Press Release

ABIONYX Pharma RACERS study data in sepsis presented at the American Society of Nephrology (ASN) 2023 Annual Meeting "Kidney Week"

CER-001 showed robust efficacy in sepsis demonstrating statistically significant sustained reduction in endotoxins (LPS) and consequent decreases in inflammatory cytokines and markers of endothelial dysfunction

Data showed a reduced severity of AKI, a trend for decreased mortality and shorter ICU stay

CER-001 shows promise as a therapeutic strategy for sepsis management, improving outcomes and mitigating inflammation and organ damage with the potential to save lives

Simultaneous publication of data from translational sepsis research project, including the RACERS study, exclusively in BMC Medicine (Nature Springer)

Toulouse, FRANCE, Lakeland MI, USA, November 2nd, 2023, 6.00 p.m. CET - **ABIONYX Pharma**, (**FR0012616852 - ABNX - PEA PME eligible**), a new generation biotech company dedicated to the discovery and development of innovative therapies based on the world's only recombinant human apoA-1, today announced the full results of the RACERS Phase 2 clinical trial of CER-001, an apoA-1-based therapy for the treatment of sepsis, in a late-breaking clinical trial poster presentation at the American Society of Nephrology (ASN) Kidney Week 2023.

Key Points from the RACERS Data:

CER-001 rapidly and significantly eliminated endotoxins, and the result was maintained ($p<0.05$ on days 3, 6 and 9), whereas even by day 9, patients on standard care alone showed no decreases in endotoxin levels relative to baseline.

Mortality for all patients at 30 days was 6.7% for the CER-001 group and 20.0% for patients treated with standard care alone. This represents a **Relative Risk Reduction (RRR) of 65%**.

Among critical care patients, mortality rates were 14.7% compared to 50.0% for patients on standard care (RRR=71%).

ICU patients treated with CER-001 were discharged earlier than patients receiving standard care, with **an average ICU stay 5 days shorter than that of patients on standard care.**

In the RACERS trial, which included patients with sepsis, CER-001 added to standard of care treatment demonstrated statistically significant and sustained endotoxin removal compared to standard care alone ($p<0.05$ on days 3, 6 and 9). Subsequent immunomodulation was observed with CER-001 treatment, which led to rapid and significant decreases in pro-inflammatory cytokines (e.g., IL-6, IL-8, TNF-α, MCP-1), endothelial dysfunction markers (sVCAM, sICAM) and a mortality biomarker (sTREM-1).

Additionally, patients treated with CER-001 had reduced severity of AKI and a trend for improved survival compared to placebo. In a subset of critically ill patients recruited from the ICUs, a trend toward improved survival and a shorter length of ICU stay due to decreased need for organ support was observed with CER-001.

"*Our RACERS data emphasize the safety and efficacy of a novel HDL-mimetic compound in sepsis*," said **Pr. Loreto Gesualdo, Head of the Nephrology, Dialysis and Transplantation Unit, University of Bari Aldo Moro, Italy, and lead investigator of the RACERS study**. "*The data provide valuable insights into the multifaceted effects of HDL in a heterogeneous population of septic patients, and the ability of CER-001 to counteract inflammation, modulate the immune response, and protect endothelial cells makes it a promising potential therapeutic option for sepsis*."

"The data of the study have profound implications for the management of sepsis and CER-001's pleiotropic effects hold promise in mitigating the severity of critical inflammation and organ failure in sepsis," said **Cyrille Tupin, CEO of ABIONYX Pharma**. "*Considering the economic burden and high mortality associated with sepsis, the 3rd leading cause of death in the world, the novel therapeutic approach represented by CER-001 offers big hope for addressing unmet medical needs in critical care."*

Detailed RACERS Results

RACERS, an open-label, randomized, pilot (Phase 2a) study, was designed to determine an optimal dose of CER-001 in combination with standard of care in septic patients based on safety, identify the effects on Acute Kidney Injury (AKI) onset and severity and assessing the changes from baseline for endotoxin and IL-6 levels, and other key inflammatory and endothelial dysfunction markers.

Participants with sepsis due to intra-abdominal cavity infection or urosepsis due to Gram-negative bacteria causing high levels of endotoxin activity and a sequential organ failure score of at least 2 points, were recruited from the Intensive Care Units (ICUs) or the sub-intensive Nephrology unit to participate in the study.

The primary endpoint of the study was to determine an optimal dose of CER-001 in combination with standard of care in septic patients based on safety. In addition, the study aims to analyze whether CER-001 treatment had an effect on AKI onset and severity according to KDIGO criteria.

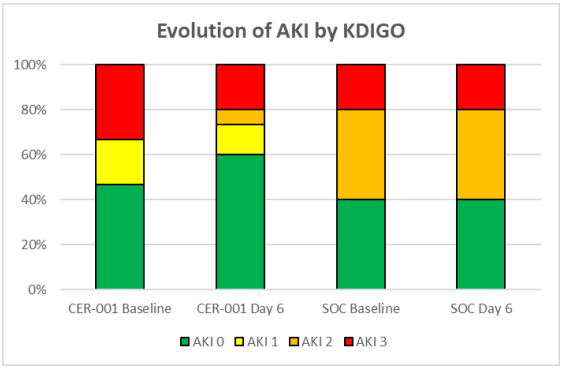
Secondary endpoints included the change from baseline (the last measurement taken prior to dosing on Day 1) to Days 3, 6 and 9 for endotoxin and IL-6 levels, SOFA score and other key inflammatory and endothelial dysfunction markers. Data on mortality at Day 30 were also reported as a pre-specified exploratory endpoint.

