

Data S1.

Supplementary procedures

Patient and study design. According to the guidance of the National Health Commission (NHC) of China, a 75-year-old male patient critically ill with COVID-19 with multiple concomitant diseases such as hypertension (for >10 years), diabetes and coronary heart disease (for >1 year) was confirmed by the reverse transcription-quantitative PCR (RT-qPCR) detection of SARS-CoV-2 RNA extracted from the nasopharyngeal swabs and enrolled on January 31, 2020. Prior to the human umbilical cord-derived mesenchymal stem/stromal cell (hUC-MSC) administration, the COVID-19-infected patient received standard treatments and was not involved in other clinical trials and did not exhibit signs of cancer.

The present study was performed at the Affiliated Hospital of Zunyi Medical University in China, and was approved with the consent of the patient and ethics committee (approval no. KLL-2020-013) and registered at the Chinese Clinical Trial Registry (approval nos ChiCTR2000030116 and ChiCTR2000031930). The detailed information of the project 'Clinical Studies on severe COVID-19 pneumonia caused acute respiratory distress syndrome (ARDS) by hUC-MSCs' was approved by the Department of Science and Technology of Jiangxi Province (approval no. 2020, to ZHa).

hUC-MSC preparation and systemic infusion. The hUC-MSC product with the certification of the National Institutes for Food and Drug Control of China (approval no. CXSL1800101) and the China Food and Drug Inspection and Research Institute (inspection report no. SZ201000890) were gratuitously provided by Jiangxi Health-Biotech Stem Cell Technology Co. Ltd. (product lot nos. 202002JF07, 202003JF02 and 202002JF05). The characterization of the signatures, including cytomorphology, immunophenotype, cell viability and multi-lineage differentiation potential of the banked hUC-MSCs have already been clarified in a recent study by the authors (1). The clinical-grade hUC-MSCs were resuspended in 100 ml saline for intravenous injection. A total amount of 1×10^6 hUC-MSCs per kg body weight (body weight, 50 kg) was then intravenously injected at a rate of 40 drops per min according to the manufacturer's instructions (2). The vital signs of the patient were meticulously observed and recorded as shown in Table SI.

RT-qPCR detection of SARS-Cov-2 nucleic acid. RT-qPCR analysis was conducted as previously reported with several modifications (3,4). Briefly, the SARS-CoV-2 nucleic acid were extracted from the lixivium of nasopharyngeal swab from the enrolled patient by the special government agencies (Chinese Center for Disease Control and Prevention). RT-qPCR was performed with the ABI PRISM 7900 (Applied Biosystems) as previously reported (4,5). The primer sequences for SARS-CoV-2 RNA detection were used as previously described by Leng *et al* (2). The sequences were as follows: BHQ1 probe, 5'-CY5CTAGTTACTACTAGCCATCCTTACTGC-3'; forward sequence, 5'-TCAGAAATGCCAATCTCCC CAAC-3'; reverse sequence, 5'-AAAGGTCCACCCGATACA TTGA-3'.

Assessment of disease severity. In general, the clinical classification of COVID-19 infection was according to NHC of China as recently reported (2). The severity of the enrolled COVID-19-infected patient was comprehensively assessed by utilizing the standard qualifications including acute physiology and chronic health evaluation II (APACHE II), sequential organ failure assessment (SOFA) and pneumonia severe index (PSI), which were based on the multiple quantized clinical parameters.

References

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3. Zhang W, Liu C, Wu D, Liang C, Zhang L, Zhang Q, Liu Y, Xia M, Wang H, Su P, *et al*: Decitabine improves platelet recovery by down-regulating IL-8 level in MDS/AML patients with thrombocytopenia. *Blood Cells Mol Dis* 76: 66-71, 2019.
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5. Wu Q, Zhang L, Su P, Lei X, Liu X, Wang H, Lu L, Bai Y, Xiong T, Li D, *et al*: MSX2 mediates entry of human pluripotent stem cells into mesendoderm by simultaneously suppressing SOX2 and activating NODAL signaling. *Cell Res* 25: 1314-1332, 2015.

Figure S1. The dynamic variations of hemogram and pro-inflammatory cytokines during treatment. (A and B) The dynamic variations of Hb (A, g/l) and PLT (B, $10^9/l$) in the peripheral blood of the patient from January 31 to April 16, 2020. (C and D) The dynamic immunosuppression of IL-2 (C, pg/ml), and IL-4 (D, pg/ml) in the peripheral blood of the patient from January 31 to April 16, 2020. Hb, haemoglobin; PLT, platelet.

