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Original Article

Study on the effects of statin use in immunotherapy for elderly cancer patients on immune-related adverse reactions and quality of life

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Abstract: Objective: To assess the effects of statins on immune-related adverse reactions, quality of life, and clinical outcomes in older adults receiving cancer immunotherapy. Methods: We retrospectively enrolled 150 elderly cancer patients admitted to Beijing Shunyi Hospital between August 2023 and March 2025, who were categorized into a study group (n=94) and a control group (n=56) depending on their use of oral statins. Clinical efficacy, laboratory parameters, quality of life, and adverse reactions were compared between groups. Patients on statins with biomarker elevations ≤2.5 times the upper limit of normal (ULN) (n=78) were further divided into discontinuation (n=35) and continuation (n=43) subgroups to compare biomarker normalization rates. Progression-free survival (PFS) was assessed, and Cox regression analyses were performed to identify PFS-associated factors. Results: No significant differences were observed in general characteristics, clinical efficacy, or most laboratory indicators between the two groups (all P>0.05). Following treatment, the study group demonstrated more pronounced improvements in inflammatory/tumor markers and lipid profiles (all P<0.05), with better quality of life (P<0.05), while overall adverse reaction incidence and cardiac biomarker elevations remained comparable between groups (all P>0.05). Normalization rates in statin users with mild elevations did not differ by discontinuation status. Median PFS was numerically longer in the statin group (11.5 vs 10.9 months) but not statistically significant (all P>0.05). Conclusion: In elderly cancer patients receiving immunotherapy, concomitant statin use did not increase adverse reactions, may improve quality of life, and did not compromise clinical efficacy. The observed PFS benefit was modest. Statins should be considered as an adjunctive therapy, with decisions individualized based on lipid profile and cardiovascular risk.

Keywords: Immunotherapy, elderly cancer patients, statins, immune-related adverse reactions, quality of life

Introduction

In 2022, there were over 20 million new cancer cases globally, resulting in 9.7 million deaths [1]. Cancer has become the second leading cause of death worldwide, with an increasing burden among the elderly. This trend has brought great pressure to the social economic structure and medical service system. Pro-gramed death-1 (PD-1)/programed death ligand-1 (PD-L1) inhibitors are among the most effective cancer treatments. These agents harness the body's immune system to block the PD-1/PD-L1 signalling pathway, thereby promoting tumor cell elimination and significantly prolonging patient survival. Approved drugs include camrelizumab, nivolumab, toripalimab, and atezolizumab. Among them, camrelizumab has a wide range of clinical applications and is suitable for the treatment of malignant tumors in the lungs, esophagus, liver, stomach and other sites [2].

Elderly patients usually have poor tolerance to systemic treatments such as chemotherapy. In contrast, immune checkpoint inhibitors (ICIs) not only show better efficacy but are also associated with a lower incidence of adverse reactions than traditional chemotherapy, offering distinct advantages for application in elderly patients. However, a significant proportion of elderly patients take oral statins. If these medications were to potentially increase adverse reactions to ICIs, the rationale for continuing their use during ICI treatment would require reassessment. Recent research suggests that

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beyond their well-established role in cholesterol reduction and cardiovascular risk mitigation, statins demonstrate additional pleiotropic properties [3]. Craig et al. [4] found that patients who used statins exhibited a decreased risk of advanced prostate cancer and enhanced prognostic results. Maeda-Minami et al. [5] discovered that after adjusting for multiple confounding factors, individuals using statins had a lower cancer risk than those not using statins. Das and Freedland [6] proposed that statins may have anti-cancer activity, and research by Chen et al. [7] supports this view, indicating that statins have a protective effect on both the risk and prognosis of gastric cancer.

Although existing studies have shown that statins may have anti-tumor activity, high-quality evidence on the safety of combining statins with ICIs in elderly cancer patients remains limited. Therefore, this retrospective study aimed to evaluate the effects of statins on immune-related adverse reactions, quality of life and prognosis during ICI treatment in elderly patients, in order to provide a theoretical basis for the clinical use of this combination.

Materials and methods

Research subjects

A retrospective cohort study was conducted involving 150 elderly cancer patients admitted to Beijing Shunyi Hospital between August 2023 and March 2025. All patients presented with dyslipidaemia requiring lipid-lowering therapy. They were grouped based on oral statin use: the study group comprised patients taking statins (n=94), while the control group included those not taking statins (n=56). Patients in the control group had a history of statin allergy or intolerance (e.g., rash, urticaria, angioedema or statin-associated myopathy), which met the diagnostic criteria outlined in the Chinese Guidelines for the Prevention and Treatment of Dyslipidaemia in Adults (2016 Revised Edition) [8]. To ensure lipid management and ethical compliance, these patients uniformly received the alternative lipid-lowering agent probucol. Study group patients had no history of statin allergy and required routine oral statin therapy due to dyslipidaemia. A posteriori sample size validation was conducted based on the primary endpoint of progression-free survival (PFS). With a hazard ratio (HR) of 0.713, α=0.05, and 1-β=0.80, the minimum required sample size was determined to be 142 patients. The study ultimately enrolled 150 patients, thereby meeting the statistical power requirements.

