**Primary data source**

**Protocol: Higher vs. Lower Doses of Dexamethasone in Patients with COVID-19 and Severe Hypoxia: the COVID STEROID 2 trial**

**Department: 4131**

**Hospital: Rigshospitalet**

**Investigator: Marie Warrer Petersen**

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|  | **Data** | **Primary data source** |
|  | Consent | Samtykkeerklæring |
|  | **SCREENING FORM** |  |
| S1 | National identification number | SP-Header |
|  | **Inclusion criteria** |  |
| S2 | ≥18 years old | SP-Header |
| S3 | Documented COVID-19 | SP-Forside -> rapportindex -> diagnoser |
| S4 | Oxygen supplementation through an open system with an oxygen flow of at least 10 L/min | SP- Vurderingsskema -> resp |
|  | **Either of the following inclusion criteria must be fulfilled** |  |
| S5 | Respiratory support in a closed system | SP- Vurderingsskema -> resp |
| S5a | Invasive mechanical ventilation | SP- Vurderingsskema -> resp |
| S5b | Non-invasive ventilation | SP- Vurderingsskema -> resp |
| S5c | Continuous CPAP (NOT including intermittent CPAP) | SP- Vurderingsskema -> resp |
|  | **Exclusion criteria** |  |
| S6 | Does the patient have an indication for use of systemic corticosteroids in doses higher than 6 mg dexamethasone or equivalents? | SP-Resume -> MDA-historikSP-Resume -> MDA-overblik |
| S7 | Has the patient received systemic corticosteroids for COVID-19 for ≥ 5 consecutive days? | SP-Resume -> MDA-historikSP-Resume -> MDA-overblik |
| S8 | Does the patient have an invasive fungal infection? | 1) SP-Resultater -> resultatgennemgang2) SP-Resultater -> mere -> parakliniske systemer -> mikrobiologi3) SP-forside -> rapportindeks -> Diagnoser |
| S9 | Does the patient have active tuberculosis? | 1) SP-Resultater -> resultatgennemgang2) SP-Resultater -> mere -> parakliniske systemer -> mikrobiologi3) SP-forside -> rapportindeks -> Diagnoser |
| S10 |  Is the patient pregnant? | SP-Notater (ublindet forsøgspersonale sikrer sig, at der er lavet urinstix og laver notat om svaret) |
| S11 |  Known hypersensitivity to hydrocortisone? | SP-Header: Cave |
| S12 |  Consent unobtainable according tonational regulations? | SP-Notater |
| S13 | For how many consecutive days has thepatient received systemic corticosteroidsfor COVID-19? | SP-Notater |

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|  | **BASELINE FORM** |  |
|  | **GENERAL PATIENT INFORMATION** |  |
| BL1 | Sex | SP-Header |
| BL2 | Hospital admission date? | SP -> vis journal -> behandlingskontakter -> flueben i indlæggelser |
| BL3 | Number of days with symptoms before hospital admission | 1) SP – Resumé 2) SP- indlæggelsesnotat |
| BL4 | Department at which the participant was included | SP - forskningsnotat |
|  | **Co-morbidities prior to hospital admission** |  |
| BL5 | History of ischemic heart disease or heart failure? | 1) SP- Diagnoseliste2) SP – Resume / indlæggelsesnotat |
| BL6 | Immunosuppressive therapy within thelast 3 months? | 1. SP – Resume / indlæggelsesnotat
2. SP-Resume -> MDA-historik
 |
| BL7 | Chronic pulmonary disease? | 1) SP- Diagnoseliste2) SP – Resume / indlæggelsesnotat |
| BL8 | Diabetes Mellitus? | 1) SP- Diagnoseliste2) SP – Resume / indlæggelsesnotat |
|  | **Baseline data** |  |
| BL9 | Participant weight | 1) SP- forside -> søg (indtast ’vægt’ i øvre højre hjørne)2) estimer med klinisk blik eller via personalet |
| BL10 | Use of any form of renal replacement therapy within the last 72 hours prior to randomisation: | 1. SP-Vurderingsskema ’CRRT’
2. SP – Notater

