Cure can be Achieved by Conversion to Microwave Ablation following Atezolizumab-Bevacizumab Therapy in Unresectable Hepatocellular Carcinoma

Running Title: Curative Conversion using MWA

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Abstract

Introduction: Atezolizumab/bevacizumab is the recommended first-line systemic therapy for unresectable hepatocellular carcinoma (uHCC) and may facilitate curative conversion through resection and locoregional therapies. However, there have been very few reports on curative conversion using microwave ablation (MWA). This study aimed to determine the curative conversion rate with MWA using atezolizumab-bevacizumab as the first-line treatment in patients with uHCC, and to compare the characteristics and survival of patients with and without curative conversion.

Methods: Consecutive patients with uHCC who were started on atezolizumab-bevacizumab from May 2021 and December 2023 in a single tertiary center were included. Objective response (ORR) and disease control rate (DCR) were based on the RECIST 1.1 and mRECIST criteria.

Results: Twenty consecutive patients with uHCC (60% advanced-stage) were included, 90% exceeding the up-to-7 criteria. The ORR and DCR were 35% and 60%, and 35% and 55% using RECIST and mRECIST, respectively. Five (25%) patients underwent successful curative conversion with MWA (4 advanced and 1 intermediate stage) despite a median HCC size of 6.1 (range: 2.4-7.3) cm. Two of these patients were tumor and drug-free 132-133 weeks from the 1st atezolizumab-bevacizumab dose. Patients who underwent curative conversion had significantly longer survival than those who did not. (p=0.024) Other factors associated with survival were male sex, Child-Pugh class A, and an objective response.

Conclusions: Despite the relatively large tumor size, successful curative conversion with MWA was achieved with first-line atezolizumab-bevacizumab in uHCC. However, data from prospective multicenter trials are required to determine whether this strategy is universally applicable.
Key words: ablation; tyrosine kinase inhibitor; immune checkpoint inhibitor; locoregional therapy; thermal; combination

Introduction:

Hepatocellular carcinoma (HCC) is the sixth most common cancer worldwide and the third leading cause of cancer-related death. The high mortality rate is often due to late diagnosis, where HCC has already advanced, limiting options for potentially curative therapies. The development of immune checkpoint inhibitors (ICI) has dramatically changed the landscape of HCC, achieving objective response rates of 17-36%, compared to response rates of only 1-13% with sorafenib. Consequently, HCC downstaging, a term usually reserved for locoregional therapy or limited hepatic resection that allows HCC patients to meet liver transplant criteria, is now also being realized with systemic HCC treatment. Several investigators have designated this capability, following systemic treatment, to downgrade a previously unresectable HCC to receive potentially curative treatment as “curative conversion”.

The combination of atezolizumab, an ICI binding to the programmed cell death ligand 1 receptors of T-cells, and bevacizumab, an anti-angiogenic agent, has been recommended as the first-line treatment for unresectable and advanced stage HCC in most guidelines. This recommendation follows the IMbrave150 Phase III trial, which demonstrated its superiority over sorafenib in both overall survival (OS) and progression free survival (PFS) in patients with unresectable HCC. Notably, the relatively high objective response rate of 33.2% achieved with atezolizumab-bevacizumab combination in the trial has translated into curative conversion rates of up to 35% in intermediate stage and 13% in advanced stage patients. Curative
conversion is not only limited to atezolizumab bevacizumab but can also be achieved using other antiangiogenic and ICI combinations.\textsuperscript{9, 12, 13}

Most reports on curative conversion employ surgical modalities, with only a minority mentioning thermal ablative therapies, such as radiofrequency ablation (RFA) and microwave ablation (MWA).\textsuperscript{8, 10, 14} This is understandable because thermal ablation is usually limited to smaller tumors, and patients who undergo systemic therapy usually have large tumors at the start of treatment. However, with improvements in ablation techniques and technology, HCCs as large as 7-8 cm can be thermally ablated with a high success rate\textsuperscript{15, 16}, and consequently extend the indications for ablation. Therefore, thermal ablation can be a good option to surgical resection of HCC that is downsized to a size deemed suitable for ablation, according to the expertise available at the institution. Therefore, we aimed to present the curative conversion rates using MWA as a potential curative treatment in consecutive patients with intermediate-to-advanced HCC who were initially treated with a combination of atezolizumab and bevacizumab. We also compared the survival rates of patients who achieved curative conversion to those who did not.

