

Appendix 1 Search strategy

PubMed

- #1. ex20ins OR EGFRex20ins OR Exon20ins OR “ex20 ins” OR “EGFR e20ins” OR “exon 20 insertion*” OR “exon 20 in-frame insertion*” OR “Exon 20 mutation*”
- #2. “epidermal growth factor receptor*”[tw] OR EGFR[tw]
- #3. #1 and #2
- #4. “exon 14 mutat*” OR “exon 14 skipping” OR METex14 OR METex14del OR “MET exon 14delta” OR “MET ex14 skipping” OR “MET ex14 mutat*”
- #5. “mesenchymal-epithelial transition”[tw] OR MET[tw]
- #6. #4 and #5
- #7. #3 or #6
- #8. “China”[Mesh] OR China OR Chinese OR Taiwan OR Taiwanese OR “Hong kong” OR Hongkong OR Macau OR Macao OR Beijing OR Shanghai OR Tianjin OR Chongqing OR “Inner Mongolia” OR Tibet OR Guangxi OR Sinkiang OR Ningxia OR Xinjiang OR Hebei OR Shanxi OR Liaoning OR Jilin OR Heilongjiang OR Jiangsu OR Zhejiang OR Anhui OR Fujian OR Jiangxi OR Shandong OR Henan OR Hubei OR Hunan OR Guangdong OR Hainan OR Sichuan OR Guizhou OR Yunnan OR Shaanxi OR Gansu OR Qinghai
- #9 #7 and #8

EMBASE

- #1. (ex20ins OR EGFRex20ins OR Exon20ins OR “ex20 ins” OR “EGFR e20ins” OR “exon 20 insertion*” OR “exon 20 in-frame insertion*” OR “Exon 20 mutation*”):ti,ab,kw
- #2. (“epidermal growth factor receptor*” OR EGFR):ti,ab,kw
- #3. #1 and #2
- #4. (“exon 14 mutat*” OR “exon 14 skipping” OR METex14 OR METex14del OR “MET exon 14delta” OR “MET ex14 skipping” OR “MET ex14 mutat*”):ti,ab,kw
- #5. (“mesenchymal-epithelial transition” OR MET):ti,ab,kw
- #6. #4 and #5
- #7. #3 or #6
- #8. ‘China’/exp OR (China OR Chinese OR Taiwan OR Taiwanese OR “Hong kong” OR Hongkong OR Macau OR Macao OR Beijing OR Shanghai OR Tianjin OR Chongqing OR “Inner Mongolia” OR Tibet OR Guangxi OR Sinkiang OR Ningxia OR Xinjiang OR Hebei OR Shanxi OR Liaoning OR Jilin OR Heilongjiang OR Jiangsu OR Zhejiang OR Anhui OR Fujian OR Jiangxi OR Shandong OR Henan OR Hubei OR Hunan OR Guangdong OR Hainan OR Sichuan OR Guizhou OR Yunnan OR Shaanxi OR Gansu OR Qinghai):ti,ab,ad,ff
- #9. #7 and #8

Cochrane Library:

- #1. ex20ins OR EGFRex20ins OR Exon20ins OR “ex20 ins” OR “EGFR e20ins” OR “exon 20 insertion*” OR “exon 20 in-frame insertion*” OR “Exon 20 mutation*”
- #2. (“epidermal growth factor receptor*” OR EGFR):ti,ab,kw
- #3. #1 and #2
- #4. “exon 14 mutat*” OR “exon 14 skipping” OR METex14 OR METex14del OR “MET exon 14delta” OR “MET ex14 skipping” OR “MET ex14 mutat*”
- #5. (“mesenchymal-epithelial transition” OR MET):ti,ab,kw
- #6. #4 and #5
- #7. #3 or #6
- #8. MeSH descriptor: [China] explode all trees
- #9. China OR Chinese OR Taiwan OR Taiwanese OR “Hong kong” OR Hongkong OR Macau OR Macao OR Beijing

OR Shanghai OR Tianjin OR Chongqing OR “Inner Mongolia” OR Tibet OR Guangxi OR Sinkiang OR Ningxia OR Xinjiang OR Hebei OR Shanxi OR Liaoning OR Jilin OR Heilongjiang OR Jiangsu OR Zhejiang OR Anhui OR Fujian OR Jiangxi OR Shandong OR Henan OR Hubei OR Hunan OR Guangdong OR Hainan OR Sichuan OR Guizhou OR Yunnan OR Shaanxi OR Gansu OR Qinghai

#10. #8 or #9

#11. #7 and #10

Web of Science:

#1. TS=(ex20ins OR EGFRex20ins OR Exon20ins OR “ex20 ins” OR “EGFR e20ins” OR “exon 20 insertion*” OR “exon 20 in-frame insertion*” OR “Exon 20 mutation*”)

#2. TS=(“epidermal growth factor receptor*” OR EGFR)

#3. #1 and #2

#4. TS=(“exon 14 mutat*” OR “exon 14 skipping” OR METex14 OR METex14del OR “MET exon 14delta” OR “MET ex14 skipping” OR “MET ex14 mutat*”)

#5. TS=(“mesenchymal-epithelial transition” OR MET)

#6. #4 and #5

#7. #3 or #6

#8. CU=(China) OR TS=(China OR Chinese OR Taiwan OR Taiwanese OR “Hong kong” OR Hongkong OR Macau OR Macao OR Beijing OR Shanghai OR Tianjin OR Chongqing OR “Inner Mongolia” OR Tibet OR Guangxi OR Sinkiang OR Ningxia OR Xinjiang OR Hebei OR Shanxi OR Liaoning OR Jilin OR Heilongjiang OR Jiangsu OR Zhejiang OR Anhui OR Fujian OR Jiangxi OR Shandong OR Henan OR Hubei OR Hunan OR Guangdong OR Hainan OR Sichuan OR Guizhou OR Yunnan OR Shaanxi OR Gansu OR Qinghai) OR AD=(China OR Chinese OR Taiwan OR Taiwanese OR “Hong kong” OR Hongkong OR Macau OR Macao OR Beijing OR Shanghai OR Tianjin OR Chongqing OR “Inner Mongolia” OR Tibet OR Guangxi OR Sinkiang OR Ningxia OR Xinjiang OR Hebei OR Shanxi OR Liaoning OR Jilin OR Heilongjiang OR Jiangsu OR Zhejiang OR Anhui OR Fujian OR Jiangxi OR Shandong OR Henan OR Hubei OR Hunan OR Guangdong OR Hainan OR Sichuan OR Guizhou OR Yunnan OR Shaanxi OR Gansu OR Qinghai)

#9. #7 and #8

CNKI:

#1. (SU%=表皮生长因子受体20插入+ EGFR 20插入+ex20ins+EGFRex20ins+ Exon20ins+”ex20 ins”+ “EGFR e20ins” OR TKA % (表皮生长因子受体20插入+ EGFR 20插入+ex20ins+EGFRex20ins+ Exon20ins+ “ex20 ins”+ “EGFR e20ins”))

#2. (SU%=MET 14跳跃+MET 14跳读+MET 14突变+”METex14”+”METex14del”+ “MET exon 14delta”+ “MET ex14” OR TKA % (MET 14跳跃+MET 14跳读+MET 14突变+”METex14”+”METex14del”+ “MET exon 14delta”+ “MET ex14”))

