Supplementary

Table S1 Searching strategy of database

Database	Strategy
Pubmed	(((local therapy[Title/Abstract] OR surgery[Title/Abstract] OR resection[Title/Abstract] OR stereotactic body radiotherapy[Title/Abstract] OR SBRT[Title/Abstract] OR radio frequency[Title/Abstract] OR stereotactic ablation body radiation[Title/Abstract] OR radio therapy[Title/Abstract] OR radiation[Title/Abstract]) AND (systemic therapy[Title/Abstract] OR chemotherapy[Title/Abstract] OR tyrosine kinase Inhibitor[Title/Abstract] OR immunotherapy[Title/Abstract] OR TKI[Title/ Abstract] OR PD1[Title/Abstract] OR PDL1[Title/Abstract])) AND (stage IV[Title/Abstract] OR advanced[Title/Abstract] OR oligometasta*[Title/Abstract] OR metasta*[Title/Abstract])) AND (NSCLC[Title/Abstract] OR non-small cell lung cancer[Title/ Abstract] OR non small cell lung cancer[Title/Abstract] OR non-small-cell lung cancer[Title/Abstract])
Web of knowledge	((local therapy OR surgery OR resection OR stereotactic body radiotherapy OR SBRT OR radio frequency OR stereotactic ablation body radiation OR radio therapy OR radiation) AND (systemic therapy OR chemotherapy OR tyrosine kinase Inhibitor OR immunotherapy OR TKI OR PD1 OR PDL1) AND (stage IV OR advanced OR oligometasta* OR metasta*) AND (NSCLC OR non-small cell lung cancer OR non small cell lung cancer OR non-small-cell lung cancer))
Embase	('local therapy':ab,ti OR surgery:ab,ti OR resection:ab,ti OR 'stereotactic body radiotherapy':ab,ti OR sbrt:ab,ti OR 'radio frequency':ab,ti OR 'stereotactic ablation body radiation':ab,ti OR 'radio therapy':ab,ti OR radiation:ab,ti) AND ('systemic therapy':ab,ti OR chemotherapy:ab,ti OR 'tyrosine kinase inhibitor':ab,ti OR immunotherapy:ab,ti OR tki:ab,ti OR pd1:ab,ti OR pd11:ab,ti) AND ('stage iv':ab,ti OR advanced:ab,ti OR oligometasta*:ab,ti OR metasta*:ab,ti) AND (nsclc:ab,ti OR 'non- small cell lung cancer':ab,ti OR 'non small cell lung cancer':ab,ti OR 'non-small-cell lung cancer':ab,ti)

Time interval 2001.1.1-2020.12.31

Study	Intervention	ТХ	T1	T2	Т3	T4	N0	N1	N2	N3
Gray 2014	LT		/	/	/	/	/	/	/	/
	ST		/	/	/	/	/	/	/	/
Xanthopoulos 2015	LT		/	/	/	/	/	/	/	/
	ST		/	/	/	/	/	/	/	/
Johnson 2016	LT	0	9	7	5	1	17	5	0	0
	ST	2	2	4	4	1	0	0	13	0
Huang 2017	LT		/	/	/	/	1	2	7	0
	ST		/	/	/	/	0	0	12	0
lyengar 2018	LT		/	/	/	/	5	1	6	2
	ST		/	/	/	/	5	3	6	1
Xu 2018	LT		4	0	1	1	3	8	1	3
	ST		1	4	2	25	1	9	2	20
Gomez 2019	LT		/	/	/	/	1	2	1	1
	ST		/	/	/	/	1	3	1	3
Wang 2020	LT		/	/	/	/	/	/	/	/
	ST		/	/	/	/	/	/	/	/

Table S2 Clinical thoracic stage of patients included

LT, local aggressive lung therapy; ST, systemic therapy.





Figure S1 Risk bias table of randomized controlled trials. (A) Bias item presented as percentages; (B) judgements about each risk of bias item.

Cturdu /	New Ottawa Scale								
Study -	Selection	Comparativity	Results	Total					
Gray 2014	3	0	2	5					
Xanthopoulos 2015	3	0	2	5					
Johnson 2016	2	0	2	4					
Huang 2016	3	0	2	5					
Xu 2018	3	0	3	6					

Table S3 Newcastle-Ottawa Scale of retrospective studies included



Figure S2 Correlationship between single distant lesion status and median survival time by linear regression analysis. (A) Single distant lesion status and median OS in ST group; (C) single distant lesion status and median PFS in LT group; (D) single distant lesion status and median PFS in ST group; LT, local aggressive lung therapy; ST, systemic therapy; OS, overall survival; PFS, progression-free survival.



