

SEARCH STRATEGY

1. Searching in MEDLINE, CENTRAL and EMBASE

All databases were searched using both controlled vocabulary (namely MeSH in MEDLINE and EMTREE in EMBASE) and a wide range of free-text terms (Higgins 2011)

Search code for MEDLINE (accessed via PubMed) and CENTRAL

Patients		
Lung cancer	#1	lung neoplasms[MeSH] OR carcinoma, non small cell lung[MeSH] OR lung carcinom*[tiab] OR lung neoplasm*[tiab] OR lung cancer[tiab] OR NSCLC[tiab] OR non small cell lung[tiab]
Advanced	#2	"Neoplasm Metastasis"[MeSH] OR advanced[tiab] OR stage IV[tiab] OR stage 4[tiab] OR stage four[tiab] OR metastatic[tiab] OR metastases[tiab]
Intervention		
Chemotherapy	#3	chemotherapy[tiab] OR chemotherapies[tiab] OR docetaxel[tiab] OR taxotere[tiab] OR "docetaxel"[Supplementary Concept] OR pemetrexed[tiab] OR alimta[tiab] OR "pemetrexed"[Supplementary Concept] OR gemcitabine[tiab] OR "gemcitabine"[Supplementary Concept] OR vinorelbine[tiab] OR "vinorelbine"[Supplementary Concept] OR paclitaxel[tiab] OR "Paclitaxel"[MeSH] OR "Vinblastine"[Supplementary Concept] OR vinblastine[tiab] OR "Ifosfamide"[MeSH] OR Ifosfamide[tiab] OR "irinotecan"[Supplementary Concept] OR irinotecan[tiab] OR "Mitomycin"[MeSH] OR mitomycin[tiab] OR vindesine[tiab] OR "Vindesine"[MeSH]
EGFR Targeted therapy	#4	"protein kinase inhibitors"[MeSH] OR "kinase inhibitor"[tiab] OR "kinase inhibitors"[tiab] OR gefitinib[tiab] OR iressa[tiab] OR "gefitinib"[Supplementary Concept] OR erlotinib[tiab] OR tarceva[tiab] OR "erlotinib"[Supplementary Concept] OR "icotinib"[Supplementary Concept] OR "icotinib"[tiab] OR afatinib[tiab] OR "BIBW 2992" [Supplementary Concept] OR "cetuximab"[Supplementary Concept] OR cetuximab[tiab]
VEGF targeted therapy	#5	bevacizumab[tiab] OR "bevacizumab"[Supplementary Concept] OR "vandetanib"[tiab] OR sunitinib[tiab] OR "sunitinib"[Supplementary Concept] OR sorafenib[tiab] OR "sorafenib"[Supplementary Concept] OR Ramucirumab[tiab] OR "ramucirumab"[Supplementary Concept] OR "nintedanib"[Supplementary Concept] OR nintedanib[tiab]
Second line	#6	second line[tiab] OR pretreat*[tiab] OR previously treated[tiab] OR refractory[tiab] OR recurrent[tiab]
Cochrane Highly Sensitive Search Strategy	#7	(randomized controlled trial[Publication Type] OR controlled clinical trial[Publication Type] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab]) NOT (animals[mh] NOT humans[mh])
Search algorithm	#8	#1 AND #2 AND (#3 OR #4 OR #5) AND #6 AND #7

