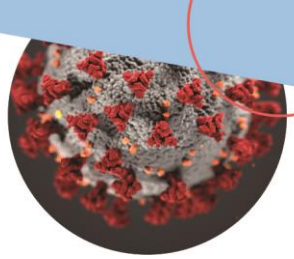
taskforce on bbvs
sexual health and covid-19



ASHM COVID-19 Taskforce update on registered COVID-19 studies in Australia and New Zealand. *Prepared by members of the Taskforce's Research Studies in Australasia and Overseas Cluster Group and the Taskforce Chair, June 2020*

Document last updated: May 31st 2020

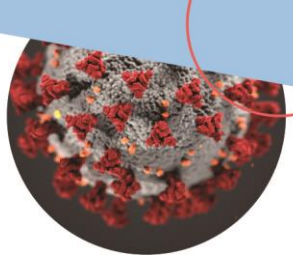
Disclaimer: This ASHM document is designed to provide available, relevant information to clinicians and other healthcare providers to optimise the health and wellbeing of people living HIV, hepatitis B or hepatitis C during the COVID-19 pandemic**.** The recommendations provided are the opinions of the authors and are not intended to provide a standard of care, or practice. This document does not reflect a systematic review of the evidence, but will be revised to include relevant future systematic review findings of the National COVID-19 Clinical Evidence Taskforce(1) and other relevant information.

Summary of key findings in this report

- Australia and New Zealand are actively involved in designing research studies that address the COVID-19 illness that occurs following infection with SARS-CoV-2
- Several clinical trials have been registered in Australasia that are designed to look at the prevention and treatment benefits of diverse therapeutic agents including a vaccine study
- Several observational studies, including a study of immunosuppressed populations, neonatal outcomes, a biobanking study and a study of the role of physiotherapy in intensive care are underway to help characterise the COVID-19 illness and its sequelae
- Several studies are looking at the psychological impact of the COVID-19 pandemic on healthcare workers and the general population
- Two registries have been established to look at the impact of COVID-19 illness upon cardiac function and pregnancy outcomes
- People living with blood borne viruses are eligible for several studies
- Recently published data are available that address the safety and efficacy of remdesivir and hydroxychloroquine for treatment of COVID-19 illness

Background:

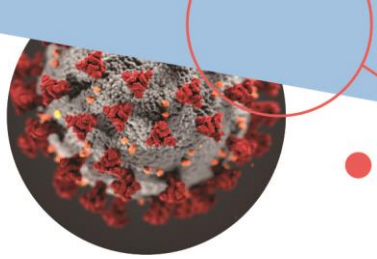
Australia and New Zealand are actively involved in research that addresses the COVID-19 illness that occurs following infection with SARS-CoV-2. Of these, those that have been registered with the Australian and New Zealand Clinical Trials Registry (ANZCTR)(2) and/or the United States ClinicalTrials.gov(3) have been selectively summarised in Table 1. For information on other registered studies not listed in Table 1 and for daily updates on new COVID-19 studies refer to ANZCTR(2), ClinicalTrials.gov(3) and the WHO COVID-19 Clinical Trials Registry(4).



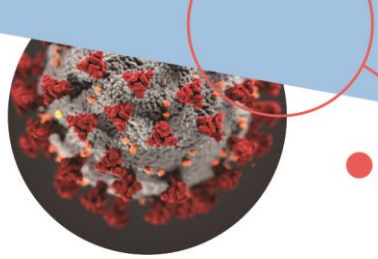
Some of the treatment and prevention studies listed in Table 1 indicate that people living with HIV are eligible for enrolment: HIV positive people are eligible for the REMAP-COVID study and the ASCOT treatment studies, but in the ASCOT study only participants who are on antiretroviral therapy are eligible; HIV positive people are not eligible for the DAS 181 study, the BCG study, or the MEND study. People living with hepatitis B and hepatitis C are not eligible for the MEND study. People living with untreated hepatitis B and primary or secondary immunodeficiency are not eligible for the Tocilizumab study. People living with HIV, hepatitis B or hepatitis C are not eligible for the Novavax vaccine study.

Table 1. Selected COVID-19 treatment, prevention, observational and psychological studies and registries that have been registered in Australasia at May 31st 2020

