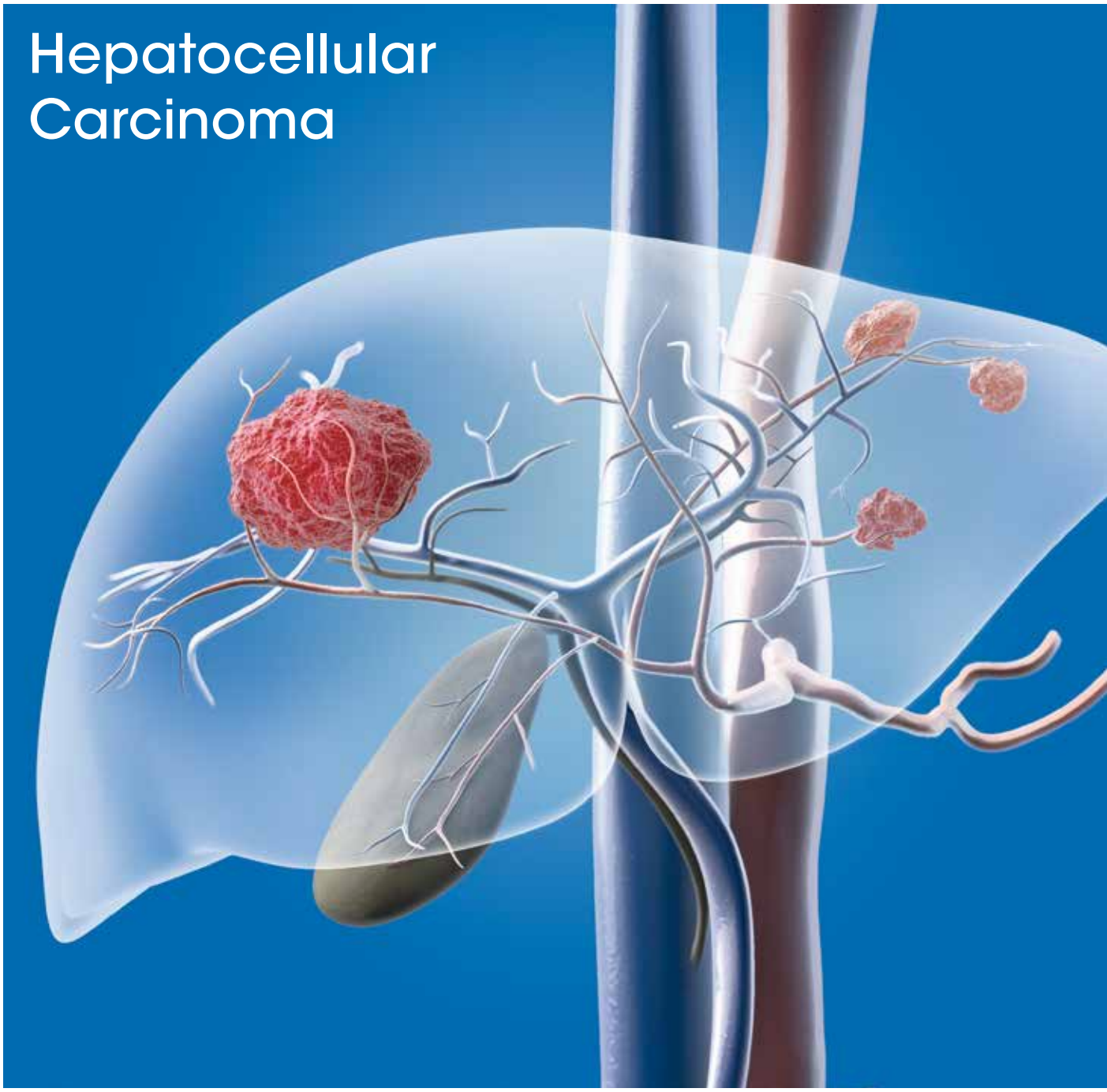
INDICATION

EmboCept® S

the universal short-term embolizate



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

CLASSIFICATION AND TREATMENT

