Table: Mistletoe (Viscum album) for quality of life / treatment-related adverse events in cancer

Source: CAM-Cancer Collaboration. Mistletoe (*Viscum album*) [online document]. Mistletoe | Quality of Life, October 2026.

Review characteristics	PICO of included studies	Results and conclusions	Assessment
Loef M, Walach H. Quality of life in cancer patients treated with mistletoe: a systematic review and meta-analysis. BMC Complement Med Ther. 2020 Jul 20;20(1):227. doi: 10.1186/s12906-020-03013-3.			
Type of review SR with MA **Studies n and design** 26 publications with 30 data sets 25 RCTs, 5 nRCTs, **Search strategy** **Databases** PubMed, Embase, CENTRAL, CINAHL, PsycINFO, Science Citation Index, ClinicalTrials.gov, Google Scholar, OpenGrey, Manual reference list searches Additionally hand searches, Google Scholar and VfK. Search dates not reported. No language restrictions. **Dates** From 1995 to 2019. **Risk of bias / quality assessment** RCTs: Cochrane RoB 2. nRCTs: ROBINS-I.	**Participants** Patients with various cancers. Total participants around 2,500+ across all studies, depending on outcome. **Interventions** Iscador, Helixor, Eurixor, Lektinol, AbnobaVISCUM, others, as adjuvant or sole treatment. **Control** Same oncological treatment without mistletoe (e.g. ctx, rt, surgery, supportive care), placebo injections, active comparators (e.g. lentinan), supportive care alone. **Outcome measures** Quality of life; EORTC QLQ-C30 (n=9), Self-regulation scales (n=6), one or multiple other instruments in the remaining studies: GLQ-8, FACT-G, Spitzer QoL Index, Karnofsky Performance Index, ECOG, **Measure of treatment effect** SMD of the changes from baseline to post-intervention between groups. Reported per outcome and subdomain.	**Results for risk of bias assessment of primary studies included in the review** RCTs RoB2: Most studies are at high risk of bias or of some concern. 65% had an overall high RoB (85% high RoB in the measurement of outcome: lack of blinding w self-reported QoL) All nRCTs had an overall score of 7 out of a maximum of 9. **Certainty of evidence** No GRADE or other formal assessment. **Results for outcome measures** Statistically significant improvement of global QoL, combined SMD d=0.61 (95% CI 0.41–0.81, p<0.00001). QoL dimensions: SMD of seven out of 14 were significant (p≤0.05): role functioning, social functioning, pain, nausea and vomiting, dyspnoea, diarrhoea, financial difficulties. Not significant QoL dimensions: physical functioning, emotional functioning, cognitive functioning, ***fatigue***, insomnia, appetite loss, constipation **Subgroup analysis** Subgroup analyses suggested that the beneficial effect of mistletoe therapy on QoL was generally observed across a variety of study and patient characteristics. Some variation between studies reported regarding factors such as study design, patient characteristics, treatment-related variables, and methodological features but overall conclusion that the positive association remained broadly robust across the examined subgroups **Adverse events** Not assessed **Conclusion**	**Quality assessment of the SR** Moderate to high according to AMSTAR2. Incorporation of RoB into discussion: despite 65% of included studies rated as high RoB, interpretation does not appropriately downgrade confidence based on study limitations. **Comments** Multiple sensitivity and subgroup analyses No GRADE assessment. Safety not reported. Substantial heterogeneity of included studies in terms of all PICO. Subgroup and sensitivity analyses could not account for the heterogeneity. High risk of bias, especially due to lack of blinding. Some studies small or poorly reported. **Funding** Förderverein komplementärmedizinische Forschung*, Arlesheim, Switzerland. **Competing interests** No conflicts of interest declared. * Association for the Promotion of Complementary Medicine Research (not official translation)

© 2026 The CAM Cancer Collaboration. The website cam-cancer.org is managed by Norway's National Research Centre for Complementary and Alternative Medicine