#3. #1 OR #2

CBM:

#1. ((“表皮生长因子受体”[常用字段:智能] OR “EGFR”[常用字段:智能]) AND “20插入”[常用字段:智能])

#2. (“ex20ins”[常用字段:智能] OR “EGFRex20ins”[常用字段:智能] OR “Exon20ins”[常用字段:智能] OR “ex20 ins”[常用字段:智能] OR “EGFR e20ins”[常用字段:智能])

#3. “MET”[常用字段:智能] AND (“14跳跃”[常用字段:智能] OR “14跳读”[常用字段:智能] OR “14突变”[常用字段:智能])

#4. “MET14”[常用字段:智能] AND (“跳跃”[常用字段:智能] OR “跳读”[常用字段:智能] OR “突变”[常用字段:智能])

#5. (“MET14”[常用字段:智能] OR “METex14”[常用字段:智能] OR “METex14del”[常用字段:智能] OR “MET exon 14delta”[常用字段:智能] OR “MET ex14”[常用字段:智能] OR “exon 14”[常用字段:智能])

#6. #1 OR #2 OR #3 OR #4 OR #5

Wanfang:

主题:(表皮生长因子受体 OR EGFR) AND “20插入”) OR 主题:(ex20ins OR EGFRex20ins OR Exon20ins OR “ex20 ins” OR “EGFR e20ins”) OR 主题:(MET AND (“14跳跃” OR “14跳读” OR “14突变”)) OR 主题:(“MET14” AND (“跳跃” OR “跳读” OR “突变”)) OR 主题:(“MET14” OR “METex14” OR “METex14del” OR “MET exon 14delta” OR “MET ex14” OR “exon 14”)

VIP:

M= (表皮生长因子受体20插入 OR EGFR 20插入 OR MET 14跳跃 OR MET 14跳读 OR MET 14突变)

Appendix 2 List of included studies

1. Ai X, Yu Y, Zhao J, et al. Comprehensive analysis of MET mutations in NSCLC patients in a real-world setting. *Ther Adv Med Oncol* 2022;14:17588359221112474.
2. Chang JW, Huang CY, Fang YF, et al. Epidermal growth factor receptor tyrosine kinase inhibitors for non-small cell lung cancer harboring uncommon EGFR mutations: Real-world data from Taiwan. *Thorac Cancer* 2023;14:12-23.
3. Chen D, Song Z, Cheng G. Clinical efficacy of first-generation EGFR-TKIs in patients with advanced non-small-cell lung cancer harboring EGFR exon 20 mutations. *Onco Targets Ther* 2016;9:4181-6.
4. Chen H, Luo Y, Lin M, et al. Clinical and pathological characteristics of 11 NSCLC patients with c-MET exon 14 skipping. *Transl Cancer Res* 2022;11:880-7.
5. Chen K, Cheng G, Zhang F, et al. PD-L1 expression and T cells infiltration in patients with uncommon EGFR-mutant non-small cell lung cancer and the response to immunotherapy. *Lung Cancer* 2020;142:98-105.
6. Chen K, Pan G, Cheng G, et al. Immune microenvironment features and efficacy of PD-1/PD-L1 blockade in non-small cell lung cancer patients with EGFR or HER2 exon 20 insertions. *Thorac Cancer* 2021;12:218-26.
7. Chen K, Xu Y, Huang Z, et al. Sintilimab plus anlotinib as second- or third-line therapy in metastatic non-small cell lung cancer with uncommon epidermal growth factor receptor mutations: A prospective, single-arm, phase II trial. *Cancer Med* 2023;12:19460-70.
8. Chen K, Yu X, Wang H, et al. Uncommon mutation types of epidermal growth factor receptor and response to EGFR tyrosine kinase inhibitors in Chinese non-small cell lung cancer patients. *Cancer Chemother Pharmacol* 2017;80:1179-87.
9. Cheng T, Gu Z, Song D, et al. Genomic and clinical characteristics of MET exon14 alterations in a large cohort of Chinese cancer patients revealed distinct features and a novel resistance mechanism for crizotinib. *J Cancer* 2021;12:644-51.
10. Chow DYL, So TH, Leung DKC, et al. First-line Afatinib in Epidermal Growth Factor Receptor-mutant Metastatic Non-small Cell Lung Cancer: a Clinical Retrospective Study. *Hong Kong Journal of Radiology* 2022;25:184-91.
11. Dai J, Zuo Z, Guo P, et al. Combined Detection and Analysis of Ten Driver Gene Mutations in Non-Small Cell Lung Cancer. *Journal of Cancer Control and Treatment* 2020;33:979-87.
12. Ding C, Qiu Y, Zhang J, et al. Clinicopathological characteristics of Non-Small Cell Lung Cancer (NSCLC) patients with c-MET exon 14 skipping mutation, MET overexpression and amplification. *BMC Pulm Med* 2023;23:240.
13. Dong X, Li X, Chen J, et al. Phase 1 Study of the Selective c-MET Inhibitor, HS-10241, in Patients With Advanced Solid Tumors. *JTO Clin Res Rep* 2023;4:100449.
14. Duan J, Wu L, Yang K, et al. Safety, Tolerability, Pharmacokinetics, and Preliminary Efficacy of YK-029A in Treatment-Naive Patients With Advanced NSCLC Harboring EGFR Exon 20 Insertion Mutations: A Phase 1 Trial. *J Thorac Oncol* 2024;19:314-24.
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16. Feng Y, Feng G, Lu X, et al. Exploratory analysis of introducing next-generation sequencing-based method to treatment-naive lung cancer patients. *J Thorac Dis* 2018;10:5904-12.
17. Gao QY, Lin XC, Chen YQ, et al. Explore and Analyze the Therapeutic Effects and Tumor Immune Microenvironment of Driver Gene-Positive Lung Squamous Cell Carcinoma. *The Journal of Evidence-Based Medicine* 2022;22:105-18.

