

Placenta-Derived Cell Therapy to Treat Patients With Respiratory Failure Due to Coronavirus Disease 2019

Journal Club

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COVID-19 pandemic



- SARS-CoV-2
- Hyperinflammatory Syndrome in severely affected patients

Treatment

- Supportive care and supplemental oxygen with invasive mechanical ventilatory support
- Immune-modulatory treatment
 - Hydroxychloroquine
 - Interleukin (IL)-6 antagonist
 - IL-1 antagonists
- Dexamethasone
- Mesenchymal stromal cell (MSC) therapeutics
- PLacental eXpanded (PLX)-PAD Treatment

Objectives

- Benefit of Placental cell therapy **PLacental eXpanded (PLX)-PAD** in treatment of critically ill patients suffering from ARDS due to COVID-19
- Design → Retrospective case report

PLacental eXpanded (PLX)-PAD Treatment

- regenerative and immunomodulatory properties
- ↓ proinflammatory cytokines → TNF- α , interferon- γ , IL-17A
- ↑ anti-inflammatory cytokines → IL-10, IL-1Ra
- ↑ T-regulatory cells
- ↓ T cell proliferation
- macrophage population → M2 phenotype

- peripheral artery disease
- muscle injuries
- critical limb ischemia

Ⓢ PLX-PAD is an investigational product in the clinical development stage and is not authorized for sale in any country. Ⓢ

Treatment Procedure – PLX-PAD

ONE TREATMENT



300 MILLION CELLS



15 INTRAMUSCULAR INJECTIONS

Study Population

8 critically ill patients on invasive mechanical ventilation, suffering from ARDS due to COVID-19