		"Mistletoe extracts produce a significant, medium-sized effect on QoL in cancer. Risk of bias in the analyzed studies is likely due to the specific type of treatment, which is difficult to blind; yet this risk is unlikely to affect the outcome." *Our analysis provides evidence that global QoL in cancer patients is positively influenced by VAE. Because the risk of bias and the heterogeneity is high, future research needs to better assess the actual impact. Large studies in homogeneous patient populations are required to address these problems.*	
Breast cancer Loef M, Paepke D, Walach H. Quality of Life in Breast Cancer Patients Treated With Mistletoe Extracts: A Systematic Review and Meta-Analysis. Integr Cancer Ther. 2023 Jan-Dec;22:15347354231198074. doi: 10.1177/15347354231198074.			
Type of review SR with MA; PROSPERO registered, conducted and reported according to PRISMA **Studies n and design** Sixteen studies (15 publications), thereof 9 RCTs and 7 nRCTs. **Search strategy** Databases Medline, Embase, CENTRAL, ClinicalTrials.gov, Google Scholar, and the Society for Cancer Research database; they also screened two prior systematic reviews. Search date not reported. Assume no language restrictions as in previous SRs. Dates Searches were conducted up to January 2023. **Risk of bias / quality assessment** RCTs: Cochrane RoB 2; nRCTs: ROBINS-I.	**Participants** Breast cancer, any stage. 833 participants (RCTs), 2831 participants (nRCTs). **Interventions** Any mistletoe extract: Iscador (n=4 RCTs), Helixor Eurixor, Lektinol (n=2), unspecified ME; as adjuvant or sole treatment. **Control** Conventional oncological treatment (ctx, rt, surgery) alone (no additional treatment) or placebo + conventional therapy. **Outcome measures** EORTC QLQ-30: 6 studies (3 RCTs, 3 nRCTs) "Self-regulation": 3 studies Clinician reported: 3 nRCTs Remaining studies: Spitzer, FLIC, GLQ—8, FACT-G, "QoL scale". **Measure of treatment effect** SMD of the changes from baseline to post-intervention between group, and 95% CI	**Results for risk of bias assessment of primary studies included in the review.** RCTs, RoB2: Six RCTs were of high RoB, 2 some concerns, and 1 study low RoB. High RoB was mostly due to outcome measurement. nRCTS, ROBINS I: serious RoB in all 6 studies, mostly because of bias due to confounding and measurement of outcome. **Certainty of evidence** GRADE: Moderate for RCTs, very low for nRCTs. **Results for outcome measures** RCTs: medium effect size on QoL with low heterogeneity between RCTs. Estimated pooled effect size is SMD = 0.61 (0.47-0.75). Tendency for methodologically more rigorous studies to yield higher or equally high effect sizes compared to less rigorous ones. nRCTs: SMD = 0.46 (0.1-0.82), high heterogeneity for nRCTs, subgroup analysis indicates outcome measurement (self-administered vs clinician-reported) as factor. **Subgroup analysis** Prespecified subgroup analyses examined blinding status, tumour stage, mistletoe preparation, and risk of bias in the RCTs, while analyses among NRSIs examined differences according to the type of quality-of-life measurement used.	**Quality of SR** According to AMSTAR2 moderate to high. While high RoB of most RCTs is acknowledged and included in GRADE, the results are interpreted by the authors as "clinically relevant" and "support inclusion into current guidelines". **Comments** First meta-analysis focused on a single cancer entity (breast cancer) receiving ME, reducing cross-cancer heterogeneity. Safety not reported. Heterogeneity including cancer stage; QoL scales, blinding, RoB. Use of surrogate parameters for QoL in some studies. **Funding** Stiftung Integrative Medizin & Pharmazie, Stuttgart (Integrative Medicine & Pharmacy Foundation), Germany. **Competing interests** No conflicts of interest declared.

