PreventSepticShock Report Summary
Project ID: 666328
Funded under: H2020-EU.3.1.3.

Periodic Reporting for period 2 - PreventSepticShock (Bioactive AdrenoMedullin is a Novel Outstanding Marker to Predict and Prevent Septic Shock)

Reporting period: 2016-04-01 to 2017-03-31

Summary of the context and overall objectives of the project

Sepsis is a life-threatening condition that arises when the body’s response to an infection damages its own tissues and organs. Although sepsis is initiated by infection, it is not the infection per se, which kills a patient, but rather the body’s response to it, in particular, development of a shock, which is initiated by deterioration of blood vessel system, hypotension, insufficient perfusion and organ oxygenation and finally organ failure. For a clinician this situation occurs suddenly and there is no diagnostic tool to predict this event early enough to initiate adequate measures to guide the patient and prevent its death. Despite of large efforts and developments in the last decade septic shock is still one of the world biggest killer causing 5-6 million deaths a year worldwide. Thus the septic shock prediction and stratification of high risk patients is still an unmet medical need.

Bio-ADM is a novel marker in sepsis to reliably identify patients with a high risk of developing septic shock, who are having a high mortality and a need for vasopressor treatment.

During the project scientists of Sphingotec (SPH) developed bio-ADM as a powerful marker to predict fatal shock progression in severe sepsis.

Accordingly, main goal of the project was to validate the clinical utility of bio-ADM as biomarker in European intensive and emergency care for identification of critically ill patients with the highest risk of developing shock, in order to enable earlier treatment options. This will change the standard of care in sepsis patient management. Furthermore, all necessary dissemination was made to guarantee quick market uptake and broad clinical marker application.

Within project, Sphingotec fulfilled all objectives:

1. Prototyping for clinical application
   Sphingotec estabilished a highly reliable in-vitro diagnostic (IVD) bio-ADM assay for routine clinical application.

2. Clinical validation
   Sphingotec conducted a large observational clinical study with 585 sepsis patients on the Intensive Care Units (ICU). In the study: (i) we confirmed significant data from the pilot study of Marino et al 2014 Crit Care, (ii) we confirmed the cut-off-value for bio-ADM measurement in clinical routine to identify patients with highest risk to die and to indicate vasopressor therapy at the earliest stage and thus help to save lives, (iii) we showed high performance of the marker in comparison to established clinical chemistry parameters (according to international sepsis guidelines), (iv) we delivered clinical data for a broad clinical exploitation of the biomarker.

3. Establishing automation of assay to enhance European and worldwide exploitation
   bio-ADM analysis was adapted for automation as random access format of the assay and for point-of-care platform (POC) together with designated industrial licensing parties.

4. Scale-up of production capacity and preparation of the company for growth
New staff for the project (for research, development, clinical profiling, production and marketing) has been employed. Structure for continuous growth of company after the project were implemented.

5. Market replication
For dissemination of bio-ADM as clinical marker, several retrospective studies for the application of bio-ADM in analogous clinical questions had to be conducted, e. g. bio-ADM in German and international cohorts for sepsis, septic shock and in acute heart failure.

6. Prepare product launch
Launch of bio-ADM as clinical marker in 2017 was prepared and conducted.

7. Fulfilling regulatory requirements
During the project all work for the bio-ADM assay was in compliance with the European Directive on In Vitro Diagnostic Medical Devices (98/79/EC) as well as all regulatory ethic and data safety requirements were fulfilled.

**Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far**

In project all planned work has been performed. A brief overview is given in the following:

In WP 1 - Routine assay in IVD format (i) small batches of assay components have been produced and validated, (ii) material for all serial tests to be used in the project has been produced, (iii) all technical assay data have been acquired to ensure IVD conform test performance, (iv) technical documentation including preparation and quality protocols for all components for CE declaration of conformity IVD registration via DIMDI are accomplished.

In WP 2 - Sepsis cohort study 26 study sites were conducted according to international standards.

In WP 3 - Forwarding to automation bio-ADM assay components were produced and transferred to several potential licensing partners for assay feasibility studies.

In WP 4 - Dissemination and exploitation action (i) presentation materials were prepared, (ii) a marketing website explaining the Prevent Septic Shock concept was published, (iii) more than 15 oral presentations were given on national and international conferences, (iv) Sphingotec attended relevant commercial exhibitions, (v) introduced information for bio-ADM to 9 potential licensing parties, and (vi) furthermore, large studies were conducted which confirm the positive result of the Prevent Septic Shock study and established bio-ADM as powerful marker for Acute Heart Failure. (vii) A strategy for marketing and dissemination was developed and executed.

In WP 5 - Project management several meetings were held, as well as regular biweekly telephone conferences with clinical contract research partner EDDH. Critical documents were transferred from Sphingotec to study partner and vice versa. EDDH gave monthly short reports on the progress of recruitment. Contacts to all parties conducting reference studies and to licensing parties were organized as well.

**Progress beyond the state of the art and expected potential impact (including the socio-economic impact and the wider societal implications of the project so far)**

In WP 1 - Routine assay in IVD format a chemiluminescence assay in 96 well format, including standard and control samples has been designed and is ready to be used in clinical environment. Its technical performance is excellent.

In WP 2 - The multi-centre observational study was performed successfully (i) confirming the cut-off-value for bio-ADM measurement in clinical routine to identify patients with highest risk to die and to indicate vasopressor therapy at earliest stage and thus help to save lives, (ii) showing high performance of marker in comparison to established clinical chemistry parameters (according to international sepsis guidelines), and (iii) delivering clinical data for a broad clinical exploitation of the biomarker.

In WP 3 – Bio-ADM was successfully transferred to automated random access format and to point-of-care platform.

In WP 4 - Dissemination and exploitation a strategy was developed and is being executed. Bio-ADM showed its outstanding performance in sepsis and in second application such as Acute Heart Failure. Bio-ADM was presented in most important conferences for acute and intensive care. New licensing partners have been acquired. Europe-wide sales are currently
established.

In WP 5 - Project management several meetings were held, technical and administrative management has been preceded continuously.

Importantly, all ethical requirements have been fulfilled in all participating centres as well as gender bias is avoided within the scientific community through distribution of relevant publications (Helsinki report).

Related information

![Image](666328-preventsepticshock-interim-report.png)

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