Inclusion criteria: ① Pathologically and/or cytologically confirmed diagnosis of cancer, with at least one evaluable target lesion ≥1.0 cm in measurable dimension; ② Age ≥70 years; ③ Expected survival ≥12 weeks; ④ Eastern Cooperative Oncology Group Performance Status (ECOG-PS) score of 0-2 [9]; ⑤ Effective communication and treatment compliance; ⑥ Complete clinical documentation; ⑦ Exclusive atorvastatin therapy in the study group versus exclusive probucol therapy in the control group. Exclusion criteria: ① Concurrent malignant tumors; ② Inability to undergo or intolerance to antineoplastic treatment regimens; ③ Concurrent active inflammation or acute phase of other diseases; ④ Significant proteinuria or abnormal hepatic/renal function; ⑤ Active viral hepatitis, cardiac dysfunction or severe arrhythmia, history of cerebral hemorrhage or cerebral infarction; ⑥ Concurrent immune dysfunction or coagulation abnormalities; ⑦ Concomitant use of other treatments along with statins during the study period. All enrolled patients underwent multidisciplinary team assessment and met the approved indications for camrelizumab as outlined in the product label, with no contraindications present. This study was approved by the Ethics Committee of Beijing Shunyi Hospital.

Treatment methods

All patients received intravenous infusion of camrelizumab for Injection (Suzhou Shengdiya Biopharmaceutical Co., Ltd., National Drug Approval Number S20190027, specification: 200 mg/vial) at a dose of 200 mg every three weeks. Each infusion was administered intravenously on Day 1 of the treatment cycle and continued until disease progression or intolerable toxicity occurred. Patients in the study group concurrently received oral atorvastatin calcium tablets (Qilu Pharmaceutical Co., Ltd., National Drug Approval Number H20193143, specification: 10 mg) at a dose of 10 mg once daily [10]. Atorvastatin was selected because it is the most commonly prescribed and readily available statin; patients using other statins were excluded to minimize heterogeneity in pharmacokinetic and pharmacodynamic characteris-