Methods:

This retrospective cohort study of consecutive patients diagnosed with unresectable HCC (uHCC) who received atezolizumab-bevacizumab combination therapy as a first-line systemic treatment from May 2021 to December 2023. Criteria for HCC unresectability were based on the Barcelona Clinic Liver Cancer (BCLC) staging system, which includes portal vein invasion, distant extrahepatic spread, diffuse and infiltrative bilobar tumor involvement, and an Eastern Cooperative Oncology Group (ECOG) score of 1-2 at the staging work-up. Patients with a liver reserve of Child-Pugh classification (CPC) C and ECOG \( \geq 3 \) were excluded.
Information collected from the medical records included patients’ age, sex, ECOG, alpha-fetoprotein (AFP), HCC etiology, and tumor characteristics. Tumor size and number were further characterized according to the up-to-7 criteria, where the size of the largest HCC (in cm) and the number of intrahepatic HCC present were summed to obtain a value.\textsuperscript{17} Patients were then categorized as beyond (>7) or within (≤7) up-to-7 criteria depending on the value computed. All patients were administered atezolizumab and bevacizumab with the end goal of achieving the following criteria for curative conversion with MWA: (a) tumor size of ≤7.5 cm in diameter, which is the tumor size limit where the complete ablation rate with thermal ablation reaches at least 80\%, based on the institution’s experience (S. Wong, unpublished data); b) interval disappearance of arterial enhancement of thrombosis with shrinkage or disappearance of baseline intrahepatic vein thrombosis; and c) extrahepatic metastasis amenable to microwave ablation.

Atezolizumab–bevacizumab was administered intravenously every three weeks at standard pharmaceutical doses of 1,200 mg and 15 mg/kg, respectively. Patients were followed up with laboratory tests every three weeks, and dynamic imaging studies using computed tomography (CT) or magnetic resonance imaging (MRI) were repeated every 12 weeks. For patients who experienced progressive disease (PD) based on the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 or modified RECIST (mRECIST), systemic therapy was shifted to either lenvatinib monotherapy or lenvatinib in combination with pembrolizumab at standard recommended doses for HCC, depending on the patient’s preference. In selected cases, patients with stable or progressive disease while on systemic therapy were offered MWA as long as the criteria for MWA were met. Transarterial chemoembolization (TACE) was performed as needed in some patients to achieve further reduction in tumor size in synergy with systemic therapy.
Radiological responses were evaluated according to the RECIST and mRECIST. The objective response rate (ORR) was defined as the percentage of patients with a confirmed complete response (CR) or partial response (PR). Disease control rate (DCR) refers to the percentage of patients with complete response, partial response, and stable disease (SD). The primary end point was curative conversion using MWA. Patients were followed up with dynamic imaging one month after MWA to confirm complete ablation using mRECIST, and then every four months thereafter for recurrence surveillance. The patients were given the option to continue systemic treatment after curative conversion or surveillance only. Overall survival (OS) was computed from the time of the first infusion of atezolizumab-bevacizumab and estimated using Kaplan-Meier analysis. Outcomes and baseline characteristics were compared between patients who achieved curative conversion and those who did not. All continuous variables are presented as medians (range) and compared using the Mann-Whitney U test, while categorical variables are presented as numbers (%) and compared using Fisher’s exact test. The log-rank test or Cox regression analysis was used to compare variables affecting OS. Statistical significance was set at P < 0.05.

All procedures were in accordance with the ethical standards of the responsible committee on human experimentation and the Helsinki Declaration of 1975, as revised in 2008. This study was approved by the institutional Ethics Review Board (protocol reference number 2023-09-082-TF-AP).