Figure S3 Subgroup analysis of included studies stratified by study type (randomized controlled trials or retrospective cohort studies). (A) Progression-free survival; (B) overall survival.

				Hazard Ratio		Haza	rd Ratio		
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Fixed, 95% Cl	Year	IV. Fix	ed. 95% Cl		
1.5.1 Overall survival	of local therapy for lur	ng and	d metasta	1505					
Huang 2017	-0.0513	0.44	5.7%	0.95 [0.40, 2.25]	2017	_	-		
Xu 2018	-0.8675 0.1	1987	27.8%	0.42 [0.28, 0.62]	2018				
Gomez 2019	-0.7765 0.3	3911	7.2%	0.46 [0.21, 0.99]	2019		-		
Wang 2020	-0.3821 0.1	1953	28.8%	0.68 [0.47, 1.00]	2020		Н		
Subtotal (95% CI)			69.5%	0.55 [0.43, 0.71]		•			
Heterogeneity: Chi ² = 4	.81, df = 3 (P = 0.19); P	= 389	6						
Test for overall effect: 2	Z = 4.69 (P < 0.00001)								
1.5.2 Overall survival	of local therapy for lur	ng							
Gray 2014	-0.9163	0.35	9.0%	0.40 [0.20, 0.79]	2014	-	·		
Xanthopoulos 2015	-0.6733	0.25	17.6%	0.51 [0.31, 0.83]	2015		·		
Johnson 2016	-1.1394	0.53	3.9%	0.32 [0.11, 0.90]	2016		-1		
Subtotal (95% CI)			30.5%	0.45 [0.31, 0.65]		•			
Heterogeneity: Chi ² = 0	.78, df = 2 (P = 0.68); I ²	= 0%							
Test for overall effect: 2	z = 4.24 (P < 0.0001)								
Total (95% CI)			100.0%	0.52 [0.42, 0.64]		•			
Heterogeneity: Chi ² = 6	47. df = 6 (P = 0.37): P	= 7%				<u>⊢ ⊢ ⊢ · ·</u>	+ +		
Test for overall effect: 2	Z = 6.25 (P < 0.00001)					0.01 0.1	1 10	100	
Test for subgroup differ	rences: Chi ² = 0.89, df =	1 (P)	= 0.35), l²	= 0%		Favours [LT	Favours [ST]		

Figure S4 Subgroup overall survival analysis of included studies stratified by local aggressive lung therapy sites (lung only or both lung and metastases).



Figure S5 Subgroup analysis of included studies stratified by systemic therapy regimens (chemotherapy alone or targeted therapy); (A) progression-free survival; (B) overall survival.

6	LT	W -4-1	ST			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Fixed, 95% CI	M-H. Fixed, 95% Cl
Gomez 2019	5	25	3	24	30.1%	1.75 [0.37, 8.30]	
lyengar 2018	4	14	3	15	25.5%	1.60 [0.29, 8.90]	
Wang 2020	8	68	4	65	44.4%	2.03 [0.58, 7.11]	
Total (95% CI)		107		104	100.0%	1.84 [0.79, 4.29]	-
Total events	17		10				
Heterogeneity: Chi ² = 0	.05, df = 2	2 (P = 0).97); I ² =	0%			
Test for overall effect: 2	Z = 1.41 (P = 0.1	6)				Favours [LT] Favours [ST]

Figure S6 Forest plot of merged odds ratio of adverse effects between local aggressive lung therapy and systemic therapy groups.

Ctudy and quant	Local t	herapy	Systemi	c therapy	
Sludy and event	Grade 1-2	≥Grade 3	Grade 1-2	≥Grade 3	
lyengar 2018					
Gastrointestinal	6		6		
Hematologic	4	1 (7.1%)	6	2 (13.4%)	
Infectious		1 (7.1%)		1 (6.7%)	
Respiratory	2	2 (14.2%)	5		
Skin	1				
NOS [†]	5		7		
Gomez 2019					
Creatinine			1 (4.2%)		
Fatigue			1 (4.2%)	1 (4.2%)	
Anemia		1 (4.0%)		1 (4.2%)	
Extremity edema				1 (4.2%)	
Esophagitis	1	2 (8.0%)			
Rib fracture		1 (4.0%)			
Wang 2020					
Pneumonitis	NA	5 (7.3%)	NA	2 (2.9%)	
Esophagitis	NA	3 (4.4%)	NA	2 (3.0%)	

Table S4 Adverse effects reported in local therapy and systemic therapy groups

NA, not applicable; NOS is not defined in original study.

