Transarterial Chemoembolization: cTACE vs DEB TACE vs DSM TACE

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Disclosure

Speaker name:
Thomas Vogl

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other: travel grant

- I do not have any potential conflict of interest
TACE Techniques

- C-TACE (conventional TACE): Lipiodol® and chemo
- DEB-TACE (beads loaded with chemo)
- DSM-TACE: degradable starch microspheres EmboCept® S and chemo
- TACE characteristics: multidrug therapy, repeatable, reversible / permanent embolization
A search of the literature published between January 1, 1980 and June 30, 2013 was performed using MEDLINE and EMBASE databases. Of a total of 1,564 articles reviewed, 101 articles, including a total of 10,108 patients treated with lipiodol TACE, were selected for the efficacy analysis. **Objective response rate was 52.5% (95% confidence interval [CI]: 43.6-61.5).** **Overall survival (OS) was 70.3% at 1 year, 51.8% at 2 years, 40.4% at 3 years, and 32.4% at 5 years.** **Median OS was 19.4 months (95% CI: 16.2-22.6).** A total of 217 articles presenting precise description on numbers of adverse events (AEs) were selected for the safety review: In these studies, a total of 21,461 AEs were reported in 15,351 patients.
Frankfurt Liver Cancer Center

cTACE: Method and Materials

- Retrospective study: April 2003 – February 2013
- Patients:
  - n = 356 with histopathologically proven HCC
  - male : female = 259 : 97
- cTACE sessions:
  - n = 1,664
  - TACE sessions: $\bar{x} = 4.7$ (range: 1-21)
  - repetitive treatments in 4-week intervals
  - Mitomycin C/Lipiodol
Frankfurt Liver Cancer Center
cTACE: Results

- **Median survival rates:**
  - since first diagnosis: 35.45 months
  - since 1st TACE: 26.22 months

- **Survival rates:**
  - Neoadjuvant intervention and resection:
    - since first diagnosis: 12.00 months
    - since 1st TACE: 6.60 months
  - Neoadjuvant intervention and transplantation:
    - since first diagnosis: 21.88 months
    - since 1st TACE: 21.12 months
  - Neoadjuvant intervention followed by ablation:
    - since first diagnosis: 28.55 months
    - since 1st TACE: 19.58 months
Chemoembolization (TACE): Hepatocellular Carcinoma

Before intervention

After intervention
Overall Survival Data

- **cTACE**
  - More than 10,000 patients involved in clinical studies published in peer-reviewed journals
  - 5 major RCTs since 2002
  - 4 international clinical guidelines from Europe, United States, Japan & China endorsing cTACE as Standard-of-Care for treatment of intermediate stage HCC
- **Median survival of intermediate stage HCC patients**\(^{(1)}\)
  - No treatment: 16 months
  - cTACE: 19-20 months \(\rightarrow 3\text{-}4\) additional months
- **Shortest & longest survival of intermediate stage HCC patients following cTACE**\(^{(1)}\)
  - Worst case scenario: 14 months
  - Best case scenario: 36-45 months \(\rightarrow 22\text{-}31\) additional months

\(^{(1)}\)EASL-EORTC Clinical Practice Guidelines Management of Hepatocellular Carcinoma. J. Hepatol. 2012; 56: 908-943
2 meta-analyses:

- Significant reduction of overall mortality after 2 years for cTACE vs. Placebo\(^{(1)}\)
- Significant improvement of survival rate after 2 years compared to systemic chemotherapy or conservative treatment\(^{(2)}\)

Asian cooperation study between Japan and Korea:

- 2-year survival rate in 99 HCC patients: 75\%\(^{(3)}\)
- Median overall survival: 3.1 years

The increasing use of microcatheters, c-arm angiography systems and state of the art imaging software in the past years may have a positive influence on these data.

1. Camma C. et al., Radiology 2002
2. Llovet J. et al., Hepatology 2003
Problems: 1) Arterial Damage

DEB-TACE and c-TACE induce a permanent occlusion of pre-neoplastic arterial vessels: it may be difficult to repeat the procedure.

