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Efficacy of Atezolizumab Plus Bevacizumab Combined with Transarterial Chemoembolization for Unresectable Hepatocellular Carcinoma: A Real-World Study

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Purpose: Transarterial chemoembolization (TACE), when used in combination with immunotherapy and antiangiogenic therapy, has been shown to have synergistic anticancer effects. The aim of this study was to further assess the efficacy and safety of TACE combined with atezolizumab and bevacizumab in the treatment of unresectable hepatocellular carcinoma (HCC) in the real world.

Methods: Between August 2021 and September 2023, clinical information was collected from consecutive HCC patients who received treatment via TACE-Atezo/Bev at four tertiary institutions. This study evaluated the objective response rate (ORR), overall survival (OS), and progression-free survival (PFS) as outcomes. Predictors for OS and PFS were also analyzed. Treatment-related adverse events (TRAEs) were recorded and assessed.

Results: Ninety-two patients were enrolled in this study, with a median follow-up duration of 14.1 months. The ORRs based on the modified Response Evaluation Criteria in Solid Tumors (RECIST) and RECIST 1.1 criteria were 54.3% and 41.3%, respectively. The median OS and PFS of the patients were 15.9 months [95% confidence interval (CI), 14.5–17.2 months] and 9.1 months (95% CI, 7.4–10.8 months), respectively. Multivariate analyses revealed that the Eastern Cooperative Oncology Group score and neutrophil–lymphocyte ratio were independent risk factors for OS, whereas tumor size and extrahepatic metastasis were independent risk factors for PFS. Grade 3/4 TRAEs occurred in 16.3% (15/92) of the patients and were controlled conservatively.

Conclusion: The combination of Atezo/Bev with TACE demonstrated acceptable synergistic therapeutic effects and manageable safety profiles in patients with unresectable HCC.

Keywords: atezolizumab, bevacizumab, efficacy, hepatocellular carcinoma, transarterial chemoembolization

Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies and a leading cause of cancer-related death worldwide.[1] The majority of patients are often diagnosed at an intermediate or advanced stage, which restricts treatment options and results in a dismal prognosis.[2,3]

Systemic therapies, including molecular therapies and immunotherapies, have transformed the treatment of unresectable HCC (uHCC), with the support of robust clinical trials.[4] The IMbrave 150 trial, the most representative study, demonstrated that atezolizumab plus bevacizumab (Atezo/Bev) was superior to sorafenib for patients with uHCC.[5] Consequently, Atezo/Bev was approved for first-line systemic therapy according to the American Society of Clinical

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Oncology guidelines.[6] Many studies have been conducted on the combination of antiangiogenic agents (including bevacizumab) with transarterial chemoembolization (TACE) to counteract TACE-induced vascular endothelial growth factor (VEGF) release, and encouraging results have been obtained.[7] TACE, which induces antigen release and the expression of programmed cell death 1 ligand 1 (PD-L1), promotes the formation of an immunosuppressive microenvironment to enhance the response to PD-L1 inhibitors.[8] Driven by theory, there is growing interest in combining tyrosine kinase inhibitors and PD-1 inhibitor therapies with TACE for treating HCC, which has shown encouraging therapeutic effects and tolerable safety profiles.[9,10] Recently, in a Phase III trial of TACE combined with durvalumab with bevacizumab, EMERALD-1 the exciting primary research endpoint of an improvement in median PFS (15.0 months) was achieved, and a high ORR of 43.6% was demonstrated via RECIST.[11] Given these findings, the rationale for the combination strategy of Atezo/Bev and TACE may be more comprehensive.

Wang et al preliminarily explored the therapeutic effect of TACE combined with Atezo/Bev in patients with BCLC stage B HCC, with an ORR of 42.9% according to RECIST and 61.9% according to mRECIST.[12] In addition, the IMbrave 150 trial for HCC focused on patients with preserved liver function (Child–Pugh A). Researchers in a previous study had attempted to extend the inclusion criteria to a limited number of patients with Child–Pugh B liver disease.[13] However, in the context of the Atezo/Bev and TACE treatment model, evidence supporting whether patients with Child–Pugh B disease enjoy safety profiles and outcome benefits to those of patients in the IMbrave 150 trial is lacking.

Therefore, we conducted this real-world retrospective study to evaluate the efficacy and safety of Atezo/Bev and TACE treatment and to analyze the associations of these variables with prognosis in these HCC patients.

