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(54)	Title	COMBINATION OF EGFR INHIBITOR AND MEK INHIBITOR FOR USE IN THE TREATMENT OF NRAS MUTATED CANCER
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(56)	References	
	Cited:	US-A1- 2013 053 409 C. H. DIEP ET AL: "Synergistic Effect between Erlotinib and MEK Inhibitors in KRAS Wild-Type Human Pancreatic Cancer Cells", CLINICAL CANCER RESEARCH, vol. 17, no. 9, 8 March 2011 (2011-03-08), pages 2744-2756, XP055132319, ISSN: 1078-0432, DOI: 10.1158/1078-0432.CCR-10-2214 MISALE SANDRA ET AL: "Blockade of EGFR and MEK intercepts heterogeneous mechanisms of acquired resistance to anti-EGFR therapies in colorectal cancer", SCIENCE

TRANSLATIONAL MEDICINE 19 FEB 2014, vol. 6, no. 224, 19 February 2014 (2014-02-19), page 224ra26, XP002740843, ISSN: 1946-6242

SONG JI-YOUNG ET AL: "Dual inhibition of MEK1/2 and EGFR synergistically induces caspase-3-dependent apoptosis in EGFR inhibitor-resistant lung cancer cells via BIM upregulation.", INVESTIGATIONAL NEW DRUGS DEC 2013, vol. 31, no. 6, December 2013 (2013-12), pages 1458-1465, XP002740844, ISSN: 1573-0646

FEI-YU NIU ET AL: "Novel agents and strategies for overcoming EGFR TKIs resistance", EXPERIMENTAL HEMATOLOGY & ONCOLOGY, BIOMED CENTRAL LTD, LONDON, UK, vol. 3, no. 1, 11 January 2014 (2014-01-11), pages 1-5, XP021175239, ISSN: 2162-3619, DOI: 10.1186/2162-3619-3-2

HUANG MING-HUNG ET AL: "MEK inhibitors reverse resistance in epidermal growth factor receptor mutation lung cancer cells with acquired resistance to gefitinib", MOLECULAR ONCOLOGY, ELSEVIER, AMSTERDAM, NL, vol. 7, no. 1, 1 February 2013 (2013-02-01), pages 112-120, XP008165510, ISSN: 1574-7891, DOI: 10.1016/J.MOLONC.2012.09.002 [retrieved on 2012-10-13]

SUN CHONG ET AL: "Intrinsic resistance to MEK inhibition in KRAS mutant lung and colon cancer through transcriptional induction of ERBB3", CELL REPORTS 10 APR 2014, vol. 7, no. 1, 27 March 2014 (2014-03-27), pages 86-93, XP002740911, ISSN: 2211-1247

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (<http://worldwide.espacenet.com>) or via the search engine on our website here: <https://search.patentstyret.no/>

Patentkrav

1. EGFR-hemmer til bruk i behandlingen av NRAS-mutert ikke-småcellet lungekreft, der EGFR-hemmeren blir administrert i kombinasjon med en MEK-hemmer, og NRAS-mutasjonen er valgt blant E63K, G12V, G12R, eller en økning av kopitallet hos *NRAS*-genet.
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2. EGFR-hemmer til bruk ifølge krav 1, der EGFR-hemmeren er valgt blant gefitinib, erlotinib, afatinib, AZD9291 og CO1686; eller et farmasøytisk akseptabelt salt av dette.
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3. EGFR-hemmer til bruk ifølge krav 1 eller krav 2, der EGFR-hemmeren er valgt blant AZD9291 og CO 1686; eller et farmasøytisk akseptabelt salt av dette.
4. EGFR-hemmer til bruk ifølge et av kravene 1 til 3, der MEK-hemmeren er valgt
15 blant selumetinib, trametinib, MEK-162 og kobimetinib; eller et farmasøytisk akseptabelt salt av dette.
5. EGFR-hemmer til bruk ifølge et av kravene 1 til 4, der EGFR-hemmeren er AZD9291 eller et farmasøytisk akseptabelt salt av dette.
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6. EGFR-hemmer til bruk ifølge et av kravene 1 til 5, der MEK-hemmeren er selumetinib eller et farmasøytisk akseptabelt salt av dette.
7. EGFR-hemmer til bruk ifølge krav 1, der EGFR-hemmeren er AZD9291 eller et
25 farmasøytisk akseptabelt salt av dette, og MEK-hemmeren er selumetinib eller et farmasøytisk akseptabelt salt av dette.