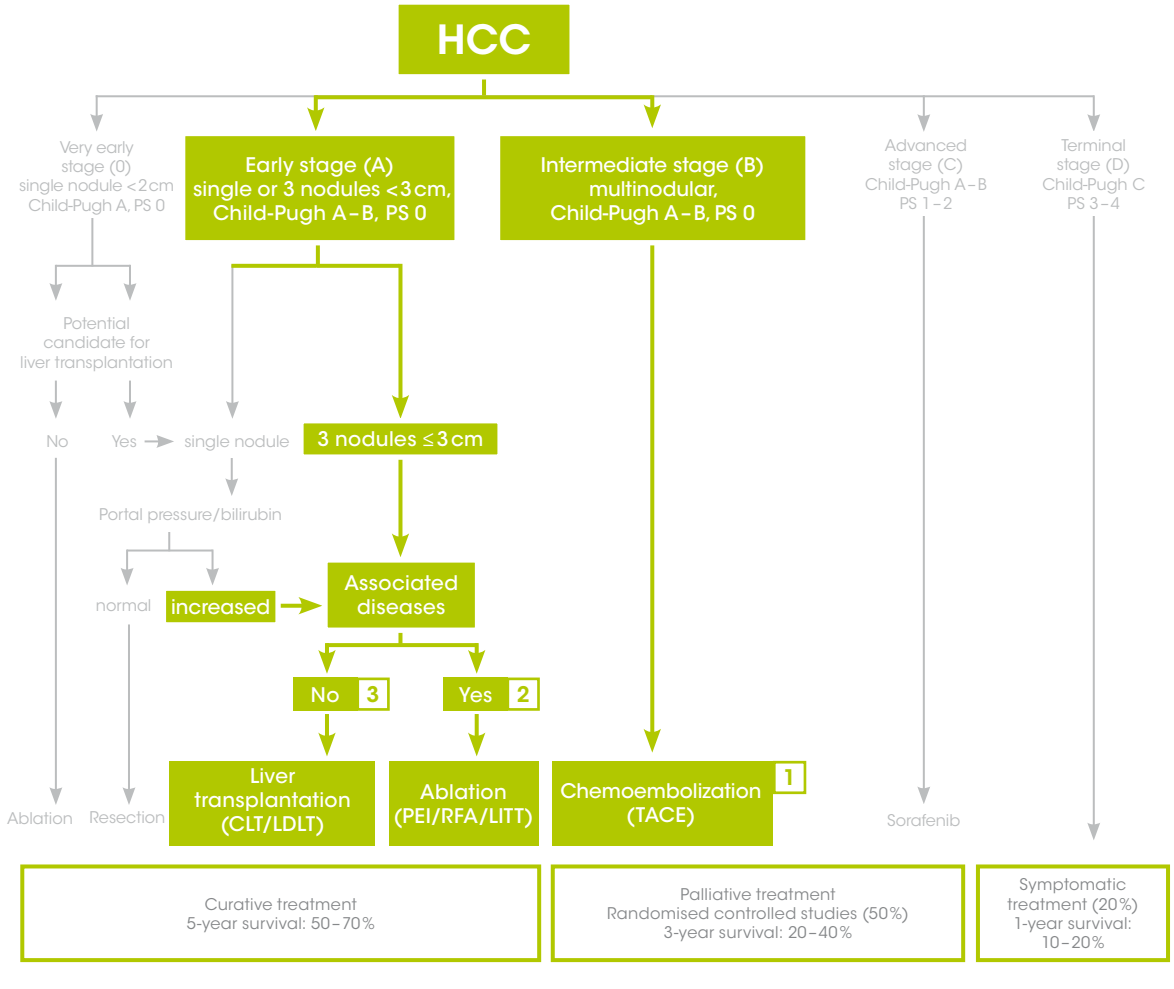
Guideline-compliant treatment options

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



*Barcelona Clinic Liver Cancer adapted from Llovet, J.M. et al. [1] and Forner, A. et al.[5]