Methods

The procedures followed in this research conformed to the guidelines of the World Medical Association Declaration of Helsinki and were approved by the ethics committee of our institution. This retrospective study was approved by the local institutional ethics review board of the Ethics Committee of the First Affiliated Hospital with Nanjing Medical University (ethical review no. 2022-SR-332). Written informed consent was waived for this retrospective study. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Patients

Patients diagnosed with uHCC from four tertiary institutions between August 2021 and September 2023 were retrospectively reviewed for this study. HCC was diagnosed on the basis of clinical or pathological findings according to the Guidelines for Diagnosis and Treatment of Primary Liver Cancer in China.[14] The inclusion criteria were as follows: (1) aged ≥18 years; (2) HCC at Barcelona Clinic Liver Cancer (BCLC) stages B and C; (3) first-line treatment with Atezo/Bev in combination with TACE; (4) Child–Pugh class A/B; (5) Eastern Cooperative Oncology Group (ECOG) score of 0–1; and (6) at least one measurable target lesion that could be assessed via Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1, and modified RECIST (mRECIST).[15,16] The exclusion criteria were as follows: (1) patients who had other primary malignant tumors; (2) patients who received fewer than two cycles of systemic therapy; and (3) patients who were lost to follow-up or whose medical information was incomplete.

TACE and Atezo/Bev Treatment

TACE was performed initially before the first cycle of Atezo/Bev. During the TACE procedure, programmed angiography, including angiography of the celiac artery, superior mesenteric artery, and hepatic artery, was conducted with a 5F catheter, mostly via the femoral artery under local anesthesia. After confirming the tumor number, size, localization and tumor-feeding arteries, embolization through a coaxial microcatheter (2.7F or 2.4F) was superselectively administered via a lipiodol (5–20 mL)-epirubicin (10 mg) mixture, followed by gelatin sponges or particles. Subsequent TACE was performed on demand. In some cases, hepatic arterial infusion chemotherapy [FOLFOX, oxaliplatin (85 mg/m2) for 4 h, leucovorin (400 mg/m2) for 4 h, 5-fluorouracil (400 mg/m2) for 8 h, and (2400 g/m2)] was also administered for 46 h after repeat embolization.

Prior to systemic treatment, the patient underwent an esophagogastroduodenoscopy examination; varices or ulcers were assessed and treated. On the basis of the degree of varices, patients were prescribed bevacizumab at 15 or 7.5 mg/kg.

Patients received atezolizumab (1200 mg) plus bevacizumab intravenously 3–7 days after initial TACE and then at approximately 3-week intervals. The treatment was interrupted or the dose was adjusted according to the drug manufacturer's instructions if there was disease progression, an intolerable adverse event (AE), or a clinician decision for treatment cessation.

Outcomes and Assessments

The patients were followed up regularly (approximately every 1.5–2 months) until the end of the study (March, 2024) or until death. To assess treatment efficacy, enhanced CT or MRI and laboratory tests were performed at each visit. Progression-free survival (PFS), overall survival (OS), tumor response, and treatment-related adverse effects (AEs) were evaluated. OS was defined as the time between the initial TACE procedure and the date of death from any cause or the last follow-up. PFS was defined as the time from initial TACE to disease progression or death. Tumor responses were classified as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD) on the basis of mRECIST and RECIST version 1.1. The objective response rate (ORR) was defined as the proportion of patients who achieved CR or PR and were evaluated at 2–3 months after the initial treatment. The disease control rate (DCR) was defined as the proportion of patients who achieved CR, PR or SD. The time to response (TTR) was defined as the time from the initial TACE procedure to the date of the first confirmed response (either CR or PR) in all responders. AEs were assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.

Statistical Analysis

Continuous data are presented herein as the means and standard deviations. Categorical data are presented as frequencies and percentages. PFS and OS were calculated via the Kaplan–Meier method. Univariate and multivariate analyses of the predictors of PFS and OS were performed via Cox proportional hazards regression. Factors with $P < 0.1$ in the univariate analysis were considered potential predictors and were further analyzed in the multivariate analysis. SPSS software (version 27.0) was used for the statistical analyses in this study. $P < 0.05$ was considered to indicate statistical significance.

