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晚期肝細胞癌患者 atezolizumab 合併 bevacizumab 與 durvalumab 合併 tremelimumab 的比較療效：真實世界臨床應用的觀察性研究

Comparative effectiveness of atezolizumab plus bevacizumab versus durvalumab plus tremelimumab in patients with advanced hepatocellular carcinoma: an observational study based on real-world practice

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Comparative effectiveness of atezolizumab plus bevacizumab versus durvalumab plus tremelimumab in patients with advanced hepatocellular carcinoma: an observational study based on real-world practice

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中文摘要

背景：Atezolizumab 合併 bevacizumab（Atezo/Bev）與 durvalumab 合併 tremelimumab（Durva/Treme）已被確立為晚期肝細胞癌（hepatocellular carcinoma, HCC）的第一線治療方案。然而目前仍缺乏直接比較這兩種治療組合療效與安全性的研究資料，尤其於真實世界臨床實務中的表現更為有限。

目的：本研究利用真實世界電子健康紀錄資料，比較 Atezo/Bev 與 Durva/Treme 做為晚期肝細胞癌第一線治療的療效與安全性。

方法：本研究為回溯性世代研究，資料來源為 TriNetX Global Collaborative Network 此一跨國電子健康紀錄平台。納入 2022 年 10 月 1 日至 2025 年 10 月 31 日期間，接受 Atezo/Bev 或 Durva/Treme 做為第一線全身性治療的成人（≥18 歲）肝細胞癌患者；排除先前曾接受其他全身性治療者。主要療效指標為整體存活期（overall survival），次要指標為安全性事件，包括腸胃道出血、非腸胃道出血、新發高血壓以及需接受治療之免疫相關不良反應（treatment-requiring immune-related adverse events, irAEs）；其中需接受治療之 irAEs 以處方系統性類固醇做為代理指標。採用 1:1 最近鄰傾向分數配對（propensity score matching），以調整包括年齡、性別、種族、門靜脈栓塞、食道靜脈曲張、病毒性及酒精性肝病、肝硬化、先前肝切除、血清生化指標（白蛋白、總膽紅素、凝血酶原時間及 INR、血小板、ALT、AST、肌酐酸、甲型胎兒蛋白）等共變數之基線差異。配對後之族群以 Kaplan–Meier 法估算累積事件發生率，並以 Cox 比例風險模式估算校正後風險比（aHR）及 95% 信賴區間（CI）。

結果：於符合條件之 3,362 位患者中（Atezo/Bev 2,149 位、Durva/Treme 830 位），經 1:1 傾向分數配對後納入 765 對患者進行最終分析，兩組基線特徵皆達充分平衡

（所有共變數標準化平均差均＜0.1）。Atezo/Bev 組中位追蹤時間為 14.8 個月，Durva/Treme 組為 17.5 個月。兩組整體存活期無顯著差異，中位存活期分別為 14.6 與 17.3 個月（aHR 0.96；95% CI 0.83–1.12；P = 0.62）；此結果於依年齡、性別、種族、病因及是否有肝硬化之次族群分析中亦一致。安全性方面，兩組腸胃道出血（17.1% vs 15.2%；aHR 0.88；95% CI 0.68–1.13）及非腸胃道出血（3.8% vs 2.6%；aHR 1.06；95% CI 0.60–1.89）發生率相當；新發高血壓於 Atezo/Bev 組較常見（34.7% vs 25.2%），但未達統計顯著（aHR 1.24；95% CI 0.87–1.76）。需接受治療之免疫相關不良反應於 Atezo/Bev 組明顯較低（20.2% vs 24.6%；aHR 0.61；95% CI 0.48–0.77），且此差異於治療初期即出現並持續存在。

結論：在真實世界臨床應用中，Atezo/Bev 與 Durva/Treme 做為晚期肝細胞癌的第一線治療，整體存活效益及主要安全性事件相當；但 Atezo/Bev 組需接受治療之免疫相關不良反應發生率顯著較低，可能有助於臨床醫師依個別患者特性選擇適當之免疫治療方案。

關鍵詞：肝細胞癌；免疫治療；不良反應；真實世界研究；傾向分數配對

ABSTRACT

Background and Aims: Atezolizumab plus bevacizumab (Atezo/Bev) and durvalumab plus tremelimumab (Durva/Treme) are established first-line therapies for advanced hepatocellular carcinoma (HCC). However, direct comparisons between these regimens remain limited. This study aimed to evaluate their comparative effectiveness and safety in real-world practice.

Methods: We conducted a retrospective cohort study within the TriNetX Global Collaborative Network, including adults with HCC who initiated Atezo/Bev or Durva/Treme as first-line systemic therapy between October 1, 2022, and October 31, 2025. Outcomes were defined using standardized diagnostic, procedural, and medication codes. Propensity score matching (1:1) was applied to minimize baseline differences between groups.

