Conventional TACE vs. drug-eluting beads

Ulf Teichgräber, MD, MBA
Department of Radiology
University Hospital Jena
Disclosure of conflict of interest

Speaker name: Ulf Teichgräber, MD, MBA

Potential conflicts of interest related to the presentation:

- Research grant, honoraria: Celonova (Boston Scientific)

Potential conflicts of interest not related to the presentation:


- Master research agreements with Siemens Healthcare, GE Healthcare
Classics

Ferdinand Porsche

Marcel Guerbet

Source: Volkswagen AG
TACE with Lipiodol

Embolization
- Mixture of Lipiodol mit chemotherapeutic agent 1:1
- e.g. with Doxorubicin (50mg) / Cisplatin (50mg)

Before TACE

After TACE

Source: own images
Disadvantage

Emulsion instead of chemical binding of embolizing agent with the chemotherapeutic substance

Source: Filipebvarela / fotolia.com
Interactive chemical groups

TACE with Drug-loaded Beads

- Chemical binding of the therapeutic substance
- After application
  - Local effect
  - High local drug release for 7 d
- Minimal systemic effect

Source: Sirtex
Prospective Randomized Study of Doxorubicin-Eluting-Bead Embolization in the Treatment of Hepatocellular Carcinoma: Results of the PRECISION V Study

Johannes Lammer · Katarina Malagari · Thomas Vogl · Frank Pilleul · Alban Denys · Anthony Watkinson · Michael Pitton · Geraldine Sergent · Thomas Pfammatter · Sylvain Terraz · Yves Benhamou · Yves Avajon · Thomas Gruenberger · Maria Pomoni · Herbert Langenberger · Marcus Schuchmann · Jerome Dumortier · Christian Mueller · Patrick Chevallier · Riccardo Lencioni · On Behalf of the PRECISION V Investigators

Received: 9 June 2009 / Accepted: 21 August 2009 / Published online: 12 November 2009
© Springer Science+Business Media, LLC and the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) 2009
• 212 patients with Child-Pugh A/B cirrhosis and large and/or multinodular, unresectable HCCs were randomized.
• Primary Endpoint TR @ 6 months.
• The DC-beads group showed higher rates of CR, OR, and DC compared with the cTACE group (27% vs. 22%, 52% vs. 44%, and 63% vs. 52%) (P=0.11).

→ Hypothesis of superiority of DC-beads was not met!
• 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 ($P = 0.0001$).
Systematic review comparing the safety and efficacy of conventional and drug-eluting bead transarterial chemoembolization for inoperable hepatocellular carcinoma


Hepatobiliary Surgery Department, Affiliated Tumor Hospital of Guangxi Medical University, Nanning, China
Meta-analysis data on objective TR

<table>
<thead>
<tr>
<th>Study</th>
<th>RR (95 CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrer et al. 2011</td>
<td>1.26 (0.75, 2.10)</td>
<td>8.82</td>
</tr>
<tr>
<td>Gollieri et al. 2014</td>
<td>1.01 (0.92, 1.12)</td>
<td>48.20</td>
</tr>
<tr>
<td>Lammer et al. 2010</td>
<td>1.19 (0.89, 1.59)</td>
<td>26.72</td>
</tr>
<tr>
<td>Malensstein et al. 2011</td>
<td>2.65 (0.12, 60.21)</td>
<td>0.33</td>
</tr>
<tr>
<td>Recchia et al. 2012</td>
<td>1.38 (0.66, 2.92)</td>
<td>5.33</td>
</tr>
<tr>
<td>Sacoo et al. 2011</td>
<td>1.37 (0.92, 2.04)</td>
<td>10.60</td>
</tr>
<tr>
<td>Overall (I-squared = 27.3%, p = 0.230)</td>
<td>1.14 (1.01, 1.29)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Zhi-Bo Xie et al. Hepatology Research 2015; 45: 190-200
DEB-TACE was associated with a significantly higher objective tumor response rate (RR = 1.14, 95% CI = 1.01-1.29, P = 0.03) and a slightly lower incidence of adverse events.

As a matter of fact DC beads do not provide greater survival benefit than cTACE.

Zhi-Bo Xie et al. Hepatology Research 2015; 45: 190-200
Embozene TANDEM®

- Capable of loading doxorubicin-HCl and irinotecan-HCl up to 50 mg/ml Microspheres.

