Hepatocellular carcinoma: from guidelines to individualized treatment

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Il sottoscritto dichiara di aver avuto negli ultimi 12 mesi conflitto d’interesse in relazione a questa presentazione:

_Bayer, BMS, Roche_
Hepatocellular carcinoma: from guidelines to individualized treatment

Items

• Guidelines produced by scientific societies over the world give different recommendations
• The “grey area” lacking scientific evidence is wide and the rate of application of guidelines in the real world is variable
• The role of molecular signatures is unknown
• The choice of the proper treatment must take into account the paucity of evidences and the individual complexity
• In this context, the role of the Hepatologist worldwide and in Italy would be crucial, but it is often marginal
HCC treatment guidelines: recently updated or in-progress

- AASLD (published 2010)\(^4\)
- NCCN guidelines (published 2010)\(^1\)
- BCLC staging system/treatment algorithm (2008)\(^2\)
- APASL (presented 2009 and published 2010)\(^3\)
- JSH (published in 2011)\(^5\)
- EASL (currently being updated)


AASLD Guidelines (2011)

Stage 0
PST 0, Child–Pugh A

Stage A–C
PST 0–2, Child–Pugh A–B

Stage D
PST >2, Child–Pugh C

Very early stage (0)
1 HCC < 2cm
Carcinoma in situ

Early stage (A)
1 HCC or 3 nodules ≤ 3cm, PST 0

Intermediate stage (B)
Multinodular, PST 0

Advanced stage (C)
Portal invasion, N1, M1, PST 1–2

End stage (D)

Portal pressure/bilirubin
1 HCC
3 nodules ≤3cm
Increased
Associated diseases
Normal
No
Yes

Resection
Liver transplantation
PEI/RFA
TACE
Sorafenib
Symptomatic treatment

Curative treatments
Randomized controlled trials

Evidence-based benefits in the treatment of hepatocellular carcinoma according to the strength of study design and of end-points as defined by an expert panel of the National Cancer Institute

<table>
<thead>
<tr>
<th>Treatments assessed</th>
<th>Benefit</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgical treatments</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical resection</td>
<td>Increase survival</td>
<td>3iiA</td>
</tr>
<tr>
<td>Liver transplantation</td>
<td>Increase survival</td>
<td>3iiA</td>
</tr>
<tr>
<td><strong>Loco-regional treatments</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percutaneous ablation</td>
<td>Increase survival</td>
<td>3iiA</td>
</tr>
<tr>
<td>Percutaneous ethanol injection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radiofrequency ablation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemoembolization</td>
<td>Increase survival</td>
<td>1iiA</td>
</tr>
<tr>
<td>Arterial chemotherapy</td>
<td>Treatment response</td>
<td>3ii Diii</td>
</tr>
<tr>
<td>Internal radiation (I(^{131}), Y(^{90}))</td>
<td>Treatment response</td>
<td>3ii Diii</td>
</tr>
<tr>
<td><strong>Systemic treatments</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>No benefit</td>
<td>1iA</td>
</tr>
<tr>
<td>Systemic chemotherapy</td>
<td>No benefit</td>
<td>1iiA</td>
</tr>
<tr>
<td>Interferon</td>
<td>No benefit</td>
<td>1iiA</td>
</tr>
<tr>
<td>Sorafenib</td>
<td>Benefit</td>
<td>1iA</td>
</tr>
</tbody>
</table>
Hepatocellular Carcinoma

**CLINICAL PRESENTATION**

- Inadequate hepatic reserve
- Tumor location

Evaluate whether patient is a candidate for transplant (See UNOS criteria under Surgical Assessment HCC-4)

**TREATMENT**

Transplant candidale ➔ Transplant ➔

**SURVEILLANCE**

- Imaging every 3-6 mo for 2 y, then annually
- AFP, if initially elevated, every 3 mo for 2 y, then every 6 mo

