



The Importance of Elm Mistletoe in the Therapy of Malignant Pleural Mesothelioma

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Abstract

Despite improved surgical techniques and the addition of tyrosine kinase inhibitors, only a few therapeutic advances were achieved in the treatment of pleural mesothelioma. This seems to be different if the mistletoe of the elm is used either partially or primarily. All 8 patients treated in practice in the last 13 years are documented. Median survival increases to more than five years.

Keywords: Pleural mesothelioma; Elm mistletoe; Iscador U.c. Hg

Case Series

Pleural mesotheliomas are rare and account for less than 1% of all cancers. The therapy of pleural mesothelioma remains a difficult challenge. A review by Neumann et al. [1] concludes survival times of 4 months to 12 months on average. The percentage of people with a survival time of more than five years is 8% on average in the United States. Pleural mesothelioma is the worst of all types of cancer after pancreatic cancer (7%) [2]. Paul Kraus [3], a Holocaust survivor diagnosed in 1997, is considered the longest currently living (as of 2019) mesothelioma survivor in the world [3]. Survival time increase only slightly with an extra pleural pleuropneumectomy, chemotherapy alone or radiotherapy. However, survival currently seems to improve with the addition of the checkpoint inhibitor Durvalumab. 54 patients who had not previously been irradiated received the combination treatment of chemotherapy and PD-L1 blockers for a maximum of six cycles, after which they continued treatment with Durvalumab alone-until the disease progressed further, or for a maximum of one year.

After six months, an initial evaluation showed that the disease had not progressed in 71 percent of patients treated with Durvalumab. The therapy proved to be relatively well tolerated [4]. However, at the moment it is unclear how substantial the actual survival benefit will be under this therapy.

Therefore, allow me to recall a therapy method with an "old-timer" of cancer therapy: mistletoe. However, it is not mistletoe per se, but more precisely the elm mistletoe, which shows unexpectedly impressive qualities in this disease. These have been known with regard to lung cancer for some time, but have never been consistently followed up in studies [5,6]. The effect on lung cancer, especially in smokers, is already considerable, but its specific effect seems to be on pleural mesothelioma. Allow me to therefore briefly introduce all patients with this diagnosis who have been treated by me in the last 13 years and who have received supplementary or even exclusive therapy with elm mistletoe Iscador U.c. Hg. I was able to find eight patients in my database.

According to the retrieved data, I have often been able to achieve survival times of five years or more. With all due caution, a therapy concept seems to have been found here that is waiting for confirmation in the next few years. The therapy is simple, does not require treatment in specialized medical centers and can therefore be carried out regularly in family doctors' practices.

Patient 1

75-year-old patient with a malignant pleural mesothelioma of the epithelioid type, cytokeratin 5/6 positive, strongly calretinin positive, negative for SP-A and TTF-1. April 2006 the diagnosis of a malignant pleural mesothelioma with formation of a hand-width pleural effusion was made. Negative for SSP-A and TTF-1 in the pleural puncture, but the tumor cells show a membrane-bound reaction with the antibody against EMA. They are partly moderately to strongly vimentin-positive, clearly cytokeratin 5/6 positive and strongly calretinin positive. Constant coughing. Non-smoker.

Patient received s.c. injections with elm mistletoe Iscador U.c. Hg Series II 2-3x/week since 07/2006 alternating with oak mistletoe Iscador qu. Series II.

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Under mistletoe therapy, the patient developed pneumonia with fever and severe swelling after a few days [7,8]. The pleural effusion increased to up to two hand widths.

Yet he refused a pleural drainage. We actively waited and checked the course of the disease every fortnight by chest X-ray. After four months the effusion was declining and has not been detectable since November 2006. Being an allergy sufferer, he reacted very sensitively to the mistletoe compound even years later, and so the mistletoe injections had to be paused in November 2006. As of November 2006, he continued to inject both types of mistletoe at a reduced frequency (instead of 2x/week now 2x/month) for several years. On a visit 6 years later, he reports unchanged well-being. After a last consultation with the daughter (internist) July 2019, the patient lives unchanged, but now suffers from dementia at the age of 88.

Patient 2

A 66-year-old patient with a pleural mesothelioma ED January 2008 and partial pleural resection and talcum pleurodesis. Histologically malignant pleural mesothelioma, positive for calretinin, cytokeratin 5/6, cytokeratin 8; negative for TTF1, HEA 125, proliferation marker K167 with a focal proliferation rate of 10%. Six cycles of chemotherapy with Cisplatin/Pemetrexed. Irradiation of the thoracic drainage outlet.

Patient worked in the car industry and had contact with asbestos for years. For four years there was right-thoracic pain, especially after physical exertion. Negative history of allergy and nicotine. No night sweats or weight loss. The CT reveals a large space-demanding pleural effusion on the right and suspected pleural mass in the upper and especially in the lower field. In January 2008 the parietal pleura was partially resected and a talcum pleurodesis performed.

