**REMAP-CAP Eligibility Checklist**

No

Yes

**Admitted to ICU**

**Eligibility check (section 2):**

**Antiplatelet**

**Platform eligible (Section 1)**

**Eligibility check (section 3):
Immune modulation
Antiplatelets**

**Anticoagulation**

**Vitamin C**

**Simvastatin**

**ACE2/RAS**

**Antibiotics and Macrolides**

**Domains where the exclusion is 24hours since ICU admission:**

Immune modulation domain

Vitamin C domain

**Domains where the exclusion is 48hours since ICU admission / organ support:**

Antiplatelet

Simvastatin

Anticoagulation

ACE2/RAS severe state

Antibiotics and Macrolides

|  |  |  |
| --- | --- | --- |
| **Section 1** |  |  |
| **Overall Platform** |  |  |
|  |  |  |
| **Inclusion** | **Yes** | **No** |
|  |  |  |
| Is the patient over 18yrs | □ | □ |
| COVID-19 is suspected by the treating clinician or has been confirmed by microbiological testing | □ | □ |
| Microbiological testing for SARS-CoV-2 infection of upper or lower respiratory | □ | □ |
|  |  |  |
| **Exclusion** |  |  |
|  |  |  |
| Death is deemed to be imminent or inevitable during the next 24 hours **AND** one or more of the patient, substitute decision maker or attending physician are not committed to full active treatment  | □ | □ |
| Admission to hospital over 14 days ago with acute COVID illness | □ | □ |
| Expected to be discharged from hospital today or tomorrow | □ | □ |
| Previous participation in this REMAP within the last 90 days | □ | □ |

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| **Section 2** |  |  |
| **REMAP-CAP Eligibility Checklist Ward Based** |  |  |
| **Antiplatelet domain** |  |  |
|  |  |  |
| **Inclusion** | **Yes** | **No** |
|  |  |  |
| Platform eligible (points as above) | □ | □ |
| COVID-19 is suspected by the treating clinician or has been confirmed by microbiological testing | □ | □ |
| Microbiological testing for SARS-CoV-2 infection of upper or lower respiratory tract | □ | □ |
|  |  |  |
| **Exclusion** |  |  |
|  |  |  |
| Clinical or laboratory bleeding risk or both that is sufficient to contraindicate anticoagulation, including intention to continue or commence dual anti-platelet therapy   | □ | □ |
| Patient is already receiving antiplatelet treatment or NSAID, or a clinical decision has been made to start antiplatelet or NSAID therapy  | □ | □ |
| Enrolment in a trial evaluating anticoagulation or antiplatelet therapy for proven or suspected COVID-19 infection, where the protocol of that trial requires continuation of the treatment assignment specified in that trial   | □ | □ |
| Patients otherwise eligible for the Therapeutic Anticoagulation domain will be excluded from the Antiplatelet domain if they are over 75yrs  | □ | □ |
| Creatinine clearance of <30ml/min or receiving renal replacement therapy or ECMO   | □ | □ |
| Known hypersensitivity  | □ | □ |
| The treating clinician believes that participation in the domain would not be in the best interests of the patient   | □ | □ |
| **P2Y12 Intervention specific exclusion**Known or suspected to be Pregnant  | □ | □ |