**Unresectable**

- Extensive liver disease

---

* See Principles of Locoregional Therapy (HCC-C)
* See Child-Pugh Score (HCC-A)
* The impact of sorafenib on patients potentially eligible for transplant is unknown. Data are inadequate to define dosing for patients with abnormal liver function (Child-Pugh Class B or C).
* There are limited data to support the use of RT in this setting.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
APASL guidelines

HCC

Confined to the liver
Main portal vein patent
Resectable

Yes
Resection/RFA (for < 3 cm HCC)

No
Solitary tumor ≤ 5 cm ≤ 3 tumors ≤ 3 cm No venous invasion

Child–Pugh A
Local ablation

Child–Pugh B
Transplantation

Child–Pugh C
TACE

Extrahepatic metastasis
Main portal vein tumor thrombus

Child–Pugh A/B
Sorafenib or systemic therapy trial

Child–Pugh C
Supportive care

Tumor > 5 cm > 3 tumors
Invasion of hepatic/portal vein branches

Child–Pugh A/B
Supportive care

Child–Pugh C
Supportive care

Guidelines based on EBM - Limits

Extent of the “grey area” lacking scientific evidence
Limits of the Evidences derived from RCTs

- Studies industry-sponsored performed for economical purposes
- Only selected patients (exclusion of comorbidities)
- Priviliged cultural and organization background (super-expert centers)

Applicability in the “real world?
- Individual characteristics not recognized
- Demostration valid only for selected patients corresponding to the inclusion criteria
Actual application of the AASLD guidelines in the real world - The BLOG experience

Population characteristics

✓ 227 patients with HCC on cirrhosis at the first diagnosis November 2005 – June 2010;

✓ 180 males, 47 females;

✓ Diagnosis of HCC based on AASLD 2005 diagnostic criteria.

Leoni et al AISF, DLD, 44:S36, 2012
RESULTS

✓ Application of guidelines in different BCLC stages

Leoni et al AISF, DLD, 44:S36, 2012
RESULTS – BCLC A4

Treatment
- Percutaneous 22/63
- Resection 11/63
- TACE 23/63
- Other 7/63

Reason for non application
- Resection:
  - Mild portal hypertension, subcapsular lesions, proximal to other structures (n=11)
- TACE:
  - Poor visibility US and difficult approach PEI/RF (n=21)
  - Diameter > 4 e < 5 cm (n=2)
- Other:
  - Location, Ascites (n=7)

Leoni et al’ AISF, DLD, 44:S36, 2012
RESULTS – BCLC B

Treatment
- TACE 34/50
- Yttrium/Irinotecan 8/50
- Capecitabine 1/50
- Sorafenib 6/50
- Palliation 1/50

Reason for non application
- Multifocality (number of nodules > 4) (n=3)
- Nodule ø > 5 cm (n=13)

Leoni et al AISF, DLD, 44:S36, 2012
AASLD Guidelines have been applied in 60.8% of cases.

Main reasons for non application (less aggressive treatment) include:

- Age and comorbidities
- Visibility at conventional US
- Feasibility of the percutaneous approach
- Size and number of nodules (within the same BCLC stage)
- Liver decompensation
- Eligibility and compliance to OLT

A subgroup of patients has been treated with a more aggressive approach; in these cases other prognostic indexes such as the MELD score, bilirubin levels, severity of portal hypertension have been taken into account.

Leoni et al AISF, DLD, 44:S36, 2012
(Suspected) HCC – management in the BLOG

The physician in charge brings the following to the discussion: the patient’s history, clinical data, laboratory findings, and any available clinical images (films or CD to be reviewed)

Can a diagnosis of HCC be made?
Is staging complete (have all the nodules been characterized)?

Yes

Does the patient meet the guidelines?

