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(73)	Proprietor	F. Hoffmann-La Roche AG, Grenzacherstrasse 124, 4070 Basel, Sveits
(72)	Inventor	GUARDINO, Alice, Elizabeth, 1 Dna Way, South San Francisco, CA 94080, USA SAMANT, Meghna, 1 Dna Way, South San Francisco, CA 94080, USA STRASAK, Alexander, 1 Dna Way, South San Francisco, CA 94080, USA SMITT, Melanie, 1 Dna Way, South San Francisco, CA 94080, USA PATRE, Monika, 1 Dna Way, South San Francisco, CA 94080, USA
(74)	Agent or Attorney	PLOUGMANN VINGTOFT, C. J. Hambros plass 2, 0164 OSLO, Norge

(54) Title **METHODS OF TREATING HER2-POSITIVE PREVIOUSLY UNTREATED METASTATIC BREAST CANCER**

(56) References Cited:

SUNIL VERMA ET AL: "Trastuzumab Emtansine for HER2-Positive Advanced Breast Cancer", NEW ENGLAND JOURNAL OF MEDICINE, THE - NEJM -, vol. 367, no. 19, 8 November 2012 (2012-11-08), pages 1783-1791, XP055297991, ISSN: 0028-4793, DOI: 10.1056/NEJMoa1209124

K. D. MILLER ET AL: "Phase IIa Trial of Trastuzumab Emtansine With Pertuzumab for Patients With Human Epidermal Growth Factor Receptor 2-Positive, Locally Advanced, or Metastatic Breast Cancer", JOURNAL OF CLINICAL ONCOLOGY, vol. 32, no. 14, 14 April 2014 (2014-04-14), pages 1437-1444, XP055196925, ISSN: 0732-183X, DOI: 10.1200/JCO.2013.52.6590

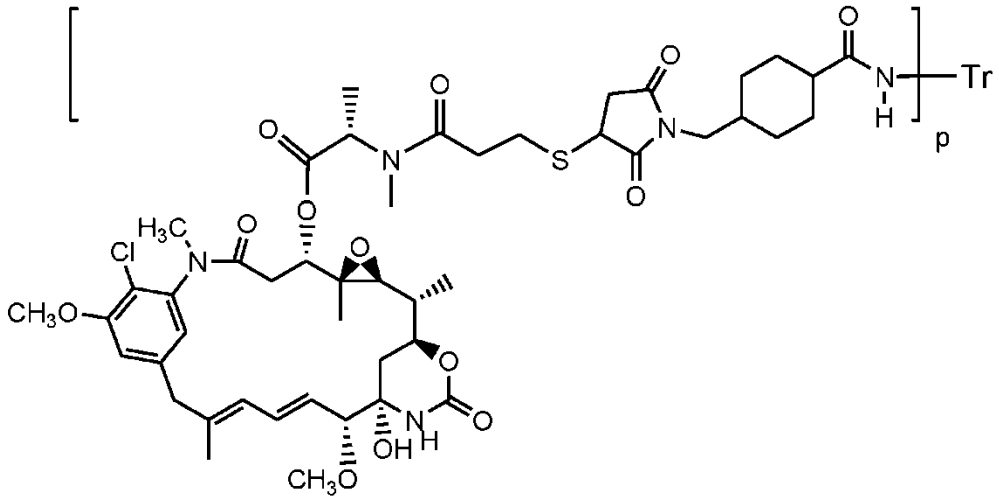
THOMAS H. PILLOW ET AL: "Site-Specific Trastuzumab Maytansinoid Antibody-Drug Conjugates with Improved Therapeutic Activity through Linker and Antibody Engineering", JOURNAL OF MEDICINAL CHEMISTRY, vol. 57, no. 19, 9 October 2014 (2014-10-09), pages 7890-7899, XP055268691, US ISSN: 0022-2623, DOI: 10.1021/jm500552c

G. D. LEWIS PHILLIPS ET AL: "Targeting HER2-Positive Breast Cancer with Trastuzumab-DM1, an Antibody-Cytotoxic Drug Conjugate", CANCER RESEARCH, vol. 68, no. 22, 15 November 2008 (2008-11-15), pages 9280-9290, XP055013498, ISSN: 0008-5472, DOI: 10.1158/0008-5472.CAN-08-1776