$\textbf{Table S5} \ \text{Adverse effects reported in local therapy group}$

Ctudy and avent	Addition of local therapy				
	Grade 1-2	≥Grade 3			
Xanthopoulos 2015					
Pneumonitis	14%	14%			
Esophagitis	24%	21%			
Xu 2018					
Pneumonitis	NA	7.7%			
Esophagitis	NA	16.9%			

NA, not applicable.

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				Hazard Ratio		Hazard Ratio	
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV. Random, 95% CI Yea	ur	IV. Random, 95% Cl	
lyengar 2018	-1.204	0.5119	11.6%	0.30 [0.11, 0.82] 201	8		
Xu 2018	-1.1394	0.2398	33.1%	0.32 [0.20, 0.51] 201	8		
Gomez 2019	-1.0498	0.3393	21.7%	0.35 [0.18, 0.68] 201	9		
Wang 2020	-0.478	0.2365	33.6%	0.62 [0.39, 0.99] 202	0		
Total (95% CI)			100.0%	0.40 [0.28, 0.59]		•	
Heterogeneity: Tau ² =	0.05: Chi ² = 4.71, df =	3 (P = 0),19); l ² =	36%	<u> </u>		_
Test for overall effect:	Z = 4.75 (P < 0.00001)			0.01	0.1 1 10 Eavours II TL Eavours ISTL	100
						rationa [21] Tationa [01]	
В							
В				Hazard Ratio		Hazard Ratio	
B Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV. Random, 95% CI Yea	ır	Hazard Ratio IV, Random, 95% Cl	
B Study or Subgroup Xu 2018	log[Hazard Ratio] -0.8675	SE 0.1987	Weight 41.5%	Hazard Ratio IV. Random, 95% CI Yes 0.42 [0.28, 0.62] 201	ur8	Hazard Ratio	
B Study or Subgroup Xu 2018 Gomez 2019	log[Hazard Ratio] -0.8675 -0.7765	SE 0.1987 0.3911	Weight 41.5% 16.3%	Hazard Ratio IV. Random, 95% CI Yes 0.42 [0.28, 0.62] 201 0.46 [0.21, 0.99] 201	ar 8 9	Hazard Ratio	
B Study or Subgroup Xu 2018 Gomez 2019 Wang 2020	log[Hazard Ratio] -0.8675 -0.7765 -0.3828	SE 0.1987 0.3911 0.1953	Weight 41.5% 16.3% 42.2%	Hazard Ratio IV. Random, 95% Cl Yes 0.42 [0.28, 0.62] 201 0.46 [0.21, 0.99] 201 0.68 [0.47, 1.00] 202	8 9 9	Hazard Ratio	
B Study or Subgroup Xu 2018 Gomez 2019 Wang 2020	log[Hazard Ratio] -0.8675 -0.7765 -0.3828	SE 0.1987 0.3911 0.1953	Weight 41.5% 16.3% 42.2%	Hazard Ratio IV. Random, 95% CI Yes 0.42 [0.28, 0.62] 201 0.46 [0.21, 0.99] 201 0.68 [0.47, 1.00] 202 0.52 [0.37, 0.74]	ar 8 9 20	Hazard Ratio	
B Study or Subgroup Xu 2018 Gomez 2019 Wang 2020 Total (95% Ci)	log[Hazard Ratio] -0.8675 -0.7765 -0.3828	SE 0.1987 0.3911 0.1953	Weight 41.5% 16.3% 42.2% 100.0%	Hazard Ratio IV. Random, 95% Cl Yes 0.42 [0.28, 0.62] 201 0.46 [0.21, 0.99] 201 0.68 [0.47, 1.00] 202 0.52 [0.37, 0.74]	ar 8 9 00	Hazard Ratio	
B <u>Study or Subgroup</u> Xu 2018 Gomez 2019 Wang 2020 Total (95% Ci) Heterogeneity: Tau ^a =	<u>log[Hazard Ratio]</u> -0.8675 -0.7765 -0.3828 0.03; Chi ^a = 3.17, df =	SE 0.1987 0.3911 0.1953 = 2 (P = 0	Weight 41.5% 16.3% 42.2% 100.0% 0.21); I ² =	Hazard Ratio <u>IV. Random, 95% Cl Yes</u> 0.42 [0.28, 0.62] 201 0.46 [0.21, 0.99] 201 0.68 [0.47, 1.00] 202 0.52 [0.37, 0.74] 37%	ar 8 9 10 	Hazard Ratio	+ 100

Figure S7 Sensitivity analysis by excluding low quality retrospective cohort studies. (A) Progression-free survival; (B) overall survival.