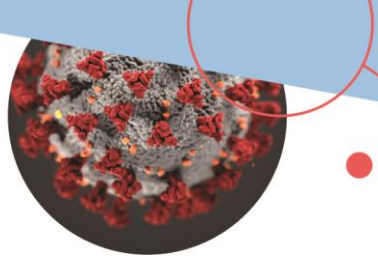
Name & Sponsor & Trial number	Intervention	Number (N) & Design & Note if eligibility statement provided regarding people living with blood borne viruses	Sites	Noted to be Open
PREVENTION of COVID-19				
Evaluation of the Safety and Immunogenicity of a SARS-CoV-2 rS (COVID-19) Nanoparticle Vaccine With/Without Matrix-M Adjuvant Novavax NCT04368988	Phase 1 2 IM injections at a 21-day interval (Day 0 and Day 21) of: NSS Saline Placebo versus SARS-CoV-2 rS - 25 µg without Matrix-M versus SARS-CoV-2 rS - 5 µg with 50 µg Matrix-M versus SARS-CoV-2 rS - 25 µg with 50 µg Matrix-M versus SARS-CoV-2 rS - 25 µg with 50 µg Matrix-M followed by Placebo	N=131 A phase I/II blinded, randomised, placebo controlled trial People with HIV, hepatitis B and hepatitis C are excluded	Victoria Queensland	Yes
Effectiveness of Prophylactic Hydroxychloroquine on incidence of COVID-19 infection in Front-line Health and Allied Health Care Workers: The COVID-SHIELD Trial	Hydroxychloroquine orally once daily; 400mg (>=65kg body weight) or 200mg (<65kg body weight) for 4 months versus placebo once daily for 4 months	N=2250 Blinded randomised controlled trial People with immunosuppressive conditions, or medications (sic) are excluded	Victoria, South Australia, New South Wales, Australian Capital Territory	No



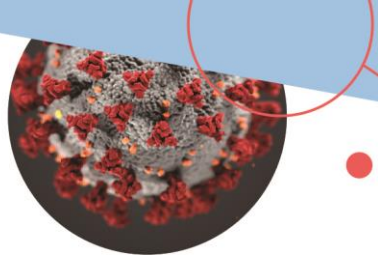
Walter and Eliza Hall Institute of Medical Research ACTRN12620000501943p				
BCG Vaccination to Protect Healthcare Workers Against COVID-19. The BRACE study. Murdoch Research Children's Institute NCT04327206	Single dose BCG 0.1ml	N= 4,170 Open label, phase 3 randomised controlled trial HIV positive people excluded because of risk of dissemination BCG infection	Victoria, Western Australia, South Australia	Yes
Chloroquine RepurpOsing to healthWorkers for Novel CORONAvirus mitigaTION (CROWN CORONA) Washington University School of Medicine NCT04333732	Low-dose (300mg chloroquine base weekly) versus Medium-dose (300mg chloroquine base twice weekly) versus High-dose (150 mg chloroquine base daily) versus placebo	N=55,000 Bayesian, adaptive, pragmatic, participant level randomisation, international, placebo-controlled trial Randomization will be stratified by age (<50 and ≥50) and study site	Victoria	No
Multi-Site, Randomized, Open-Label, Parallel-Group, Placebo-Controlled Study to Assess the Chemoprophylactic Efficacy of Chloroquine Against SARS-CoV-2/COVID-19 in Healthcare Workers at High-Risk of Exposure Australian Defence Force Malaria and Infectious Disease Institute ACTRN12620000417987	Oral 500mg chloroquine phosphate tablets prophylactic weekly regimen against COVID-19 over 10 week trial period versus Vitamin C placebo	N= 680 Multi-Site, Randomized, Open-Label, Parallel-Group, Placebo-Controlled Study	Queensland	Yes
TREATMENT of COVID-19				
International ALLIANCE Study of Therapies to Prevent Progression of COVID-19 National Institute of Integrative Medicine, Australia	Participants will be randomized to azithromycin, hydroxychloroquine, zinc, Vitamin D3/B12 and IV Vitamin C for 14 days	N=200 Open label, randomised controlled trial Adaptive design	Not stated	



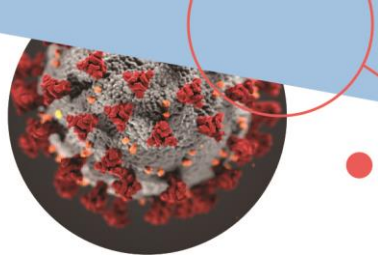
Catholic Health Initiatives NCT04395768	Versus Azithromycin, zinc and hydroxychloroquine, Vitamin D3/B12 for 14 days			
The MEND (MEseNchymal coviD-19) Trial: a pilot study to investigate early efficacy of mesenchymal stem cells in adults with COVID-19. The MEND trial. Cynata Therapeutics Limited ACTRN12620000612910	Mesenchymoangioblast-derived mesenchymal stem cells (CYP-001) at a dose of 2 million cells/kg (up to a maximum of 200 million cells) by IV infusion on two occasions (Day 1 and Day 3) PLUS standard of care in ICU versus Standard of care in ICU	N= 24 Phase I/II , open label, randomised controlled trial People with HIV 1, HIV 2, hepatitis B, hepatitis C virus or any other infection which the opinion of the Investigator is likely to impact on the ability of the patient to participate in the study are excluded	New South Wales	No
Tocilizumab for the treatment of COVID-19 in intensive care patients: effect on days free of ventilatory support. QIMR Berghofer Medical Research Institute ACTRN12620000580976p	Patients in the intensive care setting will be randomized 2:1 to receive a single dose of intravenous 400mg Tocilizumab plus standard of care in ICU Versus Standard or care in ICU	N=150 Open label randomised controlled trial Patients with untreated hepatitis B and primary and secondary immunodeficiency are excluded	Queensland	No
BEAT COVID-19: A Phase III Bayesian adaptive randomisation platform controlled trial to evaluate the efficacy of drug interventions for COVID-19 on hospital admission or death in the community setting for high risk older people University of Sydney ACTRN12620000566932p	Initial treatment will be hydroxychloroquine 200mg bd for 7 days versus Placebo i bd for 7 days	N=3000 Blinded randomised placebo controlled trial	New South Wales	No
Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community- Acquired Pneumonia (REMAP-CAP)	REMAP-COVID will include the following drugs in the comparator arms: -Lopinavir-ritonavir	Phase 4, randomised, embedded, multifactorial, adaptive platform trial	New South Wales, Northern Territory,	Yes



