Table S1. Studies showing the abscopal effect in different clinical settings.

AUTHORS	STUDY TYPE	TYPE OF CANCER (n. pts)	STAGE	LOCATION OF METASTASES	RADIOTHERAPY	SITE TREATED	CONCOMITANT THERAPY	ABSCOPAL RESPONSE
Ye et al. [1] 2021	Phase I clinical trial	Lung cancer (31)	Progressive advanced		HFRT	Selected lesions	Nivolumab	HFRT increased response to nivolumab; OOR: 39.13%; CR rates: 13.04%
Bassanelli et al. [2] 2021	Observational, retrospective study	NSCLC (95)	Advanced		RT		Nivolumab	RT during Nivolumab: better outcomes; Median OS: 11.9 months
Maity et al. [3] 2021	Phase I trial	Melanoma (22)	IV		RT		Ipilimumab	5/22: partial response; 3/22: stable disease
Mattes et al. [4] 2021	Trial PCT	NSCLC (35)	Metastatic		SBRT	A single extracranial target lesion	Checkpoint inhibitor alone (19) or in combination with Carboplatin/pemetrexed (16)	15 pts: grade 1 to 2 toxicities (pneumonitis and fatigue); the best ORR1: 53%
Li et al. [5] 2021	Retrospective study	Solid tumors (32)	Metastatic		Hypofractionated RT		PD-1 inhibitor	RT+immunotherapy: no AE
Kazandjian et al. [6] 2021	Pilot study	Relapsed/refractory multiple myeloma			Hypofractionated RT	Focal lesion	Avelumab	RT+ CI: no apparent anti-tumor response
Margulis et al. [7] 2021	Phase II Trial	RCC (6)	3/6 Metastatic	Inferior vena cava (IVC) tumor thrombus (TT)	SABR	IVC-TT		1/3 metastatic pts: CR; 2/3: PR
Segal et al. [8] 2021	Phase II study	CRC (24)	Metastatic		EBRT		Durvalumab+Tremelimumab	Rare cases of AE
Theelen et al. [9] 2021	2 clinical trials (ph 2: PEMBRO-RT; ph 1/2: MDACC)	NSCLC (148)	Metastatic		EBRT	Lung metastases, lung primary disease and intrathoracic lymph nodes	Pembrolizumab (76 only pembro; 72 pembro+radiotherapy)	ARR: 19.7% with pembro.; 41·7% with pembro.+RT. ACR: 43.4% with pembro.; 65.3% with pembro.+RT

Singh et al. [10] 2020	Data evaluation	NSCLC	Metastatic	Brain	SRS		35% of patients received immunotherapy; 46% chemotherapy; 18% EGFR/ALK targeted therapy	Immunotherapy+SRS: improved PFS compared to other therapies
Lieverse et al. [11] 2020	Phase II clinical trial	NSCLC (126)	IV		SABR		L19-IL2	Their Phase I study: response in 2/6 pts; results of this Phase II study: expected in 2023
Funck-Brentano et al. [12] 2020	Retrospective analysis	Melanoma (26)	Advanced		Hypofractioned RT (n 23)- Palliative RT (n 2)- Brain radiosurgery (n 1)		Pembrolizumab or Nivolumab	AE in 35% of pts
Yano M et al. [13] 2020	Case report	Endometrial Carcinosarcoma (1)	Metastatic	Bone,lung and mediastinal LN	EBRT	Pelvis	Pembrolizumab	CR lasted for 2 months
Watanabe T et al. [14] 2020	Case report	Melanoma (2)	Metastatic	Case1: liver, muscle, groin Case 2: liver, lung, abdominal LN	SBRT SBRT	Liver Liver, LN	Nivolumab Pembrolizumab	CR CR lasted for 2,5 years
Ellerin BE et al. [15] 2020	Case report	Parotid gland cancer (1)	cT3 cN2b M1 (IVC)	Cervical LN, lung, hilar, subcarinal and paratracheal LN	VMAT	Parotid mass	No	Reduction: lung lesions; regression: LN lesions lasted for 1 year

