The comparative effectiveness of first-line treatment EGFR TKIs in Asian lung cancer population: A systematic review and meta-analysis

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APPENDIX

Appendix A. Literature searching term

P	:	Asian EGFR mutation
I	:	tyrosine kinase inhibitor = gefitinib, erlotinib, afatinib, osimertinib, dacomitinib, osimertinib
C	:	-
O	:	overall survival or progress free survival or time treatment failure

(1) Science Direct: Journal, searching range: 1995 – 2022: 287 results
Comparative Effectiveness Research AND Lung Cancer OR non-small cell lung cancer AND Tyrosine kinase inhibitor OR epidermal growth factor receptor mutation AND Asian:

(2) ProQuest (updated 20210420): searching range: Jan 1995 – May 2022, Document type: article, dissertation/thesis, report – Language: English:117 results
ti(Comparative Effectiveness Research) AND ti(Lung Cancer) OR ti(non-small cell lung cancer) AND ti(tyrosine kinase inhibitor) OR ti(epidermal growth factor receptor mutation) AND Asian

(3) EBSCOhost (updated 20210602): searcing range: 1995 – May 2022, Subject Subset: Cancer - Language: English, Academic Journals: MEDLINE: 298 results

TI Comparative Effectiveness Research AND TI (lung cancer or lung neoplasms or lung tumor or lung adenocarcinoma) OR TI (non-small cell lung cancer or nsclc) AND TI tyrosine kinase inhibitor OR TI epidermal growth factor receptor mutation AND asian

(4) Scopus (updated 20210630): 12 results

"Comparative Effectiveness Research" AND TITLE-ABS-KEY-AUTH (*carcinoma* OR *"Non-Small-Cell Lung"*) AND TITLE-ABS-KEY-AUTH (*"tyrosine kinase inhibitor"*) AND *asian*

(5) Cochrane Library (updated 20201027): 382 result

#1 Comparative Effectiveness Research with publication date Jan 1995 and May 2022, in Trials:	20,263
#2 MeSH descriptor: [Lung Neoplasms] explode all trees:	8,631
#3 MeSH descriptor: [Carcinoma, Non-Small-Cell Lung] explode all trees:	4,828
#4 (tyrosine kinase inhibitor): ti,ab,kw :	2,688
#5 (epidermal growth factor receptor mutation): ti,ab,kw	1,057
#6 (asian): ti,ab,kw	8,306
#7 #1 AND #2 OR #3 AND #4 OR #5 AND #6 with publication date Jan 1995 and May 2022	385

3 cochrane reviews result and 382 Trials result

(6) PubMed: 277 results

(((("comparative effectiveness research"[MeSH Terms] OR ("comparative"[All Fields] AND "effectiveness"[All Fields] AND "research"[All Fields]) OR "comparative effectiveness research"[All Fields]) AND "lung neoplasms"[MeSH Terms]) OR "carcinoma, non-small cell lung"[MeSH Terms]) AND (("protein tyrosine kinases"[MeSH Terms] OR ("protein tyrosine"[All Fields] AND "kinases"[All Fields]) OR "protein tyrosine kinases"[All Fields] OR ("tyrosine"[All Fields] AND "kinase"[All Fields]) OR "tyrosine kinase"[All Fields]) AND ("antagonists and inhibitors"[MeSH Subheading] OR ("antagonists"[All Fields] AND "inhibitors"[All Fields]) OR "antagonists and inhibitors"[All Fields] OR "inhibitors"[All Fields] OR "inhibitor"[All Fields] OR "inhibitor s"[All Fields])) AND (("erbb receptors"[MeSH Terms] OR ("erbb"[All Fields] AND "receptors"[All Fields]) OR "erbb receptors"[All Fields] OR ("epidermal"[All Fields] AND "growth"[All Fields] AND "factor"[All Fields] AND "receptor"[All Fields]) OR "epidermal growth factor receptor"[All Fields]) AND ("mutate"[All Fields] OR "mutated"[All Fields] OR "mutates"[All Fields] OR "mutating"[All Fields] OR "mutation"[MeSH Terms] OR "mutation"[All Fields] OR "mutations"[All Fields] OR "mutation s"[All Fields] OR "mutational"[All Fields] OR "mutator"[All Fields] OR "mutators"[All Fields])) AND ("asians"[MeSH Terms] OR "asians"[All Fields] OR "asian"[All Fields])

