Interventional radiology in the treatment of liver cancer patients

Professor Thierry de Baere, France
TACE | 4D CT
Radioembolisation

Radiofrequency

Microwave
Liver Radiofrequency Ablation

MegaPEG
RF ablation **local efficacy**:

- HCC complete necrosis

**Livraghi, Radiology 1999**
- Smaller than 3 cm: 90%
- 3.1 to 5 cm: 61%
- Greater than 5 cm: 23%

**Livraghi, Radiology, 2000**
- Smaller than 3 cm: 97.2%

**Livraghi T, Hepatology 2007**
- 2cm or smaller: 97.2%
RF ablation local efficacy: Microsatellites

Microsatellites at pathology 46/100

- Tumor < 2.5 cm
- No satellites farther than 5 mm

RF ablation local efficacy: Microsatellites

Microsatellites at pathology  46/100

- Tumor > 2.5 cm
  satellites farther than 5 mm
  You treat what you see but not the satellites

CT during treatment

CT after treatment
A randomized controlled trial of radiofrequency ablation and surgical resection in the treatment of small hepatocellular carcinoma

Kai Feng1,2,3, Jun Yan1,†, Xiaowu Li1, Feng Xia1, Kuansheng Ma1,*, Shuguang Wang1, Ping Bie1, Jiahong Dong1

- 168 patients, 49% Child A
- Up to 2 HCC tumors ≤ 4 cm
Long-term effectiveness of resection and radiofrequency ablation for single hepatocellular carcinoma <3 cm. Results of a multicenter Italian survey

729 consecutive single HCC <3 cm treated with surgery (n=302) or RFA (n=427)
Long-term effectiveness of resection and radiofrequency ablation for single hepatocellular carcinoma \(<3\) cm. Results of a multicenter Italian survey

729 consecutive single HCC \(<3\) cm treated with surgery (n=302) or RFA (n=427)

<table>
<thead>
<tr>
<th>Variable</th>
<th>RES (n = 246)</th>
<th>RFA (n = 298)</th>
<th>p value</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>67 (35-85)</td>
<td>68 (36-88)</td>
<td>0.188</td>
<td></td>
</tr>
<tr>
<td>Men (%)</td>
<td>200 (81.3)</td>
<td>175 (58.7)</td>
<td>(&lt;0.001)</td>
<td></td>
</tr>
<tr>
<td>Anti-HCV positive (%)</td>
<td>144 (58.5)</td>
<td>213 (\sim)</td>
<td>0.325</td>
<td></td>
</tr>
<tr>
<td>HBsAg positive (%)</td>
<td>24 (9.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse (%)</td>
<td>31 (12.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed etiology of cirrhosis (%)</td>
<td>22 (8.8)</td>
<td>38 (13.4)</td>
<td>0.635</td>
<td></td>
</tr>
<tr>
<td>Other etiology of cirrhosis (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Portal hypertension (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet count (x10^{12}/L)</td>
<td>138 (52.3)</td>
<td>103 (28.6)</td>
<td>(&lt;0.001)</td>
<td>0.859</td>
</tr>
<tr>
<td>Mild ascites (%)</td>
<td>21 (8.6)</td>
<td>30 (10.1)</td>
<td>0.005</td>
<td>0.605</td>
</tr>
<tr>
<td>Encephalopathy (%)</td>
<td></td>
<td></td>
<td>0.267</td>
<td>n.c.</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>1.0 (0.3-4.1)</td>
<td>(&lt;0.001)</td>
<td>0.551</td>
<td></td>
</tr>
<tr>
<td>MELD score</td>
<td>8 (6-18)</td>
<td>6.4 (4.5-10)</td>
<td>0.182</td>
<td>0.069</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>65 (14-222)</td>
<td>60 (14-212)</td>
<td>0.072</td>
<td>0.143</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.90 (0.10-5.16)</td>
<td>0.90 (0.10-5.16)</td>
<td>0.019</td>
<td>0.211</td>
</tr>
<tr>
<td>AFP (ng/mL)</td>
<td>9 (1-9000)</td>
<td>29 (2-2200)</td>
<td>(&lt;0.001)</td>
<td>0.440</td>
</tr>
<tr>
<td>Tumor size (cm)</td>
<td>2.5 (0.8-3.0)</td>
<td>2.3 (1.0-3.0)</td>
<td>0.153</td>
<td>0.052</td>
</tr>
<tr>
<td>HCC (&lt;)2 cm (%)</td>
<td>99 (40.2)</td>
<td>109 (36.6)</td>
<td>0.381</td>
<td>0.086</td>
</tr>
</tbody>
</table>

