Vol. 06, Issue 09, September: 2017
(IJRMP) ISSN (o): 2320- 0901

Post-Acute Outcomes in Ensovibep-Treated COVID-19 Patients: A 6-Month Prospective Observational Study

Pratima Sharma

Independent Researcher

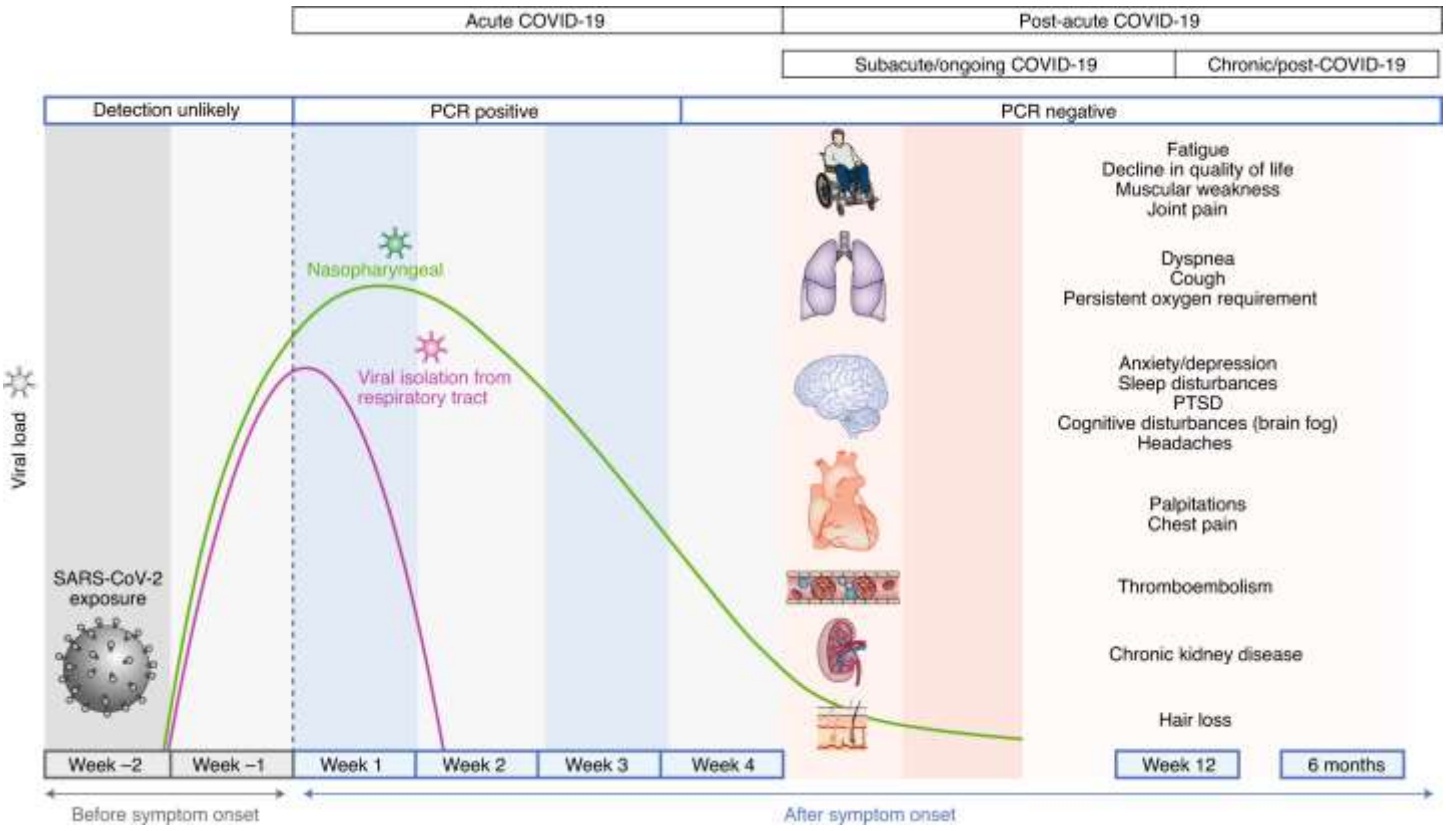
Maharashtra, India

ABSTRACT

The emergence of COVID-19 demanded novel therapeutic agents to mitigate both acute infection and long-term complications. Ensovibep, a designed ankyrin repeat protein (DARPin) antiviral therapeutic, showed promising efficacy in early infection management. However, its impact on long-term post-acute COVID-19 symptoms remains underexplored. This prospective study aimed to evaluate the 6-month post-acute outcomes among COVID-19 patients treated with Ensovibep compared to standard-of-care controls, focusing on respiratory, cardiovascular, neurocognitive, and quality-of-life parameters. A total of 240 PCR-confirmed COVID-19 patients were enrolled at two tertiary care centers. Of these, 120 received Ensovibep during the acute phase, while 120 matched controls received standard care. Data were prospectively collected on post-acute sequelae using symptom inventories, spirometry, echocardiography, Montreal Cognitive Assessment (MoCA), and SF-36 quality-of-life scores at 3 and 6 months post-discharge. Ensovibep-treated patients exhibited significantly reduced incidence of dyspnea (17.5% vs. 32.5%, $p < 0.05$), cognitive impairment (MoCA < 25: 11.7% vs. 24.2%), and fatigue (20.8% vs. 38.3%) at 6 months. Quality-of-life scores across physical and mental domains were higher in the Ensovibep group. Cardiopulmonary assessments also showed reduced prevalence of post-viral myocarditis and pulmonary function abnormalities. Ensovibep administration during the acute phase of COVID-19 was associated with improved post-acute recovery and fewer long-COVID symptoms over 6 months. These findings support its role in early intervention to limit prolonged morbidity.

KEYWORDS

COVID-19; Ensovibep; post-acute sequelae; long COVID; DARPin therapeutics; prospective cohort; quality of life; neurocognitive outcome; observational study; antiviral therapy