© 2026 The CAM Cancer Collaboration. The website cam-cancer.org is managed by Norway's National Research Centre for Complementary and Alternative Medicine

		Overall, the subgroup analyses showed that the beneficial effect of mistletoe extracts on quality of life was generally consistent across subgroups and supported the robustness of the main findings. **Adverse events** Not assessed **Conclusions** *"Our results indicate a clinically relevant, medium-sized effect of mistletoe extracts on the QoL in breast cancer patients which may be based on the immunomodulating effects of mistletoe extracts during chemotherapy. The limitations of evidence include the risk of bias which is mainly caused by the difficulty of blinding. Further RCTs and real-world evidence need to confirm this result, especially in the setting of neoadjuvant chemotherapy and in breast cancer survivors."*	
Fatigue Pelzer F, Loef M, Martin DD, Baumgartner S. Cancer-related fatigue in patients treated with mistletoe extracts: a systematic review and meta-analysis. Support Care Cancer. 2022 Aug;30(8):6405-6418. doi: 10.1007/s00520-022-06921-x. (Pelzer 2022)			
Type of review SR with MA **Studies n and design** 12 RCTs, 7 nRCTs. **Search strategy** Databases Medline (EuropePMC), Embase, CENTRAL, Clinicaltrials.gov, opengrey.org, VfK. Content experts. **Dates** Inception to October 2020. **Risk of bias assessment** RCTs: Cochrane RoB 2. NRSIs: ROBINS I.	**Participants** 1494 participants RCTs), 2668 participants (nRCTs). Various cancers. **Interventions** Any mistletoe extract: Iscador (n=6), Helixor (n=2), Lektinol (n=2), Eurixor, AbnobaVISCUM, "anthroposophic mistletoe extracts"; as adjuvant or sole treatment. **Control** Conventional oncological treatment, ctx, rt, surgery, hormone therapy; no (additional) treatment; active comparator; placebo. **Outcome measures** Cancer-related fatigue severity or prevalence. EORTC QLQ-30: 12 studies (9 RCTs, 3 nRCTs) Clinician reported: 4 nRCTs Remaining studies: GLQ8 2 RCTs, TCM 1 RCT.	**Results for risk of bias assessment of primary studies included in the review** RCTs: most studies (92%) were at a high risk of bias. Most high-risk judgments were derived from the measurement of the outcome. nRCTs: overall RoB was serious for all studies. Primarily driven by concerns regarding confounding. **Certainty of evidence** No formal GRADE or other assessment. **Results for main outcome measures** RCTs: 14 of 23 SMDs were significant, moderate effect size, SMD–0.48 (–0.82 to –0.14; p = 0.006). nRCTs: OR of 0.36 (0.20 to 0.66; p = 0.0008). **Subgroup analysis** Subgroups were based on factors such as country, cancer type, blinding status, mistletoe extract type, control type, additional treatments, fatigue measurement instrument, risk of bias, baseline fatigue level, study size, and intervention duration. Overall, the subgroup analyses did not identify a clear single factor that reliably explained the substantial heterogeneity observed	**Quality of SR** Moderate to high according to AMSTAR2. One critical domain shows some concern, due to overly confident/optimistic interpretation in light of consistently high/serious risk of bias in included studies. **Comments** High risk of bias 11/12 in RCTs and serious in all nRCTs. Only 2/12 RCTs were double-blind. 6/7 nRCTs were retrospective. No GRADE assessment for certainty of evidence. Small number of trials, small trials. High heterogeneity of included studies. Different fatigue instruments used. **Funding** Society for Cancer Research (VfK*)Arlesheim, Switzerland. Gesellschaft fur klinische Forschung e.V.**, Berlin, Germany.

