



(11) **EP 1 666 881 A3**

(12) **EUROPEAN PATENT APPLICATION**

(88) Date of publication A3:
19.09.2007 Bulletin 2007/38

(51) Int Cl.:
G01N 33/53 (2006.01) G01N 33/68 (2006.01)

(43) Date of publication A2:
07.06.2006 Bulletin 2006/23

(21) Application number: **06002477.5**

(22) Date of filing: **04.05.2002**

(84) Designated Contracting States:
**AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE TR**

(30) Priority: **04.05.2001 US 288871 P**
28.08.2001 US 315642 P

(62) Document number(s) of the earlier application(s) in
accordance with Art. 76 EPC:
02734211.2 / 1 322 957

(71) Applicant: **Biosite Incorporated**
San Diego, CA 92121 (US)

(72) Inventors:
• **Valkirs, Gunars E.**
Escondido, CA 92025 (US)
• **Dahlen, Jeffrey R.**
San Diego, CA 92126 (US)
• **Kirchick, Howard**
San Diego, CA 92121 (US)
• **Buechler, Kenneth F.**
Rancho Santa Fe, CA 92067 (US)

(74) Representative: **Viering, Jentschura & Partner**
Postfach 22 14 43
80504 München (DE)

(54) **Diagnostic markers of acute coronary syndromes and methods of use thereof**

(57) The present invention relates to a method of diagnosing myocardial ischemia in a patient, the method comprising: determining a level of N-terminal B-type natriuretic peptide (NT pro-BNP) in a sample obtained from said patient; determining a level of at least two further diagnostic markers in a sample obtained from said patient, wherein one of the at least two further diagnostic markers is an inflammatory marker and the other one of

the at least two further diagnostic markers is an ischemic marker, and correlating the level of NT pro-BNP and of said at least two further diagnostic markers to the presence or absence of myocardial ischemia in said patient. The invention also relates to kit for diagnosing myocardial ischemia in a patient and/or for determining a prognosis of a patient diagnosed with acute coronary syndrome.

EP 1 666 881 A3



DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	HUNT P J ET AL: "IMMUNOREACTIVE AMINO-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE (NT-PROBNP): A NEW MARKER OF CARDIAC IMPAIRMENT" CLINICAL ENDOCRINOLOGY, BLACKWELL SCIENTIFIC PUBLICATIONS, OXFORD, GB, vol. 47, 1997, pages 287-296, XP000913471 ISSN: 0300-0664 * abstract * * page 287, column 2, paragraph 3 * * page 294, column 2, last paragraph * * page 295, column 1, last paragraph * * page 293, column 2, paragraph 3 *	1-11	INV. G01N33/53 G01N33/68
A	SAGNELLA G A: "Measurement and significance of circulating natriuretic peptides in cardiovascular disease." CLINICAL SCIENCE (LONDON, ENGLAND : 1979) NOV 1998, vol. 95, no. 5, November 1998 (1998-11), pages 519-529, XP009052621 ISSN: 0143-5221 * abstract; table I * * page 522, column 2, paragraph 2 *	1-11	TECHNICAL FIELDS SEARCHED (IPC) G01N
P,A	SABATINE MARC S ET AL: "Multimarker approach to risk stratification in non-ST elevation acute coronary syndromes: Simultaneous assessment of troponin I, C-reactive protein, and B-type natriuretic peptide" CIRCULATION, AMERICAN HEART ASSOCIATION, DALLAS, TX, US, vol. 105, no. 15, 16 April 2002 (2002-04-16), pages 1760-1763, XP002262207 ISSN: 0009-7322 * abstract *	1-11	
The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 9 August 2007	Examiner Bigot-Maucher, Cora
<p>CATEGORY OF CITED DOCUMENTS</p> <p>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</p> <p>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</p> <p>& : member of the same patent family, corresponding document</p>			

6
EPO FORM 1503 03.82 (P04C01)



DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
E	WO 02/083913 A (BIOSITE DIAGNOSTICS, INC; DAHLEN, JEFFREY, R; VALKIRS, GUNARS, E; BUEC) 24 October 2002 (2002-10-24) * abstract; claims 11,16,17,20,21 * * page 7, paragraph 2 - page 8, paragraph 2 * * page 1, paragraph 1 * -----	2-11	
T	JAMES STEFAN K ET AL: "N-terminal pro-brain natriuretic peptide and other risk markers for the separate prediction of mortality and subsequent myocardial infarction in patients with unstable coronary artery disease: a Global Utilization of Strategies To Open occluded arteries (GUSTO)-IV substudy." CIRCULATION 22 JUL 2003, vol. 108, no. 3, 22 July 2003 (2003-07-22), pages 275-281, XP002445654 ISSN: 1524-4539 * abstract * -----	1-11	
The present search report has been drawn up for all claims			TECHNICAL FIELDS SEARCHED (IPC)
Place of search Munich		Date of completion of the search 9 August 2007	Examiner Bigot-Maucher, Cora
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	

6

EPO FORM 1503 03 82 (P04C01)

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 06 00 2477

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.

