100 Jahre Zukunft
Die Mistel in der Krebstherapie

Ergebnisse zur Misteltherapie aus der Versorgungsforschung

Dr. Friedemann Schad

Leiter Onkologisches Zentrum, Abt. Interdisziplinäre Onkologie und Palliativmedizin

Gemeinschaftskrankenhaus Havelhöhe, Berlin

Havelhöhe

DKG Krebsgesellschaft | Zertifiziertes Onkologisches Zentrum

Klinische Forschung

Der Mensch ist ein komplexes System

Krebs ist eine komplexe Systemerkrankung

Integrative Medizin: komplexe Interventionen

Wissenschaftliche Methodik: „komplex“

⇨ Methodenpluralismus

Havelhöhe

Integrative Onkologie: “mixed method approach”

- Cognition Based Medicine, Einzelfallstudien
- Randomised Controlled Trial (RCT)
- Kohortenstudien
- Outcome/Versorgungsforschung, SER/whole system research - PROMS, Überleben

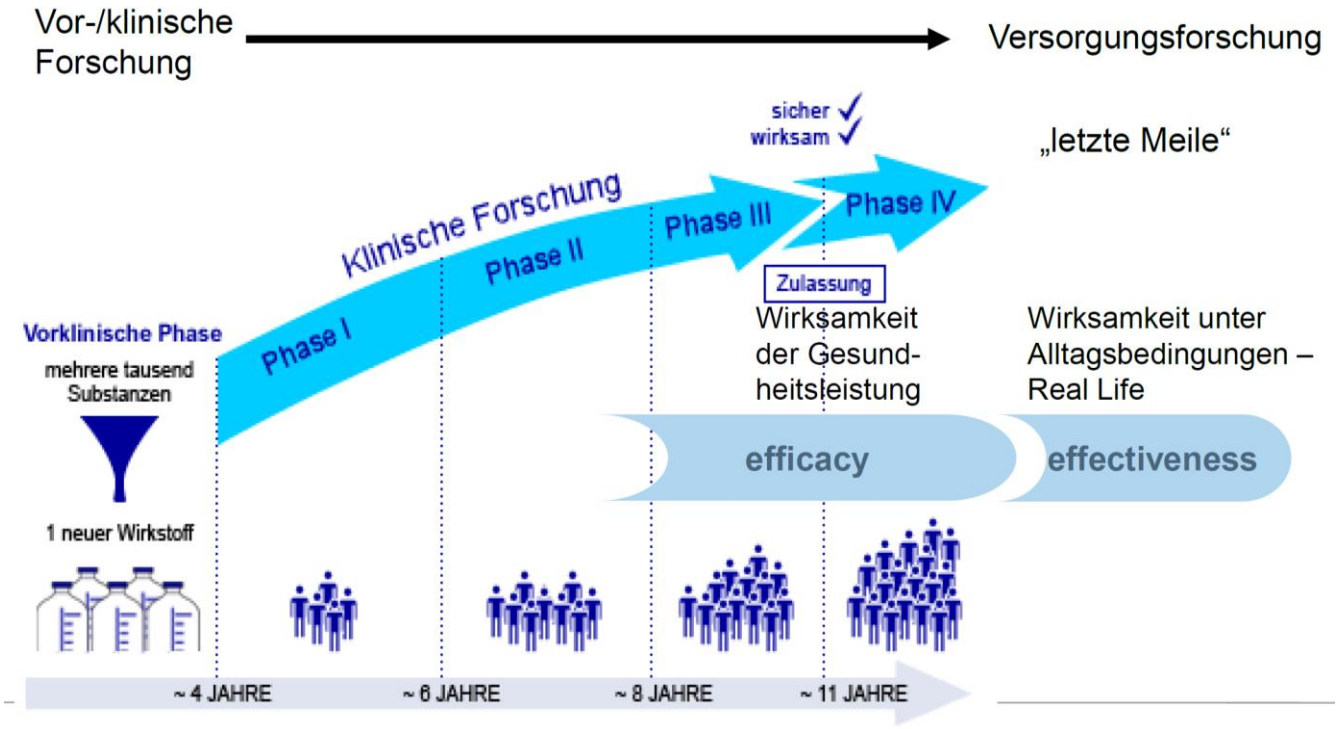
Studien, Konzeptforschung

Unbedenklichkeit, Hypothesengenerierung

NO-Basis: klinische Registerdaten

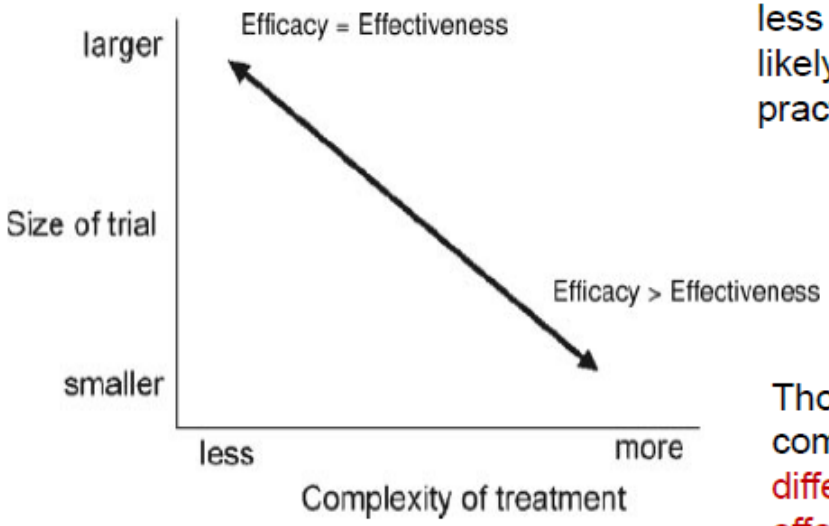
Havelhöhe

Stellung der Versorgungsforschung



Univ.-Prof. Dr. Prof. Dr. h.c. Edmund A.M. Neugebauer
Deutscher Kongress für Versorgungsforschung, 7.-8.10.2015
Deutsches Netzwerk Versorgungsforschung,
Probleme Klinischer Studien

Generalisierbarkeit und Versorgungsforschung



Trials that are larger and that evaluate less complex therapies are the most likely to be applicable in routine clinical practice (ie, efficacy = effectiveness).

