Table 1 Selected prospective studies

Author	*Phase*	*Tumor type*	*Line*	*Number of lesions*	*Scenario*			*Brain disease*	*Randomized*	*Number of patients*	*Intervention*	*Primary tumor RT*	*RT type*	*RT dose*	*Control arm*	*LC*	*High grade toxicity (G3-5)*	*mFU*	*mPFS*	*mOS*
					Synchr	Metachr	Induced													
Wang (8)	III [†]	EGFRm NSCLC	1st line (TKI)	1-5 mets, ≤2 per organ	Y	?	N	Not allowed	Y (1:1)	133	Upfront SBRT to all disease + TKI	?	SBRT	25–40 Gy, 5# (BED 37.5–72 Gy)	TKI	?	G3-4 pneumonitis: I: 7.3% *vs.* C: 2.9%; G3-4 Esophagitis: I: 4.4% *vs.* C: 3.0%	19.6 m (IQR 9–41)	I: 20.2 m; C: 12.5 m (HR: 0.62)	I: 25.5 m; C: 17.4 m (HR: 0.68)
Palma (9,10)	II	Mixed	Any	1-5 mets, controlled primary	Y	Y	?	Allowed	Y (1:2)	99	SBRT to all disease + SOC systemic therapy	N	SBRT	Various (BED 41.6–151 Gy)	SOC systemic therapy	I: 63%; C: 46%	G >=2 AE: I: 29% *vs.* C: 9%; G5 AE: I: 4.5% *vs.* C: 0%	51m (IQR 46–58)	I: 11.6 m; C: 5.4 m (HR: 0.48)	I: 50 m; C: 28 m (HR: 0.47)
Gomez (6,7)	II	NSCLC	After 1[st] line and no PD	1-3 mets, N1-N3 nodes collectively counted as 1 lesion	Y	Y	Y	Allowed, Treatment of brain disease allowed in both arms.	Y (1:1)	49	(C)RT or surgery to all disease (incl primary tumor and nodes)	Y	SBRT, hypofr RT, conv (C)RT	Physician choice curative intent	SOC maint therapy or observation	?	G3 AE: I: 20% *vs.* C: 8.3%	38.8 m (range 28–61m)	I: 14.2 m; C: 4.4 m (P=0.022)	I: 41.2 m; C: 17.0 m (P=0.017)
Iyengar (2017) (5)	II	NSCLC	After 1[st] line (platinum-based chemo) and no PD. EGFRm/ALKp/local PD within 3 m of previous RT to local disease: exclusion	1-6 extracran lesions (incl primary), ≤3 in liver/lung each. Mets in GI tract or skin not allowed	Y	Y	N	Allowed if treated & controlled	Y (1:1)	29	SBRT to all disease (incl primary if agreed by PI) followed by SOC maint therapy	if agreed by PI	SBRT, hypofr RT	21–27 Gy in 1#; 26.5–33 Gy in 3#; 30–37.5Gy in 5# 45 Gy in 15#	SOC maint therapy	I: 100%; C: 53%	I: 4 G3 AE (not due to SBRT) C: 2 G3 AE, 1 G4 AE	9.6m (range 2–30m)	I: 9.7 m; C: 3.5 m (HR: 0.30)	I: NR; C: 17 m
Iyengar (2014) (15)	II	NSCLC	After at least 1 line of chemo. PD after previous treatment. No previous EGFR inhibitor	1-6 extracran lesions (incl primary unclear), ≤3 in liver/lung each. Mets in GI tract or skin not allowed.	Y	Y	?	Allowed if previously treated >3 m prior to trial. (no pts received RT to brain)	N	24	SBRT to all disease + concurrent erlotinib	?	SBRT	19–24 Gy in 1#; 27–33 Gy in 3#; 35–40 Gy in 5#	NA	86%	2 G3 AE due to SBRT 1 G4 AE possibly due to SBRT 1 G5 AE possibly due to SBRT	16.8 m (range 3–60 m)	14.7 m	20.4 m
Petty (3)	II	NSCLC	After 1[st] line chemo and no PD	1-5 mets, not incl primary, Ipsilat supraclav lnn allowed, Contralat mediast/hilar lnn excl	Y	Y	?	Allowed if not active	N	27	RT to all disease (incl primary and nodes if applicable)	Y	SBRT, Conv RT	54 Gy in 3#; 50 Gy in 5#; 24 Gy in 1#; 27 Gy in 3#; 60 Gy in 30#	NA	85%	No G3-5 AE	24.2 m	11.2 m	28.4 m
