

## **Supplementary Note 1. Draft of search strategy**

**Search term:** (oligometastasis OR oligometastases OR oligometastatic OR “limited metastatic” OR “limited metastasis” OR “limited metastases”) AND survival AND (randomised OR randomized OR versus OR comparison OR compare OR controlled)

### **Search strategy in Embase and Medline**

Embase search:

#1 ('oligometastasis'/exp OR oligometastasis OR oligometastases OR oligometastatic OR 'limited metastatic' OR 'limited metastasis' OR 'limited metastases') AND ('survival'/exp OR survival) AND (randomised OR randomized OR versus OR 'comparison'/exp OR comparison OR compare OR controlled)

#2 ('oligometastasis'/exp OR oligometastasis OR oligometastases OR oligometastatic OR 'limited metastatic' OR 'limited metastasis' OR 'limited metastases') AND ('survival'/exp OR survival) AND (randomised OR randomized OR versus OR 'comparison'/exp OR comparison OR compare OR controlled) AND ('article'/it OR 'article in press'/it)

#3 ('oligometastasis'/exp OR oligometastasis OR oligometastases OR oligometastatic OR 'limited metastatic' OR 'limited metastasis' OR 'limited metastases') AND ('survival'/exp OR survival) AND (randomised OR randomized OR versus OR 'comparison'/exp OR comparison OR compare OR controlled) AND ('article'/it OR 'article in press'/it) NOT ('animal cell'/de OR 'animal model'/de OR 'animal tissue'/de OR 'case report'/de OR 'ex vivo study'/de OR 'human cell'/de OR 'human tissue'/de OR 'in vitro study'/de OR 'in vivo study'/de OR 'meta analysis'/de OR 'nonhuman'/de OR 'systematic review'/de)

\*#1 is our basic strategy using Emtree; #2 is to filter studies with irrelevant formats (e.g. reviews, editorials, letters, conference abstracts); #3 is to filter studies which is not relevant clinical studies (e.g. case reports, in vivo studies, systematic reviews)

### **Search strategy in Pubmed and Cochrane library**

Using search query, filters to include clinical trial (I-IV), comparative study, clinical study, controlled clinical trial, multicenter study, and observational study were used. We did not use any filter in Cochrane library..

**Supplementary table 1. General information from the included studies**

Author, target disease	Affiliation	Publication	Patient recruit	Study type	LCT group compared to control	Total No. of patients	NOS score	Type of oligometastases; Preceding Tx. For primary dz.	Defined No. of oligomets.	Conflicts of interest
He, NSCLC	Sun Yat-sen University, China.	2017	2003–2013	R	N/A	21	7	Synchronous and metachronous; OP	≤3, in lung	None
Iyengar, NSCLC	University of Texas Southwestern, US	2017	2014–2016	P	RCT	29	9	Synchronous; PR or SD after CTx.	Up to 6 lesions (including primary) in 3 organs	None
Sheu, NSCLC	MDACC, US	2014	1998–2012	R	PSM, balanced except higher age	74	9	Synchronous; no PD after CTx.	≤3	None
Yano, NSCLC	Kyushu University, Japan	2010	1994–2004	R	N/A	93	7	Metachronous; surgery	Controllable with surgery or RTx	None
Frost, NSCLC	Charité, Evangelische Lungenklinik, DRK Klinikum Berlin-Mitte, Germany.	2018	2000–2016	R	PSM	180	9	Synchronous	1–4 in one organ	None
Gomez, NSCLC	MDACC, London health center, University of Colorado, US & UK	2019	2012–2016	P	RCT	49	9	Synchronous and metachronous; CTx.	≤3	None
Gray, NSCLC	Harvard Medical School, US	2014	2000–2011	R	younger age (p=0.027)	66	7	Synchronous	≤4, brain only	Industrial
Hu, NSCLC	Shanghai Jiaotong University, China.	2019	2010–2016	R	more brain mets, less lung mets. (P<0.001)	231	8	Synchronous; TKI	≤5 in single organ	None
Song, NSCLC	Cancer Hospital of China Medical University, Liaoning Cancer Hospital and Institute	2020	2005–2019	R	PSM, more peripheral location of mets. (p=0.048)	70	9	Synchronous	≤5	None
Xu Q, NSCLC	Tongji University, China	2018	2010–2016	R	Lower T and N stage	90	7	Synchronous; PR or SD after TKI	≤5	None
Ni, NSCLC	Shandong First Medical University, China.	2020	2015–2018	R	no significant difference	86	8	Synchronous	≤5	None
Shang, NSCLC (postop)	Shandong University, China.	2019	2005–2016	R	no significant difference except mets. location	152	8	Synchronous	≤5	None
Gore, SCLC (extended)	57 centers	2017	2010–2015	P	RCT, more old age in control, p=0.03)	86	9	Synchronous; PR or CR after CTx.	≤4	Industrial
Xu SCLC (extended)	Tianjin Medical University, China	2017	2010–2015	R	PSM, more weight loss patient	44	9	Synchronous	in one organ or in single RT portal	None
Bouman-Wammes, prostate	VUMC, Netherland	2017	2009–2015	R	higher PSA at Dx. (p=0.015), more single mets (p=0.003)	63	7	Metachronous; prostatectomy or RTx.	≤3	Industrial
Lan, prostate	Lanzhou General Hospital of Lanzhou Command, China.	2019	2005–2016	R	lower PSA (p=0.003), cT (p<0.001), N stage (p=0.015), fewer bone mets (p=0.019)	111	7	Synchronous	≤5	None