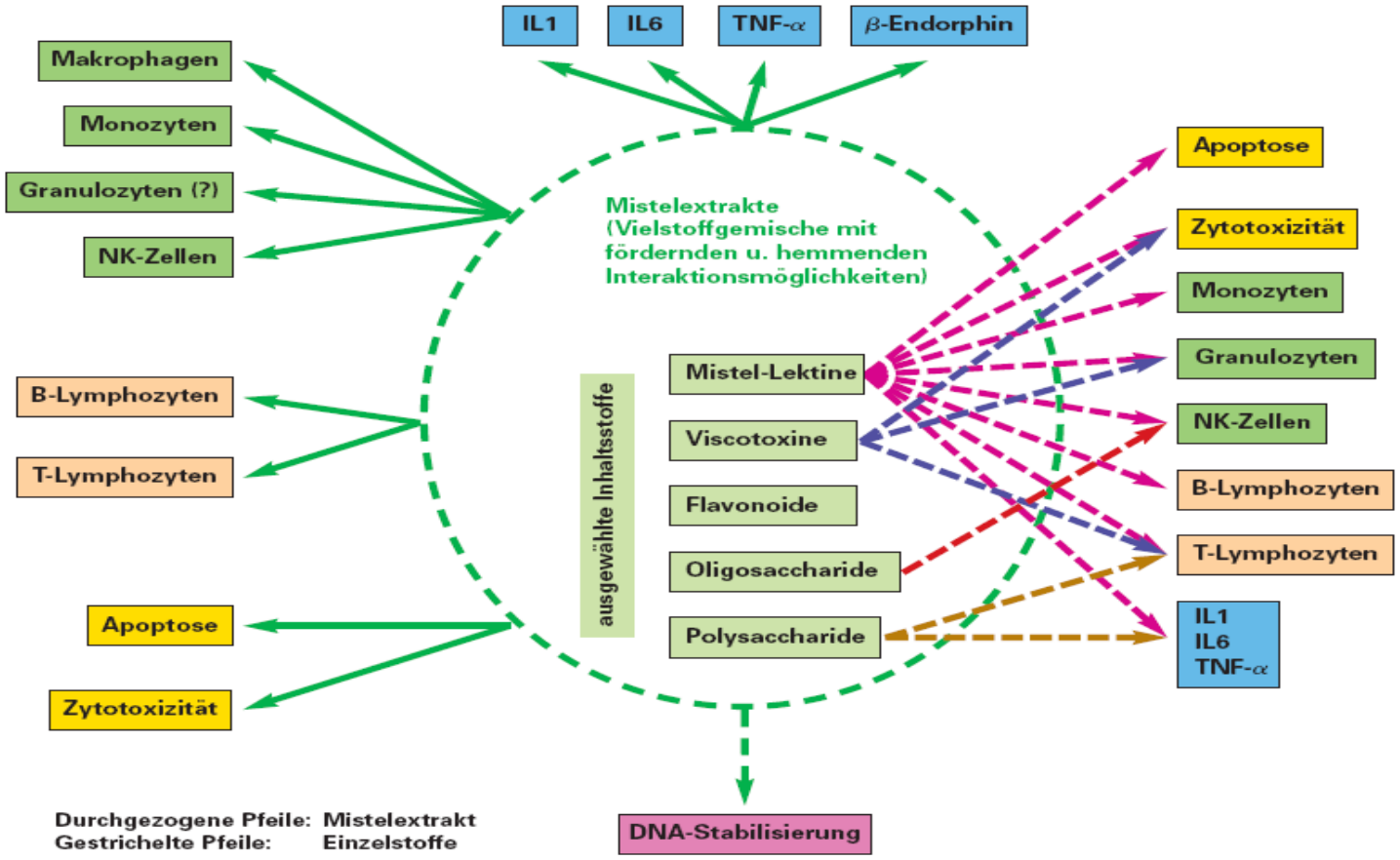
Those that are smaller and evaluate complex therapies may have important differences between efficacy and effectiveness

Flather M et al. Generalizing results of randomized trials to clinical practice: reliability and cautions. Clin Trials 2006; 3:508-512

- Beschreibung der Gesundheitsversorgung im Alltag
- Vielfalt und Komplexität der Versorgung
- Nutzenbewertung und Patientensicherheit über die Möglichkeit von RCTs hinaus
- Pharmakovigilanz nur über Register realisierbar

Prof. Dr. Neugebauer E,
Deutsches Netzwerk Versorgungsforschung, Probleme Klinischer Studien
Deutsches Ärzteblatt, Jg 114, Heft 24, 6-2017

Zelluläre Effekte von *Viscum album L.*



Dr. M. Reif, IKF, Berlin

eCAM Evidence-Based Complementary and Alternative Medicine

Mistletoe: From Basic Research to Clinical Outcomes in Cancer and Other Indications

Guest Editors: Matthias Kröz, Gunver Sophia Kienle, Gene Feder, Srini Kaveri, and Steven Rosenzweig

Hindawi Publishing Corporation
Evidence-Based Complementary and Alternative Medicine
Volume 2014, Article ID 724258, 11 pages
http://dx.doi.org/10.1155/2014/724258

Hindawi

Research Article

Adverse Drug Reactions and Expected Effects to Therapy with Subcutaneous Mistletoe Extracts (*Viscum album* L.) in Cancer Patients

Megan L. Steele,[1] Jan Axtner,[1] Antje Happe,[1] Matthias Kröz,[1,2,3] Harald Matthes,[1,2] and Friedemann Schad[1,2]

[1] *Research Institute Havelhoehe, 14089 Berlin, Germany*
[2] *Hospital Havelhoehe, 14089 Berlin, Germany*
[3] *Institute for Social Medicine, Epidemiology and Health Economics, Charité-University Medical Center, 10117 Berlin, Germany*

Correspondence should be addressed to Friedemann Schad; fschad@havelhoehe.de

Received 23 September 2013; Accepted 16 December 2013; Published 19 January 2014

Academic Editor: Gene Feder

Hindawi Publishing Corporation
Evidence-Based Complementary and Alternative Medicine
Volume 2014, Article ID 236310, 10 pages
http://dx.doi.org/10.1155/2014/236310

Hindawi

Research Article

Safety of Intravenous Application of Mistletoe (*Viscum album* L.) Preparations in Oncology: An Observational Study

Megan L. Steele,[1] Jan Axtner,[1] Antje Happe,[1] Matthias Kröz,[1,2,3,4] Harald Matthes,[1,2] and Friedemann Schad[1,2]

[1] *Research Institute Havelhoehe, 14089 Berlin, Germany*
[2] *Hospital Havelhoehe, 14089 Berlin, Germany*
[3] *Institute for Social Medicine, Epidemiology and Health Economics, Charité-University Medical Centre, 10117 Berlin, Germany*
[4] *Institute of Integrative Medicine, Witten/Herdecke University, 58313 Herdecke, Germany*

Correspondence should be addressed to Friedemann Schad; fschad@havelhoehe.de

Received 21 November 2013; Revised 2 April 2014; Accepted 3 April 2014; Published 15 May 2014

Academic Editor: Srini Kaveri

Sicherheit von Mistelgesamtextrakten

Sc. n=1923; iv. n = 475; it. n = 123 Patienten

- Die meisten UAW's (80%) waren "General disorders and administration site conditions" und nahezu alle UAW's (99%) waren sog. erwartete Reaktionen.
- 98% aller UAW's waren von milder bis moderater Intensität
- Nur 8.4% (sc.) bzw. 4.6% (iv.) der Patienten hatten eine UAW's
- Traditional sc. und iv. Applikation von VA sind sicher in der Anwendung
- Off-label sc. and it. Applikation resultieren in deutlich höheren UAW-Raten (26.1% and 21.1%); keine schwerwiegende UAW trat auf.

Steele M, Axtner J, Happe A, Kröz M, Matthes H, Schad F "Adverse Drug Reactions and Expected Effects to Therapy with **Subcutaneous** Mistletoe Extracts (Viscum album L.) in Cancer Patients," Evidence-Based Complementary and Alternative Medicine, vol. 2014

Steele M, Axtner J, Happe A, Kröz M, Matthes H, Schad F "Safety of **Intravenous** Application of Mistletoe (Viscum album L.) Preparations in Oncology: An Observational Study," Evidence-Based Complementary and Alternative Medicine, vol. 2014

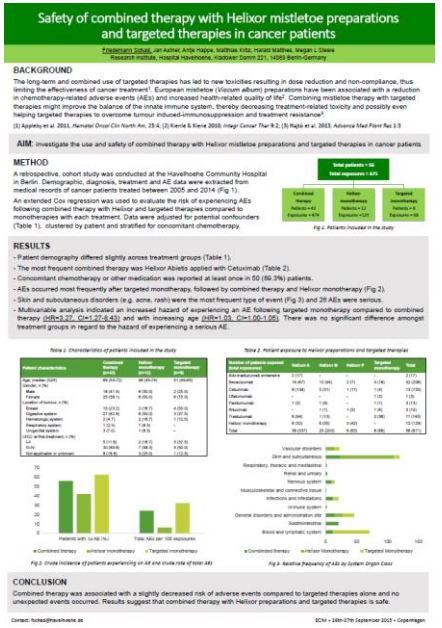
Steele, M. L., Axtner, J., Happe, A., Kröz, M., Matthes, H., & Schad, F. (2014). Use and Safety of **Intratumoral** Application of European Mistletoe (Viscum album L) Preparations in Oncology. Integrative cancer therapies, 1534735414563977.

Safety of combined treatment with targeted anticancer therapies and Helixor *Viscum album* L. preparations

- Helixor und Antikörper intravenös zeitgleich gegeben / versus Helixor alleine oder Antikörper alleine.

