DCBead™

Improving outcomes as a monotherapy or in patients receiving sorafenib
DC Bead™
delivering the standard of care in intermediate HCC

DC Bead™ has been shown in multiple studies to offer benefits to patients vs conventional TACE in terms of improved response, survival and time to progression, and reduced systemic exposure.²,³,⁴,⁵ New data now demonstrate DC Bead™ is well tolerated by patients receiving sorafenib.¹,⁶

DC Bead™
Giving HCC patients more treatment options
**DC Bead™**

in patients receiving sorafenib is well tolerated with favourable disease control

Phase II Trial of Sorafenib Combined with Concurrent Transarterial Chemoembolization with Drug-Eluting Beads for Hepatocellular Carcinoma


- Prospective, single-centre phase II study
- 35 intermediate HCC patients
- Combined protocol of sorafenib and DC Bead™
- **Most toxicities were minor**
  (grade 1/2 = 83%; grade 3/4 = 17%)
- Toxicities were manageable with dose adjustment of sorafenib
- Promising preliminary efficacy data

"In summary, the combination of sorafenib and DEB-TACE in patients with unresectable HCC was well tolerated."


**Inclusion Criteria**

- ECOG Status 0 or 1
- Child-Pugh A or B
- ALT and AST <8 x ULN (upper limit of normal)
- Bilirubin <3mg/dl and albumin >2.0mg/dl
- Life expectancy >12 weeks
- Adequate bone marrow, renal & cardiac function

Patients with prior sorafenib use of <3 months were eligible

**Efficacy of DC Bead™ in Patients Receiving Sorafenib**

<table>
<thead>
<tr>
<th>Response (%)</th>
<th>Complete Response</th>
<th>Partial Response</th>
<th>Stable Disease</th>
<th>Progressive Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECIST</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td>0%</td>
<td>9%</td>
<td>5%</td>
<td>3.5%</td>
</tr>
<tr>
<td>EASL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0%</td>
<td>0%</td>
<td>53.5%</td>
<td>43%</td>
<td>0%</td>
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</table>

**Study Schema (one cycle)**

<table>
<thead>
<tr>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5</th>
<th>Week 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sorafenib 400mg x 2 daily</td>
<td>Sorafenib 400mg x 2 daily</td>
<td>Sorafenib 400mg x 2 daily</td>
<td>Sorafenib 400mg x 2 daily</td>
<td>Sorafenib 400mg x 2 daily</td>
<td>Sorafenib 400mg x 2 daily</td>
</tr>
</tbody>
</table>

+ DC Bead™

- Dose reductions and interruptions permitted if toxicities seen
- A maximum of five DC Bead™ treatments were given (one per 6-week cycle)
  The median number of DC Bead™ treatments was one (range 1-5)

"Preliminary efficacy results for combined sorafenib and DEB-TACE were promising, as demonstrated by an excellent disease control rate."

DC Bead™
in patients receiving sorafenib is well tolerated

Sorafenib or Placebo in Combination with Transarterial Chemoembolization (TACE) with Doxorubicin-Eluting Beads for Intermediate-Stage Hepatocellular Carcinoma: Phase II, Randomized, Double-Blind, Placebo-Controlled SPACE Trial

Lencioni R, Llovet JM, Han G et al. Plenary presentation, March 2010, Society of Interventional Radiology (SIR), Tampa, Florida, USA

- **First randomised, double-blind, placebo-controlled phase II trial** to measure efficacy and safety of administering sorafenib in addition to DC Bead™
- 307 intermediate HCC patients randomised to receive DC Bead™ + placebo vs DC Bead™ + sorafenib
- 85 centres in 13 countries (Europe, North America and Asia)
- Patients in the sorafenib group showed a **statistically significant improvement in time to progression** vs patients receiving DC Bead™ alone ($p = 0.072$)

**DC Bead™ in patients receiving sorafenib is well tolerated**

† Pre-defined one-sided alpha of 0.15. HR: 0.797 (95% CI: 0.588 - 1.080).