Rusthoven (liver) (21)	I/II	Mixed	Any	1-3 liver mets (each max diameter 6 cm) Other disease had to be 'low burden' and treaf with surgery, RT or approved systemic treatments	Y	Y	?	Allowed	N	47	SBRT to liver mets	N	SBRT	36–60 Gy in 3#	NA	92%	1 G3 AE	16m (range 6–54 m)	6.1 m	20.5 m
Rusthoven (lung) (20)	I/II	Mixed	Any	1-3 lung mets (cum max diameter 7 cm). Other disease had to be 'low burden' and treatable with surgery, RT or approved systemic treatments	Y	Y	?	Allowed	N	38	SBRT to lung mets	N	SBRT	48–60 Gy in 3#	NA	96%	3 G3 AE	51.4 m (range 6–48 m)	8.4 m	19 m
Salama (22)	I	Mixed	Any	1-5 mets (each max diameter 10 cm or 500 mL in volume)	Y	Y	?	Allowed if treated and controlled	N	61	SBRT to all mets	N	SBRT	24–60 Gy in 3#	NA	65%	8 G3 AE	20.9 m (range 3–61m)	5.1 m	NR
De Ruysscher (16)	II	NSCLC	At diagnosis	1-5 mets, untreated local disease	Y	N	N	Allowed	N	39	(C)RT or surgery to all disease	Y (RT or surgery)	SBRT, hypofr RT, conv (C)RT	Various	NA	95%	G3 esophagitis in 15%; G3 cough in 3%	27.7 m (range 17–46m)	12.1 m	13.5 m
Collen (23)	II	NSCLC	After induction chemo	1-5 disease sites (each ln station counted as 1)	Y	?	?	Allowed	N	26	SBRT to all disease (incl primary)	Y	SBRT	50 Gy in 10#	NA	50%	G3 AE in 8%	16.4 m (range 3–40 m)	11.2 m	23 m
Bauml (24)	II	NSCLC	Any	1-4 mets	Y	Y	N	Allowed if treated	N	45	(C)RT, RFA or surgery to all disease (incl primary and nodes) with adj pembro	Y (RT, RFA or surgery)	SBRT, hypofr RT, conv (C)RT	Various	NA	87%	G3-4 pneumonitis in 7%[‡]; G3 colitis in 4%[‡]; G3 adrenal insuff in 2%[‡]	25.0 m	19.1 m	41.6 m
Milano (25)	Pilot	Mixed	Any	1-5 mets	Y	Y	?	Allowed	N	121	SBRT	Y	SBRT	50 Gy in 10# preferred. Brain: 10–20 Gy in 1#	NA	65% for non-BC 87% for BC	G3 AE in 1%	1.7yr (range 0.3–8.9yr) for non-BC 4.5yr (range 0.6–10.4 yr) for BC	2 yr FFDM: 35%; 4 yr FFDM: 26%; 6 yr FFDM: 21%	2 yr OS: 50%; 4 yr OS: 28%; 6 yr OS: 20%

Table of selected prospective studies of radiotherapy to metastatic disease and/or the primary tumor in patients with oligometastatic non-small cell lung cancer. #, fraction(s); ?, not reported; †, interim results; ‡, patients received both local treatment as well as adjuvant pembrolizumab, the patients with pneumonitis all received initial thoracic radiotherapy. adj, adjuvant; AE, adverse event; ALKp, anaplastic lymphoma kinase positive; ARDS, acute respiratory distress syndrome; BC, breast cancer patients; BED, biologically effective dose; C, control arm; chemo, chemotherapy; (C)RT, (chemo)radiotherapy; cum, cumulative; EGFRm, epidermal growth factor receptor mutant; G, grade; GI, gastro-intestinal; Gy, Gray; hypofr, hypofractionated; HR, hazard ratio; I, interventional arm; IQR, interquartile range; LC, local control (percentage of patients without local progression of irradiated disease); m, months; maint, maintenance; max, maximum; mets, metastases; N, no; NA, not applicable; NR, not reached; NSCLC, non-small cell lung cancer; pembro, pembrolizumab; PI, principal investigator; R, randomisation; RFA, radiofrequency ablation; SOC, standard of care; TKI, tyrosine kinase inhibitor; Y, yes; yr, years.