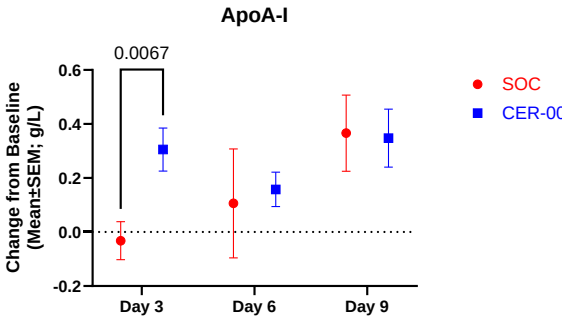
No safety issues were identified for any of the CER-001 dosing regimens. Most patients (11/20; 55%) already had AKI by the time they were randomized into the study. In these patients, no improvement was seen by Day 6 on standard of care alone (0/3) while 50% of patients treated with CER-001 saw improvement (4/8).

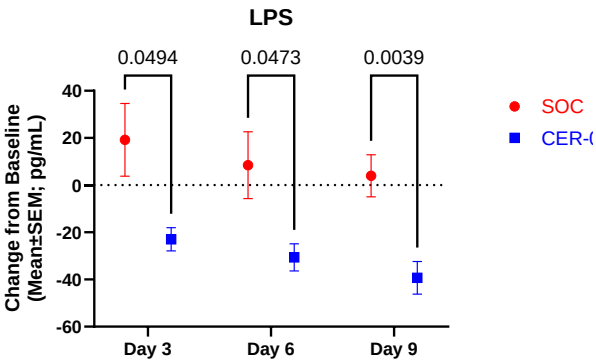
ApoA-I levels, known to be markedly decreased in patients with sepsis and septic shock,[1,2,3] increased rapidly when CER-001 was added to standard of care (p=0.0067 on Day 3). Endotoxins from Gram-negative bacteria, also called lipopolysaccharide (LPS), were elevated for all patients at baseline, as part of the study entry criteria. CER-001 rapidly and significantly removed LPS and the result was sustained (p<0.05 on Days 3, 6 and 9), whereas patients on standard of care alone still had levels of LPS higher the baseline at Day 9.

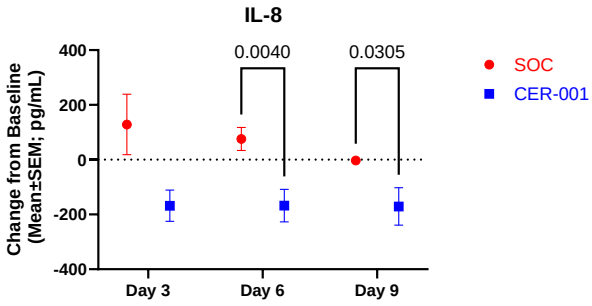
A recent scoping review[4] of studies that investigated circulating protein and lipid markers to inform non-COVID-19 sepsis diagnosis and prognosis identified IL-8 and ICAM as important markers correlated not only with detecting sepsis, but also strongly associated with patient outcome. In the RACERS study, patients treated with CER-001 on top of standard of care had significant decreases in IL-8 (p=0.004) and ICAM (p=0.002) by Day 6 of the study compared to standard of care alone.

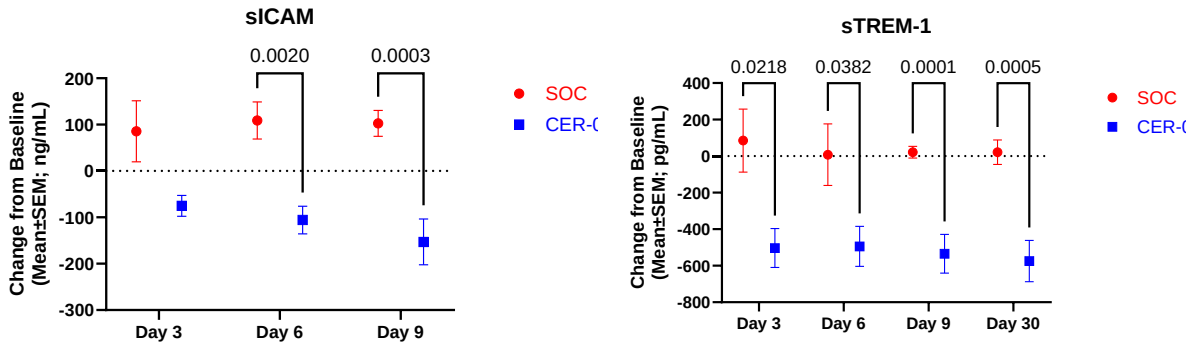
Soluble triggering receptor expressed on myeloid cells 1 (sTREM-1) has also been reported as a predictor of progression from sepsis to septic shock and of mortality.[5] CER-001-treated patients showed significant rapid and sustained decreases of sTREM-1, from Day 3 (p=0218) through Day 30 (p=0.0005) while patients treated with standard of care only saw minimum decreases from baseline levels.











