Determining Hepatocellular Carcinoma Staging:
Liver Disease Staging, Performance Status and RECIST Criteria
Factors Determining Prognosis of Hepatocellular Cancer

- Severity of chronic liver disease (liver function)
- Performance status (overall patient health)
- Cancer staging classification
- Response-to-treatment
The severity of chronic liver disease (CLD) helps measure outcomes.

In general, higher (worse) scores correlate to poorer outcomes.

Scoring systems that predict outcomes in chronic liver diseases include:
- Child-Pugh (CTP)
- Model for End Stage Liver Disease (MELD)
## Assessing Severity of CLD: Child-Turcotte-Pugh Score

<table>
<thead>
<tr>
<th>Clinical and Lab Criteria</th>
<th>Points*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>&gt; 3.5</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td></td>
</tr>
<tr>
<td>Seconds prolonged</td>
<td>&lt;4</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>&lt;1.7</td>
</tr>
</tbody>
</table>

**Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)**

- **Class A = 5 to 6 points** (least severe liver disease)
- **Class B = 7 to 9 points** (moderately severe liver disease)
- **Class C = 10 to 15 points** (most severe liver disease)
Assessing Severity of CLD: MELD Score

- For a given patient, MELD score = 
  \[9.6 \log_e (\text{creatinine [mg/dl]}) + 3.8 \log_e (\text{bilirubin [mg/dl]}) + 11.2 \log_e (\text{INR}) + 6.4\]

- Scores can range from 6 (healthy) to 40 (gravely ill)

- Useful for continuous measure of liver disease severity and an accurate predictor of 3-month mortality
  - Patients with HCC awaiting liver transplant have their MELD scores adjusted according to an evolving policy from UNOS, because the MELD cannot predict mortality in HCC patients

- Sodium is now the 4\(^{th}\) component of the MELD score (MELD-Na)

*Stage I = single nodule < 2 cm; stage II = nodule between 2 and 5 cm, or 2 or 3 nodules each < 3 cm
Impact of adding Sodium to the MELD Score
How does Sodium affect the MELD Score?

Example: Revised MELD Score (with Sodium)

If the MELD is 15 and the Na = 125, the new score would be 25.
If the MELD is 15 and the Na = 135, the new score would be 17.
If the MELD is 30 and the Na = 125, the new score would be 34.
If the MELD is 25 and the Na = 137, the new score would be 25.
Assessing Severity of CLD: Child-Pugh vs. MELD scores

- Child-Pugh scores are based on 3 clinical, subjective parameters (ascites, encephalopathy and nutritional status) and 2 biochemical, objective parameters (serum albumin and bilirubin).
- MELD scores are based entirely on objective parameters.

### Comparison of Child–Pugh and MELD scores

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Child–Pugh</th>
<th>MELD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of variables in the score</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Quantitative variables</td>
<td>3/5</td>
<td>3/3</td>
</tr>
<tr>
<td>Selection of variables</td>
<td>Empirical</td>
<td>Statistical</td>
</tr>
<tr>
<td>Variables are weighted according to their influence</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>‘Ceiling’ effect for quantitative variables</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Logarithmic transformation of variables</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Needs computation</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Variables can be influenced by personal judgement</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Type of score</td>
<td>Discrete</td>
<td>Continuous</td>
</tr>
</tbody>
</table>

Performance status is highly correlated with survival, need for services, and may help predict ability to tolerate therapies.

<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG Performance Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled; cannot carry on any selfcare; totally confined to bed or chair</td>
</tr>
<tr>
<td>5</td>
<td>Dead</td>
</tr>
</tbody>
</table>

ECOG = Eastern Cooperative Oncology Group
Importance of Staging Systems in HCC

- Predict prognosis of patients
- Stratify patients according to prognostic variables in the setting of clinical trials
- Allow exchange of information among researchers
- Guide the therapeutic approach

A globally accepted staging system for HCC is not available; many staging systems exist.