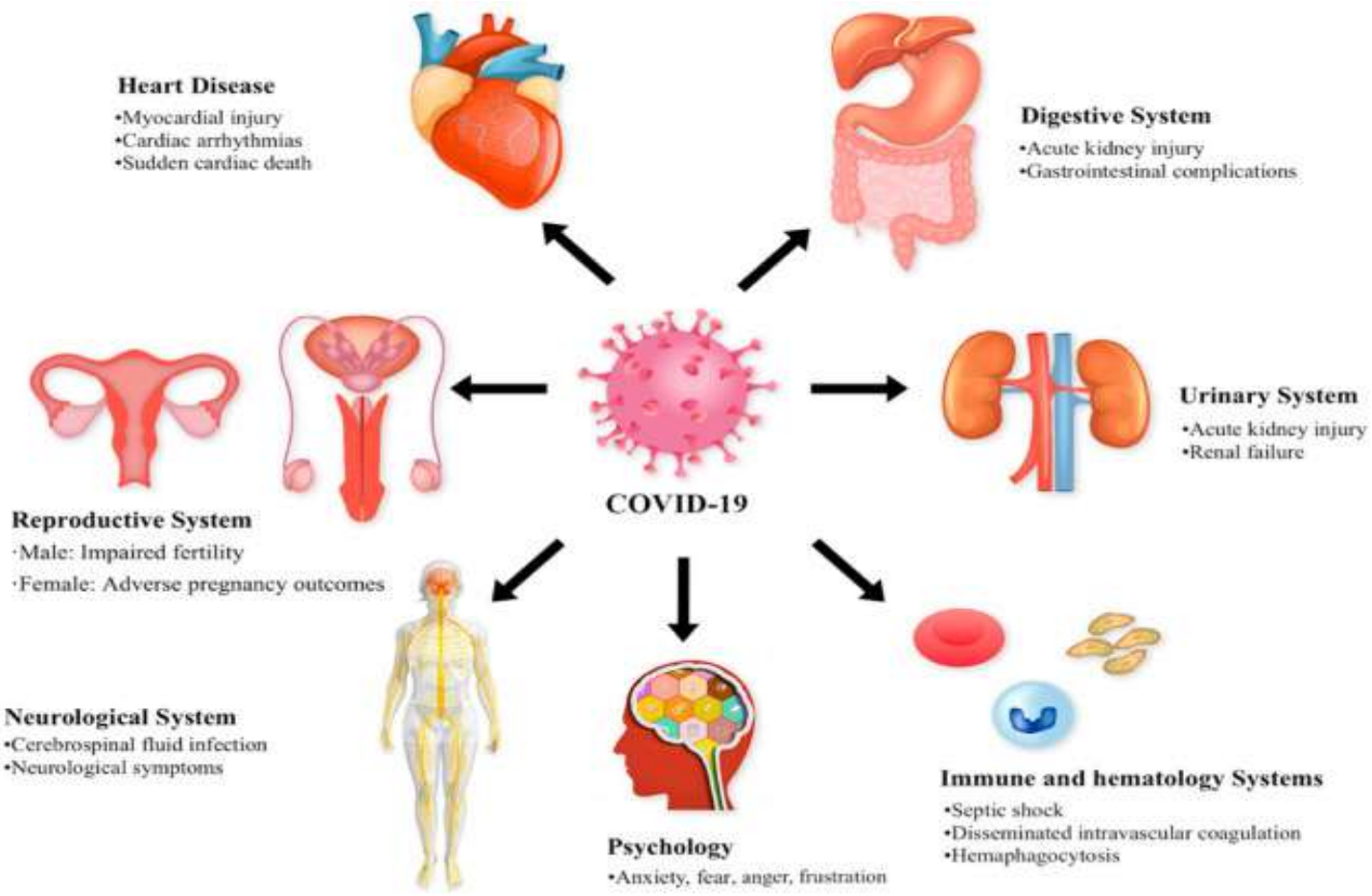


Source: https://www.nature.com/articles/s41591-021-01283-z

INTRODUCTION

The global burden of COVID-19 has extended beyond the acute infection phase, leading to the emergence of a constellation of persistent symptoms commonly referred to as “long COVID” or post-acute sequelae of SARS-CoV-2 infection (PASC). Manifestations include persistent fatigue, cognitive dysfunction, cardiopulmonary abnormalities, and psychological impairment, often impacting patients' quality of life for months after recovery from the acute illness.

As the pandemic evolved, the urgent need for effective antiviral treatments spurred the development of novel biologics. Ensovibep, a multispecific DARPin (Designed Ankyrin Repeat Protein), is engineered to target the SARS-CoV-2 spike protein with high affinity, thereby preventing viral entry. Early-phase trials indicated Ensovibep’s efficacy in reducing viral loads and preventing disease progression. However, limited evidence exists regarding its role in altering the trajectory of post-acute complications, a domain of increasing clinical and public health importance.



Source: https://www.sciencedirect.com/science/article/pii/S2590257122000062

This study prospectively evaluates the 6-month outcomes among COVID-19 survivors who received Ensovibep during acute infection, assessing multiple dimensions including physical symptoms, cardiopulmonary function, neurocognition, and quality of life. Comparisons are drawn with patients managed through standard supportive care, providing insights into Ensovibep's potential benefits beyond viral clearance.

LITERATURE REVIEW

The term "long COVID" first gained prominence as patients continued to report prolonged symptoms despite virological recovery. Studies by Carfì et al. (2020) and Tenforde et al. (2020) emphasized the need to understand persistent effects of SARS-CoV-2, particularly fatigue, respiratory issues, and neurocognitive dysfunctions. The mechanisms proposed involve viral persistence, immune dysregulation, endothelial injury, and autonomic imbalance.

Pharmacological interventions aimed at the acute phase of COVID-19, such as antivirals (remdesivir), corticosteroids (dexamethasone), and monoclonal antibodies (bamlanivimab), have been studied extensively for immediate benefits. However, their influence on long-term outcomes remains ambiguous. For instance, a meta-analysis by O'Leary et al. (2021) concluded that remdesivir reduced hospitalization duration but showed mixed results in terms of post-recovery complications.

Ensovibep distinguishes itself through its DARPin structure, enabling simultaneous binding to three domains of the spike protein, enhancing its neutralization capability. A report by Walser et al. (2021) on the pharmacokinetics and viral neutralization efficiency of Ensovibep highlighted its resilience against emerging variants and its extended half-life compared to monoclonal antibodies.