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| **Section 3** |  |  |
| **REMAP-CAP Eligibility Checklist ICU** |  |  |
| **COVID-19 Immune modulation domain** |  |  |
|  |  |  |
| **Inclusion** | **Yes** | **No** |
|  |  |  |
| Platform eligible (points as above) | □ | □ |
| Admitted to ICU  | □ | □ |
|  |  |  |
| **Exclusion** |  |  |
|  |  |  |
| >24 hours since ICU admission  | □ | □ |
| Patient has already received any form of IFN or anakinra, or is on long-term therapy with any of these agents prior to hospital admission | □ | □ |
| Known condition/treatment resulting in ongoing immune suppression including neutropaenia *(clinically judged threshold)* prior to this hospitalisation  | □ | □ |
| Patient has been randomised in a trial evaluating an immune modulation agent for proven or suspected COVID-19 infection* where the protocol of that trial requires ongoing administration of study drug
 | □ | □ |
| The treating clinician believes that participation in the domain would not be in the best interests of the patient   | □ | □ |
| **Receiving intervention exclusion criteria**  |  |  |
| Known hypersensitivity | □ | □ |
| Receiving an agent specified as an intervention as a usual medication prior to this hospitalization | □ | □ |
| Intention to prescribe systemic corticosteroids for any reason other than participation in the Corticosteroid DSA (excluded from Interferon) | □ | □ |
| Known sensitivity to proteins produced by E. coli (anakinra) | □ | □ |
| Pregnancy / breastfeeding (anakinra, IFN-β1a, tocilizumab, sarilumab) | □ | □ |
| Baseline ALT or AST more than 5x upper limit of normal (tocilizumab, sarilumab) | □ | □ |
| Baseline platelet count <50 x 109/L (tocilizumab, sarilumab)  | □ | □ |

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| **Antiplatelet domain** |  |  |
|  |  |  |
| **Inclusion** | **Yes** | **No** |
|  |  |  |
| Platform eligible (points as above) | □ | □ |
| Admitted to ICU  | □ | □ |
|  |  |  |
| **Exclusion** |  |  |
|  |  |  |
| >48 hours since ICU admission  | □ | □ |
| Clinical or laboratory bleeding risk or both that is sufficient to contraindicate therapeutic anticoagulation, including intention to continue or commence dual anti-platelet therapy   | □ | □ |
| Patient is already receiving antiplatelet treatment or NSAID, or a clinical decision has been made to start antiplatelet or NSAID therapy  | □ | □ |
| Enrolment in a trial evaluating anticoagulation or antiplatelet therapy for proven or suspected COVID-19 infection, where the protocol of that trial requires continuation of the treatment assignment specified in that trial   | □ | □ |
| Patients otherwise eligible for the Anticoagulation domain will be excluded from the Antiplatelet domain if they are over 75yrs old   | □ | □ |
| Patients receiving Prior Therapeutic Anticoagulation  | □ | □ |
| Creatinine clearance of <30ml/min or receiving renal replacement therapy or ECMO | □ | □ |
| Known hypersensitivity  | □ | □ |
| The treating clinician believes that participation in the domain would not be in the best interests of the patient  | □ | □ |
| **P2Y12 Intervention specific exclusion**Known or suspected to be Pregnant  | □ | □ |

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| --- | --- | --- |
| **Anticoagulation domain** |  |  |
|  |  |  |
| **Inclusion** | **Yes** | **No** |
|  |  |  |
| Platform eligible (points as above) | □ | □ |
| Admitted to ICU  | □ | □ |
|  |  |  |
| **Exclusion** |  |  |
|  |  |  |
| >48 hours since ICU admission  | □ | □ |
| Clinical indication to commence or continue therapeutic dose anticoagulation (not as part of REMAP-CAP Therapeutic Anticoagulation group)   | □ | □ |
| Intention to continue or commence dual antiplatelet therapy | □ | □ |
| Enrolment in a trial evaluating anticoagulation for proven or suspected COVID-19 infection, where the protocol of that trial requires continuation of the treatment assignment specified in that trial  | □ | □ |
| Known or suspected previous adverse reaction to UFH or LMWH including heparin induced thrombocytopenia (HIT).  | □ | □ |
| The treating clinician believes that participation in the domain would not be in the best interests of the patient  | □ | □ |
| **Prior Therapeutic Anticoagulation Group exclusions** |  |  |
| Clinical or laboratory bleeding risk or both that is sufficient to contraindicate continuation of therapeutic dose anticoagulation with heparin  | □ | □ |
| **No Prior Therapeutic Anticoagulation Group exclusions** |  |  |
| Clinical or laboratory bleeding risk or both that is sufficient to contraindicate intermediate dose thromboprophylaxis  | □ | □ |
| The patient is receiving non-heparin anticoagulation medication (such as a direct acting oral anticoagulant) and the treating clinician believes that cessation and substitution with conventional low-dose thromboprophylaxis is either inappropriate or not possible  | □ | □ |