Results: Among 3,362 eligible patients, 765 matched pairs were included in the final analysis. Over a median follow-up of 14.8 months for Atezo/Bev and 17.5 months for Durva/Treme, overall survival was comparable between the regimens (median 14.6 vs. 17.3 months; aHR 0.96; 95% CI 0.83–1.12). Safety outcomes were broadly similar, including gastrointestinal bleeding (aHR 0.88; 95% CI 0.68–1.13), and non-gastrointestinal bleeding (aHR 1.06; 95% CI 0.60–1.89). Treatment-requiring immune-related adverse events (irAEs) occurred significantly less frequently with Atezo/Bev (aHR 0.61; 95% CI 0.48–0.77), with curve separation evident early after treatment initiation. Incident hypertension was numerically more frequent with Atezo/Bev but was not statistically significant (aHR 1.24; 95% CI 0.87–1.76).

Conclusions: Atezo/Bev and Durva/Treme demonstrated similar overall survival in patients with HCC, with largely comparable safety profiles. The lower rate of treatment-requiring immune-related adverse events observed with Atezo/Bev may assist clinicians in tailoring regimen selection for individuals with advanced HCC.

Keywords: Hepatocellular carcinoma; Immunotherapy; Adverse event; Real-world study; Propensity score matching

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy and one of the leading causes of cancer-related mortality worldwide. It accounts for more than 80% of primary liver cancers and is the third leading cause of cancer death globally. Despite advances in surveillance and therapeutic strategies, HCC is projected to cause over one million deaths by 2030.

Immune checkpoint inhibitors (ICIs) targeting PD-1, PD-L1, and CTLA-4 represent a major therapeutic breakthrough in oncology. In advanced HCC, two ICI-based regimens have demonstrated superior overall survival compared with the historic standard-of-care sorafenib, a multi-kinase inhibitor, in pivotal phase III randomized trials.

The IMbrave150 trial evaluated atezolizumab (anti–PD-L1) plus bevacizumab (anti-VEGF) versus sorafenib in patients with unresectable HCC. Atezolizumab plus bevacizumab (Atezo/Bev) significantly improved median overall survival (19.2 vs 13.4 months) and prolonged median progression-free survival (6.9 vs 4.3 months). The HIMALAYA trial assessed a single priming dose of tremelimumab (anti–CTLA-4) combined with durvalumab (anti–PD-L1) compared with sorafenib monotherapy. The durvalumab plus tremelimumab (Durva/Treme) regimen achieved a median overall survival of 16.4 months versus 13.8 months with sorafenib. Collectively, these findings have led to major guideline updates and a paradigm shift toward immunotherapy-based combinations in the first-line treatment of advanced HCC.

However, despite the establishment of Atezo/Bev and Durva/Treme as standard first-line options, a critical evidence gap remains. There are no prospective or randomized head-to-head trials directly comparing the efficacy and safety of these two regimens. Moreover, their relative performance in real-world clinical practice—where patient populations are more heterogeneous and management more complex than in clinical trials—remains uncertain.

To address this unmet need, we conducted a large-scale, retrospective, real-world comparative analysis of the effectiveness and safety of Atezo/Bev versus Durva/Treme using data from the TriNetX Global Collaborative Network.

MATERIALS AND METHODS

Data source

This is a retrospective cohort study with data drawn from the TriNetX Global Collaborative Network, a federated electronic health records (EHR) platform aggregating standardized, de-identified data including demographics, diagnoses, procedures, medications, and laboratory results from over 215 healthcare organizations worldwide across the Asia-Pacific, Europe, Middle East, and Africa, Latin America, and the United States.

The TriNetX platform aggregates de-identified clinical data coded with established standards—diagnoses (ICD-10-CM), procedures (ICD-10-PCS/CPT), medications (ATC/RxNorm), and laboratory results (LOINC). This uniform coding enables consistent cohort construction and outcome ascertainment across participating sites. All analyses were executed within the secure, cloud-based TriNetX analytics environment, which supports epidemiologic workflows including precise cohort construction, propensity score matching, and time-to-event modeling. The study was approved by the Institutional Review Board of Chia-Yi Christian Hospital (IRB2025075). Because only aggregate results from de-identified data were produced, the requirement for informed consent was waived. Procedures conformed to the principles of the Declaration of Helsinki.

Study population

Patients ≥ 18 years with HCC receiving Atezo/Bev or Durva/Treme as the first-line systemic treatment between October 1, 2022 and October 31, 2025 were included in this analysis. Patients with prior exposure to other systemic treatment for hepatocellular carcinoma were excluded. The index date was the first prescription date of the assigned regimen. To preserve the new-user design and mitigate bias from prior exposure, we excluded patients who had received the alternative regimen before index. Patients were classified by index regimen and followed under an intention-to-treat framework from index until censoring.

