|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |  |  | **Intensive care unit** |  |  |  | **Home** |
| **Day of hospitalization** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** |
| **COVID-19 test RT-PCR**  | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | - | - |
| **Encephalopathy Symtoms** | **Agitation** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Deliriums** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Disoriented in time** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Disoriented in space** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Vomitting** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Unable to follow commands** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Seizure** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **CIGB-258 Therapy** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

 Figure 1. Development of hepatic encephalopathy symptoms throughout the course of COVID-19. Schedule of the CIGB-258 therapy

**Table 1.** Clinical Laboratory tests

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| *Blood cell count* | Ref Range and Units | Day of Admission(Day 1) | Day of ICU admission(Day 10) | CIGB-258 therapy |
| **Day 11** | **Day 12** | **Day 13** | **Day 14** | **Day 16** |
| White blood cell (109/L) | 4 - 11 | 11,24 | 22 | 14 | - | 14,6 | 10,2 | - |
| Platelet count (109/L) | 150 - 450 | - | 380 | 214 | 245 | 247 | 280 | - |
| *Prognostic Markers* |  |  |  |  |  |  |  |  |
| LDH (U/L) | 230-460 | 459 | 3846 | 4730 | 1992 | 1706 | 1904 | 1134 |
| Ferritine (µg/L) | 30-300 | - | 383 | 536 | 403 | 344 | 348 | 274 |
| C-Reactive Protein (mg/L) |  ≤ 5 | 3,32 | 37,17 | 91,99 | 56 | 20 | 11,25 | 5,71 |
| IL-6 (pg/mL) |  ≤ 6 | - | 46,49 | 26,67 | 16,45 | 13,06 | 17,46 | 20,8 |
| IL-10 (pg/mL) | ≤7,8 | - | 349,35 | 68,05 | 64,37 | 49,95 | 60,01 | 41,58 |
| *Metabolic Panel* |  |  |  |  |  |  |  |  |
| Creatinine (µmol/L) | 47-125 | 105 | 119 | 180 | 127 | 98,43 | 85, 18 | 81,54 |
| AST (U/L) | 32-39 | 26 | 1214 | 1004 | 402 | 303 | 325 | 160 |
| ALT (U/L) | 32-40 | 39 | 460 | 480 | 323 | 252 | 282 | 166 |
| Ammonia (μmol/L) | 25-76 | - | 170 | 165 | 110 | 85 | 70 | 62 |
| Alkaline Phosphatase (U/L) | 35-126 | 184 | 178 | 143 | 500 | 143 | 19 | - |

LDH: Lactate dehydrogenase , AST: Aspartate aminotransferase , ALT: Alanine aminotransferase, ICU: Intensive care unit

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| Figure 2. Therapy with CIGB-258 caused the reduction of Calprotectin in the patient. Concentrations of Calprotectin in the serum were measured by a specific ELISA (Quantikine, R&D Systems), according to the manufacturer’s instructions. Serum samples were obtained before and during the treatment. Normal range: 481-6540 (ng/mL) |