

CLAIMS

1. A method of treating a subject suffering from peritoneal carcinomatosis with a “plasminogen activator inhibitor 1”(PAI-1) inhibitor, the method comprising
5 determining the concentration of PAI-1 and determining the level of phosphorylation of “signal transducer and activator of transcript 3” (STAT3) in a sample obtained from the subject;
administering the PAI-1 inhibitor to the subject showing (a) an increase in PAI-1 concentration and an increase in STAT3 phosphorylation, or (b) a decrease in PAI-1 concentration and an increase in STAT3
10 phosphorylation;
wherein the increase and/or decrease of the concentration of PAI-1 and STAT3 phosphorylation is compared to a reference value.
2. A method of detecting or determining susceptibility of a subject suffering from peritoneal
15 carcinomatosis to a treatment with a “plasminogen activator inhibitor 1”(PAI-1) inhibitor, the method comprising
determining the concentration of PAI-1 and determining the level of phosphorylation of “signal transducer and activator of transcript 3” (STAT3) in a sample obtained from a subject;
wherein the subject is susceptible to the treatment if the subject shows (a) an increase in PAI-1
20 concentration and an increase in STAT3 phosphorylation, or (b) a decrease in PAI-1 concentration and an increase in STAT3 phosphorylation;
wherein the subject is not considered to be susceptible to treatment if the subject shows (c) a decrease in PAI-1 concentration and a decrease in STAT3 phosphorylation;
wherein the increase and/or decrease of the concentration of PAI-1 and the level of STAT3
25 phosphorylation is compared to a reference value.
3. The method of any one of the preceding claims, wherein the concentration of PAI-1 is determined by measuring the concentration of PAI-1 directly, and/or in one or more complexes.
- 30 4. The method of any one of the preceding claims, wherein the level of STAT3 phosphorylation is determined by measuring the concentration of one or more surrogate markers, and/or by measuring the concentration of STAT3 phosphorylation directly.
5. The method of claim 4, wherein the surrogate markers are selected from the group consisting of
35 IL6, IL10, CCL2, MMP9, ANGPT1, TGFB1, POSTN, VSIG4, CD44, and CXCL10.

6. The method of any one of claims 4 to 5, wherein the surrogate markers are selected from the group consisting of IL6, IL10, CCL2, MMP9 and ANGPT1.
7. The method of any one of claims 4 to 6, wherein the surrogate markers are selected from the group consisting of IL6, IL10, CCL2, and MMP9.
8. The method of any one of claims 4 to 7, wherein the surrogate markers comprise IL6, IL10, CCL2, MMP9 and ANGPT1; or wherein the surrogate markers comprise at least IL6, IL10, CCL2, and MMP9.
9. The method of any one of claims 4 to 8, wherein the surrogate markers are selected from the group consisting of IL6, TGFB1, POSTN, VSIG4, CD44, and CXCL10.
10. The method of any one of claims 4 to 9, wherein the surrogate markers are selected from the group consisting of TGFB1, POSTN, VSIG4, CD44, and CXCL10.
11. The method of any one of the preceding claims, wherein the PAI-1 inhibitor is an anti-cancer drug or an anti-cancer treatment.
12. The method of claim 11, wherein the anti-cancer drug or the anti-cancer therapy is selected from the group consisting of a small molecule, a chemotherapeutic agent, a peptide, an antibody, combinations thereof, and combination therapy.
13. The method of any one of claims 11 to 12, wherein the anti-cancer drug is selected from the group consisting of TM5441 (5-Chloro-2-[[2-[2-[[3-(3-furanyl)phenyl]amino]-2-oxoethoxy]acetyl]amino]benzoic acid sodium salt; CAS 1190221-43-2), TM5007 (N, N-bis [3,3'-carboxy-4,4'-(2,2'-thienyl)-2,2'-thienyl] hexanedicarboxamide; CAS 342595-05-5), TM5275 (5-Chloro-2-[[2-[2-[4-(diphenylmethyl)-1-piperazinyl]-2-oxoethoxy]acetyl]amino]-benzoic acid sodium salt; CAS 1103926-82-4), tiplaxtinin (2-(1-Benzyl-5-(4-(trifluoromethoxy)phenyl)-1H-indol-3-yl)oxoacetic acid; CAS 393105-53-8), ZK4044, and derivatives thereof.
14. The method of any one of the preceding claims, wherein the PAI-1 inhibitor is administered intraperitoneally.
15. The method according to any one of the preceding claims, wherein the peritoneal carcinomatosis is selected from the group consisting of colorectal peritoneal carcinomatosis, small bowel peritoneal carcinomatosis, mesothelioma, endometrial peritoneal carcinomatosis, gastric peritoneal carcinomatosis,

ovarian peritoneal carcinomatosis, appendiceal peritoneal carcinomatosis, pancreatic peritoneal carcinomatosis, urothelial carcinomatosis and Pseudomyxoma peritonei (PMP).

16. The method according to any one the preceding claims, wherein the sample is a solid sample or a liquid sample.
17. The method according to any one the preceding claims, wherein the sample is selected from the group consisting of ascites, blood, serum, urine, drain fluid, surgical drain fluid, supernatant obtained from cells, supernatant obtained from organs, supernatant obtained from tissues, lymph, supernatant obtained from lymph nodes, liquid biopsy samples and supernatant obtained from biopsy samples.
18. The method according to any one of the preceding claims, wherein the method is performed in a treatment setting selected from the groups consisting of neoadjuvant setting, adjuvant setting, palliative setting and prophylactic setting.
19. The method of any of the preceding claims, wherein the reference group comprises subjects suffering from peritoneal carcinomatosis.
20. The method of any of the preceding claims, wherein administration of the PAI-1 inhibition leads to inhibition of PAI-1 activity compared to patients suffering from the same disease.
21. A panel of markers for treating a patient suffering from peritoneal carcinomatosis with a “plasminogen activator inhibitor 1” (PAI-1) inhibitor, or for detecting or determining susceptibility of a subject suffering from peritoneal carcinomatosis to a treatment with a “plasminogen activator inhibitor 1” (PAI-1) inhibitor, wherein the panel of markers comprises PAI-1, and one or more surrogate markers of STAT3 phosphorylation or p-STAT3.
22. Use of a panel of markers in the method of any one of claims 1 to 19, wherein the panel comprises PAI-1 and one or more surrogate markers of STAT3 phosphorylation, or PAI-1 and p-STAT3.
23. The panel of claim 21 or the use of claims 22, wherein the panel comprises PAI-1, and one or more or all of IL6, IL10, CCL2, and MMP9.
24. The panel of claims 21 and 23 or the use of claims 22 to 23, wherein the panel comprises PAI-1, and one or more or all of IL6, IL10, CCL2, MMP9 and ANGPT1.
25. The panel of claim 21 or the use of claim 22, wherein the panel comprises PAI-1, and one or more or all of TGFB1, POSTN, VSIG4, CD44, and CXCL10.

26. The panel of claims 21 and 25 or the use of claims 22 and 25, wherein the panel comprises PAI-1, and one or more or all of IL6, TGFB1, POSTN, VSIG4, CD44, and CXCL10.