General Characteristics of the Patients

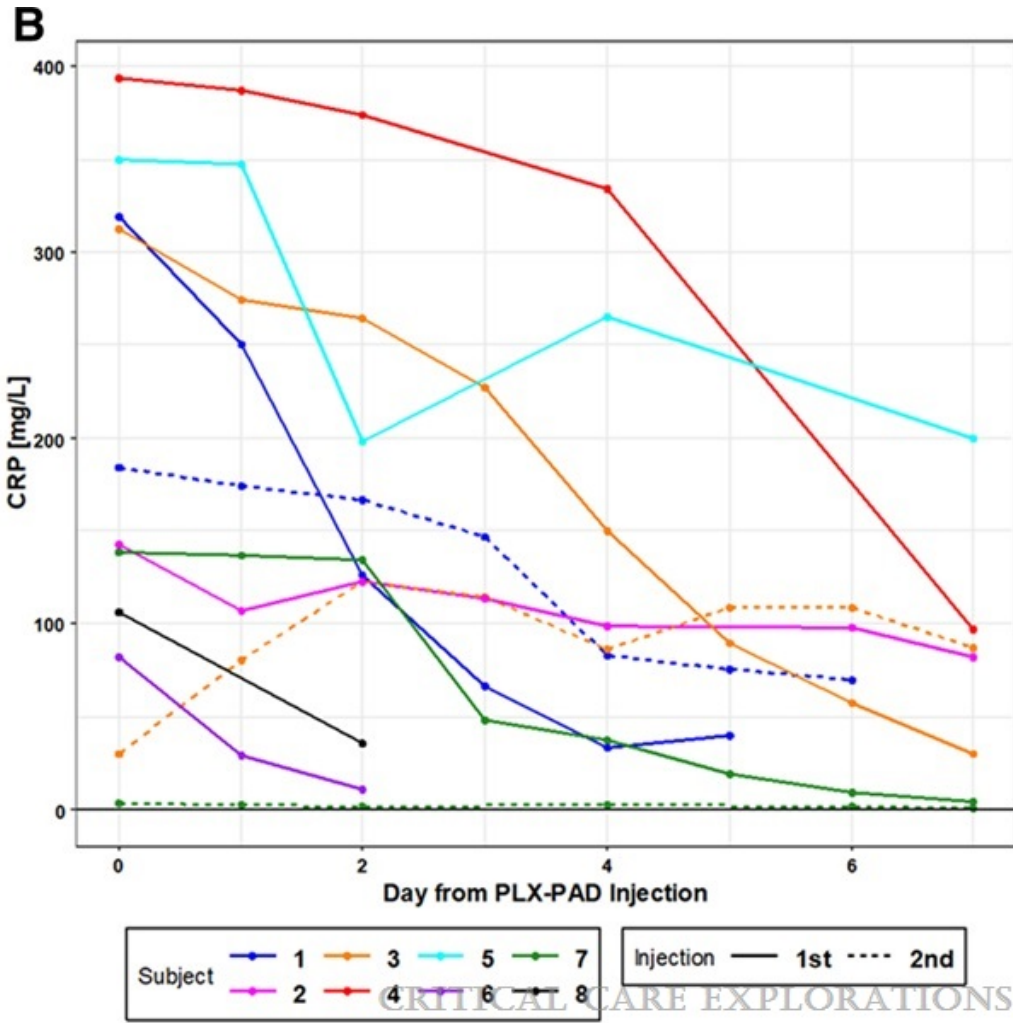
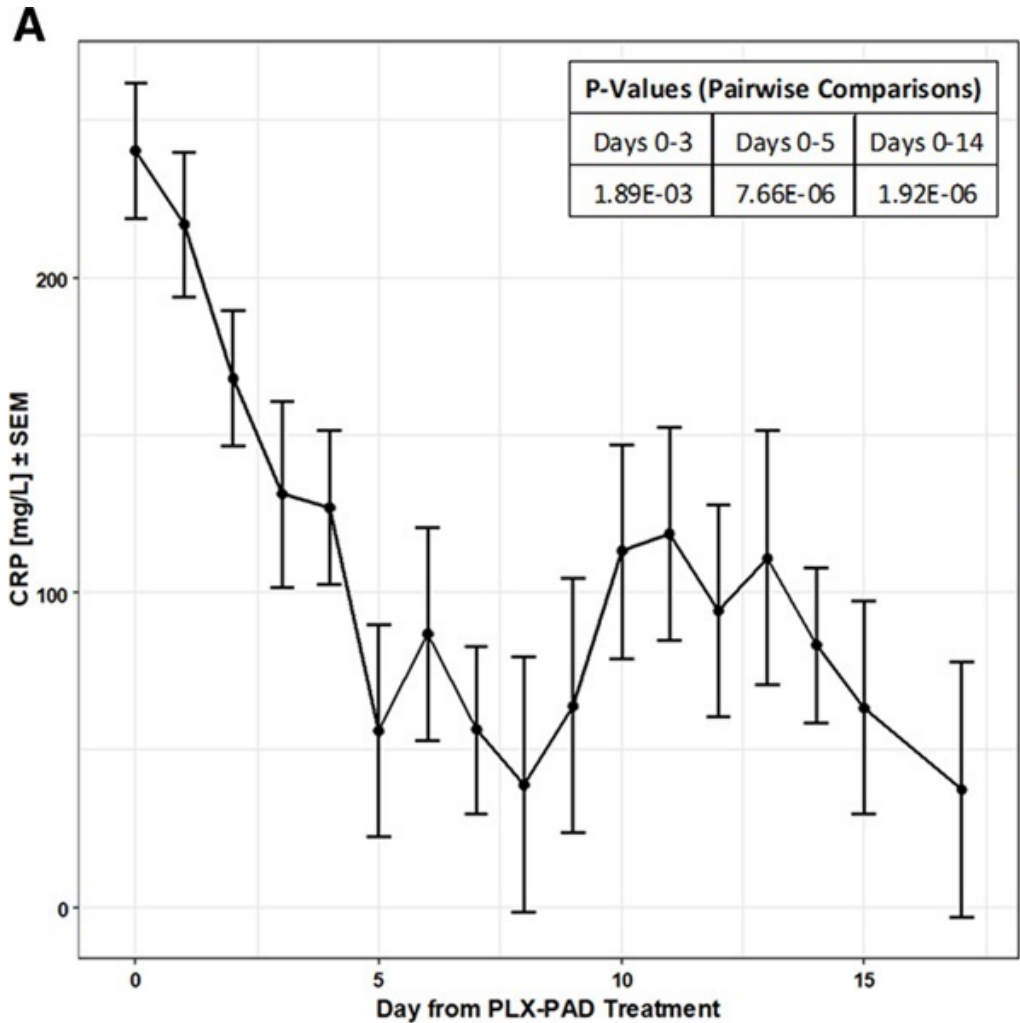
Table 1. - General Characteristics of Severe Acute Respiratory Syndrome Coronavirus 2 Infected Patients Who Received PLacental eXpanded-PAD Treatment

Characteristic Site	Subject 1 Rambam	Subject 2 Bnai Zion	Subject 3 Rambam	Subject 4 Assuta	Subject 5 Assuta	Subject 6 Assuta	Subject 7 Bnai Zion	Subject 8 Holy Name
Age	71	79	56	54	53	22	65	49
Sex	Male	Male	Male	Male	Male	Male	Female	Male
Body mass index	> 30	> 30	29.5	24.4	30	30.5	> 30	27.8
Active smoker	No	No	No	No	No	No	No	No
Diabetes	Yes	No	Yes	No	Yes	No	Yes	No
Hypertension	Yes	Yes	Yes	No	No	No	Yes	No
Chronic obstructive pulmonary disease	No	No	No	No	No	No	No	No
Ischemic heart disease	No	No	No	No	No	No	No	No
Number of PLacental eXpanded-PAD treatments	2	1	2	1	1	1	2	1
Other investigational drugs	Hydroxychloroquine, lopinavir	Hydroxychloroquine, remdesivir	Hydroxychloroquine, lopinavir	Hydroxychloroquine, anti-IL-6	Hydroxychloroquine, anti-IL-6	Hydroxychloroquine	Hydroxychloroquine, lopinavir, anti-IL-6	Hydroxychloroquine, remdesivir
Steroids	Yes	Yes	No	No	No	Yes	No	Yes
Number of hospital days	26	69	22	NA	27	48	NA	56
Days intubated before treatment	5	14	1	10	10	2	2	22
Days intubated after treatment	20	16	7	Ongoing	14	NA	35	11
Status	Died	Discharged	Discharged	In Hospital	Discharged	Discharged	In Hospital	Discharged

