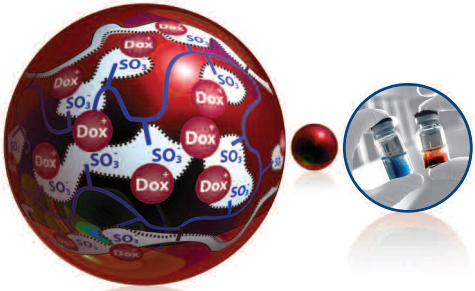
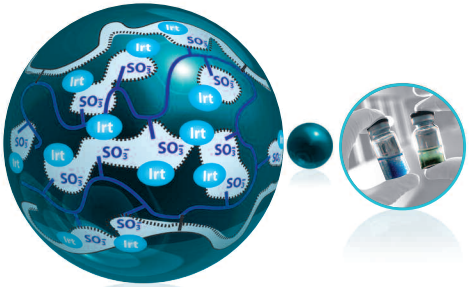
DC Bead®

DC Bead® is an embolic Drug-Eluting Bead capable of loading and releasing chemotherapeutic agents in a controlled manner.

DC Bead is CE-Mark approved for loading with doxorubicin (DEBDOX™) and irinotecan (DEBIRI™)





DEBDOX
(Drug-Eluting Bead doxorubicin)

DC Bead is intended to be loaded with doxorubicin for the purpose of:

- Embolisation of vessels supplying malignant hypervascularised tumour(s)
- Delivery of a local, controlled, sustained dose of doxorubicin to the tumour(s)

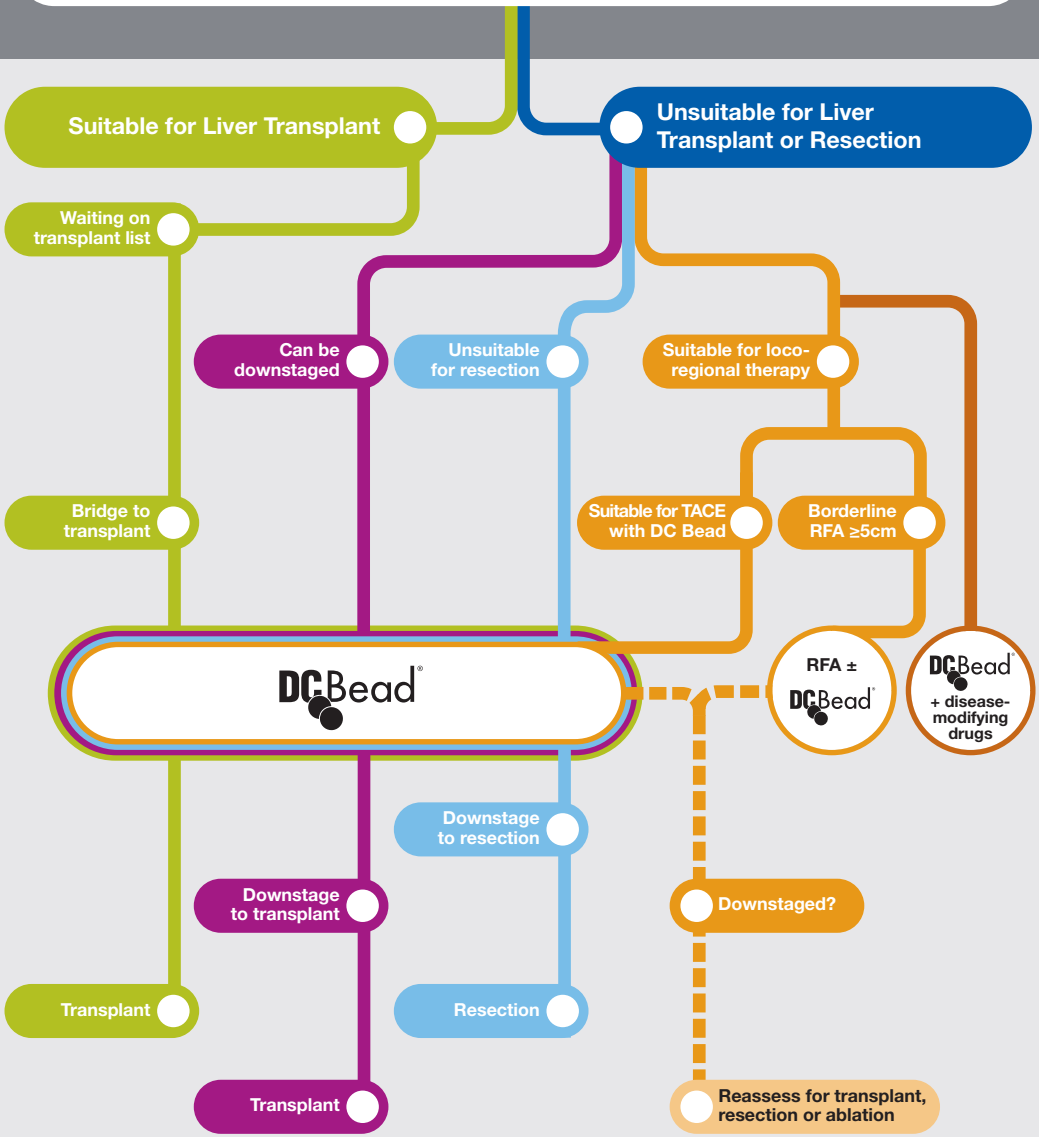
DEBIRI
(Drug-Eluting Bead irinotecan)