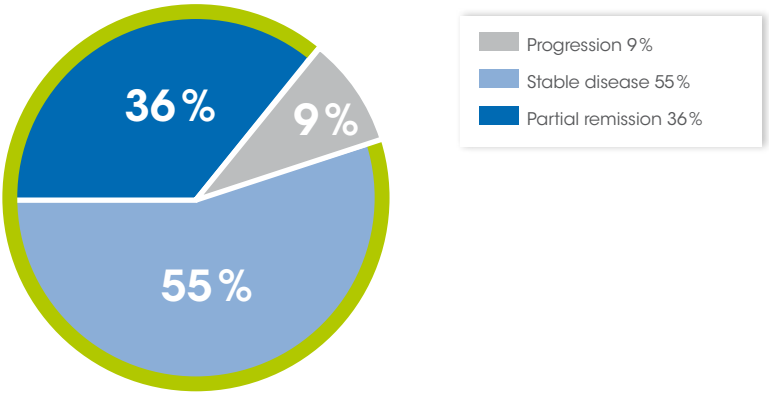
TACE with EmboCept® S offers treatment strategies for the curative and palliative treatment of HCC.

RESPONSE RATE

High response rate for TACE with DSM

Total 91 %
Stable disease
+ Partial remission

Median survival
> 2 years



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

EmboCept®S performs well in clinical practice

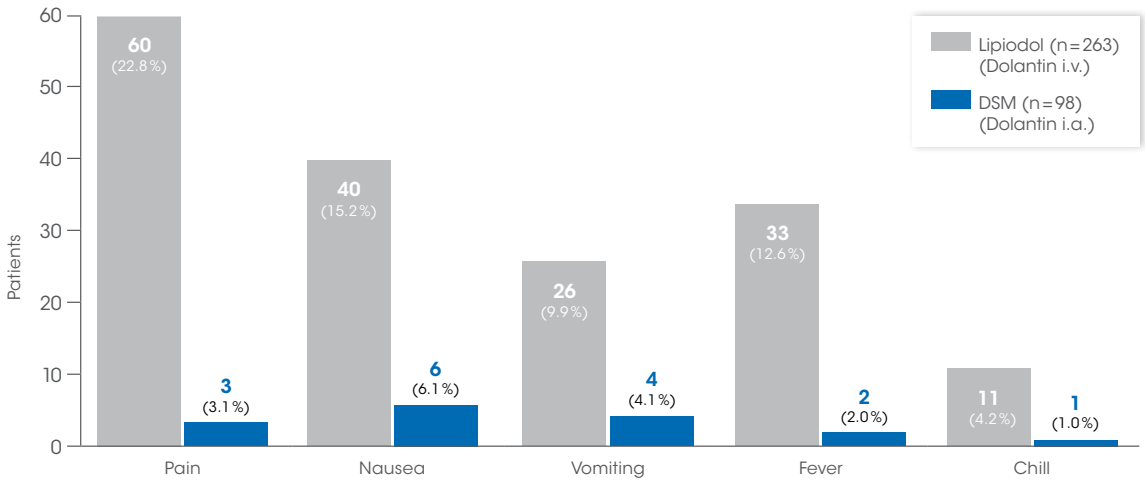
"Our TACE protocol implementing DSM combined with Carboplatin and Docetaxel exhibited good tolerability and low toxicity as well as encouraging survival rates in advanced HCC patients. No case of typical post-embolization syndrome occurred under 117 chemoembolizations."