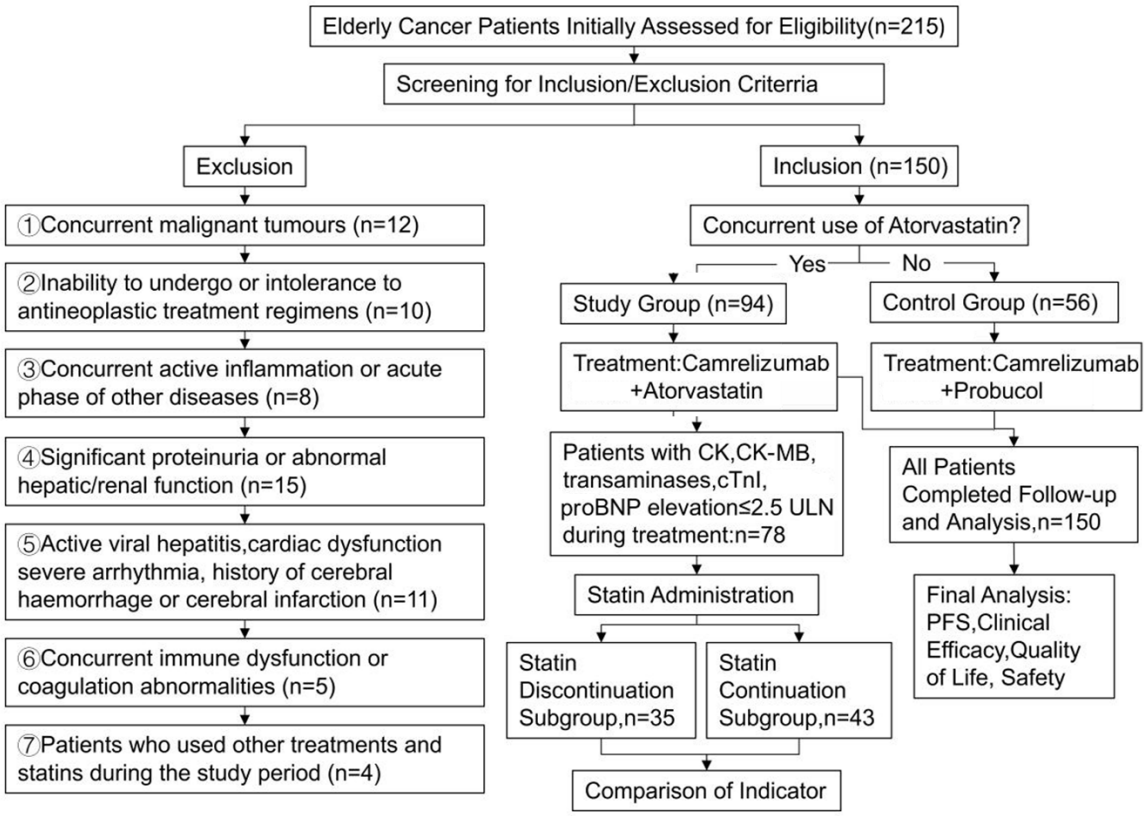


Figure 1. The flowchart depicting patient screening, grouping, and analysis. Note: CK, creatine kinase; CK-MB, creatine kinase MB isoenzyme; cTNI, cardiac troponin I; proBNP, pro-B-type natriuretic peptide; ULN, upper limit of normal; PFS, progression-free survival.

tics. Patients in the control group received oral probucol tablets (Qilu Pharmaceutical Co., Ltd., National Drug Approval No. H20237019, specification: 0.25 g) at a dose of 0.5 g twice daily with meals. Each treatment cycle lasted 3 weeks, with both groups continuing treatment for at least 4 cycles. For patients in the study group who discontinued atorvastatin due to adverse events, subsequent lipid-lowering regimens were determined by clinicians based on patients' lipid levels and tolerability. Among these, 28 patients received no further lipid-lowering medication, while 7 patients switched to probucol for continued treatment. Specific treatment protocols and dosages during the study period were formulated and adjusted according to multidisciplinary clinical opinions and individual patient tolerability. The flowchart is presented in **Figure 1**.

Observation indicators

General information: Including gender, age, marital status, educational attainment, smoking history, drinking history, cardiovascular history, pathological type, Tumor, Node, Metastasis staging, tumor diameter, number of tumors, surgical history, treatment modality, Child-Pugh liver function classification, and ECOG-PS score.

Clinical efficacy: Following four treatment cycles, computed tomography or magnetic resonance imaging examinations were conducted. According to the Response Evaluation Criteria in Solid Tumors [11], outcomes were classified as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD). CR was defined as complete disappearance of lesions persisting for at least four weeks; PR as a reduction in lesion size exceeding 30%; SD as a reduction <30% without meeting CR or PR criteria, or an increase <20%; PD as the emergence of new lesions or an increase in existing lesion size exceeding 20%. Disease control rate = (Number of CR cases + Number of PR cases + Number of SD cases)/Total number of patients × 100%; Objective remission

rate (ORR) = (Number of CR cases + Number of PR cases)/Total number of patients × 100%.

Laboratory parameters: Blood counts, inflammatory markers, hepatic and renal function indicators, lipid profiles, and tumor markers were collected prior to treatment and after four treatment cycles. Blood count parameters included white blood cell count, red blood cell count, haemoglobin, and platelet count Inflammatory markers encompassed C-reactive protein, interleukin-6 (IL-6), absolute lymphocyte count, neutrophil count, and platelet count, with calculation of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio. Hepatorenal function indicators comprised alanine transaminase, aspartate aminotransferase, creatinine. Lipid parameters encompassed total cholesterol (TC), total triglycerides, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Serum tumor markers comprised alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA).

Quality of life: Before and after four treatment cycles, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 [12] was employed to assess patients' quality of life. This encompassed three domains: functional, symptom, and overall health/quality of life. Each domain was scored on a scale of 0 to 100 points. Higher scores in the overall health/quality of life domain and functional domains indicate higher quality of life, while higher scores in symptom domains indicate lower quality of life. The Chinese version of this questionnaire has a Cronbach's alpha coefficient of 0.860 [13, 14].

Adverse reactions: Adverse reactions were assessed according to the World Health Organization's grading system for acute and subacute toxicities of antineoplastic agents [15]. These included hematological toxicity, gastrointestinal reactions, and endocrine toxicity, categorized by severity from grade 0 to grade 4. Clinical observation during treatment was used to determine the occurrence and severity of adverse reactions.

