



(11)

EP 1 585 966 B8

(12) **CORRECTED EUROPEAN PATENT SPECIFICATION**

(15) Correction information:
Corrected version no 1 (W1 B1)
Corrections, see
Bibliography INID code(s) 73

(51) Int Cl.:
A61K 39/395 (2006.01)

(86) International application number:
PCT/US2003/021590

(48) Corrigendum issued on:
07.03.2012 Bulletin 2012/10

(87) International publication number:
WO 2004/008099 (22.01.2004 Gazette 2004/04)

(45) Date of publication and mention
of the grant of the patent:
30.11.2011 Bulletin 2011/48

(21) Application number: **03755724.6**

(22) Date of filing: **11.07.2003**

(54) **Treatment of cancer with the anti-ErbB2 antibody rhuMAb 2C4**

Behandlung von Krebs mit dem anti-ErbB2-Antikörper rhuMAb 2C4

Traitement de cancer par l'anticorps rhuMAb 2C4

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR
HU IE IT LI LU MC NL PT RO SE SI SK TR

(74) Representative: **Walton, Seán Malcolm et al**
Mewburn Ellis LLP
33 Gutter Lane
London
EC2V 8AS (GB)

(30) Priority: **15.07.2002 US 396290 P**
20.06.2003 US 480043 P

(43) Date of publication of application:
19.10.2005 Bulletin 2005/42

(56) References cited:
WO-A-01/00245 WO-A-01/09186
WO-A-01/89566 US-A- 5 811 098
US-A- 5 811 098 US-A1- 2002 064 805
US-B1- 6 417 168 US-B1- 6 417 168

(60) Divisional application:
10176072.6 / 2 263 691

(73) Proprietor: **F.Hoffmann-La Roche AG**
4070 Basel (CH)

- **XIA W ET AL: "Combination of EGFR, HER-2/neu, and HER-3 is a stronger predictor for the outcome of oral squamous cell carcinoma than any individual family members." CLINICAL CANCER RESEARCH : AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. DEC 1999, vol. 5, no. 12, December 1999 (1999-12), pages 4164-4174, XP002400085 ISSN: 1078-0432**
- **GILBERTSON RICHARD J ET AL: "Prognostic significance of HER2 and HER4 coexpression in childhood medulloblastoma" CANCER RESEARCH, vol. 57, no. 15, 1997, pages 3272-3280, XP008069241 ISSN: 0008-5472**

(72) Inventors:

- **KOLL, Hans**
85247 Oberroth (DE)
- **BOSENMAIER, Birgit**
82229 Seefeld (DE)
- **MÜLLER, Hans-Joachim**
82377 Penzberg (DE)
- **SLIWKOWSKI, Mark, X.**
San Carlos, CA 94070 (US)
- **KELSEY, Stephen, Michael**
Montara, CA 94037 (US)

Note: Within nine months of the publication of the mention of the grant of the European patent in the European Patent Bulletin, any person may give notice to the European Patent Office of opposition to that patent, in accordance with the Implementing Regulations. Notice of opposition shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

