Treatment with Allocetra–OTS in 21 severely/critically ill patients with COVID-19, leading to swift discharge and cytokine storm resolution

Vernon Van Heerden[1], Avi Abutbol[1], Yehudit Shabat[2], Barak Reicher[2], Dror Mevorach, M.D.[1]

[1] Hadassah-Hebrew University Medical Center, Jerusalem Israel. [2] Research, Enlivex

Background

COVID-19 has become pandemic, with mortality estimated between 1–4% (in Alpha and Delta variants) and complications among hospitalized patients resulting in up to 15–25% of inpatients being admitted to the intensive care unit (ICU).

Two studies (one of 5 and one of 16 patients), were designed to determine the safety and efficacy of treatment with Allocetra-OTS for reprogramming macrophages and resolution of cytokine storm in patients with severe/critical COVID-19.

The two studies were approved by the Ministry of Health's (MOH) Ethical Committee.

Methods

Two clinical studies were done in three medical centers in Israel.

Patient inclusion criteria was severe or critical condition by NIH criteria. Further details are found in NCT04590053 and NCT04513470.

Allocetra-OTS preparation. An enriched mononuclear cell fraction was collected via leukapheresis from healthy, eligible human donors, prepared by Enlivex Therapeutics Ltd. As described (Van Heerden et al. Frontiers in Immunology 2021). Following sighing an informed consent every patient received a single dose of 10^9 Allocetra–OTS cells. The patients were followed-up for 28 days and monitored for any adverse events, and blood samples were cell counted and analyzed for serum cytokines.

Results

Administration of Allocetra-OTS in 21 COVID–19 patients (11 severe and 10 critical, with non-invasive oxygen support-airvo) was safe, with only five unrelated serious adverse events (SAEs). 18/21 patients had significant ARDS.

Allocetra-OTS was well tolerated when given in conjunction with standard therapy (Remdesivir, Enoxaparin, and Dexamethasone) and showed early recovery, with 5.5 days in average till discharge.

Only 2/21 patients were still hospitalized by day 28 (end of study).18 patients had mild-to severe ARDS and 16/18 (88.8%) completely recovered within few days.

The cytokine storm was resolved in all discharged patients as shown by laboratory and 30 cytokine/chemokine measurements.

Clinical Trial	# Patients enrolled	Disease Severity	Clinical Outcome		Hospitalization Post Administration of Allocetra-OTS	
			Recovered Day 28	Mortality Day 28	Discharged Day 28	Duration (days, avg.)
Phase Ib	5	2 Severe, 3 Critical	5/5 (100%)	0/5 (0%)	5/5 (100%)	6.6
Phase II	16	9 Severe, 7 Critical	14/16 (87.5%)	0/16 (0%)	14/16 (87.5%)	5.3
Total	21	11 Severe, 10 Critical	19/21 (90.5%)	0/21 (0%)	19/21 (90.5%)	5.6

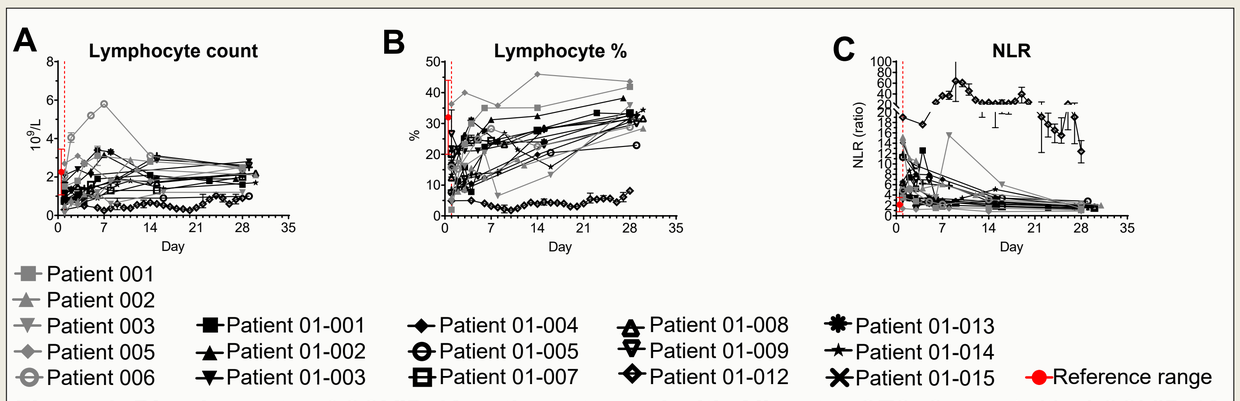

Figure 1. Blood counts of COVID-19 patients treated with Allocetra-OTS. Severe/critical COVID-19 patients from studies NCT04513470 (gray symbols) and NCT04590053 (black symbols) were treated with Allocetra-OTS on Day 1 (red dotted line); blood samples were analyzed. Presented here are for (**A-B)** lymphocyte, and (**C**) neutrophil : lymphocyte ratio (NLR) at the indicated timepoints; the first blood sampling of each patient was taken before i.v administration of Allocetra-OTS. Data are shown as average ± range.