Outcomes and definitions

The primary outcome was overall survival. Secondary outcomes included adverse events such as gastrointestinal (GI) bleeding, non-GI bleeding, incident hypertension, and immune-related adverse events (irAEs). Because irAEs, a key consideration in ICI-based therapy, cannot be reliably distinguished using diagnostic codes alone within the TriNetX network, we defined treatment-requiring irAEs using prescriptions for systemic corticosteroids as a proxy indicator. All outcomes and variables were defined according to TriNetX operational standards using diagnostic, procedure, and medication codes. For adverse event analyses, patients with relevant diagnoses prior to initiation of Atezo/Bev or Durva/Treme were excluded to ensure that only incident events were captured.

Statistical analysis

To minimize potential confounding and balance baseline characteristics between treatment groups, we estimated a propensity score for patients receiving Atezo/Bev vs Durva/Treme using multivariable logistic regression for covariates including age, sex, race, portal vein thrombosis, esophageal varices, viral hepatitis, alcoholic liver disease, liver cirrhosis, prior hepatectomy, and serum biomarkers (albumin, total bilirubin, prothrombin time and International Normalized Ratio, platelets, alanine aminotransferase, aspartate aminotransferase, creatinine, and alpha-fetoprotein), then applied 1:1 nearest-neighbor matching with a caliper of 0.1 standard deviations on the logit of the propensity score. Covariate balance was assessed using standardized mean differences (SMD), with SMD < 0.1 indicating adequate balance.

In the matched cohort, we plotted Kaplan–Meier curves with log-rank tests and fitted Cox proportional hazards models to estimate adjusted hazard ratios (aHRs) with 95% confidence intervals (CIs). E-values for point estimates and CIs quantified the minimum strength of unmeasured confounding required to explain away observed associations. Two-sided $P < 0.05$ was considered statistically significant. All analyses were performed within the integrated TriNetX analytic environment.

RESULTS

Study population and baseline characteristics

We identified 137,679 patients with HCC in the TriNetX network, of whom 2,411 initiated Atezo/Bev and 951 initiated the Durva/Treme regimen between October 1, 2022 and October 31, 2025. 2,149 Atezo/Bev initiators and 830 Durva/Treme initiators remained eligible for matching; 1:1 propensity score matching yielded 765 vs 765 well-balanced patients (Figure 1).

Before matching, the Durva/Treme cohort carried a subtly higher baseline risk profile including age (68.0 ± 9.8 vs 67.1 ± 9.4 years; P = 0.032), higher cirrhosis (69.3% vs 60.1%; P < 0.001) and more frequently had portal-hypertensive features—portal vein thrombosis (21.3% vs 16.2%; P = 0.001), esophageal varices (27.8% vs 23.4%; P = 0.015), lower serum albumin (3.4 ± 0.6 vs 3.6 ± 0.6 g/dL; P < 0.001), longer prothrombin time (14.3 ± 3.2 vs 13.8 ± 2.8 s; P = 0.001), and lower platelets (189 ± 115 vs 203 ± 117 $\times 10^3/\mu L$; P = 0.004). Following 1:1 matching, covariate balance was achieved across all baseline characteristics (all SMDs < 0.1; Table 1).

Table 1. Baseline Patient Characteristics before and after Propensity Score Matching

	Before matching				**After matching**		
	Atezo/Bev (N=2,149)	**Durva/Treme (N=830)**	**P**		**Atezo/Bev (N=765)**	**Durva/Treme (N=765)**	**P**
Age	67.1 (9.4)	68.0 (9.8)	0.032		68.0 (8.9)	67.9 (9.8)	0.94
Male	1,656 (78.8)	629 (80.3)	0.35		631 (82.5)	616 (80.5)	0.32
Race †							
White	1,369 (65.1)	497 (63.5)	0.42		483 (63.1)	487 (63.7)	0.83
Black	354 (16.8)	132 (16.9)	0.99		129 (16.9)	128 (16.7)	0.95

