Mistletoe in Cancer – an Overview 2014

Mistletoe extracts (*Viscum album* L., VAE) are among the most widely used integrative cancer care treatments, particularly in Europe [1-5]. They are an old herbal remedy [6,7], but were introduced into cancer treatment in 1920 by Rudolf Steiner and Ita Wegman, founders of Anthroposophic Medicine [8]. Viscum album is a hemiparasitic shrub, growing on different host trees. Different mistletoe preparations are available for the treatment of cancer (currently Abnobaviscum®, Helixor®, Iscador®, Iscucin® and Lektinol®). They are available from different host trees such as oak, apple, pine and others. They are applied parenteral, particularly subcutaneously, but also intravenously, intratumorally, intrapleurally, intraperitoneally and else.

Several pharmacologically active compounds have been isolated from VAE, such as mistletoe lectins (ML I, II and III) [9], viscotoxins [10,11], oligo- and polysaccharides [12,13], lipophilic extracts [14] and various others [6,7]. The most prominent properties of VAE are their cytotoxic and growth-inhibiting effects, *in vitro*, on a variety of human tumour cell lines, lymphocytes and fibroblasts [6,7] . The cytotoxic effects of VAE are mainly due to the apoptosis-inducing mistletoe lectins [15-17], while the viscotoxins induce necrotic cell death [16,18]. VAE are also recognized for their immune-modulating activity: *In vitro* and *in vivo* studies have demonstrated activation of monocytes/macrophages, granulocytes, natural killer (NK) cells, T-cells (especially T-helper-cells) and the induction of various cytokines [6,7]. VAE also possess DNA stabilizing properties, they reduce chromosome damage and improve DNA repair [19-22]. VAE show antiangiogenetic effects [23]. In animals, VAE displays potent antitumor effects when administered either directly into the tumour or systemically [6,7,24].

Clinical effectiveness of mistletoe extracts in cancer has been investigated in a great number of studies, among these 43 prospective randomized controlled trials [25-71]: They predominantly report significant clinical benefits. With regard to quality of studies and consistency of results, the best evidence concerning efficacy of mistletoe therapy exists for the improvement of *quality of life* and *improved tolerability of cytoreductive therapies* (chemotherapy, radiotherapy, surgery) [72,73]. Regarding *survival,* a well-designed randomized controlled trial has recently shown a highly significant benefit in advanced pancreatic cancer [26]. Other studies showed similar results [74-77]. Effectiveness seems to depend on the duration of the mistletoe therapy, in addition to factors relating to dosage, host tree and choice of preparation. *Tumour remissions* have been repeatedly observed after local application of high dose mistletoe extracts. This finding is consistent with the preclinical research on cytotoxicity and treatment of tumors in animals. During customary low-dose mistletoe therapy, tumour remissions are rare exceptions. Tumor remissions have therefore been reported primarily in case series and single cases. (e.g. [24,78-85])

Highly individualized and comprehensive treatment – individually adjusted and selected dosage, preparation, host tree, injection site, rhythm of administration, and supplementation with other interventions – is regarded to lead to far better health outcomes, according to highly experienced practitioners. This still needs to be investigated. [86,87]

Clinical application of mistletoe extracts is safe, even in high dosages [6,8,88-91].

22. August 2014 – Dr. med. Gunver S. Kienle, IFAEMM Freiburg, gunver.kienle@ifaemm.de

Enclosed, exemplary literature:

1. Tröger W, Galun D, Reif M, Schumann A, Stankovic N, Milicevic M: **Quality of life of patients with advanced pancreatic cancer during treatment with mistletoe—a randomized controlled trial.** *Dtsch Arztebl Int* 2014, **111:**493-502
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