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SUPPLEMENTARY EUROPEAN SEARCH REPORT

Application Number
EP 15 85 5548

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	TANIKAWA, S., ET AL: "Predictive markers for hepatic veno-occlusive disease after hematopoietic stem cell transplantation in adults: a prospective single center study", BONE MARROW TRANSPLANTATION, vol. 26, 1 January 2000 (2000-01-01), pages 881-886, XP002778345, * abstract, bridging paragraph on pages 883 and 885 *	3,9	INV. G01N33/68 G01N30/72 A61B5/00 A61B5/145
X	LEE, J-H., ET AL: "Plasminogen activator inhibitor-1 is an independent diagnostic marker as well as severity predictor of hepatic veno-occlusive disease after allogenic bone marrow transplantation in adults conditioned with busulphan and cyclophosphamide", BRITISH JOURNAL OF HAEMATOLOGY, vol. 118, 1 January 2002 (2002-01-01), pages 1087-1094, XP002778346, * abstract, page 1089, left-hand column, last paragraph. *	3	TECHNICAL FIELDS SEARCHED (IPC) G01N
X	CN 102 858 985 A (SIGMA ALDRICH CO) 2 January 2013 (2013-01-02) * the whole document *	2	

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The supplementary search report has been based on the last set of claims valid and available at the start of the search.

Place of search	Date of completion of the search	Examiner
Munich	21 February 2018	Lindberg, Pia

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	FRIED, MW., ET AL: "Serum hyaluronic acid in patients with veno-occlusive disease following bone marrow transplantation", BONE MARROW TRANSPLANTATION, vol. 27, 1 January 2001 (2001-01-01), pages 635-639, XP002778347, * abstract, page 636 left-hand column, 3rd full paragraph, figure 1. *	3-7	
X	UEDA NORIHIRO ET AL: "Predictive Value of Circulating Angiopoietin-2 for Endothelial Damage-Related Complications in Allogeneic Hematopoietic Stem Cell Transplanta", BIOLOGY OF BLOOD AND MARROW TRANSPLANTATION, vol. 20, no. 9, 2 May 2014 (2014-05-02), pages 1335-1340, XP029040958, ISSN: 1083-8791, DOI: 10.1016/J.BBMT.2014.04.030 * abstract, page, 1336 right-hand column, 1st paragraph; page 1337, right-hand column, 1st par.; page 1338, right-hand column, last par. *	3-7,9-13	TECHNICAL FIELDS SEARCHED (IPC)
A	HOLTAN, S.G., ET AL: "Acute graft-versus-host disease: a bench-to-bedside update", BLOOD, vol. 124, no. 3, 9 June 2014 (2014-06-09), pages 363-373, XP002778348, * page 363, left-hand column, 1st paragraph; bridging paragraph on pages 365 and 366 *	1-14	

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EP 15 85 5548

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X,P	AKIL AYMAN ET AL: "Biomarkers for Diagnosis and Prognosis of Sinusoidal Obstruction Syndrome after Hematopoietic Cell Transplantation", BIOLOGY OF BLOOD AND MARROW TRANSPLANTATION, KLUGE CARDEN JENNINGS PUBLISHING, CHARLOTTESVILLE, VA, US, vol. 21, no. 10, 11 July 2015 (2015-07-11) , pages 1739-1745, XP029267511, ISSN: 1083-8791, DOI: 10.1016/J.BBMT.2015.07.004 * the whole document * -----	1-14	

TECHNICAL FIELDS SEARCHED (IPC)

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Application Number

EP 15 85 5548

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing claims for which payment was due.

☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due and for those claims for which claims fees have been paid, namely claim(s):

☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for those claims for which no payment was due.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

☐ All further search fees have been paid within the fixed time limit. The present (supplementary) European search report has been drawn up for all claims.

☒ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

☐ Only part of the further search fees have been paid within the fixed time limit. The present (supplementary) European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

☐ None of the further search fees have been paid within the fixed time limit. The present (supplementary) European search report has been drawn up for those parts of the European patent application which relate to the first mentioned in the claims, namely claims:

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LACK OF UNITY OF INVENTION
SHEET B

Application Number
EP 15 85 5548

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-14

A biomarker panel and a method for diagnosing or aiding diagnosis of sinusoidal obstructive syndrome in a subject receiving HSCT, by measuring in a biological sample from the subject the expression of at least one biomarker, and wherein the at least one biomarker is suppressor of tumorigenicity 2 (ST2).

1.1. claims: 1, 3-8(all partially)

A biomarker panel and a method for diagnosing or aiding diagnosis of sinusoidal obstructive syndrome in a subject receiving HSCT, by measuring in a biological sample from the subject the expression of at least one biomarker, and wherein the at least one biomarker is angiopoietin 2 (ANG2).

1.2. claims: 1, 3-8(all partially)

A biomarker panel and a method for diagnosing or aiding diagnosis of sinusoidal obstructive syndrome in a subject receiving HSCT, by measuring in a biological sample from the subject the expression of at least one biomarker, and wherein the at least one biomarker is L-Ficolin.

1.3. claims: 1, 3-8(all partially)

A biomarker panel and a method for diagnosing or aiding diagnosis of sinusoidal obstructive syndrome in a subject receiving HSCT, by measuring in a biological sample from the subject the expression of at least one biomarker, and wherein the at least one biomarker is hyaluronic acid.

1.4. claims: 1, 3-8(all partially)

A biomarker panel and a method for diagnosing or aiding diagnosis of sinusoidal obstructive syndrome in a subject receiving HSCT, by measuring in a biological sample from the subject the expression of at least one biomarker, and wherein the at least one biomarker is vascular cell adhesion molecule 1 (VCAM1).