Results:

Twenty consecutive uHCC patients who received atezolizumab were included in this study. The majority (85%) of the patients were male, with a median age of 68 (30-80) years. The median tumor size was 10 cm (1.4-26.9), with most patients (60%) classified as BCLC stage C. More than half of the cases (65%) were secondary to chronic viral hepatitis (hepatitis
B=12, hepatitis C=1), while the rest were secondary to nonalcoholic fatty liver disease (NAFLD) (Table 1).

TUMOR RESPONSES:

Radiological responses using RECIST and mRECIST were assessed in 17 and 16 of the 20 patients, respectively. Three patients were not evaluated for radiological responses due to death before the first scheduled assessment. Another patient was assessed for RECIST using plain MRI but not for mRECIST because of renal dysfunction. In intention-to-treat analysis, ORR after 12 weeks were 25% (RECIST) and 30% (mRECIST). The disease control rates were 65% (RECIST) and 60% (mRECIST). After a median of 6.5 cycles (1-28), the ORR at the last data cutoff was 35% for both RECIST and mRECIST, whereas the DCR was 60% (RECIST) and 55% (mRECIST) (Table 2). Four patients experienced PD after 2-4 cycles while one had 16 cycles before PD. All patients with PD were treated with a combination of lenvatinib and pembrolizumab.

Curative conversion with MWA was achieved in 5 patients (25 %) (Figure 1). Median follow-up period after curative MWA was 43.7 weeks. Three patients had intrahepatic vessel invasion, one had isolated lung metastasis after successful locoregional treatment of intrahepatic HCC, and the last was BCLC stage B at the start of atezolizumab-bevacizumab. No baseline characteristics predicted the curative conversion. In the 12-week radiological assessment, an objective response using mRECIST, but not RECIST, was associated with curative conversion. An objective response at the last available assessment using both the mRECIST and RECIST was associated with curative conversion (Table 1). A brief description of the clinical course of each patient who achieved curative conversion is provided below.

Patient 1 was a 72-year-old male with nonalcoholic fatty liver disease (NAFLD)-related cirrhosis. CT tomography showing a solitary, 13.6 cm-sized HCC. The baseline BCLC stage
was B with CPCA. Nine cycles of atezolizumab-bevacizumab were administered with one conventional TACE performed after the 1st cycle. Reassessment showed PR with a tumor size of 7.3 cm. Uncomplicated MWA was performed 55 weeks after the 1st dose of atezolizumab bevacizumab, and complete ablation was documented. (Figures 2a-c) Patient opted for no further systemic treatment and remained tumor- and drug-free for 133 weeks after the 1st atezolizumab-bevacizumab dose.

Patient 2 was a 71-year-old male with chronic hepatitis C-related cirrhosis. The patient had CPC A and was classified as having BCLC C because of multiple (>3) classic HCC, with the largest tumor at 10.5 cm, and segmental portal vein thrombosis (PVT). The patient developed immune-mediated hepatitis during atezolizumab-bevacizumab treatment, which resulted in only three cycles being administered before the first radiological assessment. Fortunately, the CT scan showed PR with shrinkage of the tumor to 6.1 cm, and the disappearance of most of the other liver nodules and PVT. Patient underwent MWA 44 weeks after the 1st dose of atezolizumab-bevacizumab. Repeat scans revealed complete tumor ablation. (Figures 3a-f) However, the patient developed duodenal perforation post-MWA due to non-apparent adhesion between the tumor and the duodenum. This was resolved using an endoscopic over-the-scope clip and the patient was still tumor- and drug-free 132 weeks after the 1st dose of atezolizumab bevacizumab.

Patient #3 was a 69-year-old male with alcohol-related cirrhosis (CPC A) who initially presented with a solitary 2.5 cm HCC lesion and lung metastasis after previous successful TACE and MWA for HCC. After four cycles of atezolizumab-bevacizumab, SD was documented, though with an 8% increase in tumor size and elevated AFP levels. It was then decided to shift the patient to lenvatinib and pembrolizumab combination therapy. After another four cycles, a new intrahepatic 2.4 cm-sized HCC with stable lung metastases was also observed. MWA was then performed for both intrahepatic and lung HCC 34 weeks after the
1st atezolizumab-bevacizumab dose. A post-ablation scan showed complete ablation. However, patient developed a lung abscess as a complication, which resolved with medical therapy. On lenvatinib monotherapy after MWA, the patient experienced multiple intrahepatic and lung metastasis recurrences with inferior vena cava (IVC) thrombosis 41 weeks after MWA. Pembrolizumab was reintroduced into the regimen.

