Hepatocellular Carcinoma

The ideal combination partner for optimization of locoregional cancer treatment in HCC patients
CLASSIFICATION AND TREATMENT

Guideline-compliant treatment options

1. TACE with Degradable Starch Microspheres (DSM) for guideline-compliant palliative treatment of unresectable HCC patients in the intermediate stage. [1]

2. TACE with DSM for curative treatment in combination with ablation and PEI. [2] [3]

3. TACE with DSM for neoadjuvant treatment to prolong the waiting time in HCC patients with increased risk of relapse or progression prior to liver transplantation. [4]

BCLC classification* of HCC

HCC

Early stage (A) single or 3 nodules < 3 cm, Child-Pugh A – B, PS 0

Intermediate stage (B) multinodular, Child-Pugh A – B, PS 0

Advanced stage (C) Child-Pugh A – B PS 1 – 2

Terminal stage (D) Child-Pugh C PS 3 – 4

No Yes

single nodule

3 nodules ≤ 3 cm

Portal pressure/bilirubin normal increased

Associated diseases

No 3 Yes 2

Liver transplantation (CLT/LDLT) Ablation (PEI/RFA/LITT) Chemoembolization (TACE) Sorafenib

Curative treatment 5-year survival: 50 – 70%

Ablation

Resection

Palliative treatment Randomised controlled studies (50%) 3-year survival: 20 – 40%

Symptomatic treatment (20%) 1-year survival: 10 – 20%

*Treatment options for the curative and palliative treatment of HCC.
RESPONSE RATE

High response rate for TACE with DSM

Total 91%
- Stable disease 55%
- Partial remission 36%
- Progression 9%

Median survival >2 years

TACE treatment of unresectable HCC patients using DSM, Cisplatin (50mg/m²), Doxorubicin (50mg/m²) and Lipiodol leads to high response rates and a median survival of 26 months. [6]

EmboCept®S performs well in clinical practice

"Our TACE protocol implementing DSM combined with Carboplatin and Docetaxel exhibited good tolerability and low toxicity as well as encouraging survival rates in advanced HCC patients. No case of typical post-embolization syndrome occurred under 117 chemoembolizations."

Prof. T. Albrecht; Vivantes Klinikum Neukölln; German Congress of Radiology, Hamburg 2012

TACE with EmboCept®S is recommended by experts as an ideal partner in the treatment of HCC.
QUALITY OF LIFE

TACE with DSM shows very good tolerability

Comparison of side-effects between TACE with Degradable Starch Microspheres and conventional TACE with Lipiodol shows significantly better tolerability for TACE with DSM. [7]

TACE with EmboCept®S offers advantages in the anti-tumour strategy

Comparison of temporary vs. permanent embolization clearly demonstrates the advantages of treatment with EmboCept®S.

Improved tolerability of TACE with EmboCept®S enhances the quality of life of your HCC patients.
**SURVIVAL**

**Significant increase in overall survival**

In unresectable patients in the intermediate stage, TACE with DSM leads to a significant increase in overall survival compared to TACE with Doxorubicin (30mg/m²) alone. [10]

**Significant increase in progression-free survival**

Median progression-free survival in patients following TACE with DSM, Cisplatin (80mg) and Lipiodol is significantly better compared to TACE with Lipiodol (p=0.035) or DSM alone (p=0.02). [11]

TACE with EmboCept®S significantly prolongs the life of your HCC patients.
A sequential TACE protocol with DSM, Carboplatin (450 mg) and Docetaxel (80 mg) as well as a change of chemotherapy (liposomal-encapsulated Carboplatin or liposomal-encapsulated Doxorubicin) following progression leads to median survival of 27 months in unresectable HCC patients. \(^{(13)}\)

**TREATMENT OPTIONS**

Combination therapy, including bridging therapy

### TACE with DSM

<table>
<thead>
<tr>
<th>Type of treatment</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Combination</td>
<td>Increased survival</td>
</tr>
<tr>
<td>TACE and PEI (^{(2)})</td>
<td></td>
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<tr>
<td>TACE and LITT (^{(3)})</td>
<td>Downsizing and 36-month median survival</td>
</tr>
<tr>
<td>TACE and RFA (^{(12)})</td>
<td>Downsizing of lesions 3–8 cm</td>
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<tr>
<td>Bridging</td>
<td>Extension of medium waiting time</td>
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<td>TACE prior to liver transplantation (^{(4)})</td>
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</table>

TACE with EmboCept\(^{®}\)S is a universal partner with high response rates in combination therapy.