18. Gao X, Wei XW, Zheng MY, et al. Impact of EGFR amplification on survival of patients with EGFR exon 20 insertion-positive non-small cell lung cancer. *J Thorac Dis* 2020;12:5822-32.
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21. Geng D, Guo Q, Huang S, et al. Clinical and molecular characteristics of epidermal growth factor receptor exon 20 insertion mutations in non-small-cell lung cancer. *Clin Transl Oncol* 2022;24:379-87.
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25. He C, Xu YH, Xu K, et al. Evaluation of EGFR-TKI treatment efficacy in non-small cell lung cancer patients with uncommon EGFR mutations. *Chinese Journal of Cancer Prevention and Treatment* 2020;27:1081-7.
26. Hou H, Zhu H, Zhao H, et al. Comprehensive Molecular Characterization of Young Chinese Patients with Lung Adenocarcinoma Identified a Distinctive Genetic Profile. *Oncologist* 2018;23:1008-15.
27. Hu MM, Liu ZC, Zhang HM, et al. EGFR Mutation Status and PD-L1 Expression in Patients ≤ 40 Years Old with NSCLC. *Cancer Research on Prevention and Treatment*. 2022;49:687-91.
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29. Huang CH, Ju JS, Chiu TH, et al. Afatinib treatment in a large real-world cohort of nonsmall cell lung cancer patients with common and uncommon epidermal growth factor receptor mutation. *Int J Cancer* 2022;150:626-35.
30. Huang HM, Zhu ZP, Wei Y. Analysis of epidermal growth factor receptor gene mutations in patients with non-small cell lung cancer in Shiyan, Hubei. *Cancer Research and Clinic* 2022;34:921-4.
31. Ji XK, Ma Y, Guo X, et al. Relationship between LAPT4B and multigene mutation status and EGFR-TKIs resistance in lung cancer. *Chinese Journal of Clinical and Experimental Pathology*. 2022;38:1176-80, 1186.
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33. Ju S, Cui Z, Hong Y, et al. Detection of multiple types of cancer driver mutations using targeted RNA sequencing in non-small cell lung cancer. *Cancer* 2023;129:2422-30.
34. Ko HW, Shie SS, Wang CW, et al. Association of smoking status with non-small cell lung cancer patients harboring uncommon epidermal growth factor receptor mutation. *Front Immunol* 2022;13:1011092.
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53. Peng W, Li B, Li J, et al. Clinical and genomic features of Chinese lung cancer patients with germline mutations. *Nat Commun* 2022;13:1268.
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58. Shen CI, Ho HL, Yeh YC, et al. Epidermal growth factor receptor mutations in non-small cell lung cancer undetected by high-sensitivity allele-specific real-time polymerase chain reaction-based assays. *J Chin Med Assoc* 2020;83:345-9.
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60. Shi C, Xing R, Li M, et al. Real-world clinical treatment outcomes in Chinese non-small cell lung cancer with EGFR exon 20 insertion mutations. *Front Oncol* 2022;12:949304.
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63. Song Y, Li G, Ju K, et al. Mesenchymal-Epithelial Transition Exon 14 Skipping Mutation and Amplification in 5,008

Patients With Lung Cancer. *Front Oncol* 2021;11:755031.

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65. Sun YY, Zhou XL, Gu WX, et al. Clinicopathology observation of primary pulmonary sarcomatoid carcinoma: 15 cases. *Chinese Journal of Thoracic and Cardiovascular Surgery* 2019;35:649-54.
66. Tang Y, Wang WY, Zheng K, et al. EGFR mutations in non-small cell lung cancer: an audit from West China Hospital. *Expert Rev Mol Diagn* 2016;16:915-9.
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- Molecular heterogeneity and treatment outcome from nationwide real-world study. *Lung Cancer* 2020;145:186-94.
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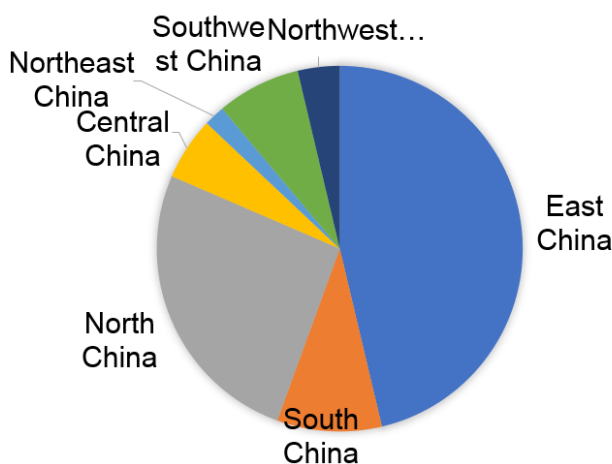


Figure S1 Number of included studies in seven geographical regions of China. Studies that did not report location were excluded. Northeast China: Heilongjiang Province, Jilin Province and Liaoning Province. Eastern China: Shanghai, Jiangsu Province, Zhejiang Province, Anhui Province, Fujian Province, Jiangxi Province, Shandong Province, and Taiwan. North China: Beijing, Tianjin, Shanxi Province, Hebei Province, Inner Mongolia Autonomous Region. Central China: Henan Province, Hubei Province, Hunan Province. South China: Guangdong Province, Guangxi Zhuang Autonomous Region, Hainan Province, Hong Kong Special Administrative Region, Macao Special Administrative Region; South China: Sichuan Province, Guizhou Province, Yunnan Province, Chongqing Municipality, Tibet Autonomous Region. Northwest Region: Shaanxi Province, Gansu Province, Qinghai Province, Ningxia Hui Autonomous Region, Xinjiang Uygur Autonomous Region.

Table S1 Detection methods of mutations in the included studies

Methods	Number of studies	Percentage (%)
RT-PCR	27	24.32%
NGS	35	31.53%
ARMS-PCR	5	4.50%
cSMART	1	0.90%
Sanger sequencing	2	1.80%
Mixed*	35	31.53%
Not report [#]	6	5.40%

*, Studies defined as mix, detection methods of mutations include any combination of the following, ARMS-PCR, NGS, CGP, PCR, FISH. [#], One of these six studies reported the use of PCR, without describing the method of sequencing. ARMS: amplification refractory mutation system; CGP: Comprehensive genomic profiling; cSMART: circulating single-molecule amplification and resequencing technology; FISH: fluorescence in situ hybridization; NGS: next generation sequencing; PCR: polymerase chain reaction; RT-PCR: reverse transcription-polymerase chain reaction.

Table S2 Summary of study characteristics in the scoping review

Characteristics	Number of studies	Percentage (%)
Age		
Predominantly or exclusively elderly (>60y)	8	7.21%
Non-elderly only (≤60y)	0	0.0%
Mixed elderly and non-elderly ages	48	43.24%
NR	55	49.55%
Tumour histology		
Adenocarcinoma (n)	58	52.25%
Adenosquamous (n)	18	16.22%
Large cell carcinoma (n)	5	4.50%
Sarcomatoid carcinoma (n)	13	11.71%
Squamous cell carcinoma (n)	31	27.93%
Poorly differentiated carcinoma (n)	2	1.80%
Undefined pathology (n)	8	7.21%
Other (Specific)	11	9.91%
Not reported	54	48.65%
Stage at diagnosis		
I	13	11.71%
II	10	9.01%
III	27	24.32%
IV	38	34.23%
I-II	3	2.70%
I-III	3	2.70%
I-IV	2	1.80%
III-IV	4	3.60%
Stage-Unknown (n)	6	5.41%
Not reported	65	58.56%
First three genetic subtypes		
A763_Y764insFQEA	19	17.12%
S768_D770 dupSVD	15	13.51%
A767_V769dupASV	12	10.81%

NR: not reported.