Patient #4 is a 60-year-old male with hepatitis B-related cirrhosis. Patients were classified as CPC B and BCLC C because of multiple (>3) classic HCC, with the largest being 8.3 cm, and thrombosis of the right hepatic vein, and nine sub-centimeter lung metastases. After 12 cycles of atezolizumab, the patient achieved PR with disappearance of most of the smaller HCC, shrinkage of the main HCC to 5.5 cm, non-enhancement of the hepatic vein thrombosis, and disappearance of the lung metastasis (two remaining nodules were classified as granulomas). Curative conversion was then performed using MWA for the remaining HCC and hepatic vein thrombosis 40 weeks after the 1st cycle. The patient required therapeutic thoracentesis for symptomatic pleural effusion after MWA. The patient was maintained on lenvatinib after MWA, was asymptomatic, and remained tumor-free for 78 weeks after the 1st atezolizumab-bevacizumab dose.

Patient #5 was a 61-year-old male with hepatitis B-related cirrhosis diagnosed with BCLC C due to two HCCs, the largest being 9.4 cm, with invasion into the IVC. The patient underwent TACE with drug-eluting beads and lipiodol after the 12th cycle. A repeat scan after the 15th cycle showed PR with an HCC size of 7.3 cm with nonenhancement, lipiodol deposition, and shrinkage of the IVC thrombus to 0.1 cm. Uncomplicated MWA was then performed 50 weeks after the 1st atezolizumab-bevacizumab cycle with documented complete ablation, and the patient is presently tumor-free 51 weeks after the 1st cycle and will continue systemic treatment.
SURVIVAL AND ADVERSE EVENTS:

After a median follow-up of 56.9 weeks (1.4-132.7), eight patients had died, two due to sepsis and the rest due to liver-related events. The median overall survival of the entire patient population was 101.7 weeks (95% CI: 35.3-168.1). Curative conversion (HR: 52.255; 95% CI: 1.117-23367.109; p=0.024), an objective response (RECIST [HR: 46.186; 95% CI: 1.074-28715.445; p=0.012] and mRECIST [HR: 50.003; 95% CI: 1.119-21057.759; p=0.025]) at the 12-week assessment (Figures 4a-c), male gender (HR: 10.067; 95% CI: 1.981-51.153; p=0.005), and CPC A (HR: 6.035; 95% CI: 1.286-28.324; p=0.023) were all associated with better overall survival.

Treatment with atezolizumab and bevacizumab was well-tolerated. The most common treatment-related adverse event was hypertension (20%). Immune-mediated hepatitis occurred in two (10%), which resolved with oral steroids and allowed continuation of treatment. One patient (patient 13) had grade IV plantar erythrodysesthesia and discontinued atezolizumab-bevacizumab. No treatment-related deaths occurred.

Discussion:

The objective response rate of 35% achieved in our study with the combination of atezolizumab and bevacizumab was comparable to the rates published in the registration trial for the drug combination.\(^4\) This allowed curative conversion with MWA to be performed in 4 of the 7 patients with an objective response (Figure 1) and in 1 of the 4 patients with stable disease. While it can be argued that maintaining patients on a combination therapy that is currently used may already result in acceptable survival, the long-term follow-up of patients who achieve a partial or even complete response to combination immunotherapy demonstrates
that some of these patients eventually experience progressive disease, even while being on maintenance treatment. Studies using atezolizumab-bevacizumab have shown that despite continued treatment, up to 38% and 3% of patients with partial\textsuperscript{18} and complete\textsuperscript{19} radiologic responses, respectively, eventually develop progressive disease. Additionally, another study using different ICI and anti-angiogenic combinations showed that residual tumors were still seen in 67% of resected specimens even after a complete radiologic response.\textsuperscript{9} The ability to convert these patients to potentially curative HCC treatment presents a unique opportunity to further extend the survival of these patients instead of just treating them until disease progression occurs. Achieving curative conversion has indeed been found to result in better overall survival not only in the overall population of patients administered systemic treatment, but also among those with partial radiologic response.\textsuperscript{14} Our study also shows a similar benefit in survival (Figure 4a) and contributes to the increasing evidence that upfront systemic treatment in patients who are initially deemed to be poor candidates for TACE and/or resection can still receive potentially curative treatments later.\textsuperscript{8,10-12,14}