Translations Comparative Effectiveness Research: "comparative effectiveness research"[MeSH Terms] OR ("comparative"[All Fields] AND "effectiveness"[All Fields] AND "research"[All Fields]) OR "comparative effectiveness research"[All Fields]

lung cancer[MeSH Terms]: "lung neoplasms"[MeSH Terms]

non-small cell lung cancer[MeSH Terms]: "carcinoma, non-small-cell lung"[MeSH Terms]

tyrosine kinase: "protein-tyrosine kinases"[MeSH Terms] OR ("protein-tyrosine"[All Fields] AND "kinases"[All Fields]) OR "protein-tyrosine kinases"[All Fields] OR ("tyrosine"[All Fields] AND "kinase"[All Fields]) OR "tyrosine kinase"[All Fields]

inhibitor: "antagonists and inhibitors"[Subheading] OR ("antagonists"[All Fields] AND "inhibitors"[All Fields]) OR "antagonists and inhibitors"[All Fields] OR "inhibitors"[All Fields] OR "inhibitor"[All Fields] OR "inhibitor's"[All Fields]

epidermal growth factor receptor: "erbb receptors"[MeSH Terms] OR ("erbb"[All Fields] AND "receptors"[All Fields]) OR "erbb receptors"[All Fields] OR ("epidermal"[All Fields] AND "growth"[All Fields] AND "factor"[All Fields] AND "receptor"[All Fields]) OR "epidermal growth factor receptor"[All Fields]
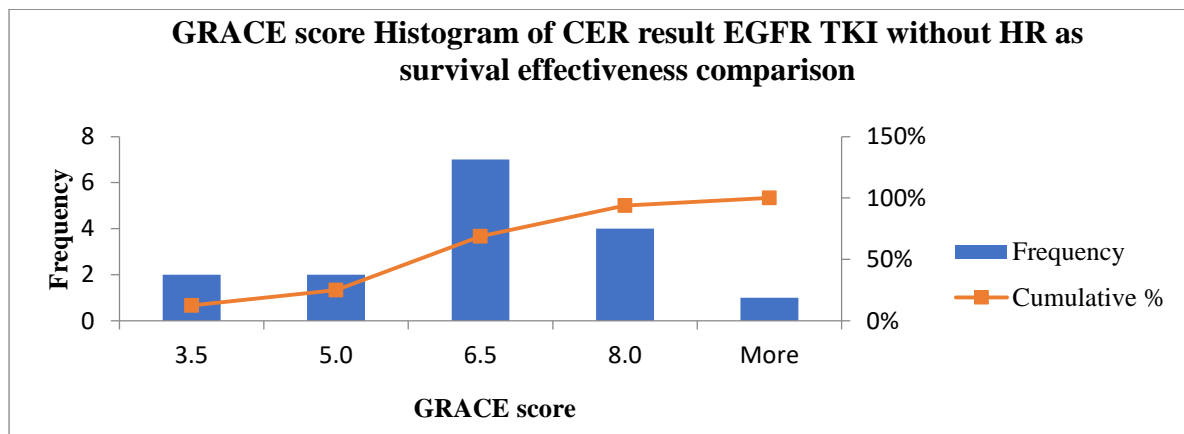
mutation: "mutate"[All Fields] OR "mutated"[All Fields] OR "mutates"[All Fields] OR "mutating"[All Fields] OR "mutation"[MeSH Terms] OR "mutation"[All Fields] OR "mutations"[All Fields] OR "mutation's"[All Fields] OR "mutational"[All Fields] OR "mutator"[All Fields] OR "mutators"[All Fields]

Asian: "asians"[MeSH Terms] OR "asians"[All Fields] OR "asian"[All Fields]

Appendix B. Analysis of founded articles result

(a) Descriptive analysis result of GRACE score from the 17 articles with two or more EGFR-TKIs without HR as EGFR-TKI survival comparison

