

RCT-Table: Randomized Controlled Trials on Mistletoe Therapy in Cancer. [19-21]

Author, Year	Site	Stage	Intervention (evaluable patients)	Survival	Tumour behaviour	Other Results	Comments; Attrition Rate (AR)
Grossarth 2009 [16a]	Cervical Dysplasia		<ul style="list-style-type: none"> ● Iscador (42) ● None (42) 	Death due to cancer 5 Pat. 12 Pat.	Cancer incidence 6 Pat. 13 Pat.		Embedded in a long-term epidemiologic cohort study; AR: 9%
Eisenbraun 2009 [8a]	Stomach	IB, II	<ul style="list-style-type: none"> ● Surgery, Capecitabine, Abnobaviscum (16) ● Surgery, Capecitabine (16) 			EORTC C30 ↑*; leucocytes ↑*	Poster presentation, abstract
Hekal 2009 [17a]	Bladder	pTa; T1	<ul style="list-style-type: none"> ● Surgery, Abnobaviscum (no data) ● Surgery, BCG (no data) 		Recurrence 73%* 30%	Development of invasive cancer 5 pat. 5 pat.	Poster/abstract; total patient number: n=60
Longhi 2009 [24b]	Osteo-sarcoma	no meta-stases or relapse after 2nd surgery	<ul style="list-style-type: none"> ● Iscador (6) ● Etoposide (4) 		Median disease-free survival (months) 8,5 (3-18) 3 (3-11)	EORTC C30/POQOL : pos. trend	Interim analysis; study still in progress
Tröger 2009 [36, 36a]	Breast	T1-3, N0-2, M0	<ul style="list-style-type: none"> ● CAF, Iscador or Helixor (59) ● CAF (30) 			Reduction of neutropenia * EORTC C30 ↑* (pain*, diarrhoea*, role*, insomnia*, nausea/vomiting*)	AR: 6%
Büssing 2008 [4a]	Breast	No data	<ul style="list-style-type: none"> ● (F)EC, Iscador (32) ● (F)EC (33) 			Reduction of EC-related side effects (nausea, constipation, pain, stomatitis). * Granulocyte function, lymphocytes, vomiting, EORTC C30, BR 23: no difference	Only few data, only abstract; possible bias regarding co-intervention; AR: no data
Grossarth 2008 [15a]	Uterus	IA-C	<ul style="list-style-type: none"> ● Iscador (30) ● None (30) 	Overall survival HR 0.36 (0.16-0.82) *		Psychosomatic self regulation ↑*	Embedded in an epidemiologic cohort study; AR: 21%
Grossarth 2008 [15a]	Uterus	IVA-B	<ul style="list-style-type: none"> ● Iscador (26) ● None (26) 	Overall survival HR 1 (0.46-2.16)			Embedded in an epidemiologic cohort study; AR: 0%
Grossarth 2007 [15b]	Ovary	IA-C	<ul style="list-style-type: none"> ● Iscador (21) ● None (21) 	Overall survival HR 0.40 (0.15-1.03)		Psychosomatic self regulation ↑*	Embedded in an epidemiologic cohort study; AR: 16%
Grossarth 2007 [15b]	Ovary	IV	<ul style="list-style-type: none"> ● Iscador (20) ● None (20) 	Overall survival HR 0.33 (0.12-0.92) *			Embedded in an epidemiologic cohort study; AR: 17%
Grossarth 2007 [16]	Melanoma	>1.5 mm no metastases	<ul style="list-style-type: none"> ● Iscador (22) ● None (22) 	Overall survival HR 0.47 (0.19-1.14)	Time to event HR 0.49 (0.32-0.75)*	Psychosomatic self regulation ↑*	Embedded in an epidemiologic cohort study; AR: 0% No difference regarding time to diagnosis of brain metastases, HR: 0.5 (0.09-2.73)
Grossarth 2007 [15]	Cervix	FIGO IVA-IVB	<ul style="list-style-type: none"> ● Iscador (19) ● None (19) 	Overall survival HR 0.46 (0.18-1,21)		Psychosomatic self regulation ↑*	Embedded in an epidemiologic cohort study; AR: 0%
Schink 2007 [34]	Colon, rectum	II-IV	<ul style="list-style-type: none"> ● Surgery, Iscador (11) ● Surgery (11) 			Reduced surgery-induced suppression of NK-cell activity *	Perioperative mistletoe infusion. Small sample size; sequential design allows study termination as soon as results are significant
Grossarth 2006 [13, 14]	Breast	T1-3, N0, M0	<ul style="list-style-type: none"> ● Iscador (38) ● None (38) 	Overall survival HR 0.65 (0.34-1.25)	Time to event HR 0.65 (0.47-0.91)*	Psychosomatic self regulation ↑*	Embedded in an epidemiologic cohort study; AR: 36%
Auerbach 2005 [1]	Breast	T1-2, N0-1, M0	<ul style="list-style-type: none"> ● CMF, radiation, Helixor (11) ● CMF, radiation, placebo (9) 			CMF-induced NK-cell-decrease ↓*, SCE- increase ↓, QoL: no difference	RCT according to modern standards; double blinding, but largely unblinded; small sized pilot study; AR: 17-30%

