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Pharmaceuticals

DPP3 biomarker to advance prediction of organ function progression in septic patients

- ***Dipeptidyl Peptidase 3 (DPP3) is an enzyme involved in the degradation of cardiovascular mediators and has been shown to be a marker of refractory shock***
- ***Monitoring DPP3 levels predicts improvement of organ function and survival in sepsis***
- ***DPP3 levels at admission were superior to lactate and procalcitonin for mortality prediction***
- ***DPP3 blood levels correlate with sepsis severity opening doors for early intervention***

Hennigsdorf/ Berlin, Germany, XXXXX - 4TEEN4 Pharmaceuticals GmbH ("4TEEN4") announced today new published data on the prognostic value of DPP3 in sepsis. In this recent study, DPP3 predicted the progression of organ function and survival in septic patients more accurately than standard parameters such as lactate and procalcitonin (1,2). This has the potential to ultimately ease individualized clinical management. Therefore, DPP3 measurements in the early phase of sepsis could aid individualized clinical management.

Sepsis remains a major health problem of the 21st century, with a high fatality rate and an ever-increasing incidence (3). Septic shock, the most severe form of sepsis, is associated with an even greater mortality risk (3). DPP3 is an enzyme responsible for degradation of cardiovascular mediators that plays an important role in disease progression in critically ill patients. Although intracellular DPP3 is involved in normal metabolic processes (3), massive cell death leads to DPP3 release into the bloodstream. Circulating DPP3 inactivates Angiotensin II, a hormone regulating the renin-angiotensin-aldosterone system (RAAS), which ultimately controls hemodynamics (4,5). Angiotensin II depletion leads to cardiovascular depression (3,5,6,7), reduced vascular tone (3,4) and hemodynamic instability that quickly escalates into multiple organ failure. DPP3 proved added value in various critical care settings such as cardiogenic shock (4,5) and burn shock (6).

The published data from the AdrenOSS-1 study, an observational, multi-centered study with more than 500 patients with sepsis and septic shock, showed that DPP3 levels predict multiple organ injury, need for organ support therapies and poor short-term outcome in this patient population (1,3). In addition, DPP3 levels reflected patient severity with septic shock patients displaying significantly higher DPP3 levels than patients with sepsis (1,3). The data further demonstrated the importance of DPP3 normalization in the first days after ICU admission. The study concludes that serial DPP3 measurements in the first 24h of ICU admission could guide intensivists in the early management of septic patients. Apart from its predictive power as a biomarker of clinical outcome in sepsis, DPP3 has been shown to exert negative inotropic effects and works as a cardiac depressant factor. These destructive effects were reversed by Procizumab, a humanized monoclonal anti-DPP3 neutralizing antibody, currently in preclinical development (9). Therefore, DPP3 is not only a prognostic marker but also represents a therapeutic target in sepsis.

Dr. Andreas Bergmann, founder and CEO of 4TEEN4 mentioned: "The marked prognostic value of DPP3 in sepsis combined with the preclinical data demonstrating beneficial effects of DPP3 inhibition shows that the modulation of the DPP3 pathway is an avenue worth pursuing."

References

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About 4TEEN4
At 4TEEN4 we are dedicated to improve critically ill patient lives who suffer from hemodynamic instability, end-organ hypoperfusion and multiple organ failure with our first-in-class humanized monoclonal antibody" Procizumab" targeting human dipeptidyl peptidase 3 (DPP3).
4TEEN4 licensed its novel biomarker DPP3 for diagnostic purposes in critical care conditions.
4TEEN4 Pharmaceuticals GmbH ("4TEEN4") was established in 2013 in Hennigsdorf near Berlin, Germany, by Dr. Andreas Bergmann, CEO of 4TEEN4, as part of his Medicine4Future Initiative.
For further information please visit www.4teen4.de

About DPP3
Dipeptidyl peptidase 3 an active enzyme which, when released into the blood, inactivates angiotensin II, and Enkephalin, hormones that are important for the hemodynamic balance as well as cardiac and renal function. This inactivation leads to hemodynamic instability and consequently to cardiac depression. The DPP3 release is a newly identified disease mechanism explaining short-term organ failure in critically ill patients. Early identification of DPP3 release may allow better patient stratification and earlier therapy escalation to improve outcomes.

About Procizumab

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Procizumab is a humanized monoclonal antibody in preclinical development specifically binding circulating Dipeptidyl Peptidase 3 (DPP3). It will be a first-in-class drug that targets and modulates DPP3 as an essential regulator of cardiovascular function. Procizumab has an innovative mode of action, relevant in acute diseases. Massive cell death and release of DPP3 into the bloodstream lead to degradation of its substrates, including angiotensin II and enkephalin, that are responsible for cardiac and renal function regulation. Procizumab inhibits the activity of DPP3, thereby reducing bioactive peptide degradation, stabilizing hemodynamics, cardiovascular function and potentially increasing survival chances e.g., in cardiogenic and septic shock. Preclinical studies of Procizumab in models of cardiovascular failure showed instant efficacy.

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