DC Bead is intended to be loaded with irinotecan for the purpose of:

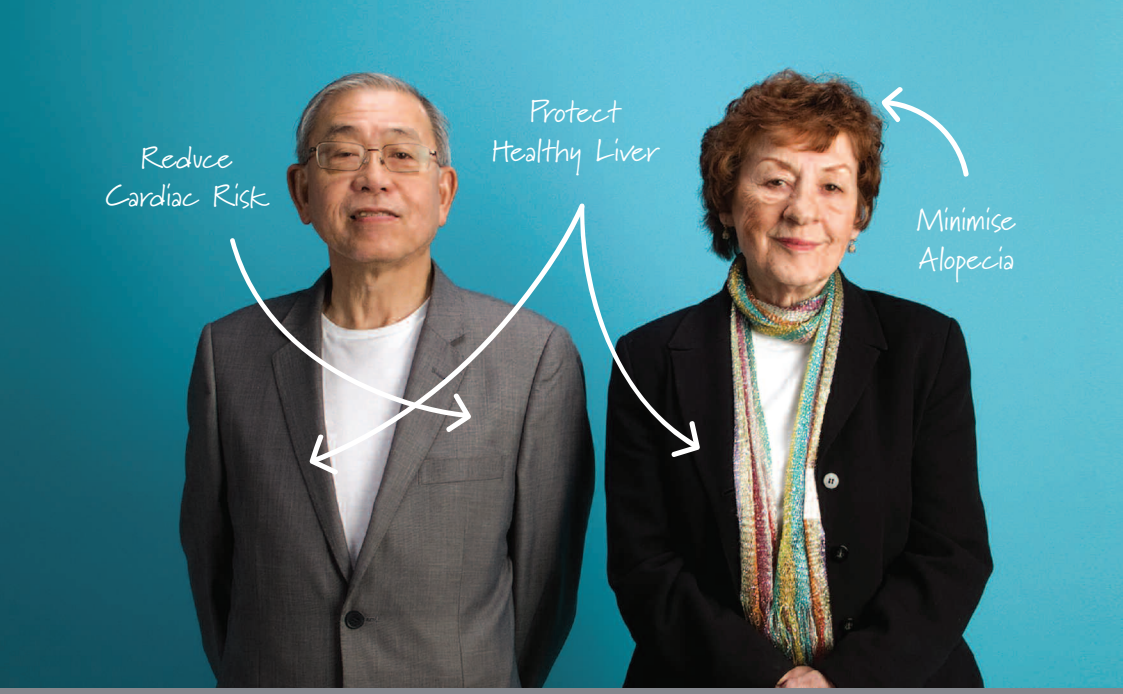
- Embolisation of vessels supplying malignant colorectal cancer metastasised to the liver (mCRC)
- Eluting a local, controlled, sustained dose of irinotecan to hepatic metastases of colorectal cancer

Biocompatibles

Biocompatibles' Hepatocellular Carcinoma Clinical Programme



The DC Bead® clinical programme targets treatment of a wide range of HCC patients by using the products alone and in combination with surgery and other treatment modalities



Protect your patients. **Improve** response.

