## **Intensive Care Medicine**

# Early rise in circulating Endothelial Protein C Receptor correlates with poor outcome in severe sepsis

Christophe Guitton <sup>1, 2</sup>, Nathalie Gérard <sup>1</sup>, Véronique Sébille <sup>3, 4</sup>, Cédric Bretonnière <sup>2</sup>, Olivier Zambon <sup>2</sup>, Daniel Villers <sup>2</sup> and Béatrice Charreau <sup>1</sup>

#### **Corresponding author:**

Dr. Christophe GUITTON, M.D.;

Service de Réanimation Médicale Polyvalente ; Hôtel Dieu, CHU de Nantes ; 30 Boulevard Jean Monnet ; 44093 NANTES Cedex 1 ; FRANCE

Phone + 33 2 40 08 73 65; Fax + 33 2 40 08 75 50

E-Mail christophe.guitton@chu-nantes.fr

<sup>&</sup>lt;sup>1</sup> INSERM, U643, Nantes, F44000 France; CHU Nantes, Institut de Transplantation et de Recherche en Transplantation, ITERT, Nantes, F44000 France; UMR643 Université de Nantes, Faculté de Médecine, Nantes, F44000 France.

<sup>&</sup>lt;sup>2</sup> Service de Réanimation Médicale Polyvalente, CHU de Nantes, F44000 France.

<sup>&</sup>lt;sup>3</sup> EA 4275, Faculté de Pharmacie, Université de Nantes, Nantes, F44000 France.

<sup>&</sup>lt;sup>4</sup> Plateforme de Biométrie, CHU de Nantes, F44000 France.

#### **ESM 1:**

### **Inclusion Criteria:**

Patients with severe sepsis were included using the following inclusion criteria according to the ACCP consensus definition for severe sepsis

-Suspected or proven infection- Patients had to have a known infection or a suspected infection, as evidenced by one or more of the following: white blood cells in a normally sterile body fluid; perforated viscus, radiographic evidence of pneumonia in association with the production of purulent sputum; and a syndrome associated with a high risk of infection.

- Patients had to meet at least 3 of the following 4 criteria- a core temperature of at least 38°C or below 36°C; a heart rate of at least 90 beats/min, except in patients with a medical condition known to increase the heart rate or those receiving treatment that would prevent tachycardia; a respiratory rate of at least 20 breaths/min or a PaCO2 of no more than 32 mmHg or the use of mechanical ventilation for an acute respiratory process; a white blood cell count between 12000/ mm³ and 40000/ mm³ or a differential count showing more than 10% immature neutrophils.

- Criteria for dysfunctional organs or systems- Patients had to meet at least 1 of the following criteria within the 24 hours period immediately preceding enrolment. The onset of the first organ dysfunction had not to precede the inclusion more than 24 hours For cardiovascular system dysfunction, arterial systolic blood pressure had to be no more than 90 mmHg or the mean arterial pressure of no more than 70 mmHg for at least 1h despite adequate fluid resuscitation, adequate intravascular volume status, or the use of vasopressors in an attempt to maintain a systolic blood pressure of at least 90 mmHg or a mean arterial pressure of at least 70 mmHg. For kidney dysfunction, urine output had to be less than 30 mL/h for 1h and/or serum creatinin concentration more than 200 μmol/L, despite adequate fluid resuscitation. For respiratory-system dysfunction, the ratio PaO2/FiO2 had to be below 250 in the presence of other dysfunctional organs or below 200 if the lung was the only dysfunctional organ. For hematologic dysfunction, the platelet count had to be below 50000/mm3

or to have decreased by 50% in the 3 days preceding enrolment. In the case of unexplained metabolic acidosis, the pH had to be no more than 7.30 and a plasma lactate level above 2 mmol/ L. For hepatic dysfunction, bilirubin above 50  $\mu$ mol/ L or alcalin phosphatase more than 3-fold upper limit of the normal reference range were considered. For neurologic dysfunction, coma Glasgow score had to be below 13.