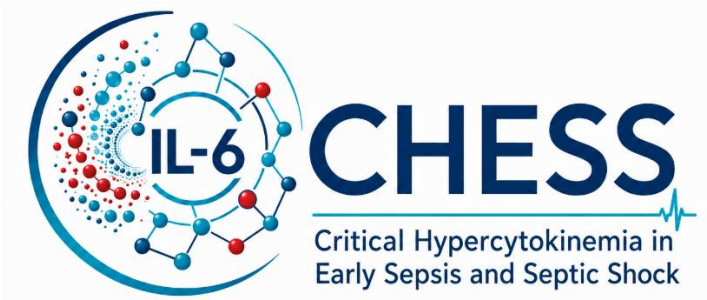

CHESS STUDY (Critical Hypercytokinemia in Early Sepsis and Septic shock)

We have recently published a study entitled "Critical Hypercytokinemia in Sepsis and Septic Shock: Identifying Interleukin-6 Thresholds Beyond Which Mortality Risk Exceeded Survival Probability." In this single-centre cohort of patients with severe sepsis and septic shock, we identified a plasma interleukin-6 threshold above 15,000 pg/mL as a clinically relevant marker associated with severe organ dysfunction and increased mortality. We have defined this level of IL-6 as "critical hypercytokinemia", reflecting an extreme hyperinflammatory state in which the risk of death exceeds the probability of survival.

Based on these findings, we are now launching an external validation study called CHESS (Critical Hypercytokinemia in Early Sepsis and Septic Shock). The main objective of CHESS is to validate, in an independent multicentre cohort, whether early IL-6 levels can identify this hyperinflammatory endotype of sepsis associated with poor clinical outcomes.

We are currently looking for hospitals that routinely measure IL-6 or have measured during the early phase of sepsis or septic shock, ideally within the first 12–24 hours from diagnosis or clinical onset. Participation would involve the collection of anonymised clinical, microbiological, laboratory and outcome data from patients with sepsis or septic shock in whom IL-6 was measured as part of routine clinical practice or in a research study.

The study is observational, retrospective and non-interventional. The aim is to build an international collaborative cohort that may help externally validate the concept of critical hypercytokinemia and define clinically meaningful IL-6 thresholds. This could support the future development of precision medicine strategies in sepsis, including patient selection for immunomodulatory therapies.

We believe your centre could make a valuable contribution to this project. We would be very grateful if you could let us know whether IL-6 is measured in your hospital during the early phase of sepsis or septic shock, and whether you would be interested in participating in CHESS.

We would be pleased to share the study protocol, data collection form and further details about authorship and collaboration.

This study does not have funding.

Thank you very much for considering this invitation.

Kind regards,

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