Asian	168 (8.0)	73 (9.3)	0.25		65 (8.5)	71 (9.3)	0.59
Other	102 (4.9)	43 (5.5)	0.48		44 (5.8)	42 (5.5)	0.82
Unknown	82 (3.9)	25 (3.2)	0.37		33 (4.3)	24 (3.1)	0.22
Etiology †							
HBV	142 (6.8)	51 (6.7)	0.94		41 (5.2)	50 (6.5)	0.28
HCV	429 (20.4)	153 (19.5)	0.61		142 (18.6)	152 (19.9)	0.52
Alcohol	324 (15.4)	149 (19.0)	0.019		136 (17.8)	144 (18.8)	0.60
Cirrhosis of liver	1,264 (60.1)	543 (69.3)	<0.001		527 (68.9)	526 (68.8)	1.00
Esophageal varices	493 (23.4)	218 (27.8)	0.015		203 (26.5)	208 (27.2)	0.77
Portal vein thrombosis	341 (16.2)	167 (21.3)	0.001		158 (20.7)	159 (20.8)	0.95
Prior hepatectomy	580 (27.6)	208 (26.6)	0.59		201 (26.3)	206 (26.9)	0.77
Laboratory †							
Creatinine, mg/dL	1.6 (9.9)	1.1 (0.8)	0.11		1.6 (8.6)	1.1 (0.8)	0.19
Platelets, $10^3/\mu L$	203 (117)	189 (115)	0.004		185 (117)	190 (114)	0.43
ALT, U/L	53.2 (62.1)	50.4 (51.9)	0.28		52.9 (68.3)	50.6 (52.3)	0.47
AST, U/L	81.1 (88.0)	86.0 (92.2)	0.21		83.2 (86.4)	86.1 (92.7)	0.55
Total bilirubin, mg/dL	1.3 (1.8)	1.5 (2.5)	0.007		1.4 (2.1)	1.5 (2.3)	0.55
Albumin, g/dL	3.6 (0.6)	3.4 (0.6)	<0.001		3.5 (0.6)	3.4 (0.6)	0.27
Prothrombin time, sec	13.8 (2.9)	14.3 (3.2)	0.001		14.4 (3.5)	14.2 (3.1)	0.37
INR	1.2 (0.3)	1.2 (0.3)	0.012		1.3 (0.3)	1.2 (0.3)	0.16
AFP, ng/mL							

AFP < 400	543 (25.8)	224 (28.6)	0.13		218 (28.5)	218 (28.5)	-
AFP ≥ 400	336 (16.0)	135 (17.2)	0.41		114 (14.9)	127 (16.6)	0.362

Categorical variables expressed as n (%); continuous variables as mean (SD). † Missing data in some patients. AFP, alpha-fetoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Atezo/Bev, atezolizumab + bevacizumab; Durva/Treme, durvalumab + tremelimumab; HBV, hepatitis B virus; HCV, hepatitis C virus; INR, International Normalized Ratio.

Comparison of overall survival

Over a median follow-up of 14.8 months in the Atezo/Bev group and 17.5 months in the Durva/Treme group, median overall survival was similar between the two regimens (14.6 vs 17.3 months; aHR 0.96; 95% CI 0.83–1.12; P = 0.62) (Figure 2). Subgroup analyses showed consistent findings, with comparable overall survival across categories defined by age, sex, race, underlying etiology, and the presence or absence of cirrhosis (Figure 3).

Comparison of adverse events

During the study period, safety profiles were broadly comparable regarding GI bleeding (17.1% vs 15.2%; aHR 0.88; 95% CI 0.68–1.13), and non-GI bleeding (3.8% vs 2.6%; aHR 1.06; 95% CI 0.60–1.89) (Table 2; Figure 4C and 4D). Treatment-requiring irAEs were significantly lower with Atezo/Bev (20.2% vs 24.6%; aHR 0.61; 95% CI 0.48–0.77), with early and sustained separation of Kaplan–Meier curves (Table 2; Figure 4A). Incident hypertension occurred more often in the Atezo/Bev group (34.7% vs 25.2%), although the difference was not statistically significant (aHR 1.24; 95% CI 0.87–1.76) (Table 2; Figure 4B). This pattern of significantly lower treatment-requiring irAEs in Atezo/Bev patients was consistent across most subgroups.

Table 2. Safety Outcomes after Propensity Score Matching

	Atezo/Bev	**Durva/Treme**	**aHR (95% CI)**	**E-value (CI)**
GI bleeding	17.1%	15.2%	0.88 (0.68–1.13)	1.53 (1.00)
Non-GI bleeding	3.8%	2.6%	1.06 (0.60–1.89)	1.31 (1.00)

Hypertension	34.7%	25.2%	1.24 (0.87–1.76)	1.79 (1.00)
Treatment-requiring irAEs	20.2%	24.6%	0.61 (0.48–0.77)	2.66 (1.92)

Safety outcomes were analyzed after excluding patients with the corresponding diagnosis prior to Atezo/Bev or Durva/Treme use. aHR, adjusted hazard ratio; CI, confidence interval; GI, gastrointestinal; irAEs, immune-related adverse events.

DISCUSSION

In this retrospective analysis using data from the TriNetX Global Collaborative Network, 3,362 patients with HCC receiving Atezo/Bev or Durva/Treme as first-line systemic therapy were identified. Following rigorous propensity score matching, 765 well-balanced patients in each group were included for evaluation. We observed no significant difference in overall survival between the two regimens (14.6 months for Atezo/Bev vs 17.3 months for Durva/Treme), indicating comparable real-world effectiveness. Safety outcomes were also broadly similar with respect to GI bleeding, non-GI bleeding, and hypertension. Notably, Atezo/Bev was associated with significantly lower rates of treatment-requiring irAEs, with divergence emerging early after treatment initiation. These patterns were consistent across clinically relevant subgroups.