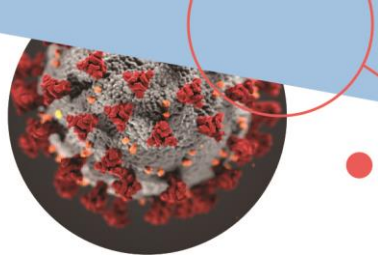
REMAP-COVID is a sub-platform of REMAP-CAP MJM Bonten NCT02735707	-Hydroxychoroquine -Lopinavir-ritonavir plus Hydroxychoroquine - Interferon-β1a - Anakinra (interleukin1 receptor antagonist) - Tocilizumab - Sarilumab		Queensland, South Australia, Victoria, Western Australia	
Australasian COVID-19 Trial (ASCOT). A multi-centre randomised clinical trial to assess clinical, virological and immunological outcomes in patients with SARS-CoV-2 infection (COVID-19) treated with lopinavir/ritonavir and/or hydroxychloroquine compared to standard of care University of Melbourne ACTRN12620000445976	-Lopinavir-ritonavir versus - Hydroxychloroquine versus - Lopinavir-ritonavir plus hydroxychloroquine versus - standard care	N= 2,500 Phase 3, randomized open, controlled trial HIV positive people are excluded if they are not on antiretroviral therapy	All States and Territories and New Zealand	Yes
Cord Blood Therapy to prevent progression of COVID-19 related pneumonia Monash Health ACTRN12620000478910	Intravenous umbilical cord blood versus standard care	N= 24 Randomised controlled trial	Victoria	No
A Phase III Randomized Placebo-Controlled Study to Examine the Efficacy and Safety of DAS181 for the Treatment of Lower Respiratory Tract Parainfluenza Infection in Immunocompromised Subjects (Substudy: DAS181 for COVID-19) Ansun Biopharma, Inc. NCT03808922	DAS181 for 7 or 10 days (For the COVID-19 substudy)	N= 250 International, randomised controlled study HIV positive subjects are excluded	New South Wales, Queensland, Victoria	Yes
A Randomised, Double Blind, Placebo-Controlled Trial of the Efficacy of Hydroxychloroquine for the Community-Based Treatment of Adults With Diagnosed COVID-19	Hydroxychloroquine versus placebo for five days	N= 70 Blinded, randomised placebo- controlled trial	New Zealand	No



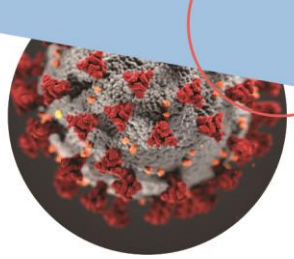
Medical Research Institute of New Zealand ACTRN12620000457943p				
High-dose intravenous zinc (HDIVZn) as adjunctive therapy in COVID-19 positive critically ill patients: A pilot randomized controlled trial **Austin Hospital, Victoria** **ACTRN12620000454976**	**Intravenous zinc chloride for 7 days** **versus** **intravenous normal saline placebo daily for 7 days**	**N= 160** **Blinded randomised controlled trial** **HIV positive subjects are excluded**	**Victoria**	**No**
EXPANDED ACCESS TREATMENT TRIALS				
Expanded Access Treatment Protocol: Remdesivir (RDV; GS-5734) for the Treatment of SARS-CoV2 (CoV) Infection Gilead Sciences NCT04323761	Intravenous remdesivir	N= not stated Open label access study	Victoria, New South Wales	Yes
RESEARCH PLATFORMS & BIOBANKS				
Covid-19 Biobank: a clinical database and biological bank of clinical samples from individuals with COVID-19 infection to better characterise the clinical course and pathogenesis of the infection and provide insights into potential therapeutic agents Alfred Hospital ACTRN12620000609954	N/A	N=250 There are no exclusion criteria	Victoria	Yes
OBSERVATIONAL STUDIES				
ADAPT - COVID-19 Study - Characterizing pathophysiological, immunological and clinical outcomes relating to COVID-19 infection in the patient population of St Vincent's Hospital Sydney	N/A	N=300 Prospective, observational cohort study of all patients at St Vincent's Hospital Sydney who test positive for COVID-19 infection. The cohort will consist of two	New South Wales	No