Since March 2008 the patient has been consistently receiving mistletoe therapy with Iscadur U.c. Hg Series II 2x/week and fir mistletoe ISCUCIN ABIET is with a concentration of F 1x/week. From January 2008 to March 2009 6 cycles of chemotherapy with Cisplatin/Pemetrexed. He soon feels very well again and has been back in action since autumn 2008. Only a CT control December 2010 gives rise to the suspicion of renewed growth, so that now and in the following years the chemotherapy is repeated as required. April 2017 he dies. Until then the consistent implementation of mistletoe therapy had remained unchanged and, according to his wife (telephone call 08/19), he enjoyed an excellent quality of life for many years.

Patient 3

In the 53-year-old patient, a pleural mesothelioma with extensive involvement of the parietal/vi cellular pleura and the diaphragm had been diagnosed March 2011. Resection of the visceral pleura April 2011 after a complete pleurectomy and partial diaphragm resection and refixation. Histological mesothelioma of the epithelioid type, cat. A hyperthermic intrathoracic chemotherapy with Cisplatin and Doxorubicin April 2011 as well as radiotherapy of the thoracotomy scar and stitch channel radiation. Among these, no progression from April 2011 to June 2014. June 2014 low growth of pleural metastases and the decision to start mistletoe therapy.

From 03/2015 on, consistent implementation of mistletoe therapy with U.c. Hg. series II 2x/week. Supplement Bryonia/Stannum WALA 2x daily 5 to 10 globuli. This was initially followed by a palm-sized swelling at the injection site, which subsided as time went on. Two thousand fifteen to two thousand sixteen (2015-2016) he felt very comfortable under this therapy. According to his wife's statement on

the phone (August 2019), the progress then slowly increased. He died December 2018.

Patient 4

70-year-old female patient with unilateral pleural effusion on the left-hand side September 2014. December 2014: multiple small foci of an infiltratively growing mesothelial proliferation in the excised tissue sample of the visceral pleura. Positive with Calretinin and WT 1 as evidence of mesothelial origin, negative for BerEp4. Positive for GLUT 1 on the papillary structured parts. Diagnosed with highly differentiated pleural mesothelioma. She received a talcum pleurodesis and from October 2014 to March 2015, 5 cycles of Pemetrexed/Cisplatin.

Since January 2015 consistent administration of elm mistletoe Iscadur U.c. Hg 2-3x/week s.c. No changes in findings up to the last PET-CT February 2019 and a good and stable quality of life until the last consultation December 2019.

Patient 5

A 70-year-old female patient (epithelioid pleural mesothelioma) had been primarily treated with 2 cycles of Cisplatin and Alimta in October 2008. This was followed by a pleuropneumectomy on the left November 2008. The patient had already been prescribed Iscadur P by her pulmonologist from approx. January 2009 onwards. This she injected 3 times a week.

At first contact in the office May 2010, 19 months had passed. Now skin metastases appeared and the PET-CT showed nodular compressions of the right lung. The switch from pine to elm mistletoe was of limited value here, as increasing pain, shortness of breath and night sweats occurred from July 2010 onwards. Then change to the lime mistletoe *Iscucutilliae* C 2x/week s.c., *Arandisit* D15 ampoules Weleda 2-3x/week s.c. and *Bryonia/Stannum* 2x-3x daily 5 to 10 globuli. However, no real improvements were noticeable here either. She died in spring 2011, after a total of about 2.5 years.

Patient 6

In this 73-year-old patient an extensive sinistral partially epithelioid intrathoracic and intraabdominal pleural mesothelioma was found in August 2017. A comprehensive surgical therapy with partial pleurectomy and diaphragm reconstruction followed. The surgeon was not able to remove all parts of the tumor, especially between the 10th and 11th rib.

Upon the sole injection of elm mistletoe 2x/week s.c., a slight regression of the tumor was found in CT after one year of therapy, which continues to this day (January 2020). Patient is stable, continues his work as a weaver and seldomly complains about limitations 2.5 years after the initial diagnosis.

Patient 7

A 82-year-old female patient with epithelioid pleural mesothelioma October 2016 accompanied by a primary pleural effusion on the right side. Condition after a breast carcinoma on the left with irradiation 1998 and squamous cell carcinoma of the skin 2015.