© 2026 The CAM Cancer Collaboration. The website cam-cancer.org is managed by Norway's National Research Centre for Complementary and Alternative Medicine

	Measure of treatment effect RCTs: SMD 95% CI differences in CRF score changes from baseline to post-intervention between groups. nRCTs: OR	between studies, although differences in population characteristics and study methodology were considered likely contributors. **Adverse events** AEs were reported in 18 of 20 studies. Mean HR 1.20±0.19 (SD) AE per 1000 prescribed doses. Most AEs were local reactions at the injection site, including all grade 3 AEs. Systemic AEs included fever, flu-like symptoms, nausea, diarrhea, hypotension, and acute allergic reaction. **Conclusions** *"Treatment with mistletoe extracts shows a moderate effect on cancer-related fatigue of similar size to physical activity. These results need to be confirmed by more placebo- controlled trials."*	**Competing interests** Society for Cancer Research (VfK*) and Gesellschaft fur klinische Forschung e.V.** are shareholders of Iscador AG, manufacturer of mistletoe extracts. Two of the authors are (part-time) employees of VfK and Iscador, third author Gesellschaft. One author declared no conflict of interest.

Abbreviations
CI – confidence interval
Ctx, rt – chemotherapy, radiotherapy
DFS –disease free survival
HR – hazard ration
MA meta-analysis
MD – mean difference
ME – mistletoe extract
nRCT – non-randomized controlled trial
OS – overall survival
PFS – progression-free survival
PICOS - **P**opulation, **I**ntervention, **C**ontrol, **O**utcome, **S**tudies
RCT – randomized controlled trial
RoB Risk of bias
RR - relative risk
TCM-Traditional Chinese Medicine Index
VfK – Verein fuer Krebsforschung
VfK took over the responsibility for all business units of Iscador.

© 2026 The CAM Cancer Collaboration. The website cam-cancer.org is managed by Norway's National Research Centre for Complementary and Alternative Medicine

References

Loef M, Walach H. Survival of Cancer Patients Treated with Non-Fermented Mistletoe Extract: A Systematic Review and Meta-Analysis. Integr Cancer Ther. 2022 Jan-Dec;21:15347354221133561. doi: 10.1177/15347354221133561.

Loef M, Paepke D, Walach H. Quality of Life in Breast Cancer Patients Treated With Mistletoe Extracts: A Systematic Review and Meta-Analysis. Integr Cancer Ther. 2023 Jan-Dec;22:15347354231198074. doi: 10.1177/15347354231198074.

Pelzer F, Loef M, Martin DD, Baumgartner S. Cancer-related fatigue in patients treated with mistletoe extracts: a systematic review and meta-analysis. Support Care Cancer. 2022 Aug;30(8):6405-6418. doi: 10.1007/s00520-022-06921-x. Epub 2022 Mar 3.

Excluded

Freuding M, Keinki C, Kutschan S, Micke O, Buentzel J, Huebner J. Mistletoe in oncological treatment: a systematic review : Part 2: quality of life and toxicity of cancer treatment. J Cancer Res Clin Oncol. 2019 Apr;145(4):927-939. doi: 10.1007/s00432-018-02838-3. Epub 2019 Jan 23. [low quality according to AMSTAR2]

Cogo E, Elsayed M, Bhardwaj S, Cooley K, Aycho C, Liang V, Papadogianis P, Psihogios A, Seely D. Mistletoe Extracts during the Oncological Perioperative Period: A Systematic Review and Meta-Analysis of Human Randomized Controlled Trials. Curr Oncol. 2023 Sep 6;30(9):8196-8219. doi: 10.3390/curroncol30090595. [QoL not primary outcome]

Hofinger J, Kaesmann L, Buentzel J, Scharpenberg M, Huebner J. Systematic assessment of the **influence of quality** of studies on mistletoe in cancer care on the results of a meta-analysis on overall survival. J Cancer Res Clin Oncol. 2024 Apr 29;150(4):219. doi: 10.1007/s00432-024-05742-1. [low quality according to AMSTAR2]

© 2026 The CAM Cancer Collaboration. The website cam-cancer.org is managed by Norway's National Research Centre for Complementary and Alternative Medicine