Results of Neoadjuvant Hepatic Arterial Infusion Chemotherapy in Inoperable HCC Patients with Child-Pugh Class A

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Introduction

Not Suitable for Liver Resection and Liver Transplantation

PVTT

N >4

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Different Thinking in Treatment of HCC

- Surgeon vs Hepatologist
- Eastern Country vs Western Country

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Guidelines for the Diagnosis and Treatment of HCC in Asian Country

Korean Guidelines

Japan Guidelines
Guidelines for HCC in Western Country

• **BCLC** staging classification
  – Llovet JM, Bruix J et al. 1999 Semin Liver Dis 19:329-
  – Bruix J, Llovet JM. 2009 Lancet 373: 614-

• **AASLD** practice guidelines
  – Bruix J, Sherman M. 2005 Hepatology 42:1208-

• **British** Society of Gastroenterology
  – Ryder SD. 2003 Gut 52 (suppl. III):iii1-
Japan Guidelines for HCC Treatment


HCC

Liver Damage (Child-Pugh)

Tumor No.

Tumor Size

Treatment

Resection Ablation† Resection Ablation Resection TAE TAE HAI Transpl. Supportive

†Recommended for Child B, ‡≤ 5cm for solitary lesion

*Excluding patients with tumor thrombus or extrahepatic lesions
Japan Guidelines for HCC Treatment

Consensus-based in Japan Hepatology 2010

HCC

- Extrahepatic spread
  - Liver function
    - Vascular invasion
      - Number
        - Size
          - Treatment
            - Intensive follow-up
            - Ablation
            - Resection
            - TACE
            - TACE+ Ablation
            - Sorafenib
              (TACE refractory, Child-Pugh A)
            - Sorafenib
              (TACE/HAIC refractory, Child-Pugh A)
            - TACE
            - HAIC
            - Resection
            - Ablation
            - HAIC
            - Sorafenib
              (Vp3,4)
            - TACE
              (Vp1,2)
            - Resection
              (Vp1,2)
            - Transplantation
              TACE/Ablation for Child-Pugh C
              or Child-Pugh A
            - Palliative care
            - Sorafenib

- Child-Pugh A/B
  - No
  - Yes
    - Child-Pugh C
      - No
      - Yes
        - Child-Pugh B/C
          - Child-Pugh A
            - Yes
              - ※1, 2
Rationale of IA Chemo.

✓ IA chemo vs Systemic Chemo:
  20~400 effective

✓ Less systemic toxicity

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Purpose

To investigate the role of Neoadjuvant IA Chemotherapy in inoperable HCC patients with Child Pugh Class A

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Material and Methods

1. From January 2003 to December 2012
2. 46 inoperable HCC patients with Child Pugh Class A

- 5-FU / Cisplantin
  - 5-FU 750 mg/m²/2hr
  - Cisplatin 25 mg/m²/1hr
  - Q every 4 weeks

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Results

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## Patient Characteristics

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex (M:F)</strong></td>
<td>28:6 (82.4:17.6)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>54±10</td>
<td></td>
</tr>
<tr>
<td><strong>Portal vein thrombosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main trunk</td>
<td>9(26.5)</td>
<td></td>
</tr>
<tr>
<td>Rt</td>
<td>12(35.3)</td>
<td></td>
</tr>
<tr>
<td>Lt</td>
<td>3(8.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Tumor morphology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multinodular</td>
<td>9(26.5)</td>
<td></td>
</tr>
<tr>
<td>Huge, massive</td>
<td>25(73.5)</td>
<td></td>
</tr>
<tr>
<td><strong>AFP (ng/mL)</strong></td>
<td>29067±90281</td>
<td></td>
</tr>
<tr>
<td><strong>Treatment prior to Chemotherapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TACE</td>
<td>4(11.8)</td>
<td></td>
</tr>
<tr>
<td>Radiation and TACE</td>
<td>1(2.9)</td>
<td></td>
</tr>
<tr>
<td>No treatment</td>
<td>29(85.3)</td>
<td></td>
</tr>
</tbody>
</table>

N = 34

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Results

- Twelve patients who could not receive more than 2 cycles HAI chemotherapy were excluded

<table>
<thead>
<tr>
<th>Tumor response</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>4(11.8%)</td>
</tr>
<tr>
<td>PR</td>
<td>9(26.5%)</td>
</tr>
<tr>
<td>SD</td>
<td>16(47.1%)</td>
</tr>
<tr>
<td>PD</td>
<td>5(14.7%)</td>
</tr>
</tbody>
</table>

| Response rate | 13(38.3%) |

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Overall Survival Rate

Median Survival: 16.6±2.8
6 months : 81.2%
12 months : 44.0%
18 months : 28.7%
24 months : 19.1%
IA Neoadjuvant Chemotherapy

- 20% resectable
- Resection
- 80% unresectable (n=?)
  - Child-Pugh Class A (n=46)
    - 17.4% become resectable (n=8)

Total resectable: 20%

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Overall Survival Rate after Resection

The 6, 12, 18 and 24-month cumulative survival rate 87.5%, 75.0%, 62.5%, and 62.5%, respectively

N=8
Median survival : 32.4±7.5
Summary

1. Response Rate: 13/34 (38.3%)
   - CR: 4/34 (11.8%), PR: 9/34 (26.5%)
2. The 6, 12, 18 and 24-month cumulative survival rate are 80.2%, 44.0%, 28.7% and 19.1%, respectively.
3. Liver resection in 8 patients (17.3%) and the median survival was \(32.4 \pm 7.5\) months.

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M/ 53

Rt/ main portal vein invasion

AFP 950ng/mL

After 6 cycle

AFP 19.29ng/mL

S#6, 7 segmentectomy

Postop: 50 months

AFP 2.56ng/mL

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Tumor necrosis: 100% of tumor
M/52

Rt lobe huge HCC with PVTT

AFP  5066ng/mL

TACE + RTx After 6 cycle

AFP  3955ng/mL

Rt lobectomy

Postop: 46months

AFP  2.24ng/mL

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Tumor necrosis: Approximately 95% of tumor
M/ 58

Ruptured multiple bilobar HCC
PIVKA 75000mAU/mL

After TACE
After 6 cycle
PIVKA 111mAU/mL

S# 4,5
Segmentectomy
S#6 wedge resection
Post op : 6 months
PIVKA 21mAU/mL

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Liver, segment 4b and 5, segmentectomy:

**No viable tumor**

with 1) tumor number: One
2) satellite nodule: Absent
3) gross type: Expanding nodular
4) tumor location: Segment 4b and 5
5) tumor size: 4.3 cm
6) Histologic grade (Edmondson-Steiner grade): Cannot be assessed
7) histologic type: Cannot be assessed
8) cell type: Cannot be assessed
9) **tumor necrosis**: Approximately 100% of tumor
   (preoperative therapy administered)
10) fatty change: Cannot be assessed
11) fibrous capsule formation: Complete capsule

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F/74

Main portal vein invasion and multiple bilobar tumor

AFP 3170ng/mL

After 2 cycle

AFP 19.07ng/mL

No recurrence 15 months After 6 cycle

AFP 11.92ng/mL

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Donor Organ Shortage in Asian Country

Confucianism:
- Don’t touch our body even after death..

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The metroticket paradigm

- If vascular (-) → No limit for LT
- But Size, Number ↑ → Vascular invasion ↑

Number of Nodules

Tumor Size (cm)

75-80 % 50-75 % 35-50 %

Expected 5-year survival
Conclusion

Neoadjuvant HAI chemotherapy can be another good option to treat HCC patients with good liver function, not suitable for liver resection and transplant.

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Thank You for Your Attention