Talcum pleurodesis Tumor pos. for Calretinin and Podoplanin with negativity for TTF1. No chemotherapy. December 2016 introduction of mistletoe therapy with Iscadur U.c. Hg. series I 2x/week, Series II 2x/week afterwards. March 2017 switch to pine mistletoe Iscadur P.c. Hg. series II in an external clinic and the

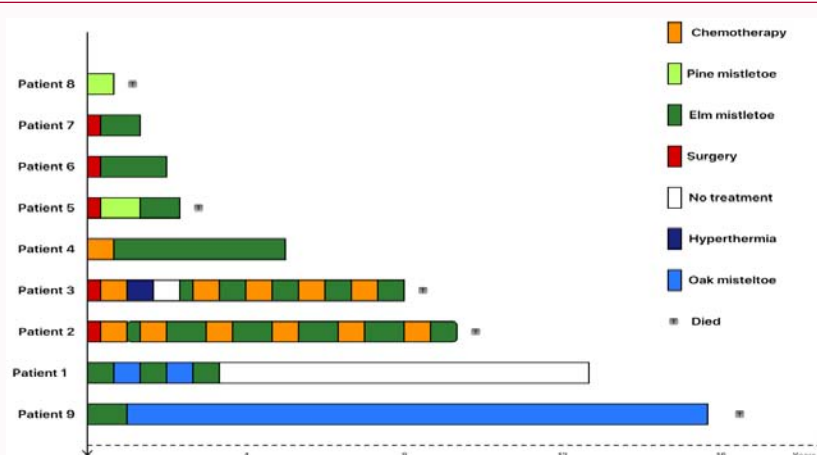


Figure 1: Graphically slightly simplified presentation of survival times and essential therapies.

Christmas rose [7] *Helleborus niger* aquos. Helixor D6 2x/week s.c. Last contact December 2017, no further information after that. Thus at least 14 months of survival.

Patient 8

A 51-year-old Turkish patient with an epithelioid pleural mesothelioma. She came for the first consultation in August 2016. No papers and concrete findings in this case. Pleural effusion on the right-hand side since April 2016. Patient received Helixor P serial pack I 2x/week as well as the Christmas rose [7] *Helleborus niger* D12 Helixor. Last phone contact January 2017, further inquiries remained unanswered. Thus about 6 months to 8 months of survival.

Patient 9

My good experiences with pleural mesothelioma, and especially the elm mistletoe, have not remained my own solely. I received the following casuistry from Dr. Frank Meyer, general practitioner in Nuremberg: Former car mechanic (exposure to asbestos) born 1924 (Figure 1).

Conventional therapy: On 21st October 1998 Attempt of pleurodesis with talcum, 30th November 1998 to 14th January 1999 and 16th February 1999 to 3rd March 1999 palliative radiotherapy of the left thoracic wall in the vicinity of the puncture site, up to 70Gy total, Aim of the radiation therapy: Preventing the carryover of tumor cells through pleural puncture.

Mistletoe therapy: From 13th January 1999 Iscadur U.c. Hg, beginning with 0.01 mg s.c., dose increase to a final maintenance dose of 60 mg in August 1999 at 3 x/w. s.c. injections with varying dosages of 30 mg to 60 mg (weekly dose up to 120 mg; Monday 30 mg, Wednesday 30 mg, Friday 60 mg). From April 2000 transition to Iscadur Qu 5 mg special, initially 3 × 1 ampoules, later 3 × 2 ampoules. From September 2009 optimization of the therapy by increasing the dose on Iscadur Qu 20 mg 3 × weekly 1 ampoule (will continue until death). Concomitant disease multiple basal cell carcinomas: From April to December 2000, a basal cell carcinoma of approx. 2 cm × 3 cm on the left breast and a basal cell carcinoma of approx. 1 cm × 1 cm on the left forehead receded under Iscadur injections. The excision advised by the dermatologist thereby became superfluous. Quote: "The development of the external ulcer on the chest is particularly impressive for me; I was able to follow the regression from injection to injection. For me as a layperson, this was the proof of it working". - CT-Thorax 12th December 2001, follow-up

examinations by professional radiation specialists, last on 9th January 2002: "Stable tumor situation to weight increase from 79 kg to 83 kg (176 cm), no complaints except for slight stress dyspnoea, can walk straight for 3 h to 4 h without restrictions. Regular holidays in the mountains. Stroke on 29th October 2002 (basal ganglia infarction on the right with hemiparesis on the left, trigger probably embolism during atrial fibrillation), since then Marcumar. Self-injection of Iscadur Qu 5 mg special during the clinic treatment and the follow-up treatment. Fully mobilized since January 2003. Patient can walk short distances with only the assistance of a cane died of a stroke in September 2014.

Results

In general, Schad et al. [9] was able to demonstrate that bronchial carcinomas benefit from mistletoe therapy. Mistletoe therapy is not just mistletoe therapy, however, but depends very much on the tree selected [10]. For many years, the elm mistletoe has been my daily companion for lung tumors. It has proved its worth to me and leads to considerable survival times even in stages III and IV [5,6]. Patients suffering from pleural mesothelioma seem to benefit specifically from the treatment with elm mistletoe and should therefore be treated more regularly.

Conclusion

In the therapy of pleural mesothelioma, a malignant tumor of the pleura with an unfavorable prognosis, progress has recently been made in the treatment of this disease with the addition of tyrosine kinase inhibitors and checkpoint inhibitors. Surprisingly, mistletoe from the elm (Iscadur U.c. Hg.) seems to be even more successful in this tumor entity. All eight patients treated in the practice over the last 13 years are documented. The median survival increases to more than five years.

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