## Supplement 2: Table summarising UK and available international guidelines for PIMS-TS published prior to July 29<sup>th</sup> 2020

| Source<br>(Hospital or<br>network)                         | Date<br>published<br>(2020) | Туре  | Process                   | Antiviral                                      | IVIG  | Glucocorticoids  | Biologics  | Antiplatelet  | Anticoagulation   |
|--|-----------------------------|---|---------------------------|--|---|--|--|---|---|
| Nottingham   | 4 May                       | Internal  | MDT                       |  | If KD   | MP 30mg/kg 3 days<br>if KD or severe or<br>IVIG resistant (all<br>PICU patients) | Anakinra if IL-1<br>raised or MAS<br>features<br>Tocolizumab if<br>IL-6 raised | If coronary involvement                                     | If coronary<br>involvement  |
| Evelina London   | 11 May                      | Internal,<br>available online                   | MDT                       |  | 2g/kg   | MP 3-10mg/kg OD<br>3 days  | Consider   | High dose<br>Aspirin  | LMWH prophylaxis  |
| Manchester   | 12 May                      | Internal  | MDT                       |  | 2g/kg   | All shocked patients<br>MP 10 – 30mg/kg<br>OD (max 1g) for<br>three days         | Discuss with rheumatology if no improvement with IVIG or MP                    | High dose if KD   |   |
| North Thames Paediatric Network (St Mary's)                | 19 May                      | Internal,<br>available online                   | MDT from multiple centres | Consider if PCR positive                       | Yes   | yes  | No mention   | Low dose aspirin  | LMWH  |
| Leeds  | 22 May                      | Internal  | MDT                       |  | 2g/kg<br>Repeat dose if<br>poor response 48<br>hours                | Consider MP 10-<br>30mg/kg   | MDT to consider  | Aspirin 5mg/kg<br>(max 75mg) but<br>12.5mg/kg QDS<br>if KD  | GCS if non- mobile.<br>Consider LMWH if<br>not on high dose<br>aspirin    |
| St George's  | 26 May                      | Internal,<br>available online                   | MDT                       | Consider                                       | Consider  | Consider   | No mention   | Consider (no dose)  | Consider heparin  |
| Great Ormond<br>Street                                     | 28 May                      | Internal  | MDT                       |  | Consider 1 or 2g/kg   | Consider MP (10-<br>30mg/Kg OD, max<br>1g)                                       | Discuss<br>Anakinra,<br>Infliximab,<br>Tocilizumab                             | High dose aspirin<br>30mg/kg/day<br>then 3-<br>5mg/Kg/day   | LMWH  |
| Oxford   | May                         | Internal  | MDT                       |  | 2g/kg if KD   | Consider 10mg/kg<br>MP if TSS, give if<br>refractory to IVIG                     | Consider if refractory to treatment  | Aspirin (no dose)   | Advised (not specified)   |
| Birmingham/<br>KIDS intensive<br>care transfer<br>service  | May                         | Internal,<br>available online                   | MDT                       |  | 2g/kg   | 10mg/kg IV MP up<br>to 30mg/kg max 1g  | Consider<br>Infliximab or<br>Anakinra  | Aspirin<br>12.5mg/kg QDS<br>until afebrile then<br>2-5mg/kg |   |
| UK PIMS-TS<br>National<br>Consensus<br>Management<br>Group | 23 July                     | Pre-peer review <sup>1</sup> , available online | Delphi                    | Consider<br>Remdesivir if<br>PCR positive      | 2g/kg<br>Consider 2 <sup>nd</sup><br>dose if not fully<br>responded | Enrol RECOVERY<br>trial<br>if high risk or<br>unwell 24 hours post<br>IVIG       | Enrol<br>RECOVERY<br>trial, consider if<br>no response                         | Low dose aspirin<br>or high dose if<br>KD                   | GCS if >12 years  |
| King's College   | July                        | Internal  | MDT                       |  | 2g/kg   | All patients with<br>shock- variable<br>dosing                                   | Consider   | All<br>Dose by MDT  | LMWH  |
| Leicester<br>Children's                                    | July                        | Internal,<br>available online                   | MDT                       | Consider if PCR positive and in Recovery trial | KD complete or incomplete criteria                                  | Resistant or refractory disease  | No mention   | Aspirin (no dose)   | Heparin if critical<br>illness. Consider:<br>mild/moderate cases<br>or KD |
| Cardiff, Wales   | July                        | Internal  | MDT                       |  | 2g/kg   | MP at 48 hours if culture negative   | At 96h<br>Infliximab,<br>Anakinra,<br>Tocilizumab via<br>RECOVERY<br>trial     | Aspirin (no dose)   |   |
| Cambridge  | July                        | Internal  | MDT                       |  | 2g/kg   | MP 10mg/kg to<br>30mg/kg (max 1g)  | Discuss<br>Anakinra,<br>Infliximab,<br>Tocilizumab                             | 12.5mg/kg QDS<br>Aspirin                                    | LMWH  |