Table S3 Summary of EGFR exon20ins and MET exon14 skipping co-occurring genetic alteration in the included studies

Study ID	Total sample size of NSCLC	Number of EGFR/MET mutations	Number of EGFRex20ins/METex14	Number of cases of EGFRex20ins/METex14 with co-occurring genetic alterations	Specific information on co-occurring genetic alterations
EGFRex20ins mutation with co-occurring genetic alterations					
Caixia Ding, 2023	257	NR	17	3	KRAS, ALK fusion, EGFR L858R
Chao Shi, 2022	7831	3686	129	NR	TP53; EGFR; BRCA; CTNNB1
Cheng He, 2020	113	113	20	1	L858R
D. Geng, 2021	283	283	283	103	NR
Dan Chen, 2016	3910	1560	29	3	20INS + 19DEL; 20INS + L858R
Guangjian Yang, 2022	NR	NR	122	73	TP53, EGFR amplification, PIK3CA, RB1, BIM deletion polymorphism, alterations of PTEN, CREBBP
Guangjian, Yang 2020	165	165	165	NR	P53-60; EGFR amplification-19; PTEN-7; PIK3CA-5; MYC amplification-4; RB1 mutation-4; BIM deletion polymorphism-4
Haiyan Tu, 2017	5363	1837	67	1	19DEL+20INS; 20INS+21L858R
Huanlan Sa, 2023	NR	NR	53	43	TP53; EGFR amplification; MET amplification; CDKN2A deletion; RB1 mutation
Jenny Wu, 2008	515	253	5	1	P772_H773insYNP + H773Y
Jenny Wu, 2019	3805	2112	84	1	N771_H73dupNPH+H773_V774insG
Jie Dai, 2020	406	207	16	2	EGFR-L858R
Kaiyan Chen, 2020	1270	504	35	NR	TP53, PIK3CA, CDKN2A and EGFR amplification
Kaiyan Chen, 2023	21	NR	12	9	G719A; L861Q or G709X
Lifeng Wang, 2022	3892	2208	77	NR	ALK, KRAS, PIK3CA, TP53
Qi Gui, 2018	57	57	2	2	NR
Wenfeng Fang, 2019	2316	1095	53	10	EGFR L858R-1; EGFR amp-1
Xue Yang, 2015	24	24	3	6	NR
Yan Gao, 2017	86	40	2	2	19 and 20-T790M-1, 20-T790M and 20-Ins-1
Yue Wang, 2020	8348	2426	55	39	NR
Yunlang She, 2022	8437	5358	155	4	19Del, L858R, G719X, L861Q
MET exon14 skipping mutation with co-occurring genetic alterations					
Haiyan Yang, 2020	11242	NR	117	62	NR
Hanmin Wang, 2021	NR	NR	15	15	TP53, MYC, CDK4, MDM2, RBI, ATM, PIK3CA, CDKN2A, NRAS, KRAS, HGF
Kang Miao, 2023	NR	34	17	3	EGFR mutations
Li Liu, 2021	74	74	31	20	TP53 mut-7, PIK3CA mut-3, LZTR1 mut-1, ERBB2 CN amp-2, RET CN amp-1, CCND3 mut-1, MET CN amp-4, BRAF CN amp-4, CDKN2A mut-1, NRAS mut-1, EGFR CN amp-2, LRP1B mut-1
Shun Lu, 2021	NR	NR	70	48	TP53-32; MDM2-16;
Siyang Liu, 2016	1296	12	1	1	KRAS G12D mutation
Xiaorong Dong, 2022	27	5	1	1	amplified MET
Xinghao Ai, 2022	NR	564	117	21	MET copy number gain(CNG), gain of function (GOF) ,GOF single-nucleotide variant (SNV) ,EGFR,KRAS CNG/mutation, ERBB2 CNG
Yan Li, 2018	77	NR	16	3	KRAS mutated with METex14 skipping mutation, FGFR4 mutation (P458 L) with METex14 skipping mutation, KRAS mutation (G12 A) with METex14 skipping mutation, PIK3CA mutation (E542 K) with METex14 skipping mutation, ALK mutation (C1255 S) with METex14 skipping mutation
Yang Gao, 2021	58	NR	5	2	amplified MET
Yang Xia, 2023	NR	NR	29	9	TP53, NF1, PI3K,RAS, SMARCA4, STK11, KEAP1, PTEN
Yaolin Song, 2021	4955	NR	45	3	EGFR exon 21 L858R, EGFR exon19 19-Del, and BRAF exon 15 V600E
Yongfeng Yu, 2022	NR	NR	46	35	TP-53,POT1,TERT, KRAS,DNMT3A
Ziguang Xu, 2020	951	NR	16	10	TP53-6; PTEN-1; PIK3CA-1; EGFR-1; MET-1

ALK: anaplastic lymphoma kinase; BIM: Bcl-2 interacting mediator; CCND3: cyclin D3; DEL: deletion; EGFR: epidermal growth factor receptor; FGFR: fibroblast growth factor receptor; INS: insertion; KRAS: Kirsten rat sarcoma viral oncogene homolog; LZTR1: leucine-zipper-like transcription regulator 1; MET: mesenchymal-epithelial transition factor; NR: not reported; NSCLC: non-small cell lung cancer; PIK3CA: phosphatidylinositol 3-kinase catalytic subunit α ; PTEN: phosphate and tension homology deleted on chromosome ten.

Table S4 Study characteristics of the EGFRex20ins mutation in the included studies