Results

Baseline Patient Characteristics

In total, 92 eligible patients were enrolled in this study. The patients' baseline characteristics are summarized in Table 1. The median age was 59.0 years, and 85.9% (79/92) of the patients were male. Sixty-two (67.4%) patients had Child–Pugh grade A liver function, whereas 30 (32.6%) patients had Child–Pugh grade B liver function. The study cohort had high tumor burdens, with the average size of the maximum tumor being 9.2 cm. Fifty-seven patients (62.0%) had BCLC

Table 1 Baseline Characteristics of Patients

Characteristics	Number	Percentage
Age		
< 60	52	56.5%
≥ 60	40	43.5%
Gender		
Female	13	14.1%
Male	79	85.9%
BCLC stage		
B	35	38.0%
C	57	62.0%
ECOG PS		
0	71	77.2%
1	21	22.8%

(*Continued*)

Table 1 (Continued).

Characteristics	Number	Percentage
Child-Pugh class		
A	62	67.4%
B	30	32.6%
ALBI grade		
1	30	32.6%
2	62	67.4%
Etiology		
HBV	79	85.9%
Others	13	14.1%
AFP		
< 400 ng/mL	54	58.7%
≥ 400 ng/mL	38	41.3%
NLR		
< 2.68	42	45.7%
≥ 2.68	50	54.3%
Tumor size		
< 10 cm	58	63.0%
≥ 10 cm	34	37.0%
Tumor number		
< 3	44	47.8%
≥ 3	48	52.2%
Macroscopic vascular invasion		
Absent	45	48.9%
Present	47	51.1%
Extrahepatic metastasis		
Absent	65	70.7%
Present	27	29.3%

Abbreviations: BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group; AFP, alpha-fetoprotein.

stage C disease, and 21 patients (22.8%) had an ECOG score of 1. Forty-seven (51.1%) patients presented macroscopic vascular invasion, and 27 (29.3%) patients exhibited extrahepatic metastasis.

ORR, PFS, and OS

The tumor responses are shown in Table 2. The ORRs based on the RECIST 1.1 and mRECIST criteria were 41.3% and 54.3% (Supplementary Figure 1A), respectively. The DCR was 79.3%. Among responders, the median TTR for mRECIST was 2.4 months (range: 1.2–6.6 months). The size changes in the intrahepatic target lesion are shown in Figure 1. In addition, the ORR in the CP-A group was 64.5% with mRECIST, which was significantly higher than the ORR of 33.3% in the CP-B group (P = 0.005, Supplementary Figure 1B). There were no obvious differences in ORR between BCLC-B and BCLC-C patients (P = 0.518, Supplementary Figure 1C) or between patients with a neutrophil-lymphocyte ratio (NLR) < 2.68 and patients with an NLR ≥ 2.68 (P = 0.212, Supplementary Figure 1D).

The median follow-up was 14.1 months (range, 5.9–30.7 months). A total of 279 TACE procedures were performed, with a median of three sessions (range, 1–9 sessions). At the time of analysis, 58 patients showed disease progression, and 32 patients had died. Here, five patients underwent hepatectomy after achieving a tumor response of PR. The median OS was 15.9 months [95% confidence interval (CI), 14.5–17.2 months; Figure 2A]. The median PFS was 9.1 months (95% CI, 7.4–10.8 months; Figure 2B).

In addition, the median OS was 16.4 months (95% CI, 14.9–17.8 months) for patients with CP-A and 15.4 months (95% CI, 12.4–18.3 months) for patients with CP-B (P = 0.453) (Supplementary Figure 2A). The median PFS was 9.6

Table 2 Radiological Response According to mRECIST and RECIST1.1

Response	N = 92	
	mRECIST	RECIST v1.1
CR	0	0
PR	50 (54.3%)	38 (41.3%)
SD	23 (25.0%)	35 (38.0%)
PD	19 (20.7%)	19 (20.7%)
ORR (CR + PR)	50 (54.3%)	38 (41.3%)
DCR (CR + PR + SD)	73 (79.3%)	73 (79.3%)

Abbreviations: CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; DCR, disease control rate; ORR, objective response rate; mRECIST, modified Response Evaluation Criteria in Solid Tumors; RECIST, Response Evaluation Criteria in Solid Tumors.

months (95% CI, 7.5–11.7 months) for patients with CP-A and 7.9 months (95% CI, 4.2–11.5 months) for patients with CP-B (P = 0.346) (Supplementary Figure 2B).