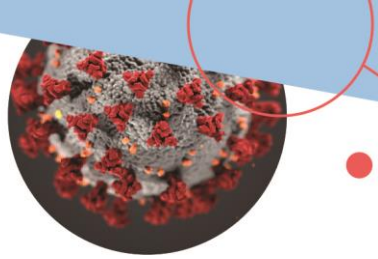
St Vincent's Health Network ACTRN12620000554965		components. Cohort A - Mild disease patients recruited through the community cohorts Cohort B - Moderate-severe patients recruited via St Vincent's Hospital Sydney		
Coronavirus Outcomes Registries in Immunocompromised Individuals Australia (CORIA): a Multisite Registry and Optional Biorepository in People With COVID-19 and Selected Conditions Affecting Immune Function Kirby Institute NCT04354818	N/A	N=1000 Prospective observational cohort study of immunosuppressed patients with COVID-19 HIV positive subjects are eligible	New South Wales	No
Loss of SMELL as an earlY marker in patients with COVID-19. The SMELLY study Royal North Shore Hospital ACTRN12620000575932	N/A	N=100 Observational study The prevalence of olfactory dysfunction in patients with COVID-19 will be determined using the validated University of Pennsylvania Smell Identification Test (UPSIT).	New South Wales	Yes
Recovery of Patients From COVID-19 After Critical Illness (COVID-Recovery) Australian and New Zealand Intensive Care Research Centre NCT04401254	N/A	N=300 Prospective observational study of the physiotherapy interventions provided to patients with COVID-19 admitted to the ICU and health outcomes	Victoria	No
Neonatal CoVID-19 Study to evaluate the population health impacts of COVID-19 in mothers and their newborn infants cared for in tertiary and non-tertiary hospitals in Australia. Hunter New England LHD	N/A	N=1000 Prospective observational study of COVID-19 confirmed infants or infants born to COVID-19 confirmed mothers	All States and Territories	No



ACTRN12620000527965				
PSYCHOLOGICAL STUDIES				
Randomised controlled trial of an app-based intervention, Anchored, to support the mental health of Australians recently unemployed due to COVID-19. University of New South Wales ACTRN12620000555954	Randomised to use 'Anchored' a smartphone app versus Being placed in a waitlist group and being provided with support referral services	N=492 Randomised controlled trial	All States and Territories	No
Psychological impact of COVID-19 pandemic on perioperative staff at the Royal Melbourne Hospital – a longitudinal study Royal Melbourne Hospital ACTRN12620000590965p	N/A	N= 90 Prospective observational study	Royal Melbourne Hospital, Victoria	No
Stress-reduction Using Probiotics to Promote Ongoing Resilience Throughout COVID-19 for Healthcare Workers: A randomised placebo-controlled trial University of Auckland ACTRN12620000480987p	Daily capsules containing either the probiotic Lactobacillus rhamnosus HN001 for 12 weeks versus a placebo for 12 weeks	N=507 Randomised controlled trial	New Zealand	No
Impact of Social Isolation on Mental Health during the COVID-19 Pandemic: a large international multi-centre cohort study The George Institute for Global Health ACTRN12620000479909p	Not applicable	N= 3,000 International observational study	All States and Territories	No



Randomised Controlled Trial of Problem Management Plus versus Enhanced Treatment as Usual, on Anxiety and Depression in People Distressed by Covid 19 UNSW ACTRN12620000468921p	Problem Management Plus Comprising 6 x 60 minutes sessions via teleconference versus Referral to portal with stress coping strategies	N= 140 Blinded randomised controlled trial	NSW	No
Home telerehabilitation for people with COVID-19: Implementing telehealth approaches to care and its effect on reintegration into the community Flinders Medical Centre ACTRN12620000443998p	Telerehabilitation using a Coaching model versus a traditional model for 11 sessions	N=58 Blinded, randomised controlled trial	South Australia	No
REGISTRIES				
Angiotensin II Infusion in COVID-19-Associated Vasodilatory Shock: A multinational, multicentre registry Rinaldo Bellomo, Austin Health ACTRN12620000620921	Not applicable	N= 315 Patients admitted to ICU with COVID-19 who are, or who are not treated with angiotensin II and other novel therapies will be enrolled in the registry retrospectively and prospectively	New South Wales, Victoria	No
AUSTRALIAN CARDIOVASCULAR COVID-19 REGISTRY (AUS-COVID) Royal North Shore Hospital ACTRN12620000486921	Not applicable	Patients admitted to hospital with confirmed SARS-CoV-2 infection will be enrolled in the registry will	New South Wales, Queensland, South Australia, Victoria, Western Australia	No



Prospective registry of maternal, perinatal and neonatal outcomes from pregnancies infected with SARS-COV2 (COVID-19) University of Melbourne ACTRN12620000449932	Not applicable	N=200 Observational study	All States and Territories	No

A quick primer on several of the therapeutic interventions planned for use in the treatment and prevention studies listed in Table 1.