Patients with HCC receiving PRECISION TACE™ with DC Bead®, experience less toxicity with improved response, compared to those receiving conventional chemoembolisation[1,2,3,4]

Results from the PRECISION V clinical trial[1]

✔ **Reduce Cardiac Risk**
DC Bead patients had maintained or improved cardiac function compared to those receiving conventional chemoembolisation.[1]

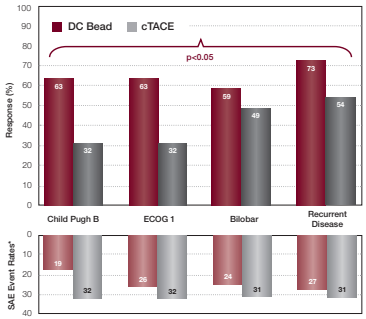
✔ **Improve Response**
DC Bead patients with more advanced disease showed a significant improvement in response ($p<0.05$) without a compromise in safety.[1]

✔ **Protect Healthy Liver**
DC Bead patients experienced significantly less elevation of liver enzymes ($p<0.01$) after each of three treatments.[1]

✔ **Minimise Alopecia**
DC Bead patients benefit from a highly significant ($p<0.001$) reduction in doxorubicin related SAEs.[1]

DC Bead, minimise the toxicity of TACE, for your patients and you

Response and Adverse Events - Advanced Disease
PRECISION TACE vs Conventional TACE[1]
Objective Response ($p=0.038$) and Disease Control ($p=0.026$)



*Per 100 patients, event within 30 days of treatment

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

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www.biocompatibles.com

Trials for Hepatic Metastases

	Design	Endpoint	Regimen	Status	n	Location
Colorectal	**Drug-Eluting Bead, Irinotecan (DEBIRI) Therapy of Liver Metastases from Colon Cancer with Concomitant Systemic Oxaliplatin, Fluorouracil and Leucovorin Chemotherapy, and Anti-Angiogenic Therapy**					
	Feasibility phase: 10 patients (complete) Randomised phase: 60 patients	Safety Efficacy	FOLFOX + Avastin (IV) vs FOLFOX + Avastin + DEBIRI	Recruiting	70	USA

Schema

Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7
FOLFOX + Avastin	LC Bead 100mg Irinotecan	FOLFOX +Avastin	LC Bead 100mg Irinotecan	FOLFOX + Avastin	Break	FOLFOX + Avastin

- Then repeat CT to evaluate initial response

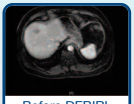
Response Rates and Pharmacokinetics to Date

- 3 and 6-month response rate: 100% (2 CR, 8 PR)

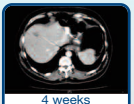
Surgical Downstaging

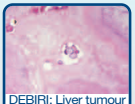
- 5 (50%) patients downstaged to resection
- All tolerated surgical resection
- Pathologic response rates >90%

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)					
Feasibility study	Feasibility Safety Efficacy	FOLF + Cetuximab + DEBIRI	Protocol in development	20	Belgium
A Single-arm Phase II Study of Neoadjuvant Therapy Using Irinotecan Bead in Patients with Resectable Liver Metastases from Colorectal Cancer					
Single-arm, multicentre	Rate of R0 at Resection	DEBIRI Prior to Resection	Recruiting	40	UK, Spain, France


Before DEBIRI


No DEBIRI: Viable liver tumour cells


4 weeks after DEBIRI


DEBIRI: Liver tumour cell death

Response Rates to Date

- 19 patients recruited and embolised
- 17 now operated
- 50% demonstrate 90-100% tumour necrosis
- 30% demonstrate 50-90% tumour necrosis
- 20% demonstrate <50% tumour necrosis

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					
Multicentre Randomised controlled trial	Safety Efficacy	Cetuximab + DEBIRI vs Cetuximab + irinotecan	Recruiting	80	Germany
DC Bead®/LC Bead™ International Registry					
Registry	Safety Efficacy	DEBIRI in current clinical practice	Recruiting	735	Global
Phase II Study of Drug-Eluting Irinotecan Beads (DEBIRI) in Refractory Metastatic Colorectal Cancer with Liver-only or Liver-predominant Disease					
Feasibility study	Safety Efficacy	LC Bead + Irinotecan	Recruiting	32	USA
Melanoma	**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**				
Multicentre pilot study	Feasibility Safety Efficacy	LC Bead + Doxorubicin	Recruiting	40	USA + Germany
Neuroendocrine	**Transarterial Chemoembolisation of Liver Metastases from Well Differentiated Gastroenteropancreatic Endocrine Tumours with Doxorubicin-Eluting Beads**				
Single-arm, prospective study	Feasibility Safety Efficacy	DC Bead + Doxorubicin	Published JVIR 19 (6) 2008	30	France