Prognostic Factor Analysis

The prognostic factors for OS are shown in Table 3. Univariate analysis revealed that the ECOG score, NLR, and α-fetoprotein (AFP) level were predictors of OS, and multivariate analysis revealed that the ECOG score [hazard ratio (HR) = 3.12; 95% CI, 1.45–6.71; P = 0.004] and the NLR (HR = 2.53; 95% CI, 1.08–5.91; P = 0.033) were significant independent risk factors for OS.

The prognostic factors for PFS are shown in Table 4. Univariate analysis revealed that ALB and AFP levels, tumor size, and extrahepatic metastasis were related factors for PFS, and multivariate analysis revealed that tumor size (HR = 1.83; 95% CI, 1.06–3.15; P = 0.030) and extrahepatic metastasis (HR = 2.61; 95% CI, 1.49–4.58; P <0.001) were independent risk factors for PFS.

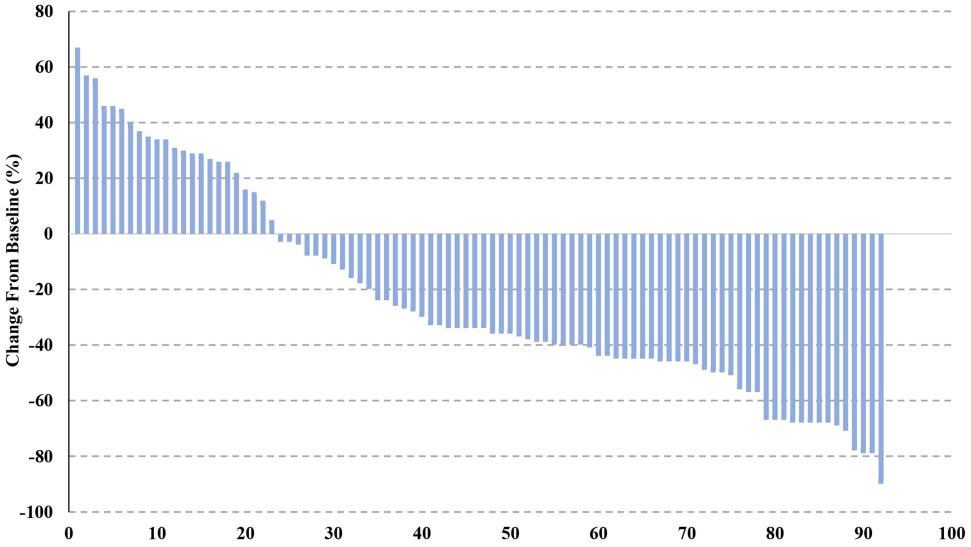

Figure 1 Waterfall plots of the best percentage changes from baseline in the size of the intrahepatic target lesions assessed with the modified Response Evaluation Criteria in Solid Tumors (mRECIST).