Mortality in all patients at 30-days was 6.7% for CER-001 and 20.0% for standard of care alone (RRR=65%); in the subset of critically ill patients recruited from the ICUs, the rates were respectively 14.7% and 50.0% (RRR=71%). Additionally, ICU patients treated with CER-001 were discharged to step-down care sooner than those on standard of care alone, with an average ICU stay 5 days shorter than patients on standard of care alone (23.2 vs 28.5 days).

The late-breaking clinical results poster from ASN Kidney Week, presenting the RACERS data is available on the Company's website.

The full results of the RACERS study are published simultaneously and exclusively in the prestigious journal BMC Medicine (Nature Springer).

About sepsis:

Sepsis is characterized by a dysregulated immune response and metabolic alterations, including decreased High-Density Lipoprotein cholesterol (HDL-C) and apoA-I levels. Our recent research highlighted the diverse properties of HDL/apoA-I, including LPS scavenging, anti-inflammatory effects, and preservation of endothelial integrity in an LPS-induced AKI swine model treated with CER-001.

The severity in sepsis is related to the sequential organ failure assessment score (SOFA) which detects mortality in patients. A SOFA score of less than two is associated >90% survival, while a score of more than 20 is associated with >94% mortality.

About CER-001

CER-001 is a novel engineered HDL-mimetic comprised of recombinant human apoA-I and phospholipids that was designed to mimic the beneficial properties of nascent pre-β HDL. The binding of pathogen-associated lipids to HDL leads to sequestration, neutralization, and inactivation of their pro-inflammatory effects. HDL constitute an arm of the innate immune system. Pathogen-associated HDL can be removed from the body via the reverse lipopolysaccharide transport pathway in which HDL play a key role. Independent of the capacity for sequestration, the direct anti-inflammatory effects of HDL may counteract the development of sepsis.

About BioMed Central (Springer Nature)

BioMed Central (BMC) is a United Kingdom-based, for-profit scientific open access publisher that produces over 250 scientific journals. BioMed Central is the first and largest open access science publisher. It was founded in 2000 and has been owned by Springer Nature since 2008.

About ABIONYX Pharma

ABIONYX Pharma is a new generation biotech company that aims to contribute to health through innovative therapies in indications where there is no effective or existing treatment, even the rarest ones. Thanks to its partners in research, medicine, biopharmaceuticals and shareholding, the company innovates on a daily basis to propose drugs for the treatment of renal and ophthalmological diseases, or new apoA-I vectors used for targeted drug delivery.

Contacts:

NewCap
Investor relations
Nicolas Fossiez
Louis-Victor Delouvrier
abionyx@newcap.eu
+33 (0)1 44 71 98 53

NewCap
Media relations
Arthur Rouillé
abionyx@newcap.eu
+33 (0)1 44 71 00 15

---

[1] Cirstea M, Walley KR, Russell JA, Brunham LR, Genga KR, Boyd JH. Decreased high-density lipoprotein cholesterol level is an early prognostic marker for organ dysfunction and death in patients with suspected sepsis. J Crit Care. 2017 Apr;38:289-294. doi: 10.1016/j.jcrc.2016.11.041. Epub 2016 Dec 7. PMID: 28013095.

[2] Roveran Genga K, Lo C, Cirstea M, Zhou G, Walley KR, Russell JA, Levin A, Boyd JH. Two-year follow-up of patients with septic shock presenting with low HDL: the effect upon acute kidney injury, death and estimated glomerular filtration rate. J Intern Med. 2017 May;281(5):518-529. doi: 10.1111/joim.12601. Epub 2017 Mar 19. PMID: 28317295.

[3] Tanaka S, Couret D, Tran-Dinh A, Duranteau J, Montravers P, Schwendeman A, Meilhac O. High-density lipoproteins during sepsis: from bench to bedside. Crit Care. 2020 Apr 7;24(1):134. doi: 10.1186/s13054-020-02860-3. PMID: 32264946; PMCID: PMC7140566.

[4] Barber G, Tanic J, Leligdowicz A. Circulating protein and lipid markers of early sepsis diagnosis and prognosis: a scoping review. Curr Opin Lipidol. 2023 Apr 1;34(2):70-81. doi: 10.1097/MOL.0000000000000870. PMID: 36861948.

[5] Jedynak M, Siemiatkowski A, Mroczko B, Groblewska M, Milewski R, Szmitkowski M. Soluble TREM-1 Serum Level can Early Predict Mortality of Patients with Sepsis, Severe Sepsis and Septic Shock. Arch Immunol Ther Exp (Warsz). 2018 Aug;66(4):299-306. doi: 10.1007/s00005-017-0499-x. Epub 2017 Dec 27. PMID: 29282483; PMCID: PMC6061141.