Our findings are consistent with recent comparative studies. A network meta-analysis of phase III trials demonstrated that Atezo/Bev was not statistically superior to Durva/Treme in reducing the risk of death (HR 0.74; 95% CI 0.52–1.06). A multicenter retrospective U.S. cohort of 452 patients (Atezo/Bev: 336; Durva/Treme: 116) similarly reported no differences in overall survival (14.0 months for Atezo/Bev vs 14.6 months for Durva/Treme), time to treatment discontinuation, objective response rate, or disease control, with clinical outcomes driven primarily by underlying liver function and Child–Pugh class. Another study using TriNetX data—although not evaluating safety outcomes—also demonstrated comparable overall survival between the two regimens (15.4 months for Atezo/Bev vs 15.5 months for Durva/Treme) in routine clinical practice, with 309 well-matched patients in each group. Together, these studies corroborate our findings and further indicate that both regimens exhibit similar real-world effectiveness across diverse clinical settings.

Importantly, our study is among the first to directly compare adverse events between the two regimens. We observed significantly lower rates of treatment-requiring irAEs in the Atezo/Bev group compared with the Durva/Treme group, with divergence emerging early after treatment initiation. This finding is biologically plausible: Atezo/Bev combines a single immune checkpoint inhibitor with an anti-VEGF agent, whereas the Durva/Treme regimen incorporates dual immune checkpoint blockade at the first dose

before transitioning to durvalumab monotherapy. In addition, because treatment-requiring irAEs were defined by the need for systemic corticosteroids, another potential explanation is physician prescribing behavior—clinicians may be more inclined to initiate steroids for patients receiving Durva/Treme due to heightened concern for toxicities associated with dual ICI therapy. An additional area of interest is whether the development of irAEs correlates with improved clinical outcomes. One recent meta-analysis has suggested that irAEs—particularly dermatologic, endocrine, and low-grade events—may be associated with better survival. However, further data are needed to clarify this relationship in the context of advanced HCC and contemporary first-line immunotherapy combinations.

Compared with IMbrave150 and HIMALAYA, the overall rates of GI bleeding, non-GI bleeding, and incident hypertension in our study were higher. This likely reflects the higher clinical heterogeneity of real-world populations. Patients with Child–Pugh B cirrhosis, substantial comorbidities, or impaired performance status—groups excluded from the pivotal trials—may occasionally receive these regimens in real-world practice. In addition, concerns about bleeding risk with bevacizumab, the anti-VEGF component of the Atezo/Bev regimen, may also contribute to these differences. Patients at high risk for gastrointestinal bleeding—such as those with large varices, recent variceal hemorrhage, or active peptic ulcers—were excluded from IMbrave150, and all participants were required to undergo upper endoscopy before enrollment. In routine practice, clinicians may preferentially select Durva/Treme for patients perceived to have higher bleeding risk, and international guidance similarly recommends Durva/Treme over Atezo/Bev for patients with a high risk of gastrointestinal bleeding. Such treatment selection patterns could influence the observed frequency of bleeding events in our real-world cohort. Regarding hypertension, which is more closely associated with VEGF inhibition, the substantially lower rate of hypertension reported in the HIMALAYA trial (5.9%) compared with IMbrave150 (29.8%) underscores regimen-specific differences, although direct cross-trial comparisons should be interpreted cautiously. This pattern is also reflected in our findings: incident hypertension was numerically higher in the Atezo/Bev group than in the Durva/Treme group, although the difference did not reach statistical significance.

The strengths of this study include its large sample size and the use of a globally representative, multi-institutional electronic health record network, which enhances the external validity of our findings. The diversity of the study population—spanning multiple regions, healthcare systems, and clinical practice environments—allows the results to reflect real-world treatment patterns that are not captured in single-center or country-restricted cohorts. In addition, the application of a rigorously constructed propensity score model incorporating a wide range of demographic, clinical, and laboratory variables helped minimize confounding and achieve well-balanced comparison groups. Importantly, our study also provides the first comprehensive evaluation of adverse events between Atezo/Bev and Durva/Treme in routine clinical practice, filling a notable gap in the current literature and offering clinically relevant information that may guide regimen selection for patients with advanced HCC.

Several limitations should be acknowledged. Detailed radiologic information, clinical response assessments, and standardized toxicity grading were not available within the EHR-derived dataset. Key prognostic indicators, such as Child–Pugh scores, were also not consistently captured. Variability in clinical practice patterns across institutions may introduce heterogeneity, and coding-based identification of adverse events may misclassify or undercapture certain events. Although we implemented a carefully constructed and clinically informed propensity score model to minimize selection bias and balance measured covariates between treatment groups, the possibility of unmeasured confounding cannot be fully excluded, as is inherent to all observational studies. In addition, several clinically relevant subgroups were underrepresented in our cohort, limiting our ability to explore potential heterogeneity in treatment effects across patient characteristics.

