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1: Eur J Med Res. 2003 Mar 27;8(3):109-19.

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## Mistletoe in cancer - a systematic review on controlled clinical trials.

**Kienle GS, Berrino F, Bussing A, Portalupi E, Rosenzweig S, Kiene H.**

Institute for Applied Epistemology and Medical Methodology, Bad Krozingen/Freiburg, Germany. Gunver.Kienle@ifaemm.de

**BACKGROUND:** Mistletoe preparations are among the most widely used unconventional cancer therapies in Central Europe. Their clinical effectiveness, however, is controversial. **OBJECTIVE:** To investigate whether prospective controlled clinical trials provide evidence for efficacy of mistletoe therapy in cancer. **DESIGN:** Systematic review. **MATERIAL AND METHODS:** Search of 11 electronic databases, reference lists and expert consultations. Criteria based analysis was performed to assess methodological quality of the studies. **RESULTS:** Twenty-three studies were identified: 16 randomized, 2 quasi-randomized and 5 non-randomized. Cancer sites included breast, lung, stomach, colon, rectum, head and neck, kidney, bladder, melanoma, glioma, and genital. Among these studies, statistically significant positive outcomes were reported for survival (n = 8), tumor remission (n = 1), overall quality of life (QOL) (n = 3), and QOL in relation to side effects during cytoreductive therapy (n = 3). Further, positive trends were reported for survival (n = 8), disease-free-survival (n = 1), and tumor remission (n = 2). Several studies reported no effect on survival (n = 4), disease-free-survival (n = 1), recurrence (n = 2), remission (n = 3), and QOL (n = 1). One study showed a negative trend for disease-free-survival. However, methodological quality of the studies was sometimes far below the standard that is today regarded as optimal or necessary. In view of substantial heterogeneity of the studies and potential positive and negative biases, we considered effect size estimation by quantitative synthesis to be unreliable and decided on a non-quantitative synthesis and discussion. Mistletoe therapy was well tolerated, and no major side effects were noted. **CONCLUSIONS:** Among 23 identified studies evaluated for clinically relevant outcome measures, 12 studies showed one or more statistically significant, positive results, another 7 studies showed at least one positive trend, 3 showed no effect and 1

had a negative trend. All studies, however, suffered from methodological shortcomings to some degree, and many of the studies are not conclusive. As several reasonably well conducted studies indicate beneficial effects, further properly designed trials should be encouraged. Future controlled studies should take into account the methodological limitations and potential biases of these past mistletoe trials.

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