<table>
<thead>
<tr>
<th>Staging Systems for HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Barcelona Clinic Liver Cancer (BCLC)</strong></td>
</tr>
<tr>
<td>American Joint Commission on Cancer (AJCC)/Union Internacional</td>
</tr>
<tr>
<td>Cancer of the Liver Italian Program (CLIP)</td>
</tr>
<tr>
<td>Chinese University Prognostic Index (CUPI)</td>
</tr>
<tr>
<td>Contra la Cancrum (UICC) Tumor Node Metastasis (TNM)</td>
</tr>
<tr>
<td>Group d’Etude de Traitement du Carcinoma Hepatocellulaire (GRETCH)</td>
</tr>
<tr>
<td>Japanese Staging System and Japan Integrated Staging score (JIS)</td>
</tr>
<tr>
<td>Okuda Staging System</td>
</tr>
</tbody>
</table>

The BCLC, devised from the results of cohort studies and randomized clinical trials, is a widely accepted staging system recommended by EASL and AASLD guidelines.

Treatment Recommendations According to BCLC Stage

MWA, microwave ablation; BSC, best supportive care; 1L, first-line therapy; 2L, second-line therapy
Radiologic Diagnostic Criteria for HCC

FIGURE 3: LI-RADS categories.
Modified Response Evaluation Criteria in Solid Tumors (mRECIST)

- Defines standard measurement methods for converting radiology image observations into a quantitative and statistically tractable framework for measuring the response of tumor size to therapy

<table>
<thead>
<tr>
<th>Assessment of Target Lesion Response</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complete Response (CR)</strong></td>
</tr>
<tr>
<td><strong>Partial Response (PR)</strong></td>
</tr>
<tr>
<td><strong>Stable Disease (SD)</strong></td>
</tr>
<tr>
<td><strong>Progressive Disease (PD)</strong></td>
</tr>
</tbody>
</table>

mRECIST, modified Response Evaluation Criteria in Solid Tumors
## Response Evaluation Criteria In Solid Tumors

<table>
<thead>
<tr>
<th>Target lesions</th>
<th><strong>Response category</strong></th>
<th><strong>RECIST</strong></th>
<th><strong>mRECIST</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>CR</strong></td>
<td>Disappearance of all target lesions</td>
<td>Disappearance of any intratumoral arterial enhancement in all target lesions</td>
</tr>
<tr>
<td></td>
<td><strong>PR</strong></td>
<td>At least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum of the diameters of target lesions</td>
<td>At least a 30% decrease in the sum of the diameters of viable (enhancement in the arterial phase) target lesions, taking as reference the baseline sum of the diameters of target lesions</td>
</tr>
<tr>
<td></td>
<td><strong>SD</strong></td>
<td>Any cases that do not qualify for either PR or PD</td>
<td>Any cases that do not qualify for either PR or PD</td>
</tr>
<tr>
<td></td>
<td><strong>PD</strong></td>
<td>An increase of at least 20% in the sum of the diameters of target lesions, taking as reference the smallest sum of the diameters of target lesions recorded since treatment started</td>
<td>An increase of at least 20% in the sum of the diameters of viable (enhancing) target lesions, taking as reference the smallest sum of the diameters of viable (enhancing) target lesions recorded since treatment started</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-target lesions</th>
<th><strong>Response category</strong></th>
<th><strong>RECIST</strong></th>
<th><strong>mRECIST</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>CR</strong></td>
<td>Disappearance of all non-target lesions</td>
<td>Disappearance of any intratumoral arterial enhancement in all non-target lesions</td>
</tr>
<tr>
<td></td>
<td><strong>IR/SD</strong></td>
<td>Persistence of one or more non-target lesions</td>
<td>Persistence of intratumoral arterial enhancement in one or more non-target lesions</td>
</tr>
<tr>
<td></td>
<td><strong>PD</strong></td>
<td>Appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions</td>
<td>Appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions</td>
</tr>
</tbody>
</table>

### mRECIST recommendations

<table>
<thead>
<tr>
<th>Pleural effusion and ascites</th>
<th>Cytopathologic confirmation of the neoplastic nature of any effusion that appears or worsens during treatment is required to declare PD.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Porta hepatis lymph node</td>
<td>Lymph nodes detected at the porta hepatis can be considered malignant if the lymph node short axis is at least 2 cm.</td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td>Malignant portal vein thrombosis should be considered as a non-measurable lesion and thus included in the non-target lesion group.</td>
</tr>
<tr>
<td>New lesion</td>
<td>A new lesion can be classified as HCC if its longest diameter is at least 1 cm and the enhancement pattern is typical for HCC. A lesion with atypical radiological pattern can be diagnosed as HCC by evidence of at least 1 cm interval growth.</td>
</tr>
</tbody>
</table>
RECIST vs mRECIST