Yes

Treatment (+ any possible trials) including transplantation
Definite judgment made on achieving downstaging criteria for LT

No

Further investigations (usually imaging/biopsy)

Yes

No

Proposal by the group of an individualized treatment strategy including ongoing trials
Actual application of the AASLD guidelines in the real world
The case of Sorafenib

- Global experience – The Gideon study

- Italian experience - Market Research Kantar Health 2011
Child-Pugh B patients are included

GIDEON second interim analysis: OS by BCLC stage at study entry

<table>
<thead>
<tr>
<th>Stage</th>
<th>(n)</th>
<th>Median (95% CI)</th>
<th>Survival distribution function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage A</td>
<td>117</td>
<td>413 (413, NE)</td>
<td>13.6 months</td>
</tr>
<tr>
<td>Stage B</td>
<td>311</td>
<td>384 (312, 419)</td>
<td>12.6 months</td>
</tr>
<tr>
<td>Stage C</td>
<td>877</td>
<td>240 (198, 260)</td>
<td>7.9 months</td>
</tr>
<tr>
<td>Stage D</td>
<td>93</td>
<td>104 (77, 148)</td>
<td>3.4 months</td>
</tr>
</tbody>
</table>

CI, confidence interval; NE, not evaluable

Lencioni R et al. Oral presentation at ECCO/ESMO Congress 2011 Stockholm - Abstract 6500
Treatments prescribed at BCLC C stage in Italy

Out of 100 patients in BCLC C stage for whom you are personally involved in the treatment decision, for how many does the treatment consist of …? [ESTIMATED VALUES]

In BCLC C stage, the estimates given by the doctors show a distinct shift towards the systemic therapy.
The Italian experience with Sorafenib

Prescribed by hepatologists and oncologists, the image and use of Sorafenib differ among the two specialists, because of their different perspective of the disease:

**ONCOLOGISTS**
- Good level of enthusiasm
- High propensity to use it
- Comparison with chemotherapy drugs

Sorafenib is the key to enter the world of HCC with a really effective drug, a weapon to personally fight a battle that has just begun

**HEPATOLOGISTS**
- Very limited enthusiasm
- Low propensity to use it
- Comparison with the other treatments

Sorafenib is little more than a palliative treatment, to be used strategically in patients that need some more time

Source: Qualitative and quantitative HCC market researchs Kantar Health 2011
Open issues in the guidelines of HCC leading to individualized treatment

- Role of surgery in early (and intermediate) stages
- Use of TACE outside the guidelines recommendations
- Strategies for repeating/stopping TACE and switching to other treatment
- Role of combined/sequential treatments
- Management of Child B patients
- Poor definition of Intermediate patients (BCLC B)
- Treatment of elderly patients
- Management of cases not suitable to PEI or RF
- Strategies for retreating patients with stage migration
- Role of Yttrium Radioembolization
Role of surgery in early (and intermediate) stages
The BLOG policy

Cirrhotic patient eligible for liver resection

- MELD score
  - < 9
  - 9-10
  - > 10

- Serum sodium level
  - ≥ 140 mEq/L
  - < 140 mEq/L

- Major hepatectomy (up to 4 segments)
- Segmentectomy or bisegmentectomy
- Segmentectomy or limited resection
- Risk of IPLF > 15% in all types of hepatectomies

Cescon et al, Arch Surg 2009
Derangement from the Guidelines: the case of TACE

Prospctive Cohort Study of Transarterial Chemoembolization for Unresectable Hepatocellular Carcinoma in 8510 Patients

KENICHI TAKAYASU,* SHIGEKI ARII,** IWAO IKAI,† MASAO OMATA,†† KIWAMU OKITA,*
TAKAFUMI ICHIDA,‡ YUTAKA MATSUYAMA,** YASUNI NAKANUMA,** MASAMICHI KOJIRO,*
MASATOSHI MAKUUCHI,†† and YOSHIO YAMAOKA** for the Liver Cancer Study Group of Japan