**Study Schema**

- **Inclusion Criteria**
  - Unresectable, multinodular, HCC
  - Child-Pugh A without ascites or encephalopathy
  - ECOG Status of 0

- First TACE with DC Bead™ performed 3-7 days after start of treatment with sorafenib or placebo
- Subsequent TACE with DC Bead™ performed on day 1 (+/- 4 days) of cycles 3, 7, and 13, and every 6 cycles thereafter
- Patients allowed optional TACE with DC Bead™ sessions between cycles 7 and 13 and cycles 13 and 19, if deemed necessary by the investigator
DC Bead™ improves overall 5-year survival rate

Chemoembolization with Doxorubicin-Eluting Beads for Unresectable Hepatocellular Carcinoma: Five-year Survival Analysis

- Prospective study to measure efficacy of DC Bead™
- 173 BCLC A/B patients unsuitable for curative treatments
- DC Bead™ resulted in **high 5-year survival rate (22.5%)** and **mean overall survival (OS) of 43.8 months**, exceeding results previously reported for cTACE⁷,⁸
- Child-Pugh A patients had longer OS than Child-Pugh B patients
- Response rate observed after first DC Bead™ treatment improved after second and third treatments

![Graph showing Overall Survival (OS) for Child-Pugh A and B patients.](image)

**Study Schema**

**Inclusion Criteria**
- BCLC Stage A/B HCC
- Bilirubin <3 mg/dl
- AST and ALT <270 units/litre

- Three DC Bead™ procedures were scheduled, unless complete response was achieved within two treatments
- Additional embolisations using DC Bead™ were conducted ‘on demand’ if progressive disease was noted during follow-up
- Mean number of embolisations was 5.6 (range 1–9)
Interventional Radiology + Hepatology

References:
5 Varela M, Real MI, Burrel M et al. J Hepatol 46 (2007): 474-481
6 Lencioni R, Llovet JM, Han G et al. Plenary presentation, March 2010, Society of Interventional Radiology (SIR), Tampa, Florida, USA

Important Safety Information

DC Bead Indications:
• DC Bead is CE marked and is indicated for the treatment of malignant hypervascular tumours and loading with doxorubicin drug.
• DC Bead is also indicated for loading with irinotecan for the treatment of metastatic colorectal cancer (mCRC).

Note: Doxorubicin is not indicated for the treatment of HCC.

DC BeadM1 Indications:
• DC BeadM1 is primarily intended as an embolic agent for the treatment of malignant hypervascularised tumours.
• DC BeadM1 is compatible with irinotecan, which can be loaded prior to embolisation and then, as a secondary action, elute a local, controlled and sustained dose to the tumour after embolisation.

Note: Doxorubicin is not indicated for the treatment of HCC.

For full instructions for use, please refer to: www.biocompatibles.com/dcbead-ifu

DC Bead and DC BeadM1 are manufactured by Biocompatibles UK Ltd.

Cautions:
DC Bead and DC BeadM1 should only be performed by a physician with appropriate interventional occlusion training in the region intended to be embolised.

- Do not use the i.v. or packaging damaged.
- Consideration should be given to 99mTc-MAA scanning if there is suspicion of AV shunting.
- Do not use if the vial or packaging appear damaged.
- Do not use if the vial or packaging appear damaged.
- The maximum amount of irinotecan that can be loaded is 100mg irinotecan per 2ml vial of DC Bead/DC BeadM1. Exceeding this amount may lead to some irinotecan remaining free in solution. This free solution should be removed prior to use to prevent the patient receiving the excess dose as a bolus.

Potential Complications:
- Undesirable reflux or passage of DC Bead/DC BeadM1 into normal arteries adjacent to the targeted lesion or through the lesion into other arteries or arterial beds.
- Non-target embolisation.
- Pulmonary embolisation.
- Ischaemia at an undesirable location.
- Capillary bed saturation and tissue damage.
- Ischaemic stroke or ischaemic infarction.
- Vessel or lesion rupture and haemorrhage.
- Neurological deficits including cranial nerve palsies.
- Vasospasm.
- Death.
- Recanalisation.
- Foreign body reactions necessitating medical intervention.
- Infection necessitating medical intervention.
- Clot formation at the tip of the catheter and subsequent dislodgement causing arterial thromboembolic sequelae.

WARNING: Studies have shown that DC Bead and DC BeadM1 do not form aggregates and, as a result, penetrate deeper into the vasculature as compared to similarly sized PVA particles.

Ordering Information:

<table>
<thead>
<tr>
<th>Product Name</th>
<th>DC BeadM1</th>
<th>DC Bead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Label Colour and Size</td>
<td>70-150µm</td>
<td>100-300µm</td>
</tr>
<tr>
<td>Volume of Beads</td>
<td>2ml</td>
<td>2ml</td>
</tr>
<tr>
<td>Product Code</td>
<td>DC2V001</td>
<td>DC2V013</td>
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</tbody>
</table>

For more information, please contact:
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email: marketing@biocompatibles.com
www.biocompatibles.com

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