BCG

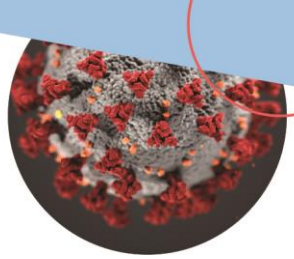
The Bacille Calmette-Guérin vaccine, in addition to its role in preventing infection with Mycobacterium tuberculosis, has immunomodulatory properties and is used for this purpose to induce an immune response against tumour cells in non-invasive bladder cancer. As noted in a recent commentary by Dr Nigel Curtis(5) who is leading the Australian COVID-19 BCG study listed in Table 1, BCG has been shown to induce memory in the innate immune system and reduce mortality beyond its role in the prevention of tuberculosis(6).

Chloroquine

Chloroquine is an anti-malarial drug. In vitro data from a recent study showed that low concentrations of chloroquine blocked SARS-CoV-2 infection in Vero E6 cells(7). Chloroquine is known to block infection with the first SARS virus, SARS-CoV, by changing the pH of cells' endosomes and by interfering with the glycosylation of SARS-CoV receptors(8). There has been a brief publication that referred to 15 COVID-19 treatment trials in China, which stated that chloroquine was effective in treating over 100 people(9), however the contents of this publication has been met with caution(10).

Hydroxychloroquine

Hydroxychloroquine is a metabolite of chloroquine and is used to treat a number of autoimmune disorders. Two French studies examined the impact of hydroxychloroquine on the PCR positivity of nasopharyngeal swabs for SARS-CoV-2. An open-label study undertaken in Paris reported that when hydroxychloroquine was combined with azithromycin for treatment of 11 patients consecutively admitted to hospital with COVID-19 illness, PCR assays from nasopharyngeal swabs remained positive for 5-6 days following commencement of treatment (11). This was in contrast to findings of a study undertaken in Marseille of patients hospitalised with COVID-19, which reported that at day 6, 70% of 20 patients treated with hydroxychloroquine +/- azithromycin had negative nasopharyngeal swabs versus only 12.5% of the 16 controls(12). However, as summarised by Ferner(10) concerns



about this study included that the findings from six patients' in the treatment arm were not evaluated (12).

There has been one randomised study from China which examined both viral clearance and clinical outcomes in 30 patients hospitalised with COVID-19 illness(13). This study reported no difference in PCR positivity of pharyngeal swabs at day 7 between those randomised to receive five days of hydroxychloroquine versus standard treatment and no difference in clinical outcomes(13).

The Marseille study team recently reported on a retrospective study on 1061 people with symptomatic or asymptomatic SARS-CoV-2 infection who were treated with combination hydroxychloroquine and azithromycin for 10 and 9 nine days, respectively. The authors concluded that the treatment was safe with 2.3% reporting adverse events; QT prolongation was observed in nine patients but no arrhythmias, cardiac events or sudden deaths occurred. The authors noted that good clinical outcome and virological clearance was observed in 91.7% of patients(14).

Results were released recently from a large international registry study of 96, 032 hospitalised patients with COVID-19, which examined the association between in-hospital mortality and treatment with hydroxychloroquine, or chloroquine either alone or with a macrolide antibiotic (15). There were 14, 888 patients who received these treatments and 81,144 patients who did not and served as the control group. The authors found that use of either of these drugs either alone or with a macrolide was associated with decreased in-hospital survival and an increased risk of clinically significant cardiac arrhythmias when compared to controls. Most importantly this study was not a randomised controlled trial. Since its release there have been concerns raised regarding the study's recruitment methodology and its statistical analysis(10). Following this study's publication the World Health Organisation instructed that there be a 'temporary pause' of the hydroxychloroquine arm in the WHO Solidarity trial(11).

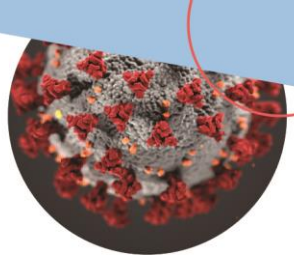
In Australia, the ASCOT study is waiting for further data to become available and the study remains open and the COVID SHIELD study remains open.

Lopinavir-ritonavir

Lopinavir is a protease inhibitor of HIV-1 and has in vitro activity against SARS-CoV(16). In a recent randomised controlled study of 199 patients hospitalised with COVID-19 illness, there was no difference in time to clinical improvement or discharge from hospital between participants who were randomised to 14 days of treatment with lopinavir-ritonavir versus standard care(17).