Ost, prostate	Six institutions in Belgium	2018	2012–2015	P	RCT	62	9	Metachronous; OP, RTx.	≤3	Industrial
Steuber, prostate	Six European and one US center	2019	1993–2014	R	PSM	659	9	Metachronous; OP & adjuvant RTx (biochemical failure)	≤5	None
Parker, prostate	117 centers in UK and Swiss	2018	2013–2016	P	RCT	819	9	Synchronous	≤3 (low burden subgroup)	Industrial and government
Tsumura, prostate	Kitasato University, Japan.	2019	2003–2013	R	N/A	40	7	Synchronous	≤5	None
Giessen, colorectal	48 German centers	2013	2000–2004	P	more N-, better PS	253	7	Synchronous and metachronous; OP (95%)	1 (~95% of patients)	Industrial
Ruers, colorectal	22 European centers	2017	2002–2007	P	RCT	119	9	Synchronous and metachronous	≤9, all resectable or ablatable	None
Ruo, colorectal	Memorial Sloan Kettering Cancer Center, US	2003	1996–1999	R	more comorbidity (p=0.04), more liver only and single mets. (p=0.02)	230	7	Synchronous	≤3	None
Palma, multiple	10 institutions in Canada, Netherlands, Scotland, and Australia	2019	2012–2016	P	RCT	99	9	Metachronous; no progression after definitive Tx.	≤5	Industrial
Chen Y, esophagus	Wuhan, Zengzhou Univ, China	2019	2012–2015	R	no significant difference	461	8	Synchronous	≤3	None
Depypere, esophagus	University Hospitals Leuven, Belgium	2018	2002–2015	R	N/A	20	7	Synchronous or metachronous; NAC(R)T	3–5 mets in single organ	None
Chen J, HCC	Sun Yat-sen University Cancer Center, China.	2018	2013–2016	R	PSM	68	9	Synchronous	≤5 in lung	None
Pan, HCC	Sun Yat-sen University Cancer Center, China.	2017	2004–2013	R	PSM	92	9	Synchronous	N/A	None
Morino, bile duct	Kyoto University, Japan.	2020	1996–2015	R	PSM, more ICC (p<0.001), more local mets. location (p=0.005)	67	8	Metachronous; R0 or R1 resection	≤3	None
Schulz, head and neck	Klinikum rechts der Isar, Germany.	2018	2001–2016	R	intentioned match	47	7	Synchronous and metachronous; OP, CTx., RT	1 (77%), but ranged up to 10	None
Falk, sarcoma	15 centers, France	2015	2000–2012	R	smaller primary tumor (p=0.04), more controlled primary (p=0.0003), less lung mets (p=0.006)	281	7	Synchronous and metachronous; OP 93%, R0 62% R1 23%	≤5	Industrial