EP 1 585 966 B8

- LANE HEIDI A ET AL: "ErbB2 potentiates breast tumor proliferation through modulation of p27Kip1-Cdk2 complex formation: Receptor overexpression does not determine growth dependency" MOLECULAR AND CELLULAR BIOLOGY, vol. 20, no. 9, May 2000 (2000-05), pages 3210-3223, XP002400087 ISSN: 0270-7306
- LYNE J C ET AL: "Tissue expression of neu differentiation factor/herregulin and its receptor complex in prostate cancer and its biologic effects on prostate cancer cells in vitro." THE CANCER JOURNAL FROM SCIENTIFIC AMERICAN. 1997 JAN-FEB, vol. 3, no. 1, January 1997 (1997-01), pages 21-30, XP002400088 ISSN: 1081-4442
- OLAYIOYE M: "The Erbbeta Signaling Network: Receptor Heterodimerization in Development and Cancer" EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 19, no. 13, January 2000 (2000-01), pages 3159-3167, XP002985171 ISSN: 0261-4189
- MOTOYAMA ANDREA B ET AL: "The efficacy of ErbB receptor-targeted anticancer therapeutics is influenced by the availability of epidermal growth factor-related peptides" CANCER RESEARCH, vol. 62, no. 11, 11 June 2002 (2002-06-11), pages 3151-3158, XP001155498 ISSN: 0008-5472
- CHEN XINMEI ET AL: "Enhanced drug resistance in cells coexpressing ErbB2 with EGF receptor or ErbB3" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 277, no. 3, 2 November 2000 (2000-11-02), pages 757-763, XP002400090 ISSN: 0006-291X
- BROCKHOFF GERO ET AL: "Epidermal growth factor receptor, c-erbB2 and c-erbB3 receptor interaction, and related cell cycle kinetics of SK-BR-3 and BT474 breast carcinoma cells" CYTOMETRY, vol. 44, no. 4, 1 August 2001 (2001-08-01), pages 338-348, XP002400091 ISSN: 0196-4763
- NEVE RICHARD M ET AL: "Effects of oncogenic ErbB2 on G1 cell cycle regulators in breast tumour cells" ONCOGENE, vol. 19, no. 13, 23 March 2000 (2000-03-23), pages 1647-1656, XP002400092 ISSN: 0950-9232
- AGUS D.B. ET AL: 'Targeting ligand-activated ErbB2 signaling inhibits breast and prostate tumor growth' CANCER CELL vol. 2, August 2002, pages 127 - 137, XP002988666
- TZAHAH E. ET AL: 'The ErbB-2/HER2 oncogenic receptor of adenocarcinomas: from orphanhood to multiple stromal ligands' BIOCHEMICAL BIOPHYSICAL ACTA vol. 1377, 20 February 1998, pages M29 - M34, XP004281795
- SLIKOWSKI M.X. ET AL: 'Coexpression of erbB2 and erbB3 proteins reconstitutes a high affinity receptor for heregulin' THE JOURNAL OF BIOLOGICAL CHEMISTRY vol. 269, no. 20, 20 May 1994, pages 14661 - 14665, XP000605388
- QIAN X. ET AL: 'p185c-neu and Epidermal Growth Factor Receptor Associated into Structure Composed of Activated Kinases' PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES vol. 89, February 1992, pages 1330 - 1334, XP002988667
- GORDON MICHAEL S ET AL: "Clinical activity of pertuzumab (rhuMab 2C4), a HER dimerization inhibitor, in advanced ovarian cancer: potential predictive relationship with tumor HER2 activation status", JOURNAL OF CLINICAL ONCOLOGY, AMERICAN SOCIETY OF CLINICAL ONCOLOGY, US, vol. 24, no. 26, 10 September 2006 (2006-09-10), pages 4324-4332, XP002492090, ISSN: 0732-183X, DOI: DOI: 10.1200/JCO.2005.05.4221 [retrieved on 2006-08-07]
- BASELGA, J. ET AL.: "Objective response rate in a phase II multicenter trial of pertuzumab (P), a HER2 dimerization inhibiting monoclonal antibody, in combination with trastuzumab (T) in patients (pts) with HER2-positive metastatic breast cancer (MBC) which as progressed during treatment with T", JOURNAL OF CLINICAL ONCOLOGY, vol. 25, no. 18S, 20 June 2007 (2007-06-20), page 1004,
- MAKHIJA, S. ET AL.: "Results from a phase II randomized, placebo-controlled, double-blind trial suggest improved PFS with the addition of pertuzumab to gemcitabine in patients with platinum-resistant ovarian, fallopian tube, or primary peritoneal cancer", JOURNAL OF CLINICAL ONCOLOGY, vol. 25, no. 18S, 20 June 2007 (2007-06-20), page 5507,
- CHEE M NG ET AL: "Rationale for Fixed Dosing of Pertuzumab in Cancer Patients Based on Population Pharmacokinetic Analysis", PHARMACEUTICAL RESEARCH, KLUWER ACADEMIC PUBLISHERS-PLENUM PUBLISHERS, NL, vol. 23, no. 6, 26 May 2006 (2006-05-26), pages 1275-1284, XP019405128, ISSN: 1573-904X, DOI: DOI: 10.1007/S11095-006-0205-X
- ALLISON, D. ET AL.: "Pharmacokinetics (PK) of Pertuzumab (rhuMab 2C4) in Phase II Studies of Ovarian, Breast, Prostate, and Lung Cancers", , 2005, page 2532,

专利名称(译)	用抗ErbB2抗体rhuMAb 2C4治疗癌症		
公开(公告)号	EP1585966B8	公开(公告)日	2012-03-07
申请号	EP2003755724	申请日	2003-07-11
[标]申请(专利权)人(译)	健泰科生物技术公司		
申请(专利权)人(译)	基因泰克 , INC. F.HOFFMANN-LA ROCHE AG		
当前申请(专利权)人(译)	F.HOFFMANN-LA ROCHE AG		
[标]发明人	KOLL HANS BOSENMAIER BIRGIT MULLER HANS JOACHIM SLIWKOWSKI MARK X KELSEY STEPHEN MICHAEL		
发明人	KOLL, HANS BOSENMAIER, BIRGIT MÜLLER, HANS-JOACHIM SLIWKOWSKI, MARK, X. KELSEY, STEPHEN, MICHAEL		
IPC分类号	A61K39/395 C07K14/485 C07K16/32 G01N33/50 G01N33/53 G01N33/574		
CPC分类号	A61K2039/505 A61P35/00 A61P35/02 A61P43/00 C07K16/32 C07K2317/24 G01N33/57492 G01N2333/485 G01N2333/71 G01N2800/52		
优先权	60/396290 2002-07-15 US 60/480043 2003-06-20 US		
其他公开文献	EP1585966B1 EP1585966A3 EP1585966A2 EP1585966A4		
外部链接	Espacenet		

摘要(译)

通过检测HER2 / HER3和/或HER2 / HER1蛋白复合物的存在或肿瘤细胞样品中的HER2磷酸化, 鉴定肿瘤对用抗HER2抗体治疗有反应。患有包含HER / 2 / HER1和/或HER2 / HER3异二聚体和/或HER2磷酸化的肿瘤的患者用抗HER2抗体如rhuMAb 2C4处理。