

**Supplementary Table 1: Response methodology for landmark analyses**

| System   | Classification      | Radiologic Interpretation (6 or 12 months)                | Imaging Finding (6 or 12 months)   |
|--|---------------------|---|--|
| <b>World Health Organization Guidelines (WHO)</b>                        | <b>RESPONDER</b>    | <b>Complete Response (CR)</b>                             | 100% decrease in cross-product of index lesion   |
|  |                     | <b>Partial Response (PR)</b>                              | ≥50% decrease in cross-product of index lesion   |
|  | <b>NONRESPONDER</b> | <b>Stable Disease (SD)</b>                                | <50% decrease to ≤25% increase in cross-product of index lesion  |
|  |                     | <b>Progressive Disease (PD)</b>                           | >25% increase from maximum response of index lesion, new lesions or metastases, development of vascular invasion   |
| <b>European Association for the Study of the Liver Guidelines (EASL)</b> | <b>RESPONDER</b>    | <b>Complete Response (CR)</b>                             | 100% decrease in amount of enhancing tissue in index lesion  |
|  |                     | <b>Partial Response (PR)</b>                              | ≥50% decrease in amount of enhancing tissue in index lesion  |
|  | <b>NONRESPONDER</b> | <b>Stable Disease (SD)</b>                                | <50% decrease in to ≤25% increase in amount of enhancing tissue in index lesion  |
|  |                     | <b>Progressive Disease (PD)</b>                           | >25% increase in amount of enhancing tissue in index lesion, new lesions or metastases, development/progression of vascular invasion<br><br>AND/OR<br><br>Any new enhancement in previously treated index lesion warranting further locoregional therapy |
| <b>Alpha-fetoprotein (AFP) response</b>                                  | <b>Responder</b>    | >50% decrease in the level of AFP from baseline           |  |
|  | <b>Nonresponder</b> | <50% decrease from baseline or any increase from baseline |  |
| <b>AFP response (quantitative)*</b>                                      | <b>Responder</b>    | AFP level decrease to <500 ng/mL                          |  |
|  | <b>Nonresponder</b> | AFP levels did not decrease to <500 ng/mL                 |  |

\* only in patients with AFP >500 ng/mL at baseline

**Supplementary Table 2: Percentage AFP reduction stratified by baseline AFP**

|                    |                                  | Baseline AFP level (ng/mL) |                     |                 |         |
|--------------------|----------------------------------|----------------------------|---------------------|-----------------|---------|
| 3-months<br>(n=43) |                                  | 200-1000<br>(n=17)         | 1000-3000<br>(n=14) | >3000<br>(n=12) | Total   |
|                    | any increase -<br><50% reduction | 6 (35)                     | 4 (29)              | 3 (25)          | 13 (30) |
|                    | 50-75% reduction                 | 1 (6)                      | 1 (7)               | 1 (8)           | 3 (7)   |
|                    | >75-90% reduction                | 4 (24)                     | 1 (7)               | 2 (17)          | 7 (16)  |
|                    | >90% reduction                   | 6 (35)                     | 8 (57)              | 6 (50)          | 20 (47) |
| 6-months<br>(n=23) |                                  | 200-1000<br>(n=8)          | 1000-3000<br>(n=7)  | >3000<br>(n=8)  | Total   |
|                    | any increase -<br><50% reduction | 1 (12)                     | 1 (14)              | 2 (25)          | 4 (17)  |
|                    | 50-75% reduction                 | 1 (12)                     | 0 (0)               | 1 (12)          | 2 (9)   |
|                    | >75-90% reduction                | 0 (0)                      | 0 (0)               | 0 (0)           | 0 (0)   |
|                    | >90% reduction                   | 6 (76)                     | 6 (86)              | 5 (63)          | 17 (74) |