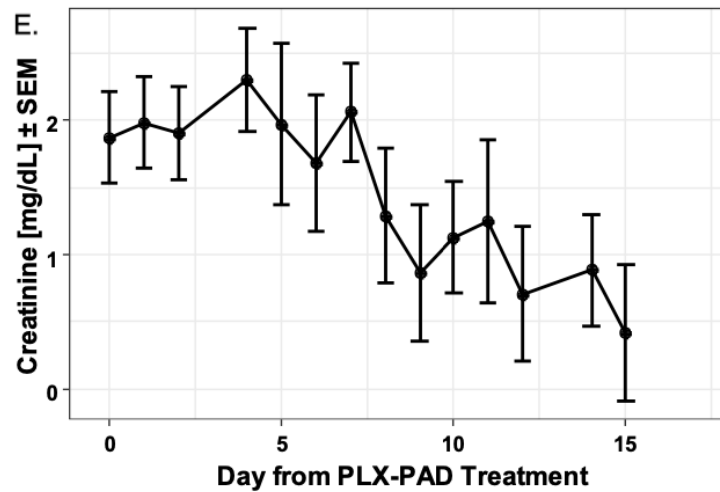
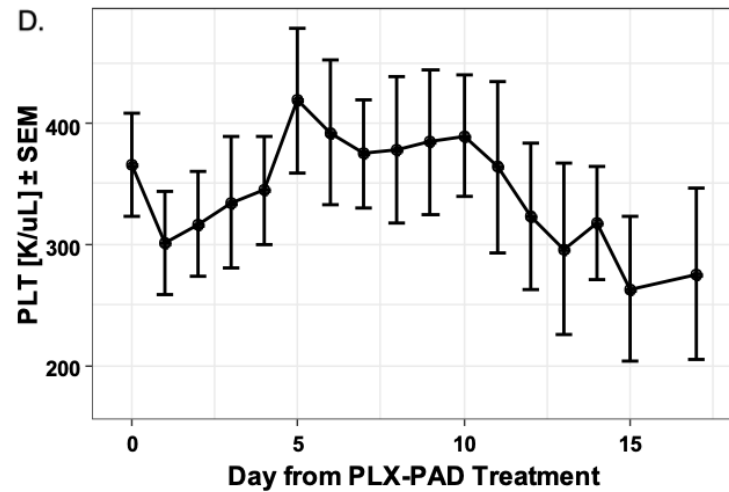
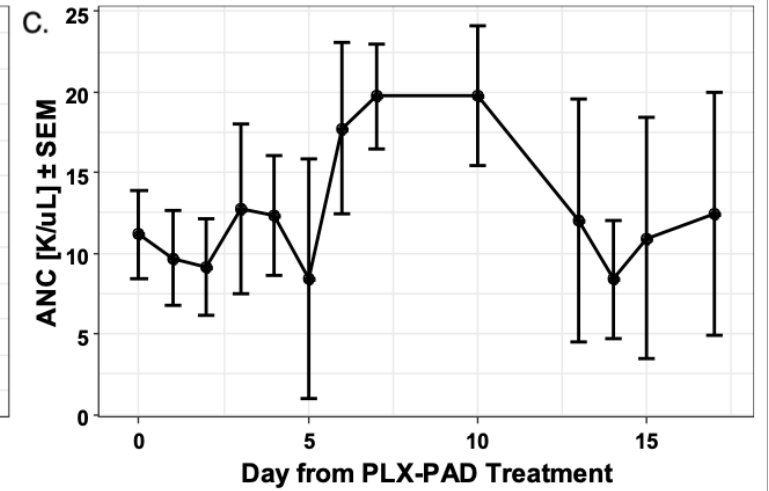
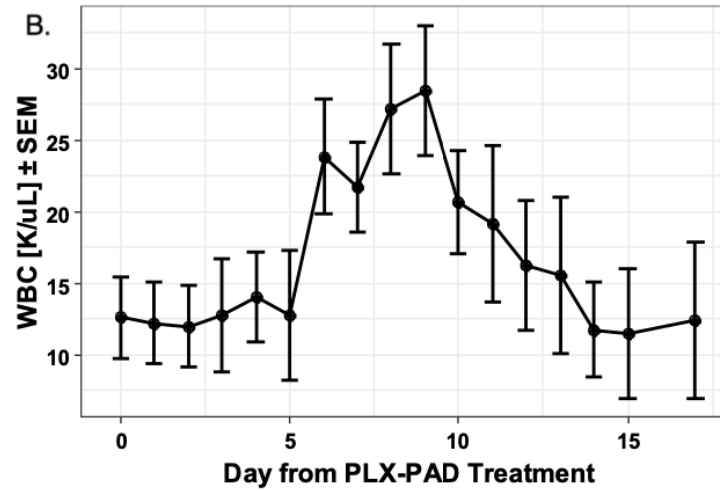
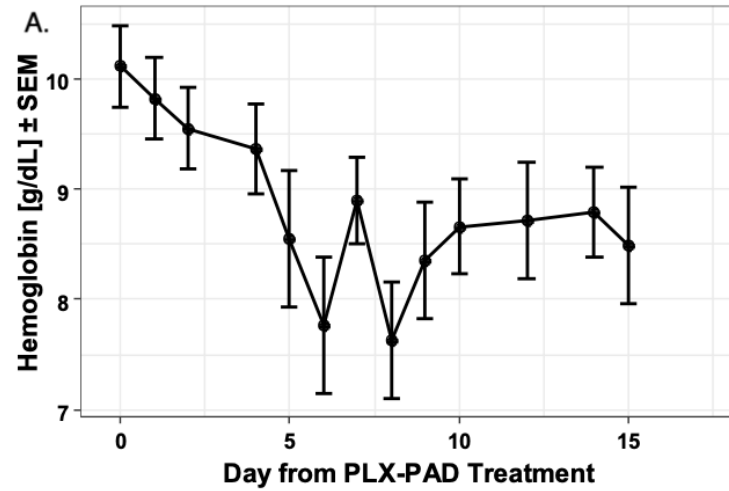
anti-IL-6 = anti-interleukin 6, NA = not available.

