Suggested Protocol for Treatment of confirmed COVID-19 Infection

A. General information:

1- The purpose of the protocol is to assist physicians in management of patients with confirmed COVID-19 infection.
2- Those recommendations are based on case series, registered and observational trials on patients with MERS CoV, SARS and COVID-19.
3- Strict infection control measures should be maintained all the time.

B. Collection of swabs: **(Table 1)**

1- Strict infection control measures should be maintained all the time.
2- Samples should be collected in negative pressure room (if not available single room with HEPA FILTERS)
3- Staff should wear full personal protective equipment PPE (Gown, gloves, N95 mask, face shield (goggles))
4- Combined Nasopharyngeal/ Oropharyngeal swab is recommended.
5- If positive, repeat the swab every 7 days (for patient whom home isolation is suitable like Nationals, stable resident with families…) or every 14 days (for patients whom home isolation is not suitable e.g. laborers…) from the first sample collection date till negative.
6- If negative repeat after 24 hours.
7- If 2 consecutive negative results patient can be discharge home if the patient will stay in the hospital for another reason then we advise to keep under droplet and contact for 2 weeks more .
   - Lower respiratory specimen is preferred when the patient is intubated.
   - Airborne / contact isolation is recommended
   - Confirmed cases can be cohorted in case of shortage of single isolation rooms
   - For further information contact your infection control practitioner

C. Collection of other laboratory diagnostic tests: **(Table 2)**

1- Request CBC, CMP, CRP, Respiratory panel including COVID-19 PCR, Chest X-ray as baseline investigations.
2- Request G6PD level.
3- Request electrocardiogram (ECG) for all patients.
4- Consider QuantiFERON test for patient whom will be started on Tocilizumab.
5- Consider repeating other blood tests if indicated and for patients in ICU
6- CT Chest if clinically indicated
7- Appropriate PPE should be applied during laboratory investigation (specimen collection and transport) performing ECG and radiological investigations.

D. Supportive therapy and monitoring:

1- No evidence linking NSAIDS to COVID-related clinical deterioration. This has not been proven clinically to date, so we cannot make a recommendation for or against their use at this time.
2- American Heart Association, the Heart Failure Society of America and the American College of Cardiology all recommend that ACE inhibitors or ARBs be continued in people who have an indication for these medications We do not currently routinely recommend stopping these agents

3- All patients with COVID-19 should receive standard prophylactic anticoagulation with LMWH/ Unfractionated heparin if no contraindications
4- Continue statins if already prescribed where no contraindications and to prescribe it for those for those whom it is indicated for
5- Postexposure Prophylaxis for Healthcare Workers: There is currently no proven role for post exposure prophylaxis for people with a known COVID-19 exposure. They should follow self-quarantine for 14-days and monitor for symptoms.
6- Monitor for drug -drug interactions (consult with your clinical pharmacist)
7- Give supplemental oxygen therapy immediately to patients with COVID-19 and respiratory distress, hypoxemia, or shock. Initiate oxygen therapy at 5 L/min and titrate flow rates to reach target SpO2 ≥90% in non-pregnant adults and SpO2 ≥92-95 % in pregnant patients.
8- All areas where patients with COVID-19 are cared for should be equipped with pulse oximeters, functioning oxygen systems and disposable, single-use, oxygen-delivering interfaces (nasal cannula, simple face mask, and mask with reservoir bag). Use contact precautions when handling contaminated oxygen interfaces of patients with COVID-19 infection.
9- Use conservative fluid management in patients with COVID-19 when there is no evidence of shock.
10- Give empiric antimicrobials to treat all likely pathogens causing secondary bacterial infection in COVID-19 patients. Give antimicrobials within one hour of initial patient assessment for patients with sepsis. According to HMC local protocol (CG 10015)
11- Do not routinely give systemic corticosteroids for treatment of viral pneumonia or ARDS unless they are indicated for another reason. **(Table 3)**
12- Closely monitor patients with COVID-19 for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and apply supportive care interventions immediately.
13- Understand the patient's co-morbid condition(s) to tailor the management of critical illness and appreciate the prognosis. Communicate early with patient and family.
14- Discharged patients will be kept in Home isolation /Quarantine for 4 weeks from the first positive COVID-result or 2 weeks after the last negative swab (whichever is longer).
15- Home isolation:
    - Stay at home in a separate room to other family members, preferably one with an en-suite bathroom, and ensure proper and regular ventilation
    - Avoid any direct contact with other family members
    - Don't allow visitors into your house
    - Use your phone if you need to contact anyone else in the house
    - Ask others - a family member or friend - to run errands for you like buying food or medicine
    - You must not leave your house. In the event of a medical emergency call 999.
    - Only one member of the family should be allowed to provide care to you. Your caregiver should wear a facemask and gloves every time he or she enters your room and should dispose of the mask and gloves and wash their hands immediately after leaving the room.
    - A distance of at least one-two meter shall always be maintained between you and your caregiver.
16- For case definition please see **Appendix 1**
17- For Medication related consideration please see **Appendix 2**
18- For COVID-19 infection in special population please see **Appendix 3**