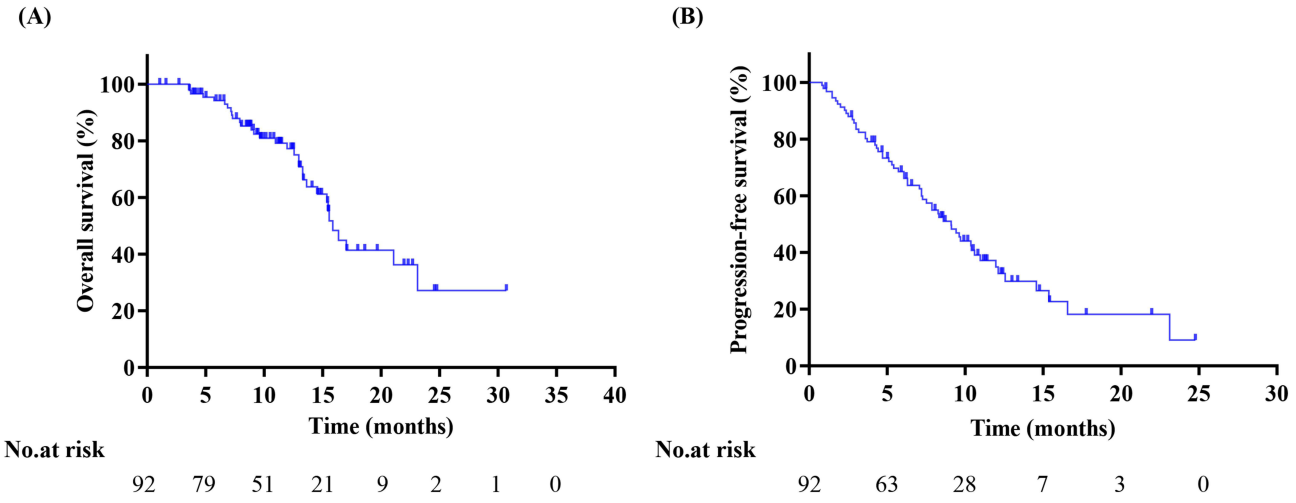

Figure 2 Kaplan–Meier curves for progression-free survival (**A**) and overall survival (**B**).

Adverse Events

Common AEs are summarized in Table 5. The frequency of common AEs of all grades was 85.9% (79/92). The most common treatment-related AEs (TRAEs) included elevated aspartate aminotransferase (AST) (67.4%), elevated alanine aminotransferase (ALT) (59.8%) and abdominal pain (48.9%). The most common grade 3–4 AEs were elevated AST (6.5%), hypertension (5.4%), and anemia (5.4%). No treatment-related deaths occurred in this study. Four patients (4.3%) suspended Atezo/Bev treatment for grade 4 AEs. Bevacizumab was discontinued in two patients who developed esophageal and gastric venous hemorrhage and one patient who developed albuminuria. One patient discontinued atezolizumab due to immune myocarditis.

Discussion

In theory, TACE + immunotherapy + anti-VEGF therapy induces enhanced antitumor activity through immune activation and inhibition of tumor neovascularization. Studies have also shown that TACE combined with tyrosine kinase inhibitors and immunotherapy can exert synergistic antitumor effects.[17–20] In this study, a median PFS of 9.1 months and a median

Table 3 Univariate and Multivariate Analyses for Predictive Factors of OS

Variables	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Sex (male)	1.63 (0.56,4.75)	0.370		
Age (≥60)	0.88 (0.43,1.78)	0.720		
Child-Pugh class (B)	1.01 (0.49,2.07)	0.448		
BCLC stage (C)	1.31 (0.60,2.57)	0.544		
ECOG (1)	2.84 (1.32,6.08)	0.007	3.12 (1.45,6.71)	0.004
Etiology (HBV)	1.25 (0.44,3.58)	0.675		
ALBI (2)	1.60 (0.69,3.73)	0.275		
NLR (≥2.68)	2.68 (1.16,6.20)	0.021	2.53 (1.08,5.91)	0.033
AFP (≥400 ng/mL)	1.83 (0.90,3.72)	0.096	1.82 (0.88,3.75)	0.107
Tumor number (≥3)	1.23 (0.60,2.50)	0.570		
Tumor size (≥10 cm)	1.12 (0.55,2.28)	0.750		
Macroscopic vascular invasion	1.53 (0.76,3.10)	0.232		
Extrahepatic metastasis	1.43 (0.70,2.94)	0.328		

Abbreviations: OS, overall survival; BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group; ALBI, albumin bilirubin score; NLR, neutrophil to lymphocyte ratio; AFP, α-fetoprotein.

Table 4 Univariate and Multivariate Analyses for Predictive Factors of PFS

Variables	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Sex (male)	1.12 (0.50,2.51)	0.780		
Age (≥60)	0.76 (0.45,1.30)	0.320		
Child-Pugh class (B)	1.32 (0.77,2.26)	0.309		
BCLC stage (C)	1.15 (0.67,1.98)	0.614		
ECOG (1)	1.58 (0.87,2.85)	0.130		
Etiology (HBV)	0.63 (0.32,1.26)	0.196		
ALBI (2)	1.72 (0.93,3.14)	0.080	1.40 (0.74,2.57)	0.313
NLR (≥2.68)	1.25 (0.73,2.15)	0.419		
AFP (≥400 ng/mL)	1.69 (1.00,2.85)	0.049	1.14 (0.66,1.97)	0.643
Tumor number (≥3)	1.13 (0.67,1.91)	0.644		
Tumor size (≥10 cm)	1.98 (1.16,3.36)	0.012	1.83 (1.06,3.15)	0.030
Macroscopic vascular invasion	1.20 (0.71,2.02)	0.496		
Extrahepatic metastasis	2.83 (1.64,4.88)	<0.001	2.61 (1.49,4.58)	<0.001

Abbreviations: PFS, progression free survival; BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group; ALBI, albumin bilirubin score; NLR, neutrophil to lymphocyte ratio; AFP, α-fetoprotein.