- 5 fach geringere UAW-Rate bei der Kombination Helixor und Antikörper

Fazit: sichere Anwendung eines Mistelgesamtextraktes mit Antikörper


Safety of combined therapy with Helixor mistletoe preparations and targeted therapies in cancer patients

BACKGROUND

AIM: investigate the use and safety of combined therapy with Helixor mistletoe preparations and targeted therapies in cancer patients

METHOD

RESULTS

CONCLUSION

Combined therapy was associated with a slightly decreased risk of adverse events compared to targeted therapies alone and no unexpected events occurred. Results suggest that combined therapy with Helixor preparations and targeted therapies is safe.

Schad F, Axtner J, Kröz M, Matthes H & Steele M. (2016). Safety of Combined Treatment with Monoclonal Antibodies and Viscum album L preparations. Integr Cancer Ther.

Klinische Sicherheit: kombinierte Gabe von Immune Checkpoint Inhibitoren und VA bei Patienten mit fortgeschrittenen Krebserkrankungen

Clinical safety of combined therapy of immune checkpoint inhibitors and *Viscum album L.* therapy in patients with advanced or metastasized cancer

Anja Thronicke, Megan Steele, Christian Grah, Burkhard Matthes, Friedemann Schad
Research Institute Havelhoehe, Hospital Havelhoehe, Berlin, Germany

BACKGROUND

Despite improvement of tumour response rates in patients with progressive and metastatic cancer, anti-PD-1/PDL-1 and CTLA-4 immune checkpoint monoclonal antibodies (ICM) potentiate toxicities in cancer patients. *Viscum album L.* (VA) extracts have been safely and effectively applied as add-on therapy in antineoplastic concepts and have been shown to support health related quality of life and to reduce chemotherapy-induced adverse side effects in cancer patients.

OBJECTIVE

As a first step towards determining the safety profile of combinatory ICM/VA therapy, we compared the adverse event (AE) profiles of patients with advanced or metastasized cancer who received either ICM treatment alone or combinatory ICM/VA therapy.

METHODS

ICM or combinational ICM/VA therapies were applied in an integrative oncology setting of a certified Cancer Centre (GKH Havelhöhe). AE rates of both therapy groups were compared. Initial assessment of disease response was performed. Statistics: Application of univariate analysis for detection of differences in AE rates and tumour response rates; performance of adjusted multivariate regression analyses for identification of safety associated factors in ICM treated patients.

Variables	n (%)
Number of patients, N (%)	16 (100)
Age, years, median (IQR)	64 (57.8; 69.3)
Gender, male, n (%)	7 (43.8)
Lung cancer, n (%)	11 (68.8)
Malignant melanoma, n (%)	3 (18.8)
Pleural mesothelioma, n (%)	1 (6.3)
Uveal melanoma, n (%)	1 (6.3)
UICC stage IIIA, n (%)	4 (25.0)
UICC stage IV, n (%)	12 (75.0)

Table 1. Baseline characteristics of patients receiving ICM

RESULTS

1. How were the patients treated?

ICM alone (ICM)/ 7 patients (43.8%)	Combined therapy (ICM/VA)/ 9 patients (56.3%)
ICM – nivolumab, n=4	ICM/VA – nivolumab/Abnoba Viscum, n=6
ICM – ipilimumab, n=2	ICM/VA – nivolumab/Helixor P, n=1
ICM – pembrolizumab, n=1	ICM/VA – nivolumab/Iscador Qu, n=1
	ICM/VA – ipilimumab/Abnoba Viscum, n=1

Table 2. Treatment scheme of patients receiving either ICM or ICM/VA

- 44.4% of the ICM/VA patients received VA subcutaneously (SC), 66.7% intravenously (IV)
- None of the 16 patients received chemotherapy during ICM or ICM/VA treatment

2. What types of AEs and how many occurred for each treatment group?

- ICM alone: 71.4% of patients experienced an adverse event
- ICM/VA: 66.7% of patients experienced an adverse event
- Differences between treatment groups with respect to AE or ADR rate were not significant
- No serious AEs and serious adverse reactions in total cohort
- 85% of AEs were expected ICM reactions
- Malaise (18.8%), pyrexia (12.5%), bronchitis (12.5%), and skin reactions (12.5%) were most frequent AEs in total cohort

System Order Class	ICM	ICM/VA
Gastrointestinal	g, h, k	a,c
General disorders and administration site	g, k	a, b
Metabolism and nutrition disorder	j	a, e
Musculoskeletal and connective tissue		b
Nervous system		b
Renal and urinary		a
Respiratory, thoracic and mediastinal	j,k,l	c,d,f
Skin and subcutaneous	k	a,e
Surgical and medical procedures	-	a
AE rate, %	71.4%	66.7%
ADR rate, %	14.3*%	11.1*%

Table 3. Frequency of adverse events grouped by System Organ Class for each treatment group; Individual patients having experienced AEs during treatment are indicated by letters a-l (i was dismissed); *One ADR per treatment group: nausea

3. Which relevant safety-associated factors were detected?

- No association between concomitant VA treatment and occurrence of AE (OR: 1.467, 95%CI: 0.183-11.693 p=0.720)
- No association between occurrence of AEs and:
  - greater cycle-numbers (>10) of ICM treatment
  - pre-treatment with platinum-based chemotherapy, targeted therapy or with VA

4. What was the disease response in both treatment groups?

- Differences between treatment groups for CR, PR, SD and PD were not significant, see table 4
- 33.3% partial response in the ICM/VA group vs. no response in the ICM group
- Combined ICM/VA treatment in partial response patients:
  - stabilized size and number of metastases (1 patient)
  - size reduction of metastases and lymph nodes (2 patients)

Disease response	ICM	ICM/VA	P-value
Complete response, n (%)	0	0	NA
Partial response, n (%)	0	3 (33.3)	0.21
Stable disease, n (%)	2 (28.6)	2 (22.2)	NA
Progressive disease, n (%)	5 (71.4)	4 (44.4)	0.36

Table 4. Tumour response after therapy with immune checkpoint inhibitors

CONCLUSIONS

- Approval of known toxicity profile of current PD-1/PDL-1 and CTLA-4 immune checkpoint inhibitors (ICM)
- No grade 3 and 4 AEs (CTC)
- IV and SC applications of *Viscum album L.* (VA) extracts during therapy with ICM did not alter the AE rate for ICM → first indication for a safe concomitant SC and IV application of VA extracts to ICM therapy
- Positive ICM-induced disease response has been maintained during additive VA therapy

Poster ID # P3.02c-037/ Abstract ID #5056 IASLC WCLC 2016, 4-7 October, Vienna, Austria

Thronicke, A., M. Steele, C. Grah, B. Matthes, Friedemann Schad.: P3.02c-037 Clinical Safety of Combinational Therapy of Immune Checkpoint Inhibitors and Viscum Album L. in Patients with Advanced or Metastasized Cancer. Journal of Thoracic Oncology 2017; 12: p. S1295–S1296

Klinische Sicherheit: kombinierte Gabe von Immune Checkpoint Inhibitoren und VA bei Patienten mit fortgeschrittenen Krebserkrankungen

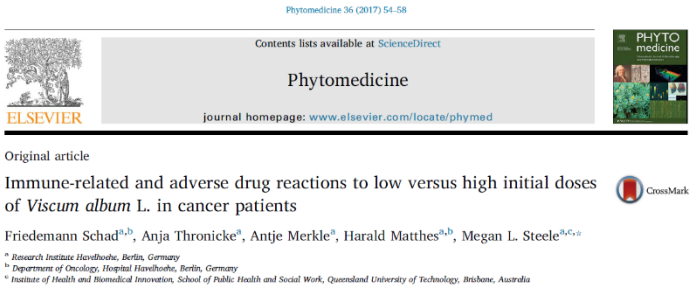
System Order Class	AE (preferred term), grade 1-2	ICM (n=7)	VA+ICM (n=9)
Gastrointestinal	Constipation §		f
	Vomiting[3)] §		g
	Abdominal pain upper §	a, b	
	Abdominal colic §	c	
	Diarrhoea §	c	
	Nausea[3)] §	c	
General disorders and administration site	Decreased appetite §		f
	Pyrexia §	a	h
	Pain §		f
	Malaise §	c	f, h
Metabolism and nutrition disorder	Hyponatraemia §		i
	Marasmus		f
	Hypercholesterolemia §	d	
Musculoskeletal and connective tissue	Pain in extremity §		h
Nervous system	Altered visual depth perception §		h
Renal and urinary	Urinary tract infection §		f
Respiratory, thoracic and mediastinal	Bronchitis chronic		k
	Respiratory distress §		g
	Pneumonia staphylococcal §		g
	Bronchitis §	e	l
	Cough §	d	
	Pneumonia §	c	
Skin and subcutaneous	Decubitus ulcer		f
	Skin reaction §	c	i
Surgical and medical procedures	Supportive care		f
Total number of patients experiencing AE		5 (71.4[2)])	6 (66.7[1)])

§ erwartete Nebenwirkung laut ICI Fachinformation (85%)

Fazit: Die zusätzliche VA-Gabe erhöht **nicht** das Nebenwirkungsprofil der ICI-Therapie bei fortgeschrittenem Lungenkarzinom und Melanom.