Ion-exchange mechanism

DEB-TACE non-ionic CA → drug releasing via ion exchange
Embozene Microspheres

- Hyrogel Core
- Surface Nano Coating: Polyzene-F-Shell
- Precise calibration: tight size distribution
- highly biocompatible
- minimize inflammatory response
- Stable suspension: no aggregation, no catheter clotting
- High elasticity and structural integrity
Embozene Tandem

- TANDEM® Microspheres are capable of loading doxorubicin-HCl and irinotecan-HCl up to 50 mg/ml microspheres
- Available in three sizes
- Available in two pre filled syringe volumes
- Ideal for passage through microcatheters.

<table>
<thead>
<tr>
<th>Size</th>
<th>2 ml Syringe</th>
<th>3 ml Syringe</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 ± 10 µm</td>
<td>10420-TS0</td>
<td>10430-TS0</td>
</tr>
<tr>
<td>75 ± 15 µm</td>
<td>10720-TS0</td>
<td>10730-TS0</td>
</tr>
<tr>
<td>100 ± 25 µm</td>
<td>11020-TS0</td>
<td>11030-TS0</td>
</tr>
</tbody>
</table>
Tight size distribution allows better steerable vessel occlusion

Calibration

TANDEM™ 40 µm

TANDEM™ 75 µm

TANDEM™ 100 µm

DC-BEADS (100 – 300 µm)

Source: Celonova
Principle

- **Aim**: Embolization of pre-capillary bed
- **Better and deep tumor vessel penetration**
- **Particle size** $\leq 75 \mu m$
HCC before Embozene-TACE
Embozene Tandem Embolization

Before Embolization

After Embolisation

3 ml Embozene Tandem 100µm
(100 mg Doxorubicin)

Source: own images
Follow-up @ 6 weeks

Partial Response

Source: own images
Observational study on the Response Evaluation of Doxorubicin-loaded Embozene TANDEM® Microspheres with different Particle Sizes for Transarterial Chemoembolization of the Hepatocellular Carcinoma

CT/MRT baseline → 1.TACE → CT/MRT 1. follow-up → 2.TACE → CT/MRT 2. follow up → Etc.

Tumor Response mRECIST Assessment

Preliminary Results
Target Lesion – mRECIST (2010)

- Consideration: every hypervascularized lesion $\geq 1$ cm
- CE lesions in the arterial phase in CT or MRT $\rightarrow$ vital tumor

Lencioni 2010
Therapy Response with mRECIST

- RECIST stable
  - mRECIST stable
- RECIST stable (<30% reduction)
  - mRECIST stable
- RECIST complete response
  - mRECIST complete response
- RECIST partial response
  - mRECIST partial response
Patients

- 56 TANDEM® TACE in 36 patients

- In average 1.6 TACE/patient

<table>
<thead>
<tr>
<th># TACE</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>&gt;3</td>
<td>6</td>
</tr>
</tbody>
</table>
Results

Therapy Response:
- with 100 µm Tandem: 79 %
- with 75 µm Tandem: 84 %
- with 40 µm Tandem: 94 %

p<.05
n.s.
Injected Dose of Doxorubicin

<table>
<thead>
<tr>
<th>Particle Size:</th>
<th>100 µm</th>
<th>75 µm</th>
<th>40 µm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applied dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Of Doxorubicin:</td>
<td>38.4 mg</td>
<td>43.1 mg</td>
<td>36.1 mg</td>
</tr>
</tbody>
</table>

*not statistically Significant*
Advanced Embolization

Source: own images
Quo vadis?

- **GIGALIX X-ray tube**
  - Flat emitter technology
  - Small square focal spots

- **New large HDR detector**
  - Enhanced soft-tissue resolution in 3D imaging
  - High dose efficiency
Axial plane view

Arterial phase 64-row CT

Large Volume DynaCT

Source: own images
Coronar plane view

Arterial phase 64-row CT

Large Volume DynaCT

Source: own images
Large Volume dynaCT

Source: own images
Another Case Example

Baseline CE-CT

Baseline CE-MRI

Source: own images
Superselective Embolization

Before TACE

After TACE
2 ml Embozene Tandem
40µm
(50 mg Doxorubicin)

Source: own images
syngo iFlow

Visualization of a complete DSA run in a color-coded single image

Source: own images
Conclusion

Superiority of Embozene Tandem®

- Better and deep tumor vessel penetration
- Depending on embolization target selection of particle size
- EMBOZENE TANDEM: Effective prolonged drug-release at the embolization target
- Trend towards smaller Microsphere sizes: Aim: Embolization of pre-capillary tumor vessels

100-300 µm

100 µm

75 µm

40 µm
Conventional TACE vs. drug-eluting beads

Ulf Teichgräber, MD, MBA
Department of Radiology
University Hospital Jena