G. D. L. PHILLIPS ET AL: "Dual Targeting of HER2-Positive Cancer with Trastuzumab Emtansine and Pertuzumab: Critical Role for Neuregulin Blockade in Antitumor Response to Combination Therapy", CLINICAL CANCER RESEARCH, vol. 20, no. 2, 4 October 2013 (2013-10-04), pages 456-468, XP055197050, ISSN: 1078-0432, DOI: 10.1158/1078-0432.CCR-13-0358
MYRA BARGINEAR ET AL: "Trastuzumab-DM1: A Clinical Update of the Novel Antibody- Drug Conjugate for HER2-Overexpressing Breast Cancer", MOLECULAR MEDICINE, vol. 18, no. 11, 1 January 2012 (2012-01-01), page 1, XP055298134, WASHINGTON, DC; US ISSN: 1076-1551, DOI: 10.2119/molmed.2012.00302
F. Hoffmann-La Roche Ltd. ET AL: "Medienmitteilung: Roche informiert über Phase-III-Studie MARIANNE bei nicht vorbehandeltem, HER2-positivem fortgeschrittenem Brustkrebs", , 19 December 2014 (2014-12-19), XP055329487, Basel Retrieved from the Internet: URL:http://www.roche.com/dam/jcr:48c3b136- 996b-4c55-83c7-b4cec27341ee/de/med-cor-2014-12-19-d.pdf [retrieved on 2016-12-15]
Nih: "A Study of Trastuzumab Emtansine (T-DM1) Plus Pertuzumab/Pertuzumab Placebo Versus Trastuzumab [Herceptin] Plus a Taxane in Patients With Metastatic Breast Cancer (MARIANNE) - Full Text View - ClinicalTrials.gov", , 12 January 2015 (2015-01-12), XP055329506, Retrieved from the Internet: URL:https://clinicaltrials.gov/ct2/show/NC T01120184 [retrieved on 2016-12-15]
SANDHYA GIRISH ET AL: "Clinical pharmacology of trastuzumab emtansine (T-DM1): an antibody-drug conjugate in development for the treatment of HER2-positive cancer", CANCER CHEMOTHERAPY AND PHARMACOLOGY, SPRINGER, BERLIN, DE, vol. 69, no. 5, 20 January 2012 (2012-01-20), pages 1229-1240, XP035047349, ISSN: 1432-0843, DOI: 10.1007/S00280-011-1817-3

PATENTKRAV

1. Trastuzumab-MCC-DM1 for anvendelse i en fremgangsmåte for behandling av HER2-positiv metastatisk brystkreft som ikke har mottatt behandling i den metastatiske tilstanden, fremgangsmåten omfattende administrering til en menneskelig pasient som har brystkreften av en terapeutisk effektiv mengde av trastuzumab-MCC-DM1 alene, hvori den menneskelige pasienten mottok behandling med et taksan før den metastatiske tilstanden, og administreringen av trastuzumab-MCC-DM1 forekommer ≥ 6 måneder etter den tidligere behandlingen med et taksan og hvori trastuzumab-MCC-DM1 er et antistoff-legemiddelkonjugat, som har strukturen:



hvori Tr er trastuzumab koblet gjennom bindeleddelen MCC til maytansinoidlegemiddeldelen DM1, og hvori p representerer forholdet mellom legemiddel og antistoff og varierer i heltallsverdier fra 1 til 8.

2. Trastuzumab-MCC-DM1 for anvendelse i fremgangsmåten ifølge krav 1, hvori behandlingen før den metastatiske tilstanden med et taksan ble administrert i adjuvanstilstanden.

3. Trastuzumab-MCC-DM1 for anvendelse i fremgangsmåten ifølge krav 1, hvori behandlingen før den metastatiske tilstanden med et taksan ble administrert i neoadjuvanstilstanden.

4. Trastuzumab-MCC-DM1 for anvendelse i fremgangsmåten ifølge krav

1, hvori trastuzumab-MCC-DM1 administreres hver tredje uke ved 3,6 mg/kg.

5. Trastuzumab-MCC-DM1 for anvendelse i fremgangsmåten ifølge krav 1, hvori trastuzumab-MCC-DM1 administreres hver uke ved 2,4 mg/kg.