CRITICAL CARE EXPLORAT

Changes in Blood C-Reactive Protein (CRP) Levels



Blood Measurements



F.

Parameter	P-Values (Pairwise Comparisons)		
	Days 0-3	Days 0-5	Days 0-14
Hemoglobin [g/dL]	n.s.	1.53E-02	2.76E-03
WBC [K/uL]	n.s.	n.s.	n.s.
ANC [K/uL]	n.s.	n.s.	n.s.
PLT [K/uL]	n.s.	n.s.	n.s.
Creatinine [mg/dL]	n.s.	n.s.	3.24E-02

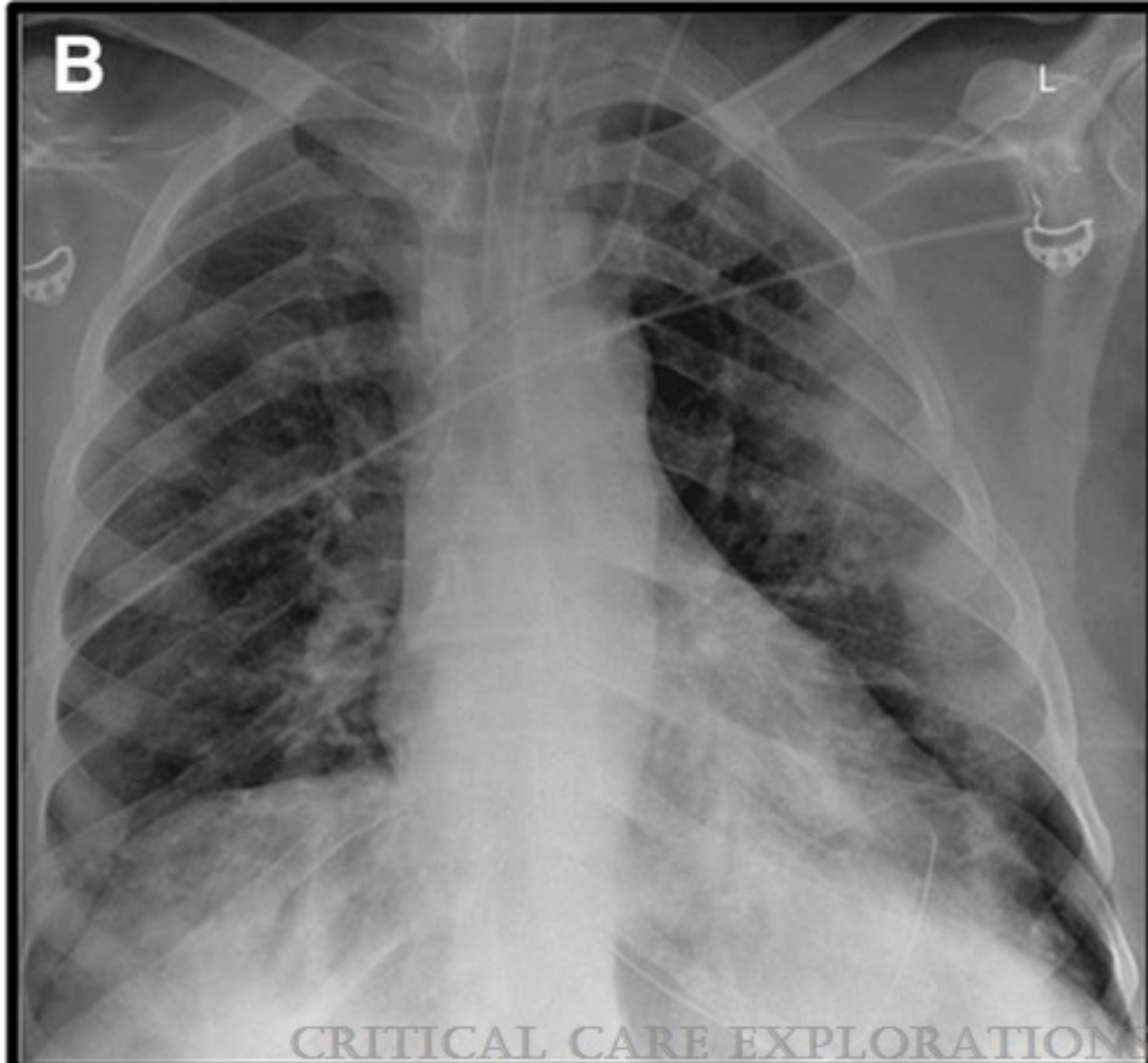
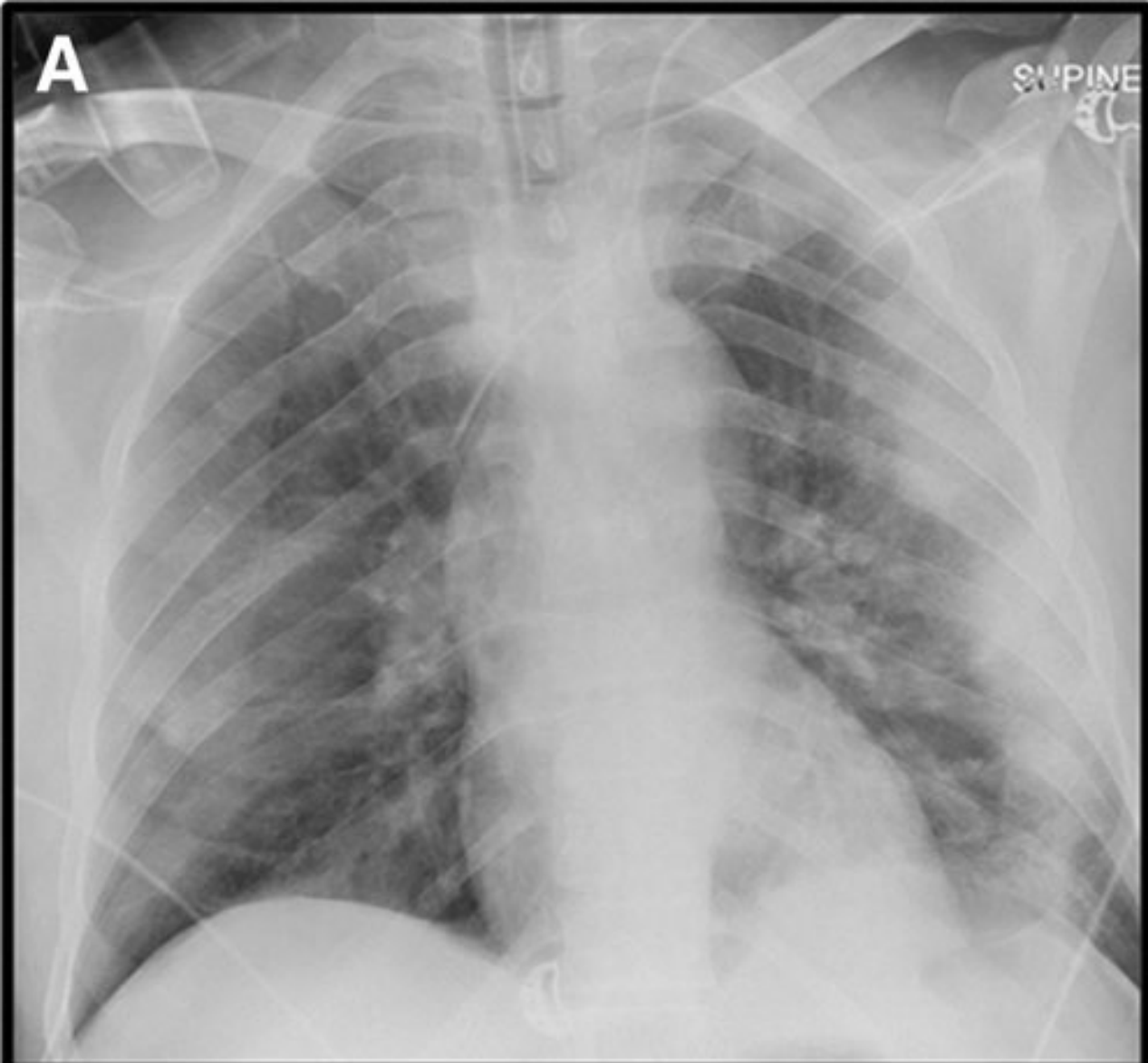
Patient No.	Before Treatment	24-hr Post Treatment	48-hr Post Treatment
1	160	229	170
2	140	172.5	177.5
3	143	151	217
4	149	107	92
5	106	145	197
6	173	205	151
7	172	93	95
8	342.5	Not available	425