First author/year	Region	Mutation test Institution	Detection methods	Sample size (NSCLC)	Frequency in NSCLC	Sample size (EGFR)	Frequency in EGFR Positive
Northeast China (1)							
Yu Wang, 2019	Liaoning, Dalian	NR	NGS; PCR	102	1.96%	42	4.76%
Eastern China (32)							
Anxin Zuo, 2022	Jiangsu, Nanjing	Department of Pathology, Nanjing Jiangning Hospital	ARMS-PCR	83	3.61%	41	7.32%
Biao Zhang, 2017	Jiangsu, Nanjing	Department of Pathology, Gulou Hospital, School of Medicine, Nanjing University	PCR-direct sequencing	236	3.81%	129	6.98%
Cheng He, 2020	Anhui, Hefei	NR	ARMS-PCR	NR	NR	113	17.70%
Chia-I Shen, 2020	Taiwan, Taipei	Department of Pathology and Laboratory Medicine, Taipei Veterans General Hospital	ASPR; Sanger	98	3.06%	6	50.00%
Chia-I Shen, 2022	Taiwan	NR	NGS	62	8.06%	7	71.43%
Chihhsien Huang, 2021	Taiwan, Taoyuan	NR	PCR	NR	NR	516	2.52%
Dan Chen, 2016	Zhejiang, Hangzhou	NR	Amplification refractory mutation system-based EGFR mutation detection kit	3910	0.70%	1560	1.90%
Dongmei Zhou, 2019	Fujian, Fuzhou	NR	ARMS-PCR	1252	1.04%	NR	NR
Fangfang, Zhong 2015	Anhui, Wuhu	NR	ARMS-PCR	20	5.00%	8	12.50%
Helei Hou, 2018	Shandong, Qingdao	NR	NGS	177	3.95%	96	7.29%
How-Wen Ko, 2022	Taiwan	NR	ARMS-PCR	NR	NR	3155	2.73%
Jenny Wu, 2008	Taiwan, Taipei	NR	PCR	515	1.00%	253	2.00%
Jenny Wu, 2019	Taiwan, Taipei	NR	PCR	3805	2.21%	2112	3.80%
Jiahui Zhang, 2022	Shandong	NR	ARMS-PCR; NGS	5338	1.31%	2000	3.50%
Jie Qian, 2022	Shanghai	Shanghai Chest Hospital	PCR; NGS	NR	NR	58	12.07%
John Wen-Cheng Chang, 2022	Taiwan	NR	NR	NR	NR	2420	2.27%
Junchang Jiang, 2015	Zhejiang, Hangzhou	NR	ARMS-PCR; general-PCR; Sanger sequencing	359	0.56%	337	0.59%
Kaiyan Chen, 2017	Zhejiang, Hangzhou	NR	Amplification refractory mutation system-based EGFR mutation detection kit	NR	NR	755	1.20%
Kaiyan Chen, 2020	Zhejiang, Hangzhou	NR	NR	NR	NR	600	0.80%
Kaiyan Chen, 2020	Zhejiang, Hangzhou	NR	CGP; PCR	1270	2.76%	504	6.90%
Kaiyan Chen, 2023	Zhejiang, Hangzhou	NR	ARMS-PCR; NGS	NR	NR	21	57.10%
Liping Gu, 2023	Shanghai	NR	ARMS-PCR; NGS	NR	NR	837	3.11%
Qi Gui, 2018	Jiangsu, Suzhou	Burning Stone Medical genetic testing	NGS	NR	NR	57	3.51%
Qingyue Lin, 2022	Zhejiang	The First Affiliated Hospital, School of Medicine, Zhejiang University, Department of Respiratory and Critical Care Medicine.	NGS; PCR	2132	1.69%	NR	NR
Ran ZHAO, 2022	Shanghai	NR	NGS	650	1.38%	389	2.31%
Yenting Lin, 2017	Taiwan, Taipei	NR	RT-PCR; DNA direct sequencing	3534	2.04%	1721	4.18%
Yicheng Shen, 2017	Taiwan, Taichung	NR	PCR	1632	1.30%	840	2.60%
Ying-Ting Liao, 2023	Taiwan	Oncomine Focus Assay and FoundationOne CDx	RT-PCR	NR	1.27%	NR	3.53%
Yue Wang, 2020	Shanghai	NR	PCR-direct sequencing; NGS	8348	1.21%	2426	4.16%
Yufang Feng, 2018	Jiangsu, Zhangjiagang	Zhangjiagang First People's Hospital	NGS	61	6.56%	27	14.81%
Yunjian Pan, 2014	Shanghai	NR	Direct dideoxynucleotide sequencing	1086	2.85%	662	4.68%
Yunlang She, 2022	Shanghai	Shanghai Pulmonary Hospital	PCR	8437	1.84%	5358	2.89%
North China (13)							
Guangjian Yang, 2020	Beijing	PCR and NGS for exon 18–21 were tested at these patients' treating hospitals or via commercially available platforms in China. PCR testing probe for EGFR ex20ins in National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences is designed to detect the following three ex20ins variants.	PCR; NGS	NR	NR	165	100.00%
Guangjian Yang, 2021	Beijing	NR	Genetic testing; NGS	NR	NR	62	100.00%
Jing Zhang, 2008	Beijing	NR	PCR-direct sequencing; Scorpions ARMS	82	2.40%	42	4.80%
Jing Zhang, 2010	Beijing	NR	PCR	170	2.40%	84	4.80%
Jingjing Wang, 2022	Beijing	NR	RT-PCR; NGS	NR	NR	14	50.00%
Mingming Hu, 2022	Beijing	NR	ARMS-PCR	141	2.84%	61	6.56%

Table S4 (continued)

Table S4 (continued)

First author/year	Region	Mutation test Institution	Detection methods	Sample size (NSCLC)	Frequency in NSCLC	Sample size (EGFR)	Frequency in EGFR Positive
Xiaoyan Si, 2021	Beijing	NR	NGS	7395	2.00%	3821	3.87%
Xue Yang, 2015	Beijing	NR	ARMS-PCR	NR	NR	24	12.50%
Yan Li, 2018	Beijing	NR	NGS	231	1.73%	72	5.56%
Yan Zhang, 2017	Beijing	NR	ARMS-PCR; direct sequencing	128	13.20%	128	13.20%
Ye Wang, 2020	Beijing	Department of Pathology, China-Japan Friendship Hospital	RT-PCR	630	1.90%	322	3.72%
Yun Ling, 2015	Beijing	NR	PCR-direct sequencing	431	2.56%	231	4.76%
Zheng Wang, 2009	Beijing	NR	PCR	91	4.40%	27	10.80%
Central China (4)							
Chao Shi, 2022	Henan	NR	NGS	7831	1.60%	3686	3.50%
D. Geng, 2021	Henan, Zhengzhou	NR	PCR; NGS	NR	NR	283	100.00%
Huimin Huang, 2022	Hubei	NR	ARMS-PCR	173	0.58%	76	1.32%
Limeng Zhu, 2022	Henan	Zhengzhou Jinyu clinical laboratory Center	NGS	895	1.56%	483	2.90%
South China (5)							
DYL Chow, 2022	Hong Kong	NR	NR	NR	NR	85	5.88%
Haiyan Tu, 2017	Guangdong, Guangzhou	NR	ADx-ARMS; Sanger sequencing	5363	1.20%	1837	3.60%
Qingyun Gao, 2022	Guangdong, Guangzhou	NR	NGS	231	0.87%	18	11.11%
Wenfeng Fang, 2019	Guangdong, Guangzhou	Origimed (Shanghai, China)	NGS	2316	0.26%	1095	0.56%
Xin Gao, 2020	Guangdong, Guangzhou	Burning Rock Biotech	NGS	NR	NR	39	100.00%
Southwest China (7)							
Jianping Zhou, 2018	Sichuan, Panzhihua	Sangong Bioengineering (Shanghai) Co., LTD	PCR-direct sequencing	72	4.17%	42	7.14%
Jibing Liu, 2022	Sichuan, Zhongjiang	NR	PCR; NGS	192	1.56%	76	3.95%
Jie Dai, 2020	Sichuan, Chengdu	NR	PCR; ARMS-PCR	406	3.94%	207	7.73%
Jie Zheng, 2019	Chongqing	NR	ARMS-PCR; NGS	1560	0.64%	406	2.46%
Mai Zhang, 2023	Sichuan	NR	ARMS-PCR; NGS	NR	NR	5940	2.29%
Yan Gao, 2017	Yunnan, Honghe Hani and Yi Autonomous Prefecture	NR	PCR-direct sequencing	86	2.32%	40	5.00%
Yuan Tang, 2016	Sichuan, Chengdu	NR	ARMS-PCR	3894	0.70%	1872	1.44%
Northwest China (3)							
Lingling Tian, 2023	Gansu	NR	ARMS-PCR	143	1.40%	54	3.70%
Yuanyang Lai, 2013	Shaanxi, Xi'an	Tangdu Hospital, Fourth Military Medical University	ADx-ARMS	697	0.29%	243	0.82%
Zhiyun Shi, 2020	Ningxia, Yinchuan	NR	ARMS-PCR	225	1.33%	113	2.65%
Mix or NR (5)							
Chunwei Xu, 2020	NR	NR	NGS	9142	2.10%	3748	5.12%
Lifeng Wang, 2022	Mix	NR	NGS	3892	1.98%	2208	3.49%
Panli Peng, 2021	NR	Origimed (Shanghai, China)	NGS	13976	0.02%	127	3.15%
Shiwang Wen, 2019	NR	Origimed (Shanghai, China)	NGS	1200	1.83%	571	3.85%
Tao Wang, 2022	Mix	Tongxiang First People's Hospital, First Medical Center of PLA General Hospital and Affiliated Qingdao Central Hospital	NGS	NR	NR	1012	5.04%

ADx: amoy diagnostics, xiamen; ARMS: amplification refractory mutation system; ASPR: allele-specific real-time polymerase; CGP: comprehensive genomic profiling; DNA: deoxyribonucleic acid; EGFR: epidermal growth factor receptor; NGS: next generation sequencing; NR: not reported; NSCLC: non-small cell lung cancer; RT-PCR: reverse transcription-polymerase chain reaction.