Havelhöhe

Sicherheit auch bei initial hohen Mistelstärken



Phytomedicine 36 (2017) 54–58

Contents lists available at ScienceDirect

Phytomedicine

journal homepage: www.elsevier.com/locate/phymed

Original article

Immune-related and adverse drug reactions to low versus high initial doses of *Viscum album* L. in cancer patients

Friedemann Schad[a,b], Anja Thronicke[a], Antje Merkle[a], Harald Matthes[a,b], Megan L. Steele[a,c,*]

[a] Research Institute Havelhoehe, Berlin, Germany
[b] Department of Oncology, Hospital Havelhoehe, Berlin, Germany
[c] Institute of Health and Biomedical Innovation, School of Public Health and Social Work, Queensland University of Technology, Brisbane, Australia

Von 1361 Krebspatienten starteten 516 (39%) mit ≤ 0.02 mg VA (low inititial dose) und 845 (62%) mit > 0.02 mg VA (high initial dose)

Ergebnisse:

- ADR-Inzidenz in der „High initital dose“ Gruppe signifikant höher (20.7% vs. 0.8% in der Niedrigdosisgruppe, p<0.001)
- Wahrscheinlichkeit um 38fach erhöht, in der „High initial“ Gruppe ein VA-basiertes ADRs zu erhalten (adjustierte multivariable Regression, p<0.001)
- Trotz erhöhter Inzidenz waren die Nebenwirkungen:
  - Von milder und moderater Intensität
  - erwartete Reaktionen (Fieber, lokale Reaktionen)
  - Reaktionen an der Verabreichungsstelle, immunbezogene und Allgemeinerkrankungen
  - Keine schwerwiegenden Nebenwirkungen

Schad F, Thronicke A, Merkle A, Matthes H, Steele M. Immune-related and adverse drug reactions to low versus high initial doses of Viscum album L. in cancer patients. Phytomedicine : international journal of phytotherapy and phytopharmacology. 2017. https://doi.org/10.1016/j.phymed.2017.09.004

Sicherheit bei initial hohen Mistelstärken

System organ class	Low dose group		High dose group	
	No. of patients	No. of ADRs (%)	No. of patients	No. of ADRs (%)
Blood and lymphatic system disorders	–	–	1	1 (0.4)
Cardiac disorders	–	–	1	1 (0.4)
Gastrointestinal disorders	–	–	5	7 (2.6)
General disorders and administration site conditions	2	2 (50.0)	174	253 (92.7)
Investigations	–	–	2	2 (0.7)
Nervous system disorders	–	–	3	3 (1.1)
Respiratory, thoracic and mediastinal disorders	–	–	1	1 (0.4)
Skin and subcutaneous tissue disorders	2	2 (50.0)	3	5 (1.8)
TOTAL	4	4 (100.0)	175*	273* (100.0)

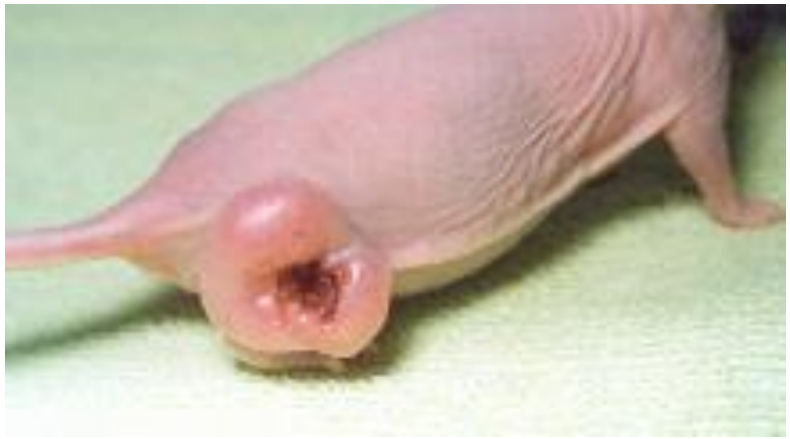
No. = number; % = percentage of total adverse drug reactions (ADRs) per dose group;
*Some patients experienced multiple ADRs.

Fazit: Die Initiierung einer VA-Therapie mit höheren als nach Fachinformation vorgegebenen Stärken ist unter fachgerechter Anwendung sicher.

Schad F, Thronicke A, Merkle A, Matthes H, Steele M. Immune-related and adverse drug reactions to low versus high initial doses of Viscum album L. in cancer patients. Phytomedicine : international journal of phytotherapy and phytopharmacology. 2017. https://doi.org/10.1016/j.phymed.2017.09.004

Intrakutanes, humanes Adenokarzinom vor und nach 35 Tagen unter peritumoraler Injektion von Mistelgesamtextract (Pini)

Before



After 35 days

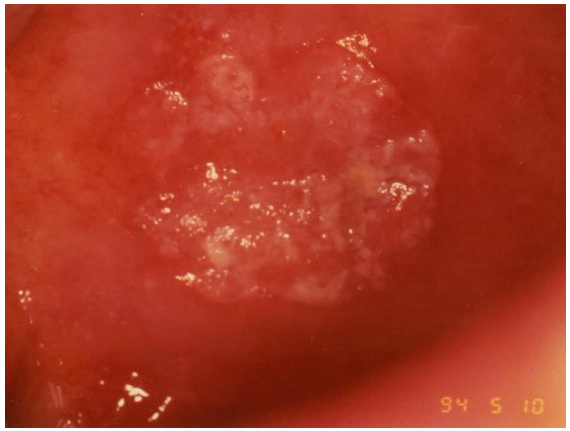
Klopp R et al. DZO 35 2003: 5-14 Changes of microcirculation in tumor and surrounding tissues after application of standardised mistletoe extract .

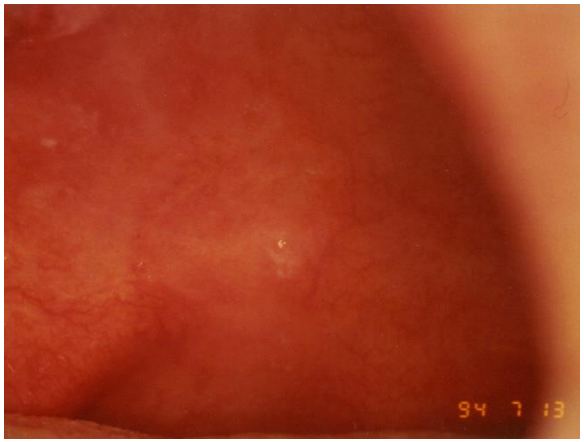
Einzelfälle mit intratumoraler Mistelapplikation

