

# Drug-Eluting Bead TACE with DC Bead® [DEBDOX™] in the Treatment of Hepatocellular Carcinoma (HCC)

## Review of Published Clinical Data

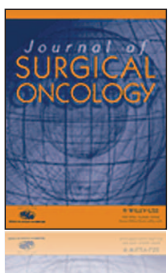


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For many years, transcatheter arterial chemoembolisation with Lipiodol® (conventional TACE) has been considered standard of care for patients with multifocal hepatocellular carcinoma without vascular invasion and good liver function and performance status. TACE with DC Bead® [DEBDOX™] is a new technique to improve patient response and tolerability of chemoembolisation. In reviewing the recent literature comparing DEBDOX and conventional TACE (cTACE), it is apparent that DEBDOX is superior to cTACE. DEBDOX results in improved response rates for patients with HCC, especially those with more advanced cancer or more advanced liver disease. In addition, DEBDOX appears to be safer in patients with worse prognostic factors, including CTP B cirrhosis, bilobar disease, recurrent disease, and worse ECOG performance status. Given these results, DEBDOX should replace cTACE in most patients undergoing chemoembolisation for treatment of hepatocellular carcinoma.

1 **Comparison of Conventional Transarterial Chemoembolization (TACE) and Chemoembolization with Doxorubicin Drug Eluting Beads (DEB) for Unresectable Hepatocellular Carcinoma.**



*Dhanasekaran R, Kooby D, Staley C et al  
J of Surg Onc 101 (2010): 476-480*

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2 **Prospective Randomized Study of Doxorubicin-Eluting-Bead Embolization in the Treatment of Hepatocellular Carcinoma: Results of the PRECISION V Study.**



*Lammer J, Malagari K, Vogl T et al  
Cardiovasc Interv Radiol 33 (2010): 41-52*

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3 **Single-Centre Phase II Trial of Transarterial Chemoembolization with Drug-Eluting Beads for Patients with Unresectable Hepatocellular Carcinoma: Initial Experience in the United States.**



*Reyes D, Vossen, J, Geschwind J et al  
The Cancer Journal 15 (6) 2009: 526-532*

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4 **Transarterial Chemoembolization with Epirubicin-eluting Beads versus Transarterial Embolization before Liver Transplantation for Hepatocellular Carcinoma.**



*Nicolini A, Martinetti L, Crespi S et al  
J Vasc Interv Radiol 21 (2010): 327-332*

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5 **Prognostic factors for survival in patients with unresectable hepatocellular carcinoma undergoing chemoembolization with doxorubicin drug-eluting beads: a preliminary study.**



*Dhanasekaran R, Kooby D, Kim H et al  
HPB (12) 2010: 174-180*

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6 **Prospective Randomized Comparison of Chemoembolization with Doxorubicin-Eluting Beads and Bland Embolization with Bead Block for Hepatocellular Carcinoma.**



*Malagari K, Pomoni M, Kelekis A et al  
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# Drug-Eluting Bead in the Treatment of

## 1 Comparison of Conventional Transarterial Chemoembolization (TACE) and Chemoembolization with Doxorubicin Drug Eluting-Beads (DEB) for Unresectable Hepatocellular Carcinoma

Dhanasekaran R, Kooby D, Staley C et al. *J of Surg Onc* 101 (2010): 476-480

### ABSTRACT

**Background and Objectives:** Chemoembolization with doxorubicin drug-eluting beads (DEB) is a novel locoregional treatment modality for unresectable hepatocellular carcinoma (HCC). Initial animal studies and clinical trials suggest that treatment with DEB [DEBDOX™] may provide safer and more effective short-term outcomes than conventional chemoembolization. Current study explores long-term survival benefits.

**Methods:** Consecutive patients who received transcatheter therapy with DEB or conventional chemoembolization as sole therapy between 1998 and 2008 were studied. Statistical analysis was performed using Kaplan-Meier estimator with log-rank testing, chi-squared, and independent *t*-tests.

**Results:** Seventy-one patients were included in this study, 45 (63.4%) received therapy with DEB (group A) and 26 (36.6%) underwent conventional chemoembolization (group B). Median survival from diagnosis of HCC in groups A and B were 610 (351–868) and 284 days (4–563; *P*=0.03), respectively. In Okuda stage I, survival in groups A and B were 501 (421–528) and 354 days (148–560, *P*=0.02). In Child–Pugh classes A and B, survival in groups A and B were 641 (471–810) and 323 days (161–485, *P*=0.002). Median survival in patients with Cancer of Liver Italian Program (CLIP) score ≤ 3 in groups A and B were 469 (358–581) and 373 days (195–551, *P*=0.03). NCI CTCAEv3 Grade 5 clinical toxicity was similar.