1. Suggested Treatment protocol for asymptomatic adult patients with positive COVID-19 PCR

No risk factors for severe disease (Table 4)		
Admit the patient to quarantine facility for observation after baseline investigations, no treatment is recommended Strict infection control measures should be maintained all the time.		
With Risk factors for severe disease (Table 4)		
Admit the patient to hospital/quarantine facility for observation after bassline investigations		
+		
Hydroxychloroquine 400 mg BID for 1 day then 400 mg OD	PO	For 5 days
+		
Azithromycin 500 mg OD	PO	For 5 days

2. Suggested Treatment protocol for asymptomatic pregnant females with positive COVID-19 PCR

No risk factors for severe disease (Table 4)		
Admit the patient to quarantine facilities for observation after bassline investigations, no treatment is recommended Strict infection control measures should be maintained all the time. To be evaluated by obstetrician.		
With Risk factors for severe disease (Table 4)		
Admit the patient to hospital		
+		
Chloroquine phosphate 250 mg (150 mg base)300 mg (base) (2 tablets) BID OR Hydroxychloroquine 400 mg BID for 1 day then 400 mg OD	PO	For 5 days
+		
Azithromycin 500 mg OD	PO	For 5 days

1. Efficacy and Safety of Hydroxychloroquine for Treatment of Pneumonia Caused by 2019-nCoV (HC-nCoV) - Full Text View - ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04261517?cond=SARS+%28Severe+Acute+Respiratory+Syndrome%29&draw=5 (accessed March 16, 2020).

2. Fei Zhou, Ting Yu*, Ronghui Du*, Guohui Fan, Ying Liu*, Zhibo Liu, Jie Xiang, Yeming Wang, Bin Song, Xiaoying Gu, Lulu Guan, Yuan Wei,Hui Li, Xudong Wu, Jiuyang Xu, Shengjin Tu, Yi Zhang, Hua Chen, Bin Cao
Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study http://www.thelancet.com/ published on line March 9 ,2020

Suggested Treatment protocol for symptomatic adult patients with positive COVID-19 PCR

1. Positive COVID-19 PCR with Uncomplicated Upper Respiratory Tract Infection (for definition see Table 5)

No risk factors for severe disease (Table 4)		
Admit the patient to COVID-19 Hospital Strict infection control measures should be maintained all the time.		
+		
Hydroxychloroquine 400 mg BID for 1 day then 400 mg OD	PO	For 5 days
+		
Azithromycin 500 mg OD	PO	For 5 days
With Risk factors for severe disease (Table 4)		
Admit the patient to COVID-19 Hospital Strict infection control measures should be maintained all the time.		
+		
Hydroxychloroquine 400 mg BID for 1 day then 400 mg OD	PO	For 5 days
+		
Azithromycin 500 mg OD	PO	For 5 days
+		
Oseltamivir 150 mg BID	PO	For 5 days