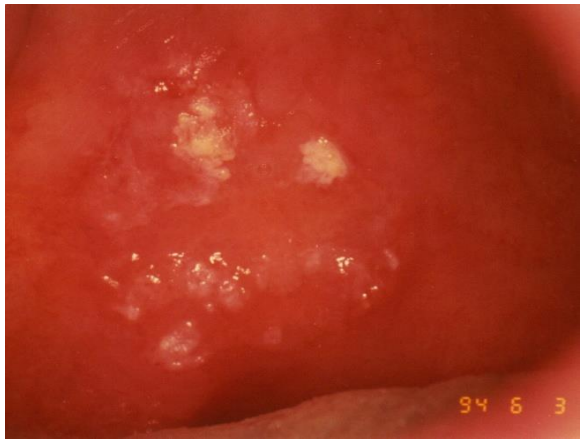
- HCC
- Ösophagus Carcinoma
- Colon Carcinoma
- Oropharynx Carcinoma
- Breast Cancer
- Duodenal Carcinoma
- Merkel Cell Carcinoma
- Cutaneous Squamous Cell Carcinoma

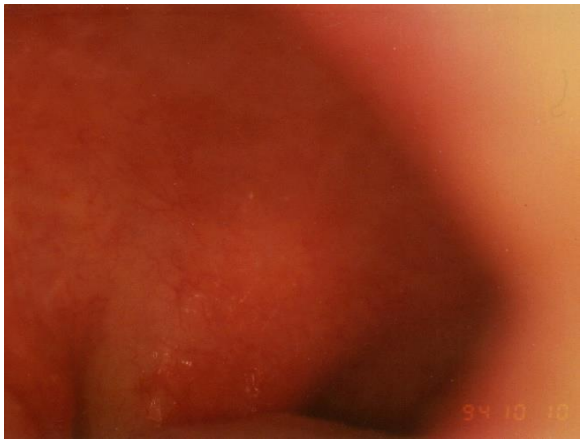
Werthmann PG, Sträter G, Friesland H, Kienle GS. Phytomedicine 2013;20(3):324-327
Orange M, Fonseca M, Lace A, von Laue HB, Geider S. Eur J Integr Med. 2010;2(2):63-69.
Orange M, Lace A, Fonseca M, et al.2009: Eur J Integr Med. 1;223–260
Kröz, M., F. Schad, et al. 2002: Forsch Komplementarmed Klass Naturheilkd 9(3): 160-7
Nabrotzki M, Scheffler A. Die Misteltherapie in der Tumortherapie, KVC Verlag Essen 2001;453-464.
Schad, F., M. Kröz, et al. 1999: Merkurstab 52(6): 399-406
Schad, F., B. Matthes, et al. 1999: Der Merkurstab 52(2): 120-22
Scheffler, A., H. Mast, et al. 1996: Grundlagen der Misteltherapie. Hippokrates Verlag

Intratumorale Mistelapplikation: Oropharynxkarzinom





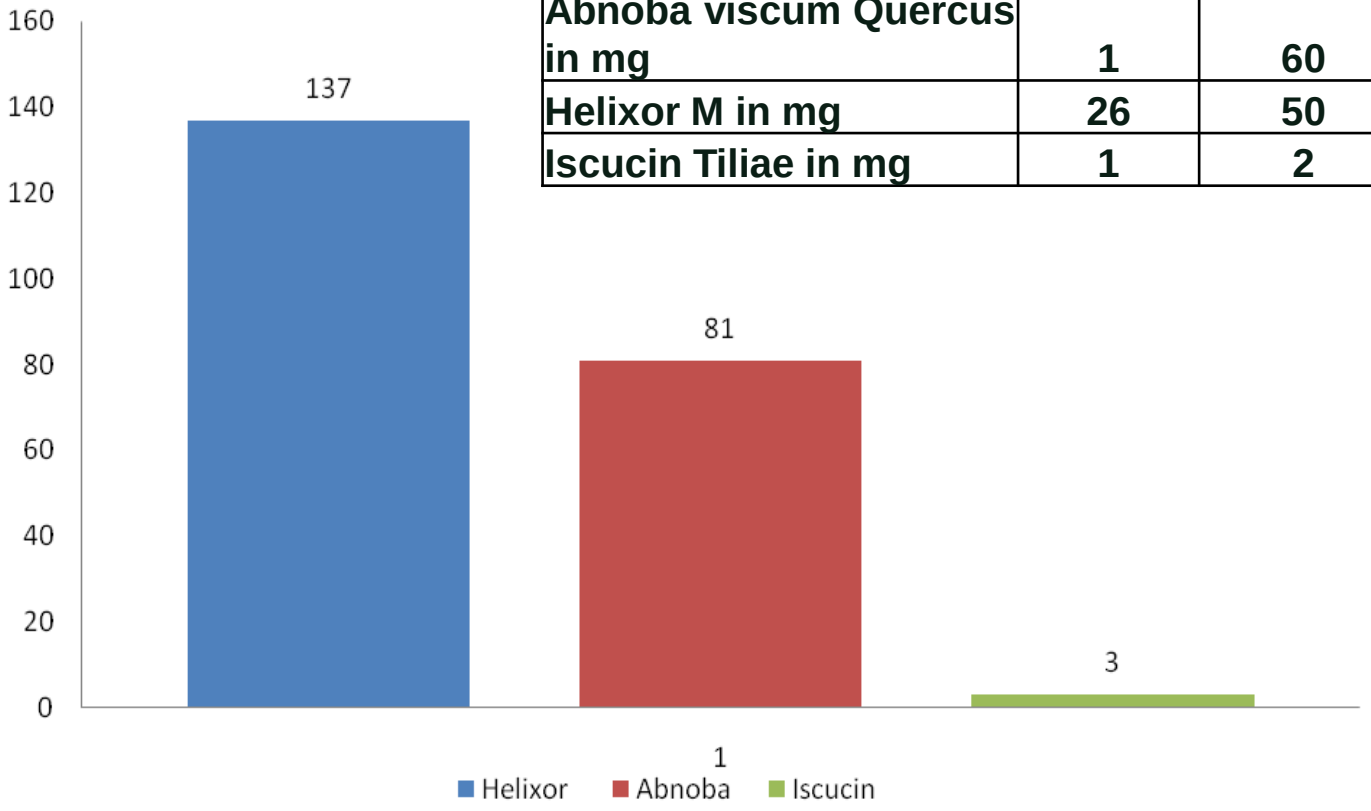




Scheffler, A., H. Mast, et al. 1996: Grundlagen der Misteltherapie. Hippokrates Verlag

