

sample obtained from the subject; wherein if the subject shows (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 phosphorylation, the subject is to be administered the medicament; wherein the increase and/or decrease of the concentration of PAI-1 and STAT3 phosphorylation is compared to a reference value;

5 wherein the sample is selected from the group consisting of ascites, tumour samples, and biopsy samples; wherein the reference values are obtained from a reference group comprising subjects suffering from peritoneal carcinomatosis. In one example, there is described a method of treating a subject suffering from peritoneal carcinomatosis 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

10 “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 phosphorylation; wherein the increase and/or decrease of the concentration of PAI-1 and STAT3 phosphorylation is compared to a reference value.

15 [007] In another aspect, the present disclosure refers to a method of detecting or determining susceptibility of a subject suffering from peritoneal 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

20 shows (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 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 phosphorylation is compared to a reference value; wherein the sample is selected from ascites,

25 tumour samples, and biopsy samples; wherein the reference values are obtained from a reference group comprising subjects suffering from peritoneal carcinomatosis.

[008] In one aspect, the present disclosure refers to 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 two or more surrogate markers of STAT3 phosphorylation, or p-STAT3, wherein the two or more surrogate markers are either (a) or (b): (a) two or more surrogate markers selected from the group consisting of IL6, IL10, CCL2, MMP9, ANGPT1, TGFB1, POSTN, VSIG4, CD44, and CXCL10, wherein one of the at least two surrogate markers is MMP9, or (b) TGFB1, POSTN, VSIG4,

30 CD44, and CXCL10; wherein the panel of markers is to be measured in a sample selected from ascites,

35 tumour samples, and biopsy samples.

CLAIMS

1. Use of a “plasminogen activator inhibitor 1” (PAI-1) inhibitor in the manufacture of a medicament for treating a subject suffering from peritoneal carcinomatosis, wherein the subject is to be identified by
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;
wherein if the subject shows (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 phosphorylation, the subject is to be administered the medicament;
wherein the increase and/or decrease of the concentration of PAI-1 and STAT3 phosphorylation is compared to a reference value;
wherein the sample is selected from the group consisting of ascites, tumour samples, and biopsy samples;
wherein the reference values are obtained from a reference group comprising subjects suffering from peritoneal carcinomatosis.
2. A method of detecting or determining susceptibility of a subject suffering from peritoneal 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 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 phosphorylation is compared to a reference value;
wherein the sample is selected from ascites, tumour samples, and biopsy samples;
wherein the reference values are obtained from a reference group comprising subjects suffering from peritoneal carcinomatosis.
3. The use of claim 1 or the method of claim 2, wherein the concentration of PAI-1 is determined by measuring the concentration of PAI-1 directly, and/or in one or more complexes.
4. The use of claim 1 or 3, or the method of claims 2 to 3, wherein the level of STAT3 phosphorylation is determined by measuring the concentration of two or more surrogate markers, and/or

by measuring the concentration of STAT3 phosphorylation directly, wherein the two or more surrogate markers are selected from the group consisting of IL6, IL10, CCL2, MMP9, ANGPT1, TGFB1, POSTN, VSIG4, CD44, and CXCL10, wherein one of the two or more surrogate markers is MMP9.

5 5. The use or the method of claim 4, wherein the two or more surrogate markers are selected from the group consisting of IL6, IL10, CCL2, MMP9 and ANGPT1, wherein one of the two or more surrogate markers is MMP9.

10 6. The use or the method of any one of claims 4 to 5, wherein the two or more surrogate markers are selected from the group consisting of IL6, IL10, CCL2, and MMP9, wherein one of the two or more surrogate markers is MMP9.

15 7. The use or the method of any one of claims 4 to 6, wherein the two or more surrogate markers comprise IL6, IL10, CCL2, MMP9 and ANGPT1, wherein one of the two or more surrogate markers is MMP9; or wherein the surrogate markers comprise at least IL6, IL10, CCL2, and MMP9, wherein one of the two or more surrogate markers is MMP9.

20 8. The use of claim 1 or 3 to 7, or the method of any one of claims 2 to 7, wherein the PAI-1 inhibitor is an anti-cancer drug or an anti-cancer treatment.

9. The use or the method of claim 8, 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.

25 10. The use or the method of any one of claims 8 to 9, 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), and ZK4044.

30

35 11. The use of claim 1 or claims 3 to 10, wherein the PAI-1 inhibitor is to be administered intraperitoneally.

12. The use of claim 1 or claims 3 to 11, or the method according to any one of claims 2 to 10, 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).

5 13. The use of claim 1 or claims 3 to 12, or the method according to any one of claims 2 to 10 and 12, wherein the treatment is to be performed in a treatment setting selected from the groups consisting of neoadjuvant setting, adjuvant setting, palliative setting and prophylactic setting.

10 14. The use of claim 1 or claims 3 to 13, or the method of any of claims 2 to 10 and 12 to 13, wherein administration of the PAI-1 inhibition leads to inhibition of PAI-1 activity compared to patients suffering from the same disease.

15 15. 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 two or more surrogate markers of STAT3 phosphorylation or p-STAT3, wherein the two or more surrogate markers are either (a) or (b):
(a) two or more surrogate markers selected from the group consisting of IL6, IL10, CCL2, MMP9, ANGPT1, TGFB1, POSTN, VSIG4, CD44, and CXCL10, wherein one of the at least two surrogate
 20 markers is MMP9, or
(b) TGFB1, POSTN, VSIG4, CD44 and CXCL10;
 wherein the panel of markers is to be measured in a sample selected from ascites, tumour samples, and biopsy samples.

25 16. Use of a panel of markers in the use of claim 1 or claims 3 to 14, or the method of any one of claims 2 to 10 and 12 to 14, wherein the panel comprises PAI-1 and two or more surrogate markers of STAT3 phosphorylation, wherein at least one of the surrogate markers of STAT3 phosphorylation is MMP9, or PAI-1 and p-STAT3; wherein the two or more surrogate markers are selected from the group consisting of IL6, IL10, CCL2, MMP9, ANGPT1, TGFB1, POSTN, VSIG4, CD44, and CXCL10,
 30 wherein one of two or more surrogate markers is MMP9.

17. ~~The panel of claim 15 or the use of claim 15 or 16,~~ wherein the panel comprises PAI-1, and two or more or all of IL6, IL10, CCL2, and MMP9, wherein one of the surrogate markers is MMP9.

35 18. ~~The panel of claims 15 and 17 or the use of claims 16-15~~ to 17, wherein the panel comprises PAI-1, and one or more or all of IL6, IL10, CCL2, MMP9 and ANGPT1, wherein one of the surrogate markers is MMP9.