Table 5 Safety Profiles and Adverse Events

Adverse Event	Any Grade	Grades 3–4
Elevated AST	62 (67.4%)	6 (6.5%)
Elevated ALT	55 (59.8%)	4 (4.3%)
Abdominal pain	45 (48.9%)	1 (1.1%)
Fever	41 (44.6%)	0
Vomiting	31 (33.7%)	2 (2.2%)
Hyperbilirubinemia	28 (30.4%)	0
Weight decrease	25 (27.2%)	0
Thrombocytopenia	23 (25.0%)	0
Anemia	22 (23.9%)	5 (5.4%)
Fatigue	22 (23.9%)	0
Hypertension	19 (20.7%)	5 (5.4%)
Albuminuria	15 (16.3%)	1 (1.1%)
Diarrhea	13 (14.1%)	0
Hypothyroidism	11 (12.0%)	0
Gastrointestinal bleeding	11 (12.0%)	2 (2.2%)
Abdominal distention	7 (7.6%)	0
Epistaxis	3 (3.2%)	0
Immunological myocarditis	1 (1.1%)	1 (1.1%)

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase.

OS of 15.9 months were achieved with TACE followed by Atezo/Bev, with relatively safe profiles. The ORRs based on the modified RECIST and RECIST 1.1 criteria were 54.3% and 41.3%, respectively. Multivariate analyses revealed that the ECOG score and NLR were independent risk factors for OS. In addition, compared with our latest published study,[3] which was also sub research of the protocol TACE combined with immune checkpoint inhibitors (ICI) and antiangiogenic agents for the treatment of HCC, the current study contained different study population including BCLC stages B and stage C, systemic treatment by using Atezo/Bev, and research design (Supplementary Table 1). The published article was a control study comparing the effectiveness difference of TACE-ICI-antiangiogenic agents and ICI-antiangiogenic agents in the HCC with PVTT patients, while this study was a single arm study, aimed at exploring

the effectiveness and safety of TACE combined with single first-line systemic therapy regimen (Atezo/Bev). Therefore, we believe that the current research could provide novelty and clinical practice information.

In the IMbrave 150 trial, the ORR, median PFS, and median OS were 27.3% according to RECIST 1.1 and 33.2% according to mRECIST, 6.9 months, and 19.2 months with atezo/bev, respectively, for these uHCCs.[5,21] In addition, a previous study revealed that the median OS of Atezo/Bev treatment for advanced HCC patients was 16.4 months in a real-world scenario,[22] which was similar to our results. In contrast, the current study demonstrated that TACE-Atezo /Bev yielded a superior tumor response rate and median PFS, rather than median OS, after Atezo/Bev treatment. These results may be explained as follows: (1) 32.6% of cases had a B classification on the Child–Pugh liver function scale, which was beyond that in the eligibility criteria for liver function in the IMbrave 150 trial. A previous study demonstrated that Atezo/Bev may be safely administered even beyond the inclusion criteria of the IMbrave150 trial.[23] (2) the proportion of patients with macrovascular invasion was 51.1%, which was numerically higher than that in the IMbrave 150 trial (38%). Therefore, in fact, these findings are more representative of the clinical characteristics of the population in clinical practice. There are also rationales for combining TACE with Atezo/Bev. TACE can activate tumor-associated antigens and induce the expression of PD-L1.[24] Subsequently, the TACE-induced hypoxic microenvironment leads to the release of VEGF, thereby stimulating neoangiogenesis and tumor progression.[25] Here, atezolizumab influences the PD-L1 pathway. Bevacizumab, a VEGF inhibitor, can delay revascularization and reverse VEGF-mediated immunosuppression,[18] thereby further enhancing the synergistic antitumor immune response. This study demonstrated that even in the Child–Pugh liver function class B group, the ORR reached 33.3%, with median PFS and OS rates of 7.9 months and 14.6 months, respectively. This demonstrated the scalability of this treatment model in the target population. In addition, 32 patients died by the time of analysis. Owing to the relatively short follow-up time, the immature event rate may also have compromised the final median OS; therefore, we will also update these data.