GASTROENTEROLOGY 2006;131:461–469

<table>
<thead>
<tr>
<th>Background factors</th>
<th>Number of patients</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
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<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>1871</td>
<td>22</td>
</tr>
<tr>
<td>≥60</td>
<td>6639</td>
<td>78</td>
</tr>
<tr>
<td>Sex</td>
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<td></td>
</tr>
<tr>
<td>Male</td>
<td>6122</td>
<td>72</td>
</tr>
<tr>
<td>Female</td>
<td>2386</td>
<td>28</td>
</tr>
<tr>
<td>Degree of liver damage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>4008</td>
<td>51</td>
</tr>
<tr>
<td>B</td>
<td>3053</td>
<td>39</td>
</tr>
<tr>
<td>C</td>
<td>766</td>
<td>10</td>
</tr>
<tr>
<td>HBV and HCV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCV Ab positive</td>
<td>6063</td>
<td>74</td>
</tr>
<tr>
<td>HBs Ag positive</td>
<td>900</td>
<td>11</td>
</tr>
<tr>
<td>Both positive</td>
<td>211</td>
<td>3</td>
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<tr>
<td>Both negative</td>
<td>971</td>
<td>12</td>
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<tr>
<td>Maximum tumor size (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2</td>
<td>1989</td>
<td>24</td>
</tr>
<tr>
<td>2.1–3</td>
<td>1981</td>
<td>24</td>
</tr>
<tr>
<td>3.1–5</td>
<td>2318</td>
<td>28</td>
</tr>
<tr>
<td>≥5.1</td>
<td>2076</td>
<td>25</td>
</tr>
<tr>
<td>No. of lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3648</td>
<td>44</td>
</tr>
<tr>
<td>2–3</td>
<td>2675</td>
<td>32</td>
</tr>
<tr>
<td>4&lt;–/&gt;</td>
<td>2066</td>
<td>25</td>
</tr>
</tbody>
</table>
Derangement from the Guidelines: the case of TACE

Superselective transarterial chemoembolization for hepatocellular carcinoma. Validation of treatment algorithm proposed by Japanese guidelines

Kenichi Takayasu1, Shigeki Arii2, Masatoshi Kudo3, Takafumi Ichida4, Osamu Matsui5,6, Namiki Izumi5, Yutaka Matsuyama2, Michie Sakamoto3, Osamu Nakashima4, Yonson Ku9,10,11, Norihiro Kokudo11, Masatoshi Makuuchi12,1

<table>
<thead>
<tr>
<th>Background factors</th>
<th>No. of patients</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, yr</strong></td>
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<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>756</td>
<td>15</td>
</tr>
<tr>
<td>≥60</td>
<td>4205</td>
<td>86</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>3369</td>
<td>68</td>
</tr>
<tr>
<td>F</td>
<td>1597</td>
<td>32</td>
</tr>
<tr>
<td><strong>Child-Pugh classification</strong></td>
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<td></td>
</tr>
<tr>
<td>A</td>
<td>3229</td>
<td>69</td>
</tr>
<tr>
<td>B</td>
<td>1296</td>
<td>28</td>
</tr>
<tr>
<td>C</td>
<td>167</td>
<td>4</td>
</tr>
<tr>
<td><strong>HBV and HCV</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCV Ab positive</td>
<td>3479</td>
<td>73</td>
</tr>
<tr>
<td>HBs Ag positive</td>
<td>449</td>
<td>9</td>
</tr>
<tr>
<td>Both positive</td>
<td>89</td>
<td>2</td>
</tr>
<tr>
<td>Both negative</td>
<td>768</td>
<td>16</td>
</tr>
<tr>
<td><strong>Maximum tumor size (cm)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2</td>
<td>1549</td>
<td>32</td>
</tr>
<tr>
<td>2.1-3</td>
<td>1178</td>
<td>24</td>
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<tr>
<td>3.1-5</td>
<td>1291</td>
<td>27</td>
</tr>
<tr>
<td>≥5.1</td>
<td>811</td>
<td>17</td>
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<tr>
<td><strong>No. of lesions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2252</td>
<td>46</td>
</tr>
<tr>
<td>2</td>
<td>1003</td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td>565</td>
<td>12</td>
</tr>
<tr>
<td>≥4</td>
<td>1092</td>
<td>22</td>
</tr>
</tbody>
</table>
# Derangement from the Guidelines: the case of TACE