DC Bead®

Clinical Trials for Hepatocellular Carcinoma

	Study Design	Endpoint	Status	n	Location
Bridge to Liver Transplant	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				
	Multicentre, Randomised, Phase II	Histological Response and Transplantability	Recruiting	72	Germany
	Assessment of Chemoembolisation using Doxorubicin-Eluting Beads in Patients Listed for Orthotopic Liver Transplantation with Hepatocellular Carcinoma with Explant Correlation				
	Single-Centre, Phase II	Histological Response and Transplantability	Recruiting	30	New Zealand
	LC Drug-Eluting Bead for Treatment of Liver Cancer Which Cannot be Surgically Removed (HCC)				
	Single-Centre, Phase II	Histological Response and Resectability	Recruiting	20	USA
Unsuitable for Liver Transplant or Resection	Chemoembolization of Hepatocellular Carcinoma with Drug-Eluting Beads: Efficacy and Doxorubicin Pharmacokinetics (PRECISION I)				
	Single-Centre, Phase II	Safety, Efficacy and Pharmacokinetics (Dose Escalation)	Published: Varela M, Real MI, Burrel M et al: Journal of Hepatology 46 (2007) 474-481	27	Spain
	A Phase I/II Trial of Chemoembolization for Hepatocellular Carcinoma using a Novel Intra-arterial Drug-Eluting Bead (PRECISION II)				
	Prospective, Single-Arm, Phase I/II	Phase I: Dose Escalation Phase II: Safety and Efficacy	Published: Poon R, Tso W, Pang R et al: Journal Clinical Gastroenterology and Hepatology 5 (2007) 1100-1108	35	Hong Kong
	Prospective Randomised Study of Doxorubicin in the Treatment of Hepatocellular Carcinoma by Drug-Eluting Bead Embolisation (PRECISION V)				
	International Multicentre, Prospective, Randomised, Single-Blind, Phase II	Safety and Efficacy	Published: Lammer J, Malagari K, Vogl T et al: Cardiovasc Intervent Radiol 33 (2010) 41-52[1]	212	International Multicentre
	Doxorubicin-eluting Bead-enhanced Radiofrequency Ablation of Hepatocellular Carcinoma: a Pilot Clinical Study				
	Prospective, Single-Arm, Pilot	Safety and Efficacy	Published: Lencioni R, Crocetti L, Petruzzi P et al: Journal of Hepatology 49 (2008) 217-222	20	Italy
	Prospective Randomized Comparison of Chemoembolization with Doxorubicin-Eluting Beads and Bland Embolization with BeadBlock for Hepatocellular Carcinoma				
	Prospective, Randomised, Single-Centre	Efficacy, Safety, Time to Progression and Survival	Published: Malagari K, Pomoni M, Kelekis et al: Cardiovasc Intervent Radiol 33 (2010) 541-551	41	Greece
	Single Centre Phase II Trial of Transarterial Chemoembolization with Drug-Eluting Beads for Patients with Unresectable Hepatocellular Carcinoma				
	Prospective, Single-Arm, Phase II, Pilot	Efficacy, Safety, Feasibility, Progression-Free Survival and Overall Survival	Published: Reyes D, Vossen J, Geschwind J et al: The Cancer Journal 15 (2009) 526-532	20	USA
	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)				
	International Multicentre, Randomised, Double-Blind, Phase II	Time to Untreatable Progression	Recruiting	300	International Multicentre

Bridge to Liver Transplant

Unsuitable for Liver Transplant or Resection

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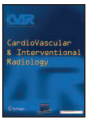

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Martin R, Joshi J, Robbins K et al
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DC Bead Ordering Information

Label Colour	Nominal Bead Size	Volume of Beads	Product Code
Yellow	100 - 300µm	2ml	DC2V103
Blue	300 - 500µm	2ml	DC2V305
Red	500 - 700µm	2ml	DC2V507

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DC Bead®

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