Are the patients / tumors the same? The major role of the multidisciplinary tumor board for treatment decision

Pompili M et al. J Hepatol 2013;59:89-97
Resection vs RF ablation (randomized):

- **180 HCC ≤ 5cm**

30 and 60 days mortality

<table>
<thead>
<tr>
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<th>Resection</th>
<th>RFA</th>
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<tbody>
<tr>
<td></td>
<td>1.1% and 1.1%</td>
<td>0%</td>
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</table>

Major complications

<table>
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<tr>
<th></th>
<th>Resection</th>
<th>RFA</th>
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<tbody>
<tr>
<td></td>
<td>50 / 90 (cirrhosis alteration)</td>
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</table>

Hospital stay

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<th>Resection</th>
<th>RFA</th>
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<tr>
<td></td>
<td>19.7 ± 5.6</td>
<td>9.18 ± 3.06</td>
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(Chen M, Ann Surg 2006)
Intra-arterial therapies

Patient not amenable to ablation or surgery
  Tumor size
  Tumor number
  Technical issue
  Underlying liver function (for surgery)
Hypothetical distribution in healthy tissue – assuming no tumor, right lobe infusion
Hypervascular Tumor (3:1) – preferentially delivered to tumor
Yttrium 90 or Holmium 166 loaded beads

Emulison of chemotherapy and radio-opaque oil (Lipiodol)

- Lipiodol
- doxorubicin nanoparticles

Tight calibration & size distribution with uniform sphericity

Yttrium 90 or Holmium 166 loaded beads
Chemo-embolization in intermediate stage HCC

- Events/patients: Orantinib group: 168/444, Placebo group: 163/444
- Median (months): Orantinib group: 31.1, Placebo group: 32.3
- HR (95% CI): 1.090 (0.878-1.332)
- Stratified log-rank test, p value: 0.435

Number at risk (number censored)

- Orantinib group: 444 (0), 422 (2), 318 (56), 209 (125), 129 (180), 70 (222), 18 (260)
- Placebo group: 444 (0), 428 (0), 326 (53), 218 (115), 140 (165), 81 (207), 24 (257)

(Kudo M Lancet Gastroenterol Hepatol 2018; 3: 37-46)
More advanced HCC: Sorafenib vs Radioembolization

Median OS (months) | Events
---|---
SIRT | 11.27 (95% CI 9.17 to 13.57) | 94
Sorafenib | 10.41 (95% CI 8.57 to 13.83) | 124

Hazard ratio 0.86 (95% CI 0.66 to 1.13); P = 0.273

Probability of Survival
Log-rank P=0.92

AEs ≥grade 3
AEs
Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma

A Overall Survival

<table>
<thead>
<tr>
<th></th>
<th>No. of Events</th>
<th>Median Overall Survival (95% CI)</th>
<th>Overall Survival at 6 Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezolizumab—Bevacizumab</td>
<td>96/336 (28.6)</td>
<td>NE</td>
<td>84.8%</td>
</tr>
<tr>
<td>Sorafenib</td>
<td>65/165 (39.4)</td>
<td>13.2 (10.4—NE)</td>
<td>72.2%</td>
</tr>
</tbody>
</table>

Stratified hazard ratio for death, 0.58 (95% CI, 0.42–0.79) P<0.001

BCLC B+C

No. at Risk

Atezolizumab—Bevacizumab

| 336 | 329 | 320 | 302 | 288 | 275 | 255 | 222 | 165 | 118 | 87 | 64 | 40 | 20 | 11 | 3 | NE |

Sorafenib

| 165 | 157 | 143 | 132 | 127 | 118 | 105 | 94  | 86  | 60  | 45  | 33  | 24  | 16  | 7  | 3  | 1  | NE |

(NE = not estimable)
Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma
Primary liver cancer is mostly HCC

Underlying liver disease limits therapeutic options

Prognostic of the disease is mostly linked with local growth and not distant metastases

Take home messages

Image guided local therapies

- are able to selectively target part of the liver and thus limits toxicity
- have usually better tolerance than more agressive treatment (surgery)
- Possible when more agressive treatment cannot be provided
- have usaully shorter hospital stay than surgery

- Are usualy delivered in a single session (radiofrequency), or in two or three session and patients have long break from treatment, when compared to systemic therapies

- Can be combined with other local therapies or systemic therapies
Thank you

Questions ?