GRACE score Descriptive	
Mean	6.15
Standard Error	0.39
Median	6.00
Mode	6.50
Standard Deviation	1.59
Sample Variance	2.52
Kurtosis	0.08
Skewness	0.17
Range	6.00
Minimum	3.50
Maximum	9.50
Sum	104.50
Count	17.00
Confidence Level (95.0%)	0.82

GRACE score	Frequency	Cumulative %
3.5	2	12.50%
5.0	2	25.00%
6.5	7	68.75%
8.0	4	93.75%
More	1	100.00%

GRACE score Histogram of CER result EGFR TKI without HR as survival effectiveness comparison

t-Test: Two-Sample Assuming Equal Variances

	multicenter	single center
Mean	5.25	6.36
Variance	0.42	3.45
Observations	4.00	11.00
Pooled Variance	2.75	
Hypothesized Mean Difference	0.00	
df	13.00	
t Stat	-1.15	
P(T<=t) one-tail	0.14	
t Critical one-tail	1.77	
P(T<=t) two-tail	0.27	
t Critical two-tail	2.16	

(b) Descriptive analysis result of GRACE score from the 13 articles with two or more EGFR-TKIs with HR as EGFR-TKI survival comparison

GRACE score Descriptive	
Mean	9.35
Standard Error	0.53
Median	10.00
Mode	10.00
Standard Deviation	1.92
Sample Variance	3.68
Kurtosis	-1.22
Skewness	-0.51
Range	5.50
Minimum	6.00
Maximum	11.50
Sum	121.50
Count	13.00
Confidence Level (95.0%)	1.16

GRACE score	Frequency	Cumulative %
6.0	1	8.33%
7.83	3	33.33%
9.67	0	33.33%
More	8	100.00%

GRACE score Histogram of CER result EGFR TKI with HR as survival effectiveness comparison
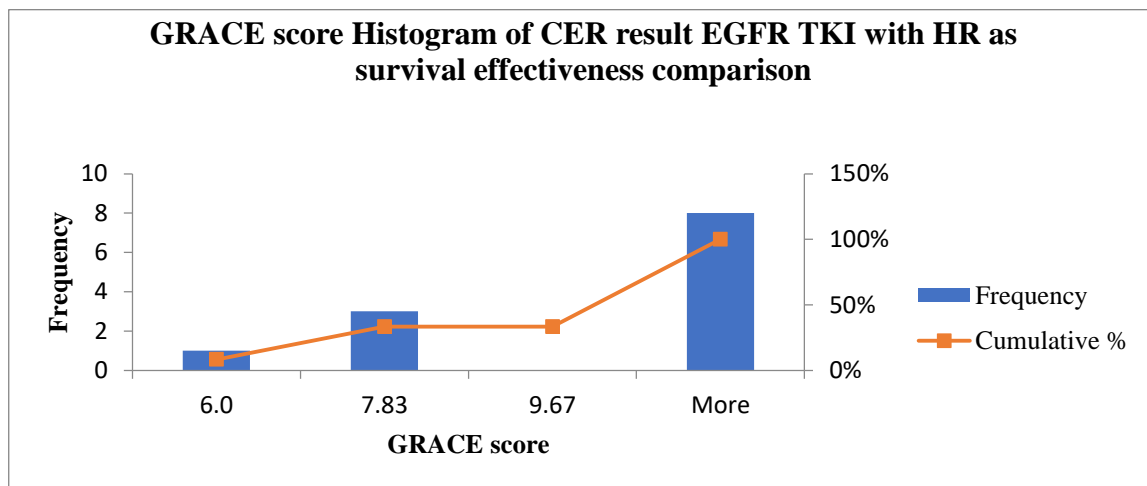
t-Test: Two-Sample Assuming Equal Variances

	multicenter	singlecenter
Mean	9.83	8.75
Variance	3.63	6.13
Observations	9.00	2.00
Pooled Variance	3.90	
Hypothesized Mean Difference	0.00	
df	9.00	
t Stat	0.70	
P(T<=t) one-tail	0.25	
t Critical one-tail	1.83	
P(T<=t) two-tail	0.50	
t Critical two-tail	2.26	