D0

- Viral Replication
- Primary immune response
- Polisegmentar Infarct Pneumonia

D5-D7

- "cytokine STORM" / ARDS
- Thromboembolic complications / MODS
- Bacterial complications

Lymphocytes (abs < 0.8)
Neutrophil to Lymphocyte Ratio (NLR) > 3

Antiviral Reduce initial viral replication	High risk • Remdesivir 200mg stat then 100mg IV OD 5/7	Start within first 72hrs of symptoms. Duration up to 5 days High risk group - Age > 65 y.o. - DM, HBP, Obesity - Other comorbidities
Reduce affinity to receptors	• Spironolactone 50mg PO OD 2/52	Inhibits TMPRSS2 and ACE2 Receptors ↓ Testosterone level ↓ Lungs congestion (diuretic)
Antithrombotic	Low risk • ASA 300mg PO OD *or* • Clopiwin 75/75 PO OD High risk • Clexane 40 – 60mg s/c OD *or* • Xarelto 10 – 15mg PO OD	Correction in renal failure if eGFR < 30ml/m2 Clexane 20-30mg OD *or* Heparin 5000-7500 IU s/c BD/TDS
Antibiotics	• Augmentin 1000mg PO BD 7/7 • Azithromycin 500mg PO OD 3/7	From Day 3 if signs of bacterial infection
General treatment	• Colchicine 1mg stat then 0.5mg PO BD 5/7 • Vitamin C 1g PO OD 2/52 • Vitamin D 50 000IU PO weekly or 4000IU PO OD • Zinc 20mg PO OD 2/52 • ACC 200 (Effervescent) 1 tab (200mg) PO TDS	Reduces symptoms but not mortality Stop all immune boosters from D6 if "cytokine storm" Avoid nephrotoxic drugs, re-consider Colchicine after D7

Increased O_2 demand (reduced SpO_2)
Increased LDH; increased CRP; increased PCT

- **Steroids**

From > Day 5 if deterioration: increase in O_2 demand / decrease in SpO_2; CRP > 20; LDH > 250

CRP	Dexamethasone OD (Methylprednisolone)	Adjustments
20 – 75	6 – 12mg **(30-60mg)**	- For 10 days - Increase to 20mg OD if CRP increase; LDH increase or increase in O_2 demand
> 75	20mg **(160mg)**	Wean by 4mg every 3 days till 10mg Change to "**Pulse therapy**" if CRP and LDH not responding or **Tocilizumab + Dexamethasone**

Good response if about 50% reduction in CRP after first dose of steroids
If no improvement within 24 hrs or deterioration:

- **Methylprednisolone** (Pulse therapy)

Elderly: 500mg IV OD Young: 1000mg IV OD 3/7, tap down by 50% every 3 days
Young patients requiring higher steroids dose than elderly OR
- **Tocilizumab (Actemra)** 8mg/kg (600 – 800mg) **IVI stat**, + **Dexamethasone 8 - 12mg OD** for 10 /7
- PCT must be < 0.5 CRP > 100
- Patient not on invasive ventilation
- No renal or Hepatic failure

Blocks LH6 receptors for 6/52 – risk of severe sepsis, despite SpO2 improvement.
LDH and WCC are septic markers after Actemra treatment NOT CRP and PCT
Antibiotics to be escalated to maximum and continue for 2 weeks.

- **Antithrombotic**

- Clexane 0.5mg/kg BD (30-50mg BD) or 1mg/kg OD (increase to 1mg/kg BD if thrombotic) *or*
- Xarelto 15-20mg PO OD
- Heparin 5000 – 7500 IU s/c TDS if eGFR < 30ml/m^2

- **Antibacterial and Antifungal cover**

PCT, CRP or WCC and β D glucan, CD_4 and culture guided

- **Respiratory support**

Face mask - Rebreathing mask – HFNC – CPAP - Vent

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From D5

- "Cytokine STORM" ARDS
- Thromboembolic complications (MODS)
- Bacterial complications

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Initial Steroids Dose						
Presentation		**Lab results CRP (excl. sepsis)**			**Age**	
On O2 mask	**CPAP needed**	**20 - 75**	**75 - 125**	**> 125**	**< 65**	**> 65**
1	**2**	**1**	**2**	**3**	**2**	**1**

Total score	**≤ 3**	**4 – 5**	**≥ 6**
Recommended initial dose	**Dexamethasone 6 - 12mg or**	**Dexamethasone 16 - 24mg or**	**Actemra 600 - 800mg IV stat + Dexamethasone 8mg or**
	Methylprednisolone 40mg	**Methylprednisolone 160mg**	**Methylprednisolone 500 - 1000mg**

(ref Alexandr Polishchuk and ICU WCH team 2021)

1) Good response consider if about 50% reduction in CRP after first dose of steroids. Maintain the same dose at least 3/7
2) Re-evaluate after 24hrs: adjust the dose if no response.
3) Consider higher dose in young patients

Name: ..... DOB: ..... Unit Number: .....