3) SP – Resume – ’Dialyse og CRRT-overblik’ |
| BL11 | Infusion of vasopressor/inotropic agent for a minimum of 1 hour to increase mean arterial blood pressure within the last 24 hours prior to randomisation? | SP-Resume -> MDA historik |
| BL12 | Use of respiratory support on a closed system at randomization? | SP- Vurderingsskema -> resp |
| BL12a | If YES, what was the latest FiO2 prior to randomization? | SP- Vurderingsskema -> resp |
| BL12b | If YES, How many days prior to randomization | SP- Vurderingsskema -> resp |
| BL12c | If NO, what was the maximum supplemental oxygen flow on an open system at randomisation (+/- 1 h) | SP- Vurderingsskema -> resp |
| BL13 | Most recent PaO2 prior to randomisation | SP- resultater |
| BL14 | Most recent arterial O2 saturation prior to randomization? | 1) SP- resultater2) SP-vurderingsskema -> resp |
| BL15 | Highest plasma lactate value in the last 24 hours prior to randomisation: | SP- resultater -> søg ‘laktat’, men OBS der vil ofte være 2 eller 3 laktat variable derfor scroll op/ned |
| BL16 | Limitations of care | SP-header -> Behandlingsniveau |
| BL17 | Chronic use of systemic corticosteroids for other indications than COVID-19 | SP-Resume -> MDA-historikSP-Resume -> MDA-overblik |
|  | **Co-interventions** |  |
| BL18 | Agents with potential anti-inflammatory action during current hospital admission? | SP-Resume -> MDA historik |
| BL18a | If YES, then Janus kinase inhibitor | SP-Resume -> MDA historik |
| BL18b | If YES, then Interleukin-6 inhibitor? | SP-Resume -> MDA historik |
| BL18c | If YES, then other? | SP-Resume -> MDA historik |
| BL19 | Use of any drug with potential antiviral activity during current hospital admission? | SP-Resume -> MDA historik |
| BL19a | If YES, then remdesivir? | SP-Resume -> MDA historik |
| BL19b | If YES, then convalescent plasma? | 1) SP-Notater2) SP-Resume -> MDA historik |
| BL19e | If YES, then other systemic antiviral drug? | SP-Resume -> MDA historik |
| BL20 | Use of any systemic anti-bacterial drugs during current hospital admission? | SP-Resume -> MDA historik |
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|  | **TRIAL MEDICATION up to 10 days** |  |
|  | **Administered Trial Medication** |  |
| ATM1 | Was the trial medication administered tothe patient on this day? | SP-Resume -> MDA-historikSP-Resume -> MDA-overblik |
|  | **Reason(s) for violation of protocol on this day** |  |
| ATM1a | If NO in ATM1, by error/lack of resources? | 1) SP-Notater2) Spørg personalet  |
| ATM1b | If NO in ATM1a, due to other reasons? | 1) SP-Notater2) Spørg personalet |

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|  | **DAILY DATA day 1-14** |  |
|  | **Major protocol violations on this day** |  |
| MPV1 | Treatment with open-label systemic corticosteroids on this day? | SP-Resume -> MDA historik |
|  | **Life-supportive interventions** |  |
| D1 | Did the patient receive invasive mechanical ventilation on this day? | SP- Vurderingsskema -> resp |
| D2 | Did the patient receive infusion of vasopressors or inotropes for at least one hour on this day? | SP-Resume -> MDA historik |
| D3 | Did the patient receive renal replacement therapy on this day? | 1. SP-Vurderingsskema ’CRRT’
2. SP – Notater

3) SP – Resume – ’Dialyse og CRRT overblik’ |
|  | **Serious Adverse Reactions** |  |
| SAR1 | Clinically important gastrointestinal bleeding on this day? | Transfusion: SP-Resultater -> mere -> parakliniske -> blodbank -> transfusionshistorikBlødning: SP-Notat |
| SAR2 | New onset septic shock on this day? | Mistænkt infektion: SP- NotaterLaktat: SP-resultaterVasopressor: SP-resume -> MDA historik |
| SAR3 | Invasive fungal infection on this day? | 1) SP-Resultater2) SP-Resultater -> mere -> parakliniske systemer -> mikrobiologi |
| SAR4 | Anaphylactic reaction to IV hydrocortison? | SP – Notat |

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|  | **DISCHARGE AND READMISSION FORM** |  |
| 1 | Date/time | SP-Resume -> SP – Behandlingstidslinje |
| 2 | Discharged to | 1) SP-Resume -> SP – Behandlingstidslinje2) SP -> vis journal -> behandlingskontakter -> flytningshistorik |
| 3 | Date/time of possible readmission | 1) SP-Resume -> SP – Behandlingstidslinje |

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|  | **WITHDRAWAL FORM** |  |
| W1+2 | Date/time of withdrawal | SP-Notat |
| W3 | Reason for withdrawal | SP-Notat |
| W3a+b | Consent not given/further data registration | Samtykkeblanket |