Bologna Liver Oncology Group experience

<table>
<thead>
<tr>
<th>Patients characteristics</th>
<th>Number of patients (151)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>115 (76)</td>
</tr>
<tr>
<td>Female</td>
<td>36 (24)</td>
</tr>
<tr>
<td>Cause of disease</td>
<td></td>
</tr>
<tr>
<td>HBV</td>
<td>14 (9)</td>
</tr>
<tr>
<td>HCV</td>
<td>93 (62)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>23 (15)</td>
</tr>
<tr>
<td>Multiple etiologies</td>
<td>11 (7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>10 (7)</td>
</tr>
<tr>
<td>Median age</td>
<td>64 (34-83)</td>
</tr>
<tr>
<td>HCC</td>
<td></td>
</tr>
<tr>
<td>Unifocal</td>
<td>63 (42)</td>
</tr>
<tr>
<td>Multifocal</td>
<td>88 (58)</td>
</tr>
<tr>
<td>Median MELD score</td>
<td>11 (7-21)</td>
</tr>
<tr>
<td>Child-Pugh score</td>
<td></td>
</tr>
<tr>
<td>Child-Pugh A</td>
<td>97 (64)</td>
</tr>
<tr>
<td>Child-Pugh B</td>
<td>51 (34)</td>
</tr>
<tr>
<td>Child-Pugh C</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Ascites</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>129 (86)</td>
</tr>
<tr>
<td>Mild-Moderate</td>
<td>17 (11)</td>
</tr>
<tr>
<td>Severe-Refractory</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>147 (97)</td>
</tr>
<tr>
<td>Mild</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
</tr>
</tbody>
</table>

Terzi et al, EASL 2011, J Hepatol 2011;44 Suppl1:S266.
Strategies for repeating and stopping TACE

Treatment strategies of viable tumor after the first TACE cycle with IR

Terzi et al, EASL 2011, J Hepatol 2011;44 Suppl1:S266.
Strategies for repeating and stopping TACE

Retreatment strategies of recurrent HCC after the first TACE with CR

Terzi et al, EASL 2011, J Hepatol 2011;44 Suppl1:S266.
Actual treatment strategies in intermediate pts

HCC

- PST 0, Child–Pugh A
  - Very early stage
    - Single < 2 cm
  - OLT

- PST 0-2, Child–Pugh A–B
  - Early stage
    - Single or 3 nodules
  - Intermediate stage
    - Multinodular, PST 0
    - TACE
    - TACE+/- RFA or PEI or TARE
    - Sorafenib (for non resp)

- Advanced stage
  - Portal invasion, N1, M1, PST 1–2
  - TACE+Sorafenib

- PST > 2, Child–Pugh C
  - Terminal stage
  - Sorafenib (for TACE unsuitable)
Proposed treatment algorithm for intermediate-stage HCC

**Patient / disease characteristics**
- No PVT
- No EHS
- Child-Pugh A or B7

**First TACE**
- CT or MRI

**Second TACE**
- CT or MRI

**Liver deterioration or major complications**

**Disease control (CR or PR or SD)**
- Follow-up / 3 months
- Consider retreatment with TACE

**Disease progression**
- New lesion
- Growth of existing lesion
- Consider sorafenib

In case of persistent vital tumour tissue

Combination of TACE with Sorafenib
The SPACE trial

• **Aim:** to evaluate the **efficacy and safety** of Sorafenib + TACE with DEBDOX in BCLC-B HCC patients

• **Results:**

<table>
<thead>
<tr>
<th>Assessment*</th>
<th>TTP</th>
<th>OS§</th>
<th>Time to VI/EHS§</th>
<th>TTUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>0.797</td>
<td>0.898</td>
<td>0.621</td>
<td>1.586</td>
</tr>
<tr>
<td>95% CI</td>
<td>0.588, 1.080</td>
<td>0.606, 1.330</td>
<td>0.321, 1.200</td>
<td>1.200, 2.096</td>
</tr>
<tr>
<td>P value (1-sided)†</td>
<td>0.072</td>
<td>0.295</td>
<td>0.076</td>
<td>0.999</td>
</tr>
</tbody>
</table>

* ITT population (all randomized pts); † predefined alpha = 0.15; § median was not reached in either group.

