

SEARCH STRATEGY (update August 2019 in red)

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).

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 navelbine[Supplementary Concept] OR paclitaxel[tiab] OR "paclitaxel"[MeSH] OR "vinflunine"[Supplementary Concept] OR vinflunine[tiab] OR nab-paclitaxel[tiab] OR "nab-paclitaxel" OR "topotecan"[MeSH] OR topotecan[tiab] OR "tegafur/uracil" OR tegafur/uracil[tiab] OR amrubicin[Supplementary Concept] OR amrubicin[tiab] OR "pralatrexate" OR pralatrexate[tiab] OR "entinostat"[Supplementary Concept] OR entinostat[tiab]
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 hydrochloride"[MeSH] OR "icotinib"[Supplementary Concept] OR "icotinib"[tiab] OR afatinib[tiab] OR "afatinib"[Supplementary Concept] OR "cetuximab"[MeSH] OR cetuximab[tiab] OR dacomitinib[tiab] OR "dacomitinib" OR matuzumab[tiab] OR "matuzumab"[Supplementary Concept] OR nimotuzumab[tiab] OR "nimotuzumab"[Supplementary Concept]
VEGF targeted therapy	#5	bevacizumab[tiab] OR "bevacizumab"[MeSH] OR "vandetanib"[tiab] OR "vandetanib" 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] OR "aflibercept"[Supplementary Concept] OR aflibercept [tiab] OR "cabozantinib"[Supplementary Concept] OR cabozantinib [tiab] OR "pazopanib"[Supplementary Concept] OR pazopanib[tiab]

Other targeted therapy	#6	tamoxifen[tiab] OR "tamoxifen"[MeSH] OR "everolimus"[tiab] OR "everolimus"[MeSH] OR selumetinib[tiab] OR "selumetinib" OR "tivantinib" OR tivantinib[tiab] OR fulvestrant[tiab] OR "fulvestrant"[Supplementary Concept] OR trametinib[tiab] OR "trametinib"[Supplementary Concept] OR "axl1717" OR axl1717[tiab] OR "dalotuzumab"[Supplementary Concept] OR dalotuzumab[tiab] OR "figitumumab"[Supplementary Concept] OR figitumumab[tiab] OR "R1507" OR R1507[tiab] OR "onartuzumab"[Supplementary Concept] OR onartuzumab[tiab]
PD1 and PDL1 targeted therapy	#7	"nivolumab"[Supplementary Concept] OR nivolumab[tiab] OR "atezolizumab"[Supplementary Concept] OR atezolizumab[tiab] OR "pembrolizumab"[Supplementary Concept] OR pembrolizumab[tiab] OR "avelumab"[Supplementary Concept] OR avelumab[tiab]
Second line	#8	second line[tiab] OR pretreat*[tiab] OR previously treated[tiab] OR refractory[tiab] OR recurrent[tiab]
Cochrane Highly Sensitive Search Strategy	#9	(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 equation	#10	#1 AND #2 AND (#3 OR #4 OR #5 OR #6 OR #7) AND #8 AND #9

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 nslc: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 'vinflunine'/exp OR vinflunine:ab,ti OR 'nab-paclitaxel'/exp OR 'nab paclitaxel':ab,ti OR 'topotecan'/exp OR topotecan:ab,ti OR 'tegafur uracil'/exp OR 'tegafur uracil':ab,ti OR amrubicin:ab,ti OR 'amrubicin'/exp OR pralatrexate:ab,ti OR 'pralatrexate'/exp OR entinostat:ab,ti OR 'entinostat'/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 'cetuximab'/exp OR cetuximab:ab,ti OR 'dacomitinib'/exp OR dacomitinib:ab,ti OR

results?q=&f_IssueNo=suppl_5&f_Volume=28&f_TocCategories=NSCLC,%20metas
tatic

-<http://www.poster-submission.com/esmo2017/visitors/search/sresult>
ESMO 2017, 8 - 12 September, 2017 Madrid, Spain, ESMO 2017, 8 - 12 September,
2017- Free poster search Advanced search for NSCLC metastatic

December 2018:

-https://academic.oup.com/annonc/search-results?q=&f_IssueNo=suppl_8&f_Volume=29&f_TocCategories=NSCLC%2c+metastatic

August 2019:

No ESMO in this period

- WCLC (World Conference on Lung Cancer)

July 2018:

-2017: 18th World Conference on Lung Cancer https://library.iaslc.org/virtual-library-search?product_id=7&author=&category=Advanced+NSCLC&date=&session_type=Poster+Session+with+Presenters+Present&session=&presentation=&keyword=

December 2018:

-2018: 19th World Conference on Lung Cancer https://library.iaslc.org/virtual-library-search?product_id=10&author=&category=Advanced+NSCLC

August 2019:

No conference in this period

2.4. Non-industry trial registries and results databases:

- 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

August 2019:

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-search/search>

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

August 2019:

<https://www.clinicaltrialsregister.eu/ctr-search/search>

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, Avelumab (Merck–Pfizer)	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/clinical

2.1. 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, Avelumab.

-European Medicines Agency:

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

https://www.ema.europa.eu/en/search/search/ema_group_types/ema_medicine?sort=field_ema_computed_date_field&order=desc&

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

2.2. Health technology assessment agencies once per year

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

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

<https://www.nice.org.uk/guidance/conditions-and-diseases/cancer/lung-cancer/products?Status=Published>

-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)

<https://integrationacademy.ahrq.gov/products/literature-collection/literature/topic/opioids-substance-use>

-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->

[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)