Online Supplemental Material

Cardiac Assessment and Inflammatory Markers in Children with Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-CoV2 (PIMS-TS) treated with Methylprednisolone Versus Intravenous Immunoglobulins: Longitudinal follow-up of the randomized controlled Swissped RECOVERY Trial.

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**Supplemental Table Legends**

**Supplemental Table 1. Follow-up protocol of the Swissped Recovery Trial.** Note, that echocardiographic and electrocardiographic, haematological, and biochemical examinations were ordered at the discretion of the treating physician and not per protocol.

**Supplemental Table 2.** **Follow-up data: Cardiac assessment on the early, intermediate, and late Follow-up (FU) in the IVIG and MPS group.** Interquartile range (IQR) displaying Q1-Q3, i.e., the 25th to 75th percentile. Note, that children in apparently good health were not examined by repeated echocardiographic examinations and have correspondingly been marked with N.A. CAA: Coronary artery aneurysm. N.A. not applicable.

**Supplemental Table 3. Follow-up data: Laboratory parameters during early, intermediate, and late FU in the IVIG and MPS group.** Note, that children in apparently good health did not receive serial blood tests and have correspondingly been marked with N.A.

ALT: Alanine-aminotransferase, CRP: C-reactive protein, N-terminal pro-B-type natriuretic peptide: NT-proBNP. N.A. not applicable.

**Supplemental Figure Legends**

**Suppl. Figure 1. Cardiac FU examinations: Biochemical assessment.** Results of laboratory analyses during the FU in children with PIMS-TS treated with IVIG or MPS as per protocol. **(A, B)** Box Whisker Plots displaying the serum concentrations of **(A)** NT-proBNP, and **(B)** Troponin at the indicated time points. Note, that we omitted the Whisker Box Plots in cases where ≤ 5 measurements were available.

**Suppl. Figure 2. Haematological FU examinations: Resolution of inflammation.** Results of laboratory analyses during FU in children with PIMS-TS treated with IVIG or MPS as per protocol. **(A-C)** Box Whisker Plots displaying the serum concentrations of **(A)** neutrophil count, **(B)** lymphocyte and **(C)** thrombocyte count at the indicated time points.

**Suppl. Figure 3. Biochemical FU examinations: Resolution of inflammation.** Results of laboratory analyses during FU in children with PIMS-TS treated with IVIG or MPS as per protocol. **(A-C)** Box Whisker Plots displaying the serum concentrations of **(A)** C-reactive protein (CRP), **(B)** D-Dimer and **(C)** ferritin at the indicated time points.

**Suppl. Figure 4. Biochemical FU examinations: Liver function test.** Results of laboratory analyses during the FU in children with PIMS-TS treated with IVIG or MPS as per protocol. **(A, B)** Box Whisker Plots displaying the serum concentrations of **(A)** albumin and **(B)** Alanin-Aminotransferase (ALT) at the indicated time points.

**Supplemental Table 1.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Early FU (week 1-3)**  | **Intermediate FU (week 4 - 8)**  | **Late FU (week 9 - month 6 )**  | **Any FU** |
| **Days in trial** | **After discharge** |
| **Clinical Assessment** |   |   |   |   |
| **Acute and past medical history** | ü | ü | ü |   |
| **Vital signs** | ü | ü | ü |   |
| **Disposition / outcome** | ü | ü | ü |   |
| **Quality of Life Assessments** |   |   | ü |   |
| **Vaccine questionnaire** |   |   | ü |   |
| **Laboratory Assessment** |  |  |  |   |
| **Haematology** | (ü) | (ü) | (ü) |   |
| **Biochemistry** | (ü) | (ü) | (ü) |   |
| **Cardiac Assessment** |  |  |  |   |
| **Echocardiography** | (ü) | (ü) | (ü) |   |
| **Electrocardiogram (ECG)** | (ü) | (ü) | (ü) |   |
|  |   |   |   |  |
| **FU Completed IVIG group (n=38)** | 29*Missing = 9* | 33*Missing = 5* | 29*Missing = 9* | 37*Missing = 1* |
| **FU Completed MPS group (n=37)** | 34*Missing = 3* | 31*Missing = 6* | 28*Missing = 9* | 37 *Missing = 0* |