Respiratory Variables Following Administration of PLX-PAD

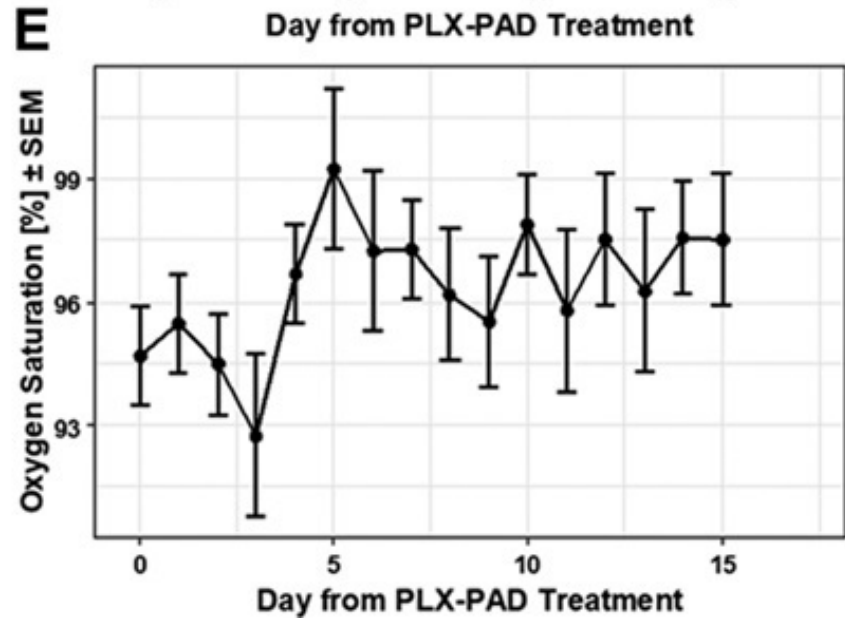
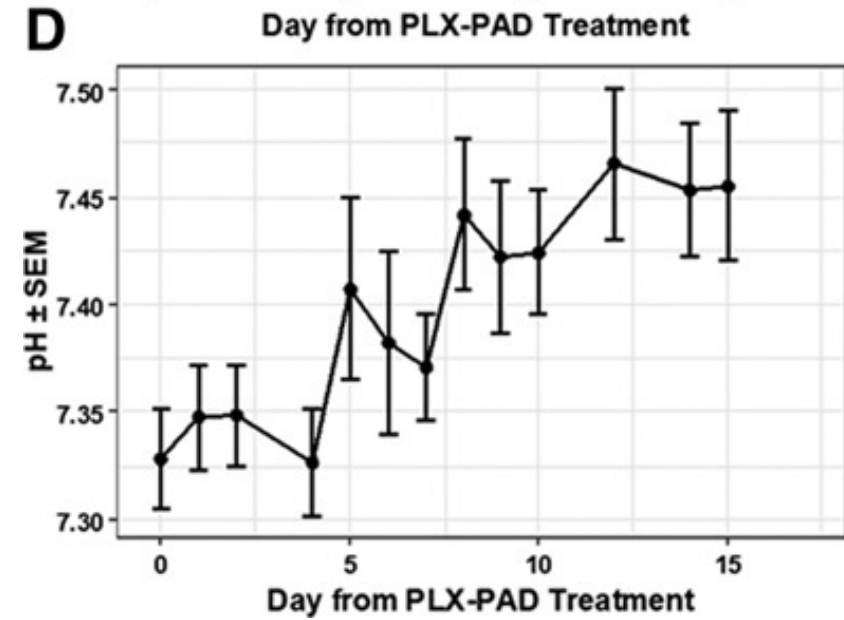