Choi JS et al. [16] 2019	Case report	Case 1: HNSCC Case 2: SCC of larynx	Metastatic Metastatic	Parotid, neck, mediastinum, hilum LN, liver, lung, stomach, adrenal, peritoneum Neck dermal, neck and axillary LN	SBRT SBRT	Submandibolar and neck LN Axilla	Atezolimumab Panitumumab+pembrolizumab	CR lasted for 13 months CR lasted for 20 months
Garelli E et al. [17] 2019	Case report	Case 1: LCNEC Case 2: Lung adenocarcinoma Case 3: Lung adenocarcinoma	cT4N0M1b cT2N3M1c cT3N2M1a	Adrenal gland, spine Mediastinal LN, brain, ocular Mediastinal LN, pleural effusion, brain	EBRT WBRT WBRT	Vertebra T2, T3 Brain Brain	Nivolumab Atezolimumab Pembrolizumab	Partial regression of adrenal metastases lasted for 10 months Partial regression: brain met.; complete remission: lung, mediastinal masses Reduction: lung mass, pleural effusion
Tubin S et al. [18] 2019	Clinical trial PCT	NSCLC (20)	IIIB/IV		SBRT-PATHY	Hypoxic tumor cells	no	AE observed in 45% (9/20) of patients
Bozorgmehr F et al. [19] 2019	Clinical trial PCT	NSCLC (130)	IV		Hypofractionated RT	All non-cerebral/non-pulmonary/non-internal organ met.	Nivolumab	

Liu X et al. [20] 2019	Case report	Case 1: ICC Case 2: ICC Case 3: ICC	IVC IIIA IIIB	Hepatic hilar and retroperitoneal LN Hepatic hilar and retroperitoneal LN Hepatic hilar and retroperitoneal LN	SBRT SBRT SBRT	Right hepatic lobe Right hepatic lobe Left hepatic lobe and left retroperitoneal LN	Nivolumab Pembrolizumab Pembrolizumab	The sum of the metastatic lesions decreased by 40,9% The sum of the metastatic lesions decreased by 86,3% CR lasted for 11 months
Tuyaerts S et al. [21] 2019	Clinical trial PCT	Cervical, endometrial carcinoma or uterine sarcoma (43)	Advanced		Hypofractionated RT		pembrolizumab	
Kuroda A et al. [22] 2019	Case report	Lung adenocarcinoma (1)	Metastatic	Supraclavicular, mediastinal and hilar LN, Lung	EBRT	Mediastinum	no	Disappearance of the lung metastases
Sundahl N et al. [23] 2019	Clinical trial	melanoma (20)	metastatic		SBRT	The largest lesion	Nivolumab	ORR 2 of 45% with 3 CR and 6 PR
Lin X et al. [24] 2019	Case report	Lung adenocarcinoma (1)	IV	Mediastinal LN, lung, pleural effusion, brain	SRT	Brain	Atezolimumab	Reduction: pleural effusion, lung, mediastinal LN lesions
Yaguchi D et al. [25] 2019	Case report	Pulmonary pleomorphic carcinoma (1)	Metastatic	Pleura, bone, brain	EBRT	Femur	Nivolumab	Near CR
Garcìa JR et al. [26] 2019	Case report	Lung adenocarcinoma (1)	metastatic	C6 vertebra	EBRT	C6	no	Reduction of the primary tumor
Gounder et al. [27] 2019	Case report	Sacral chordoma (1)	Metastatic	lung	EBRT	sacral mass	Tazemetostat+ nivolumab-ipilimumab	Regression of all lung nodules for 2 years
Mota JM et al. [28] 2019	Case report	Adrenocortical carcinoma (1)	metastatic	Liver, lung, pleura	RFA-SBRT	Liver, Lung-lung	Pembrolizumab	CR