Abbreviations: NOS, Newcastle-Ottawa scale; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; HCC, hepatocellular carcinoma; R, retrospective; N/A, not assessable; OP, operation; P, prospective; RCT, randomized controlled trial; PR, partial remission; SD, stable disease; CTx., chemotherapy; PSM, propensity score matching; TKI, tyrosine kinase inhibitor; PSA, prostate-specific antigen; RTx, radiotherapy; PS, performance status; NACT, neoadjuvant chemotherapy; NAC(R)T, neoadjuvant chemotherapy and/or radiotherapy

**Supplementary table 2. Clinical information of included studies**

Author, target disease	n	No. of oligometas.	Site	Target of LCT	Modality of LCT	n	No. of oligometas.	Site	Control	Median FU	OS (LCT arm vs. control arm)			PFS (LCT arm vs. control arm)		
											Median (months)	1/2 year rate	p	Median (months)	1/2 year rate	p
			LCT arm					Control arm								
He, NSCLC	11	1 (60%); 2 (40%)	Lung 100%	M	resection of mets. and/or CTx.	10	N/A	Lung 100%	CTx.	37.5	37 vs. 11.6	100/70% vs. 80/40%	0.026			
Iyengar, NSCLC	14	2 (50%); 3-4 (28.6%)	Lung or mediastinum >70%	M	SBRT & CTx.	15	2 (40%); 3-4(33%)	Lung or mediastinum >70%	CTx.	9.6	not reached			9.7 vs. 3.5	1yr: 35.7% vs 13.3%	0.01
Sheu, NSCLC	60	mean 1.28	Brain ~50%	M and P	conventional RTx. (76%)	14	mean 1.23	Brain (~50%)	CTx.			83.3/58.3 vs. 35.7/0%	<0.01		1yr: 46.7% vs. 18.2%	<0.01
Yano, NSCLC	44			M (recurrence)	surgery or RTx. And/or CTx.	49			CTx. or SOC	~4 year	74 vs 10.9	77.3/61.4% vs. 46.9/24.5%	<0.05			
Frost, NSCLC	90	1 (85%); 2 (8%)	Brain 57%; bone 10%; lung 9%	M and/or P	Lobectomy, CCRT, SBRT; 79% received CTx.	90	1 (76%); 2 (14%)	Brain 32%; bone 22%; lung 21%	CTx. (96%)	32 vs. 19	60.4 vs 22.5	92.2/76 vs. 81.9/45.9%	<0.001	25.1 vs. 8.2	67.8/52.2 % vs. 31/8.9%	<0.001
Gomez, NSCLC	25	0-1 (68%); 2-3 (32%)	Brain 28%; other 72%	M and/or P	RTx. or surgery & standard maintenance	24	0-1 (62%); 2-3 (38%)	Brain 25%; other 75%	Standard maintenance	38.8	41.2 vs. 17	84/68% vs. 62.5/45.8%	0.017	14.2 vs. 4.4	52/28% vs. 20.8/12.5 %	0.022
Gray, NSCLC	38	1 (50%); 2-4 (50%)	Brain 100%	P	Thoracic surgery of RTx., brain RTx. & CTx	28	1 (50%); 2-4 (50%)	Brain 100%	CTx and/or Brain RTx.		26.4 vs. 10.5	71/54% vs. 46/26%	<0.001			
Hu, NSCLC	143	1-3 (81%); 4-5 (19%)	Brain 44%; Bone 35%	M	surgery and/or radiotherapy & TKI	88	1-3 (83%); 4-5 (17%)	Bone 42%; lung 33%	CTx. (TKI)	24	34 vs. 21	95.3/72.1% vs. 84.1/40.9%	0.001	15 vs 10	60.7/18.6 % vs 33.3/10.8 %	<0.001
Song, NSCLC	35	1 (46%); 2 (29%); 3-5 (26%)	Lung 57%; bone 40%; liver 30%	M and/or P	surgery or RTx. and CTx.	35	1 (23%); 2 (40%); 3-5 (37%)	Lung 60%; bone 54%	CTx.			51.4/28.6% vs. 31.4/5.7%	0.002			
Xu Q, NSCLC	51	1 (49%); 2-3 (51%)		P and/or M	surgery or RTx. After TKI.	39	1 (41%); 2-3 (51.3%)		CTx. (TKI)	38	40.9 vs. 30.8	96.1/86.3% vs. 94.9/71.8%	<0.001	20.6 vs. 13.9	86.3/25.6 % vs. 70.5/0%	<0.001
Ni, NSCLC	34	1-3 (85%); 4-5(15%)	Lung 40%; liver 23%; adrenal gland 16%	M and/or P	TKI & MWA	52	1-3 (89%); 4-5 (11%)	Lung (32%); bone	CTx. (TKI)	36	34.8 vs. 22.7	94.1/67.6% vs. 90.3/46.2%	0.04	16.7 vs. 12.9	88.2/23.5 % vs. 61.5/0%	0.02