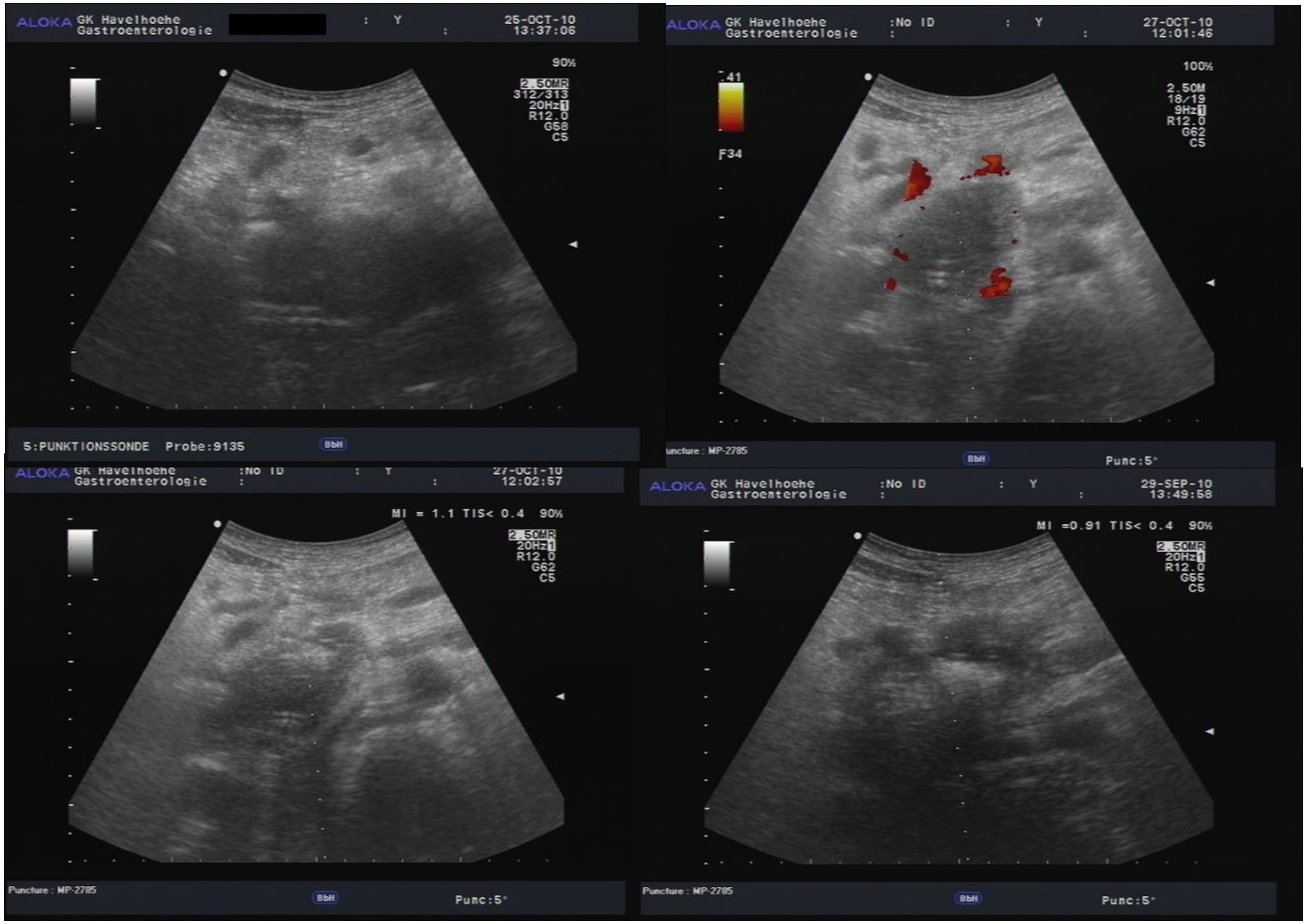
211 intratumorale Applikationen bei 39 Patienten

	n	min	max
Abnoba viscum Fraxini in mg	17	20	160
Abnoba viscum Quercus in mg	1	60	100
Helixor M in mg	26	50	1400
Iscucin Tiliae in mg	1	2	6



F Schad, J Axtner, D Buchwald, A Happe, S Popp, M Kröz, H Matthes: Integrative Cancer Therapies 2013

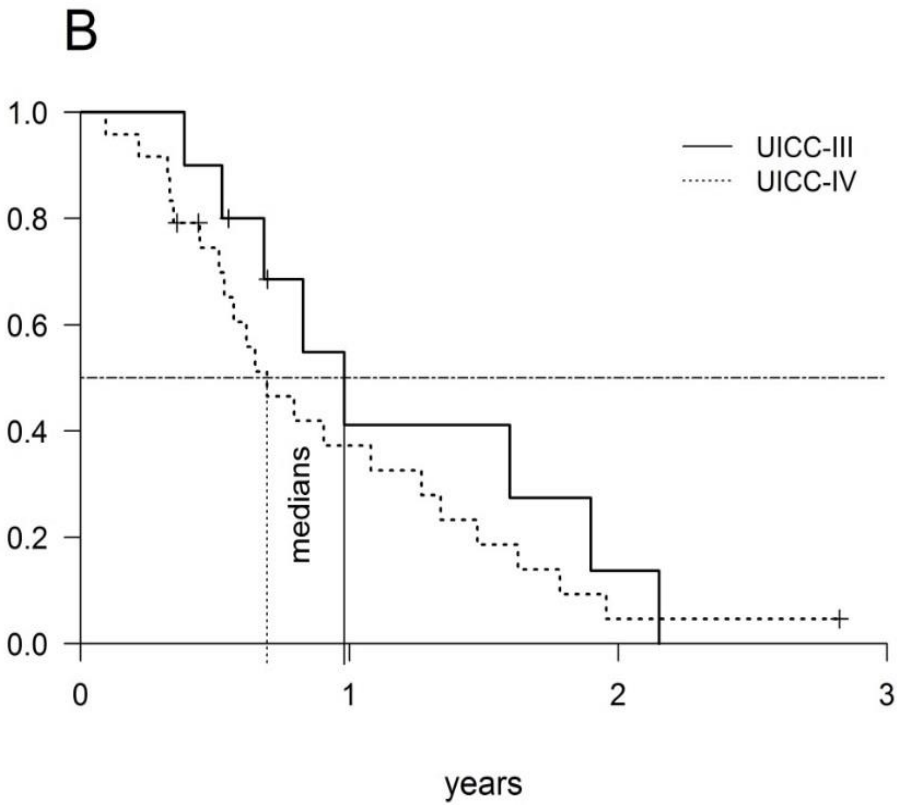
Intratumoral Mistletoe (*Viscum album L.)* Therapy in Patients With Unresectable Pancreas Carcinoma: A Retrospective Analysis



F Schad, J Axtner, D Buchwald, A Happe, S Popp, M Kröz, H Matthes: Integrative Cancer Therapies 2013

UICC stage III = 11,8 (CIlower= 8,2, CIupper= 22.8) months

UICC stage IV = 8,3 (CIlower= 6,4, CIupper= 15,2) months



F Schad, J Axtner, D Buchwald, A Happe, S Popp, M Kröz, H Matthes: Integrative Cancer Therapies 2013

MISTELTHERAPIE BEIM FORTGESCHRITTENEN PANKREASKARZINOM

Ablaufplan

Patienten mit Pankreaskarzinom der Stadien III oder IV
n = 238
Screening, Ein-/Ausschlusskriterien, Informed Consent

↓

Randomisation
n_{max} = 220
Prognose-stratifiziert nach Alter (≤/> 65), UICC (III/IV), ECOG (</≥2)

↙ ↘

Baseline-Untersuchung, Lebensqualität, Labor / Beginn der Intervention

↓ ↓

Gruppe A
Standardbehandlung
"best supportive care"
+ ME
n_{max} = 110

Gruppe B
Standardbehandlung
"best supportive care"
keine weitere Therapie
n_{max} = 110