• **Conclusions:**
  – Sorafenib + TACE **improve TTP**
  – The combination is well tolerated

Rate of allocation to treatments recommended by BCLC guidelines (red bars) is high in early patients (higher in B7 than in B8-9).

Rate of allocation to treatments recommended by BCLC guidelines (red bars) in intermediate patients is different according to individual score.

Piscaglia et al, AASLD Hepatology 2010;52 Suppl1:2010
The future: from molecular signatures to personalized treatments

G1 to G6 are the subgroups of HCCs defined by transcriptome analysis. Vertical lines indicate significantly associated features. Red and green primarily indicate over- and under-expressed genes, respectively, in that particular functional category.

Integrative transcriptome analysis reveals common molecular subclasses of human HCC

Combining Clinical, Pathology, and Gene Expression Data to Predict Recurrence of Hepatocellular Carcinoma

A 35-gene signature of vascular invasion was defined in the training set, predicting vascular invasion with an accuracy of 69%. The signature was independently associated with the presence of vascular invasion (OR 3.38, 95% CI 1.48–7.71, p = 0.003) along with tumor size (diameter greater than 3 cm, OR 2.66, 95% CI 1.17–6.05, p = 0.02).

In the validation set, the signature discarded the presence of vascular invasion with a negative predictive value of 0.77, and significantly improved the diagnostic power of tumor size alone (p = 0.045).

<table>
<thead>
<tr>
<th>Table 3. Association of vascular invasion signature and tumor diameter with presence of vascular invasion.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Univariate analysis</strong></td>
</tr>
<tr>
<td><strong>Odds ratio (95% CI)</strong></td>
</tr>
<tr>
<td>Vascular invasion signature</td>
</tr>
<tr>
<td>Tumor diameter &gt;3 cm</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4. Association of vascular invasion signature and tumor diameter with presence of vascular invasion (multivariate subgroup analysis).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis C infection (n = 54)</strong></td>
</tr>
<tr>
<td><strong>Odds ratio (95% CI)</strong></td>
</tr>
<tr>
<td>Vascular invasion signature</td>
</tr>
<tr>
<td>Tumor diameter &gt;3 cm</td>
</tr>
</tbody>
</table>
Problems in translating "molecular signatures" into clinical practice

- Lack of demonstration for correspondence to treatment efficacy and resistance
- Pathological specimens derived from surgical resection are not representative of the large majority of HCC to be treated
- For multinodular HCCs one nodule is not representative of all nodules
Conclusions

Guidelines are often not applied because:

• Careful evaluation of patients characteristics leading to individualized treatment
  ➔ “Patient oriented”

• “Grey areas” lacking evidence
  ➔ “Patient oriented-expert driven”

• Personal experience of the clinicians and availability of procedures
  ➔ “Doctor oriented”
Hepatocellular carcinoma: from guidelines to individualized treatment

The role of the hepatologist in the management of HCC:
• *limited to the underlying liver disease? BSC?*
• *extended to the active treatment of HCC?*

The actual role of different specialists in Italy

- **PEI/RF** → Interv Radiologist (Hepatologist ?)
- **Resection/OLT** → Surgeon
- **TACE/TARE** → IntervRadiologist
- **Systemic treatment** → Oncologist (Hepatologist?)

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Hepatocellular carcinoma: from guidelines to individualized treatment

- HCC on liver cirrhosis is a complex clinical challenge needing dedicated expertise for proper treatment selection.

- This expertise is not in the background of any single existing specialist and a multidisciplinary approach is requested.

- Hepatologists have the best scientific and clinical competence for liver diseases enabling the development of dedicated expertise in this field.

- The role of hepatologists should not be limited to the management of underlying liver disease or to BSC, but should be extended at least to the practice of percutaneous and systemic treatment.

- This requires a change in the mind of hepatologists and a cultural and organization effort which should be stimulated by AISF.