**Conclusions:** In our study, transcatheter therapy with DEB offers a survival advantage over conventional chemoembolization for patients with unresectable HCC.

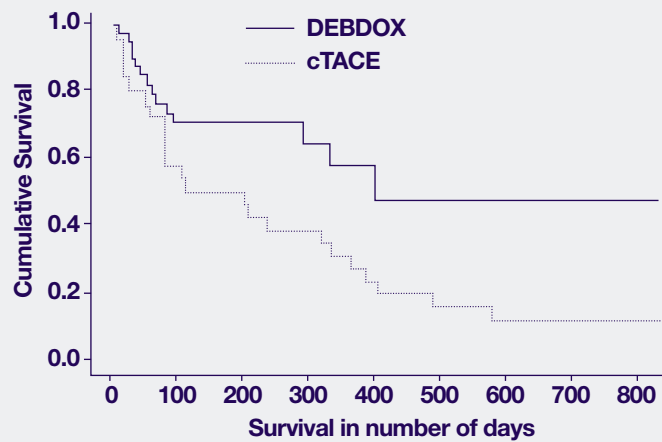
Abstract © John Wiley & Sons Inc. Reproduced with permission via republication licence for inclusion into "Drug-Eluting Bead TACE with DC Bead® [DEBDOX™] in the Treatment of Hepatocellular Carcinoma (HCC): Review of Published Clinical Data by Catherine Frenette, MD" only.

### REVIEW

This retrospective review of patients with HCC compared LC Bead™ doxorubicin [DEBDOX] and conventional TACE (cTACE). The relatively small study of only 71 patients showed similar baseline patient characteristics in the two patient populations, but an improved survival using DEBDOX over cTACE (610 days vs 284 days, respectively). In addition, the complication rate was similar between the groups. This study supports the results of the larger prospective randomised trial of PRECISION V and adds to the body of literature supporting the use of DEBDOX over cTACE.

### Kaplan-Meier Survival Curves

Comparison of survival from first transcatheter therapy between patients who received doxorubicin-eluting bead chemoembolisation [DEBDOX] (n=45) and conventional chemoembolisation (n=26).



Graph adapted from: Dhanasekaran R et al. *J of Surg Onc* 101 (2010): 476-480

### Survival Rates From First Transcatheter Therapy Stratified by Child–Pugh Class

Child–Pugh	Procedure	n	6 mths (%)	1 yr (%)	2 yrs (%)	<i>P</i> -value
Class A and B	DEBDOX	33	85	81	61	0.002
	cTACE	22	50	37	14	
Class C	DEBDOX	12	44	32	0	0.327
	cTACE	4	50	25	0	

Table adapted from: Dhanasekaran R et al. *J of Surg Onc* 101 (2010): 476-480

# Transcatheter Arterial Chemoembolization (TACE) with DC Bead<sup>®</sup> [DEBDOX<sup>™</sup>] for Hepatocellular Carcinoma (HCC)

## 2 Prospective Randomized Study of Doxorubicin-Eluting-Bead Embolization in the Treatment of Hepatocellular Carcinoma: Results of the PRECISION V Study<sup>1</sup>

Lammer J, Malagari K, Vogl T et al, *Cardiovasc Interv Radiol* 33 (2010): 41-52

### ABSTRACT

Transcatheter arterial chemoembolization (TACE) offers a survival benefit to patients with intermediate hepatocellular carcinoma (HCC). A widely accepted TACE regimen includes administration of doxorubicin-oil emulsion followed by gelatine sponge—conventional TACE.