2. Pregnant females with Positive COVID-19 PCR with Uncomplicated Upper Respiratory Tract Infection

No risk factors for severe disease (Table 4)		
Admit the patient to COVID Hospital Strict infection control measures should be maintained all the time.		
+		
Azithromycin 500 mg OD	PO	For 5 days
+		
Chloroquine phosphate 250 mg (150 mg base)300 mg (base) (2 tablets) BID OR Hydroxychloroquine 400 mg BID for 1 day then 400 mg OD	PO	For 5 days
With Risk factors for severe disease (Table 4)		
Admit the patient to COVID-19 Hospital Strict infection control measures should be maintained all the time.		
+		
Chloroquine phosphate 250 mg (150 mg base)300 mg (base) (2 tablets) BID OR Hydroxychloroquine 400 mg BID for 1 day then 400 mg OD	PO	For 5 days
+		
Oseltamivir 150 mg BID	PO	For 5 days
+		
Azithromycin 500 mg OD	PO	For 5 days

3. Suggested Treatment protocol for COVID-19 Pneumonia (Documented pneumonia in CXR/CT scan) (for definition see **Table 6**)

Admit the patient to COVID-19 Hospital Strict infection control measures should be maintained all the time.		
Start		
Hydroxychloroquine 400 mg BID for 1 day then 400 mg OD	PO	For 10 days
+		
Oseltamivir 150 mg BID	PO	For 10 days
+		
Ritonavir + Lopinavir (Kaletra) 500mg [1,2]	PO	BID for 2 weeks
+		
Azithromycin 500 mg OD	IV	For 7 days
+		
Ceftriaxone 2 gm OD*	IV	For 7 days

4. Suggested Treatment protocol for Pregnant females withCOVID-19 Pneumonia

Admit the patient to COVID Hospital Strict infection control measures should be maintained all the time.		
Start		
Chloroquine phosphate 250 mg (150 mg base)300 mg (base) (2 tablets) BID	PO	For 10 days
+		
Oseltamivir 150 mg BID	PO	For 10 days
+		
Ritonavir + Lopinavir (Kaletra) 500mg [1,2]	PO	BID for 2 weeks
+		
Azithromycin 500 mg OD	IV	For 7 days
+		
Ceftriaxone 2 gm OD*	IV	For 7 days

*Antibiotic can be switched to PO if the patient is clinically stable

1. A Prospective, Randomized Controlled Clinical Study of Antiviral Therapy in the 2019-nCoV Pneumonia - Full Text View - ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04255017?draw=2 (accessed March 16, 2020).
2. Chinese Clinical Trial Register (ChiCTR) - The world health organization international clinical trials registered organization registered platform. http://www.chictr.org.cn/showprojen.aspx?proj=49065 (accessed March 16, 2020). Randomized, open-label, controlled trial for evaluating of the efficacy and safety of Baloxavir Marboxil, Favipiravir, and Lopinavir-Ritonavir in the treatment of novel coronavirus pneumonia (COVID-19) patients

WHO Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected Interim guidance 28 January 2020

5. Suggested Treatment protocol for COVID-19 pneumonia requiring Intensive care (Septic shock/ARDS) (for definition see **Tables 7,8**)

Admit the patient to ICU in COVID-19 Hospital Strict infection control measures should be maintained all the time.		
Start		
Hydroxychloroquine 400 mg BID for 1 day then 400 mg OD	PO	For 10 days
+		
Oseltamivir 150 mg BID	PO	For 10 days
+		
Ritonavir + Lopinavir (Kaletra) 500mg [1]	PO	BID for 2 weeks
+		
Tocilizumab [3] For patients with evidence of cytokine release syndrome **(Table 9)**	IV	IV infusion: initial dose of 4–8 mg/kg infused over more than 60 minutes. If initial dose not effective, may administer second dose (in same dosage as initial dose) after 12 hours. No more than 2 doses should be given; maximum single dose is 800 mg and not to be infused in the same line with other medications
+		
Azithromycin 500 mg	IV	For 7 days
+		
Antibiotics	IV	As per local CAP guidelines
±		
Consider Convalescent Plasma Infusion **(Table 10)**	IV	2 units of CP. Each unit of plasma (200 -250 ml) will be given over 2 h with an interval of 1 h between the two units.
±		
Methylprednisolone 40 mg	IV	BID for 5 days