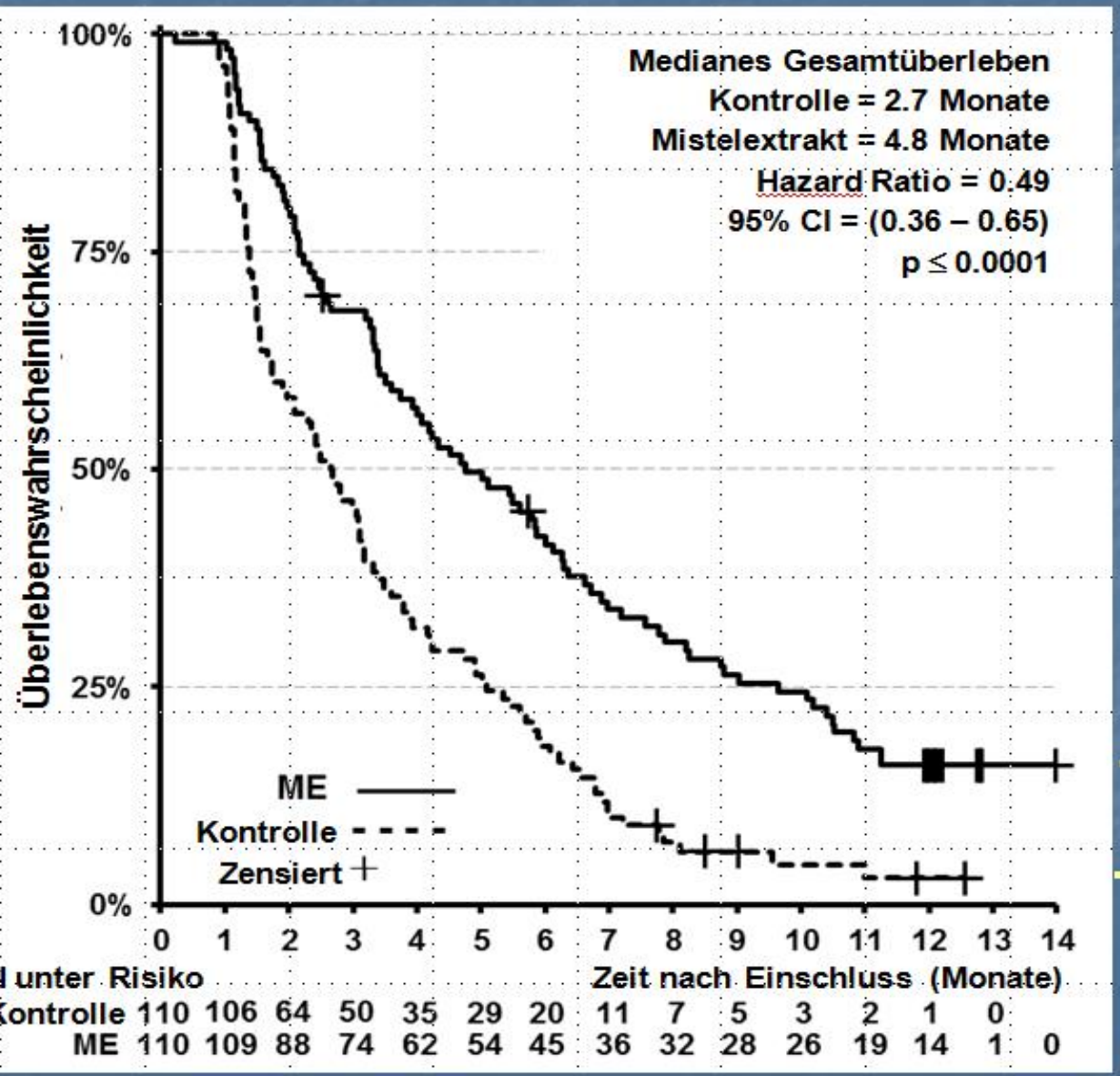
↓ ↓

6 Follow-Up Visiten innerhalb von12 Monaten (Monate 1, 2, 3, 6, 9, 12)
Datenerhebung: Todesdatum, Lokalrezidive und Metastasierung, Lebensqualität, Sicherheitslabor

↘ ↙

Analyse von 220 Patienten:
Gesamtüberleben, Lebensqualität, Unerwünschte Ereignisse

Overall Survival



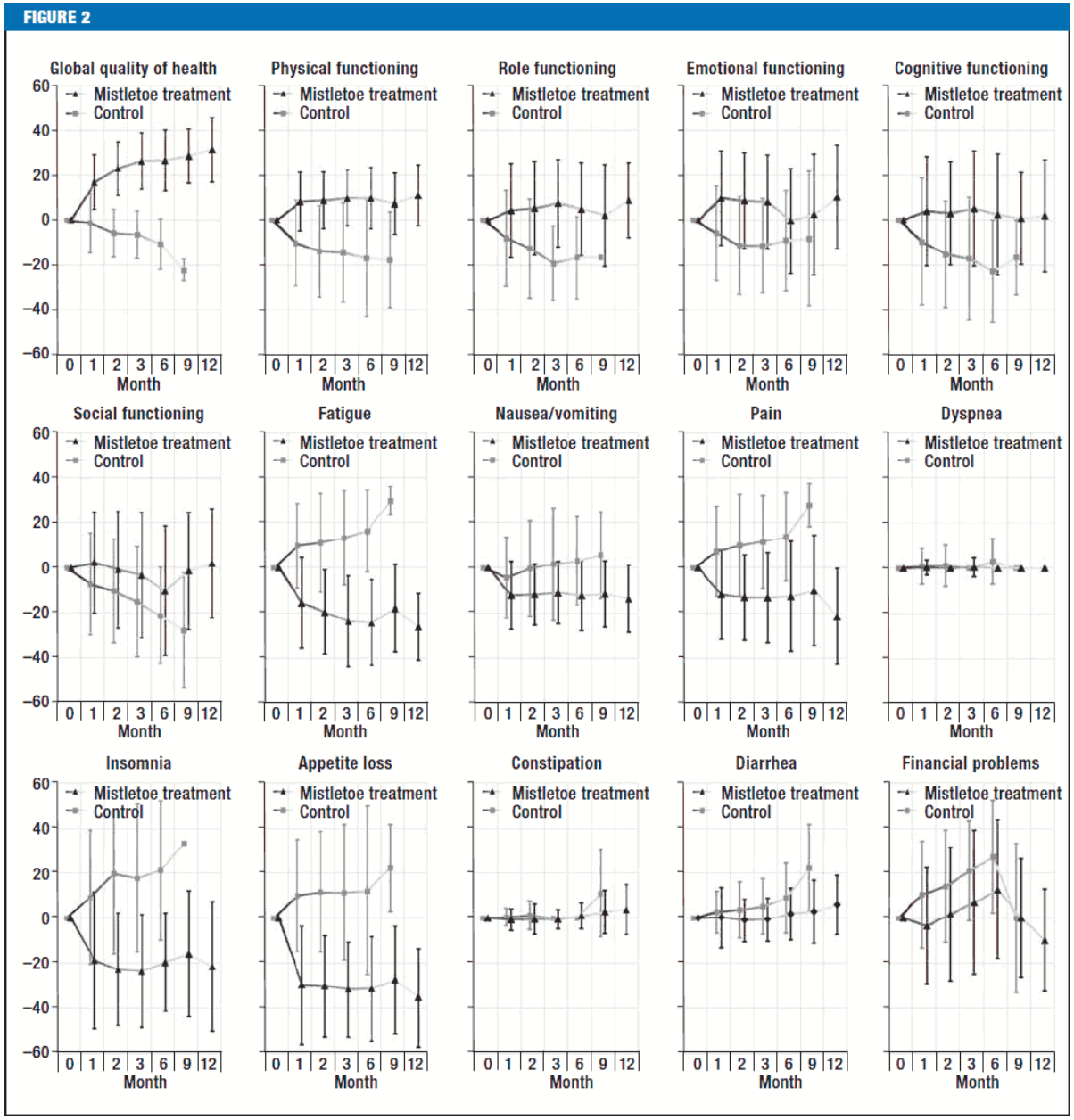
Alle Patienten

12-Monats-Überleben

→ 17 von 110 Patienten (ME)

→ 2 von 110 Patienten (Kontrolle

Cox-Regression, adjustiert auf Prognosestadium



Changes on the 15 quality-of-life scales of the EORTC-QLQ-C30 questionnaire relative to baseline (mean ± standard deviation) in patients with locally advanced or metastatic pancreatic cancer who underwent at least one follow-up examination. 96 patients were treated with mistletoe, and 72 control patients were not. The increasingly pale connecting lines are meant to represent the diminishing number of patients, as seen in *Table 4. The related data tables, along with a further* representation stratified by time of death with corresponding data tables, can be found in the *eSupplement, as can the raw data for the Figures.*

Tröger, W; Galun, D; Reif, M; Schumann, A; Stanković, N; Milićević, M

Quality of life of patients with advanced pancreatic cancer during treatment with mistletoe—a randomized controlled trial