| Available international guidance     |         |  |                    |                                |  |   |                                  |   |   |  |
|--------------------------------------|---------|--|--------------------|--------------------------------|--|---|----------------------------------|---|---|--|
| University of<br>Buffalo, New York   | 23 May  | Publication as editorial <sup>2</sup> , not peer reviewed. | MDT and CDC advice |                                | All patients<br>2g/kg                                    | ALL PICU patients High dose MP Consider if KD   | Consider                         | Aspirin if KD                                 | LMWH  |  |
| Children Hospital<br>of Philadelphia | 8 July  | Internal online  | Not reported       | Not indicated<br>even if PCR + | 2g/kg  | Oral prednisolone<br>2mg/kg/day or IV<br>MP 1mg/kg /dose<br>BD                        |                                  | Aspirin 3-5mg/kg<br>OD if coronary<br>ectasia | LMWH  |  |
| American College<br>of Rheumatology  | 23 July | Peer reviewed publication <sup>3</sup>                     | Delphi             |                                | Consider 1-2g/kg<br>but slow if poor<br>cardiac function | MP 1-2g/kg with<br>non-mild illness<br>(shock). Consider<br>higher doses with<br>LTC. | Advise Anakinra<br>if refractory | 3-5mg/kg if f KD or thrombocytosis            | LMWH if coronary<br>aneurysm (z<br>score>10) or<br>moderate LV<br>dysfunction |  |

Blank boxes indicate that guideline does not mention therapy

## Abbreviations

MDT multidisciplinary team consensus; CDC Centers for Disease Control and prevention, USA; PCR polymerase chain reaction for SARS-2-CoV; RECOVERY trial Randomised Evaluation of COVID-19 thERapY (https://doi.org/10.1186/ISRCTN50189673); KD Kawasaki disease features; OD once daily; MP methylprednisolone; TSS toxic shock syndrome features; LTC life threatening complications: KD kawasaki disease phenotype; TSS toxic shock syndrome; LMWH Low molecular weight heparin prophylaxis; GCS Graduated compression Stocking; LV left ventricle

## References

- 1: Harwood R, Allin B, Jones CE, et al. For and on behalf of the PIMS-TS National Consensus Management Study Group. A national consensus management pathway for Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-CoV-2 (PIMS-TS): The results of a national Delphi process. Pre print BMJ. https://doi.org/10.1101/2020.07.17.20156075
- 2: Hennon T, Penque M, Hicar M et al. COVID-19 associated Multisystem Inflammatory Syndrome in Children (MIS-C) guidelines; a Western New York approach Prog Pediatr Cardiol. 2020 May 23: 101232.doi: 10.1016/j.ppedcard.2020.101232.
- 3: Henderson LA, Canna SW, Friedman KG, et al. American College of Rheumatology Clinical Guidance for Pediatric Patients with Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with SARS-CoV-2 and Hyperinflammation in COVID-19. Version 1 [published online ahead of print, 2020 Jul 23]. Arthritis Rheumatol. 2020;10.1002/art.41454. doi:10.1002/art.41454