Search code for EMBASE Patients

Lung cancer	#1	'lung tumor'/exp OR 'non small cell lung cancer'/exp OR (lung NEXT/1 carcinom*):ab,ti OR (lung NEXT/1 neoplasm*):ab,ti OR 'lung cancer':ab,ti OR nslcl:ab,ti OR 'non small cell lung':ab,ti
Advanced	#2	'metastasis'/exp OR advanced:ab,ti OR 'stage IV':ab,ti OR 'stage 4':ab,ti OR 'stage four':ab,ti OR metastatic:ab,ti OR metastases:ab,ti
Intervention		
Chemotherapy	#3	'chemotherapy':ab,ti OR 'chemotherapies':ab,ti OR docetaxel:ab,ti OR taxotere:ab,ti OR 'docetaxel'/exp OR pemetrexed:ab,ti OR alimta:ab,ti OR 'pemetrexed'/exp OR gemcitabine:ab,ti OR 'gemcitabine'/exp OR vinorelbine:ab,ti OR 'navelbine'/exp OR paclitaxel:ab,ti OR 'paclitaxel'/exp OR 'vinblastine'/exp OR vinblastine:ab,ti OR 'ifosfamide'/exp OR ifosfamide:ab,ti OR 'irinotecan'/exp OR irinotecan:ab,ti OR 'mitomycin'/exp OR mitomycin:ab,ti OR vindesine:ab,ti OR 'vindesine'/exp
EGFR Targeted therapy	#4	'protein kinase inhibitor'/exp OR 'kinase inhibitors':ab,ti OR 'kinase inhibitor':ab,ti OR gefitinib:ab,ti OR iressa:ab,ti OR 'gefitinib'/exp OR erlotinib:ab,ti OR tarceva:ab,ti OR 'erlotinib'/exp OR 'icotinib'/exp OR icotinib:ab,ti OR afatinib:ab,ti OR 'afatinib'/exp OR 'bibw 2992':ab,ti OR 'cetuximab'/exp OR cetuximab:ab,ti
VEGF targeted therapy	#5	bevacizumab:ab,ti OR 'bevacizumab'/exp OR vandetanib:ab,ti OR 'vandetanib'/exp OR sunitinib:ab,ti OR 'sunitinib'/exp OR sorafenib:ab,ti OR 'sorafenib'/exp OR ramucirumab:ab,ti OR 'ramucirumab'/exp OR 'nintedanib'/exp OR nintedanib:ab,ti
Second line	#6	'second line':ab,ti OR pretreat*:ab,ti OR 'previously treated':ab,ti OR 'refractory':ab,ti OR 'recurrent':ab,ti
Filter used by the UK Cochrane Centre	#7	'crossover procedure'/exp OR 'double-blind procedure'/exp OR 'randomized controlled trial'/exp OR 'single-blind procedure'/exp OR random* OR factorial* OR crossover* OR cross NEXT/1 over* OR placebo* OR doubl* NEAR/1 blind* OR singl* NEAR/1 blind* OR assign* OR allocat* OR volunteer*
Search algorithm	#8	#1 AND #2 AND (#3 OR #4 OR #5) AND #6 AND #7

2. Searching other resources

- 2.1. Previous systematic reviews in the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effectiveness and the PROSPERO international prospective register of systematic reviews for completed or published systematic reviews

- ## 2.2. Reference lists of all selected trials

- ### 2.3. Conference abstracts

- ASCO (American Society of Clinical Oncology)

July 2018 :

https://meetinglibrary.asco.org/results/Keywords:Lung%20Cancer%20AND%20Keywords:Non-small%20Cell%20AND%20Keywords:%22Metastatic%22?filters=JTV CJT dCJT IyZml bGQl Mj I l M0 E l Mj J Z W F y J T I y J T J D J T I y d m F s d W U l M j I l M0 E l Mj I y M D E 4 J T I y J T J D J T I y c X V l c n l W Y W x 1 Z S U y M i U z Q S U y M j I w M T g l M j I l M k M l M j J a G l s Z H J l b i U y M i U z Q S U 1 Q i U 1 R C U 3 R C U y Q y U 3 Q i U y M m Z p Z W x k J T I y J T N B J T I y W W V h c i U y M i U y Q y U y M n Z h b H V l J T I y J T N B J T I y M j A x N y U y M i U y Q y U y M n F 1 Z X J 5 V m F s d W U l M j I l M0 E l M j I y M D E 3 J T I y J T J D J T I y Y 2 h p b G R y Z W 4 l M j I l M0 E l N U l l N U Q l N 0 Q l M k M l N 0 l l M j J m a W V s Z C U y M i U z Q S U y M m Z i d E 1 Z X R p b m d O Y W 1 l J T I y J T J D J T I y d m F s d W U l M j I l M0 E l M j J B U 0

-WHO ICTRP (World Health Organization International Clinical Trials Registry Platform): <http://apps.who.int/trialsearch/AdvSearch.aspx>

Title: "second line" OR pretreated OR "previously treated" OR refractory OR recurrent
Condition: "non small cell lung cancer" OR NSCLC

- *ClinicalTrials.gov*:

<https://clinicaltrials.gov/>

Search terms: ("second line" OR pretreated OR "previously treated" OR refractory OR recurrent) AND (randomized OR randomly OR random)

Condition: "non small cell lung cancer" OR NSCLC

- *EU Clinical Trials Register*: [https://www.clinicaltrialsregister.eu/ctr-](https://www.clinicaltrialsregister.eu/ctr-search/search;jsessionid=ibt6KBrHrA42yLVJt9u22qA8QXoJ_EoYVTQqjK9ARwiqaDccKsdA!3472_91559)

[search/search;jsessionid=ibt6KBrHrA42yLVJt9u22qA8QXoJ_EoYVTQqjK9ARwiqaDccKsdA!3472_91559](https://www.clinicaltrialsregister.eu/ctr-search/search;jsessionid=ibt6KBrHrA42yLVJt9u22qA8QXoJ_EoYVTQqjK9ARwiqaDccKsdA!3472_91559)