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

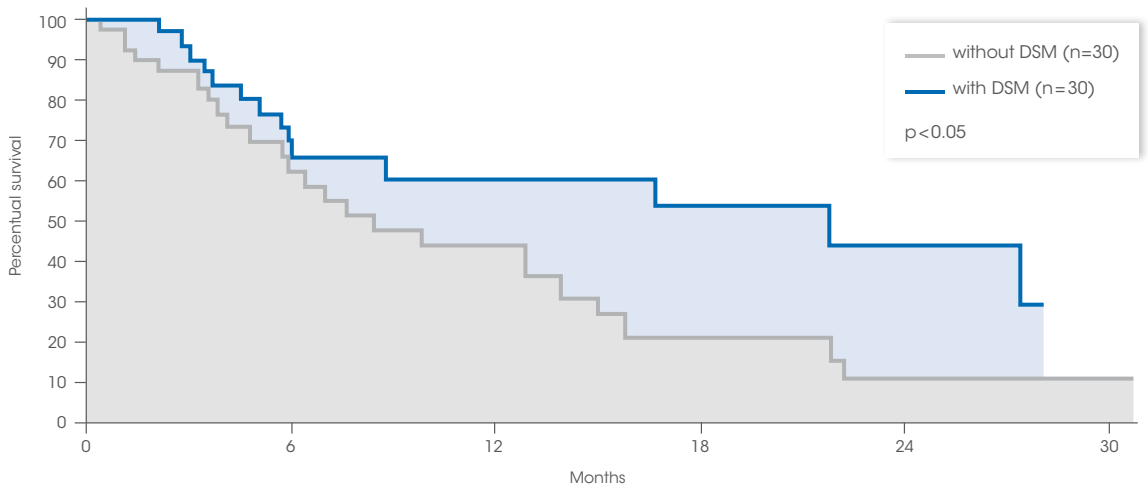
Parameter	Permanent materials [8] [9]	EmboCept®S
Degradation time	several months to permanent	limited to up to 2 hours
Ischemia	high	little
Hypoxia	high	little
Risk of tumour cell spread and new metastasis growth	given	little
Neoangiogenesis	new blood vessels supplying the tumour	unlikely
Angiogenesis inhibitors	necessary	not necessary
Reapplication of the therapy	limited	unlimited

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.

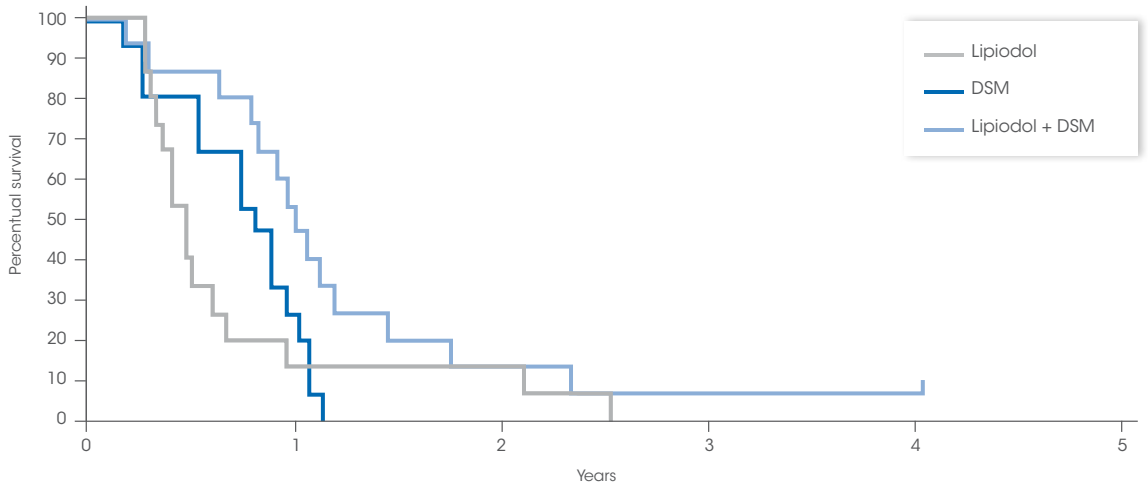
SURVIVAL

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.

