



Prospective, Randomised, Multi-centre Study of Doxorubicin in the Treatment of Hepatocellular Carcinoma by PRECISION TACE™ with DC Bead®

PRECISION V Trial Design

- Control arm of conventional transarterial chemoembolisation (cTACE) with doxorubicin
- 200 patients (100 per arm)
- 23 European centres in Austria, France, Germany, Greece, and Switzerland
- Patients receive up to 3 treatments (baseline, 2 and 4 months)
- Follow-up period: 6 months

Patient Demographics

Characteristics	DC Bead (n=102)	cTACE (n=110)
Age Mean (±sd)	67.0 years (±9.2)	67.3 years (±8.8)
Sex (Male/Female)	88/14	97/13
Aetiology (HepC/HepB/Alcohol/Other & Mixed)	20/14/41/27	12/13/52/33
Okuda (I/II)	88/14	104/6
BCLC (A/B/C)*	26/76/0	29/81/0
No. Lesions Median (interquartile range)	2 (1-4)	2 (1-4)
Sum Longest Diameter Mean (±sd)	9.4cm (±6.15)	9.0cm (±6.00)
Liver Involvement Mean (±sd)	16.9% (±15.0)	16.5% (±14.2)

*BCLC Classification according to tumour stage (Llovet et al Lancet 2003)

Product, Dose and Technique Guidelines

PRECISION TACE™ with DC Bead®

- 2 x 2ml vials of DC Bead (total 4ml) loaded at 37.5mg/ml for total dose of 150mg
- 1 vial of 300-500µm followed by 1 vial of 500-700µm

cTACE

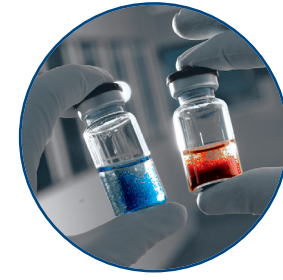
- Doxorubicin dose of 50-75mg/m² to maximum of 150mg
- Physician preference for embolic

Technique for both groups

- Unifocal tumours treated with selective segmental chemoembolisation
- Microcatheter could be used
- Bilobar disease: both lobes treated within a 3-week period
- Embolisation to stasis in 2nd or 3rd order branches
- DC Bead group: additional Bead Block™ could be used



Drug Delivery Embolisation System for PRECISION TACE



DC Bead® Bibliography



Chemoembolization of hepatocellular carcinoma with drug eluting beads: Efficacy and doxorubicin pharmacokinetics.

Varela, M., Real, M.I., Burrel, M. et al Journal of Hepatology 46 (2007) 474-481



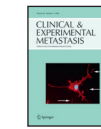
Intraarterial Hepatic Chemoembolization of Liver Metastases from Colorectal Cancer Adopting Irinotecan-eluting Beads: Results of a Phase II Clinical Study.

Florentini, G., Alberti, C., Turisi, G. et al In vivo 21: 1085-1092 (2007)



Preservation of the active lactone form of irinotecan using drug eluting beads for the treatment of colorectal cancer metastases.

Tang, Y., Czuczman, P.R., Chung, S.T. et al Journal of Controlled Release 127 (2008) 70-78



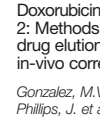
Chemoembolisation of rat colorectal liver metastases with drug eluting beads loaded with irinotecan or doxorubicin.

Eyol, E., Boleij, A., Taylor, R. et al Clinical and Experimental Metastasis (2008) 25: 273-282



Doxorubicin eluting beads-1: Effects of drug loading on bead characteristics and drug distribution.

Lewis, A.L., Gonzalez, M.V., Leppard, S.W. et al Journal of Materials Science. Special Section: Polymer Fibers 2006



Doxorubicin eluting beads-2: Methods for evaluating drug elution and in-vitro: in-vivo correlation.

Gonzalez, M.V., Tang, Y., Phillips, J. et al



Transarterial Chemoembolization of Unresectable Hepatocellular Carcinoma with Drug Eluting Beads: Results of an Open-Label Study of 62 Patients.

Malagari, K., Chatzimichail, K., Alexopoulos, E. et al Cardiovasc Intervent Radiol (2008) 31: 269-280



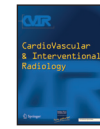
Transarterial Chemoembolization of Liver Metastases from Well Differentiated Gastropancreatic Endocrine Tumors with Doxorubicin-eluting Beads: Preliminary Results.

de Baere, T., Deschamps, F., Terlizheau, C. et al J Vasc Interv Radiol 2008, 19:855-861



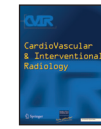
Transcatheter chemoembolization in the treatment of HCC in patients not eligible for curative treatments: mid-term results of doxorubicin-loaded DC Bead.

