

Claims

1. A method for monitoring a therapy in a subject, wherein the subject is under treatment with a binder selected from an anti-Adrenomedullin (ADM) antibody, antibody fragment and/or non-Ig Scaffold binding to SEQ ID NO. 1 (amino acid 1-52), comprising:
 - determining the level of a fragment of pre-pro-Adrenomedullin having at least 5 amino acids and selected from Midregional Proadrenomedullin (MR-proADM), C-terminal Proadrenomedullin (CT-proADM) and/or Proadrenomedullin N-terminal 20 peptide (PAMP) in a bodily fluid obtained from said subject; and
 - correlating said level of the fragment of pre-pro-Adrenomedullin selected from the group comprising MR-proADM, CT-proADM and/or PAMP with the subject's clinical/medical status of health and/or the risk for an adverse outcome and/or the requirement for adapting therapeutic measures,
 - wherein for the determination of the level of said fragment at least one binder binds to a region within the amino acid sequence selected from the group comprising SEQ ID NO. 3, SEQ ID NO. 4 and SEQ ID NO. 5, respectively.
2. A method according to claim 1, wherein the binder for the treatment is an anti-ADM antibody or an anti-adrenomedullin antibody fragment or an anti-ADM non-Ig protein scaffold, wherein said antibody or fragment or scaffold binds to the N-terminal part, aa 1-21, of adrenomedullin:

YRQSMNNFQGLRSFGCRFGTC; SEQ ID No. 19.
3. A method according to claim 1 to 2, wherein the binder for the treatment is an anti-ADM antibody or an anti-adrenomedullin antibody fragment or an anti-ADM non-Ig protein scaffold, wherein said antibody or fragment or scaffold binds to the C-terminal part, aa 42-52-amide, of adrenomedullin:

APRSKISPQGY-NH₂; SEQ ID No. 20.

4. A method according to any one of claims 1 to 3, wherein the binder for the treatment is an anti-ADM antibody or an anti-adrenomedullin antibody fragment or an anti-ADM non-Ig protein scaffold, wherein said antibody or fragment or scaffold binds to the mid-regional part, aa 21-42, of adrenomedullin:

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CTVQKLAHQIYQFTDKDKDNVA; SEQ ID No. 21.

5. A method according to any of the preceding claims, wherein the determination of the level of said fragment is performed at least once.
- 10 6. A method according to any of the preceding claims, wherein the adverse outcome is selected from worsening clinical condition such as worsening organ function, and mortality.
7. A method according to any of the preceding claims, wherein said subject suffers from a disease or condition, e.g. a chronic or acute disease or acute condition.
- 15 8. A method according to any of the preceding claims, wherein the disease the subject is suffering from is selected from: severe infections, e.g. meningitis, Systemic inflammatory Response-Syndrome (SIRS,) and sepsis; a disease such as diabetes and cancer; acute and chronic vascular diseases, e.g. heart failure, myocardial infarction, stroke, and atherosclerosis; shock, e.g. septic shock and organ dysfunction, e.g. kidney dysfunction, liver dysfunction; burnings; surgery; and trauma.
- 20 9. A method according to any of the preceding claims, where said therapeutic measures are selected from fluid resuscitation, vasopressors/inotropes, renal replacement therapy, antibiotics, hydrocortisone, insulin, and enteral nutrition/parenteral nutrition.
- 25 10. A method according to any of the preceding claims, wherein the level of said fragment of pre-pro-Adrenomedullin is determined by an immunoassay using at least one binder selected from a binder to MR-proADM or a fragment thereof and/or to CT-proADM or a fragment thereof and/or to PAMP or a fragment thereof, respectively.
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- 5 **11.** A method according to any of the preceding claims, wherein for the correlation an elevated level of said fragment of pre-pro-Adrenomedullin above a certain threshold is predictive for an enhanced risk for an adverse outcome, and/or a level of said fragment of pre-pro-Adrenomedullin or fragments thereof below a certain threshold is predictive for a reduced risk for an adverse outcome.
- 10 **12.** A method according to any of the preceding claims, wherein for the correlation of the level of the fragment of pre-pro-Adrenomedullin the determination of the level of said fragment is performed at least twice and wherein a decrease of the second measured level of said fragment in comparison to the measured first level of said fragment, is predictive for a reduced risk for an adverse outcome.
- 15 **13.** A method according to any of the preceding claims, wherein for the correlation of the level of the fragment of pre-pro-Adrenomedullin the determination of the level of said fragments is performed at least twice and wherein an increase of the second measured level of said fragment in comparison to the measured first level of said fragment, is predictive for an enhanced risk for an adverse outcome.
- 14.** A method according to any of the preceding claims, wherein said bodily fluid is selected from blood, serum, plasma, urine, cerebrospinal fluid (CSF), and saliva.
- 15.** A method according to any of the preceding claims in order to stratify said subjects into risk groups.