In conclusion, this large real-world analysis demonstrates comparable overall survival between Atezo/Bev and Durva/Treme as first-line therapy for hepatocellular carcinoma. In addition, Atezo/Bev is associated with significantly fewer treatment-requiring immune-related adverse events, with early and sustained separation of risk. Rates of GI bleeding, non-GI bleeding, and hypertension were similar between regimens. These findings suggest that both regimens remain valid first-line options, and safety

considerations—particularly the risk of immune-mediated toxicity—may help guide individualized treatment decisions.

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FIGURE LEGENDS

Figure 1. The Flow Diagram of Patient Selection and Identification. HCC, hepatocellular carcinoma.

Figure 2. Kaplan–Meier Analysis of Overall Survival. Comparison of overall survival between patients receiving Atezo/Bev and Durva/Treme after 1:1 propensity score matching.

Figure 3. Overall Survival Across Patient Subgroups. Forest plot of hazard ratios for overall survival comparing Atezo/Bev versus Durva/Treme across demographic and clinical subgroups.

Figure 4. Adverse Events-Free Survival. (A) Treatment-related irAEs-free survival. (B) Hypertension-free survival. (C) GI bleeding-free survival. (D) Non-GI bleeding-free survival. GI, gastrointestinal; irAEs, immune-related adverse events; mOS, median overall survival.

Figure 1.

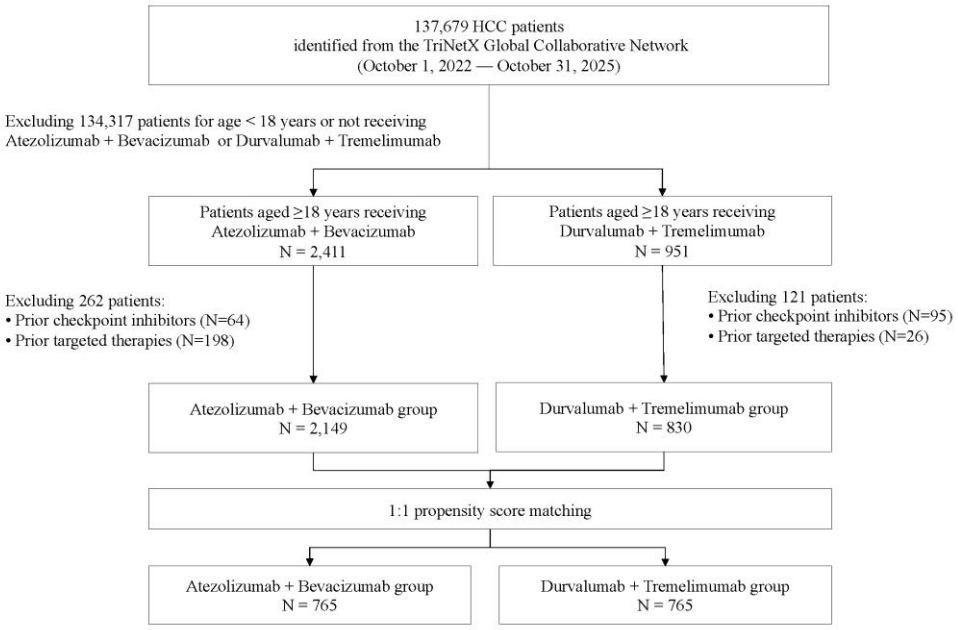


Figure 2.