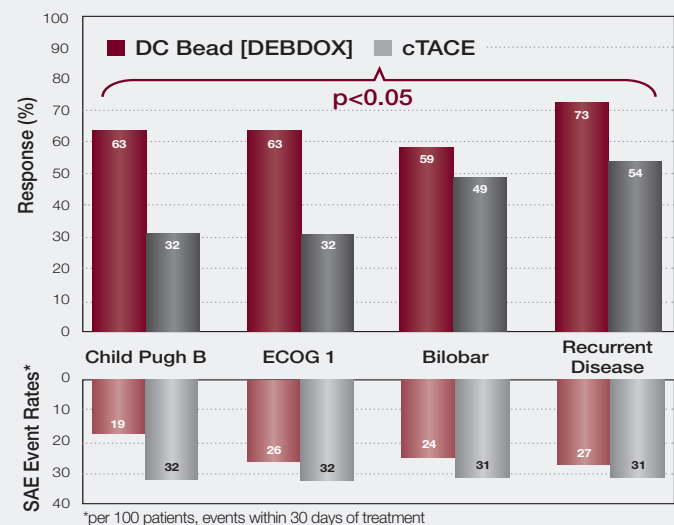
Recently, a drug-eluting bead (DC Bead<sup>®</sup>) has been developed to enhance tumor drug delivery and reduce systemic availability. This randomized trial compares conventional TACE (cTACE) with TACE with DC Bead [DEBDOX<sup>™</sup>] for the treatment of cirrhotic patients with HCC. Two hundred twelve patients with Child-Pugh A/B cirrhosis and large and/or multinodular, unresectable, N0, M0 HCCs were randomized to receive TACE with DC Bead loaded with doxorubicin or cTACE with doxorubicin. Randomization was stratified according to Child-Pugh status (A/B), performance status (ECOG 0/1), bilobar disease (yes/no), and prior curative treatment (yes/no). The primary endpoint was tumor response (EASL) at 6 months following independent, blinded review of MRI studies. The drug-eluting bead group showed higher rates of complete response, objective response, and disease control compared with the cTACE group (27% vs 22%, 52% vs 44%, and 63% vs 52%, respectively). The hypothesis of superiority was not met (one-sided  $P=0.11$ ). However, patients with Child-Pugh B, ECOG 1, bilobar disease, and recurrent disease showed a significant increase in objective response ( $P=0.038$ ) compared to cTACE. DC Bead was associated with improved tolerability, with a significant reduction in serious liver toxicity ( $P=0.001$ ) and a significantly lower rate of doxorubicin-related side effects ( $P=0.0001$ ). TACE with DC Bead and doxorubicin is safe and effective in the treatment of HCC and offers a benefit to patients with more advanced disease.

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### REVIEW

PRECISION V is the first head-to-head trial directly comparing DC Bead doxorubicin [DEBDOX] with conventional TACE (cTACE). This important trial of over 200 patients randomised them to DEBDOX (vs cTACE) at two-monthly intervals for a maximum of three chemoembolisations. Over two thirds of the patients had more advanced disease (CTP B, ECOG 1, or bilobar or recurrent disease). The overall analysis showed that DEBDOX had a disease control rate of 63.4% and cTACE had a disease control rate of 51.9% ( $P=0.11$ ). More importantly, the patients with more advanced disease who are often difficult to treat showed a better disease control rate with DEBDOX than cTACE. In addition, side effects of the treatment were consistently better with DEBDOX than cTACE. The results of this trial give reason to move to DEBDOX as standard therapy over cTACE in patients with more advanced disease, and perhaps in all patients undergoing chemoembolisation.

### Response and Adverse Events - Advanced Disease PRECISION TACE [DEBDOX] vs Conventional TACE



Objective Response ( $P=0.038$ ) and Disease Control ( $P=0.026$ )

Graph adapted from: Lammer J et al. *Cardiovasc Interv Radiol* 33 (2010): 41-52





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# Drug-Eluting Bead in the Treatment of

## 3 Single-Centre Phase II Trial of Transarterial Chemoembolization with Drug-Eluting Beads for Patients with Unresectable Hepatocellular Carcinoma: Initial Experience in the United States Reyes D, Vossen, J, Geschwind J et al, *The Cancer Journal* 15 (6) 2009: 526-532

### ABSTRACT

**Purpose:** This prospective phase II pilot study evaluated safety and efficacy of transarterial chemoembolization (TACE) with drug-eluting beads (DEBs) loaded with doxorubicin in patients with unresectable hepatocellular carcinoma (HCC).

**Methods:** Twenty patients with unresectable HCC (75% Child's A, 95% Eastern Cooperative Oncology Group performance status 0 to 1, 60% Barcelona Clinic Liver Cancer C, tumor size 6.9cm) underwent 34 DEB-TACE [DEBDOX] sessions. Primary endpoints were tumor response, assessed by contrast-enhanced magnetic resonance imaging at 1 month after treatment, using size (response evaluation criteria in solid tumors [RECIST]), contrast-enhancement (European Association for the Study of the Liver) and apparent diffusion coefficient values, and safety assessed by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE). Secondary endpoints included feasibility, progression-free survival and overall survival.