Malagari, K., Alexopoulos, E., Chatzimichail, K. et al Abdominal Imaging 2006; 33(5):512-9.



Drug-Loaded Microspheres for the Treatment of Liver Cancer: Review of Current Results.

Kettenbach, J., Stadler, A., van Katzler, I. et al (J Lammner) Cardiovasc Intervent Radiol (2008) 31: 468-476



Chemoembolization (TACE) of Unresectable Intrahepatic Cholangiocarcinoma with Slow-Release Doxorubicin-Eluting Beads: Preliminary Results.

Alberti, C., Benea, G., Tili, M. et al Cardiovasc Intervent Radiol (2008)



Doxorubicin-eluting bead-enhanced radiofrequency ablation of hepatocellular carcinoma: A pilot clinical study.

Lencioni, R., Crocetti, L., Petruzzi, P. et al Journal of Hepatology 49 (2008) 217-222



*PRECISION V Publication Committee

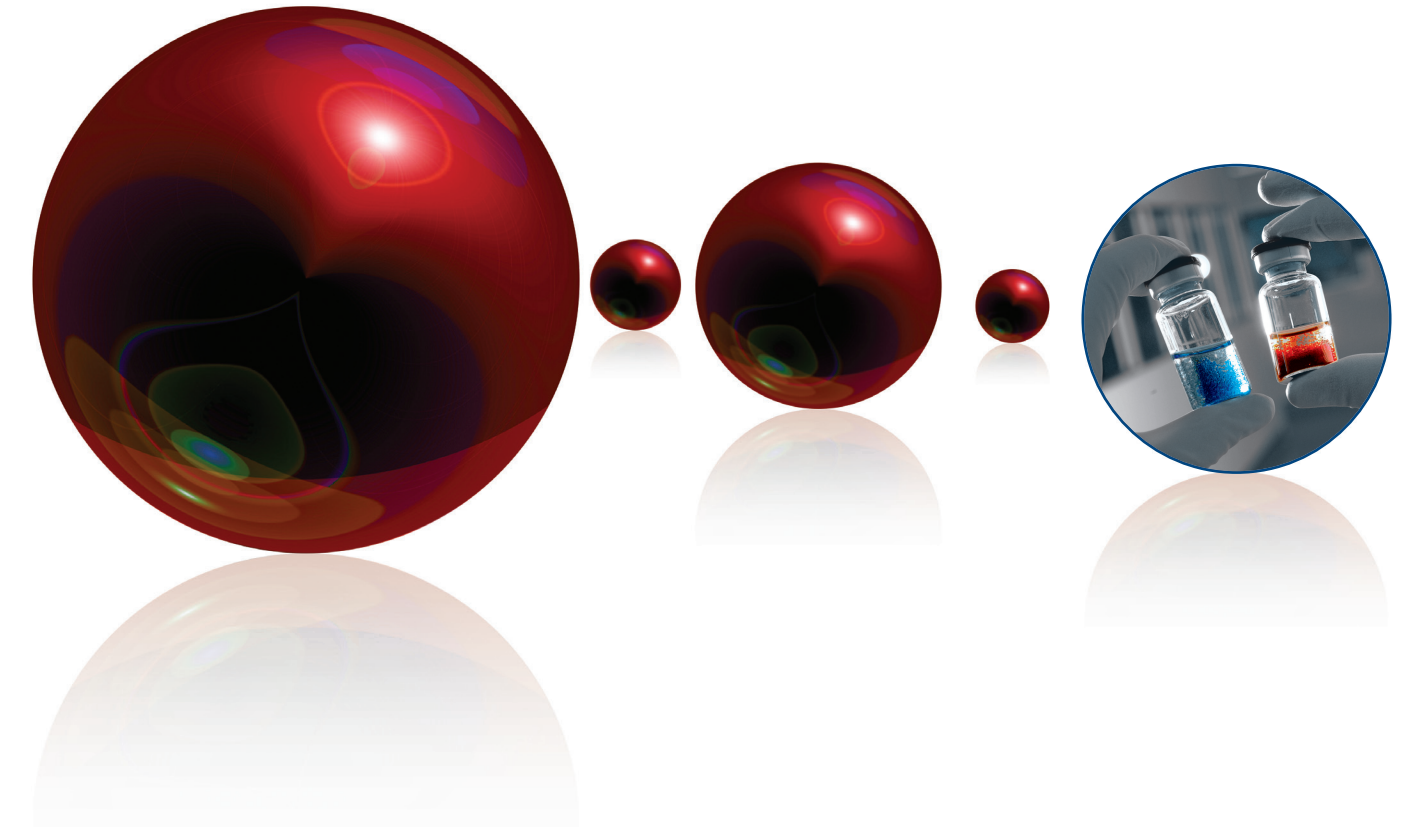
Professor Johannes Lammner, Vienna
 Professor Katarina Malagari, Athens
 Professor Alban Denys, Lausanne
 Professor Riccardo Lencioni, Pisa
 Professor Frank Pilleul, Lyon
 Professor Anthony Watkinson, Exeter
 Professor Thomas Vogl, Frankfurt