Dtsch Arztebl Int 2014; 111(29-30): 493-502; DOI: 10.3238/arztebl.2014.0493

Axtner et al. BMC Cancer (2016) 16:579
DOI 10.1186/s12885-016-2594-5

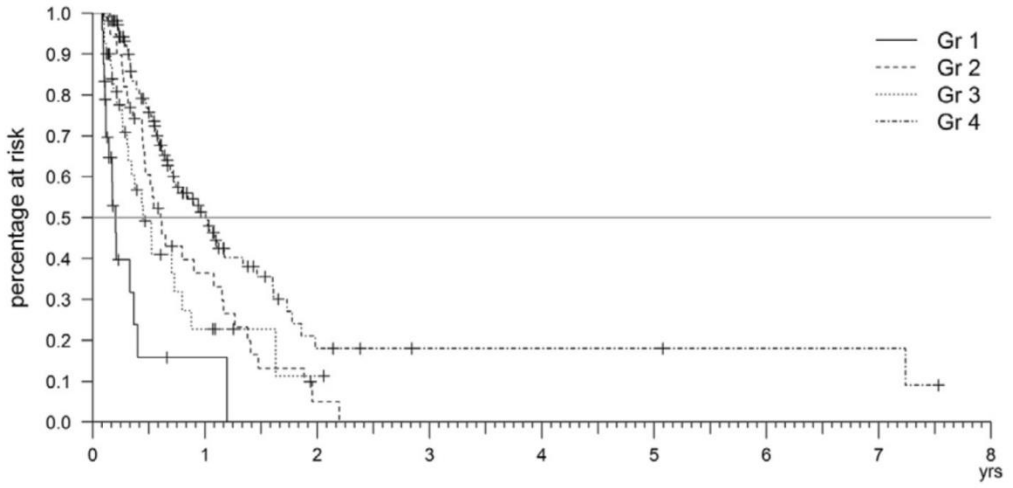
BMC Cancer

RESEARCH ARTICLE Open Access

Health services research of integrative oncology in palliative care of patients with advanced pancreatic cancer

Jan Axtner[1], Megan Steele[1,2], Matthias Kröz[1,3], Günther Spahn[4], Harald Matthes[1,3] and Friedemann Schad[1,3*]

Kaplan Meier Gesamtüberleben, UICC IV



		N	Events	Median [months]	CI [months]
Gr 1:	No or < 1 week VA & no chemotherapy	24	16	2.5	1.7 – NA
Gr 2:	No or < 1 week VA & chemotherapy	40	33	7.3	5.6 – 14.0
Gr 3:	> 4 weeks VA & no chemotherapy	43	23	5.4	3.8 – 10.6
Gr 4:	> 4 weeks VA & chemotherapy	107	57	12.1	8.7 – 17.5

Fig. 4 Kaplan Meier survival based on the UICC IV patients. Stratified for patients receiving no or less than 1 week of VA therapy and those who had it for more than 4 weeks, as well as for patients receiving chemotherapy or not

Patients receiving a combination of chemo & mistletoe therapy lived longer than patients receiving chemotherapy alone (log rank test, χ^2= 5.9, p= 0.0155).Patients receiving mistletoe therapy lived longer than patients receiving no chemotherapy and almost no mistletoetherapy (log rank test, χ^2= 7.5, p= 0.0062)

Axtner, J, Steele S, Kröz M, Spahn G, Mathes H., Schad. F. BMC Cancer 2016

Table 3 Proportional hazard models on patient survival

Covariate	w.mean	Coefficient	Exp (Coef)	SE (Coef)	Wald p
Intercept		1.613		1.730	0.351
Age	64.4	0.021	1.021	0.009	0.024
Male	0.5	0.423	1.540	0.179	0.016
Chemotherapy	0.8	-0.985	0.374	0.196	<0.001
VA therapy	0.9	-0.921	0.398	0.204	<0.001
Number of NPI	4.4	-0.010	0.990	0.032	0.765

'w.mean' is the weighted (against exposure time) means of the covariate; weighted relative frequencies of levels of factors

Axtner, J, Steele S, Kröz M, Spahn G, Mathes H., Schad. F. BMC Cancer 2016

Havelhöhe

Phase III randomized, double blind, multicenter, placebo controlled trial on overall survival and health-related quality of life

Wode et al. EUDRAC 2014-004552-64

- Karolinska University Hospital, & 3 Swedish Cancer Centers
- Inoperable Pancreatic Cancer
- 290 patients
- Iscador Qu vs. Placebo
- Primary: Survival
- Secondary: Quality of life, body weight, costs, safety

And others: Iscador /Gem and Helixor iv. palliative PCa

VEREIN FÜR KREBSFORSCHUNG
Society for Cancer Research, Arlesheim, Switzerland

Mistletoe Extract in the Palliative Therapy of Patients Suffering from Pancreatic Cancer

A multinational, multicentre, prospective, parallel, randomized open label study

(EudraCT No. 2014-002386-30)

Indication

Patients with diagnosis of locally advanced or metastatic adenocarcinoma of the pancreas (UICC stadium III or IV)

No curative surgical resection or radiation possible

Gemcitabine therapy starting within the next 4 weeks

Study Centres (Poland / Bulgaria / Serbia)

Warsaw, Grudziądz, Zielona Góra, Elbląg, Toruń, Konin; Sofia, Vratsa, Plovdiv, Kozloduy, Pleven, Gabrovo, Dobrič, Varna; Belgrade

VEREIN FÜR KREBSFORSCHUNG
Society for Cancer Research, Arlesheim, Switzerland

The following table shows the main characteristics of the actual study.

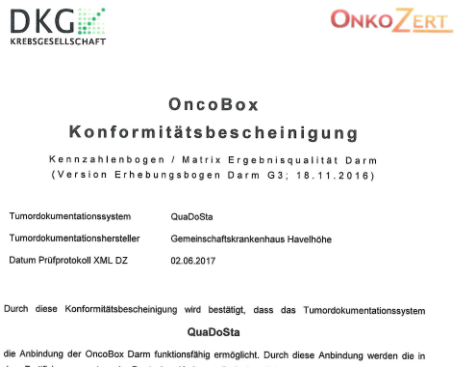
Investigational Product Fermented aqueous extract of the mistletoe plant Viscum album in dosages of 0.01 mg, 0.1 mg, 1 mg, 10 mg, and 20 mg, applied as 1ml s.c. injections three times weekly over maximally 9 months
Study Patients: Main Inclusion criteria 1. Adenocarcinoma of the pancreas (UICC stadium III or IV) 2. Age 18-90 years 3. No curative surgical resection or radiation possible 4. Planned chemotherapy with Gemcitabine Main Exclusion criteria 1. Second primary malignancy in the previous 5 years 2. Previous chemotherapy, other systemic or radiotherapy of current disease 3. Significant weight loss (≥ 20% body weight in the preceding 6 weeks) 4. Known intracranial and spinal tumours and/or metastases
Standard Therapy 1. Chemotherapy with Gemcitabine at 1000mg/m² over 30 minutes i.v. 2. Best supportive care over entire study period
Study Aims Improvement of overall survival and cancer-related fatigue, health-related quality of life, pain symptoms, body weight, neutropenia
Study Centres Poland Warsaw (2 centres), Grudziądz, Zielona Góra, Elbląg, Toruń, Konin **Study Centres Bulgaria** Sofia (4 centres), Vratsa, Plovdiv, Kozloduy, Pleven, Gabrovo, Dobrič, Varna **Study Centre Serbia** Belgrade
Coordinating Investigator Maciej Chwaliński MD, PhD, Szpital św. Elżbiety Mokotowskie Centrum Medyczne, ul. Goszczyńskiego 1, 62-616 Warsaw, Poland

Havelhöhe

Klinisches Register und OnkoZert

- Schnittstelle zum klinischen Krebsregister Brandenburg-Berlin
- www.xml-oncobox.de/de/Home/VerifizierteSysteme

XML OncoBox



DKG KREBSGESELLSCHAFT ONKOZERT

OncoBox

Konformitätsbescheinigung

Kennzahlenbogen / Matrix Ergebnisqualität Darm
(Version Erhebungsbogen Darm G3; 18.11.2016)

Tumordokumentationssystem	QuaDoSta
Tumordokumentationshersteller	Gemeinschaftskrankenhaus Havelhöhe
Datum Prüfprotokoll XML DZ	02.06.2017

Durch diese Konformitätsbescheinigung wird bestätigt, dass das Tumordokumentationssystem

QuaDoSta

die Anbindung der OncoBox Darm funktionsfähig ermöglicht. Durch diese Anbindung werden die in

- www.studybox.de/search

  mit Akkreditierung Netzwerk Onkologie und unserer Datenbank QuaDoSta

  Ethikvotum in 5 Ländern,15 Anfragen

study box

Havelhöhe

Vielen Dank für Ihr Interesse !

Havelhöhe