Table S5 Frequency of the EGFRex20ins & METex14 mutation in the different regions

Region	Frequency of EGFR Exon 20 insertion (%)				Frequency of MET Exon 14 skipping (%)			
	# Studies	NSCLC	# Studies	EGFR Positive	# Studies	NSCLC	# Studies	MET Positive
Northeast China	1	1.96%	1	4.76%	1	0.98%	0	NR
Eastern China	23	0.56–6.56%	30	0.59–71.43%	10	0.91–26.67%	3	4.06–50.00%
North China	9	1.73–13.20%	13	3.72–100.00%	7	0.32–20.78%	5	8.70–100.00%
Central China	3	0.58–1.60%	4	1.32–100.00%	4	0.71–4.17%	3	30.00–56.60%
South China	3	0.26–1.20%	5	0.56–100.00%	3	0.08–1.44%	2	8.33–100.00%
Southwest China	6	0.64–4.17%	7	1.44–7.73%	1	0.74%	0	NR
Northwest Region	3	0.29–1.40%	3	0.82–3.70%	3	0.00–6.61%	2	0.00–100.00%
Mix or NR	4	0.02–2.10%	5	3.15–5.12%	5	0.42–7.26%	3	12.20–20.74%

EGFR: epidermal growth factor receptor; MET: mesenchymal-epithelial transition factor; NR: not reported; NSCLC: non-small cell lung cancer.

Table S6 Summary of smoking status for the EGFRex20ins mutation in the included studies

Study	Total sample of NSCLC	Number of EGFR mutations	Number of EGFRex20ins	Former/ever smokers	Non-smokers	Unknown	Frequency of EGFRex20ins in smoker
Chao Shi, 2022	7831	3686	129	28	101	0	21.71%
Chia-I Shen, 2022	62	7	5	1	4	0	20.00%
Chunwei Xu, 2020	9142	3748	119	60	59	NR	50.42%
D. Geng, 2021	283	283	283	70	200	13	24.73%
Guangjian Yang, 2020	165	165	165	41	124	0	24.85%
GuangJian Yang, 2021	62	62	62	15	47	0	24.19%
Guangjian Yang, 2022	NR	NR	122	37	85	0	30.33%
Guangjian Yang, 2022	NR	NR	59	20	39	0	33.90%
How-Wen Ko, 2022	5608	3155	86	19	67	0	22.09%
Huanlan Sa 2023	NR	NR	53	9	44	0	17.00%
Jennyu Wu, 2008	515	253	5	1	4	0	20.00%
Jennyu Wu, 2019	3805	2112	84	13	71	0	15.48%
Jiahui Zhang, 2022	NR	NR	60	17	43	0	28.33%
Jibing Liu, 2022	192	76	3	0	3	0	0.00%
Jie Qian, 2022	NR	58	7	4	3	0	57.14%
Jing Zhang, 2008	82	42	2	1	1	0	50.00%
Kaiyan Chen, 2020	1270	504	35	10	25	0	28.57%
Qingyue Lin, 2022	71	NR	15	7	8	0	46.67%
Shen Zhao, 2023	NR	NR	150	48	102	0	32.00%
Tao Wang 2022	NR	1012	51	1	29	21	1.96%
Xin Gao, 2020	39	39	31	9	22	NR	29.03%
Xue Yang, 2015	24	24	3	1	1	NR	33.33%
Yenting Lin, 2017	3534	1721	6	2	4	0	33.33%
Ying-Ting Liao, 2023	NR	NR	71	30	41	0	42.30%
Yuanyang Lai, 2013	697	235	2	0	2	0	0.00%
Yunjian Pan, 2014	1086	662	31	9	22	0	29.03%
Yunlang She, 2022	8437	5358	155	32	117	6	20.65%
Zheng Wang, 2009	91	27	4	2	2	0	50.00%

EGFR: epidermal growth factor receptor; NR: not reported; NSCLC: non-small cell lung cancer.

Table S7 Frequency of EGFRex20ins mutation, grouped by age

Age	Frequency of EGFR Exon 20 insertion (%)			
	Sample size (NSCLC)	Frequency in NSCLC (%)	Sample size (EGFR)	Frequency in EGFR positive
Jie Qian, 2022				
<65 years	NR	NR	35	3 (8.57)
≥65 years	NR	NR	23	4 (17.39)
Jing Zhang, 2008				
≤60 years	42	1 (2.38)	16	1 (6.25)
>60 years	40	1 (2.50)	19	1 (5.26)
Mingming Hu, 2022				
≤40 years	47	3 (6.38)	21	3 (14.29)
≥60 years	94	1 (1.06)	40	1 (2.50)
Tao Wang, 2022				
<65 years	NR	NR	616	41(6.66)
≥65 years	NR	NR	396	10(2.53)
Ye Wang, 2020				
≤55 years	NR	NR	NR	NR (4.28)
>55 years	NR	NR	NR	NR (0.93)
Yuanyang Lai, 2013				
<60 years	378	0 (0.00)	116	0 (0.00)
≥60 years	319	2 (0.63)	119	2 (1.68)

EGFR: epidermal growth factor receptor; NR: not reported; NSCLC: non-small cell lung cancer.

