- ☐ Must tick the box for order to be implemented. Orders not checked will not be implemented
- __ Fill in blank spaces as needed/appropriate
- \- Indicates an item for consideration by Provider; is NOT an order

COVID-19 Treatment Adult (Module)

*778 (*NRGH and Victoria sites only)*

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COVID-19: Clinical Trials at VIHA