09-08-2007

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 02083913 A	24-10-2002	AU 2007201180 A1	19-04-2007
		CA 2412648 A1	24-10-2002
		EP 1311701 A1	21-05-2003
		JP 3749225 B2	22-02-2006
		JP 2004519688 T	02-07-2004
		JP 2005049351 A	24-02-2005
		NZ 523210 A	27-04-2007
		US 2004171064 A1	02-09-2004
		US 2003022235 A1	30-01-2003

专利名称(译)	急性冠状动脉综合征的诊断标志物及其使用方法		
公开(公告)号	EP1666881A3	公开(公告)日	2007-09-19
申请号	EP2006002477	申请日	2002-05-04
申请(专利权)人(译)	BIOSITE INCORPORATED		
当前申请(专利权)人(译)	BIOSITE INCORPORATED		
[标]发明人	VALKIRS GUNARS E DAHLEN JEFFREY R KIRCHICK HOWARD BUECHLER KENNETH F		
发明人	VALKIRS, GUNARS E. DAHLEN, JEFFREY R. KIRCHICK, HOWARD BUECHLER, KENNETH F.		
IPC分类号	G01N33/53 G01N33/68 C12N15/09 C12Q1/25 C12Q1/37 C12Q1/48 C12Q1/50 C12Q1/52 C12Q1/533 C12Q1/70		
CPC分类号	G01N33/53 G01N33/6887 G01N33/6893 G01N2333/58 G01N2800/324		
代理机构(译)	庆祝活动, JENTSCHURA & PARTNER		
优先权	60/288871 2001-05-04 US 60/315642 2001-08-28 US		
其他公开文献	EP1666881B1 EP1666881A2		
外部链接	Espacenet		

摘要(译)

本发明涉及诊断患者心肌缺血的方法，该方法包括：确定从所述患者获得的样品中的N-末端B型利尿钠肽 (NT pro-BNP) 的水平;确定从所述患者获得的样品中至少两种其他诊断标志物的水平，其中所述至少两种其他诊断标志物中的一种是炎性标志物，并且所述至少两种其他诊断标志物中的另一种是缺血性标志物，并将NT pro-BNP和所述至少两种其他诊断标志物的水平与所述患者中心肌缺血的存在或不存在相关联。本发明还涉及用于诊断患者的心肌缺血和/或用于确定诊断患有急性冠状动脉综合征的患者的预后的试剂盒。

DOCUMENTS CONSIDERED TO BE RELEVANT		Retrieved to obtain	CLASSIFICATION BY THE APPLICANT (IPC)
A	HUNT P J ET AL: "IMMUNOREACTIVE AMINO-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE (NT-PROBNP): A NEW MARKER OF CARDIAC IMPAIRMENT." CLINICAL ENDOCRINOLOGY, BLACKWELL SCIENTIFIC PUBLICATIONS, OXFORD, GB, vol. 47, no. 1997, pages 287-296, XP00913471 ISSN: 0306-0694 * abstract * * page 287, column 2, paragraph 3 * * page 294, column 2, last paragraph * * page 295, column 1, last paragraph * * page 293, column 2, paragraph 3 *	1-11	INV. G01N33/53 G01N33/68
A	SAGNELLA G A: "Measurement and significance of circulating natriuretic peptides in cardiovascular disease." CLINICAL SCIENCE (LONDON, ENGLAND : 1979) NOV 1998, vol. 95, no. 5, November 1998 (1998-11), pages 519-529, XP009052621 ISSN: 0143-5221 * abstract; table 1 * * page 525, column 2, paragraph 2 *	1-11	TECHNICAL FIELD SEARCHED G01N
P.A	SABATINE MARC S ET AL: "Multimarker approach to risk stratification in non-ST elevation acute coronary syndromes: Simultaneous assessment of troponin I, C-reactive protein, and B-type natriuretic peptide." CIRCULATION, AMERICAN HEART ASSOCIATION, DALLAS, TX, US, vol. 109, no. 15, 16 April 2002 (2002-04-16), pages 1760-1763, XP002262207 ISSN: 0009-7322 * abstract *	1-11	
The present search report has been drawn up for all claims			
Munich		9 August 2007	Bigot-Maucher, Cora
CATEGORY OF CITED DOCUMENTS X particularly relevant to the invention Y particularly relevant to the invention, but not directly related to the invention A document of the same category as the cited document * non-relevant document ? non-classified document			
REMARKS 1. Document cited in the application 2. Document cited for other reasons 3. Document of the same patent family, corresponding document			