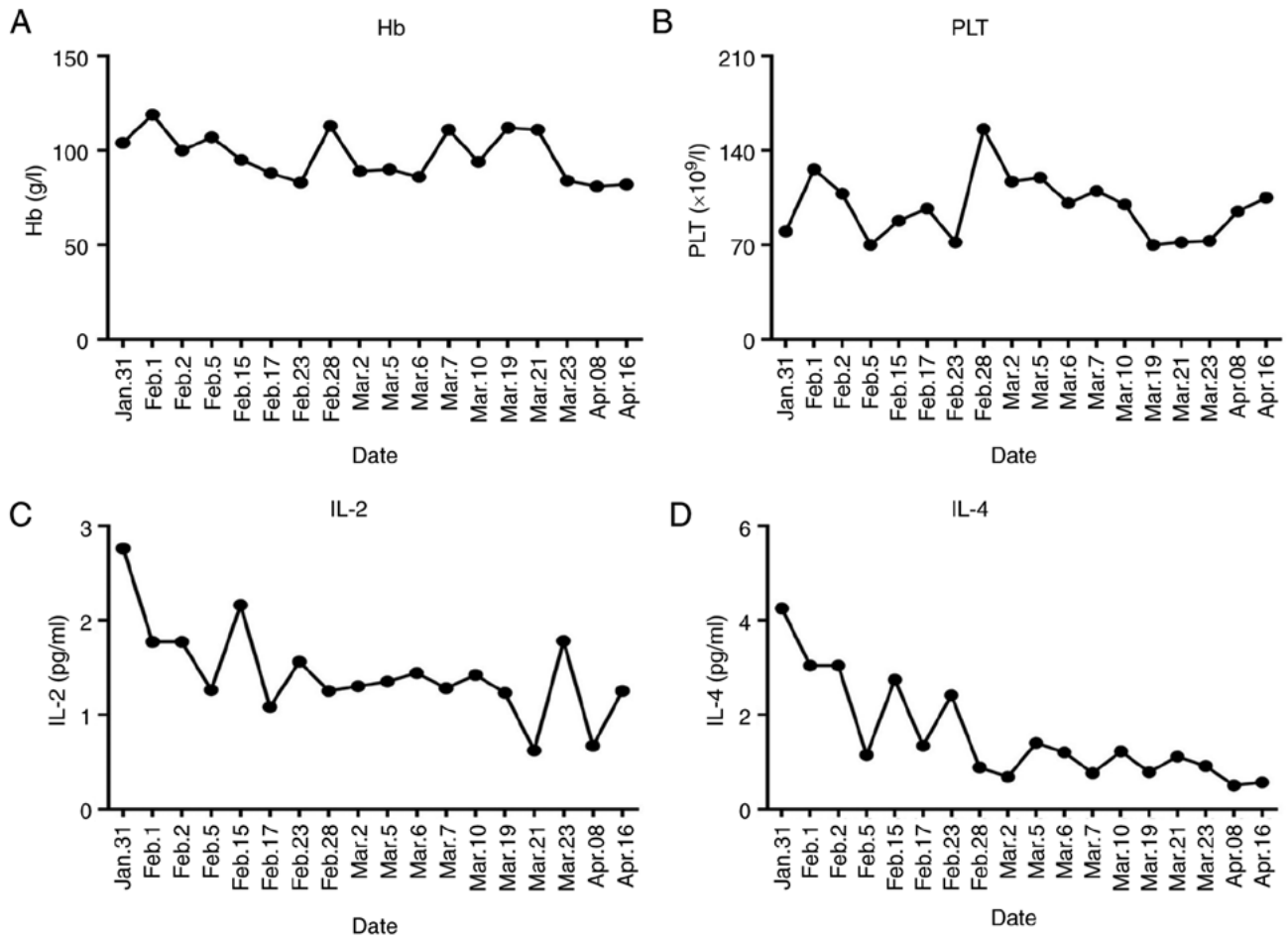


Figure S2. The dynamic variations of liver-associated parameters and the severity of illness during the patient treatment. (A-C) The dynamic variation of liver-related indicators including ALT (A, U/l), AST (B, U/l), ALB (C, g/l) and PA (D, $\mu\text{g/dl}$) in the patient from January 31 to April 16, 2020. (E) The dynamic variation of severity of illness-associated indicator (PSI value) in the patient from January 31 to April 16, 2020. ALT, alanine transaminase; AST, aspartate aminotransferase; ALB, albumin; PA, pre-serum protein.