COVID-19 Care Plan

TREATMENT PROTOCOL FOR COVID-19

7) Guidance on new IL-6 inhibiting therapies

*As of February 2021, the Department of Health has supported the use of two new IL-6 inhibiting drugs for the treatment of COVID-19; **TOCILIZUMAB** and **SARILUMAB***.*

TOCILIZUMAB is suitable for adult inpatients who meet **ALL** of the following criteria:

- ☐ Patient has confirmed COVID-19 on PCR
- ☐ Patient is already receiving dexamethasone
- ☐ Patient has a CRP result of >75mg/L
- ☐ Patient is requiring > 40% oxygen to maintain saturations > 92%
  OR is within first 24-48 hours of starting invasive ventilation, CPAP or NIV
- ☐ Decision to prescribe is made only by a Medical Consultant

If patient does not meet above oxygen criteria but Medical consultant believes potential benefits of Tocilizumab outweigh risk please contact Infectious Diseases Consultant (on call for referrals 9-5 Mon – Fri and 9-1 Sat and Sun) to discuss. Please ensure that patient is not considered to have serious underlying bacterial infection and is not prescribed intravenous antibiotics prior to discussing.

Dose and prescribing Information:

Dose is 8mg/kg IV up to a **maximum dose of 800mg**, given as a **SINGLE ONE-OFF DOSE**.

This should be diluted in 100mls of 0.9% sodium chloride (expelling any excess 0.9% sodium chloride to make 100mls volume total) given over 1 hour. Dexamethasone should be continued as usual. Tocilizumab should not be infused through an IV line at the same time as any other medications.

Cautions, considerations and contra-indications:

- Tocilizumab is contra-indicated if ANY of the following biochemical abnormalities; ALT or AST >5x upper limit of normal, neutropenia (<2.0) or thrombocytopenia (<50)
- Caution should be used in patients who may otherwise be immunosuppressed
- Caution should be used if clear evidence of a bacterial, fungal, viral or other infection besides COVID-19, including active tuberculosis, HIV or Viral Hepatitis
- Tocilizumab should be avoided in pregnancy, and used with extreme caution if patient breast-feeding (in which case, patient should not breast-feed for a period of 7 weeks after dose)
- Be aware hypersensitivity/allergic reactions are possible, and any adverse events should be reported to the MHRA by the dedicated COVID-19 Yellow Card Reporting Site.

TOCILIZUMAB given? Yes ☐ No ☐ Pending ☐

Note: Because of its immunosuppressant effects, any patient who receives **TOCILIZUMAB** should have this **specifically communicated to the GP in their discharge letter**. For example: *"This patient was given Tocilizumab to treat COVID-19 on [date]. This may make them more prone to other infections, and falsely depress CRP levels, in the short term".*

***SARILUMAB** is not yet available at UHNM.*

	Oxygen Therapy	Non-invasive CPAP/ BiPAP	Invasive Ventilation
Indications	- "Silent" or "happy hypoxic" - Sats < 90% on room air	- Sats < 86% on 15L Rebreather - Increased Work of Breathing and tiredness	- Reduced level of consciousness - Confused state or agitation
Initial Settings	FiO_2 Facemask oxygen = 0.4 Rebreather = 0.8 (at 15L/min) Encourage self-proning	- PEEP 7 → 10 → 12cm H_2O - FiO_2 1.0 → reduce when SpO_2 improving - P_{sup} 0-5 (V_t 6-8ml/kg) - Trigger 1 – 4 - "Self-proning"	- Peak 30 (34 in obese) - ΔP = Peak – PEEP <15 (keep V_t 4-6ml/kg IBW) - PEEP 7-20 Cstatic / ARDS Not protocol guided - FiO_2 1.0 → reduce when SpO_2 improving - RR 15 I:E 1:1.5 - Trigger 1-4L
Sedation	Melatonin 10mg nocte	- "Comfort Sedation" (see sedation recommendation) Lorazepam 1-2mg + Sulpiride 400mg PO Tramadol 50mg IVI/IMI BD to TDS Phenergan 25-50 mg PO/IM Morphine 1mg IV PRN or 1-2mg/hr IV infusion Zolpidem 5 - 10mg OD/BD Risperidon 2 - 4mg OD/BD Amitriptillin 25mg OD/BD Psychological support	<u><3 days</u> - Standard sedation or "Ketofol" - Precedex or Clonidine <u>>3 days</u> Keep RASS-1 – 3 Lorazepam NGT/IVI and Sulpiride Phenobarbital Load 5 - 10mg/kg Maintain 1 - 2mg/kg/day PO/IV BD **See sedation protocol** **Sedation might not provide synchronization**
Synchronization		With Trigger (pressure or flow)	**Keep on muscle relaxants first 48 - 72hrs** (to avoid self-inflicted lung injury) - Rocuronium / Atracurium - Bolus 0.5mg/kg (slowly) - Infusion 0.5mg/kg/hr Neat solution (Weight/10)÷2 = ml/hr
Target	**SpO_2 > 88%** **pCO_2 - permissive hypercapnia providing pH>7.2** **ESCALATE STEROIDS!!!** **Young patients requiring higher steroids dose than elderly**		

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