**Additional option offering change of any active substance**

TACE with DSM, Carboplatin and Docetaxel in 18 unresectable HCC patients

- Partial remission 50%
- Stable disease 22%
- Progression 28%

Change of chemotherapy

- Partial remission 20%

A sequential TACE protocol with DSM, Carboplatin (450 mg) and Docetaxel (80 mg) as well as a change of chemotherapy (liposomal-encapsulated Carboplatin or liposomal-encapsulated Doxorubicin) following progression leads to median survival of 27 months in unresectable HCC patients. \(^{(13)}\)

**TACE with EmboCept\(^{®}\)S provides increased flexibility and an option for change of any active substance.**
EmboCept® S represents simple and flexible application and can be combined with any chemotherapy.

**Low-volume chemotherapy**

Application over approx. 30 min. under continual angiographic monitoring (approx. every 10 min.): Shake mixture repeatedly to avoid sedimentation.

<table>
<thead>
<tr>
<th>Dosage examples</th>
<th>max. 7.5ml</th>
<th>max. 7.5ml</th>
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</thead>
<tbody>
<tr>
<td>1 EmboCept®S</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Active substance</td>
<td>25 ml Doxorubicin (50mg)</td>
<td>20 ml Mitomycin (10mg)</td>
</tr>
<tr>
<td>3 Mixture</td>
<td>32.5 ml (EmboCept®S + Doxorubicin)</td>
<td>27.5 ml (EmboCept®S + Mitomycin)</td>
</tr>
</tbody>
</table>

**High-volume chemotherapy**

Application over approx. 60 min. beginning with EmboCept®S-CM-mixture (approx. 2–3 ml): Administration of chemotherapy agents by perfusor (100 ml/hr.); Application of the rest of EmboCept®S-CM-mixture 2–3 ml every 10 min. under continual angiographic monitoring.

| Dosage examples | max. 7.5ml | max. 10 ml | max. 10 ml |
|-----------------|------------|------------|
| 1 EmboCept®S    |            |            |
| 2 Contrast medium (CM) |            |            |
| 3 Mixture       | 17.5 ml (EmboCept®S + contrast medium) | 17.5 ml (EmboCept®S + contrast medium) |
| 4 Active substance | 100 ml Cisplatin (100mg) | 50–70 ml Irinotecan |
|                 | - ready-to-use solution with 1 mg/ml - | - ready-to-use solution/concentrate 20 mg/ml - |
The advantages of EmboCept® S:
- Guideline-compliant treatment of HCC patients
- Significant increase in overall survival
- Significant increase in progression-free survival
- Very good tolerability
- Flexibility in treatment type and procedure
- Simple handling in treatment use

List of references


EmboCept® S 450 mg/7.5 ml, Composition: Amilomer, DSM 35/50 (Degradable Starch Microspheres), isotonic saline solution. Practical applications: Chemoembolize, EmboCept® S suspension for injection is an adjuvant for intraarterial therapy of tumours in combination with cytostatics and other active ingredients. Contraindications: EmboCept® S is not permitted for use in cases of vascular anomalies in target organs, such as shunts (> 30%), arterial occlusion, portal vein thrombosis, portal hypertension, portal vein invasion and severe liver failure. Adverse effects: Points in the region of the target organ due to vascular occlusions (normally subside after approximately 30-60 minutes and disappear after approximately 1 hour), upper abdominal complaints (sclerema pain), temporary disturbances of function in the target organ (such as elevated liver values), dyspnoea (rare, and reversible after approximately 35 minutes). Due to combination with cytostatics: nausea, vomiting, diarrhoea, inflammatory infiltration of the mucous membranes, fever, chill, coughing, ulcers in the upper gastrointestinal tract (direct correlation with embolization is not possible). Interactions with other agents: Because of the embolization effect of EmboCept® S, a local increase of the concentration of a concomitantly administered active ingredient will occur. This may impose limits on the maximum quantity of an active ingredient to be administered with EmboCept® S. Warnings: not applicable. Durability: 24 months. Special storage instructions: none. Dosage forms and package sizes: 7.5 ml injection vials. By prescription only. Information status: July 2013 Pharmaceutical manufacturer: PharmaCept GmbH, Berlin.