Adverse events: Including elevations in creatine kinase (CK), creatine kinase MB isoenzyme (CK-MB), transaminases, cardiac troponin I (cTnI), N-terminal pro-B-type natriuretic peptide (proBNP) to >2.5 times the upper limit of normal (ULN), incidence of new-onset arrhythmias or ST segment and T wave changes on electrocardiogram (ECG), and incidence of ICI discontinuation due to adverse events. During treatment, if patients exhibited elevations in CK, CK-MB, transaminases, cTnI, or N-terminal proBNP >2.5 ULN or demonstrated ECG changes, discontinuation of ICIs should be assessed based on severity. A total of 78 patients in the study group experienced elevations in these biomarkers >2.5 ULN. These patients were divided into a statin discontinuation subgroup (n=35) and a statin continuation subgroup (n=43) based on whether statin therapy was maintained. Recovery of these parameters to normal levels was then compared between the two subgroups.

Follow-up: All patients were regularly followed from the date of enrollment, with a minimum of one contact per month via outpatient review or telephone. The follow-up ended on June 30, 2025, and no follow-up loss occurred. PFS was recorded for all patients, defined as the time from the start of treatment with camrelizumab to the first occurrence of disease progression, death, or the date of last follow-up. Two full-time research nurses were assigned to manage follow-up data entry to ensure integrity and accuracy. All endpoint events (disease progression, death) were independently evaluated by two consultant oncologists. Any differences were resolved through case discussion.

Statistical analysis

This study was retrospective in nature and did not involve prior sample size estimation. All patients meeting the inclusion and exclusion criteria between August 2023 and March 2025 were included in the analysis. All data analyses were performed using Statistical Product and Service Solutions 27.0 (IBM, Armonk, NY, USA). Continuous variables that conform to a normal distribution are expressed as mean ± standard deviation, and t-tests were applied for intergroup comparisons. Categorical variables were presented as frequencies and percentages, and intergroup differences were analyzed using chi-square tests or Fisher's exact probability test. Rank-sum tests were employed for intergroup comparisons of ordinal data. The Kaplan-Meier method was employed to plot survival curves, while the log-rank test was used for analyzing these curves. Cox regression analysis

was employed to identify risk factors influencing disease progression. Factors with $P<0.05$ in univariate analysis were incorporated into multivariate Cox regression, and backward stepwise regression was used to select risk factors. $P<0.05$ indicates a statistically significant difference.

Result

Comparison of general characteristics between the control group and the study group

Comparing the general characteristics, there were no statistically significant differences between the two groups in terms of gender, age, marital status, educational attainment, smoking history, drinking history, cardiovascular history, pathological type, Tumor, Node, Metastasis staging, tumor diameter, number of tumors, surgical history, treatment modality, Child-Pugh classification, or ECOG-PS (all $P>0.05$) (**Table 1**).

Comparison of clinical efficacy between the control group and the study group

Comparing clinical efficacy, no statistically significant differences were observed in PR (21.28% vs 16.07%), SD (69.15% vs 75.00%), PD (9.57% vs 8.93%), disease control rate (90.43% vs 91.07%), or ORR (21.28% vs 16.07%) (all $P>0.05$) (**Table 2**). Subgroup analysis of ORR by primary tumor type revealed that the study group exhibited higher ORRs than the control group across all tumor subtypes; however, these differences did not reach statistical significance (all $P>0.05$) (**Table 3**).

Comparison of laboratory indicators between the control group and the study group

Comparing laboratory parameters, no statistically significant differences were observed in pre-treatment blood counts, inflammatory markers, hepatic and renal function indicators, lipid profiles, or tumor marker levels between the two patient cohorts (all $P>0.05$). Following treatment, in both patient groups, the absolute lymphocyte count increased, while levels of C-reactive protein, IL-6, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio decreased. Tumor markers AFP and CEA also decreased in both patient groups (all $P<0.05$). Post-treatment lipid parameters in the study group showed statistically significant decreases in TC and HDL-C compared to pre-treatment levels (both $P<0.05$). The LDL-C levels in the study group also showed a downward trend compared to pre-treatment levels; however, it did not reach statistical significance ($P>0.05$) (**Figure 2**).

Comparison of quality of life between the control group and the study group

Comparing symptom domain scores, overall health/quality of life domain scores, and functional domain scores, no statistically significant differences were observed between the two groups prior to treatment (all $P>0.05$). Following treatment, both groups exhibited reduced symptom domain scores and increased overall health/quality of life domain and functional domain scores, with the study group demonstrating more pronounced changes (all $P<0.05$) (**Figure 3**).

Comparison of adverse reactions between the control group and the study group

The incidence rates of adverse reactions in 150 patients were as follows: hematological toxicity 16.67% (25/150), endocrine toxicity 11.33% (17/150), hepatic toxicity 6.67% (10/150), skin toxicity 4.00% (6/150), and telangiectasia 72.67% (109/150). The incidence of grade ≥3 toxicity was 11.33% (17/150), with no fatalities reported (**Table 4**).