Anakinra, Tocilizumab and Sarilumab

Use of these agents represent a therapeutic approach to the management of the cytokine disturbance that occurs in COVID-19 illness, including in some cases, the



cytokine storm syndrome (CSS)(18). Anakinra is a recombinant human receptor IL-1 antagonist and as summarized by Cron and Chatham(19), has been used for treatment of CSS. Tocilizumab is an anti-IL-6 monoclonal antibody and has been used for the treatment of CSS including in the setting of COVID-19 illness, as reported in one small, single-centre study(20). Sarilumab is a monoclonal antibody that binds and blocks the IL-6 receptor.

DAS181

DAS181 is a recombinant sialidase fusion protein, which removes sialic acid receptors that are present on the host's respiratory epithelial cells, thereby preventing viruses from binding to these host receptors. It has activity against a number of influenza viruses, as reviewed by Koszalka et al(21).

Umbilical cord blood

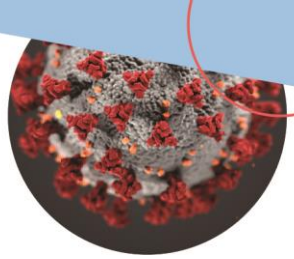
It has been postulated that the mesenchymal stem cells present in umbilical cord blood may help improve the innate immune response in the setting of COVID-19 illness(22). One small study from China has reported on seven patients who received mesenchymal stem cells(23).

Remdesivir

Remdesivir is a prodrug of a nucleotide analogue and is metabolised within cells to become an analogue of adenosine triphosphate; it inhibits RNA polymerases and has in vitro activity against several viruses including SARS-CoV-2. Remdesivir was registered in Australia in May 2020 for an expanded access treatment trial for people with COVID-19 illness.

In early April 2020 data from a small cohort study with 53 evaluable patients who were hospitalised with severe COVID-19 and received at least one dose of remdesivir were reported(24). The authors reported 18% mortality in ventilated patients and 5% mortality in non-ventilated patients over a median follow-up of 18 days(24).

Recently results were released from a large, blinded randomised controlled trial of remdesivir versus placebo in patients hospitalised with COVID-19 illness(25). The study's primary outcome was time to recovery, which was defined as discharge from hospital, or being kept in hospital solely for infection control purposes. Patients were randomized according to disease severity and study site. Results from 1089 randomised patients found a significantly shorter time to discharge for those who received remdesivir (11 days (95% confidence Interval [CI] 9-12)) versus placebo (15 days, (95% CI 13-19)). The participants whose baseline disease severity was that they required only supplemental oxygen appeared to benefit the most from remdesivir, compared to those with milder or more severe disease; this may be explained by the fact that this disease severity group had the highest number of patients. At day 14, mortality was 7.1% for remdesivir and 11.9% for placebo (hazard ratio for death, 0.70; 95%CI, 0.47-1.4). Serious adverse events occurred in 114 and 141 of



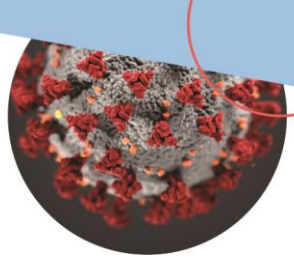
remdesivir and placebo recipients, respectively; only 2 events in each arm were attributed to study drug or placebo(25). The authors concluded that the study's findings support remdesivir's use for hospitalised patients requiring supplemental oxygen.

Importantly the authors noted the findings of a smaller blinded, randomised controlled trial conducted in 10 hospitals in Wuhan, China, which was published in late April 2020(26). Interestingly, the majority of participants' baseline disease severity in this study was that they required supplemental oxygen. However, this trial did not find that remdesivir led to faster clinical improvement compared to placebo. Of note, the study was stopped prematurely because the epidemic had waned in Wuhan and the authors noted that the study was underpowered, having required 453 patients to demonstrate benefit from remdesivir, but having enrolled only 237 patients(26).

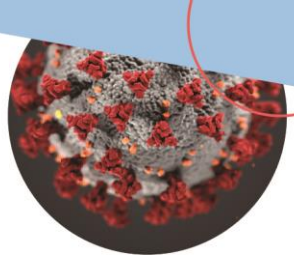
Finally a randomised open-label study of 397 patients hospitalised with COVID-19 pneumonia was published in late May 2020(27). Study participants were randomised to receive remdesivir for either five or ten days and the study's primary endpoint was the participants' clinical status at day 14. The authors did not find a difference in efficacy between the five and ten day courses of remdesivir, but noted that these findings could not be applied to critically ill patients on mechanical ventilation because only approximately 3% of study participants were mechanically ventilated(27).