Search terms: ("non small cell lung cancer" OR NSCLC) AND ("second line" OR pretreated OR "previously treated" OR refractory OR recurrent)

2.5. Industry trial registries and results databases

Pharmaceutical company	Drugs	Link
AstraZeneca	Fulvestrant, Gefitinib, Selumetinib, Vandetanib	http://www.astrazenecaclinicaltrials.com/
Axelar	AXL1717	http://www.axelar.se/rd/posters-publications/
Bayer	Sorafenib	http://pharma.bayer.com/en/research-and-development/clinical-trials/trial-finder/index.php
Boehringer Ingelheim	Afatinib, Nintedanib	http://trials.boehringer-ingelheim.com/trial_results/clinical_trials_overview/clinical_trial_result.c=i.i=10.html
Bristol-Myers Squibb	Nivolumab	http://www.bms.com/research/pipeline/Pages/default.aspx
Celgene	Nab-Paclitaxel	http://www.celgene.com/research-development/clinical-trials/celgene-sponsored-trials/
Daiichi-Sankyo	Nimotuzumab, Tivantinib	http://www.daiichisankyo.com/rd/pipeline/development_pipeline/index.html
GlaxoSmithKline	Pazopanib, Topotecan, Trametinib, Vinorelbine	http://www.gsk-clinicalstudyregister.com/
Lilly	Gemcitabine, Pemetrexed Ramucirumab (new)	http://lillytrials.com/results/ctr_toc.pdf http://lillytrials.com/results/alimta.pdf?bcsi_scan_628cd39dca2568d2=0&bcsi_scan_filename=alimta.pdf http://lillytrials.com/results/Gemzar.pdf?bcsi_scan_628cd39dca2568d2=0&bcsi_scan_filename=Gemzar.pdf
Merck	Cetuximab, Dalotuzumab, Matuzumab, Pembrolizumab	http://biopharma.merckgroup.com/en/research_development/pipeline/pipeline.html
Novartis	Everolimus	http://www.novctrd.com/ctrdWebApp/clinicaltrialrepository/public/login.jsp

Roche	Atezolizumab, Bevacizumab, R1507, Tarceva, Onartuzumab	http://www.roche-trials.com/searchFullText.action?drug=2
Sanofi	Aflibercept, Docetaxel	http://en.sanofi.com/rd/clinica

2.6. Regulatory agency online databases

- US Food and Drug Administration

<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/>

Label, Review, Summary review for: [Afatinib](#), Aflibercept, [Atezolizumab](#), Bortezomib, Docetaxel, Everolimus, Fulvestrant, Gefitinib, Gemcitabine, [Nab-Paclitaxel](#), [Nintedanib](#), [Nivolumab](#), Paclitaxel, Pazopanib, [Pembrolizumab](#), Pemetrexed, [Ramucirumab](#), Sorafenib, Tamoxifen, Topotecan, Vinorelbine.

-European Medicines Agency:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/document_library/landing/document_library_search.jsp

Search for keywords using names of drugs European public assessment reports for: [Afatinib](#), [Atezolizumab](#), Bevacizumab, Docetaxel, Erlotinib, Gefitinib, [Nintedanib](#), [Nivolumab](#), [Pembrolizumab](#), Pemetrexed, and [Ramucirumab](#)

2.7. Health technology assessment agencies

-NICE (National Institute for Health and Care Excellence):

<https://www.nice.org.uk/guidance/conditions-and-diseases/cancer/lung-cancer>

-AHRQ (Agency for Healthcare Research and Quality):

<http://www.guideline.gov/browse/by-topic-detail.aspx?id=12697&ct=1>

Guidelines by Topic: Disease/Condition >Diseases >Neoplasms >Neoplasms by Site >Thoracic Neoplasms >Respiratory Tract Neoplasms > Lung Neoplasms (58)

-IQWiG (Institute for Quality and Efficiency in Health Care):

<https://www.iqwig.de/en/projects-results/publications/iqwig-reports.1071.html>

-HAS (Haute Autorité de Santé):

[https://www.has-](https://www.has-sante.fr/portail/jcms/c_39085/en/recherche?portlet=c_39085&opSearch=&lang=en&portal=c_2566858&FACET_TYPE=opinions%2Fgenerated.AVISMedicament&FACET_THEME=c_1151682)

[sante.fr/portail/jcms/c_39085/en/recherche?portlet=c_39085&opSearch=&lang=en&portal=c_2566858&FACET_TYPE=opinions%2Fgenerated.AVISMedicament&FACET_THEME=c_1151682](https://www.has-sante.fr/portail/jcms/c_39085/en/recherche?portlet=c_39085&opSearch=&lang=en&portal=c_2566858&FACET_TYPE=opinions%2Fgenerated.AVISMedicament&FACET_THEME=c_1151682)