Hepatocellular Carcinoma (HCC)
Intralesional Therapy with
Viscum album (Mistletoe)

Case Documentation Sheet

Stamp of the Investigator/Hospital

Pat. Initials: ☐ First name ☐☐ Surname

Pat. No.: ☐

Contents

Intralesional HCC therapy

Initials: ☐ Firstn. ☐☐ Surn. Pat. No.: ☐☐☐☐☐ Today's date: ☐☐ Day ☐☐ Month ☐☐ Year

1.1 Basic documentation

Date of birth ☐☐ Day ☐☐ Month ☐☐ Year Sex M ☐ F ☐

Height (cm) ☐☐☐ Weight (kg) ☐☐☐.☐

Karnofsky score at the beginning of il. MT*: _____ % (see appendix page 1/3)

Type of documentation: ☐ 0 retrospective ☐ 1 prospective ☐ 2 retro-/prospective

prospective since: _____

2.1 Tumour diagnosis

Diagnosis _____

Initial diagnosis (ID) ☐☐ Day ☐☐ Month ☐☐ Year

Tumour stage at initial diagnosis _____ ☐ Not known

Current tumour stage***

T | N | M *or* UICC class. I | II | III | IV

Current metastasis** ☐ PUL ☐ OSS ☐ HEP ☐ BRA ☐ LYM ☐ MAR

☐ PLE ☐ PER ☐ ADR ☐ SKI ☐ SPL ☐ GEN

Other metastasis _____

Histology _____

☐ No cytology

Grading (I – III) _____

If liver cirrhosis please Child-Pugh classification*** at start of il. MT: _____

* il. MT = intralesional mistletoe therapy

**Metastasis abbreviations: PUL = lung, OSS = bone, HEP = liver, BRA = brain, LYM = lymph node, MAR = bone marrow, PLE = pleura, PER = peritoneum, ADR = suprarenal, SKI = skin, SPL = spleen, GEN = general metastasis

*** See appendix

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1.3 Patient anamnesis

☐ none

Current and chronic concomitant illnesses, previous operations

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____

If the patient has hepatic cirrhosis please state the cause:

☐ Alcohol

☐ Viral: Hepatitis A, B, B/D or C (genotype?); Since when? Please enter above.

☐ Autoimmune hepatitis

☐ Other: _____

1.4 Current concomitant medication (except mistletoe)

☐ none

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____
10. _____

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2.1 HCC therapy *prior* to il. MT

☐ none

Type of therapy	Exact description incl. dates (from – until)	Treatment outcome (according to WHO*)
Operation ☐ none	e.g. Hemihepatectomy r., vascular ligature, etc.	
Local therapy ☐ none	High-frequency induced thermotherapy (HITT), laser-induced thermotherapy (LITT), percutaneous ethanol injection (PEI)	
Chemotherapy (Scheme, substance, number of cycles) ☐ none	Transarterial chemoebolisation (TACE), systemic chemotherapy	
Other therapies		

*Complete remission = CR; partial remission = PR (remission >=50% for at least four weeks); disease unchanged = NC (remission <50% or no change in size of increase <25%); progression = PD (increase >25% or new tumour manifestation).

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2.2 HCC therapy *during and after* il. MT

☐ none

Type of therapy	Exact description incl. dates (from – until)	Treatment outcome (according to WHO*)
Operation (OP description) ☐ non	e.g. Hemihepatectomy r., vascular ligature, etc.	
Local therapy ☐ none	High-frequency induced thermotherapy (HITT), laser-induced thermotherapy (LITT), percutaneous ethanol injection (PEI)	
Chemotherapy (Scheme, substance, number of cycles) ☐ none	Transarterial chemoebolisation (TACE), systemic chemotherapy	
Other therapies		

*Complete remission = CR; partial remission = PR (remission >=50% for at least four weeks); disease unchanged = NC (remission <50% or no change in size or increase <25%); progression = PD (increase >25% or new tumour manifestation).