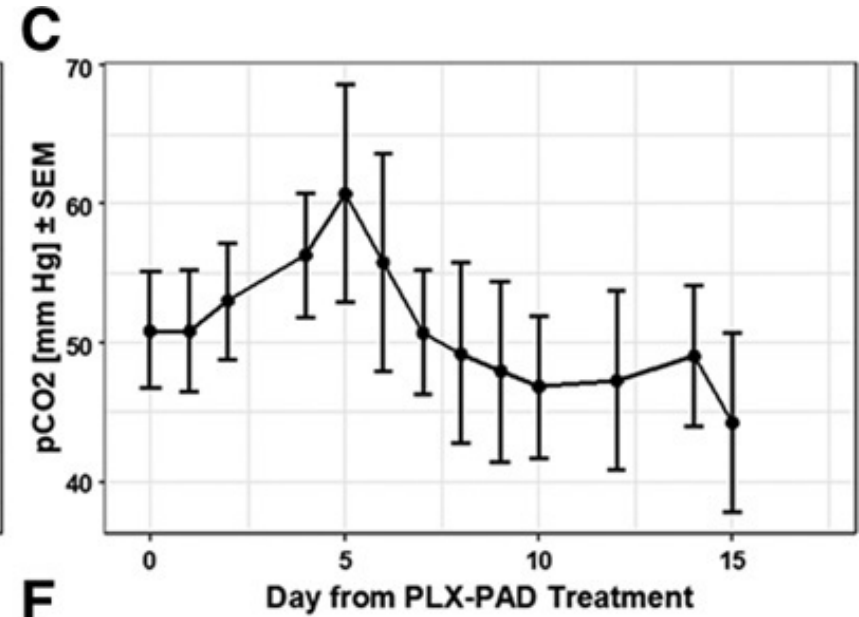
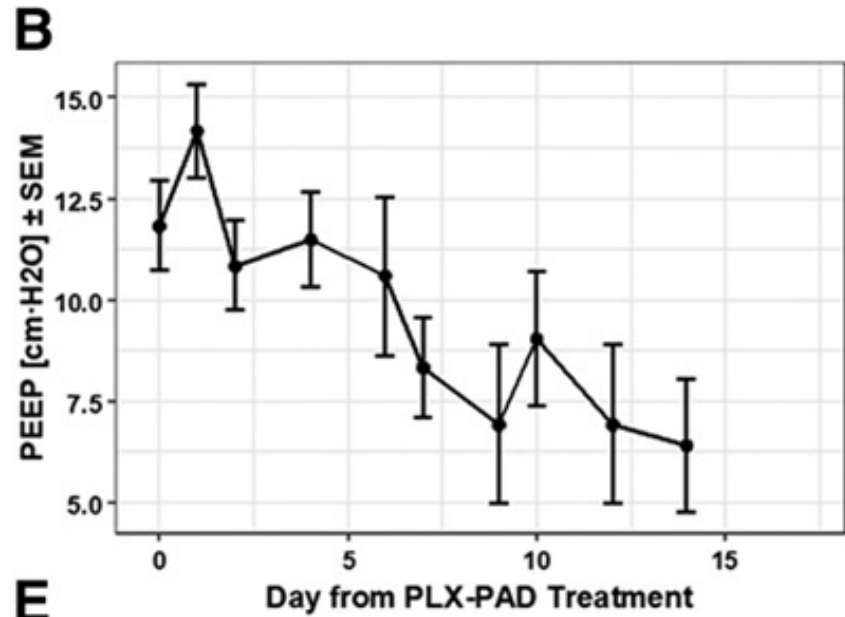
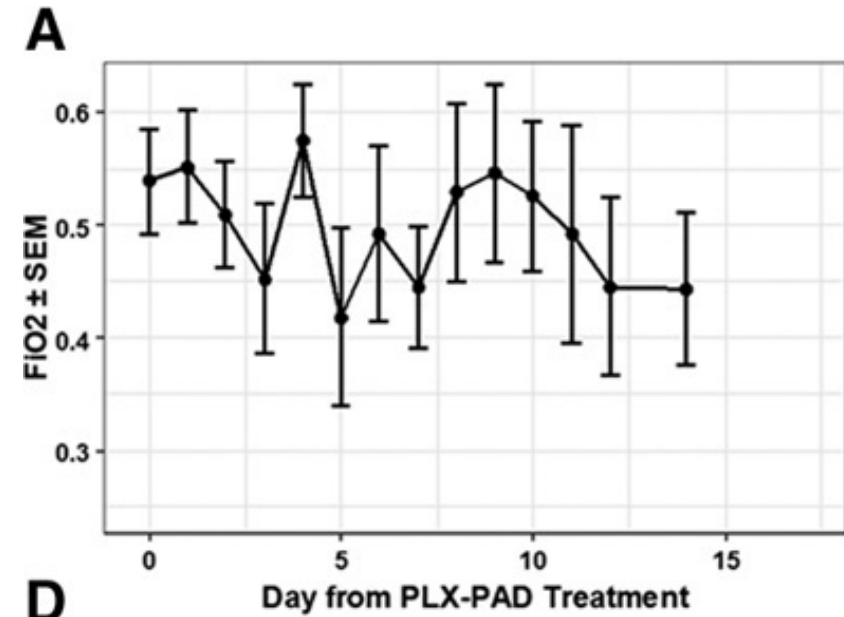