**Supplemental Table 2.**

|  |  |
| --- | --- |
|  | **Early FU** |
|  | **IVIG** | **Methylprednisolone** | **p** |
| **No. of patients** | 38 | 37 |   |
| **No. of records** | 29 | 34 |   |
| **Echocardiography (%): no** | 2 (5∙2)  | 10 (27∙0)  | 0∙05 |
| **Echocardiography (%): yes** | 27 (71∙1)  | 24 (64∙9)  |   |
| **Echocardiography (%): N.A.** | 9 (23∙7) | 3 (8∙1) |   |
| **Abnormal contractility (%): no** | 3 (7∙9)  | 6 (16∙2)  | N.A. |
| **Abnormal contractility (%): yes** | 0 (0∙0) | 0 (0∙0) |   |
| **Abnormal contractility (%): N.A.** | 35 (92∙1)  | 31 (83∙8)  |   |
| **Lowest EF (median [IQR])** | 0 | 0 | N.A. |
| **Lowest FS (median [IQR])** | 0 | 0 | N.A. |
| **CAA (%): no** | 2 (5∙3)  | 4 (10∙8)  | 0∙99 |
| **CAA (%): yes** | 1 (2∙6)  | 3 (8∙1)  |   |
| **CAA (%): N.A.** | 35 (92∙1)  | 30 (81∙1)  |   |
| **Z score (median [IQR])** | 2∙94 [2∙94, 2∙94] | 6∙36 [4∙88, 7∙85] | 0∙221 |
| **ECG (%): no** | 7 (18∙4)  | 11 (29∙7)  | 0∙66 |
| **ECG (%): yes** | 22 (57∙9)  | 23 (62∙2)  |   |
| **ECG (%): N.A.** | 9 (23∙7)  | 3 (8∙1)  |   |
| **Prolonged PR (%): no** | 5 (13∙2)  | 2 (5∙4)  | N.A. |
| **Prolonged PR (%): N.A.** | 33 (86∙8)  | 35 (94∙6)  |   |
| **Prolonged QT (%): no** | 5 (13∙2)  | 2 (5∙4)  | N.A. |
| **Prolonged QT (%): N.A.** | 33 (86∙8)  | 35 (94∙6)  |   |
| **Arrythmia (%): no** | 5 (13∙2)  | 2 (5∙4)  | N.A. |
| **Arrythmia (%): N.A.** | 33 (86∙8)  | 35 (94∙6)  |   |
| **Low voltage (%): no** | 5 (13∙2)  | 2 (5∙4)  | N.A. |
| **Low voltage (%): N.A.** | 33 (86∙8)  | 35 (94∙6)  |   |
| **ST elevation (%): no** | 5 (13∙2)  | 2 (5∙4)  | N.A. |
| **ST elevation (%): N.A.** | 33 (86∙8)  | 35 (94∙6)  |   |
| **Pericardial effusion (%): no** | 3 (7∙9)  | 6 (16∙2)  | 0∙99 |
| **Pericardial effusion (%): yes** | 0 (0∙0)  | 1 (2∙7)  |   |
| **Pericardial effusion (%): N.A.** | 35 (92∙1)  | 30 (81∙1)  |   |