### Utility of mRECIST: Efficacy Outcomes

#### Efficacy Outcomes for the Overall REFLECT Population

<table>
<thead>
<tr>
<th></th>
<th>Lenvatinib (n = 478)</th>
<th>Sorafenib (n = 476)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median OS, months</strong></td>
<td>13.6</td>
<td>12.3</td>
</tr>
<tr>
<td>95% CI</td>
<td>12.1–14.9</td>
<td>10.4–13.9</td>
</tr>
<tr>
<td><strong>ORR†, n (%)</strong></td>
<td>115 (24.1)</td>
<td>44 (9.2)</td>
</tr>
<tr>
<td>95% CI</td>
<td>20.2–27.9</td>
<td>6.6–11.8</td>
</tr>
<tr>
<td><strong>Median PFS†, months</strong></td>
<td>7.4</td>
<td>3.7</td>
</tr>
<tr>
<td>95% CI</td>
<td>6.9–8.8</td>
<td>3.6–4.6</td>
</tr>
</tbody>
</table>

**Total REFLECT Population (N = 954)**
Median OS (month) (95% CI): 13.0 months (11.9–14.1)

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*Data cutoff: November 13, 2016
†Investigator review according to mRECIST
CI, confidence interval; mRECIST, modified Response Evaluation Criteria In Solid Tumors; ORR, objective response rate; OS, overall survival; PFS, progression free survival.

Kudo M et al. Presented at ASCO GI Symposium; January 17-19, 2019; San Francisco, CA
# Tumor Assessment: Lenvatanib

<table>
<thead>
<tr>
<th>Parameter</th>
<th>mRECIST by investigator</th>
<th>mRECIST by independent review</th>
<th>RECIST v1.1 by independent review</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lenvatinib (n = 478)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORR, n (%)</td>
<td>115 (24.1)</td>
<td>194 (40.6)</td>
<td>90 (18.8)</td>
</tr>
<tr>
<td>95% CI</td>
<td>20.2–27.9</td>
<td>36.2–45.0</td>
<td>15.3–22.3</td>
</tr>
<tr>
<td>Odds ratio (95%CI)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3.13 (2.15–4.56)</td>
<td>5.01 (3.59–7.01)</td>
<td>3.34 (2.17–5.14)</td>
</tr>
<tr>
<td><strong>BOR, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete response</td>
<td>6 (1)</td>
<td>10 (2)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>Partial response</td>
<td>109 (23)</td>
<td>184 (38)</td>
<td>88 (18)</td>
</tr>
<tr>
<td>Stable disease</td>
<td>246 (51)</td>
<td>159 (33)</td>
<td>258 (54)</td>
</tr>
<tr>
<td>Durable stable disease&lt;sup&gt;b&lt;/sup&gt;</td>
<td>167 (35)</td>
<td>84 (18)</td>
<td>163 (34)</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>71 (15)</td>
<td>79 (17)</td>
<td>84 (18)</td>
</tr>
<tr>
<td>Not evaluable/unknown</td>
<td>46 (10)</td>
<td>46 (10)</td>
<td>46 (10)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Lenvatinib vs. sorafenib  
<sup>b</sup>Stable disease lasting ≥23 weeks

BOS, best overall response; CI, confidence interval; mRECIST, modified Response Evaluation Criteria In Solid Tumors; ORR, objective response rate

Lencioni R et al. Presented at ASCO GI Symposium; January 17-19, 2019; San Francisco, CA
## Tumor Assessment: Sorafenib

<table>
<thead>
<tr>
<th>Parameter</th>
<th>mRECIST by investigator</th>
<th>mRECIST by independent review</th>
<th>RECIST v1.1 by independent review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sorafenib (n = 476)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORR, n (%)</td>
<td>44 (9.2)</td>
<td>59 (12.4)</td>
<td>31 (6.5)</td>
</tr>
<tr>
<td>95% CI</td>
<td>6.6–11.8</td>
<td>9.4–15.4</td>
<td>4.3–8.7</td>
</tr>
<tr>
<td>BOR, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete response</td>
<td>2 (&lt;1)</td>
<td>4 (1)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Partial response</td>
<td>42 (9)</td>
<td>55 (12)</td>
<td>30 (6)</td>
</tr>
<tr>
<td>Stable disease</td>
<td>244 (51)</td>
<td>219 (46)</td>
<td>250 (53)</td>
</tr>
<tr>
<td>Durable stable diseaseb</td>
<td>139 (29)</td>
<td>90 (19)</td>
<td>118 (25)</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>147 (31)</td>
<td>152 (32)</td>
<td>152 (32)</td>
</tr>
<tr>
<td>Not evaluable/unknown</td>
<td>41 (9)</td>
<td>46 (10)</td>
<td>43 (9)</td>
</tr>
</tbody>
</table>