CRITICAL CARE

Improvement in Chest Radiographs Following Administration of PLX-PAD



Changes in respiratory variables

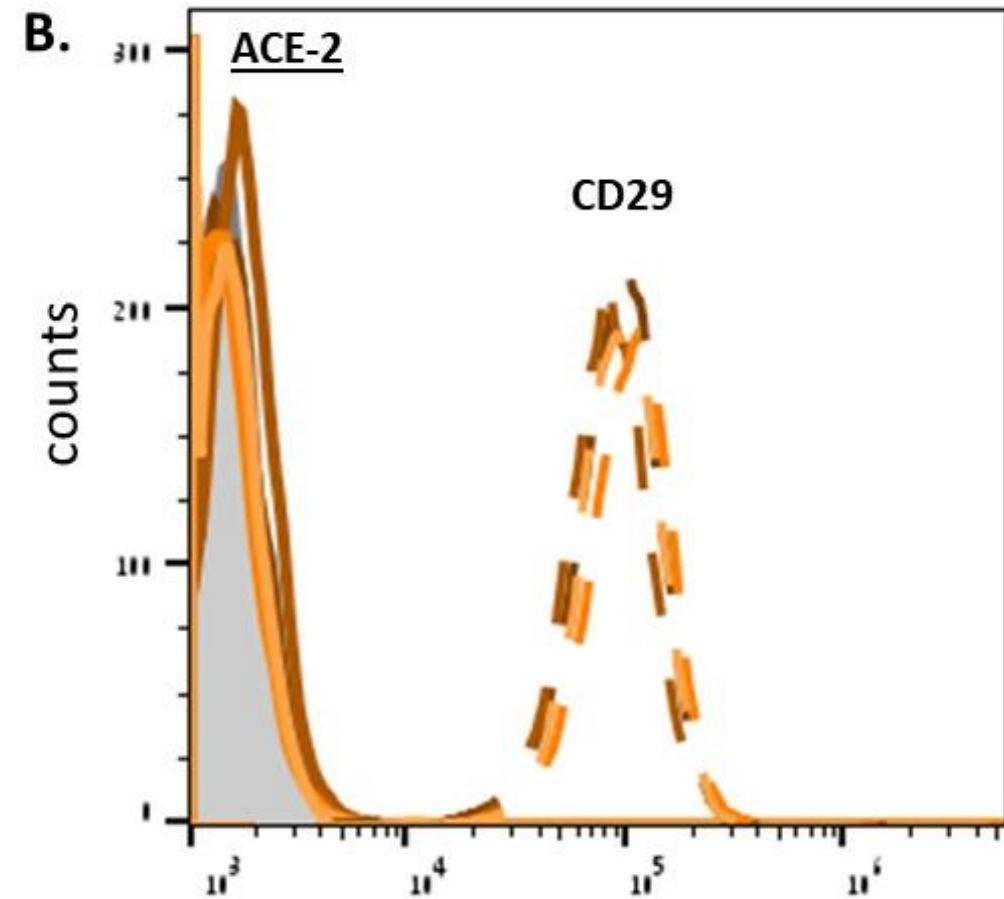
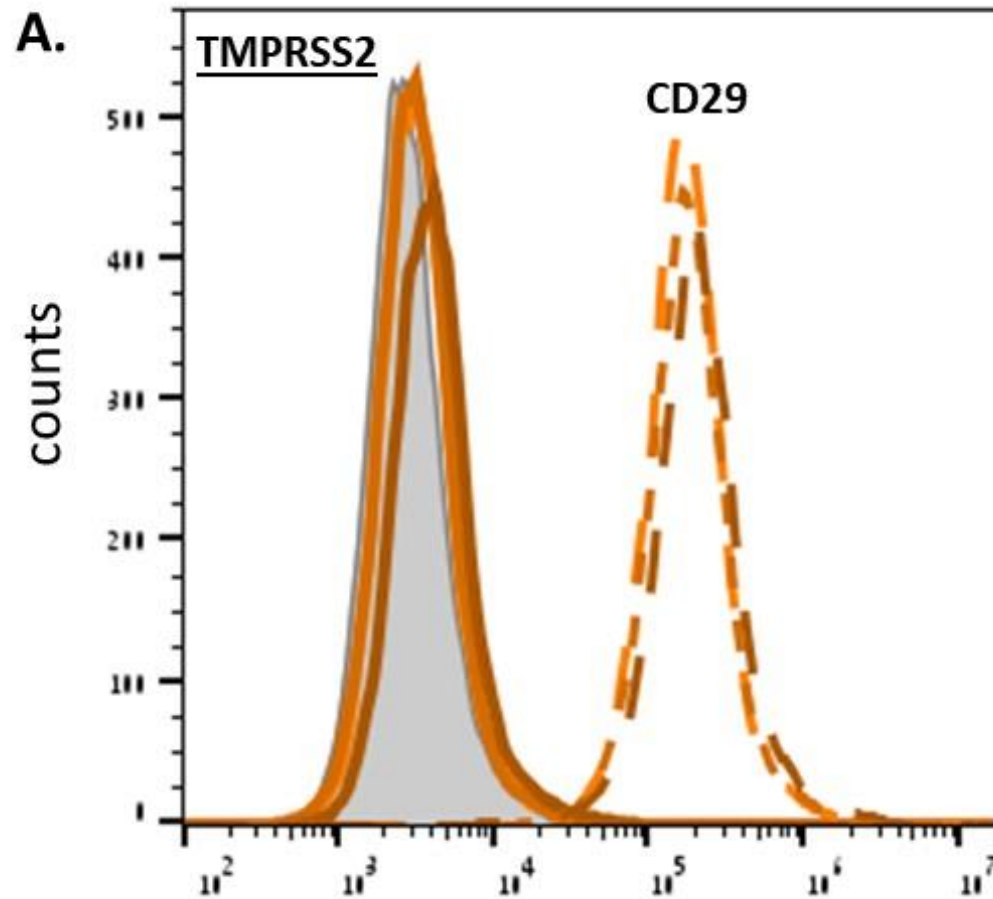


F P-Values (Pairwise Comparisons)

Parameter	P-Values (Pairwise Comparisons)		
	Days 0-3	Days 0-5	Days 0-14
FiO ₂	n.s.	n.s.	n.s.
PEEP [cm·H ₂ O]	n.s.	n.s.	3.22E-03
pCO ₂ [mm Hg]	n.s.	n.s.	n.s.
pH	n.s.	n.s.	7.19E-04
Oxygen Sat. [%]	n.s.	4.97E-02	n.s.

CRITICAL CARE EXPLORATIONS

PLX-PAD Cells Do Not Express the SARS-CoV-2 Receptor ACE2 or the Serine Protease TMPRSS2



Take Home Message

- PLX-PAD can be safely used in COVID-19 patients without being a further target for SARS-CoV-2
- PLX-PAD as a potential drug for the treatment of critically ill COVID-19 patients, showed improvement regarding: CRP, creatinine levels, P/F, radiological findings, as well as an overall improvement in the clinical status of most patients.
- PLX-PAD may reduce mortality of critically ill COVID-19 patients

Thank You !