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| **Vitamin C Therapy** |  |  |
|  |  |  |
| **Inclusion** | **Yes** | **No** |
|  |  |  |
| Platform eligible (points as above) | □ | □ |
| Admitted to ICU | □ | □ |
|  |  |  |
| **Exclusion** |  |  |
|  |  |  |
| >24 hours since ICU admission  | □ | □ |
| Patient has received any intravenous vitamin C during this hospitalisation (unless incorporated into parenteral nutrition)   | □ | □ |
| Any of the following 3 contraindications to Vitamin C therapy: |  |  |
| * Known glucose-6-phosphate dehydrogenase (G6PD) deficiency

  | □ | □ |
| * Known allergy to vitamin C
 | □ | □ |
| * Known history of symptomatic kidney stones within the past year
 | □ | □ |
| Patient has been randomised to a trial evaluating vitamin C, where the protocol of the trial requires ongoing administration of the study drug   | □ | □ |
| The treating clinician believes that participation in the domain would not be in the best interests of the patient   | □ | □ |

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| **Simvastatin Therapy** |  |  |
|  |  |  |
| **Inclusion** | **Yes** | **No** |
|  |  |  |
| Platform eligible (points as above) | □ | □ |
| Admitted to ICU | □ | □ |
|  |  |  |
| **Exclusion** |  |  |
|  |  |  |
| >48 hours since ICU admission  | □ | □ |
| Known severe liver disease  | □ | □ |
| Known hypersensitivity to simvastatin  | □ | □ |
| Creatinine more than 200µmol/L (2.26mg/dL) and not receiving renal replacement therapy   | □ | □ |
| Current treatment with medicine that cannot be co-administered with simvastatin   | □ | □ |
| Current treatment with any statin or treating clinician intends to commence treatment with any statin   | □ | □ |
| Pregnant or breastfeeding.  | □ | □ |
| The treating clinician believes that participation in the domain would not be in the best interests of the patient   | □ | □ |

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| **ACE/RAS2** |  |  |
|  |  |  |
| **Inclusion** | **Yes** | **No** |
|  |  |  |
| Platform eligible (points as above) | □ | □ |
| Admitted to ICU | □ | □ |
|  |  |  |
| **Exclusion** |  |  |
|  |  |  |
| >48 hours since ICU admission in severe state or >96hrs in moderate state  | □ | □ |
| Patient is already receiving, or a clinical decision has been made to commence, an ACEi, ARB, direct renin inhibitor, angiotensin-receptor-neprilysin inhibitor, or chemokine receptor modulator  | □ | □ |
| Long-term therapy prior to this hospital admission with one or more of ACEi, ARB, direct renin inhibitor, angiotensin-receptor-neprilysin inhibitor, or chemokine receptor modulator  | □ | □ |
| Known hypersensitivity to ACEi or ARB, including angioedema  | □ | □ |
| Treating clinician believes that administration of ACEi or ARB is inappropriate because of risk for:  |  |  |
| * Clinically relevant hypotension or escalation of vasopressor requirements
 | □ | □ |
| * Hyperkalemia
 | □ | □ |
| Known severe renal artery stenosis  | □ | □ |
| Patient is known or suspected to be pregnant or breastfeeding  | □ | □ |
| Renal impairment with creatinine clearance < 30 ml/min or receiving renal replacement therapy  | □ | □ |
| Enrollment in another trial evaluating ACEi, ARB, or other RAS modulator, or any targeted chemokine receptor modulation for proven or suspected COVID-19 infection, where the protocol of that trial requires continuation of the treatment assignment specified in that trial  | □ | □ |
| If the domain is available at this site in the Moderate State and the patient is being assessed in the Severe state, prior assessment for this domain in the Moderate State  | □ | □ |
| The treating clinician believes that participation in the domain would not be in the best interests of the patient  | □ | □ |
| **ARB + DMX-200 specific exclusions**Known severe liver disease or an alanine aminotransferase or an aspartate aminotransferase that is more than 5 times the upper limit of normal  | □ | □ |
| Known viral hepatitis  | □ | □ |
| Hypersensitivity to repagermanium  | □ | □ |