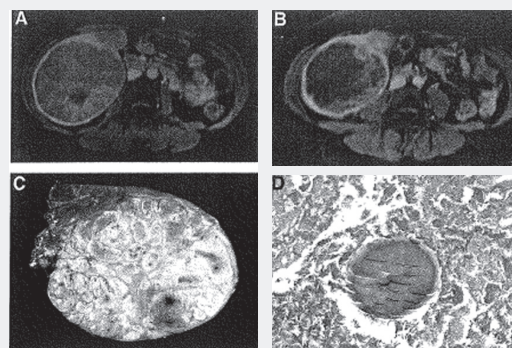
**Results:** DEB-TACE was successfully performed in 34 sessions and demonstrated a favorable safety profile. On initial (1 month) post-procedural magnetic resonance imaging, treated lesions had a mean decrease in size of 4% ( $P < 0.1129$ ). By European Association for the Study of the Liver criteria, 12 patients (60%) had objective tumor response, and 8 (40%) had stable disease. No patients had progression of a treated lesion while undergoing treatment. At 6 months, the disease control rate was 95% using RECIST. Overall survival rates at 1 and 2 years were 65% and 55%, respectively; median overall survival was 26 months.

**Discussion:** DEB-TACE is safe and effective in achieving local tumor control in patients with unresectable HCC.

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### REVIEW

This proof-of-concept study treated 20 patients with advanced, unresectable HCC with DC Bead® doxorubicin [DEBDOX]. The patient population was predominantly BCLC C patients (12/20), with good performance status and well compensated cirrhosis. The treatments were well tolerated, with few grade 3 adverse events. The response rate was excellent, with only one patient with progressive disease noted at 6-month follow-up imaging, and median overall survival of 26 months. This is an excellent survival duration given that most of the patients may have been excluded from conventional TACE treatment with BCLC stage C disease. As a pilot trial, this provided good reason to move to randomised trials with DEBDOX.



Histologic findings associated with tumour response. (A) Pre-treatment MRI showing a hypervascular lesion in segments 5 to 6. (B) Post-treatment MRI illustrating 85% to 90% tumour necrosis. (C) Gross specimen after resection. (D) Histopathology from the tumour documenting extensive necrosis and no viable tumour cells. DEB [DC Bead] is noted within the necrotic tumour.

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### Histologic Findings Associated with Tumour Response

Type of Surgery	Tumour Size (cm) on MRI Before DEBDOX	Tumour Size (cm) on MRI After DEBDOX	Percent Necrosis on MRI Before DEBDOX*	Percent Necrosis on MRI After DEBDOX	Pathology Description
Right hepatectomy	13.7	9.6	0%	> 90%	95% Necrotic
Partial hepatectomy segments V/VI	12.8	11.7	10%	85-90%	80% Necrotic
Right hepatectomy	7.2	5.9	0%	85-90%	> 50% Necrotic
Hepatic debulking radiofrequency ablation (RFA) of 3 smaller lesions	2.5	1.7	0%	100%	Not available. Lesion treated by DEBDOX was ablated
Attempted liver transplant (1 d post-DEBDOX)	4.8	3.8	0%	90%	Well-differentiated fragments of viable (25%) and necrotic (75%) HCC

\*Percent of necrosis in MRI is based on lack of contrast enhancement  
 RFA indicates radiotherapy ablation

Table adapted from Reyes D et al, *The Cancer Journal* 15 (6) 2009: 526-532

# Transarterial Chemoembolization with DC Bead<sup>®</sup> [DEBDOX<sup>™</sup>] versus Transarterial Embolization before Liver Transplantation for Hepatocellular Carcinoma (HCC)

## 4 Transarterial Chemoembolization with Epirubicin-eluting Beads versus Transarterial Embolization before Liver Transplantation for Hepatocellular Carcinoma

Nicolini A, Martinetti L, Crespi S et al, *J Vasc Interv Radiol* 21 (2010): 327-332

### ABSTRACT

**Purpose:** To retrospectively compare radiologic tumor response and degree of necrosis in explanted livers after chemoembolization with epirubicin-loaded DC Bead<sup>®</sup> versus bland embolization in patients on a transplant waiting list.