**Supplemental Table 2, cont.**

|  |  |
| --- | --- |
|  | **intermediate FU** |
|  | **IVIG** | **Methylprednisolone** | **p** |
| **No. of patients** | 38 | 37 |   |
| **No. of records** | 33 | 31 |   |
| **Echocardiography (%): no** | 6 (15∙8)  | 2 (5∙4)  | 0∙3 |
| **Echocardiography (%): yes** | 27 (71∙1)  | 29 (78∙4)  |   |
| **Echocardiography (%): N.A.** | 5 (13∙1) | 6 (16∙2) |   |
| **Abnormal contractility (%): no** | 4 (10∙5)  | 5 (13∙5)  | N.A. |
| **Abnormal contractility (%): yes** | 0 (0∙0) | 0 (0∙0) |   |
| **Abnormal contractility (%): N.A.** | 34 (89∙5)  | 32 (86∙5)  |   |
| **Lowest EF (median [IQR])** | 0 | 0 | N.A. |
| **Lowest FS (median [IQR])** | 0 | 0 | N.A. |
| **CAA (%): no** | 3 (7∙9)  | 4 (10∙8)  | 0∙99 |
| **CAA (%): yes** | 1 (2∙6)  | 2 (5∙4)  |   |
| **CAA (%): N.A.** | 34 (89∙5)  | 31 (83∙8)  |   |
| **Z score (median [IQR])** | 3∙50 [3∙50, 3∙50] | 5∙26 [3∙88, 6∙63] | 0∙99 |
| **ECG (%): no** | 5 (13∙2)  | 5 (13∙5)  | 0∙99 |
| **ECG (%): yes** | 28 (73∙7)  | 26 (70∙3)  |   |
| **ECG (%): N.A.** | 5 (13∙2)  | 6 (16∙2)  |   |
| **Prolonged PR (%): no** | 2 (5∙3)  | 2 (5∙4)  | N.A. |
| **Prolonged PR (%): N.A.** | 36 (94∙7)  | 35 (94∙6)  |   |
| **Prolonged QT (%): no** | 2 (5∙3)  | 2 (5∙4)  | N.A. |
| **Prolonged QT (%): N.A.** | 36 (94∙7)  | 35 (94∙6)  |   |
| **Arrythmia (%): no** | 2 (5∙3)  | 2 (5∙4)  | N.A. |
| **Arrythmia (%): N.A.** | 36 (94∙7)  | 35 (94∙6)  |   |
| **Low voltage (%): no** | 2 (5∙3)  | 2 (5∙4)  | N.A. |
| **Low voltage (%): N.A.** | 36 (94∙7)  | 35 (94∙6)  |   |
| **ST elevation (%): no** | 2 (5∙3)  | 2 (5∙4)  | N.A. |
| **ST elevation (%): N.A.** | 36 (94∙7)  | 35 (94∙6)  |   |
| **Pericardial effusion (%): no** | 4 (10∙5)  | 6 (16∙2)  | N.A. |
| **Pericardial effusion (%): yes** | 0 | 0 |   |
| **Pericardial effusion (%): N.A.** | 34 (89∙5)  | 31 (83∙8)  |   |