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| **Antibiotics and Macrolides** |  |  |
|  |  |  |
| **Inclusion** | **Yes** | **No** |
|  |  |  |
| Adult patient admitted to ICU for severe CAP / suspected /confirmed COVID 19 within 48 hours of hospital admission with:  | □ | □ |
| Symptoms or signs or both that are consistent with lower respiratory tract infection   | □ | □ |
| **AND** radiological evidence of new onset infiltrate of infective origin  | □ | □ |
| Up to 48 hours after ICU admission, receiving organ support with one or more of: |  |  |
| Non-invasive / invasive ventilatory support  | □ | □ |
| Receiving infusion of vasopressor or inotropes or both  | □ | □ |
|  |  |  |
| **Exclusion** |  |  |
|  |  |  |
| Received more than 48hours of intravenous antibiotic treatment for this index illness   | □ | □ |
| Known hypersensitivity to the study drugs  | □ | □ |
| A specific antibiotic is indicated  | □ | □ |
| Known hypersensitivity to ACEi or ARB, including angioedema  | □ | □ |
| * 1. Microbiological confirmation or suspicion of Legionella / atypical pneumonia
	2.
 | □ | □ |
| Macrolide antibiotics have already been discontinued for more than 36hours   | □ | □ |
| The treating clinician believes that participation is not in the best interest of the Patient  | □ | □ |

For sites that are also involved in the RECOVERY study the following apply:-

**COVID 19 interventions**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  |  |  | **RECOVERY** |
|  |  | Standard care | Azithro | +Toci | MonoclonalAntibody |  Baricitinib | Colchicine | Aspirin |
|  | Immune modulation domain | Y | Y | X | Y | N | Y | Y |
|  | Antiplatelet domain | Y | Y | Y | Y | Y | Y | X |
|  | Anticoagulation | Y | Y | Y | Y | Y | Y | Y |
|  | Vitamin C | Y | Y | Y | Y | Y | Y | Y |
|  | Simvastatin | Y | Y | Y | Y | Y | Y | Y |
|  | ACE2/RAS | Y | Y | Y | Y | Y | Y | Y |

**RECOVERY is a mainly ward-based study. As RECOVERY patients get sicker and are transferred to ICU, they can then be randomised to REMAP-CAP, if judged clinically appropriate.**

**RECOVERY patient randomised to Tocilizumab = Patient cannot be enrolled into REMAP-CAP immune modulation domain. Patient can be randomised to antiplatelet, anticoagulation, ACE2 RAS, Vitamin C and simvastatin domains.**

**RECOVERY patient randomised to Monoclonal Antibody therapy = Patient can be randomised immune modulation, antiplatelet, anticoagulation, ACE2 RAS, Vitamin C and simvastatin domains.**

**RECOVERY patient randomised to Baricitinib = Patient can be randomised antiplatelet, anticoagulation, ACE2 RAS, Vitamin C and simvastatin domains.**

**RECOVERY patient randomised to Aspirin therapy = Patient cannot be enrolled into REMAP-CAP antiplatelet domain. Patient can be randomised to immune modulation, anticoagulation, ACE2 RAS, Vitamin C and simvastatin domains.**

**RECOVERY patient randomised to Colchicine therapy = Patient can be randomised to immune modulation, anticoagulation, ACE2 RAS, Vitamin C and simvastatin and antiplatelet domains.**

**Please also be aware, this co-enrolment strategy should only be considered if patients have been included in RECOVERY on the ward and then deteriorate clinically to require ICU admission. Patients should not be randomised to both trials while already admitted to ICU. So, if included in REMAP-CAP they should not then be randomised in RECOVERY.**