Table S8 Overview of studies reporting prognostic factors

Author, year	N of participants	Population	Treatment	Predicted outcomes	Significant factors	Key results
Caixia Ding, 2023	257	17	NR	OS	IHC score, MET copy numbers	No statistical difference in OS was seen between patients with tumors showing high-MET and low-MET protein expression, as the patients were grouped by IHC score=5 P=0.532; No statistical difference OS was seen between patients with tumors showing MET amplification and not, as defined by the median (MET copy number difference OS E2 vs. others P=0.127).
Chunwei Xu, 2020	9142	119	NR	OS	histological type of NSCLC and bone-metastasis	Multivariate analysis revealed that histological type of NSCLC and bone-metastasis before treatment were independent prognostic factors for OS in all patients after adjusting all characteristic and treatment factors (P<0.05).
Guangjian Yang, 2020	165	105	platinum-based chemotherapy or TKIs	PFS	Age, gender, smoking status, diagnosis, presence/absence of CNS metastasis, molecular subtype	Univariate analysis indicated that treatment with EGFR TKIs when compared to chemotherapy demonstrated significantly worse outcome with shorter PFS (P<0.001) during first-line treatment of EGFR ex20ins mutations. Other factors including age (>60 or ≤60 years, P=0.450), gender (P=0.519), smoking status (P=0.623), stage at diagnosis (IIIB or IV, P=0.542), presence/absence of CNS metastasis (P=0.126) and molecular subtype (P=0.101) [V769_D770insASV (P=0.893); D770_N771insSVD (P=0.891); all others (P=0.902)] were not statistically significant indicators of prognosis.
GuangJian Yang, 2021	62	62	Osimertinib	PFS	TP53 mutation, baseline brain metastases, osimertinib treatment line,	"The univariate analysis showed that concurrent TP53 mutation (P=0.169), baseline brain metastases (P=0.540), and osimertinib treatment line (P=0.639) were not predictors for PFS. Whereas, those coexisting alterations resulting gain or loss of gene function that were detected by the NGS testing may be potential mechanisms for <i>de novo</i> resistance to osimertinib. Nevertheless, we observed that patients who failed to osimertinib with occurring extracranial progression had a similar PFS compared with those who failed but with intracranial progression (median, 2.3 vs. 1.9 months; P=0.142), which indicated that osimertinib was not an active agent for ex20ins patients with brain metastases. This finding was similar to that reported in our previous study, which showed the mPFS achieved by EGFR-TKIs was much shorter in patients harboring EGFR ex20ins mutations whether with brain metastases or not (2.0 vs. 2.9 months, HR =2.485, P=0.058) [27]."
Hanmin Wang, 2021	NR	12	Britinib; Crizotinib	OS; PFS	PS	Patients with PS=1 score had significantly better survival outcomes than those with PS >1 score (mPFS: 7.3 months vs. 0.4 months, P=0.002; mOS: 21.2 months vs. 9.3 months, P=0.000).
Huanlan Sa, 2023	53	53	furmonertinib	PFS	Non-significant factor: age (≥ 65 or < 65 years), sex, smoking status, presence/absence of CNS metastases, and mutation location	The univariate analysis showed that age (≥65 or <65 years, P=0.155), sex (P=0.941), smoking status (P=0.716), presence/absence of CNS metastases (P=0.232), and mutation location (P=0.640) had no statistically significant effect on PFS.
Jiahui Zhang, 2022	60	60	Chemotherapy combined with immunotherapy or chemotherapy combined with bevacizumab	OS	Smoking, TNM staging, and brain metastases	Univariate analysis showed that smoking, TNM stage and brain metastasis were the risk factors affecting the overall survival of patients, all of which were P<0.05. Smoking (P=0.013) and brain metastases (P=0.023) were independent risk factors for OS in patients with advanced NSCLC with EGFR 20INS mutations.
Kaiyan Chen, 2020	1270	35	EGFR-TKIs; targeted therapeutic strategies	OS; PFS	PD-L1	Among the patients with EGFR Ex20ins, the median OS was significantly shorter in the PD-L1-positive group than in the PD-L1-negative group (12.0 vs. 28.6 months, P=0.001) and PD-L1 was identified as an independent predictor (HR =6.21, 95% CI: 1.05–8.22, P=0.045). Median OS for the entire population with EGFR exon 20 mutations was 23.3 months (95% CI: 18.1–28.2), and half of the patients had previously received EGFR-TKIs. Specifically, 15 patients (42.9%) with tumors expressing an Ex20ins of EGFR were treated with targeted therapeutic strategies (e.g., icotinib, gefitinib or afatinib) with an ORR of 13.3%, PFS was 2.6 months.
Shen Zhao, 2023	NR	150	JMT101 plus afatinib or osimertinib	PFS	cfDNA clearance; cfDNA decrease	Meanwhile, cfDNA clearance (P=0.012) and cfDNA decrease (VAF fold change <1) on C2D1 (P<0.001) both significantly correlated with longer PFS in the study population.
Tao Wang, 2022	1012	51	NR	Exon 20 insertions percentage	Younger (<65 years) patients, nonsmoking patients, and patients with AIS	However, a higher percentage of Ex20ins occurred in younger (<65 years) patients, nonsmoking patients, and patients with AIS (6.7% vs. 2.5%, P=0.003; 5.8% vs. 0.8%, P=0.0107; and 10.6% vs. 4.7%, P=0.0423, respectively).
Ying-Ting Liao, 2023	NR	71	Platinum-based chemotherapy; EGFR-TKIs; Mono-chemotherapy; ICI	OS	Stage IVB disease	Multivariate analysis demonstrated that stage IVB disease (HR 5.59, 95% CI: 1.29–24.2; P=0.021) was the only factor significantly associated with OS.
Ying-Ting Liao, 2023	NR	71	Platinum-based chemotherapy; EGFR-TKIs; Mono-chemotherapy; ICI	1L PFS	Stage IVB disease; no baseline liver metastasis	Univariate analysis demonstrated that stage IVB disease (HR 2.09, 95% CI: 1.19–3.67; P=0.011) and no baseline liver metastasis (HR 2.62, 95% CI: 1.26–5.42; P=0.010) was the factor significantly associated with 1L PFS.

1L: 1line; AIS: adenocarcinoma in situ; C2D1: cycle 2 day 1; CNS: central nervous system; E2: estradiol; EGFR: epidermal growth factor receptor; HR: hazard ratio; ICI: immune checkpoint inhibitors; IHC: immunohistochemistry; MET: mesenchymal-epithelial transition factor; NGS: next generation sequencing; NR: not reported; NSCLC: non-small cell lung cancer; ORR: objective response rate; OS: overall survival; PD-L1: programmed death ligand 1; PFS: progress free survival; PS: performance status; TKI: tyrosine kinase inhibitors; TNM: tumor node metastasis; VAF: variant allele frequency.