**Materials and Methods:** From 2003 to 2007, 49 patients with hepatocellular carcinoma (HCC) underwent transplantation at a single centre. Sixteen patients were treated with bland embolization (n = 8) with 100–300µm Embosphere<sup>®</sup> particles or chemoembolization with epirubicin-loaded 100–300µm DC Bead particles (n = 8) every other month until complete tumor devascularization. Computed tomography was performed every 3 months until recurrence. Explanted livers were analysed to evaluate the degree of necrosis in the nodules. After orthotopic liver transplantation (OLT), patients were followed up for survival and disease status.

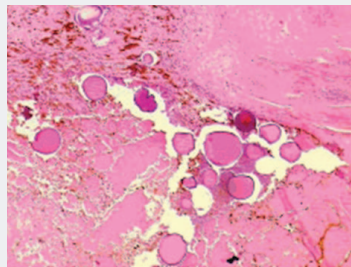
**Results:** The groups were comparable for baseline characteristics. Most patients had Child-Pugh class A disease. Solitary HCC was found in 75% of patients. Mean target lesion size was 32mm ± 15.4. Chemoembolization with drug-eluting beads achieved complete necrosis in 77% of lesions whereas bland embolization achieved complete necrosis in 27.2% of lesions. There was a significant difference between bland embolization and chemoembolization with DC Bead with regard to histologic necrosis ( $P=.043$ ). No significant treatment-related complications were observed for either group. Fifteen patients are alive with no tumor recurrence.

**Conclusions:** Chemoembolization with drug-eluting beads before OLT achieved higher rates of complete histologic response than bland embolization, with no serious adverse events observed. Because of the retrospective data analyses and small sample size, further studies are warranted to confirm these promising results.

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### REVIEW

Chemoembolisation is often used as bridging therapy for patients awaiting liver transplantation. It has been shown that patients who respond well to locoregional therapy have improved survival after liver transplantation. Nicolini et al reviewed radiologic response and explant pathology in 16 patients who underwent bland bead embolisation or DC Bead epirubicin and subsequent liver transplantation. Radiologic necrosis was very high in each group (82% in bland embolisation and 97% in Drug-Eluting Bead epirubicin). Interestingly, despite the high rates of radiologic necrosis, complete pathologic necrosis was seen in 27.2% of lesions treated with bland embolisation and 77% treated with Drug-Eluting Bead epirubicin. Given these results, it would be recommended that patients receive Drug-Eluting Bead epirubicin rather than bland embolisation, and there should be a low threshold for retreatment even in the setting of apparent radiologic necrosis.



At the top right of the image is an HCC nodule with coagulation necrosis. DC Bead (100–300µm), still perfectly round, are observed in vessels. Around the nodule, necrotic tissue within native liver is visible. A few giant cells are also present. (Hematoxylin and eosin stain, magnification x400.)

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# Drug-Eluting Bead in the Treatment of

## 5 Prognostic factors for survival in patients with unresectable hepatocellular carcinoma undergoing chemoembolization with doxorubicin drug-eluting beads: a preliminary study *Dhanasekaran R, Kooby D, Kim H et al, HPB (12) 2010: 174-180*

### ABSTRACT

**Background:** Transarterial chemoembolization (TACE) with drug-eluting beads is a new treatment modality. Little is known about prognostic factors affecting survival after DEB TACE [DEBDOX™] for patients with hepatocellular carcinoma (HCC).

**Methods:** Patients who underwent TACE with doxorubicin for unresectable HCC during 2006–2008 were studied. Survival was calculated from the day of first transcatheter therapy. Survival analysis was performed using Kaplan–Meier estimations. Survival curves were compared using the log-rank test.

**Results:** Fifty patients underwent chemoembolization with doxorubicin. They included 39 women and 11 men, with a median age of 57.5 years (range 28–91 years). Eighteen patients died during the study period and 32 remained alive. Overall survival rates at 6 months, 1 year and 2 years from the first administration of doxorubicin DEB TACE were 71%, 65% and 51%, respectively. Prognostic factors found to be significant on univariate analysis were Child–Pugh class, Okuda staging, bilirubin >2 mg/dl, albumin <3.0 g/dl, Model for End-stage Liver Disease (MELD) score, serum alphafetoprotein (AFP), Cancer of the Liver Italian Programme (CLIP) score, tumor satisfying Milan criteria, Eastern Cooperative Oncology Group (ECOG) performance status (PS) and Barcelona Clinic Liver Cancer (BCLC) staging.