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3.1 Characterisation of the HCC

Localisation: ☐ Right HL ☐ Left HL

☐ Solitary lesion ☐ Multifocal

Affected segments: _____

Diagnosis by: ☐ Clinical exam. ☐ Ultrasonography ☐ Chest X-rays

☐ CT ☐ MRI ☐ Angiography

Symptoms: ☐ Abd. pain ☐ Icterus ☐ Nausea ☐ Ascites

☐ Other: _____

Laboratory values under il. MT (if available)*:

Biopsy (Datum):	**1.** ☐☐ Day ☐☐ Month	**2.** ☐☐ Day ☐☐ Month	**3.** ☐☐ Day ☐☐ Month	**4.** ☐☐ Day ☐☐ Month
AFP				
Serum protein$_{total}$				
Serum albumin				
Serum bilirubin$_{total}$				
HB				
Other				

* You may also include a copy of the laboratory report with the documentation sheet

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3.2 Intralesional mistletoe therapy of HCC

Mistletoe preparation: ABNOBAviscum® Fraxini stage 2:

Please insert therapies in table with date:

Treatment number		Date	Localisation	Ampoules stage 2 per lesion
1.		Day Month Year		
2.		Day Month Year		
3.		Day Month Year		
4.		Day Month Year		
5.		Day Month Year		
6.		Day Month Year		
7.		Day Month Year		
8.		Day Month Year		
9.		Day Month Year		
10.		Day Month Year		
11.		Day Month Year		
12.		Day Month Year		
13.				
14.				
15.				
16.				

See the appendix for a sample therapy mode

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3.3 Reactions, ADRs during il. MT

☐ none

Please assess degree of adverse drug reactions according to WHO guidelines:

⓪ = none ① = slight / light ② = moderate / clear

③ = strong / pronounced ④ = life-threatening ⑤ = lethal therapy outcome

Treatment No.*	1.	2.	3.	4.	5.	__.	__.	__.
Abdominal pain								
Local burning (around puncture site)								
Cardiovascular reaction								
Cough								
Fever, raised temperature								
Max. Temp. on day of il. MT								
Other: _____ _____ (Tiredness, flue-like symptoms, nausea, skin rash)								
Allergic reaction grade I-IV (therapy see appendix page 1/3)								

Did ADRs have to be treated with medication? ☐ no ☐ yes, with:

Treatment No.*:	1.	2.	3.	4.	5.	__.	__.	__.
Antipyretic: _____ _____								
Antihistamine: _____								
Cortisone: _____								
Antiemetic: _____								
Volume replacement: _____								
Analgesia: _____								
Other: _____								

* If necessary copy this page and attach

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4.1 Concomitant systemic mistletoe therapy ☐ none

Was the patient systemically treated with mistletoe ***prior*** to il. MT of HCC?

☐ no ☐ yes, with:

Drug	Dose (stage, mg)	Frequency (n times / week)	Application (s.c., i.v.)	Date (from – until)

Was systemic mistletoe therapy carried out ***during and after*** il. MT of HCC?

☐ no ☐ yes, with:

Drug	Dose (stage, mg)	Frequency (n times / week)	Application (s.c., i.v.)	Date (from – until)

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4.2 Reactions to systemic mistletoe therapy

☐ none

☐ Local inflammation At what dose? _____ Size in cm? _____

Side effects: _____

_____

☐ Temperature reactions:

Time of onset? _____

At what dose? _____

Which route of application? _____

☐ Laboratory changes during therapy*:
(Complete blood count, CRP)

_____

_____

_____

*Please include copies of original results in appendix

☐ Systemic reactions after injection:
(E.g. tiredness, exhaustion, shivering, aching limbs, dizziness, skin rash)

_____

_____

_____

☐ Other:

_____

_____

_____

_____

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5.1 Assessment of il. MT of HCC

According to WHO guidelines:

☐ CR Complete remission: Complete tumour remission

☐ PR Partial remission: remission >=50% for at least four weeks

☐ NC Disease unchanged: remission <50% or no change in size
increase <25%

☐ PD Progression: increase >25% or new tumour manifestation

☐ Therapy outcome could not be recorded according to WHO guidelines.

because: ☐ patient has died ☐ patient cannot be contacted

Other reasons ☐ _____ ☐ _____

According to the doctor in charge:

1. Intralesional mistletoe therapy of HCC is:

☐ very easy ☐ often easy ☐ quite difficult ☐ very difficult

2. Are the ADRs of primary concern during therapy:

☐ very ☐ sometimes ☐ rarely ☐ never

3. For the patient the tolerability of intralesional mistletoe therapy of HCC is:

☐ very good ☐ good ☐ moderately good ☐ poor

Free space for therapy assessment:

_____

_____

_____

_____

_____

_____

APPENDIX: il. MT of HCC

Karnofsky score:

	%	Comment
A		Normal activity. No special care required.
	100	Normal state. No complaints. No evidence of disease.
	90	Capable of normal activities. Minor signs/symptoms..
	80	Some signs/symptoms and patient requires some effort to carry out normal activities.