1.5. claims: 2, 9-14(all partially)

A biomarker panel and a method for prognosing or aiding prognosis of sinusoidal obstructive syndrome in a subject receiving HSCT, by measuring in a biological sample from the subject the expression of at least one biomarker, and wherein the at least one biomarker is suppressor of tumorigenicity 2 (ST2).

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1.6. claims: 2, 9-14(all partially)

A biomarker panel and a method for prognosing or aiding prognosis of sinusoidal obstructive syndrome in a subject receiving HSCT, by measuring in a biological sample from the subject the expression of at least one biomarker, and wherein the at least one biomarker is angiopoietin 2 (ANG2).

1.7. claims: 2, 9-14(all partially)

A biomarker panel and a method for prognosing or aiding prognosis of sinusoidal obstructive syndrome in a subject receiving HSCT, by measuring in a biological sample from the subject the expression of at least one biomarker, and wherein the at least one biomarker is L-Ficolin.

1.8. claims: 2, 9-14(all partially)

A biomarker panel and a method for prognosing or aiding prognosis of sinusoidal obstructive syndrome in a subject receiving HSCT, by measuring in a biological sample from the subject the expression of at least one biomarker, and wherein the at least one biomarker is hyaluronic acid.

1.9. claims: 2, 9-14(all partially)

A biomarker panel and a method for prognosing or aiding prognosis of sinusoidal obstructive syndrome in a subject receiving HSCT, by measuring in a biological sample from the subject the expression of at least one biomarker, and wherein the at least one biomarker is vascular cell adhesion molecule 1 (VCAM1).

Please note that all inventions mentioned under item 1, although not necessarily linked by a common inventive concept, could be searched without effort justifying an additional fee.
The present application does not comply with the requirements of unity of invention, Art. 82 EPC, for the following reasons:
Independent claim 3 refers to a method of diagnosing or aiding diagnosis of sinusoidal obstructive syndrome (SOS) in a subject receiving hematopoietic stem cell transplantation, the method comprising measuring in a biological sample from the subject at least one biomarker selected from the group consisting of ST2, ANG2, L-Ficolin, HA and VCAM1, wherein an elevated biomarker expression level compared to biomarker expression in a control is indicative of SOS.
Furthermore independent claim 9 refers to a method for prognosing or aiding prognosis of SOS in a subject receiving hematopoietic stem cell transplantation, the method comprising measuring in a biological sample from the subject at least one biomarker selected from the group consisting of ST2, ANG2, L-Ficolin, HA and VCAM1, wherein an elevated

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

biomarker expression level compared to biomarker expression in a control is indicative of a prognosis of having SOS.
Document Tanikawa et al refers to predictive markers for hepatic veno-occlusive disease (VOD, sinusoidal obstructive syndrome, SOS) after hematopoietic stem cell transplantation in adults. The document states that levels of N-terminal propeptide for type III procollagen (P-III-P) were significantly higher in patients with VOD than without VOD, before preparative chemotherapy. Furthermore on day 0, levels of tissue plasminogen activator (t-PA) were significantly higher in patients with VOD than without VOD. Thus the serum P-III-P level before start of conditioning is a prognostic risk marker for VOD, and P-III-P and t-PA is stated to be a predictive/diagnostic markers for VOD after HSCT, see D1 abstract and bridging paragraph on pages 883 and 885.
Furthermore document Lee at al refers to significantly higher plasma levels of tPA antigen and PAI-1 antigen on day 7 and 14 in patients with VOD compared to those without VOD after bone marrow transplantation, see D2 abstract and page 1089, left-hand column, last paragraph.
Thus, as diagnostic and prognostic biomarkers for VOD/SOS in subjects receiving HSCT are already known from the prior art, the subject-matter of independent claim 3 therefore refers to the problem of providing alternative biomarkers for diagnosing VOD/SOS in a subject receiving HSCT to those biomarkers already disclosed in the above cited documents, and the subject-matter of independent claim 9 refers to the problem or providing alternative prognostic biomarkers for VOD/SOS in a subject receiving HSCT to those biomarkers already disclosed in Tanikawa et al.

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 15 85 5548

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

21-02-2018

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
CN 102858985 A	02-01-2013	NONE	

专利名称(译)	检测窦状隙阻塞综合征（SOS）的方法		
公开(公告)号	EP3213072A4	公开(公告)日	2018-04-04
申请号	EP2015855548	申请日	2015-10-26
[标]申请(专利权)人(译)	印第安纳UNIV RES TECH		
申请(专利权)人(译)	美国印第安纳大学研究与科技股份有限公司		
当前申请(专利权)人(译)	美国印第安纳大学研究与科技股份有限公司		
[标]发明人	PACZESNY SOPHIE		
发明人	PACZESNY, SOPHIE		
IPC分类号	G01N33/53 G01N30/72 A61B5/00		
CPC分类号	A61B5/14546 G01N33/6893 G01N2800/245 G01N2800/52 G01N30/72 G01N33/53		
代理机构(译)	HGF LIMITED		
审查员(译)	LINDBERG，PIA		
优先权	62/069394 2014-10-28 US		
其他公开文献	EP3213072A1		
外部链接	Espacenet		

摘要(译)

公开了用于在造血干细胞移植（HSCT）后早期评估具有窦性阻塞综合征（SOS）风险的受试者的生物标志物组。特别地，本公开涉及ST2，ANG2，L-纤维胶凝蛋白，HA和VCAM1中的一种或多种用于预后，诊断和/或治疗SOS的用途。

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