In addition to the rapid decrease in tumor burden initially caused by TACE, Atezo/Bev mainly induced tumor contraction, whereas tyrosine kinase inhibitors mainly induced tumor necrosis through reduced blood flow. Conversion to curative therapy is a potential option to improve the prognosis of patients who achieve a durable response with marked reductions in tumor size but are not cured.[26] Atezo/Bev may exert anti-VEGF effects, thereby enhancing the efficacy of TACE and transforming it into curative treatment.[27] In the present study, five patients underwent resection after achieving a PR. The highlighted ORRs were 54.3% and 41.3% according to the modified RECIST and RECIST 1.1 criteria, respectively. The high response rates and relative consistency of the ratios between the two evaluation methods suggest that the TACE-Atezo/Bev combination may provide an optimal choice for clinical conversion.[28]

The results of the multivariate analysis in this study revealed that the NLR and ECOG score were independent risk factors for OS. This study highlights the factors that could identify patient subgroups capable of obtaining a tumor response. The NLR is a marker of the systemic inflammatory response and reflects the balance between neutrophils and lymphocytes.[29] The predictive value of the NLR for ICI therapy in HCC patients was reported by Hugh et al.[30] Similarly, we found that a high baseline NLR (≥ 2.68) predicted shorter OS in our study. In previous real-world research on Atezo/Bev treatment for HCC, it also similarly provided significant benefits for patients with a lower NLR.[13] Given these findings, during the treatment process, the impact on the tumor microenvironment may be reflected in these early inflammatory indicators, and this effect warrants further exploration. In addition, the ECOG score was also an independent prognostic factor for OS. Previous studies have demonstrated that HCC patients with a good performance status may benefit maximally from TACE treatment.[31] In the Emerald-1 trial, the forest plot revealed that with respect to the PFS benefit, the ECOG score (1) pointed in the direction of TACE alone, instead of in the direction of combination treatment,[11] which reminded us that prioritizing a reasonable consideration of the patient's symptoms and tolerance could enable this specific subgroup to benefit more from the triple treatment method. The BCLC strategy in the 2022 update highlighted that the performance score assessment should incorporate tumor-related symptoms.[32] In this study, ECOG score influenced the prognosis but did not abolish the treatment benefit if the score did not exceed the established criteria for the final optimal outcome.

In this study, the AEs associated with the combination of TACE and Atezo/Bev were consistent with those associated with TACE or Atezo/Bev,[5,33] and no AE-related deaths occurred. The adverse reactions to a medication result from both the mechanism of action of the drug and its metabolic pathways. The most common AEs were AST and ALT elevation

and abdominal pain. These signs and symptoms were controlled and eliminated after conservative treatment. Even in HCC patients with Child–Pugh B7 liver dysfunction, TACE and atezo/bev were also well tolerated and effective.[34] Nonetheless, it is still necessary to carefully select patients who can tolerate the AEs of triple therapy and eventually achieve encouraging effects.[35]

This study has several limitations. First, it was retrospective, and the sample size was relatively small. Second, the viral replication copies were not tested in each patient, although the Atezo/Bev regimen had a lower rate of HBV reactivation. Third, bleeding is an inevitable inherent risk of bevacizumab. The dose of bevacizumab was not standardized on the basis of different endoscopy results. Therefore, further prospective clinical research is necessary to validate the benefits and safety of this treatment strategy.

Conclusion

In summary, the combination of Atezo/Bev with TACE has demonstrated a significant therapeutic effect and manageable AEs in real-world HCC patient cohorts.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Statement

The 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 1983. This study was sub project of transarterial chemoembolization combined with immune checkpoint inhibitors and antiangiogenic agents for the treatment of hepatocellular carcinoma. We hereby applied for the use of protocol and got the approval by ethics committee with ethics number (2022-SR-332) for the current study. To preserve patient privacy and data confidentiality, patient data have been deidentified before analysis. All analyses in this retrospective study were performed based on the data from anonymized patients. Due to the retrospective nature of this study, the Ethics Committee of The First Affiliated Hospital with Nanjing Medical University approved the study and determined that written informed consent was not required.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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