**Supplemental Table 2, cont..**

|  |  |
| --- | --- |
|  | **Late FU** |
|  | **IVIG** | **Methylprednisolone** | **p** |
| **No. of patients** | 38 | 37 |   |
| **No. of records** | 29 | 28 |   |
| **Echocardiography (%): no** | 4 (10∙5)  | 5 (13∙5)  | 0∙95 |
| **Echocardiography (%): yes** | 25 (65∙8)  | 23 (62∙2)  |   |
| **Echocardiography (%): N.A.** | 9 (23∙7) | 9 (24∙3) |   |
| **Abnormal contractility (%): no** | 2 (5∙3)  | 4 (10∙8)  | N.A. |
| **Abnormal contractility (%): yes** | 0 (0∙0) | 0 (0∙0) |   |
| **Abnormal contractility (%): N.A.** | 36 (94∙7)  | 33 (89∙2)  |   |
| **Lowest EF (median [IQR])** | 0 | 0 | N.A. |
| **Lowest FS (median [IQR])** | 0 | 0 | N.A. |
| **CAA (%): no** | 0 (0∙0)  | 3 (8∙1)  | 0∙39 |
| **CAA (%): yes** | 2 (5∙3)  | 1 (2∙7)  |   |
| **CAA (%): N.A.** | 36 (94∙7)  | 33 (89∙2)  |   |
| **Z score (median [IQR])** | 4∙40 [4∙35, 4∙45] | 10∙90 [10∙90, 10∙90] | 0∙221 |
| **ECG (%): no** | 4 (10∙5)  | 5 (13∙5)  | 0∙95 |
| **ECG (%): yes** | 25 (65∙8)  | 23 (62∙2)  |   |
| **ECG (%): N.A.** | 9 (23∙7)  | 9 (24∙3)  |   |
| **Prolonged PR (%): no** | 1 (2∙6)  | 3 (8∙1)  | N.A. |
| **Prolonged PR (%): N.A.** | 37 (97∙4)  | 34 (91∙9)  |   |
| **Prolonged QT (%): no** | 1 (2∙6)  | 3 (8∙1)  | N.A. |
| **Prolonged QT (%): N.A.** | 37 (97∙4)  | 34 (91∙9)  |   |
| **Arrythmia (%): no** | 1 (2∙6)  | 3 (8∙1)  | N.A. |
| **Arrythmia (%): N.A.** | 37 (97∙4)  | 34 (91∙9)  |   |
| **Low voltage (%): no** | 1 (2∙6)  | 3 (8∙1)  | N.A. |
| **Low voltage (%): N.A.** | 37 (97∙4)  | 34 (91∙9)  |   |
| **ST elevation (%): no** | 1 (2∙6)  | 3 (8∙1)  | N.A. |
| **ST elevation (%): N.A.** | 37 (97∙4)  | 34 (91∙9)  |   |
| **Pericardial effusion (%): no** | 2 (5∙3)  | 4 (10∙8)  | N.A. |
| **Pericardial effusion (%): yes** | 0 | 0 |   |
| **Pericardial effusion (%): N.A.** | 36 (94∙7)  | 33 (89∙2)  |   |