**Conclusions:** Child–Pugh class, Okuda staging, bilirubin >2 mg/dl, albumin <3 g/dl, MELD score, serum AFP, CLIP score, Milan criteria, ECOG PS and BCLC staging were found to be prognostic markers of survival after treatment with doxorubicin DEB TACE in patients with unresectable HCC.

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### REVIEW

Dhanasekaran et al reviewed 50 patients who underwent LC Bead™ doxorubicin (DEBDOX) to review prognostic markers for survival. Univariate analysis showed Child–Pugh class, Okuda staging, bilirubin >2 mg/dl, albumin <3 g/dl, MELD score, serum AFP, CLIP score, Milan criteria, ECOG PS and BCLC staging to be significant prognostic factors for survival. Unfortunately, due to the small sample size, multivariate analysis was not able to be performed. This limits the strength of this study. The most important part of this trial is that survival was not influenced by the presence of portal vein thrombosis (PVT). PVT has traditionally been considered a contraindication for transarterial therapies. However, this trial suggests that perhaps with employing proper techniques, DEBDOX would potentially be offered to these patients as treatment for their malignancy.

### Univariate Analysis of Prognostic Factors

Variable	Category	n (events)	1 yr	2 yrs	HR (95% CI)	P-value
Age at diagnosis	<60 years	27 (10)	77%	61%	1.1 (0.4–3.6)	0.819
	>60 years	23 (8)	74%	55%		
Gender	Male	39 (12)	64%	52%	1.3 (0.7–2.3)	0.291
	Female	11 (6)	72%	64%		
Ethnicity	White	37 (13)	71%	62%	0.6 (0.2–2.1)	0.372
	Non-White	13 (5)	83%	63%		
Child–Pugh class	A	24 (6)	82%	73%	6.1 (1.7–22.3)	0.002
	B	14 (4)	75%	58%		
	C	12 (8)	50%	0%		
MELD score	<15	36 (10)	75%	67%	1.1 (0.9–1.2)	0.01
	>16	14 (8)	57%	29%		
Okuda stage	I	24 (3)	90%	67%	6.6 (1.4–30.6)	0.005
	II	14 (9)	67%	24%		
	III	12 (6)	48%	0%		
AFP	<400 ng/l	43 (8)	81%	74%	3.9 (1.4–11.2)	0.005
	>400 ng/l	7 (10)	29%	14%		
Portal vein	Thrombosed	12 (5)	58%	40%	0.4 (0.1–1.1)	0.128
	Patent	38 (13)	73%	64%		
Bilirubin	<2 mg/dl	32 (9)	81%	73%	2.8 (1.0–7.8)	0.038
	>2 mg/dl	18 (9)	50%	25%		
Albumin	>3.0 g/dl	19 (4)	88%	67%	5.3 (1.1–23.6)	0.015
	<3.0 g/dl	31 (14)	46%	35%		
Tumour burden	Uni-nodular	26 (8)	70%	62%	1.3 (0.7–2.6)	0.100
	Multi-nodular	15 (4)	73%	48%		
	Diffuse	9 (6)	44%	0%		
Milan criteria	Within	31 (10)	76%	58%	0.35 (0.1–0.9)	0.038
	Beyond	19 (8)	47%	31%		
CLIP score	<3	29 (5)	89%	70%	7.3 (2.0–25.0)	<0.001
	≥3	21 (13)	35%	23%		
BCLC stage	Early-intermediate	32 (8)	73%	62%	3.9 (1.3–11.6)	0.009
	Advanced	18 (10)	28%	0%		
ECOG PS	0	33 (5)	82%	82%	4.1 (2.0–8.3)	<0.001
	1–2	17 (13)	35%	12%		

HR, hazard ratio; 95% CI, 95% confidence interval; MELD, Model of End-stage Liver Disease; AFP, alphafetoprotein; CLIP, Cancer of the Liver Italian Programme; BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group; PS, performance status

Table adapted from Dhanasekaran R et al, HPB (12) 2010: 174–180



# DEB-TACE with DC Bead<sup>®</sup> [DEBDOX<sup>™</sup>] for Hepatocellular Carcinoma (HCC)

## 6 Prospective Randomized Comparison of Chemoembolization with Doxorubicin-Eluting Beads and Bland Embolization with Bead Block<sup>™</sup> for Hepatocellular Carcinoma