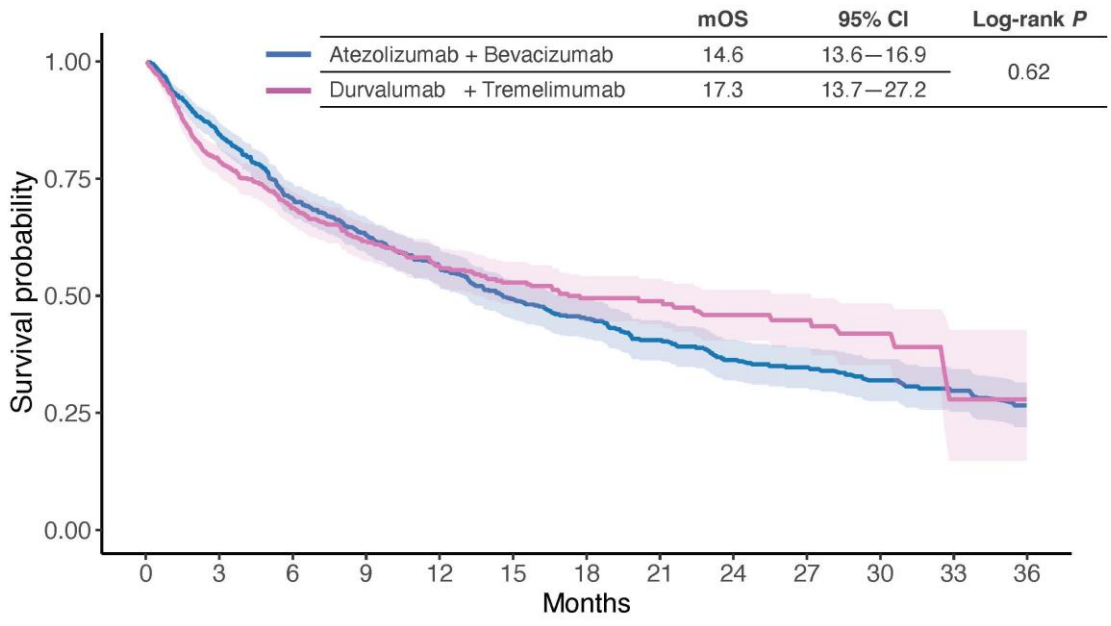


Figure 3.

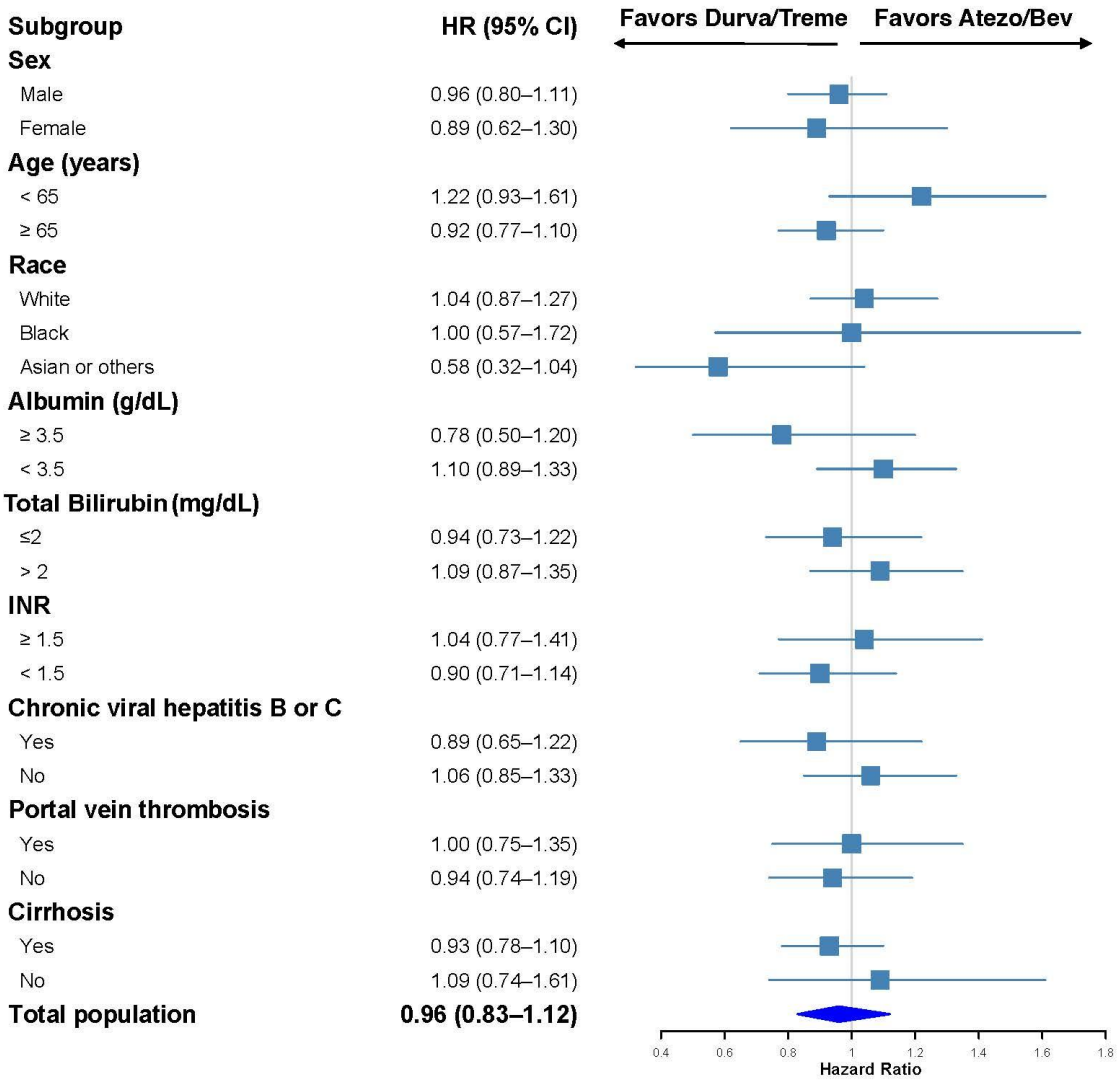
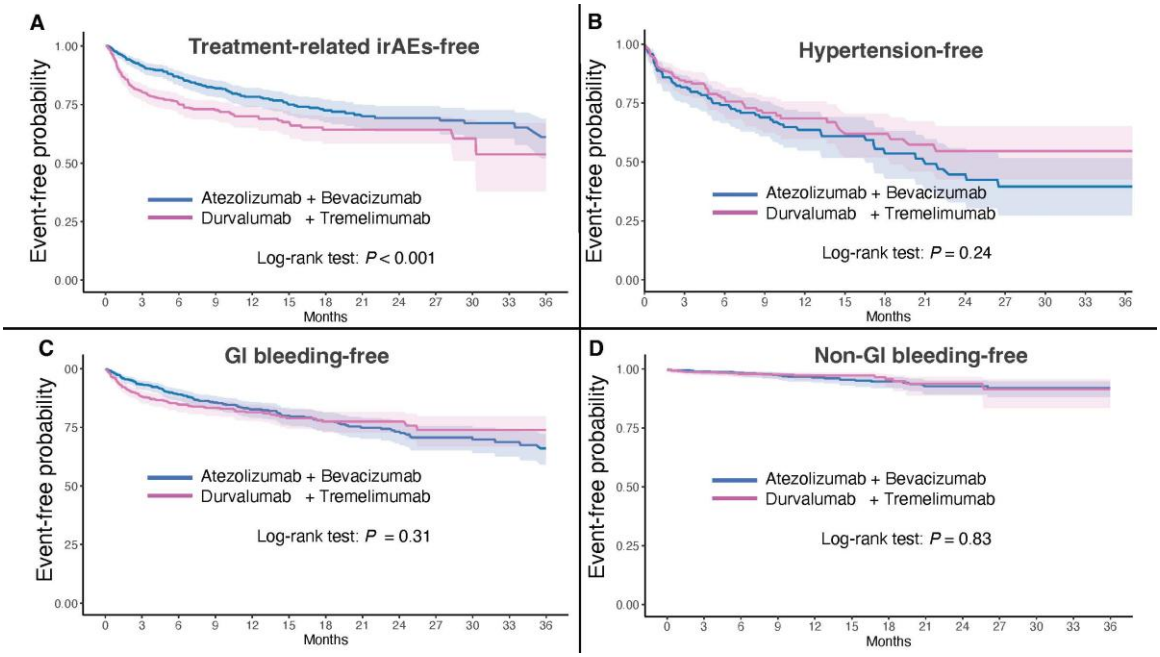