TREATMENT OPTIONS

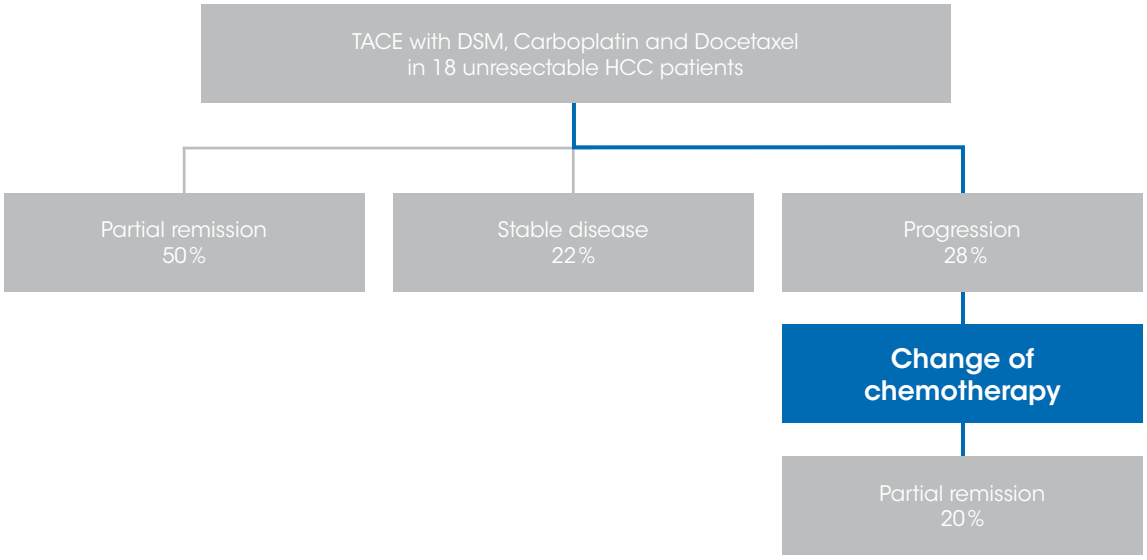
Combination therapy, including bridging therapy

TACE with DSM

Type of treatment		Outcome
Combination	TACE and PEI [2]	Increased survival
	TACE and LITT [3]	Downsizing and 36-month median survival
	TACE and RFA [12]	Downsizing of lesions 3–8 cm
Bridging	TACE prior to liver transplantation [4]	Extension of medium waiting time

TACE with EmboCept®S is a universal partner with high response rates in combination therapy.

Additional option offering change of any active substance

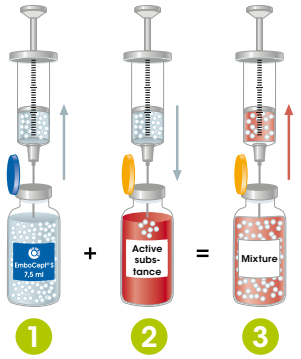


A sequential TACE protocol with DSM, Carboplatin (450 mg) and Docetaxel (80 mg) as well as a change of chemotherapy (liposomal-encapsulated Carboplatin or liposomal-encapsulated Doxorubicin) following progression leads to median survival of 27 months in unresectable HCC patients. [13]

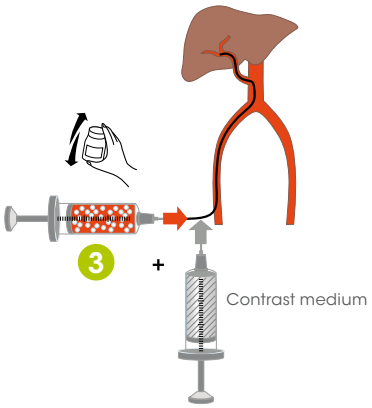
TACE with EmboCept® S provides increased flexibility and an option for change of any active substance.

HANDLING INSTRUCTIONS

Low-volume chemotherapy



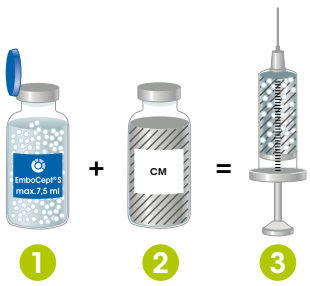
Application over approx. 30 min.
under continual angiographic monitoring (approx. every 10 min.); Shake mixture repeatedly to avoid sedimentation.