Malagari K, Pomoni M, Kelekis A et al. *Cardiovasc Interv Radiol* 33 (2010): 541-551

### ABSTRACT

The purpose of this study was to evaluate the added role of a chemotherapeutic in transarterial chemoembolization (TACE) of intermediate-stage hepatocellular carcinoma (HCC). The issue is of major importance since, as suggested by recent evidence, hypoxia or incomplete devascularization of the tumor is a potent stimulator of angiogenesis, and there are not many papers supplying level one evidence confirming the value of a chemotherapeutic. The hypothesis was that since drug-eluting bead (DEB)-TACE [DEBDOX<sup>™</sup>] is standardized and reproducible, a comparison with bland TACE can readily reveal the potential value of the chemotherapeutic. Two groups were randomized in this prospective study: group A (n = 41) was treated with doxorubicin DEB-TACE [DEBDOX], and group B (n = 43) with bland embolization. Patients were randomized for tumor diameter. Patients were embolized at set time intervals (2 months), with a maximum of three embolizations. Tumor response was evaluated using the EASL criteria and  $\alpha$ -fetoprotein levels. At 6 months a complete response was seen in 11 patients (26.8%) in the DEB-TACE group and in 6 patients (14%) in the bland embolization group; a partial response was achieved in 19 patients (46.3%) and 18 (41.9%) patients in the DEB-TACE and bland embolization groups, respectively. Recurrences at 9 and 12 months were higher for bland embolization (78.3% vs 45.7%) at 12 months. Time to progression (TTP) was longer for the DEB-TACE group ( $42.4 \pm 9.5$  and  $36.2 \pm 9.0$  weeks), at a statistically significant level ( $P=0.008$ ). In conclusion, DEB-TACE presents a better local response, fewer recurrences, and a longer TTP than bland embolization with Bead Block<sup>™</sup>. However, survival benefit and bland embolization with smaller particles must be addressed in future papers to better assess the clinical value.

### REVIEW

There remains debate as to the utility of chemoembolisation vs bland embolisation for treatment of HCC. Randomised controlled trials have been difficult to perform and interpret due to the heterogeneity of both TACE and TAE procedures. Malagari et al were able to add information to this question with a prospective randomised trial of DEB-TACE [DEBDOX] vs bland embolisation with Bead Block for treatment of HCC. The use of DEBDOX and Bead Block allows for standardisation of the procedure, which improves the ability to interpret the results. In this trial 87 patients underwent procedures every 2 months to a maximum of three procedures with beads of either 100-300 $\mu$ m or 300-500 $\mu$ m. Local response rates for complete response or stable disease were better in the DEBDOX group at both 6 and 12 month time periods. Overall response was only statistically different at 9 months, with 55% of DEBDOX having OR, compared to 31.7% of Bead Block. Time to progression was also longer in the DEBDOX group (42.4 weeks vs 36.2 weeks). Complications were similar in each group. While not every time point had statistically significant improvement with DEBDOX, all response evaluators were numerically improved with addition of doxorubicin to the embolic procedure. While there is no question that ischaemia has tumor effect, the use of doxorubicin should be incorporated into each patient treatment session unless there is a contraindication.

