CHEMOEMBOLISATION USING IODIZED OIL (LIPIIODOL®) BASED TECHNIQUES

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Disclosure

Speaker name:

Peter Huppert, M.D.

☐ I have the following potential conflicts of interest to report:
  X Consulting: Guerbet
  ☐ Employment in industry
  ☐ Stockholder of a healthcare company
  ☐ Owner of a healthcare company
  ☐ Other(s)
Rational of Transarterial Chemoembolization

- Dual blood supply with arterial vessels feeding tumors
- Selective arterial drug delivery and devascularization
- $R_{art} =$ Regional advantage of arterial drug delivery (x-times compared to systemic delivery)

\[ R_{art} = \frac{Q_A (1 - E_r)}{CL} \]

Collins 1994

<table>
<thead>
<tr>
<th>drug</th>
<th>$R_{art}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-FU</td>
<td>80</td>
</tr>
<tr>
<td>Irinotecan</td>
<td>60</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>4</td>
</tr>
<tr>
<td>Mitomycin</td>
<td>3</td>
</tr>
<tr>
<td>Cisplatin</td>
<td>2</td>
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</table>
Lipiodol® is part of „conventional“ TACE

- Emulsion = water-in-oil suspension:
  - water phase: Drug(s): Doxorubicin/Epirubicin, Cisplatin, Mitomycin
  - oily phase: Iodized oil (Lipiodol®) = oily phase

- Embolics: Gelfoam, particles
Key of success: Preparation of W/O-Emulsion & continuous refreshing

- Water-in-Oil: 1:2-3 (3 cc Epirubicin+6-9 cc Lipiodol®)*
- Slowly injection of water phase into oily phase*
- 3-way-stopcock: 2 syringes 10cc,
- „Pumping-method“: >30 times

Lipiodol-TACE is superselective TACE

- Angiographical work up of supply
- Coaxial microcatheter use
- Flow-guided injections

Intended result:
Intense & complete uptake of iodized oil
Grade 1-3 of Maki-classification
The Way of Iodized Oil & Portal Venous Overflow

The Way of iodized oil:
- Arterial feeder
- Peribiliary arterial plexus
- Sinusoids
- Portal venuoles
- Tumor vessels
- Portal venous overflow
Intense uptake of Lipiodol in HCC

- **EPR-effect** (enhanced permeability and retention):
  - interstitial deposition of macromolecules
  - caused by enhanced permeability of tumor vessels
  - lack of lymphatic drainage in tumors
  - deposition of iodized oil in satellites

cTACE in case of PV Infiltration

- 72 years old male
- Child-Pugh-Score 6
- 8 cm HCC infiltrating right PV
- 5 x TACE (Intervals: 3-5 mo.)
- Survival 63 months

In case of good liver function, PV infiltr. is no contraindication for selective TACE
Extrahepatic supply can be treated by CTACE
Lipiodol®-TACE: from the Beginning to Evidence

- First report Konno 1982*
- First choice treatment in Asia 1990-2008**
- High efficacy of superselective cTACE***


**Satake M, Uchida H, Arai Y et al.: Trancatheter arterial chemoembolization (TACE) with Lipiodol to treat hepatocellular carcinoma: Survey results from the TACE study group of Japan. Cardiovasc Intervent Radiol 2008;31:756-61


Lipiodol®-TACE: from the Beginning to Evidence

- Metaanalyses: prove of clinical efficacy: mRECIST 65-100% OR, median survival 19 Mo

**References**


The breakthrough studies

<table>
<thead>
<tr>
<th></th>
<th>Embx.</th>
<th>TACE</th>
<th>BSC</th>
<th>p</th>
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<tr>
<td><strong>35 pts.: BSC</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>37 pts.: Embolization GF</strong></td>
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<tr>
<td><strong>40 pts.: TACE:</strong> Doxo 25-75 mg/m², 10 cc iodized oil, GF</td>
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<th>TACE</th>
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<tbody>
<tr>
<td><strong>Response 6Mo. (WHO)</strong></td>
<td>43%</td>
<td>35%</td>
<td>0</td>
<td>.004</td>
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<tr>
<td><strong>Survival 1a</strong></td>
<td>75%</td>
<td>82%</td>
<td>63%</td>
<td>.009</td>
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<tr>
<td><strong>2a</strong></td>
<td>50%</td>
<td>63%</td>
<td>27%</td>
<td>.009</td>
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<tr>
<td><strong>3a</strong></td>
<td>29%</td>
<td>29%</td>
<td>17%</td>
<td>.009</td>
</tr>
<tr>
<td><strong>mean (mo.)</strong></td>
<td>25.3</td>
<td>28.7</td>
<td>17.9</td>
<td>.005</td>
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<tr>
<td><strong>40 pts. BSC</strong></td>
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<tr>
<td><strong>40 pts. TACE</strong> Cisplatin 1-30 mg, iodized oil 1-30 (mean 10) cc, GF</td>
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<th>BSC</th>
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<tr>
<td><strong>Response 3Mo. (WHO)</strong></td>
<td>39%</td>
<td>6%</td>
<td>.01</td>
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<tr>
<td><strong>Survival 1a</strong></td>
<td>57%</td>
<td>32%</td>
<td>.005</td>
</tr>
<tr>
<td><strong>2a</strong></td>
<td>31%</td>
<td>11%</td>
<td>.005</td>
</tr>
<tr>
<td><strong>3a</strong></td>
<td>26%</td>
<td>3%</td>
<td>.005</td>
</tr>
</tbody>
</table>

Llovet et al. Lancet (2002), 359; 1734-39

Lo et al. Hepatology (2002), 35; 1164-71
Conv. TACE vs. BSC in HCC: Phase III-Studies
(Random effects model pooled OR, 95% CI)

Adapted from: Llovet et al 2003, Hepatology 37; 429-42
Conv. TACE vs. BSC in HCC: Phase III-Studies
(Random effects model pooled OR, 95% CI)

Survival benefit: 6-10 months

- GETCH 1995
- Pelletier 1998
- Lo 2000
- Llovet 2002
- Pooled OR

Lo et al. Hepatology (2002), 35; 1164-71
Patients: 40
TACE: Cis 1-30 mg, iodized oil 1-30 cc, GF

Llovet et al. Lancet (2002), 359; 1734-39
Patients: 40
TACE: Doxo 25-75 mg/m², 10 cc iodized oil, GF

307 / 387 (79%) excluded
791 / 903 (88%) excluded

Pooled OR

adapted from: Llovet et al 2003, Hepatology 37; 429-42
Negative Predictors & Contraindications

- Compact type of HCC
- Diffuse type of HCC
- Infiltrative type of HCC
- Arterioportal shunts
Positive Predictors & Long Term Survival

- nodular type /pseudoencapsulation
- selective feeder
- size <10 cm
- Child A-B
- no central PV infiltration, no extrahepatic mts.

Survival today: 12 years.
Summary

Advantages of conventional Lipiodol-TACE

• Proven survival benefit in comparison to BSC of 6-12 months

• Clear feed back by iodized oil uptake in CT: guiding re-treatment

• Limited serious side effects even in multinodular and huge tumors

• Low cost / procedure
Thank You for Attention!
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