Enesel 2005 [9]	Gastro-intestinal	II-III	<ul style="list-style-type: none"> ● Surgery, Isorel (40) ● Surgery (30) 				Prevention of surgery-induced lymphocyte reduction; KPI ↑*, anxiety ↓*	Little information AR: 45%		
Kleeberg 2004 [23]	Melanoma	High risk primary (≥3MM) or LN+	<ul style="list-style-type: none"> ● Iscador, surgery (102) ● IFN-α, surgery (240) ● IFN-γ, surgery (244) ● Surgery (244/102) 	Overall survival, HR	1,21 (0,84-1,75) 0,96 (0,76-1,21) 0,87 (0,69-1,10)	Disease-free interval, HR:	1,32 (0,93-1,87) 1,04 (0,84-1,30) 0,96 (0,77-1,2)	QoL: Results not shown	2 studies (3-, and 4-arms); analysis partly separate, partly pooled; detection-bias possible; short mistletoe treatment; AR: 24%	
Piao 2004 [26]	Breast, ovary, lung (NSCLC)	T1-4, N0-3, M0-1	<ul style="list-style-type: none"> ● Helixor, chemotherapy^I (115) ● Lentinan, chemotherapy^I (109) 				FLIC ↑ (9 vs. 4,7)* TCM ↑ (-1 vs. 0)* KPI ↑ (50% vs. 32% of pat.)* chemotherapy-related adverse events ↓ (28 vs. 77)	Well conducted RCT; no blinding, but effective and popular control treatment („active placebo“); AR: 4%		
Cazacu 2003 [5]	Colon, rectum	Dukes C und D	<ul style="list-style-type: none"> ● Isorel, 5-Fu, surgery (29) ● 5-Fu, surgery (21) ● Surgery (14) 	Median mean survival (months)		<u>Dukes C D</u>	25* 17* 18 7 17 15	5-FU side effects (% of pat.) 0% 19% QoL: ↑, data not shown	Little information; unexplained disadvantage of survival in 5-FU-group; small and unequal groups sizes; AR: no data	
Borrelli 2001 [3]	Breast	IV	<ul style="list-style-type: none"> ● Iscador (20) ● Placebo (10) 				QoL (Spitzer) ↑*	Double blind RCT; small size, short duration; little information; AR: 0%		
Grossarth 2001 [11]	Breast, lung, rectum, colon, stomach	All stages	<ul style="list-style-type: none"> ● Iscador (39) ● None (39) 	Mean survival (months)			42 * 29	Psychosomatic self regulation ↑*	Embedded in an epidemiologic cohort study; AR: 20%	
Grossarth 2001 [11]	Breast	IIIA-IIIB	<ul style="list-style-type: none"> ● Iscador (17) ● None (17) 	Mean survival (months)			57,5 * 28,9	Psychosomatic self regulation ↑	Small trial; embedded in an epidemiologic cohort study, AR: 0%	
Kim 1999 [22]	Pleural effusion	Advanced	<ul style="list-style-type: none"> ● Helixor (11) ● Doxycyclin, Meperidin, Lidocain (15) 			<u>Complete part. response</u>	81% 9%* 40% 26%	Less pain, fever, and burning sensation with Helixor	Discrepancy in patient numbers in two presentations. VR: 13%	
Dold 1991 [6]	Lung	All stages	<ul style="list-style-type: none"> ● Iscador (114) ● Placebo (vitamin B) (113) ● Polyerga (110) 	Median survival (months)	9,1 7,6 9,0	<u>Compl. overall regression^{II}</u>	4% 26% 3% 20% 2% 19%	<u>Pat. subjectively improved</u>	59%* 45% 43%	Pat. recruitment difficult; unexplained high remission rates in placebo group (advanced, pre-treated disease); AR: 17%
Salzer 1991 [30]	Lung	I-IV	<ul style="list-style-type: none"> ● Iscador, surgery (87) ● surgery (96) 	Median survival (months)	33 31	Recur- rence	50% 55%		Protocol violation in study centres; more mistletoe than control patients tumour free in autopsy; AR: 16%	
Gutsch 1988 [17]	Breast	T1-3, N0-3, M0	<ul style="list-style-type: none"> ● Helixor, surgery, radiation^{III} (192) ● Surgery, radiation^{III} (274) ● CMF, surgery, radiation^{III} (177) 	5-year survival	69,1% * 59,7% 67,7% *				Major protocol violations in study centres; analysis „as treated“ (Cox Proportion Hazard Model), not „per protocol“ or „intention-to-treat“; AR: 20%	
Salzer 1987 [28]	Lung	I (II)	<ul style="list-style-type: none"> ● Iscador, surgery (12) ● Surgery (14) 	Median survival (months)	117 34,5				Major protocol violations in study centres; prognostic comparability unclear; little information; AR: 48%	
Douwes 1986 [8]	Colon, rectum	IV	<ul style="list-style-type: none"> ● Helixor, 5-Fu/FA (20) ● 5-Fu/FA (20) ● Ney Tumornin, 5-Fu/FA (20) 	Mean survival (months)		<u>Responder n-Resp</u>	27 12 14 5 24 12	<u>Compl. part. response</u>	15% 35% 15% 30% 15% 25%	Small study; little information; AR: 0%
Lange 1985 [24]	Lung, ENT, ovary	Inoperable	<ul style="list-style-type: none"> ● Radiation, cisplatin, holoxan, Helixor (23) ● Radiation, cisplatin, holoxan (21) 					KPI ↑*, nausea ↓*, vomiting ↓*, depression of myelopoiesis ↓*	Unpublished; high drop-out, otherwise well conducted; AR: 35%	
Salzer 1979, 1983 [29, 31, 33]	Stomach	II-III	<ul style="list-style-type: none"> ● Iscador, surgery (62) ● Surgery (75) 	Mean survival (months)		<u>LN + =</u>	25* 55 18 45		Major protocol violations, especially in a third chemotherapy group; AR: 57%	