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|  | **28 DAYS FOLLOW-UP** |  |
| FU1 | Date | eCRF |
| FU2 | Did the patient die within 28 days of follow-up? | 1) SP-åben journalen (kun hvis pt. er I reg H / reg S gives advarsel om at pt. er død. Hvis ikke:2) SP-Vis journal -> sundhedsjournalen  |
| FU2a | Date of death? | 1) SP-Header-> hold curser på pt-navn2) SP-Vis journal -> sundhedsjournalen |
|  | **Duration of life-support to day 28** |
| FU3 | Did the patient receive invasive mechanical ventilation from day 15-28? If yes, apply start and end dates | SP- Vurderingsskema -> resp |
| FU4 | Did the patient receive vasopressors or inotropes from day 15-28? If yes, apply start and end dates | SP-Resume -> MDA historik |
| FU5 | Did the patient receive renal replacement therapy from day 15-28? If yes, apply start and end dates | SP – Resume – ’Dialyse og CRRT overblik’ |
| FU6 | Use of extracorporeal membraneoxygenation (ECMO) within 28 days ofrandomisation? | SP-forside -> fritekstsøgning : ecmo |

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|  | **Occurrence of serious adverse reactions from day 15-28** |
| SAR1 | Clinically important gastrointestinal bleeding from day 15-28? | Transfusion: SP-Resultater -> mere -> parakliniske -> blodbank -> transfusionshistorikBlødning: SP-Notat |
| SAR2 | New onset septic shock from day 15-28? | Mistænkt infektion: SP- NotaterLaktat: SP-resultaterVasopressor: SP-resume -> MDA historik |
| SAR3 | Invasive fungal infection from day 15-28? | 1) SP-Resultater2) SP-Resultater -> mere -> parakliniske systemer -> mikrobiologi |
| SAR4 | Anaphylactic reaction to IV hydrocortison from day 15-28? | SP – Notat |

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|  | **28 DAYS FOLLOW-UP CONTINUED** **Other information** |
| FU11 | Was the patient discharged against medical advice? | SP-Notat |
| FU11a | FU11a If yes, did the patient receive life support at the time of discharge? | Invasive mechanical ventilation: SP- Vurderingsskema -> resp Circulatory support: SP-Resume -> MDA historikRenal replacement therapy: SP – Resume – ’Dialyse og CRRT overblik’ |
| FU11b | If yes, what type of life support? | Invasive mechanical ventilation: SP- Vurderingsskema -> resp Circulatory support: SP-Resume -> MDA historikRenal replacement therapy: SP – Resume – ’Dialyse og CRRT overblik’ |
| FU11c | If no, did the patient receivesupplementary oxygen at the time ofdischarge? | SP- Vurderingsskema -> resp  |
| FU11d | How much supplementary oxygen? | SP- Vurderingsskema -> resp |

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|   | **90 DAYS FOLLOW-UP** |  |
| FU1 | Date | eCRF |
| FU2 | Did the patient die within 90 days of follow-up? | 1) SP-åben journalen (kun hvis pt. er I reg H / reg S gives advarsel om at pt. er død. Hvis ikke:2) SP-Vis journal -> sundhedsjournalen |
| FU2a | Date of death? | 1) SP-Header-> hold curser på pt-navn2) SP-Vis journal -> sundhedsjournalen |
|  | **Duration of life-support to day 90** |  |
| FU3 | Did the patient receive invasive mechanical ventilation from day 29-90? If yes, apply start and end dates | SP- Vurderingsskema -> resp |
| FU4 | Did the patient receive vasopressors or inotropes from day 29-90? If yes, apply start and end dates | SP-Resume -> MDA historik |
| FU5 | Did the patient receive renal replacement therapy from day 29-90? If yes, apply start and end dates | SP – Resume – ’Dialyse og CRRT-overblik’ |
|  | **Length of hospital stay at day 90** |  |
| FU6 | Discharged alive from the hospital within 90 days? | 1) SP-Resume -> SP – Behandlingstidslinje2) SP -> vis journal -> behandlingskontakter -> flytningshistorik |
| FU6a | Date of hospital discharge (index admission) | SP -> vis journal -> behandlingskontakter -> flytningshistorik |

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|  | **180 DAYS FOLLOW-UP FORM** |  |
| FU1 | Date | eCRF |
| FU2 | Was the patient dead at 180 days follow-up? | 1) SP-åben journalen (kun hvis pt. er I reg H / reg S gives advarsel om at pt. er død. Hvis ikke:2) SP-Vis journal -> sundhedsjournalen |
| FU2a | Date of death? | 1) SP-Header-> hold curser på pt-navn2) SP-Vis journal -> sundhedsjournalen |
|  | **Quality of life at 1-year post-randomisation** |  |
| FU3 | Lost to HRQoL follow-up? | Spørgeskema |
| FU3a | Date of EQ-5D-5L and EQ-VAS interviews | Spørgeskema |
| FU5-10 | EQ-5D-5L and EQ-VAS score | Spørgeskema |
| FU11 | HRQoL follow-up conducted by proxy? | Spørgeskema |