6. Suggested Treatment protocol for COVID-19 pneumonia requiring Intensive care (Septic shock/ARDS) in pregnant females

Admit the patient to ICU in COVID Hospital Strict infection control measures should be maintained all the time.		
Start		
Chloroquine phosphate 250 mg (150 mg base)300 mg (base) (2 tablets) BID	PO	For 10 days
+		
Oseltamivir 150 mg BID	PO	For 10 days
+		
Ritonavir + Lopinavir (Kaletra) 500mg [1]	PO	BID for 2 weeks
+		
Azithromycin 500 mg	IV	For 10 days
+		
Antibiotics	IV	As per HMC CAP guidelines#
+		
Tocilizumab [3] For patients with evidence of cytokine release syndrome **(Table 9)**	IV	IV infusion: initial dose of 4–8 mg/kg infused over more than 60 minutes. If initial dose not effective, may administer second dose (in same dosage as initial dose) after 12 hours. No more than 2 doses should be given; maximum single dose is 800 mg and not to be infused in the same line with other medications
±		
Methylprednisolone 40 mg	IV	BID for 5 days

1. A Multi-centre, Double-blinded, Randomized, Placebo-controlled Trial on the Efficacy and Safety of Lopinavir / Ritonavir Plus Ribavirin in the Treatment of Severe Acute Respiratory Syndrome - Full Text View - ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT00578825 (accessed March 16, 2020).
2. Xiaoling Xu, Mingfeng Han, Tiantian Li, Wei Sun, Dongsheng Wang, Binqing Fu, Yonggang Zhou, Xiaohu Zheng, Yun Yang, Xiuyong Li, Xiaohua Zhang, Aijun Pan, Haiming Wei . Effective Treatment of Severe COVID-19 Patients with Tocilizumab [ChinaXiv:202003.00026
3. National Health Commission and State Administration of Traditional Chinese Medicine. Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7). (Mandarin; English translation.) 2020 Mar 3.

Management of community acquired pneumonia (cap) in immuno-competent adults (CG 10015)

Table 1: SAMPLE COLLECTON AND INFECTION CONTROL MEASURES

1. Samples should be collected in negative pressure room (if not available room with HEPA FILTERS) 2. Staff should wear full personal protective equipment PPE (Gown, gloves, N95 mask, face shield (goggles) 3. Combined nasopharyngeal/ oropharyngeal swab is recommended 4. If positive repeat every 7-14 days from the date of sample collection till negative. 5. If negative repeat after 24 hours 6. If 2 consecutive negative isolation can be discontinued

Table 2: Suggested Laboratories for hospitalized patients with confirmed or suspected COVID-19

Baseline investigation	• CBC with diff (esp. total lymphocyte count) • Complete metabolic panel • CPK (creatine kinase) • Ferritin/CRP • D-Dimer • LDH • G6PD level (deficiency) • ECG • HBV serologies (HepBsAb, HepBcAb, and HepBsAg) • HCV antibody • HIV 1/2 Ab/Ag
Recommended daily labs:	• CBC with diff (esp. total lymphocyte count) • Complete metabolic panel • CPK (creatine kinase) • Ferritin/CRP
If clinically indicated:	• Routine blood cultures (2 sets) • For acute kidney injury, send urinalysis and spot urine protein: creatinine • Procalcitonin • IL-6 • QuantiFERON test for patient whom will be started on Tocilizumab.
Radiology	• Chest X-ray • CT chest if clinically indicated

Table 3: use of steroids in COVID-19 patients

Steroid use
when considering patients with sepsis and septic shock for glucocorticoid therapy: • For adult patients with sepsis and septic shock, we suggest not routinely using intravenous glucocorticoid therapy as part of initial therapy • We use glucocorticoid therapy on a case-by-case basis in select patients with refractory shock (defined as a systolic blood pressure <90 mmHg for more than one hour following both adequate fluid resuscitation and vasopressor administration). Follow intensive care recommendations