Abbreviations: BCG: Bacillus Calmette-Guérin, CMF: Cyclophosphamid, Methotrexat, 5-Fu; 5-Fu: 5-Fluorouracil; FA: Folic acid; VEC: Vindesin, Epirubicin, Cyclophosphamid; Dexa: Dexamethason; QoL: Quality of life; KPI: Karnofsky Performance Index; FLIC: Functional Living Index-Cancer; TCM: Traditional Chinese Medicine Index; SCE: Sister Chromatid Exchange; HR: Hazard-Rate; Pat.: Patients, NK: Natural Killer-cells, LN: lymph nodes

* Statistically significant superior compared to control group; ^I Chemotherapy: Cyclophosphamid (C), Adriamycin (A), Cisplatin (P), 5-Fluorouracil (F), Vinorelbine (V), Mitomycin (M), Ifosfamid (I), Vindesine (Vi), Carboplatin (cP). Breast cancer.: CAP, CAF; ovarian cancer: CP, IcP; NSCLC:VP, MViP; ^{II} Not corresponding to WHO-definition of tumour response; ^{III} Co-intervention applied to part of the group, ^{IV} : patient number in ach group not mentioned, total n=60..

Dr. med. Gunver S. Kienle, MD, IFAEMM Freiburg

Last Modified: May 2010