DC Bead is a registered trademark and PRECISION TACE and Bead Block are trademarks of Biocompatibles UK Ltd. DC Bead® is not currently available for sale or distribution in the USA. EC09-020T. © 2009 Biocompatibles UK Ltd.



Hepatocellular Carcinoma

Greater tolerability
 Increased efficacy
 More safely
 for more patients



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

Biocompatibles UK Limited
 Chapman House
 Farnham Business Park
 Weydon Lane
 Farnham, Surrey, GU9 8QL, UK.
 Tel: +44 (0)1252 732 710
 Fax: +44 (0)1252 732 703
 email: marketing@biocompatibles.com
 www.biocompatibles.com



Greater tolerability
Increased efficacy
More safely
for more patients

“We believe that these results show that DC Bead® is a better treatment than conventional TACE. An improved response with significantly lower toxicity is unusual for a new cancer therapy.”

PRECISION V Publication Committee*

PRECISION V Conclusions⁵

- PRECISION TACE™ with DC Bead® is safe, efficacious and reproducible
- There is a highly significant reduction in liver toxicity in PRECISION TACE with DC Bead
- There is a significant advantage of PRECISION TACE with DC Bead in more advanced patients – those with more compromised liver function, poorer performance status, bilobar disease and recurrent disease – greater response, greater disease control and improved safety
- Currently AASLD guidelines do not recommend chemoembolisation for Child B and ECOG 1 patients. The PRECISION V data show that these patients can now be safely treated with PRECISION TACE with DC Bead

DC Bead® is a Drug Delivery Embolisation System capable of loading and releasing in a controlled manner high doses of chemotherapeutic agents.¹

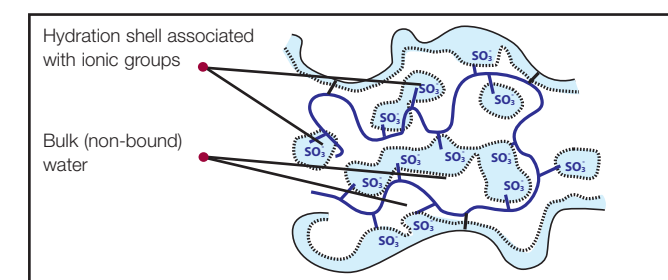
DC Bead Indication for Use

DC Bead is CE-Mark approved and is intended to be loaded with doxorubicin for the purpose of:

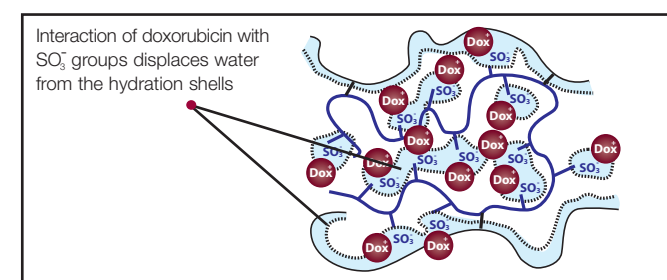
- Embolisation of vessels supplying malignant hypervascularised tumour(s)
- Delivery of a local, controlled, sustained dose of doxorubicin to the tumour(s)
- Doxorubicin maximum dose of 37.5mg/ml and 150mg per treatment with 4ml DC Bead