Table 4: Risk factors for severe disease

Epidemiological	Vital Signs	Labs
1. Older adults Age > 55 2. Patients of all ages with underlying medical conditions, particularly if not well controlled, including: • Patients with chronic lung disease or moderate to severe asthma • Patients who have serious heart conditions • Diabetes with Hb_{A1c} > 7.6% • History of hypertension • Patients with chronic kidney disease undergoing dialysis • Patients with liver disease 3. immunocompromised patients, including cancer treatment, smoking, bone marrow or organ transplantation, immune deficiencies, poorly controlled HIV or AIDS, and prolonged use of corticosteroids and other immunosuppressants 4. Obese patients (body mass index [BMI] of 30 or higher)	1. Respiratory rate > 24 breaths/min 2. Heart rate > 125 beats/min 3. SpO2 ≤ 93% on ambient air 4. PaO2/FiO2 < 300 mmHg	1. D-dimer > 1000 mg/L 2. CPK > twice upper limit of Normal 3. CRP > 100 4. LDH > 245 U/L 5. Elevated troponin 6. Admission absolute lymphocyte count < 0.8 7. Ferritin > 500 ug/L

Table 5: Definition of Uncomplicated upper respiratory tract viral infection:

Definition of Uncomplicated upper respiratory tract viral infection:
Patients with uncomplicated upper respiratory tract viral infection, may have non-specific symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache, muscle pain or malaise. The elderly and immunosuppressed may present with atypical symptoms. These patients do not have any signs of dehydration, sepsis or shortness of breath.

Table 6: Definition of Pneumonia:

Definition of Pneumonia:	
Mild pneumonia	Patient with pneumonia and no signs of severe pneumonia.
Severe pneumonia	Adolescent or adult: fever or suspected respiratory infection, plus one of: - respiratory rate >30 breaths/min - severe respiratory distress, or SpO2 <90% on room air
N.B: CURB65 and/or PSI can be used to assess pneumonia severity	

Table 7: Definition of Sepsis &Septic shock

Definition of Sepsis &Septic shock	
Sepsis	Life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection, with organ dysfunction. Signs of organ dysfunction include altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, or laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate or hyperbilirubinemia.
Septic shock	Persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥65 mmHg and serum lactate level >2 mmol/L.

Table 8: Definition of ARDS

Definition of ARDS
Berlin Definition of ARDS requires that all the following criteria be present for diagnosis: ●Respiratory symptoms must have begun within one week of a known clinical insult, or the patient must have new or worsening symptoms during the past week. ●Bilateral opacities must be present on a chest radiograph or computed tomographic (CT) scan. These opacities must not be fully explained by pleural effusions, lobar collapse, lung collapse, or pulmonary nodules. ●The patient's respiratory failure must not be fully explained by cardiac failure or fluid overload. An objective assessment (eg, echocardiography) to exclude hydrostatic pulmonary edema is required if no risk factors for ARDS are present. ●A moderate to severe impairment of oxygenation must be present, as defined by the ratio of arterial oxygen tension to fraction of inspired oxygen (PaO2/FiO2). The severity of the hypoxemia defines the severity of the ARDS: •**Mild ARDS** – The PaO2/FiO2 is >200 mmHg, but ≤300 mmHg, on ventilator settings that include positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) ≥5 cm H2O. •**Moderate ARDS** – The PaO2/FiO2 is >100 mmHg, but ≤200 mmHg, on ventilator settings that include PEEP ≥5 cm H2O. •**Severe ARDS** – The PaO2/FiO2 is ≤100 mmHg on ventilator settings that include PEEP ≥5 cm H2O.