*a*Lenvatinib vs. sorafenib  
*b*Stable disease lasting ≥23 weeks  

BOS, best overall response; CI, confidence interval; mRECIST, modified Response Evaluation Criteria In Solid Tumors; ORR, objective response rate  

Lencioni R et al. Presented at ASCO GI Symposium; January 17-19, 2019; San Francisco, CA
Utility of mRECIST: Response Correlates with Survival

Response Correlates with Survival

OS by OR for the Overall REFLECT Population

Median OS (months) 95% CI
- Response: 22.4 (19.7–26.0)
- Nonresponse: 11.4 (10.3–12.3)

HR (95% CI): 0.61 (0.49–0.76)
Mantel-Byar Test: P Value: <0.001

Number of patients at risk:
- Response: 159 155 151 138 121 108 93 76 56 41 22 11 6 1 0
- Nonresponse: 795 721 571 441 362 291 241 180 129 83 51 26 10 5 0

CI, confidence interval; OR, objective response; OS, overall survival

Kudo M et al. Presented at ASCO GI Symposium; January 17-19, 2019; San Francisco, CA
Use of mRECIST in Clinical Practice

The AASLD guidelines state that mRECIST may be the most common criteria used to evaluate radiological response in HCC patients treated with locoregional therapy.
Case 3

- **History and physical exam**
  - An otherwise healthy, 77-year-old Caucasian male with a history of alcohol use
  - Presented to his PCP complaining of abdominal pain, fatigue and an unexplained 10-lb weight loss
  - Currently consumes 3-4 alcoholic drinks per day
  - ECOG PS 0

- **Imaging**
  - CT scan: 4.5-cm hepatic lesion with arterial hypervascularity, portal venous washout, and a pseudocapsule indicative of hepatocellular carcinoma; no evidence of vascular invasion
  - Bone scan: left-sided iliac mass (3.1 cm)
  - Chest CT: clear

- **Diagnosis: unresectable HCC with extrahepatic involvement**
  - BCLC stage C
  - Child-Pugh A
  - AFP Level: 3500 ng/mL
  - Weight: 72 kg
- **Sorafenib 400 mg BID was initiated.**
  - He experienced modest weight loss and reported loss of appetite; moderate hand-foot syndrome
  - Imaging at 16 weeks: partial response (0.5 cm); AFP 4200

- **Further treatment options?**
Case 4

Medical History and Physical Exam
- A 60-year-old Asian man presented to his gastroenterologist with abdominal pain (upper-right quadrant).
- History of diabetes, hypertension controlled, chronic hepatitis C virus (HCV), diagnosed and treated 9 years ago with interferon
- ECOG Performance Status 0

Work-up and Diagnosis
- MRI abdomen: single 7-cm lesion on right hepatic lobe
- Biopsy: confirmed hepatocellular carcinoma (HCC)
- The tumor was deemed unresectable upon surgical evaluation.
- HCV RNA detected at 483,000, genotype 3
- AFP 3700

Initial Therapy
- Transarterial radioembolization (Y-90) performed; 3 month post treatment MRI lesion reduced in size to 3 cm; amount of viable tumor difficult to verify

Follow-up
- Six months later: CT showed multifocal HCC in left abdominal wall, liver lesions, and lung metastases.
- Child-Pugh score, A5
- BCLC stage C (advanced stage)
- Weight, 79 kg
- A-Fetoprotein level, 5300 ng/mL

Further Treatment options?
Conclusions

• Treatment of HCC remains challenging because the site of the neoplasm is itself diseased in most cases.
• Outcome is affected by
  – Severity of chronic liver disease
  – Performance status
  – Extent of tumor
  – Treatment response
Back-Up Slides

Additional Staging Options
Okuda Staging System

- Positive features
  - Tumor involving >50% of the liver
  - Ascites
  - Albumin < 3 g/dL
  - Bilirubin > 3 mg/dL

- Stage I: No positive features
- Stage II: 1 or 2 positive features
- Stage III: 3 or 4 positive features