# Biocompatibles' Clinical Trial Programme

## Hepatocellular Carcinoma

Trial Details	Status
<b>Prospective Randomised Study of Transarterial Doxorubicin-Eluting Bead Embolisation vs Conventional TACE in the Treatment of Patients with Hepatocellular Carcinoma on the Liver Transplant Waiting List</b> <i>Charité Universitätsmedizin, Berlin, Germany</i>	<b>Recruiting</b>
<b>Assessment of Chemoembolisation using Doxorubicin-Eluting Beads in Patients Listed for Orthotopic Liver Transplantation with Hepatocellular Carcinoma with Explant Correlation</b> <i>Auckland City Hospital, New Zealand</i>	<b>Recruiting</b>
<b>LC Drug-Eluting Bead for Treatment of Liver Cancer Which Cannot be Surgically Removed (HCC)</b> <i>University of Pittsburgh Medical Center, PA, USA</i>	<b>Recruiting</b>
<b>A Pilot Study of Neoadjuvant Therapy for Hepatocellular Carcinoma using Doxorubicin-Eluting Embolic Beads</b> <i>Mount Sinai Hospital, New York, USA</i>	<b>Recruiting</b>
<b>Chemoembolization of Hepatocellular Carcinoma with Drug-Eluting Beads: Efficacy and Doxorubicin Pharmacokinetics (PRECISION I)</b> <i>Barcelona Clinic Liver Cancer (BCLC), Spain</i>	<b>Published:</b> Journal of Hepatology 46 (2007) 474-481
<b>A Phase I/II Trial of Chemoembolization for Hepatocellular Carcinoma using a Novel Intra-arterial Drug-Eluting Bead (PRECISION II)</b> <i>Queen Mary Hospital, Hong Kong</i>	<b>Published:</b> Journal Clinical Gastroenterology and Hepatology 5 (2007) 1100-1108
<b>Prospective Randomised Study of Doxorubicin in the Treatment of Hepatocellular Carcinoma by Drug-Eluting Bead Embolisation (PRECISION V).</b> <i>International multicentre RCT. Austria, France, Germany, Greece and Switzerland</i>	<b>Published Online:</b> Cardiovasc Intervent Radiol 33 (2010) 41-52
<b>Doxorubicin-eluting Bead-enhanced Radiofrequency Ablation of Hepatocellular Carcinoma: a Pilot Clinical Study</b> <i>Cisanello University Hospital, Pisa, Italy</i>	<b>Published:</b> Journal of Hepatology 49 (2008) 217-212
<b>Prospective Randomized Comparison of Chemoembolization with Doxorubicin-Eluting Beads and Bland Embolization with BeadBlock for Hepatocellular Carcinoma</b> <i>University of Athens, Greece</i>	<b>Published:</b> Cardiovasc Intervent Radiol 33 (2010) 541-551
<b>Single Centre Phase II Trial of Transarterial Chemoembolization with Drug-Eluting Beads for Patients with Unresectable Hepatocellular Carcinoma</b> <i>Johns Hopkins University Medical School, Baltimore, USA</i>	<b>Published:</b> The Cancer Journal 15 (2009) 526-532
<b>A Phase II Randomized, Double-blind, Placebo-controlled Study of Sorafenib or Placebo in Combination With Transarterial Chemoembolization (TACE) Performed With DC Bead and Doxorubicin for Intermediate Stage Hepatocellular Carcinoma (HCC)</b> <i>International Multicentre RCT sponsored by Bayer</i>	<b>Recruiting</b>

## Hepatic Metastases

Trial Details	Status
<b>Drug-Eluting Bead, Irinotecan (DEBIRI) Therapy of Liver Metastases from Colon Cancer with Concomitant Systemic Oxaliplatin, Fluorouracil and Leucovorin Chemotherapy, and Anti-Angiogenic Therapy</b>	<b>Recruiting</b> Pilot study (n=10) complete
<b>Chemoembolisation with Irinotecan-Loaded DC Bead® (DEBIRI) in Combination with Cetuximab in the First-line Treatment of Patients with KRAS Wild-type Metastatic Colorectal Cancer (mCRC)</b>	<b>Protocol in development</b>
<b>A Single-arm Phase II Study of Neoadjuvant Therapy Using Irinotecan Bead in Patients with Resectable Liver Metastases from Colorectal Cancer</b>	<b>Recruiting</b>
<b>A Randomised Phase II Trial of Irinotecan Drug-Eluting Beads Administered by Hepatic Chemoembolisation with Cetuximab (IV) vs Systemic Treatment with Irinotecan (IV) plus Cetuximab (IV) in Patients with Refractory Metastatic Colorectal Cancer and KRAS Wild-type Tumours</b>	<b>Recruiting</b>
<b>DC Bead®/LC Bead® International Registry</b>	<b>Recruiting</b>
<b>Chemoembolisation of Liver Metastases from Breast Carcinoma with Doxorubicin-Loaded DC Bead</b>	<b>Protocol in development</b>
<b>Transcatheter Arterial Chemoembolisation (TACE) with Doxorubicin-Loaded LC Bead in the Treatment of Liver Metastases in Patients with Stage IV Metastatic Melanoma: A Multicenter Pilot, Non-Randomised Feasibility Trial</b>	<b>Recruiting</b>
<b>Transarterial Chemoembolisation of Liver Metastases from Well Differentiated Gastroenteropancreatic Endocrine Tumours with Doxorubicin-Eluting Beads</b>	<b>Published</b> JVIR 19 (6) 2008

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