The combination of thermal ablation with ICI is of particular interest because RFA and MWA have been found to induce and enhance tumor-specific immune responses\textsuperscript{20,21} and may work synergistically with ICI's. Although there have been reports of thermal ablation as a modality for curative conversion, it has either been limited to tumors measuring 3 cm and smaller,\textsuperscript{14} or the criteria for ablation were not defined.\textsuperscript{8} This is the first study to our knowledge that use MWA for curative conversion in HCC’s that are predominantly >5 cm in diameter. This is particularly important in patients with a partial response to systemic therapy, but with contraindications to or refusal of surgery. However, the fact that three (60%) of our patients had major, albeit non-fatal, complications after curative conversion with MWA emphasizes the fact that complications are usually higher in larger tumors and that there is a need to discuss the pros and cons of treatment with a multidisciplinary team.
Our 25% curative conversion rate with MWA is not far from what has been achieved with resection in the literature and has allowed two out of our five patients (40%) to achieve curative conversion to be tumor- and drug-free after MWA. However, the need for systemic therapy after curative conversion remains controversial. Although a retrospective analysis did not show a difference in recurrence-free survival between patients who continued and discontinued systemic treatment following curative conversion with ablation or resection, the recently published IMbrave050 trial suggests otherwise, in that continued immunologic surveillance in treatment-naive patients after resection or ablation showed a benefit of longer recurrence-free survival for patients given adjuvant atezolizumab-bevacizumab. A longer follow-up period of patients with or without systemic treatment following curative conversion is required to clarify this question.

Our study was limited by the small number of patients and its retrospective nature. The survival benefit of patients who undergo curative conversion should be evaluated with caution because of the immortal time bias in favor of the conversion group. Despite the favorable prognosis of patients who underwent MWA, these results cannot be applied universally, especially because expertise in ablating larger tumors may not be uniform across centers. Moreover, other curative modalities, such as resection and liver transplantation, may yield better survival results. Resection was not performed in our study because the patients either refused or were not candidates for surgery, and liver transplantation is not readily available or accessible in our country.

In conclusion, we have shown that curative conversion with MWA can be achieved in 25% of patients with unresectable HCC treated with atezolizumab-bevacizumab. Among these patients, 40% do not require further systemic treatment. The relatively high response rates that are currently achievable with combination immunotherapy and anti-angiogenic treatments provide physicians with more flexibility in managing unresectable intermediate-advanced
stage HCC. This flexibility allows for treating HCC as a dynamic disease, making innovative adjustments in the treatment regimen based on the patient’s response to systemic therapy. Such an approach aims to prolong survival and possibly achieve curative outcomes.

Conflict of Interest

The authors did not receive any financial assistance for the work. S. Wong is a lecturer for Roche and Hi-Eisai. No potential conflicts of interests exist for all other authors.

Ethics Statement

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The study was approved by the institution’s Ethics Review Board (protocol reference number 2023-09-082-TF-AP).

Funding Statement

Not applicable

Data Availability

The data presented in this study are available upon reasonable request from the corresponding author.
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Formal analysis: SNW
Investigation: RJDF, ESSP, AAK, SNW
Methodology: RJDF, ESSP, AAK, SNW
Project administration: SNW
Software: SNW
Supervision: SNW
Validation: SNW
Visualization: SNW
Writing - original draft: RJDF
Writing – review & editing: SNW
References:


Figures:

Figure 1: Swimmer’s plot of selected baseline characteristics and outcomes of all patients.