Okuda K, et al, Cancer 1985
Score = 3 (if bilirubin level ≥ 50 umol/L), 0 otherwise
+ 2 (if alkaline phosphatase ≥ 2N), 0 otherwise
+ 2 (if alpha fetoprotein ≥ 500 ng/ml), 0 otherwise
+ 3 (if Karnofsky index < 80), 0 otherwise
+ 1 (if portal vein obstruction), 0 otherwise

• Low-risk group (A) if modified score = 0
• Intermediate-risk group (B) if modified score ≤ 5
• High-risk group (C) if score ≥ 6
Cancer of the Liver Italian Program (CLIP) Staging System

- Child-Pugh stage
  - A 0
  - B 1
  - C 2

- Tumor morphology
  - Uninodular and extent ≤ 50% of liver 0
  - Multinodular and extent ≤ 50% of liver 1
  - Massive or extent ≥ 50% of liver 2

- Alpha fetoprotein (ng/dl)
  - < 400 0
  - ≥ 400 1

- Portal vein thrombosis
  - No 0
  - Yes 1

The CLIP Investigators, Hepatology 1998
Japanese Staging System

- **T criteria**: Single tumor, < 2 cm, no vascular involvement
- **T1**: Agree with all 3 criteria
- **T2**: Agree with 2 of 3 criteria
- **T3**: Agree with 1 of 3 criteria
- **T4**: Agree with no criteria

- **Stage I**: T1 N0 M0
- **Stage II**: T2 N0 M0
- **Stage III**: T3 N0 M0
- **Stage IVA**: T4 N0 M0 or any T N0 M0
- **Stage IVB**: Any T N0-1 M1

Japan Integrated Staging Score: Modification of Japanese Staging System

- Stage I: 0
- Stage II: 1
- Stage III: 2
- Stage IV: 3
- Child-Pugh A: 0
- Child-Pugh B: 1
- Child-Pugh C: 2
• sT1: Solitary tumor without vascular invasion
• sT2: Solitary tumor with vascular invasion or multiple tumors, none > 5 cm
• sT3: Multiple tumors > 5 cm, or tumor involving a major branch of the portal or hepatic vein(s)
• F0: Grade 0-4 fibrosis (no fibrosis to moderate fibrosis)
• F1: Grade 5-6 fibrosis (severe fibrosis or cirrhosis)
• N0: No regional lymph node metastasis
• N1: Regional lymph node metastasis
• M0: No distant metastasis
• M1: Distant metastasis

AJCC/UICC TNM Staging System

- **Stage I**  
  sT1 N0 M0

- **Stage II**  
  sT2 N0 M0

- **Stage IIIA**  
  sT3 N0 M0

- **Stage IIIB**  
  Any sT N1 M0

- **Stage IV M1**  
  Any sT Any N

Chinese University Prognostic Index (CUPII)

- **TNM stage**
  - I and II: -3
  - IIa and IIb: -1
  - IVa and IVb: 0

- **Asymptomatic disease on presentation**: -4

- **Ascites**: 3

- **Alpha fetoprotein ≥ 500 ng/ml**: 2

- **Total bilirubin (umol/L)**
  - < 3: 0
  - 34-51: 3
  - ≥ 52: 4

- **Alkaline phosphatase ≥ 200 units/L**: 3

- **Risk groups**: Low, score <1; Intermediate, score 2-7; High, score > 8

Leung TW et al, Cancer 2002
CLIP Staging System

Survival Probability

<table>
<thead>
<tr>
<th>Time (Months)</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
</tr>
</thead>
<tbody>
<tr>
<td>No at Risk:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 0</td>
<td>43</td>
<td>15</td>
<td>10</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Stage 1</td>
<td>74</td>
<td>33</td>
<td>14</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 2</td>
<td>35</td>
<td>21</td>
<td>9</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 3</td>
<td>32</td>
<td>10</td>
<td>3</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Stage 4</td>
<td>34</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 5</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Log Rank P

0 vs. 1  P < .0001
1 vs. 2  P = .15
3 vs. 3  P = .18
3 vs. 4  P = .001

Marrero JA, et al, Hepatology 2005
JIS Staging System

No at Risk:
Stage 0 18 12 7 2
Stage 1 60 29 9 5
Stage 2 46 29 15 6
Stage 3 42 10 3 0
Stage 4 46 4 0 0
Stage 5 27 2 0 0
Thank you !