Comparison of adverse events between the control group and the study group

Comparing adverse event occurrence, patients in the study group exhibited higher rates of CK, CK-MB, transaminases, cTnI, proBNP elevation >2.5 ULN, and showed increased new-onset arrhythmia or ST segment and T wave changes on ECG, as well as elevated discontinuation of ICIs due to adverse events. However, all the above adverse events were not statistically significant compared with the control group (17.02% vs 16.07%, 8.51% vs 7.14%, 5.32% vs 3.57%) (all $P>0.05$) (**Table 5**).

Comparison of normalized conditions between the continuation group and the discontinuation group

During treatment, patients in the study group who experienced elevations in CK, CK-MB,

Table 1. Comparison of general characteristics between the control group and the study group

Variable	Control Group (*n*=56)	Study Group (*n*=94)	Statistic	*P*
Gender, *n* (%)			χ^2=0.304	0.581
Male	32 (57.14)	58 (61.70)		
Female	24 (42.86)	36 (38.30)		
Age (year)	75.54±3.69	76.54±4.21	*t*=1.483	0.140
Marital status, *n* (%)			χ^2=0.579	0.447
Married	48 (85.71)	76 (80.85)		
Unmarried/Divorced/Widowed	8 (14.29)	18 (19.15)		
Educational attainment, *n* (%)			χ^2=0.849	0.654
Junior secondary school and below	41 (73.21)	70 (74.47)		
Secondary technical/Secondary school	12 (21.43)	16 (17.02)		
College degree or above	3 (5.36)	8 (8.51)		
Smoking history, *n* (%)	35 (62.50)	65 (69.15)	χ^2=0.698	0.403
Drinking history, *n* (%)	22 (39.29)	41 (43.62)	χ^2=0.270	0.603
Coronary heart disease, *n* (%)	10 (17.86)	12 (12.77)	χ^2=0.727	0.394
Hypertension, *n* (%)	20 (35.71)	37 (39.36)	χ^2=0.198	0.656
Cerebral infarction, *n* (%)	5 (8.93)	8 (8.51)	χ^2=0.045	0.832
Heart failure, *n* (%)	2 (3.57)	6 (6.38)	χ^2=0.134	0.715
Pathological type, *n* (%)			χ^2=2.139	0.544
Lung cancer	39 (69.64)	74 (78.72)		
Esophageal cancer	6 (10.71)	9 (9.57)		
Liver cancer	7 (12.50)	6 (6.38)		
Nasopharyngeal carcinoma	4 (7.15)	5 (5.33)		
TNM staging, *n* (%)			χ^2=0.025	0.874
III	16 (28.57)	28 (29.79)		
IV	40 (71.43)	66 (70.21)		
Tumor diameter, *n* (%)			χ^2=1.350	0.245
<5 cm	14 (25.00)	32 (34.04)		
≥5 cm	42 (75.00)	62 (65.96)		
Number of tumors, *n* (%)			χ^2=2.213	0.137
Single	35 (62.50)	47 (50.00)		
Multiple	21 (37.50)	47 (50.00)		
Surgical history, *n* (%)	8 (14.29)	19 (20.21)	χ^2=0.835	0.361
Treatment methods, *n* (%)			χ^2=1.449	0.229
Monotherapy immunotherapy	36 (64.29)	51 (54.26)		
Combination therapy	20 (35.71)	43 (45.74)		
Child-Pugh classification, *n* (%)			χ^2=0.118	0.731
A	24 (42.86)	43 (45.74)		
B	32 (57.14)	51 (54.26)		
ECOG-PS score, *n* (%)			χ^2=0.077	0.782
≤1 score	43 (76.79)	74 (78.72)		
2 score	13 (23.21)	20 (21.28)		

Note: TNM, Tumor, Node, Metastasis; ECOG-PS, Eastern Cooperative Oncology Group Performance Status.

transaminases, cTnI, or proBNP ≤2.5 ULN continued receiving camrelizumab therapy. Among these, 35 patients discontinued atorvastatin calcium tablets, while 43 patients continued taking them. One week later, follow-up results showed a higher rate of normalization in CK and transaminase levels among patients in the discontinuation group compared to those in the

Table 2. Comparison of clinical efficacy between the control group and the study group

Clinical Efficacy	Control Group (*n*=56)	Study Group (*n*=94)	Statistic	*P*
CR (%)	0 (0.00)	0 (0.00)	*Z*=0.541	0.588
PR (%)	9 (16.07)	20 (21.28)		
SD (%)	42 (75.00)	65 (69.15)		
PD (%)	5 (8.93)	9 (9.57)		
DCR (%)	51 (91.07)	85 (90.43)	χ^2=0.017	0.895
ORR (%)	9 (16.07)	20 (21.28)	χ^2=0.610	0.435

Note: CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; DCR, disease control rate; ORR, objective remission rate.