Abbreviation: AFP: Alpha-fetoprotein

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4 **Supplementary Table 3: Median AFP at baseline and**  
5 **Landmarks**  
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|                         |                | <b>Median (ng/ml) (range)</b> |
|-------------------------|----------------|-------------------------------|
| <b>Baseline</b>         |                | 1360 (210 – 270000)           |
| <b>3-month landmark</b> | All patients   | 145 (4.5 – 478900)            |
|                         | Responders     | 51 (4.5 – 24610)              |
|                         | Non-Responders | 2087 (90.7 – 478900)          |
| <b>6-month landmark</b> | All patients   | 52 (3 – 18630)                |
|                         | Responders     | 39 (3 - 4208)                 |
|                         | Non-Responders | 9243 (1362 - 18630)           |

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20 Abbreviation: AFP: Alpha-fetoprotein  
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**Supplementary Table 4: Exploratory survival analysis at 3-month Landmark by AFP response**

| <b>Quantitative AFP response in patients with baseline AFP&gt;500 ng/mL</b> |                                     |                                      |
|---|-------------------------------------|--------------------------------------|
|   | <b>R (AFP&lt;500 ng/mL)</b>         | <b>NR (AFP &gt;500 ng/mL)</b>        |
| <b>N</b>  | 22                                  | 13                                   |
| <b>Median Survival (months)</b>   | 29.4 months                         | 6.8 months                           |
| <b>P value</b>  | <b>0.003</b>                        |                                      |
| <b>Excluding patients with PVT</b>  |                                     |                                      |
|   | <b>R (&gt;50% reduction in AFP)</b> | <b>NR (&lt;50% reduction in AFP)</b> |
| <b>N</b>  | 26                                  | 10                                   |
| <b>Median Survival (months)</b>   | 27.6                                | 4.0                                  |
| <b>P value</b>  | <b>0.0003</b>                       |                                      |

Abbreviations: AFP: Alpha-fetoprotein; R: responders; NR: nonresponders; PVT: Portal vein thrombosis

**Supplementary Table 5: Distribution of tumor size and Albumin/Bilirubin among responders and nonresponders**

| Landmark | Variable      | Size    | WHO |    |         | EASL |    |         | AFP |    |         |
|----------|---------------|---------|-----|----|---------|------|----|---------|-----|----|---------|
|          |               |         | R   | NR | P value | R    | NR | P value | R   | NR | P value |
| 3 months | Baseline Size | ≤5 cm   | 7   | 18 | 0.901   | 18   | 7  | 0.373   | 18  | 7  | 0.866   |
|          |               | 5-10 cm | 4   | 9  |         | 9    | 4  |         | 9   | 4  |         |
|          |               | >10 cm  | 1   | 4  |         | 2    | 3  |         | 3   | 2  |         |
|          | Albumin       | ≥3.5    | 3   | 5  | 0.815   | 8    | 0  | 0.078   | 8   | 0  | 0.101   |
|          |               | <3.5    | 9   | 26 |         | 21   | 14 |         | 22  | 13 |         |
|          | Bilirubin     | ≤1.2    | 5   | 18 | 0.531   | 15   | 8  | 0.993   | 15  | 8  | 0.716   |
| >1.2     |               | 7       | 13  | 14 |         | 6    | 15 |         | 5   |    |         |
| 6 months | Baseline Size | ≤5 cm   | 5   | 7  | 0.973   | 10   | 2  | 0.570   | 10  | 2  | 0.420   |
|          |               | 5-10 cm | 4   | 5  |         | 7    | 2  |         | 8   | 1  |         |
|          |               | >10 cm  | 1   | 1  |         | 1    | 1  |         | 1   | 1  |         |
|          | Albumin*      | ≥3.5    | 3   | 3  | 0.964   | 6    | 0  | 0.323   | 5   | 1  | 0.612   |
|          |               | <3.5    | 6   | 10 |         | 11   | 5  |         | 13  | 3  |         |
|          | Bilirubin**   | ≤1.2    | 4   | 4  | 0.675   | 6    | 2  | 0.669   | 6   | 2  | 0.978   |
| >1.2     |               | 4       | 9   | 10 |         | 3    | 11 |         | 2   |    |         |

\*Albumin level was not available at 6 months for 1 patient

\*\*Bilirubin levels were not available at 6 months for 2 patients

Abbreviations: AFP: Alpha-fetoprotein; EASL: European Association for the Study of the Liver; WHO: World Health Organization