

A Novel Treatment Paradigm for the Treatment of Covid-19 Induced Acute Respiratory Distress Syndrome (ARDS)

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Acute respiratory distress syndrome due to the SARS-CoV-2 virus (COVID-19 ARDS) demonstrates the same pathologic changes of diffuse alveolar damage as classic ARDS, and ARDS develops in 33%-42% of hospitalized patients with COVID-19 and in 61-81% of patients admitted to the intensive care unit (ICU).^{1,2} Regardless of etiology, ARDS treatment options are limited to supportive care with mechanical ventilation (MV) and new, effective treatments are needed.³ ExoFlo™ is an acellular extracellular vesicle (EV) product isolated from a single donor bone marrow mesenchymal stem cell (bmMSC) culture that confers the promising anti-inflammatory and regenerative benefits of bmMSCs for treatment of ARDS without the drawbacks associated with viable cell therapy.⁴⁻¹² We proposed that ExoFlo could safely reduce lung injury from COVID-19, and possibly assist in the lung's recovery process. We describe the case of a patient with severe respiratory failure and subsequent ARDS requiring prolonged mechanical ventilation who recovered after receiving ExoFlo. This case highlights this EV product as a novel therapeutic for the treatment of COVID-ARDS.

The patient is a 40-year-old female with a history of mild intermittent asthma, diverticulosis, and a remote history of thyroid cancer status post thyroidectomy. The patient had a prolonged ICU course due to COVID-19 induced ARDS that started four days after delivering her second child via a Cesarean section. Treatment for ARDS included mechanical lung ventilation with prone positioning, treatment of secondary infections with intravenous antibiotics, and supportive care for multisystem organ failure. She also received standard supportive care for COVID ARDS including lung protective ventilation, intermittent neuromuscular blockade, and intravenous steroids.

After one month of supportive care failed to improve her status, an eIND (IND #28207) was approved by the Food and Drug Administration (FDA) for the administration of 15 mL of ExoFlo. At the time of ExoFlo administration, she was sedated with an FiO₂ of 100% and PEEP of 15cm H₂O, and she was receiving norepinephrine to maintain adequate perfusion. She received two doses of ExoFlo on Day 1 and Day 2 with slight improvement. She was not considered a candidate for extracorporeal membrane oxygenation (ECMO) due to the prolonged mechanical ventilation. Seventeen days later, she continued having febrile episodes and still required maximum ventilatory support. Her FiO₂ on the ventilator was 90% and her PEEP was at 14cm H₂O. Since her lung function had not improved, an additional treatment course of ExoFlo was approved by the FDA. After the second day of her second course of ExoFlo treatment, we were able to wean the PEEP, wean sedation and she began to move her lower extremities again. Due to this clear improvement, she continued the ExoFlo treatment course with 15 mL every 24 hours for a total of 5 days. By the fifth

dose of ExoFlo, her ventilatory requirements had improved to 55% FiO₂ and a PEEP of 8. The day after her fifth dose, two months from her ARDS diagnosis, she underwent a bedside tracheostomy and PEG tube placement.

Two days following her second round of ExoFlo treatment, her sedation continued to be weaned, her urine output began to increase, and she was initiated on oral intake with ice chips. Two weeks following this treatment course, the FDA approved a third treatment course with ExoFlo. Following her third course of ExoFlo (5 days, 15 mL Q 24 hours) her tracheostomy was downsized, ventilatory support was discontinued, and she achieved 96% oxygen saturation on trach collar. (Figure 1. A. Chest computed tomography (CT) imaging before five-day course of ExoFlo. B. Chest CT showing improvement after five-day course of ExoFlo.)

Four days after her third treatment course with ExoFlo, she was discharged from the hospital to a rehabilitation facility. She was still regaining strength and remained on oxygen at rest. Eight months after discharge from the hospital, she was able to return to work part time. One year after discharge, she has regained most of her strength. She still has some fine motor deficits in her right hand, and she still requires oxygen with exertion. She has a mild restrictive pattern and mild DLCO reduction on her pulmonary function tests, but her chest CT and overall functional status have both greatly improved. Her most recent CT shows improvement in the fibrotic injury appreciated on her earlier chest CTs. (Figure 2. A. Chest CT before five-day course of ExoFlo B. Chest CT one year after discharge from hospital).

Prior to her second course of ExoFlo, the ICU team was discussing palliative care options with the family, since she was in the severe COVID ARDS category of patients who often did not recover. Once she started showing signs of major improvement during her second course of treatment with ExoFlo, it became apparent that she had a good chance for a meaningful recovery. The multiplicity of molecules contained within ExoFlo may have promoted healing and regeneration of healthy lung tissue in this patient who appeared to have irreversible ARDS. Currently a Phase III, randomized, blinded trial is underway to evaluate the efficacy of ExoFlo in patients with moderate to severe COVID related ARDS.