Table 3. Comparison of ORRs across tumor subgroups

Pathological Type	Control Group ORR (%)	Study Group ORR (%)	Statistic	*P*
Lung cancer	6 (15.38)	15 (20.27)	0.403	0.526
Esophageal cancer	1 (16.67)	2 (22.22)	0.156	0.749
Liver cancer	1 (14.29)	1 (16.67)	0.425	0.899
Nasopharyngeal carcinoma	1 (25.00)	2 (40.00)	0.056	0.580

Note: ORR, objective remission rate.

continuation group. However, the differences in the proportions of patients with normalized CK and transaminase levels, as well as those with normalized CK-MB, cTnI, and proBNP levels [54.29% vs 34.88%, 25.71% vs 23.26%], were not statistically significant between the two groups (both *P*>0.05) (**Table 6**).

PFS curves for the control group and study group

As of 30 June 2025, the median follow-up duration across all patients was 12.3 months. The median PFS in the control group was 10.9 months, while that in the study group was 11.5 months. The difference in PFS between the two groups was not statistically significant (HR=0.713, 95% confidence interval [CI] 0.415-1.223) (*P*>0.05). The survival curve trends showed that the PFS curves for both groups largely overlapped, suggesting that statins have a minimal impact on disease progression (**Figure 4**).

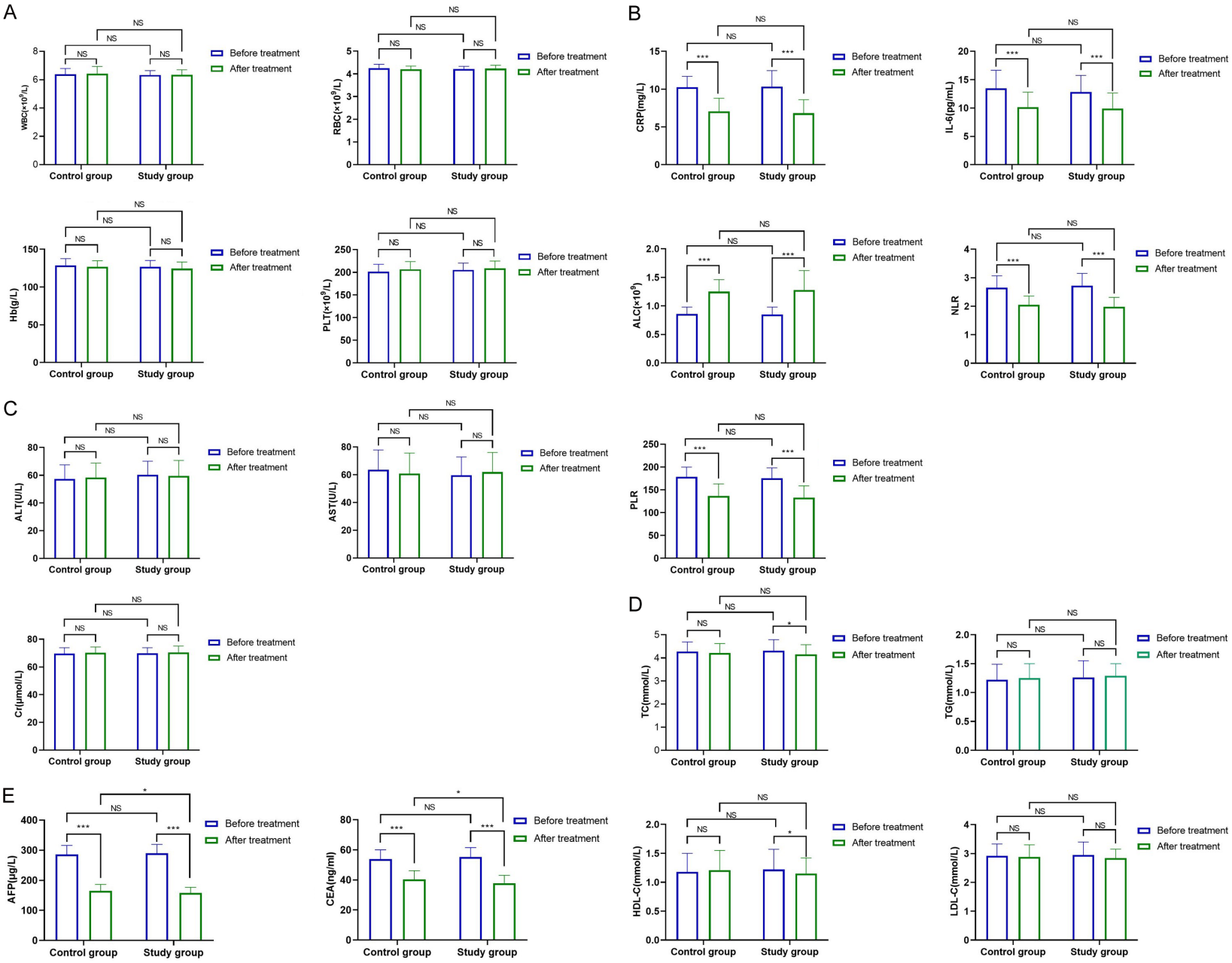
Results of univariate and multivariate Cox regression analyses