Table 9: Guidance for Tocilizumab prescription:

- **Studies indicate advanced stage disease responses to β-Coronaviruses including COVID-19 have a high IL-6 cytokine signature.**
- **Send serum IL-6 level prior to giving first dose of tocilizumab**

Establish clinical status to COVID-19	Determine treatment intervention
Grade 1 – mild reaction	No treatment
Grade 2 – moderate reaction, fever, need for IVF (no hypotension), mild oxygen requirement	Send for serum IL-6
Grade 3 – severe, liver test dysfunction, kidney injury, IVF for resuscitation, low dose vasopressor, supplemental oxygen (high flow, BiPAP, CPAP)	Send for serum IL-6; consider Tocilizumab , if no effect can repeat x 2 more doses 12 hours apart; if no response, consider low dose corticosteroids
Grade 4 – life threatening, mechanical ventilation, high dose vasopressor	Send for serum IL-6; consider Tocilizumab if no effect can repeat x 2 more doses 12 hours apart; consider corticosteroid

(adopted and based on the Penn CRS criteria)

N.B: Use for confirmed COVID-19 cases guided by IL-6 level should be prescribed by infectious disease consultant, Consider QuantiFERON test

Table10: Recommendations for Investigational COVID-19 Convalescent Plasma:

Patient inclusion Criteria	• Laboratory confirmed COVID-19 • Patients with ARDS (any severity) with or without septic shock / multiple organ dysfunction • Age ≥to 18 years. • Patient/family member to provide informed consent
Patient exclusion Criteria	• Negative RT-PCR from respiratory secretions or blood within 48 h prior to assessment of eligibility. • History of allergic reaction to blood or plasma products. • Medical conditions in which receipt of 500 mL intravascular volume may be detrimental to the patient (e.g. actively decompensated congestive heart failure). • Severe multi-organ failure, hemodynamic instability. • Other documented uncontrolled infection. • Severe DIC needing factor replacement, FFP, cryoprecipitate. • Expected survival for ≤ 48 hours
Donor inclusion criteria	1- Prior diagnosis of COVID-19 documented by a laboratory test 2- Complete resolution of symptoms at least 28 days prior to donation OR 3- Complete resolution of symptoms at least 14 days prior to donation AND Negative results for COVID-19 either from one or more nasopharyngeal swab specimens or by a molecular diagnostic test from blood 4- Male donors, female donors who have not been pregnant or female donors who have been tested since their most recent pregnancy and results interpreted as negative for HLA antibodies (if needed)
Defined SARS-CoV-2 neutralizing antibody titers	• Defined SARS-CoV2 neutralizing antibody titers, if testing can be conducted (optimally greater than 1:80) • NOTE: If neutralizing antibody titers cannot be obtained in advance, consider storing a retention sample from the convalescent plasma donation for determining antibody titers later.

• COVID-19 Convalescent Plasma, Fresh Frozen, should be frozen within 8 hours after collection, stored at -18C° or colder and have an expiration date one year from the date of collection

Appendix 1: CASE DEFINITION

Suspected case (requires diagnostic testing)	Probable case	Confirmed case
1. Acute respiratory tract infection (Sudden onset of the following: fever ≥37.8C and/or cough and/or shortness of breath) + No other etiology that fully explains the clinical presentation particularly if he/she lives or works in area reporting recent local transmission of COVID-19. OR Close contact with a confirmed or probable COVID-19 case within ≤14 days prior to onset of symptoms OR Recent travel within the previous 14 days OR History of residence in country reporting local transmission of COVID 19 Disease.	Suspected case + inconclusive COVID-19 test	Laboratory-confirmed infection, regardless of signs and symptoms
2. Severe acute respiratory infection (fever ≥37.8C and/or at least one sign / symptoms of respiratory diseases (e.g: cough, fever, shortness of breath) + Requiring hospitalization + No other etiology that fully explains the clinical presentation		
3. Individuals present with any acute respiratory illness including older adults (55 years or more) and individuals with chronic medical conditions and/or an immunocompromised state that may put them at higher risk for poor outcomes (e.g., diabetes, heart disease, receiving immunosuppressive medications, chronic lung disease, chronic kidney disease, cancer) regardless of travel history		
4. Cluster case (2 or more cases with fever of 37.8 and/or respiratory symptoms in a small area such as families, offices, school room etc. within 2 weeks		