Interaction of Doxorubicin With DC Bead Sulphonate Groups

Hydrated Beads



Loaded Beads

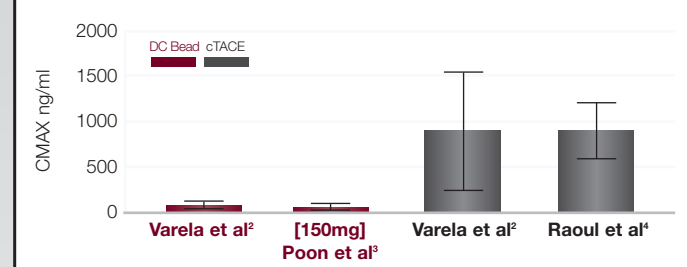


DC Bead Presentation

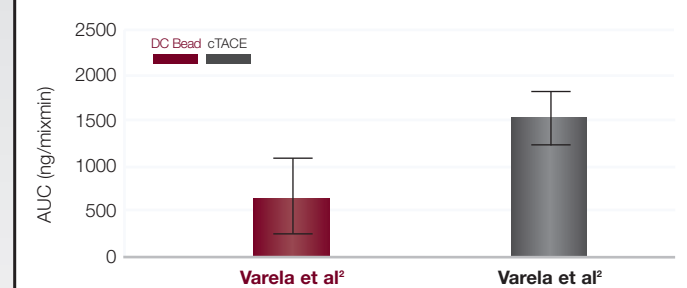
- Novel N-fil technology sulphonate modified hydrogel polymer
- Blue tinted to aid visualisation
- Delivered as vials containing 2ml Beads in 6ml saline
- Precise calibration to achieve an accurate level of embolisation



Systemic Exposure – Peak Concentration (Cmax) PRECISION TACE vs Conventional TACE

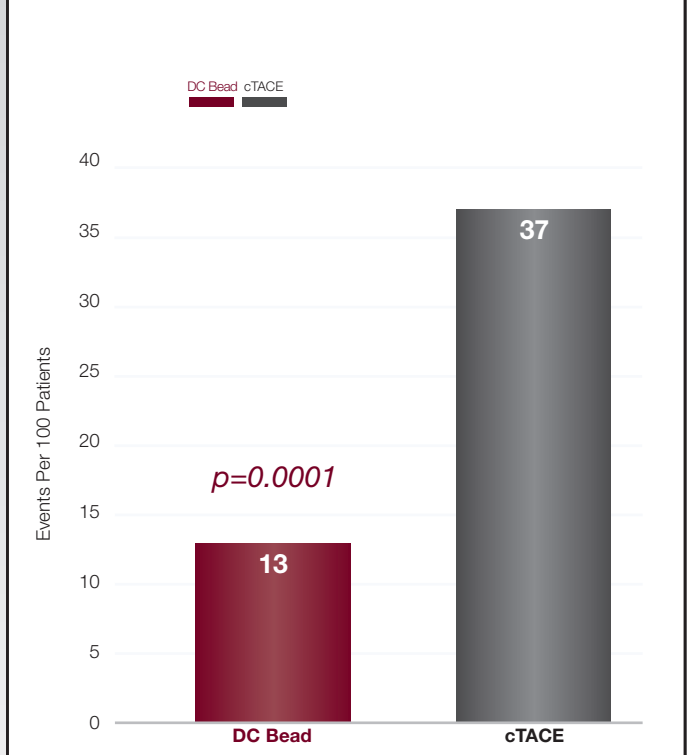


Total Systemic Exposure – Area under the Curve (AUC) PRECISION TACE vs Conventional TACE



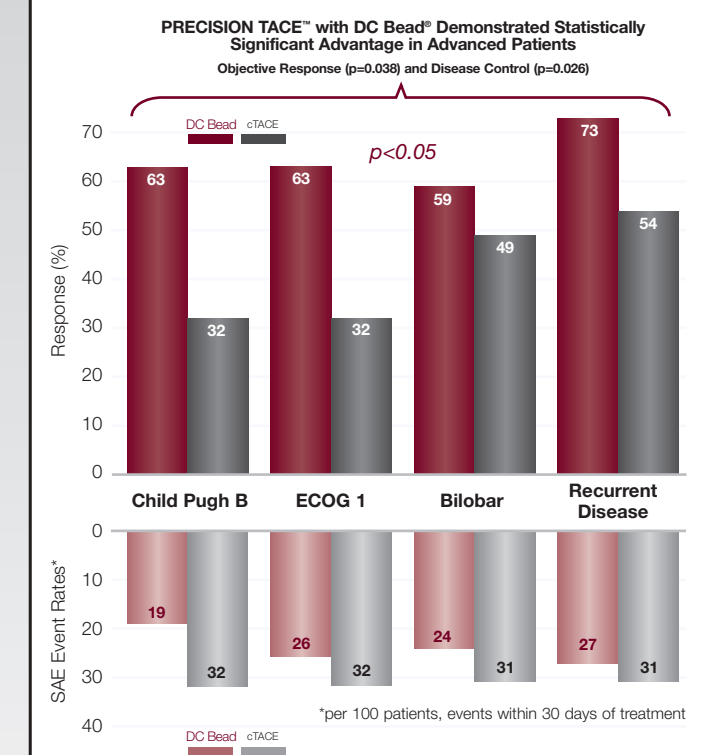
DC Bead® was shown by Varela et al² to deliver a more targeted release of doxorubicin to the tumour, with greater consistency. Patients experienced a substantial reduction in both peak concentration and total systemic exposure to doxorubicin.