								(23%); liver (20%)								
Shang, NSCLC (postop)	105	1 (73%); 2-5 (27%)	LN 46%; brain 24%; lung 19%	M and/or P	RTx. or RFA and/or CTx.	47	1 (72%); 2-5 (28%)	LN (72%) lung (32%)	CTx. or BSC	19	19 vs. 20	1yr: 72.4 vs 72.3%	0.519	10 vs. 7	1yr: 40.9 vs. 29.8%	0.006
Gore, SCLC (extended)	44	1 (32%); 2-4 (68%)	Adrenal 25%; distant LN 23%; liver 23%	P	PCI and CRTx.	42	1 (41%); 2-4 (60%)	Distant LN 31%; Bone 26%; Liver 24%	PCI	9	13.8 vs. 15.8	1yr: 50.8 vs. 60.1%	0.21	4.9 vs. 2.9	1yr: 23.9 vs. 20.5%	0.01
Xu SCLC (extended)	22			M and/or P	CTx and RTx	22			CTx.	36.4		72.7/25.2 vs. 18.2/12.7%	0.002		40.9/19.3 vs. 9.1/4.8%	0.006
Bouman-Wammes, prostate	43	1 (81%); 2 (14%)	LN 77%; bone 21%	M	SBRT	20	1 (45%); 2 (40%)	LN 65%; Bone 35%	Active surveillance					17.3 vs 4.2	72.1/35.8 % vs. 22.6/0%	<0.001
Lan, prostate	35	1 (26%) 2 (37%) 3 (20%)	Bone 100%	P	Prostatectomy & ADT	76	1(8%) 2(32%) 3(30%)	Bone 100%	ADT	35		CSS 3/5yr: 90.8/63.6% vs. 87.9/74.9%	0.773	(PSA-RFS) 32 vs. 17	82.8/62.8 % vs. 65.8/38.2 %	0.184
Ost, prostate	31	1 (58%); 2(19%); 3(22%)	LN 55%; non-nodal 45%	M	SBRT(81%) or resection	31	1 (29%); 2 (32%); 3(39%)	LN 55%; non-nodal 45%	Active surveillance	3 year				(ADT-free survival) 21 vs. 13	70.9/45.2% vs. 64.5/32.3%	0.11
Steuber, prostate	165		Pelvic LN ~90%	M	PLND or and ADT	494		Pelvic LN ~90%	ADT			CSS 5/10 yr: 98.6/95.6 vs. 95.7/84.8% OS 3/5 yr: 99.2/98.7 vs. 98.2/95.4%	0.03; 0.23			
Parker, prostate	410		Bone 76%; distant LN 36%	P	RT and ADT	409		Bone 76%; distant LN 34%	ADT	37		1/2/3 yr: 98.8/92.5/82.6 % vs. 96.7/87.7/74.8 %	0.007		89.6/72.8 % vs. 86.3/69.3 %	0.033
Tsumura, prostate	22		Bone or pelvic LN	M	metastatic RTx., prostate brachy & HTx.	18		Bone or pelvic LN	prostate brachy & HTx.	62.5					94.4/88.9% vs. 95.5/73.3%	0.027
Giessen, colorectal	38	1 (95%)	Liver 100%	M	Hepatic resection and CTx.	215	1 (100%)	Liver 100%	CTx.		48.0 vs. 17.0	97.4/89.5% vs. 68/37.6%	<0.001	16.6 vs. 6.5	63.2/36.8 % vs. 21.2/5.2%	<0.001
Ruer, colorectal	60	1-3 (48%); 4-6 (30%); 7-9 (22%)	Liver 100%	M	RFA, surgery and/or CTx.	59	1-3 (31%); 4-6 (46%); 7-9 (24%)	Liver 100%	CTx.	9.7 years	45.6 vs 40.5	91.7/75% vs. 89.8/74.5%	0.01	16.8 vs. 9.9	58.3/35% vs. 40.7/20.3 %	0.005