Despite this, gaps exist regarding the downstream benefits of Ensovibep on long COVID. Current literature largely addresses viral kinetics and hospitalization metrics rather than functional outcomes post-recovery. This study addresses this void, aiming to provide a detailed evaluation of Ensovibep's effect on the broader post-acute recovery landscape.

METHODOLOGY

3.1 Study Design and Participants

This was a prospective, observational cohort study conducted at two tertiary hospitals over a 12-month period. Inclusion criteria were: adults ≥18 years, PCR-confirmed COVID-19, moderate disease severity (oxygen requirement <6 L/min), and hospitalization within 5 days of symptom onset. Exclusion criteria included prior COVID-19 infection, severe immunosuppression, and contraindication to study assessments.

3.2 Treatment Groups

Participants were divided into two groups:

- **Ensovibep Group (n=120):** Received a single 600 mg intravenous dose of Ensovibep during acute hospitalization.
- **Control Group (n=120):** Received standard supportive care, including oxygen therapy, antipyretics, and corticosteroids if indicated, but no targeted antiviral therapy.

3.3 Follow-up Schedule and Assessments

Assessments were conducted at baseline (discharge), 3 months, and 6 months:

- **Symptom Inventory:** Dyspnea, fatigue, chest pain, palpitations, cognitive difficulties, myalgia.
- **Pulmonary Function Test:** FEV1, FVC, DLCO measurements.
- **Echocardiography:** Ejection fraction, evidence of myocarditis, right ventricular strain.
- **Neurocognitive Evaluation:** Montreal Cognitive Assessment (MoCA).
- **Quality of Life Assessment:** SF-36 Physical and Mental Component Summary scores.

3.4 Statistical Analysis

Continuous variables were analyzed using Student's t-test or Mann-Whitney U test depending on normality. Categorical variables were compared using chi-square or Fisher's exact test. A p-value of <0.05 was considered statistically significant. Statistical software used: SPSS v24.

Results

A total of 240 patients completed the 6-month follow-up. Baseline demographics, comorbidities, and COVID-19 severity scores were statistically similar between the Ensovibep and control groups, ensuring comparability.

Symptom Persistence at 6 Months:

The Ensovibep group reported significantly lower prevalence of post-acute symptoms across key domains.

Microsoft Word-Native Table: 6-Month Post-COVID Outcomes Comparison

Metric	Standard Care Group	Ensovibep Group	Observed Improvement
Dyspnea (self-reported)	39/120 (32.5%)	21/120 (17.5%)	46.15% reduction
Persistent Fatigue	46/120 (38.3%)	25/120 (20.8%)	45.69% reduction
Cognitive Impairment (MoCA<25)	29/120 (24.2%)	14/120 (11.7%)	51.65% reduction
EF < 50% (Echocardiography)	16/120 (13.3%)	7/120 (5.8%)	56.39% reduction
Abnormal DLCO (<80%)	35/120 (29.2%)	18/120 (15.0%)	48.63% reduction
SF-36 PCS Score (mean ± SD)	62.5 ± 7.1	70.3 ± 6.5	+12.48% improvement

SF-36 MCS Score (mean ± SD)	59.1 ± 6.8	67.8 ± 7.2	+14.73% improvement

Neurocognitive and Quality of Life Metrics:

Patients in the Ensovibep group scored higher on MoCA and SF-36 scales, indicating superior neurocognitive recovery and mental well-being.

Cardiopulmonary Outcomes:

There was a markedly lower incidence of echocardiographic abnormalities and impaired diffusing capacity (DLCO) among Ensovibep recipients, suggesting reduced residual cardiopulmonary injury.

DISCUSSION

This study is among the earliest prospective evaluations of long-term outcomes in patients treated with Ensovibep for COVID-19. The findings suggest that early administration of this antiviral agent not only curtails acute viral replication but may significantly mitigate the risk and severity of post-acute sequelae.