Grimaux X et al. [29] 2019	Case report	RCC (1)	Metastatic	lung, costal	EBRT	costal	Nivolumab+rituximab	Disappearance of the lung metastases
Bonanno L et al. [30] 2019	Case report	SCLC (1)	Metastatic	Liver, peripancreatic LN	SBRT	Peripancreatic LN	Nivolumab	Reduction: hepatic lesion, the primary tumor
Formenti SC et al. [31] 2018	Clinical trial PCT	NSCLC (39)	metastatic		IGRT or IMRT		Ipilimumab	Abscopal response in 18% (7/39) of patients: 2 CR and 5 PR
Chuang CH et al. [32] 2018	Case report	Colorectal adenocarcinoma (1)	Metastatic	Liver, lung, brain	WBRT	Brain	no	Regression of lung mass
Chino F et al. [33] 2018	Case report	HCC+NSCLC (1)			SBRT	Lung tumor	no	Complete regression of Hepatic lesions
Britschgi C et al. [34] 2018	Case report	NSCLC (1)	cT1a pN3 cM0 (IIIB)	Abdominal LN	SBRT	2 of 3 LN	Nivolumab	CR
Xu MJ et al. [35] 2018	Case report	Merkel cell carcinoma (2)	Metastatic	Peripancreatic mass, adrenal gland, para-aortic LN	EBRT	Adrenal gland, para-aortic LN	Pembrolizumab	CR lasted for 17 months
Wight JC et al. [36] 2018	Case report	HL (1)		Lung, pleural effusion, LN	EBRT-inverted "Y" RT	Axillary LN-Infradiaphragmatic site	Nivolumab	CR in almost all areas
Rodrìguez-Ruiz ME et al. [37] 2018	Clinical trial PCT	15	Advanced		SABR	Selected tumor lesions	Hiltonol (poly-ICLC)	
Formenti SC et al. [38] 2018	Clinical trial PCT	Breast cancer 23)	Metastatic		Focal radiotherapy	Metastatic site	Fresolimumab	Response limited to 3 stable diseases
Deipolyi AR et al. [39] 2018	Case report	Breast cancer (1)	Metastatic	LN, lung, bone, brain, liver	Radioembolization	Liver	Pembrolizumab/utomilumab - Paclitaxel/trastuzumab - MEDI6469	CR
Leung HWC et al. [40] 2017	Case report	Breast cancer (1)	cT4N3bM1 (IV)	T8, axillary LN	EBT	Breast tumor, axillary LN	no	CR
Poon DMC et al. [41] 2017	Case report	Prostate adenocarcinoma (1)	Metastatic	bone, LN	Radium-223 - SBRT	C2, T6, S1, humerus	Denosumab	Significant regression of all lesions
Kwee SA et al. [42] 2017	Case report	CPRC (2)	Metastatic	LN, bone	223-Ra-Dichloride		no	Resolution of bone disease

Komatsu T et al. [43] 2017	Case report	Lung adenocarcinoma (1)	Metastatic	Liver, intrapulmonary		Liver	Nivolumab	Reduction: the primary tumor, intrapulmonary metastases
Tubin S et al. [44] 2017	Case report	Case 1: Lung adenocarcinoma Case 2: SCC of the ear Case 3: lung SCC	Metastatic Metastatic	Neck dermal, lung, vertebra Mediastinal LN, controlateral lung	EBRT EBRT EBRT	Hypoxic tumor segment Hypoxic tumor segment Hypoxic tumor segment	No No no	70% regression of the lesion Complete regression of the primary tumor Reduction: the primary tumor; disappearance: mediastinal LN
Xie G et al. [45] 2017	Case report	RCC (1)	T2a N1 M1 (IV)	Mediastinal, retroperitoneal, pelvis, cervical LN	SBRT	Para-aortic LN	Pembrolizumab	Systemic CR
Hidaka Y et al. [46] 2017	Case report	DLBCL (1)	Metastatic	skin	Topical RT	Buttock, arm	no	Disappearance of all skin lesions lasted for 6 months
LaPlant Q et al. [47] 2017	Case report	RCC (1)	Metastatic	LN, lung, sacrum, coccyx, pelvis	DP-SBRT	Sacrum mass	Ipilimumab+nivolumab	Reduction: sacral mass; disappearance: lung, LN metastases
Sharabi A et al. [48] 2017	Case report	Neuroendocrine cervical carcinoma (1)	Metastatic	Retroperitoneal, pelvic, para-aortic LN, liver	SBRT	Cervical mss	Nivolumab	Regression of 95% of all lesions
Shi F et al. [49] 2017	Case report	Pancreatic cancer (1)	Metastatic	Liver, pleura	EBRT	Pancreatic mass	GM-CSF subcutaneous	Reduction of the metastases
Foote M et al. [50] 2017	Clinical trial PCT	Melanoma (15)	Metastatic	In-transit metastases	Hypofractionated RT		PV-10	ORR: 86,6% (33,3% CR, 53,3% PR)
Gerber DE et al. [51] 2017	Clinical trial PCT	NSCLC	III		CRT or IMRT	Thoracic	Cislatin/etoposide+Nivlumab	
Cong Y et al. [52] 2017	Case report	Adenosquamous carcinoma of the chest wall (1)	Metastatic	lung	SABR	Paramediastinal and lingual lung foci	DC-CIK	Complete response
Desar IME et al. [53] 2016	Case report	DGCT (1)	Metastatic	Lung, hilar and mediastinal LN	EBRT	Hilar LN	Imatinib	Response of lung metastases lasted for 6 months