Table S9 Study characteristics of the METex14 mutation in the included studies

First author/year	Region	Mutation test Institution	Detection methods	Sample size (NSCLC)	Frequency in NSCLC	Sample size (MET)	Frequency in MET Positive
Northeast China (1)							
Yu Wang, 2019	Liaoning, Dalian	NR	NGS; PCR	102	0.98%	NR	NR
Eastern China (11)							
Anxin Zuo, 2022	Jiangsu, Nanjing	Department of Pathology, Nanjing Jiangning Hospital	ARMS-PCR	83	2.41%	NR	NR
Chia-I Shen, 2022	Taiwan	NR	NGS	62	4.84%	NR	NR
ChienHung Gow, 2017	Taiwan, Taipei	NR	one-step RTPCR and direct sequencing	850	3.30%	NR	NR
Difan Zheng, 2016	Shanghai	NR	Quantitative Real-Time PCR, Immunohistochemistry	1770	1.30%	NR	NR
Jrhau Lung, 2019	Taiwan, Chiayi	NR	Real-time quantitative PCR	196	1.02%	NR	NR
Sheng Ju MS, 2023	Jiangsu, Suzhou	NR	NGS	NR	NR	641	4.06%
Xiaorong Dong, 2022	Shanghai	NR	NGS	27	3.70%	5	20.00%
Yangyang Sun, 2019	Jiangsu, Changzhou	NR	NR	15	26.67%	NR	NR
Yaolin Song, 2021	Shandong, Qingdao	Department of Pathology, The Affiliated Hospital of Qingdao University	NGS; ARMS-PCR	4955	0.91%	NR	NR
Yongfeng Yu, 2019	Shanghai	NR	next-generation sequencing	46	8.70%	NR	NR
Yufang Feng, 2018	Jiangsu, Zhangjiagang	Zhangjiagang First People's Hospital	NGS	61	1.64%	2	50.00%
North China (9)							
Hui Zhang, 2021	Beijing	Department of Medical Oncology, Beijing Chest Hospital, Capital Medical University	Fluorescent PCR	315	0.32%	1	100.00%
Jingjing Li, 2021	Tianjin	NR	NGS	96	1.04%	NR	NR
Jingjing Wang, 2022	Beijing	NR	RT-PCR; NGS	NR	NR	3	33.33%
Kang Miao, 2023	Beijing	NR	NGS; FISH	NR	NR	56	30.36%
Xiaokun Ji, 2022	Hebei	Cancer Screening Center, the Fourth Hospital of Hebei Medical University	RT-PCR	464	1.00%	NR	NR
Xiaoyan Si, 2021	Beijing	NR	NGS	7395	0.49%	414	8.70%
Yan Li, 2018	Beijing	NR	NGS	231	0.87%	3	66.67%
Yan Li, 2018	Beijing	NR	RT-PCR; NGS	77	20.78%	NR	NR
Yang Gao, 2021	Inner Mongolia, Baotou City	Department of Pathology, Baotou Cancer Hospital	RT-PCR	58	8.62%	NR	NR
Central China (5)							
Li Liu, 2021	Hunan, Changsha	Burning Rock Biotech	NGS	NR	NR	74	41.89%
Rui Sun, 2023	Henan, Zhengzhou	Department of Molecular Pathology of the Affiliated Cancer Hospital of Zhengzhou University	NGS	4233	0.71%	53	56.60%
Wei Wang, 2020	Henan, Zhengzhou	The laboratory co-built by Department of Pathology, The First Affiliated Hospital of Zhengzhou University and Fujian Herui Gene Technology Co., LTD	cSMART	96	4.17%	NR	NR
Wenyong Peng, 2022	Hunan	NR	NGS	1526	0.98%	50	30.00%
Ziguang Xu, 2020	Henan, Zhengzhou; Beijing	NR	NGS; RT-PCR; Sanger Sequencing	951	1.68%	NR	NR
South China (3)							
Hualin Chen, 2022	Guangdong, Zhanjiang	NR	NGS	763	1.44%	NR	NR
Qingyun Gao, 2022	Guangdong, Guangzhou	NR	NGS	166	1.20%	2	100.00%
Siyang Liu, 2016	Guangdong, Guangzhou	NR	NGS; Sanger sequencing	1296	0.08%	12	8.33%
Southwest China (1)							
Jie Dai, 2020	Sichuan, Chengdu	NR	PCR; ARMS-PCR	406	0.74%	NR	NR
Northwest China (3)							
Caixia Ding, 2023	Shaanxi	NR	ARMS-PCR	257	6.61%	NR	NR
Lingling Tian, 2023	Gansu	NR	ARMS-PCR	143	0.00%	0	0.00%
Yiqun YUAN, 2022	Xinjiang	NR	NGS	153	1.31%	2	100.00%
Mixed or NR (7)							
Haiyan Yang, 2020	NR	NR	Capture-based targeted sequencing	11242	1.04%	NR	NR
Shiwang Wen, 2019	NR	OrigiMed (Shanghai, China)	NGS	1200	0.42%	41	12.20%
Tianli Cheng, 2021	NR	Clinical Laboratory Improvement Amendments (CLIA) and College of American Pathologists (CAP)-certified genomic testing facility (Nanjing Geneseeq Technology Inc., Nanjing, China).	NGS	12848	1.08%	NR	NR
Xiaonan Wu, 2022	NR	NR	NGS	2025	1.38%	NR	NR
Xinghao Ai, 2022	NR	College of American Pathologists-accredited laboratory, GeneseeqBeijing (Beijing, China)	NGS	NR	NR	564	20.74%
Xuwen Liu, 2020	NR	Department of Medical Oncology, Sun Yat-Sen University Cancer Center	PCR-direct sequencing; Sanger sequencing	124	7.26%	NR	NR
Yu Yao, 2023	NR	Nanjing Geneseeq Technology Inc.	NGS	NR	NR	86	16.28%

ARMS: amplification refractory mutation system; cSMART: circulating single-molecule amplification and resequencing technology; DNA: deoxyribonucleic acid; FISH: Fluorescence In Situ Hybridization; MET: mesenchymal-epithelial transition factor; NGS: next generation sequencing; NR: not reported; NSCLC: non-small cell lung cancer; RT-PCR: reverse transcription-polymerase chain reaction.

Table S10 Summary of smoking status for the METex14 mutation in the included studies

Study	Total sample size of NSCLC	Number of MET mutations	Number of METex14	Former/Ever smokers	Non-smokers	Unknown	Frequency of METex14 in smoker
ChienHung Gow, 2017	850	NR	28	11	16	1	39.29%
Difan Zheng, 2016	1770	NR	23	5	18	0	21.74%
Haiyan Yang, 2020	11242	NR	117	34	91	0	29.06%
Hanmin Wang, 2021	NR	NR	15	7	8	0	46.67%
Hualin Chen, 2022	763	NR	11	5	6	0	45.45%
Jrhau Lung, 2019	196	NR	2	0	2	NR	0.00%
Kang Miao, 2023	NR	34	17	10	7	0	58.82%
Li Liu, 2021	74	74	31	16	15	0	51.61%
Shun Lu, 2021	NR	NR	70	28	42	0	40.00%
Tianli Cheng, 2021	12848	NR	139	5	17	117	3.60%
Xinghao Ai, 2022	NR	564	117	36	66	15	30.77%
Xuwen Liu, 2020	124	NR	9	5	4	NR	55.56%
Yan Li, 2018	77	NR	16	10	6	0	62.50%
Yang Gao, 2021	58	NR	5	1	4	0	20.00%
Yang Xia, 2023	NR	NR	29	7	22	0	24.14%
Yaolin Song, 2021	4955	NR	45	13	32	0	28.89%
Yiqun YUAN, 2022	153	2	2	2	0	0	100.00%
Yongfeng Yu, 2019	46	NR	4	2	2	0	50.00%
Ziguang Xu, 2020	951	NR	16	9	7	0	56.25%

MET: mesenchymal-epithelial transition factor; NR: not reported; NSCLC: non-small cell lung cancer.

Table S11 Frequency of the METex14 mutation, grouped by age

Age (years)	Frequency of MET Exon 14 skipping (%)			
	Sample size (NSCLC)	Frequency in NSCLC (%)	Sample size (MET)	Frequency in MET positive (%)
Anxin Zuo, 2022				
<60	12	0 (0)	NR	NR
≥60	54	2 (3.7)	NR	NR
Difan Zheng, 2016				
<60	914	4 (0.47)	NR	NR
≥60	856	17 (1.86)	NR	NR
Jie Dai, 2020				
<60	173	2 (1.16)	NR	NR
≥60	232	1 (0.43)	NR	NR
Kang Miao, 2023				
<60	NR	NR	12	3 (25.00)
≥60	NR	NR	22	14 (63.64)
Xuwen Liu, 2020				
<65	101	5 (8.20)	NR	NR
≥65	23	4 (17.39)	NR	NR
Yan Li, 2018				
<60	23	1 (4.35)	NR	NR
≥60	54	15 (27.78)	NR	NR
Yang Gao, 2021				
≤60	49	4 (0.82)	NR	NR
>60	9	1 (11.10)	NR	NR
Yiqun YUAN, 2022				
<60	153	1 (0.65)	1	1 (100.00)
≥60	153	1 (0.65)	1	1 (100.00)
Ziguang Xu, 2020				
<60	325	1 (0.31)	NR	NR
≥60	625	15 (2.40)	NR	NR

MET: mesenchymal-epithelial transition factor; NR: not reported; NSCLC: non-small cell lung cancer.