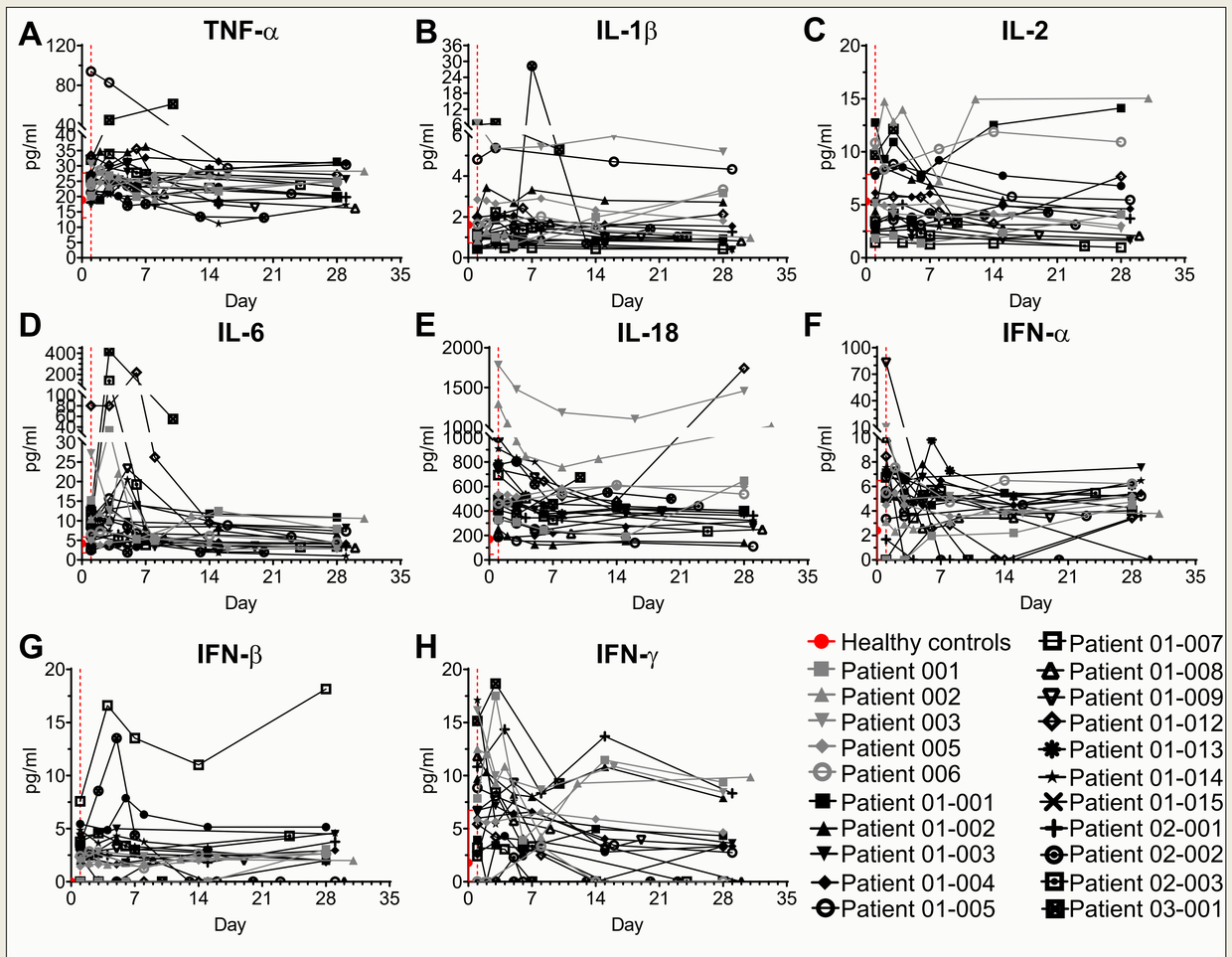

Figure 2. Pro-inflammatory cytokines of COVID-19 patients treated with Allocetra-OTS. Severe/critical COVID-19 patients from studies NCT04513470 (gray symbols) and NCT04590053 (black symbols) were treated with Allocetra-OTS on Day 1 (red dotted line); serum samples were analyzed for (**A**) TNF-α, (**B**) IL-1β, (**C**) IL-2, (**D**) IL-6, (**E**) IL-18, (**F**) IFN-α, (**G**) IFN-β, and (**H**) IFN-γ cytokine concentration at the indicated timepoints; the first blood sampling of each patient was taken before i.v administration of Allocetra-OTS. Data are shown as average ± range.

Conclusion

Allocetra–OTS showed excellent safety profile, resolution of cytokine storm, and promising clinical results in COVID-19 severe/critical patient population, of which 88.8% had ARDS associated with SARS-2.