Levy A et al. [54] 2016	Clinical trial PCT	10	Metastatic		conformal 3D RT or intracranial stereotactic RT		Darvulumab	Objective response rate was 60% (CR 2/10 and PR 8/10)
Michot JM et al. [55] 2016	Case report	HL (1)		Supradiaphragmatic and subdiaphragmatic LN	EBRT	Hilar mediastinal LN	Pembrolizumab	Regression of the sum of volume of metastatic lesions
Van de Walle M et al. [56] 2016	Case report	RCC (1)	Metastatic	Portacaval and subcutaneous abdominal LN, lung, neck	IMRT	Neck mass	no	Complete regression: lung, sucutaneous abdominal LN metastases
Siva S et al. [57] 2016	Clinical trial	NSCLC (16)			3D-CRT	Primary tumor	Cisplatin/etoposide/carboplatin/paclitaxel	Unirradiated hair follicles: abscopal DNA damage response
Saba R et al. [58] 2016	Case report	Multiple myeloma (1)		Multiple osteolytic lesions, gastric and skull plasmacytoma	EBRT	Gastric Plasmacytoma	no	Regression: all nodular lesions; stability: bony lesions
Ghodadra A et al. [59] 2015	Case report	Lung SCC (1)	IV	Liver	Yttrium-90 radioembolization	via the right hepatic artery	no	Complete regression of the nontargeted lesion in segment IVB
Golden EB et al. [60] 2015	Clinical trial PCT	Solid tumor (41)	metastatic		EBRT	Metastatic site	GM-CSF injection	AE: in 11 (26,8%) of 41 enrolled patients
Okwan-Duodu D et al. [61] 2015	Case report	Melanoma (1)	metastatic	Brain, subcutaneous tissue, mesenteric, pelvic, retroperitoneal LN	WBRT	Brain	IL-2 and CTLA-4 therapy	CR lasted for over 3 years
Thallinger C et al. [62] 2015	Case report	Melanoma (1)	Metastatic	Lung, liver, kidney, adrenal glands, brain	WBRT	Brain	ipilimumab+temozolomide	Complete regression: brain, renal lesions; partial regression: liver, lung lesions
De La Cruz V et al. [63] 2014	Case report	Melanoma (1)	Metastatic	Lung, mediastinal LN, subcutaneous nodule	EBRT	Subcutaneous nodule	no	Regression: mediastinal LN, lung disease