- Hasmukh J. Prajapati, Minzhi Xing, James R. Spivey, Steven I. Hanish, Bassel F. El-Rayes, John S. Kauh, Zhengjia Chen and Hyun S. Kim

- Survival, Efficacy, and Safety of Small Versus Large Doxorubicin Drug-Eluting Beads TACE Chemoembolization in Patients with Unresectable HCC

*AJR, December 2014, Volume 203, Number 6*
CONCLUSIONS:

DEB-TACE was associated with increased hepatic toxicities compared to cTACE. GHD, biliary injuries, and intrahepatic biloma were more frequently observed with high baseline prothrombin value, suggesting that cTACE might be more appropriate than DEB-TACE in patients with less advanced cirrhosis.
Frankfurt FAST II: Study Design

- Prospective, comparative, randomized, monocentric, open study
- N = 50 patients with hepatocellular carcinoma (HCC)
- Random assignment using a random numbers table: 25 patients/entity (TACE Lipiodol / Lipiodol + DSM EmboCept® S)
- Cytostatic drug: Mitomycin
Study population
November 2013 – April 2016
Patients randomly assigned (n = 61)

- **Group 1:** Lipiodol (n = 30)
  - received all allocated interventions (n = 19)
  - discontinued intervention (n = 11)
  - analyzed (n = 26) (excluded from analysis n=4)

- **Group 2:** Lipiodol + DSM (n = 31)
  - received all allocated interventions (n = 15)
  - discontinued intervention (n = 16)
  - analyzed (n = 28) (excluded from analysis n=3)

Materials and Methods: FAST II
Results: Response Evaluation

- **All evaluated patients:**

<table>
<thead>
<tr>
<th></th>
<th>Lipiodol</th>
<th>Lipiodol + DSM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial response</td>
<td>n = 2</td>
<td>n = 6</td>
</tr>
<tr>
<td>Stable disease</td>
<td>n = 21</td>
<td>n = 20</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>n = 3</td>
<td>n = 2</td>
</tr>
</tbody>
</table>

- **Patients who received 3 TACE sessions:**

<table>
<thead>
<tr>
<th></th>
<th>Lipiodol</th>
<th>Lipiodol + DSM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial response</td>
<td>n = 2</td>
<td>n = 6</td>
</tr>
<tr>
<td>Stable disease</td>
<td>n = 16</td>
<td>n = 9</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>n = 1</td>
<td>n = 0</td>
</tr>
</tbody>
</table>
Summary: FAST II (HCC)

- TACE with Lipiodol and DSM showed a statistically non-significant benefit in local tumor control compared to the Lipiodol-only group.

- TACE must be performed at least 3 times.

- $\Delta$ ADC as an individual predictor of the tumor volume of early response to TACE.
39-year-old Woman with HCC: Partial Response after TACE with Lipiodol+DSM

Angiography immediately after selective TACE: distribution of embolization agents
39-year-old Woman with HCC: Partial Response after TACE with Lipiodol+DSM

CT scan after selective transarterial embolization: high lipiodol uptake in the lesion – no uptake in the necrotic zone

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39-year-old Woman with HCC: Partial Response after TACE with Lipiodol+DSM

a) and b) Pretreatment volumetry - diameters of the lesion and the necrosis

c) Posttreatment volumetry

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FAST II (TACE) HCC: Preliminary Results

After 3rd TACE
C-TACE and DEB-TACE are limited by side effects, partially due to the vascular permanent occlusion and subsequent ischemic effect.

- Thomas J. Vogl, Johannes Lammer, Riccardo Lencioni, Katerina Malagari, Anthony Watkinson, Frank Pilleul, Alban Denys and Clara Lee

- Liver, Gastrointestinal, and Cardiac Toxicity in Intermediate Hepatocellular Carcinoma Treated with PRECISION TACE with Drug-Eluting Beads: Results from the PRECISION V Randomized Trial

AJR, October 2011, Volume 197, Number 4
Problems: 3) Neoangiogenesis

If TACE doesn’t obtain the complete necrosis of the whole mass, the residual malignant tissue stimulates the production of vascular endothelial growth factor (VEGF), inducing further stimulus to the tumor growth.


World J Gastroenterol 10:2878-2882, 2004


Carmeliet P, Jain RK: Angiogenesis in cancer and other diseases.

Interventional Oncology

- **Improve:**
  - HCC diagnosis (puncture guiding)

- **Guide:**
  - c-TAE procedure (angio pattern)
  - beads/DSM-TACE procedure

- **Predict:**
  - TACE efficacy (predictive factor)

- **Improve:**
  - curative therapy (combination with MWA/RFA)
20. Frankfurter Interdisziplinäres Symposium für Innovative Diagnostik und Therapie

Frankfurt/Main, 15 – 16. November 2019

www.fisi-frankfurt.de
CRC Metastases

- n = 463 patients
- Lipiodol or DSM
- Mitomycin C (n=243)
- Mitomycin C & Irinotecan (n=67)
- Mitomycin C & Gemcitabine (n=152)
- OS: 14 months
- PR: 14.7%
- SD: 48.2%
- PD: 37.1%

Overall Survival – 1-y: 62%; 2-y: 28%

Vogl TJ et al. Radiology 2009;250,28-289
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