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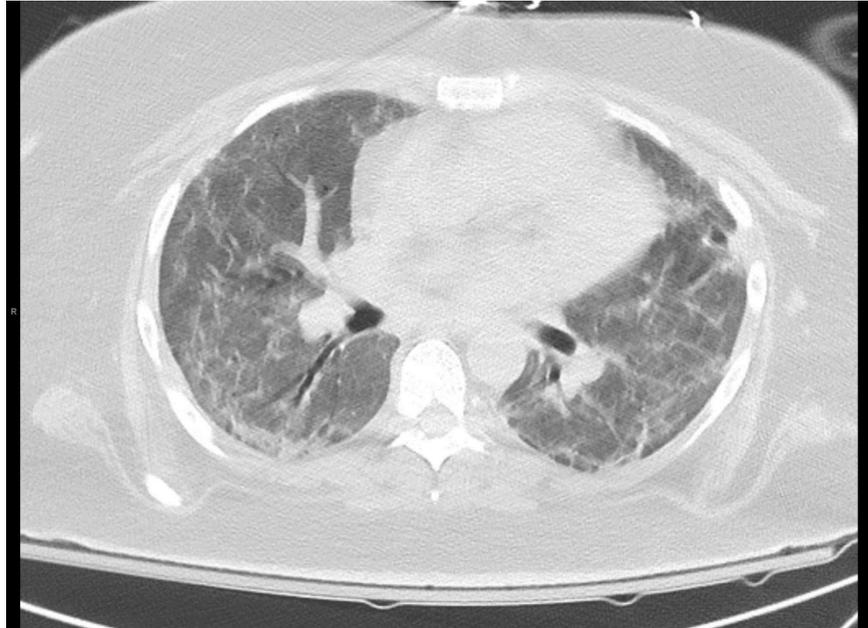




Figure 1. A. Chest CT imaging before five-day course of ExoFlo. February 8, 2022

Figure 1. B. Chest CT showing improvement after five-day course of ExoFlo. March 8, 2022.

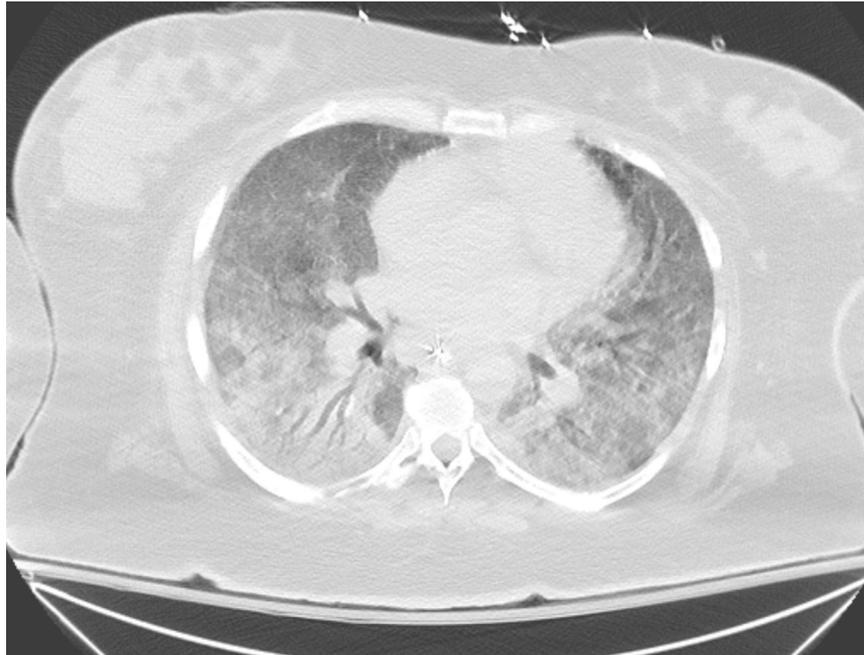


Figure 2. A. Chest CT before five-day course of ExoFlo. February 8, 2022

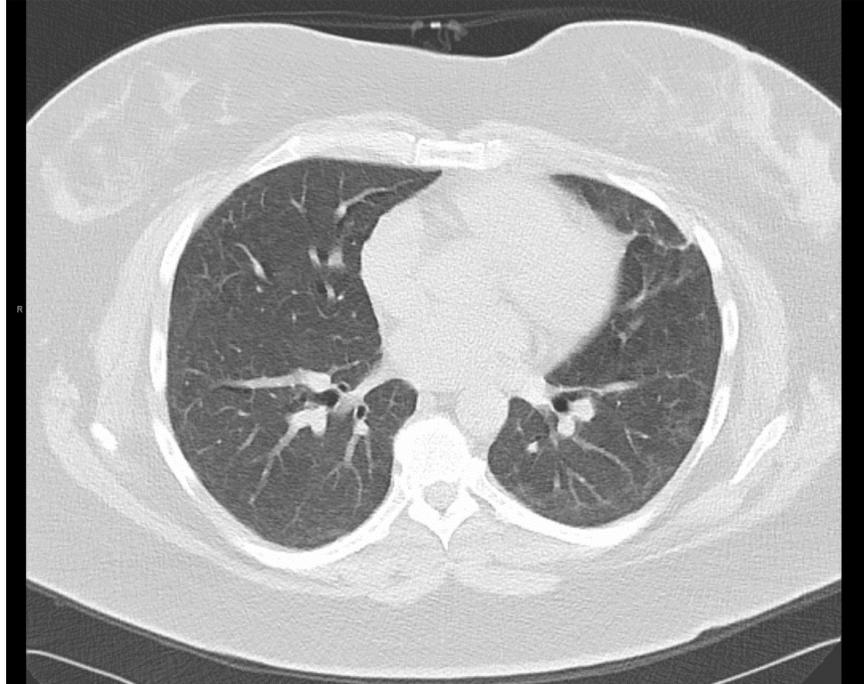


Figure 2.B. Chest CT one year after discharge from hospital. March 9, 2023

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Figure 2 Clinical Case Reports.docx available at <https://authorea.com/users/338813/articles/639690-a-novel-treatment-paradigm-for-the-treatment-of-covid-19-induced-acute-respiratory-distress-syndrome-ards>