The Havelhoehe Protocol

for intratumoural mistletoe infiltration into the mucous membranes of the gastrointestinal tract and the liver

OFF-LABEL-USE

Therapeutic regime

1. Treatment

Requirements:

It is necessary to ensure that the patient is in a sufficiently good general condition (ECOG [*Eastern Co-operative of Oncology Group*] score 0-2). In advanced medical conditions associated with tumour cachexia or severe pain, this form of treatment may place too much strain on the patient and possibly even make their general condition worse. In such cases, intravenous administration of mistletoe should be considered.

Indications:

- Locally advanced, inoperable oesophageal carcinoma
- Locally advanced, inoperable gastric carcinoma
- Locally advanced, inoperable duodenal carcinoma
- Locally advanced, inoperable hepatocellular carcinoma
- Locally advanced, inoperable cholangiocellular carcinoma
- Hepatic metastases of other tumour entities in selected cases
- In-growth and over-growth of stented tumour stenoses

Premedication:

Treatment is usually conducted with the patient under propofol sedation.

Preparation and dosage:

Induction for mucosal tumours, depending on their size:
abnobaVISCUM Fraxini 20-40 mg i.t. day 1
abnobaVISCUM Fraxini 40-80 mg i.t. day 3
abnobaVISCUM Fraxini 60-120 mg i.t. day 5

Induction for hepatic lesions:
abnobaVISCUM Fraxini 40 mg i.t. day 1
abnobaVISCUM Fraxini 80 mg i.t. day 3
abnobaVISCUM Fraxini 120 mg i.t. day 5

Consolidation:
abnobaVISCUM Fraxini, dosed individually (depending on the patient's reactions during the induction phase; if well tolerated, further increase, e.g. abnobaVISCUM Fraxini 160 mg) i.t. day 29, repeat every 4-6 weeks or even every 14 days in cases with luminal obstruction, with the intention of achieving rapid tumour destruction.
The dose increase may be given using the stated regime, provided the previous application was well tolerated and the rise in temperature was ≤ 2.5° C or the maximum temperature reached was ≤ 39.0° C.

Method of application:

Each time, the mistletoe preparation is diluted with NaCl 0.9% to 10-20 ml (2 x 10 ml), depending on the size and consistency of the local finding.
The diluted mistletoe preparation is to be shaken well before application until no more air bubbles appear in the suspension. This ensures good ultrasound confirmation of intratumoural mistletoe administration during application. Under ultrasound guidance, the needle is to be introduced as far as the posterior margin of the lesion and the mistletoe suspension applied continuously while the needle is withdrawn. Infiltrated with mistletoe, the entire tumour appears white under ultrasound guidance due to the bubbles, rendering a good demonstration of the distribution of the injected solution. Intratumoural application of the mistletoe preparation should be performed several times in a fan-shaped pattern if its distribution is difficult due to firm fibrous/septated tumour tissue or in cases of hepatic lesions.
A “large” puncture needle is to be used to treat oesophageal carcinomas. It should be borne in mind here that, basically, an oesophagotracheal fistula may develop, which should be absolutely avoided.

2. Clinical course

Rises in temperature of around 1-1.5° C or fever > 38.5° C are commonly observed in the evening and during the night after injection. At the next application, each subsequent dose should also be based on the level of fever and the patient’s general condition (e.g. exhaustion). If the medication is well tolerated and if a temperature response is absent or low, the dose should be increased.

3. Effect

An inflammatory response is induced which can result in a transient, and possibly painful, oedematous enlargement of the tumour. The febrile reaction as an expression of an immunological response associated with antigen presentation, phagocytosis and apoptosis promotion of the tumour cells is desired – provided it is well tolerated by the patient – and should not be suppressed or lowered pharmacologically.

4. Management of adverse reactions

– A (dose-dependent) pseudoallergic reaction may be triggered in patients with an allergic disposition or who have undergone previous mistletoe treatment.

– Any possible transient pain in the area of the injection site may be treated with ½ ampoule Dipidolor [*piritramide*] i.v. If excessively severe pain developed during a previous injection, then Dipidolor may also be administered as premedication. NSAIDs and novaminsulfon are undesirable because they suppress the inflammatory response to mistletoe administration.

– Attention should be paid to any possible development of transient dysphagia secondary to post-interventional swelling when treating oesophageal carcinomas.

References:

Steele ML, Axtner J, Happe A, Kröz M, Matthes H, Schad F. Use and Safety of Intratumoral Application of European Mistletoe (Viscum album L) Preparations in Oncology. Integrative Cancer Therapies. 2014:1-9.

Friedemann Schad, Jan Axtner, Dirk Buchwald, Antje Happe, Stephan Popp, Matthias Kröz and Harald Matthes 2013; Intratumoral Mistletoe (Viscum album L) Therapy in Patients with Unresectable Pancreas Carcinoma: A Retrospective Analysis.
Integr Cancer Ther. Published online 19 December 2013. DOI: 10.1177/1534735413513637.

F. Schad, D. Buchwald, A. Merkle, S. Popp, M. Kroez, H. Matthes 2011; Retrospective analysis of patients with advanced pancreatic cancer under palliative treatment and additive intratumoral application of viscum album L.
2011 ASCO Annual Meeting, J Clin Oncol 29: 2011 (suppl; abstr e14538).