**Supplemental Table 3.**

|  |  |
| --- | --- |
|  | **Early FU** |
|  | **IVIG** | **Methylprednisolone** | **p** |
| **No. of patients** | 38 | 37 |   |
| **Neutrophils (x10\*9/L) (median [IQR])** | 3∙5 [2∙2, 5∙2] | 4∙0 [3∙1, 6∙7] | 0∙21 |
| **Lymphocytes (x10\*9/L) (median [IQR])** | 2∙5 [2∙0, 3∙3] | 2∙8 [1∙7, 3∙6] | 0∙9 |
| **Thrombocytes (x10\*9/L) (median [IQR])** | 382∙0 [326∙2, 471∙5] | 335∙5 [301∙0, 476∙2] | 0∙53 |
| **ALT (U/L) (median [IQR])** | 29∙0 [19∙0, 46∙2] | 25∙5 [16∙8, 37∙8] | 0∙51 |
| **Albumin (g/L) (median [IQR])** | 36∙5 [33∙0, 39∙0] | 37∙5 [34∙0, 40∙8] | 0∙38 |
| **Ferritin (ug/L) (median [IQR])** | 193∙0 [61∙0, 218∙0] | 167∙5 [84∙5, 194∙0] | 0∙61 |
| **D-dimer (ug/L) (median [IQR])** | 631∙0 [543∙2, 671∙5] | 564∙0 [401∙0, 800∙0] | 0∙92 |
| **NT pro-BNP (ng/L) (median [IQR])** | 77∙0 [50∙0, 173∙5] | 66∙0 [49∙2, 109∙5] | 0∙31 |
| **Troponin (ng/L) (median [IQR])** | 4∙0 [3∙0, 7∙8] | 5∙0 [3∙0, 5∙0] | 0∙77 |
| **CRP (mg/L) (median [IQR])** | 1∙2 [0∙7, 5∙0] | 4∙5 [1∙9, 5∙0] | 0∙09 |
|  | **intermediate FU** |
|  | **IVIG** | **Methylprednisolone** | **p** |
| **No. of patients** | 38 | 37 |   |
| **Neutrophils (x10\*9/L) (median [IQR])** | 2∙7 [2∙4, 3∙1] | 2∙8 [2∙3, 3∙6] | 0∙81 |
| **Lymphocytes (x10\*9/L) (median [IQR])** | 2∙7 [2∙1, 3∙4] | 2∙4 [1∙9, 2∙8] | 0∙31 |
| **Thrombocytes (x10\*9/L) (median [IQR])** | 294∙0 [268∙0, 355∙0] | 309∙5 [291∙5, 386∙0] | 0∙28 |
| **ALT (U/L) (median [IQR])** | 17∙5 [13∙5, 25∙8] | 15∙0 [14∙0, 18∙0] | 0∙52 |
| **Albumin (g/L) (median [IQR])** | 44∙0 [36∙0, 46∙0] | 39∙5 [39∙2, 39∙8] | 0∙7 |
| **Ferritin (ug/L) (median [IQR])** | 54∙0 [38∙8, 61∙0] | 36∙5 [29∙0, 43∙0] | 0∙2 |
| **D-dimer (ug/L) (median [IQR])** | 330∙0 [246∙1, 451∙8] | 302∙0 [251∙0, 351∙0] | 0∙72 |
| **NT pro-BNP (ng/L) (median [IQR])** | 45∙8 [33∙5, 81∙8] | 50∙0 [24∙2, 72∙2] | 0∙83 |
| **Troponin (ng/L) (median [IQR])** | 3∙0 [3∙0, 3∙2] | 5∙0 [3∙0, 5∙0] | 0∙18 |
| **CRP (mg/L) (median [IQR])** | 1∙0 [0∙7, 5∙0] | 2∙4 [0∙4, 5∙0] | 0∙96 |
|  | **Late FU** |
|  | **IVIG** | **Methylprednisolone** | **p** |
| **No. of patients** | 38 | 37 |   |
| **Neutrophils (x10\*9/L) (median [IQR])** | 2∙8 [2∙5, 3∙2] | 3∙9 [3∙5, 4∙3] | 0∙14 |
| **Lymphocytes (x10\*9/L) (median [IQR])** | 3∙4 [2∙4, 4∙4] | 2∙5 [2∙3, 3∙3] | 0∙31 |
| **Thrombocytes (x10\*9/L) (median [IQR])** | 288∙0 [276∙0, 326∙0] | 310∙0 [296∙8, 339∙0] | 0∙22 |
| **ALT (U/L) (median [IQR])** | 19∙0 [18∙0, 23∙0] | 21∙0 [17∙0, 24∙0] | 0∙92 |
| **Albumin (g/L) (median [IQR])** | N.A. | N.A. |   |
| **Ferritin (ug/L) (median [IQR])** | 26∙5 [21∙2, 31∙8] | 33∙0 [33∙0, 33∙0] | 1 |
| **D-dimer (ug/L) (median [IQR])** | 400∙0 [400∙0, 400∙0] | N.A. [N.A., N.A.] | N.A. |
| **NT pro-BNP (ng/L) (median [IQR])** | 67∙0 [60∙5, 73∙5] | 287∙0 [287∙0, 287∙0] | 0∙22 |
| **Troponin (ng/L) (median [IQR])** | 4∙5 [3∙8, 5∙2] | 6∙0 [6∙0, 6∙0] | 0∙48 |
| **CRP (mg/L) (median [IQR])** | 0∙4 [0∙4, 1∙7] | 0∙4 [0∙4, 0∙4] | 0∙49 |

**Supplemental Figures**

**Suppl. Fig. 1.**

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**Suppl. Fig. 2.**

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**Suppl. Fig. 3.**

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**Suppl. Fig. 4.**

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