ABNOBA

The Havelhoehe Protocol

for intratumoural mistletoe infiltration of the pancreas

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.

Premedication and technical equipment:

The best access route (transabdominal or transgastral/duodenal with endoscopic-ultrasound guidance) is to be chosen under propofol sedation. A transabdominal approach is possible in the majority of cases (90%), with only 10% requiring puncture under endoscopic-ultrasound guidance. A needle with a diameter of 0.95 mm is recommended for transabdominal puncture, while a needle with a diameter of 1.2 mm should be used for hard pancreatic carcinomas. A 19 G needle is to be used for endoscopic-ultrasound guidance. Transabdominal puncture may be technically more difficult in patients with a high-riding or severely distended transverse colon or a postoperative situs, e.g. with a history of PPPD (pylorus-preserving pancreaticoduodenectomy), etc. Nevertheless, application is occasionally possible and the decision to treat is to be made after exploratory ultrasound.

Preparation and dosage:

Induction:
abnobaVISCUM Fraxini 40 mg i.t. day 1
abnobaVISCUM Fraxini 80 mg (or 60 mg) i.t. day 3
abnobaVISCUM Fraxini 120 mg (or 80 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

In cases undergoing parallel palliative chemotherapy with **Gemcitabine** (day 1, 8 and 15, repeat day 29), mistletoe instillation is administered on day 22.

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; if possible, the volume should be > 10% of the tumour volume. 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 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.

2. Clinical course

Rises in temperature of around 1-1.5° C are commonly observed in the evening and during the night after injection. Fever > 38.5°C develops in only approx. 10% of patients. 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.
So far, approx. 60 patients have been treated in this way at the Havelhoehe Community Hospital, with 1 - 20 applications carried out in each case. Fever or increased temperature occurred in 11% of patients and altogether in 20% of all injections.

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. In some patients, peritoneal irritation after the intervention, associated with nausea or vomiting, may develop in connection with the i.t. application of mistletoe. Here too, one ampoule of MCP [*metoclopramide*] as premedication in the form of a short infusion can also alleviate this effect.

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