Siva S et al. [64] 2013	Case report	Adenocarcinoma of lung (1)	IV	Adrenal gland, humeral head	EBRT + SABR	Left upper lobe tumor + right lower lobe	Carboplatin + paclitaxel	Regression: bone and adrenal lesions
Golden EB et al. [65] 2013	Case report	NSCLC (1)	IV	Liver, pelvis, TL spine, humerus, hilary/mediastinal LN	EBRT	Liver	ipilimumab	CR
Stamell Ef et al. [66] 2013	Case report	Melanoma (1)	IIIC	Skin of forehead, scalp, neck	EBRT	Primary tumor	no	CR lasted for 36 months
Sullivan RJ et al. [67] 2013	Case report	Melanoma (1)	Metastatic	Retroperitoneal, pelvic sidewall and inguinal LN, brain, bone	SRS	Brain	no	Regression: inguinal LN; bone lesion
Postow MA et al. [68] 2012	Case report	Melanoma (1)	Metastatic	Pleural-based paraspinal, hilar LN, spleen	EBRT	Paraspinal mass	Ipilimumab	Regression: treated and untreated metastases
Hiniker SM et al. [69] 2012	Pilot study PCT	Melanoma (1)	Metastatic	Liver, axillary LN	SBRT	Liver	ipilimumab	CR
Ishiyama H et al. [70] 2012	Case report	RCC (1)	pT2N0M1 (IV)	Adrenal gland, lung, bone, mediastinal and hilar LN, brain	SRS-SBRT	Brain -bone	no	Regression: lung, mediastinal disease; progression: brain metastases
Tubin et al. 2012	Case report	Medullary thyroid carcinoma (1)	pT3 pN1b (IVA)	Mediastinal LN	VMAT	Medistinal LN (level 4R)	no	32% reduction in the volume of mediastinal LN at level 6
Cotter SE et al. [71] 2011	Case report	Merkel cell carcinoma (1)	Metastatic	Skin	Brachytherapy	Skin	no	CR lasted for 25 months
Okuma K et al. [72] 2011	Case report	Hepatocellular carcinoma (1)	Metastatic	Lung, Mediastinal LN	EBRT		No	Reduction: mediastinal LN, lung lesions
Shueng PW et al. [73] 2009	Case report	Cholangiocarcinoma (1)	Metastatic	Vertebra tT8-L3, liver	HT	T8-T10	no	Acute radiation pneumonitis
Lakshmanagowda PB et al. [74] 2009	Case report	Chronic lymphocytic leukemia (1)		Axillary and cervical LN	EBRT	Axilla	no	Regression of neck LN
Isobe Y et al. [75] 2009	Case report	ENKL (1)		Submandibolar LN	EBRT	Periocular region	Chemotherapy CHOP	Eradication of all skin lesions, Regression of submandibolar LN

Nakanishi M et al. [76] 2008	Case report	Hepatocellular carcinoma (1)	Metastatic	Inferior vena cava (IVC)	EBRT	Right lobe tumor	Transcatheter arterial embolization for the posterior segment	CR of the right and left lobe tumors
Takaya M et al. [77] 2007	Case report	Uterine cervical carcinoma (1)	Advanced	Para-aortic LN	EBRT + Brachytherapy	Pelvis	no	CR
Wersäll P et al. [78] 2006	Case report	Case 1: RCC	Metastatic	Renal hilum LN, lung	SBRT	Renal mass	No	Complete regression of metastases
		Case 2: RCC	Metastatic	Lung	SBRT	Lung	No	CR: treated lung metastases; PR: untreated lung metastases
		Case 3: RCC	Metastatic	Lung	SBRT	Lung	No	CR: treated lung metastases; PR: untreated lung metastases
		Case 4: RCC	Metastatic	Kidney hilum and periaortic LN, liver	SBRT	Renal mass	No	CR
Nam SW et al. [79] 2005	Case report	Hepatocellular carcinoma (1)	Metastatic	Skull, 3-5 and 6th ribs, sternum	EBRT	Skull	No	Reduction: liver mass; CR: bone lesions
Ohba K et al. [80] 1998	Case report	Hepatocellular carcinoma (1)	Metastatic	Vertebra T2	EBRT	Vertebra	No	Reduction: liver mass
Sham RL et al. [81] 1995	Case report	Chronic lymphocytic leukemia (1)		Cervical LN, spleen	EBRT	neck, supraclavicular LN	no	Reduction: splenomegaly, WBC count
Braun MP and Maziarz RT 1994	Case report	HL (1)	4B	Spleen, liver, pulmonary, pleura, L5	EBRT	Lombosacral bone	no	Reduction of colony formation by mobilized stem cells
MacManus MP et al. [82] 1994	Case report	Renal cell carcinoma (RCC) (1)	Metastatic	Paratracheal and subcarinal LN, lung	EBRT	Renal mass	no	Reduction: paratracheal LN; regression: lung disease lasted for 9 months