Doxorubicin-Related Side Effects



In the PRECISION V clinical trial, patients who received PRECISION TACE with DC Bead® had a highly significant (p< 0.001) reduction in doxorubicin-related systemic adverse events, despite receiving 30% more doxorubicin.

Response and Adverse Events – Advanced Disease

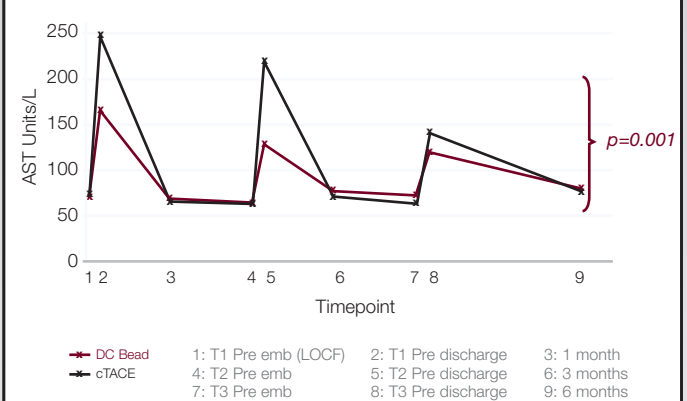


DC Bead® improved response in all treated patients. More Advanced Patients demonstrated a significant improvement (p<0.05). All DC Bead patients experienced fewer treatment-related side effects compared to the control group.

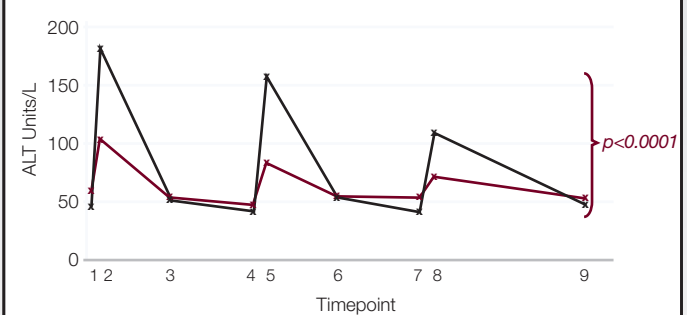
Classification	DC Bead Response (%)			cTACE Response (%)		
	DC	OR	CR	DC	OR	CR
Child Pugh B	63	44	25	32	21	16
ECOG 1	63	63	37	32	29	14
Bilobar	59	49	17	49	40	13
Recurrent Disease	73	55	27	54	31	15

DC = Disease Control OR = Objective Response CR = Complete Response

Liver Enzyme Levels (AST)



Liver Enzyme Levels (ALT)



The elevation of liver enzyme levels after each of the three treatments was significantly less in patients receiving DC Bead®, demonstrating that PRECISION TACE with DC Bead is less toxic to healthy liver.

1. Biocompatibles Instructions for use.

2. Varela, M., Real, M.J., Burrel, M. et al. Chemoembolization of hepatocellular carcinoma with drug eluting beads: Efficacy and doxorubicin pharmacokinetics. Journal of Hepatology 2007; 46:474-481.
3. Poon, R.T.P., Tso, W.K., Pang, R.W.C. et al. A phase III Trial of chemoembolization for hepatocellular carcinoma using a novel intra-arterial drug-eluting bead. Clinical Gastroenterology and Hepatology 2007; 5:100-1108
4. Raoul, J.L., Herebach, D., Bretagne, J.F. et al. Chemoembolisation of hepatocellular carcinomas: a study of the biodistribution and pharmacokinetics of doxorubicin. Cancer 1992; 70:585-590.

5. Lammer, J. Plenary Presentation September 17. CIRSE 2008.