References:

1. National COVID-19 Clinical Evidence Taskforce https://covid19evidence.net.au/.
2. Australian New Zealand Clinical Trials Registry https://anzctr.org.au/TrialSearch.aspx -&&conditionCode=&dateOfRegistrationFrom=&interventionDescription=&interventionCodeOperator=OR&primarySponsorType=&gender=&distance=&postcode=&pageSize=20&ageGroup=&recruitmentCountryOperator=OR&recruitmentRegion=&ethicsReview=&countryOfRecruitment=Australia%7cNew+Zealand&registry=&searchTxt=COVID+19+OR+%22SARS-CoV2%22+OR+%222019-nCoV%22&studyType=&allocationToIntervention=&dateOfRegistrationTo=&recruitmentStatus=&interventionCode=&healthCondition=&healthyVolunteers=&pa.
3. ClinicalTrials.gov https://clinicaltrials.gov/ct2/results?cond=COVID&term=&cntry=AU&state=&city=&dist=
4. WHO International Clinical Trials Registry Platform https://www.who.int/ictrp/search/en/

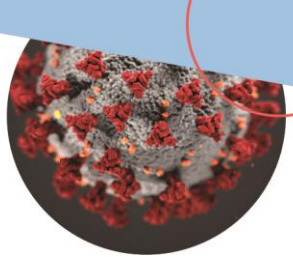


5. Curtis, N. 2019. BCG Vaccination and All-Cause Neonatal Mortality. *Pediatr Infect Dis J* 38: 195-197.
6. Higgins, J. P., K. Soares-Weiser, J. A. Lopez-Lopez, A. Kakourou, K. Chaplin, H. Christensen, N. K. Martin, J. A. Sterne, and A. L. Reingold. 2016. Association of BCG, DTP, and measles containing vaccines with childhood mortality: systematic review. *BMJ* 355: i5170.
7. Wang, M., R. Cao, L. Zhang, X. Yang, J. Liu, M. Xu, Z. Shi, Z. Hu, W. Zhong, and G. Xiao. 2020. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res* 30: 269-271.
8. Vincent, M. J., E. Bergeron, S. Benjannet, B. R. Erickson, P. E. Rollin, T. G. Ksiazek, N. G. Seidah, and S. T. Nichol. 2005. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. *Virol J* 2: 69.
9. Gao, J., Z. Tian, and X. Yang. 2020. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends* 14: 72-73.
10. Ferner, R. E., and J. K. Aronson. 2020. Chloroquine and hydroxychloroquine in covid-19. *BMJ* 369: m1432.
11. Molina, J. M., C. Delaugerre, J. Le Goff, B. Mela-Lima, D. Ponscarme, L. Goldwirt, and N. de Castro. 2020. No evidence of rapid antiviral clearance or clinical benefit with the combination of hydroxychloroquine and azithromycin in patients with severe COVID-19 infection. *Med Mal Infect*.
12. Gautret, P., J. C. Lagier, P. Parola, V. T. Hoang, L. Meddeb, M. Mailhe, B. Doudier, J. Courjon, V. Giordanengo, V. E. Vieira, H. T. Dupont, S. Honore, P. Colson, E. Chabriere, B. La Scola, J. M. Rolain, P. Brouqui, and D. Raoult. 2020. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents*: 105949.
13. Chen J, Liu D, Lui L, et al. A pilot study of hydroxychloroquine in treatment of patients with common coronavirus disease-19 COVID-19). Journal of Zhejiang University 2020; 03-03.
14. Million, M., J. C. Lagier, P. Gautret, P. Colson, P. E. Fournier, S. Amrane, M. Hocquart, M. Mailhe, V. Esteves-Vieira, B. Doudier, C. Aubry, F. Correard, A. Giraud-Gatineau, Y. Roussel, C. Berenger, N. Cassir, P. Seng, C. Zandotti, C. Dhiver, I. Ravaux, C. Tomei, C. Eldin, H. Tissot-Dupont, S. Honore, A. Stein, A. Jacquier, J. C. Deharo, E. Chabriere, A. Levasseur, F. Fenollar, J. M. Rolain, Y. Obadia, P. Brouqui, M. Drancourt, B. La Scola, P. Parola, and D. Raoult. 2020. Early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: A retrospective analysis of 1061 cases in Marseille, France. *Travel Med Infect Dis*: 101738.
15. Mehra, M. R., S. S. Desai, F. Ruschitzka, and A. N. Patel. 2020. Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis. *Lancet*.
16. Wu, C. Y., J. T. Jan, S. H. Ma, C. J. Kuo, H. F. Juan, Y. S. Cheng, H. H. Hsu, H. C. Huang, D. Wu, A. Brik, F. S. Liang, R. S. Liu, J. M. Fang, S. T. Chen, P. H. Liang,



and C. H. Wong. 2004. Small molecules targeting severe acute respiratory syndrome human coronavirus. *Proc Natl Acad Sci U S A* 101: 10012-10017.