Appendix 2: Medication related consideration

Hydroxychloroquine (HCQ)	
Baseline investigation	• G6PD level (deficiency) • ECG
Monitoring recommendations	• Monitor for symptoms or signs of hemolytic anemia including (Hg, Retic#, Retics %, LDH) closely in patient with G6PD deficiency. • Follow up ECG is recommended specially if used concurrently with other medications known to cause QT prolongation.
Common side effects/ contraindication	• QTc Prolongation. • GI symptoms (Anorexia, nausea, vomiting, diarrhea).
Drug-drug interaction	• Major Drug-Drug interaction. **Attention with:** - When HCQ is used with medication that are known to cause QTc prolongation (e.g. Fluoroquinolones, Azithromycin, Ondansetron, metoclopramide, antipsychotics, antidepressants, St. John's wort, and anti-arrhythmic medications) as it needs close monitoring of QTc interval. - When used with anti-Diabetic medications (hypoglycemia).
Lopinavir/Ritonavir (LPV/r) (Kaletra)	
Baseline investigations	• ECG (Increase PR and QTc interval) • LFT
Monitoring recommendations	• Follow up LFT • Follow up ECG is recommended (Use with caution in these with cardiac conduction abnormalities or when used with other medication that have similar effect). • Monitor for bleeding especially if used concurrently with some anticoagulant and anti-platelets.
Most common side effects	• GI Symptoms (nausea, vomiting, diarrhea) • Increase liver enzymes. • Increase PR and QTc interval.
Drug-Drug interaction	• Major Drug-Drug interaction (especially with anti-arrythmia, anticoagulant, anti-platelets, Domperidone)
Oseltamivir	
Common side effects/contraindication	• GI side effects (Diarrhea, Nausea, vomiting), • To reduce Nausea, administer with food. • CNS symptoms (delirium and abnormal behavior)
Drug-Drug interaction	• No major Drug-Drug interaction
Dose adjustment	• Needs dose adjustment based on renal function
Tocilizumab	
Baseline investigations	• Consider QuantiFERON test • CBC • LFT • Lipid profile
Most common side effects	• Injection site reaction • Infusion related reaction • Increase Liver enzymes (AST, ALT, ALP and T-bilirubin) • Neutropenia, thrombocytopenia, leukopenia
Drug-Drug interaction	• Caution with other immune suppressive medication and live attenuated vaccines

*check with your clinical pharmacist

Appendix 3: COVID-19 in special population:

Pregnancy	• Consult obstetrician • The use of therapeutic agents should be guided by individual risk-benefit analysis • Do not use statins • No contraindication to Hydroxychloroquine, Lopinavir/Ritonavir and Tocilizumab • Pregnant women with suspected or confirmed COVID-19 infection should be treated with supportive therapies as described above, considering the physiologic adaptations of pregnancy. • Emergency delivery and pregnancy termination decisions are challenging and based on many factors: gestational age, maternal condition, and fetal stability. Consultations with obstetric, neonatal, and intensive care specialists (depending on the condition of the mother) are essential. • CXR and CT scan Chest can be performed if clinically indicated and after patient consent with appropriate shield
People living with HIV	• Avoid LPV/r monotherapy in people with HIV
If IgG <400	• Consider IVIG at dose of 25 grams x 1 (unclear benefit)
Heart/Liver/Kidney Transplant Recipients	• Consult transplant and transplant ID teams • Consider decreasing Tacrolimus/Cyclosporine by 50%, • Stop Mycophenolate and Azathioprine in kidney/liver transplant patients and reduce dose by 50% in heart transplant patients. • For Kidney transplant patients approximate target Tacrolimus level 3-5 ng/ml, Cyclosporine level target 25-50 ng/ml. • Critical illness – in liver and kidney – stop all immunosuppressants except for Prednisone if they are on it at baseline
Lung transplant recipients	• Consult transplant and transplant ID teams • No change to usual immunosuppression (avoids high levels, tailor to patient) • For all those in ICU or with lower respiratory tract disease (most inpatients): pulse Methylprednisolone 125mg IV q 12 hours