

Sphingotec's critical care biomarkers early diagnose risk of loss of endothelial, kidney and heart function in severely ill COVID-19 patients

- *Results of a consensus meeting of clinical experts investigating sphingotec's diagnostic solutions for acute and critical care in COVID-19.*
- *sphingotec's biomarkers penKid, bio-ADM, and DPP3 previously shown to predict the need for organ support in numerous critical care conditions also have utility in risk stratification of severely ill COVID-19 patients.*

Hennigsdorf/Berlin, Germany, June 18, 2020 – Diagnostics company SphingoTec GmbH (“sphingotec”) announced today the results of a working group meeting of clinical experts that discussed the utility of sphingotec's diagnostic solutions for acute and critical care in supporting the triage, diagnosis, and management of severely ill COVID-19 patients. The experts representing European medical centers agreed that novel biomarkers are required for triaging and monitoring of these patients to optimally make use of the available medical resources and improve outcomes.

Diagnostic tests for sphingotec's organ-specific biomarkers for monitoring the endothelial and kidney function are currently investigated on-site in COVID-19 patients in hospitals in Germany, Switzerland, United Kingdom, France and Italy. Serial measurements of sphingotec's real-time endothelial function biomarker bio-ADM, kidney function biomarker penKid and cardiac depressant factor DPP3 were performed in these centers to investigate their utility in the management of COVID-19 patients. In a working meeting, the investigators discussed their initial findings to develop a consensus on the diagnostic needs for severely ill Covid-19 patients and how sphingotec's biomarkers can address these needs.

Prof. Thorsten Brenner (*Essen University Hospital/Essen, Germany*) commented: “To identify high risk patients, we need early and specific markers for organ failure to be measured already in the emergency departments. PenKid is a very promising biomarker that we are currently investigating for the triage and the monitoring of organ support therapies of COVID-19 patients with impaired kidney function.”

Previously gathered evidence confirmed the central role of bioactive Adrenomedullin and endothelial function in sepsis patients. First feedback on the biomarker bio-ADM in severe COVID-19 describes a strong correlation between high bio-ADM blood levels and the severity of the disease and the need for organ support which can assist in a more accurate and objective risk stratification.

Further investigations with DPP3, penKid and bio-ADM are ongoing in countries strongly affected by the COVID-19 pandemic, such as France, Italy and United Kingdom as well as in the United States and Asia. The main objective is to confirm the utility of sphingotec's biomarkers in the management of COVID-19 patients.

Dr. Marlies Ostermann, MD, PhD (*Guy's & St Thomas' Hospital/London, United Kingdom*) commented: “There is an urgent need to assess and monitor organ function of COVID-19 patients in real-time. After a first positive evaluation of these novel biomarkers we have decided to further investigate their use in clinical practice. Especially in the intensive care units, we need biomarkers for monitoring of organ

support therapies. This information will also enable us to develop strategies for individualized management of this high-risk group.”

The rapidly evolving COVID-19 pandemic has challenged health systems world-wide, with about 5% of patients requiring admission to intensive care units (ICU). Among the main complications that include respiratory, cardiovascular and kidney diseases, an emerging body of evidence shows that endothelial function (1) plays a central role in severe COVID-19 patients. Previous clinical data from more than 22,000 patients demonstrate that high bio-ADM levels independently from inflammation and co-morbidities indicate distortions in the endothelial barrier function, the inner cell sheet of blood vessels. Loss of this barrier function is considered a key driver in the development of hypotension and subsequent septic shock with loss of organ perfusion in sepsis patients (2). According to a Chinese Study in Wuhan, among the non-surviving COVID-19 patients, sepsis was present in all cases (3).

Another frequently occurring complication in COVID-19 patients is loss of kidney function. Proenkephalin (penKid) has been demonstrated to be the most accurate surrogate marker for true glomerular filtration rate in patients with renal impairment, without being biased by co-morbidities.

DPP3, sphingotec’s novel biomarker for hemodynamic instability and cardiac depression, is a major cause of short-term organ failure when released in an uncontrolled manner into the blood stream. Previously published data (4,5) has shown that high blood levels of DPP3 strongly predict poor outcome in patients with cardiogenic shock.