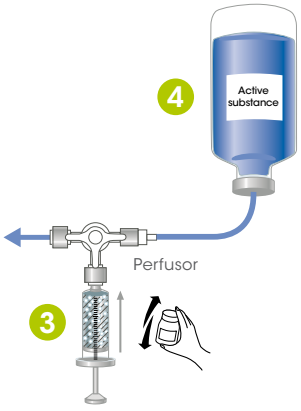
Dosage examples

1 **EmboCept®S**	max. 7.5 ml	max. 7.5 ml
2 **Active substance**	25 ml Doxorubicin (50 mg) - ready-to-use solution with 2 mg/ml -	20 ml Mitomycin (10 mg) - soluble powder -
3 **Mixture**	32.5 ml (EmboCept®S + Doxorubicin)	27.5 ml (EmboCept®S + Mitomycin)

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

1 **EmboCept®S**	max. 7.5 ml	max. 7.5 ml
2 **Contrast medium (CM)**	max. 10 ml	max. 10 ml
3 **Mixture**	17.5 ml (EmboCept®S + contrast medium)	17.5 ml (EmboCept®S + contrast medium)
4 **Active substance**	100 ml Cisplatin (100 mg) - ready-to-use solution with 1 mg/ml -	50–70 ml Irinotecan - ready-to-use solution/concentrate 20 mg/ml -

EmboCept® S represents simple and flexible application and can be combined with any chemotherapy.

SUMMARY

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

[1] Llovet, J. M. et al., Design and endpoints of clinical trials in hepatocellular carcinoma, J. Natl. Cancer Inst. 100 (2008) 698 – 711.
[2] Dettmer, A. et al., Combination of repeated single-session percutaneous ethanol injection and transarterial chemoembolization compared to repeated single-session percutaneous ethanol injection in patients with non-resectable hepatocellular carcinoma, World J. Gastroenterol 12 (2006) 3707 – 3715.
[3] Zangos, S. et al., Large-sized hepatocellular carcinoma (HCC): a neoadjuvant treatment protocol with repetitive transarterial chemoembolization (TACE) before percutaneous MR-guided laser-induced thermotherapy (LITT), Eur Radiol 17 (2007) 553 – 563.
[4] Schaudt, A. et al., Role of transarterial chemoembolization for hepatocellul ar carcinoma before liver transplantation with special consideration of tumor necrosis, Clin Transplant 23 Suppl 21 (2009) 61 – 67.
[5] Forner, A. et al., Hepatocellular carcinoma, Lancet 379 (2012) 1245 – 1255.
[6] Kirchhoff, T. D. et al., Transarterial chemoembolization using degradable starch microspheres and iodized oil in the treatment of advanced hepatocellular carcinoma: evaluation of tumor response, toxicity, and survival, HBPD INT 6 (2007) 259 – 266.
[7] Schlee, V., Komplikationen und unerwünschte Wirkungen im Rahmen intraarterieller Tumortherapien. Inauguraldissertation, Medizinische Fakultät, Universität Bonn (Betreuer: Layer G.), 1999.
[8] Kaseb, A. O. et al., Vascular endothelial growth factor in the management of hepatocellular carcinoma. Cancer 2009; 115: 4895 – 906.
[9] Xiong, Z. P. et al., Association between vascular endothelial growth factor and metastasis after transcatheter arterial chemoembolization in patients.
[10] Taguchi, T., A comparative randomized study on the treatment of primary and secondary liver tumours with intra-arterial chemotherapy with or without dagradable starch microspheres (DSM) (Spherex), Regional Cancer Treatment (1992) 117 – 120.
[11] Yamasaki, T. et al., A novel transcatheter arterial infusion chemotherapy using iodized oil and degradable starch microspheres for hepatocellular carcinoma: a prospective randomized trial, J. Gastroenterol. 46 (2011) 359 – 366.
[12] Marin, H. L. et al., Histopathologic outcome of neoadjuvant image-guided therapy of hepatocellular carcinoma, J Gastrointestin Liver Dis 18 (2009) 169 – 176.
[13] Albrecht, T., Repeated non-selective non-occlusive TACE of far advanced HCC with degradable starch microspheres (DSM) and Carboplatin – long term results, in: CIRSE Kongress München 2011.

EmboCept®S 450mg/7.5ml, Composition: Amilomer, DSM 35/50 (Degradable Starch Microspheres), isotonic saline solution. **Practical applications:** Chemoembolizate, 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:** Pains 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 (ischemia 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, diarrhea, inflammations 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:** 7.5ml injection vials. **By prescription only. Information status:** July 2013 **Pharmaceutical manufacturer:** PharmaCept GmbH, Berlin.

PharmaCept
www.pharmacept.com