Univariate and multivariate Cox regression analyses identified factors influencing PFS. Results demonstrated that multiple tumor sites [HR (95% CI): 0.380 (0.212-0.681)] and ECOG-PS score of 2 [HR (95% CI): 0.395 (0.221-0.707)] were identified as risk factors for PFS (both *P*<0.05) (**Table 7**).

Discussion

Immunotherapy constitutes a therapeutic approach that artificially modulates the body's immune function to treat immune-related diseases, with ICIs emerging as a pivotal strategy for managing malignant tumors. As a broad-spectrum PD-1 inhibitor, the anti-tumor efficacy of camrelizumab has been clinically validated [16]. This study compared the efficacy of camrelizumab monotherapy and its combination with atorvastatin in the treatment of elderly cancer patients, aiming to clarify the therapeutic value of immunotherapy combined with statins in the elderly population.

In this study, no statistically significant difference in clinical efficacy was observed between the two groups, indicating that the combined use of atorvastatin calcium tablets during camrelizumab treatment did not affect the clinical efficacy of the drug. Atorvastatin calcium tablets play a role by reducing cholesterol levels, while camrelizumab clears tumor cells by activating T cell immune response. The absence of direct target-molecule interaction between the two agents precludes synergistic effects from their combination. Although existing research suggests statins possess indirect anti-cancer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PLT(×10⁹/L)
B
CRP(mg/L)
IL-6(pg/mL)
ALC(×10⁹)
NLR
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ALT(U/L)
AST(U/L)
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TC(mmol/L)
TG(mmol/L)
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LDL-C(mmol/L)
E
AFP(μg/L)
CEA(ng/ml)
Control group
Study group
Before treatment
After treatment
NS
*
***

Figure 2. Comparison of laboratory indicators between the control group and the study group. A: Complete blood count; B: Inflammatory markers; C: Liver and kidney function indicators; D: Blood lipid levels; E: Tumor marker; Note: NS: not significant; ALC, absolute lymphocyte count; CRP, c-reactive protein; IL-6, interleukin-6; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; AFP, alpha-fetoprotein; CEA, carcinoembryonic antigen; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; WBC, white blood cell; RBC, red blood cell; Hb, hemoglobin; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine; *P<0.05; ***P<0.001.