Ruo, colorectal	127	1 (68%); 2(26%); 3(6%)	Liver 56%	P	bowel surgery and CTx.	103	1 (53%); 2(30%); 3(17%)	Liver 41%	CTx. (83.5%)		16 vs. 9	63.8/25% vs. 35.9/6%	<0.001			
Palma, multiple	66	1(46%); 2(29%); 3(18%)	lung 43%; bone 35%	M	SBRT and/or standard CTx.	33	1 (36%); 2(40%); 3(18%)	Lung 53%; bone 31%	CTx.	26 vs. 25	41 vs. 28	84.3/69.7% vs. 87.4/60.6%	0.09	12 vs. 6	54.5/36.4% vs. 22.7/15.2%	0.001
Chen Y, esophagus	196			M and P	CCRT	265			CTx	11.5	16.8 vs 14.8	72.8/27.2% vs. 63.5/17.5%	0.056	8.7 vs. 7.3	27.6/4.7% vs. 21.9/0.9%	0.002
Depypere, esophagus	10		Lung 50%; adrenal 20%	P	esophagectomy +/- lung metastectomy	10		Liver 50%; brain 30%	CTx.		21.4 vs 12.1	80/40% vs. 50/10%	0.042			
Chen J, HCC	34		Lung 100%	M and/or P	TACE, RFA, resection & sorafenib	34		Lung 100%	Sorafenib	8.4	18.4 vs. 7.4	67.6/47% vs. 35.3/23.5%	0.015	TTP: 3.1 vs. 2.3	(TTP) 11.8/0% vs. 0/0%	0.009
Pan, HCC	46	Mean 2.22 +/- 1.35	LN 100%	M (lymph node)	RFA; and BSC or sorafenib	46	Mean 2.74 +/- 1.37	LN 100%	BSC or sorafenib	14 vs 13.8	13 vs. 7.8	58.3%/11.7% vs. 17.9/0%	0.001			
Morino, bile duct	33	Median 1 (1-3)	Liver 39%; LN 27%; lung 12%	M (recurrence)	Surgery, RT, RFA, TACE and/or CTx.	34	Median 1 (1-3)	Local 35.3%; liver 29%; LN 20.5%	CTx. or BSC	12.6	48.6 vs. 14.2	97/84.8% vs. 64.7/20.5%	<0.001			
Schulz, head and neck	37	1 (70%); 2-3 (16%)	Lung 59%; bone 22%	M	RTx. or resection and/or CTx.	10	1 (100%)	Lung 90%	CTx. or BSC		24 vs. 7	67.6%/51.3% vs. 20%/10%	NA			
Falk, sarcoma	164		Lung 51%; liver 7%	M	RTx., RFA, OP +/- CTx.	117		Lung 69%; liver 7%	CTx. in majority	25.7		79.6/63.6% vs. 52.3/36.3%	<0.0001			

Abbreviations: LCT, local consolidation therapy; OS, overall survival; PFS, progression free survival; CTx., chemotherapy; M, metastases; P, primary disease; NSCLC, non-small cell lung cancer; RTx., radiotherapy; CCRT, concurrent chemoradiotherapy; SBRT, stereotactic body radiotherapy; ATT, aggressive thoracic therapy; TKI, tyrosine kinase inhibitor; MWA, microwave ablation; SCLC, small cell lung cancer; RFA, radiofrequency ablation; LN, lymph node; BSC, best supportive care; PCI, prophylactic cranial irradiation; ADT, androgen deprivation therapy; PLND, pelvic lymph node dissection; IMRT, intensity modulated radiotherapy; TACE, transarterial chemoradiotherapy; TTP, time to progression; OP, operation