	%	Comment
B		Unable to work, can live at home and care for self but requires help with certain activities.
	70	Patient is able to care for self, but is unable to carry out normal activities or active work.
	60	Patient is able to care for self, but requires occasional assistance.
	50	The patient requires medical care and much assistance with self care.

	%	Comment
C		Patient cannot look after self. Patient requires special assistance and medical care.
	40	The patient is disabled and requires special care and assistance.
	30	Patient is severely disabled and hospitalisation is necessary. Death is not imminent.
	20	The patient is very ill with hospitalisation and active life-support treatment required.
	10	Moribund. Fatal process proceeding rapidly.

Child-Pugh Classification

	Points		
	1	**2**	**3**
Albumin (mg/dL)	>3.5	2.8-3.5	<2.8
Bilirubin (mg/ dL)	<2.0	2.0-3.0	>3.0
PTT (%)	>70	40-70	<40
Ascites	none	moderate	profuse
Encephalopathy	none	grade I-II	>grade II

Total score: Child A 5-6 points; Child B 7-9 points; Child C 10-15 points

Tab. 3 Degrees of severity and therapy for allergic reactions

Clinical symptoms	***Therapy***
Grade I local reaction	
Oedema, erythema, pruritus, wheals, Quincke's oedema	- Stop allergen exposure - Antihistamines such as Fenistil 4 mg (dimetindene) or Tavegil 2 mg (clemastine) i.v. - H2-Blockers such as Tagamet 400 mg (cimetidine) i.v.
Grade II Systemic reaction	
Additional nausea, vomiting, onset of bronchospasms tachycardia, falling blood pressure	- Supply of oxygen - Infusion of 500 – 1000 ml Ringer's solution - 250 mg Solu-Decortin H (Prednisolone) - Possibly beta2-mimetics (for inhalation)
Grade III Severe systemic reaction	
Additional shock Severe bronchospasms Coma	- Volume substitution with Ringer's solution, preferably also Haes 6/10% - Adrenaline 0,1-1 mg i.v., repeat after 3 min. - Solu-Decortin 1000mg or Fortecortin 100mg - 1 Amp. Theophylline 0,24 g over 10 mg - 5-10 mg Diazepam (if fear of suffocation) with larynx- or glottis oedema
Grade IV	
Respiratory arrest, circulatory collapse	- Reanimation

APPENDIX: iI. MT of HCC

TNM classification of HCC

Primary tumour (T)

- TX - Primary tumour cannot be assessed
- T0 - No evidence of primary tumour
- T1 - Solitary tumour 2 cm or less without vascular invasion
- T2 - Solitary tumour 2 cm or less with vascular invasion or multiple tumours limited to one lobe, none more than 2 cm without vascular invasion or solitary tumour more than 2 cm without vascular invasion
- T3 - Solitary tumour more than 2 cm with vascular invasion or multiple tumours limited to one lobe none more than 2 cm with vascular invasion; or multiple tumours limited to one lobe, any more than 2 cm with or without vascular invasion
- T4 - Multiple tumours in more than one lobe or tumour(s) involve(s) a major branch of portal or hepatic vein

Regional lymph nodes (N)

- NX - Regional lymph nodes cannot be assessed
- N0 - No regional lymph node metastasis
- N1 - Regional lymph node metastasis

Distant metastasis (M)

- MX - Distant metastasis cannot be assessed
- M0 - No distant metastasis
- M1 - Distant metastasis

*Fictitious division of the liver into two lobes based on a plane running between the gallbladder and the inferior vena cava

UICC Classification of HCC

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1 T2 T3	N1 N0 N1	M0 M0 M0
Stage IV A	T4	N0, N1	M0
Stage IV B	T1-4	N0, N1	M1

Staging and prognosis according to Okuda

	0 points	**1 point**
Liver involvement	< 50%	> 50%
Ascites	no	yes
Total bilirubin	< 3 mg/dl	> 3 mg/dl
Albumin	> 3 g/dl	< 3 g/dl

Median survival	Stage I: 0 points	Stage II: 1-2 points	Stage III 3-4 points
Months	8.3	2.0	0.7

APPENDIX: il. MT of HCC

Notes:

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