Subgroup
HR (95% CI)
Favors Durva/Treme
Favors Atezo/Bev
Sex
Male
0.96 (0.80–1.11)
Female
0.89 (0.62–1.30)
Age (years)
< 65
1.22 (0.93–1.61)
≥ 65
0.92 (0.77–1.10)
Race
White
1.04 (0.87–1.27)
Black
1.00 (0.57–1.72)
Asian or others
0.58 (0.32–1.04)
Albumin (g/dL)
≥ 3.5
0.78 (0.50–1.20)
< 3.5
1.10 (0.89–1.33)
Total Bilirubin (mg/dL)
≤2
0.94 (0.73–1.22)
> 2
1.09 (0.87–1.35)
INR
≥ 1.5
1.04 (0.77–1.41)
< 1.5
0.90 (0.71–1.14)
Chronic viral hepatitis B or C
Yes
0.89 (0.65–1.22)
No
1.06 (0.85–1.33)
Portal vein thrombosis
Yes
1.00 (0.75–1.35)
No
0.94 (0.74–1.19)
Cirrhosis
Yes
0.93 (0.78–1.10)
No
1.09 (0.74–1.61)
Total population
0.96 (0.83–1.12)
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
Hazard Ratio

Figure 4.


A
Treatment-related irAEs-free
Event-free probability
Atezolizumab + Bevacizumab
Durvalumab + Tremelimumab
Log-rank test: P < 0.001
Months
B
Hypertension-free
Event-free probability
Atezolizumab + Bevacizumab
Durvalumab + Tremelimumab
Log-rank test: P = 0.24
Months
C
GI bleeding-free
Event-free probability
Atezolizumab + Bevacizumab
Durvalumab + Tremelimumab
Log-rank test: P = 0.31
Months
D
Non-GI bleeding-free
Event-free probability
Atezolizumab + Bevacizumab
Durvalumab + Tremelimumab
Log-rank test: P = 0.83
Months