Figure 2: Selected cross-sectional imaging of patient #1. a.) Pre-treatment images showing a 13.6 cm HCC. b.) Partial response after TACE and Atezolizumab-Bevacizumab. c.) Complete response after curative conversion with MWA with good surrounding ablation zone.

Figure 3: Selected cross-sectional imaging of patient #2. a.) Arterial phase CT showing a 10.5 cm HCC with satellite nodules. b.) Portal venous phase showing segmental thrombosis (black arrow). c.) Arterial phase MRI showing partial response after Atezolizumab-Bevacizumab with d.) Portal phase showing disappearance of the portal vein thrombosis. e.) Complete response after MWA curative conversion showing pre-existing hyperdensity due to ablation-induced hemorrhage in the plain film and f.) absence of enhancement in the arterial phase.

Figure 4: Comparison of overall survival between HCC patients a.) with and without curative conversion with MWA; b.) with and without ORR (RECIST) at 12 weeks; c.) with and without ORR (mRECIST) at 12 weeks.
Progression refers to progressive disease while on Atezolizumab-Bevacizumab while recurrence means new HCC occurring after curative conversion. Abbreviations: NAFLD (nonalcoholic fatty liver disease); Not NAFLD (chronic hepatitis B=12; chronic hepatitis C=1); BCLC (Barcelona clinic liver cancer); VT (venous thrombosis); Mets (extrahepatic metastasis); CPC (Child-Pugh classification)

Figure 1
Figure 2
Figure 4
Table 1. Comparison of HCC patients who achieved or did not achieve MWA curative conversion

<table>
<thead>
<tr>
<th></th>
<th>(+) Curative Conversion</th>
<th>(-) Curative Conversion</th>
<th>TOTAL</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>N=5 (25%)</td>
<td>N=15 (75%)</td>
<td>68 (30-80)</td>
<td>0.630</td>
</tr>
<tr>
<td>Male Gender</td>
<td>5 (100%)</td>
<td>12 (80%)</td>
<td>17 (85%)</td>
<td>0.539</td>
</tr>
<tr>
<td>Etiology: NAFLD</td>
<td>1 (20%)</td>
<td>6 (40%)</td>
<td>7 (35%)</td>
<td>0.613</td>
</tr>
<tr>
<td>Chronic viral hepatitis</td>
<td>4 (80%)</td>
<td>9 (60%)</td>
<td>13 (65%)</td>
<td></td>
</tr>
<tr>
<td>ECOG 0-1</td>
<td>5 (100%)</td>
<td>12 (80%)</td>
<td>17 (85%)</td>
<td>0.108</td>
</tr>
<tr>
<td>ECOG 2</td>
<td>0 (0%)</td>
<td>3 (20%)</td>
<td>3 (15%)</td>
<td></td>
</tr>
<tr>
<td>MELD-Na</td>
<td>14 (6-15)</td>
<td>13 (6-23)</td>
<td>13.5 (6-23)</td>
<td>0.662</td>
</tr>
<tr>
<td>CPC A</td>
<td>4 (80%)</td>
<td>10 (66.7%)</td>
<td>14 (70%)</td>
<td>1.000</td>
</tr>
<tr>
<td>CPC B</td>
<td>1 (20%)</td>
<td>5 (33.3%)</td>
<td>6 (30%)</td>
<td></td>
</tr>
<tr>
<td>CPC C</td>
<td>4 (80%)</td>
<td>8 (53.3%)</td>
<td>12 (60%)</td>
<td></td>
</tr>
<tr>
<td>Beyond up-to-7 criteria</td>
<td>4 (80%)</td>
<td>14 (93.3%)</td>
<td>18 (90%)</td>
<td>0.447</td>
</tr>
<tr>
<td>TACE done</td>
<td>2 (40%)</td>
<td>2 (13.3%)</td>
<td>4 (20%)</td>
<td>0.249</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>66.1 (15-355)</td>
<td>40.1 (17.2-319)</td>
<td>41.9 (15-319)</td>
<td>0.275</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>99 (25-149.7)</td>
<td>53 (36.6-236)</td>
<td>61.5 (25-236)</td>
<td>0.793</td>
</tr>
<tr>
<td>Platelets (x10⁹/L)</td>
<td>204 (89-363)</td>
<td>246 (97-550)</td>
<td>227 (89-550)</td>
<td>0.485</td>
</tr>
<tr>
<td>INR</td>
<td>1.2 (1-1.4)</td>
<td>1.1 (1-1.4)</td>
<td>1.1 (1-1.4)</td>
<td>0.896</td>
</tr>
<tr>
<td>Total bilirubin (mg/dL)</td>
<td>1.1 (0.5-2.2)</td>
<td>0.8 (0.2-2.4)</td>
<td>0.9 (0.2-2.4)</td>
<td>0.458</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.8 (0.6-1.1)</td>
<td>1 (0.7-2.6)</td>
<td>0.9 (0.6-2.6)</td>
<td>0.162</td>
</tr>
<tr>
<td>AFP ≥400 ng/mL</td>
<td>3 (60%)</td>
<td>5 (33.3%)</td>
<td>8 (40%)</td>
<td>0.347</td>
</tr>
<tr>
<td># of Atezolizumab-bevacizumab cycles</td>
<td>9 (3-15)</td>
<td>5 (1-28)</td>
<td>6.5 (1-28)</td>
<td>0.456</td>
</tr>
</tbody>
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RADIOLOGIC RESPONSES:

<table>
<thead>
<tr>
<th></th>
<th>(+) Curative Conversion</th>
<th>(-) Curative Conversion</th>
<th>TOTAL</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR (RECIST - 12 wks.)</td>
<td>3 (60%)</td>
<td>2 (13.3%)</td>
<td>5 (25%)</td>
<td>0.073</td>
</tr>
<tr>
<td>ORR (mRECIST - 12 wks.)</td>
<td>4 (80%)</td>
<td>2 (13.3%)</td>
<td>6 (30%)</td>
<td><strong>0.014</strong></td>
</tr>
<tr>
<td>ORR (RECIST – latest)</td>
<td>4 (80%)</td>
<td>3 (20%)</td>
<td>7 (35%)</td>
<td><strong>0.031</strong></td>
</tr>
<tr>
<td>ORR (mRECIST - latest)</td>
<td>4 (80%)</td>
<td>3 (20%)</td>
<td>7 (35%)</td>
<td><strong>0.031</strong></td>
</tr>
</tbody>
</table>

Abbreviations: NAFLD (nonalcoholic fatty liver disease); ECOG (Eastern cooperative oncology group); MELD-Na (Model for end-stage liver disease-sodium); CPC (Child-Pugh classification); BCLC (Barcelona clinic liver cancer); TACE (transarterial chemoembolization); ORR (objective response rate)
Table 2: Radiologic responses of the entire cohort

<table>
<thead>
<tr>
<th></th>
<th>12 wks. (RECIST)</th>
<th>12 wks. (mRECIST)</th>
<th>Latest (RECIST)</th>
<th>Latest (mRECIST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective Response Rate (ORR)</td>
<td>5 (25%)</td>
<td>6 (30%)</td>
<td>7 (35%)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>Complete response (CR)</td>
<td>1 (5%)</td>
<td>1 (5%)</td>
<td>1 (5%)</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Partial Response (PR)</td>
<td>4 (20%)</td>
<td>5 (25%)</td>
<td>6 (30%)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Stable Disease (SD)</td>
<td>8 (40%)</td>
<td>6 (30%)</td>
<td>5 (25%)</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Disease Control Rate (DCR)</td>
<td>13 (65%)</td>
<td>12 (60%)</td>
<td>12 (60%)</td>
<td>11 (55%)</td>
</tr>
<tr>
<td>Progressive Disease (PD)</td>
<td>7 (35%)*</td>
<td>8 (40%)**</td>
<td>8 (40%)*</td>
<td>9 (45%)**</td>
</tr>
</tbody>
</table>

*3 and **4 patients with missing dynamic scans were assumed to have PD