17. Cao, B., Y. Wang, D. Wen, W. Liu, J. 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, H. Li, H. Huang, S. Tu, F. Gong, Y. Liu, Y. Wei, C. Dong, F. Zhou, X. Gu, J. Xu, Z. Liu, Y. Zhang, H. 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, J. 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. 2020. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. *N Engl J Med*.
18. Wang, D., B. Hu, C. Hu, F. Zhu, X. Liu, J. Zhang, B. Wang, H. Xiang, Z. Cheng, Y. Xiong, Y. Zhao, Y. Li, X. Wang, and Z. Peng. 2020. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*.
19. Cron, R. Q., and W. W. Chatham. 2020. The Rheumatologist's Role in COVID-19. *J Rheumatol*.
20. Luo, P., Y. Liu, L. Qiu, X. Liu, D. Liu, and J. Li. 2020. Tocilizumab treatment in COVID-19: A single center experience. *J Med Virol*.
21. Koszalka, P., D. Tilmanis, and A. C. Hurt. 2017. Influenza antivirals currently in late-phase clinical trial. *Influenza Other Respir Viruses* 11: 240-246.
22. Atluri, S., L. Manchikanti, and J. A. Hirsch. 2020. Expanded Umbilical Cord Mesenchymal Stem Cells (UC-MSCs) as a Therapeutic Strategy in Managing Critically Ill COVID-19 Patients: The Case for Compassionate Use. *Pain Physician* 23: E71-E83.
23. Leng, Z., R. Zhu, W. Hou, Y. Feng, Y. Yang, Q. Han, G. Shan, F. Meng, D. Du, S. Wang, J. Fan, W. Wang, L. Deng, H. Shi, H. Li, Z. Hu, F. Zhang, J. Gao, H. Liu, X. Li, Y. Zhao, K. Yin, X. He, Z. Gao, Y. Wang, B. Yang, R. Jin, I. Stambler, L. W. Lim, H. Su, A. Moskalev, A. Cano, S. Chakrabarti, K. J. Min, G. Ellison-Hughes, C. Caruso, K. Jin, and R. C. Zhao. 2020. Transplantation of ACE2(-) Mesenchymal Stem Cells Improves the Outcome of Patients with COVID-19 Pneumonia. *Aging Dis* 11: 216-228.
24. Grein, J., N. Ohmagari, D. Shin, G. Diaz, E. Asperges, A. Castagna, T. Feldt, G. Green, M. L. Green, F. X. Lescure, E. Nicastri, R. Oda, K. Yo, E. Quiros-Roldan, A. Studemeister, J. Redinski, S. Ahmed, J. Bernett, D. Chelliah, D. Chen, S. Chihara, S. H. Cohen, J. Cunningham, A. D'Arminio Monforte, S. Ismail, H. Kato, G. Lapadula, E. L'Her, T. Maeno, S. Majumder, M. Massari, M. Mora-Rillo, Y. Mutoh, D. Nguyen, E. Verweij, A. Zoufaly, A. O. Osinusi, A. DeZure, Y. Zhao, L. Zhong, A. Chokkalingam, E. Elboudwarej, L. Telep, L. Timbs, I. Henne, S. Sellers, H. Cao, S. K. Tan, L. Winterbourne, P. Desai, R. Mera, A. Gaggar, R. P. Myers, D. M. Brainard, R. Childs, and T. Flanigan. 2020. Compassionate Use of Remdesivir for Patients with Severe Covid-19. *N Engl J Med*.
25. Beigel, J. H., 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. D. Oh, G. M. Ruiz-Palacios, T. Benfield, G. Fatkenheuer, 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, H. C. Lane, and A.-S. G. Members. 2020. Remdesivir for the Treatment of Covid-19 - Preliminary Report. *N Engl J Med*.

26. Wang, Y., D. Zhang, G. Du, R. Du, J. Zhao, Y. Jin, S. Fu, L. Gao, Z. Cheng, Q. Lu, Y. Hu, G. Luo, K. Wang, Y. Lu, H. Li, S. Wang, S. Ruan, C. Yang, C. Mei, Y. Wang, D. Ding, F. Wu, X. Tang, X. Ye, Y. Ye, B. Liu, J. Yang, W. Yin, A. Wang, G. Fan, F. Zhou, Z. Liu, X. Gu, J. Xu, L. Shang, Y. Zhang, L. Cao, T. Guo, Y. Wan, H. Qin, Y. Jiang, T. Jaki, F. G. Hayden, P. W. Horby, B. Cao, and C. Wang. 2020. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet* 395: 1569-1578.

27. Goldman, J. D., D. C. B. Lye, D. S. Hui, K. M. Marks, R. Bruno, R. Montejano, C. D. Spinner, M. Galli, M. Y. Ahn, R. G. Nahass, Y. S. Chen, D. SenGupta, R. H. Hyland, A. O. Osinusi, H. Cao, C. Blair, X. Wei, A. Gaggar, D. M. Brainard, W. J. Towner, J. Munoz, K. M. Mullane, F. M. Marty, K. T. Tashima, G. Diaz, A. Subramanian, and G.-U.-. Investigators. 2020. Remdesivir for 5 or 10 Days in Patients with Severe Covid-19. *N Engl J Med*.