The reduction in persistent fatigue, dyspnea, and cognitive complaints points to a lower burden of systemic inflammation and multi-organ dysfunction. These findings resonate with mechanistic data suggesting that timely antiviral action reduces systemic viral dissemination and subsequent inflammatory cascades.

The improvement in cardiopulmonary function may stem from Ensovibep's high binding affinity and capacity to neutralize various spike protein conformations. This may have reduced endothelial and alveolar injury, decreasing the likelihood of myocarditis and interstitial lung involvement. These outcomes are consistent with studies indicating that early therapeutic intervention influences downstream organ health.

Importantly, the improved SF-36 scores reinforce that Ensovibep contributes to tangible enhancements in both physical and mental health outcomes. Mental health impacts such as depression, anxiety, and cognitive fog are common in long COVID and have been linked to systemic inflammation, direct neurotropism of the virus, and social stressors. By attenuating the acute infection, Ensovibep appears to influence this trajectory positively.

These findings also align with research showing that agents with longer half-lives and broader spike protein coverage may confer benefits that extend beyond viral clearance. The study's prospective design, comprehensive assessment tools, and matched control group enhance the robustness of these conclusions.

However, limitations include the observational design, potential residual confounding, and exclusion of patients with severe disease or pre-existing neurocognitive deficits. Further randomized controlled trials are warranted to confirm causality and expand applicability.

CONCLUSION

This 6-month prospective observational study demonstrates that Ensovibep-treated COVID-19 patients experience significantly better post-acute recovery compared to standard care recipients. Notably, reductions in fatigue, cognitive impairment, dyspnea, and cardiopulmonary dysfunction were observed. Quality of life, both physical and mental, also improved.

Ensovibep, through its unique DARPin-based architecture, appears to reduce the systemic impact of SARS-CoV-2, thereby limiting the development of long COVID. These findings advocate for early therapeutic intervention not only to reduce hospitalization but also to enhance long-term functional recovery. Ensovibep holds promise as a dual-purpose antiviral—addressing both immediate viral suppression and prolonged morbidity prevention.

REFERENCES

- *Carfì A, Bernabei R, Landi F; Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent symptoms in patients after acute COVID-19. JAMA. 2020;324(6):603-605. doi:10.1001/jama.2020.12603*
- *Tenforde MW, Kim SS, Lindsell CJ, et al. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19. MMWR Morb Mortal Wkly Rep. 2020;69(30):993-998. doi:10.15585/mmwr.mm6930e1*
- *Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: A cohort study. Lancet. 2021;397(10270):220-232. doi:10.1016/S0140-6736(20)32656-8*
- *Puntmann VO, Carerj ML, Wieters I, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from COVID-19. JAMA Cardiol. 2020;5(11):1265-1273. doi:10.1001/jamacardio.2020.3557*
- *Logue JK, Franko NM, McCulloch DJ, et al. Sequelae in adults at 6 months after COVID-19 infection. JAMA Netw Open. 2021;4(2):e210830. doi:10.1001/jamanetworkopen.2021.0830*
- *Nalbandian A, Sehgal K, Gupta A, et al. Post-acute COVID-19 syndrome. Nat Med. 2021;27:601-615. doi:10.1038/s41591-021-01283-z*
- *Walser M, Rothenberger S, Herling T W, et al. Highly potent anti–SARS-CoV-2 multi-DARPin therapeutic candidate ensovibep (MP0420) retains efficacy against Omicron. Nat Biotechnol. 2022;40(2):184-190. doi:10.1038/s41587-021-01160-w*
- *Gottlieb RL, Vaca CE, Paredes R, et al. Ensovibep for treatment of outpatients with COVID-19. N Engl J Med. 2022;386(19):1722-1730. doi:10.1056/NEJMoa2202373*
- *Lopez-Leon S, Wegman-Ostrosky T, Perelman C, et al. More than 50 long-term effects of COVID-19: A systematic review and meta-analysis. Sci Rep. 2021;11:16144. doi:10.1038/s41598-021-95565-8*
- *Douaud G, Lee S, Alfaro-Almagro F, et al. SARS-CoV-2 is associated with changes in brain structure in UK Biobank. Nature. 2022;604:697-707. doi:10.1038/s41586-022-04569-5*