Dr. Andreas Bergmann, founder and CEO of sphingotec said: “To support the critical care community in the management of acute care patients, including COVID-19 patients, we have made available rapid tests for our biomarkers penKid®, bio-ADM® and DPP3 on our whole-blood Nexus IB10 point-of-care platform.”

The novel biomarker tests complement a wide-range of assays for acute care settings that are already available on sphingotec’s widely used Nexus IB10 point-of-care platform that can be flexibly deployed in laboratory as well as near-patient settings such as emergency departments and intensive care units.

References:

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- (2) Mebazaa et al (2018): *Circulating adrenomedullin estimates survival and reversibility of organ failure in sepsis: the prospective observational multinational Adrenomedullin and Outcome in Sepsis and Septic Shock-1 (AdrenOSS-1) study*, *Crit Care*, doi: [10.1186/s13054-018-2243-2](https://doi.org/10.1186/s13054-018-2243-2)
- (3) Zhou et al (2020): *Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study*. Doi: [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3)
- (4) Takagi (2019) *Circulating dipeptidyl-peptidase 3 and alteration in hemodynamics in cardiogenic shock: Results from the OptimaCC Trial*, *European Journal of Heart Failure*, doi: [10.1002/ejhf.1600](https://doi.org/10.1002/ejhf.1600)
- (5) Deniau (2019) *Circulating dipeptidyl peptidase-3 is a myocardial depressant factor: DPP3 inhibition rapidly and sustainably improves hemodynamics*, *European Journal of Heart Failure*, doi: [10.1002/ejhf.1601](https://doi.org/10.1002/ejhf.1601)

About sphingotec

SphingoTec GmbH ("sphingotec"; Hennigsdorf near Berlin, Germany) develops and markets innovative in vitro diagnostic (IVD) tests for novel and proprietary biomarkers for the diagnosis, prediction and monitoring of acute medical conditions, such as sepsis, acute heart failure, circulatory shock, and acute kidney injury in order to support patient management and provide guidance for

treatment strategies. sphingotec's proprietary biomarker portfolio includes Bioactive Adrenomedullin (bio-ADM®), a unique biomarker for real-time assessment of endothelial function in conditions like sepsis or congestive heart failure, Proenkephalin (penKid®), a unique biomarker for real-time assessment of kidney function, and Dipeptidyl Peptidase 3 (DPP3), a unique biomarker for cardiac depression. In addition, sphingotec develops a portfolio of novel biomarkers, which predict the risks of developing obesity, breast cancer and cardiovascular diseases. IVD tests for sphingotec's proprietary biomarkers are made available as sphingotest® microtiterplate tests as well as point-of-care tests on the Nexus IB10 immunoassay platform by sphingotec's subsidiary Nexus Dx Inc. (San Diego, CA, USA) alongside a broad menu of established and commonly used tests for acute and critical care.

About bio-ADM®

sphingotest® bio-ADM® measures blood levels of bioactive adrenomedullin (bio-ADM®), a hormone maintaining endothelial function. The endothelium contributes to blood pressure and separates blood from the surrounding tissue. Elevated blood levels of bio-ADM® predict blood pressure break down and leaky vessels resulting in oedema. Imbalanced endothelial function is the major cause of shock ultimately resulting in organ dysfunction and death. Early identification of an imbalance in endothelial function allows guidance of vasopressor and diuretic therapy in critically ill patients to improve outcomes.

About DPP3

IB10 sphingotest® DPP3 is a rapid point-of-care (POC) immunoassay for the in vitro quantitative determination of Dipeptidyl peptidase 3 an active enzyme which, when released into the blood, inactivates angiotensin II, a hormone that is important for the heart function. This inactivation leads to hemodynamic instability and consequently 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 penKid®

sphingotest® penKid® measures proenkephalin (penKid®), a stable fragment of the kidney stimulating hormone enkephalin. penKid® has been demonstrated to be a real-time surrogate biomarker for glomerular filtration rate, the gold standard to assess renal function. Measuring penKid® blood concentrations allows for timely information on kidney function in critically ill patients. Early assessment of worsening and improving of renal function on intensive care units and in emergency departments allows adjustment of nephrotoxic drug administration and the initiation of kidney-protective strategies to prevent acute kidney injury and thereby improve outcomes.