Rees GJ et al. [83] 1983	Case report	Case 1: Adenocarcinoma of esophagus Case 2: Adenocarcinoma of lung	Metastatic Metastatic	Lung Forehead, chest wall, deltoid muscle	EBRT EBRT	Esophagus Mediastinum and lower left lung	No No	Regression: primary and lung disease lasted for 14 months Regression: forehead and deltoid lesions lasted for 3 weeks
Rees GJ et al. [84] 1981	Retrospective survey	Case 1: Mixed-cellularity HL Case 2: LPHL Case 3: HL Case 4: Mixed-cellularity HL Case 5: Follicular lymphoma Case 6: Follicular lymphoma Case 7: Lymphosarcoma Case 8: NHL Case 9: Reticulum-cell sarcoma Case 10: Follicular lymphoma	III III III III		EBRT EBRT EBRT EBRT EBRT EBRT EBRT EBRT EBRT EBRT	Mantle Mantle Para-aortic and pelvic LN Mantle Abdomen Right axilla, chest wall Right groin Right breast, pelvis Para-aortic and pelvic LN Neck, supraclavicular aerea	no no no no no no no no no no	Reduction: pelvic LN Reduction: pelvic, para-aortic LN Reduction: axillary LN lasted for 3 months Reduction: para-aortic LN Regression: pleural effusion lasted for 6 months Regression: left axillary LN, spleen lesions Regression: right neck LN lasted for 6 months Regression: mediastinal mass Regression: right axillary LN lasted for 6 months Regression: bilateral axillary LN

Robins H I et al. 1981	Case report	Histiocytic lymphoma (1)	IV B	Right and Left kidneys	EBRT	Right kidney	Chemotherapy BACOP	24% reduction: the maximal axis of the rigth kidney;12,6% reduction: the left
Fairlamb DJ et al. [85] 1981	Case report	Clear cell carcinoma (1)	Metastatic	Lung, hila, pubic bone	EBRT	Groin mass	no	Regression: lung deposits
Antoniades J et al. [86] 1977	Case report	Case 1: lymphocytic lymphoma Case 2: Lumphocytic lymphoma	IV III	Axillary, supraclavicular, periaortic and pelvic LN, lung Axillary, periaortic and pelvic LN, spleen	EBRT EBRT	LN above diaphram, Waldeyer's ring, lung LN above diaphram, Waldeyer's ring	No No	LN regressed to <40% LN regressed to <60%
Kurlander R et al. [87] 1975	Case report	Chronic lymphocytic leukemia (1)		Cervical, axillary and inguinal LN, spleen	EBRT	Spleen	no	Hyperkalemia attributed to the necrosis of leukemic cells
Kingsley D P [88] 1975	Case report	Melanoma (1)	Metastatic	Inguinal, iliac, para-aortic LN	Fast neutrons	Inguinal region	no	Complete regression of LN diseases
Ehlers G et al. [89] 1973	Case report	Papillary adenocarcinoma of unknown origin (1)	Metastatic	Supraclavicular LN, axilla	EBRT	Neck, supraclavicular area	no	Regression: supraclavicular, axillary lesions
Nobler M P [90] 1969	Case report	Follicular lymphoma (1)	IV	Cervical, axillary, inguinal, femoral, pelvic and para-aortic LN, liver, spleen	EBRT	Para-aortic, pelvic, femoral LN	no	CR

ACR= Abscopal disease control rate; AE= Abscopal effect; ARR= abscopal response rate; CR= complete response; CRC= colorectal cancer; CRT= 3D-conformal radiation therapy; DGCT= diffuse-type giant cell tumor; DP-SBRT= dose-painting SBRT; EBRT= external beam radiation therapy; EBT= electron beam therapy; ENKL= extranodal NK/T cell lymphoma, nasal type; HT= helical tomotherapy; HNSCC= head and neck squamous cell carcinoma; HT= helical tomotherapy; ICC= intrahepatic cholangiocarcinoma; IGRT= image-guided radiotherapy; IMRT= intensity modulated radiotherapy; LCNEC= Large-cell neuroendocrine carcinoma; LPHL= Lymphocyte predominant Hodgkin lymphoma; NHL= non-Hodgkin lymphoma; NSCLC= Non-small-cell lung carcinoma; OOR= overall objective response; ORR= overall response rate; PR= partial response; RCC= Renal cell carcinoma; RFA= radiofrequency ablation; SABR= stereotactic ablative body radiotherapy; SBRT= Stereotactic body radiation therapy; SBRT-PATHY= SBRT targeting partial tumor hypoxic; SCC= squamous cell carcinoma; SRS= Stereotactic radiosurgery; SRT= stereotactic radiotherapy; VMAT= volumetric modulated arc therapy; WBRT= Whole-brain radiotherapy

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