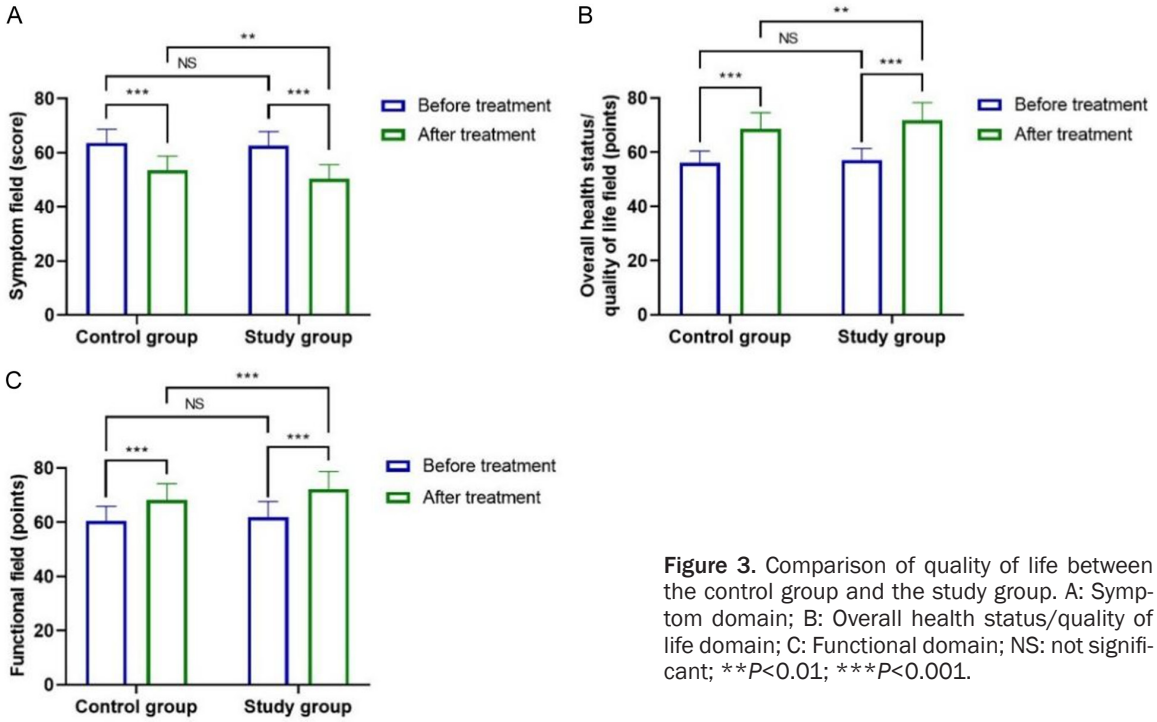

Figure 3. Comparison of quality of life between the control group and the study group. A: Symptom domain; B: Overall health status/quality of life domain; C: Functional domain; NS: not significant; **P<0.01; ***P<0.001.

Table 4. Comparison of adverse reactions between the control group and the study group

Adverse Reactions	Control Group (n=56)		Study Group (n=94)	
	Overall Incidence Rate (%)	Incidence Rate ≥ Grade 3 (%)	Overall Incidence Rate (%)	Incidence Rate ≥ Grade 3 (%)
Endocrine toxicity	5 (8.93)	1 (1.79)	12 (12.76)	2 (2.13)
Skin toxicity	2 (3.57)	0 (0.00)	4 (4.26)	2 (2.13)
Cutaneous telangiectasia	42 (75.00)	1 (1.79)	67 (71.28)	0 (0.00)
Liver toxicity	4 (7.14)	1 (1.79)	6 (6.38)	2 (2.13)
Renal toxicity	1 (1.79)	0 (0.00)	2 (2.13)	0 (0.00)
Pulmonary toxicity	0 (0.00)	0 (0.00)	1 (1.06)	0 (0.00)
Cardiac toxicity	1 (1.79)	0 (0.00)	1 (1.06)	0 (0.00)
Infusion reaction	1 (1.79)	0 (0.00)	2 (2.13)	0 (0.00)
Diarrhea	2 (3.57)	0 (0.00)	1 (1.06)	0 (0.00)
Pancreatic toxicity	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Neurotoxicity	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Ocular toxicity	1 (1.79)	0 (0.00)	1 (1.06)	0 (0.00)
Hemotoxicity	7 (12.50)	3 (5.36)	18 (19.15)	5 (5.32)

properties such as anti-inflammatory and antioxidant effects, elderly patients may experience increased fluctuations in blood drug concentrations due to diminished metabolic func-

Table 5. Comparison of adverse events between the control group and the study group

Adverse Events	Control Group (*n*=56)	Study Group (*n*=94)	Statistic	*P*
CK, CK-MB, transaminases, cTNI, proBNP elevated >2.5 ULN (%)	9 (16.07)	16 (17.02)	χ^2=0.023	0.880
New-onset arrhythmias or ST-T changes on electrocardiogram (%)	4 (7.14)	8 (8.51)	χ^2=0.001	0.989
Discontinuation of ICIs treatment due to adverse events (%)	2 (3.57)	5 (5.32)	χ^2=0.008	0.928

Note: CK, creatine kinase; CK-MB, creatine kinase MB isoenzyme; cTNI, cardiac troponin I; proBNP, pro-B-type natriuretic peptide; ST-T, ST segment and T wave; ICI, immune checkpoint inhibitor.

Table 6. Comparison of normalized conditions between the continuation group and the discontinuation group

Normalized Conditions	Discontinuation group (*n*=35)	Continuation group (*n*=43)	Statistic	*P*
CK and transaminase levels returned to normal (%)	19 (54.29)	15 (34.88)	χ^2=2.954	0.086
CK-MB, cTnI, proBNP return to normal (%)	9 (25.71)	10 (23.26)	χ^2=0.063	0.801

Note: CK, creatine kinase; CK-MB, creatine kinase MB isoenzyme; cTNI, cardiac troponin I; proBNP, pro-B-type natriuretic peptide.

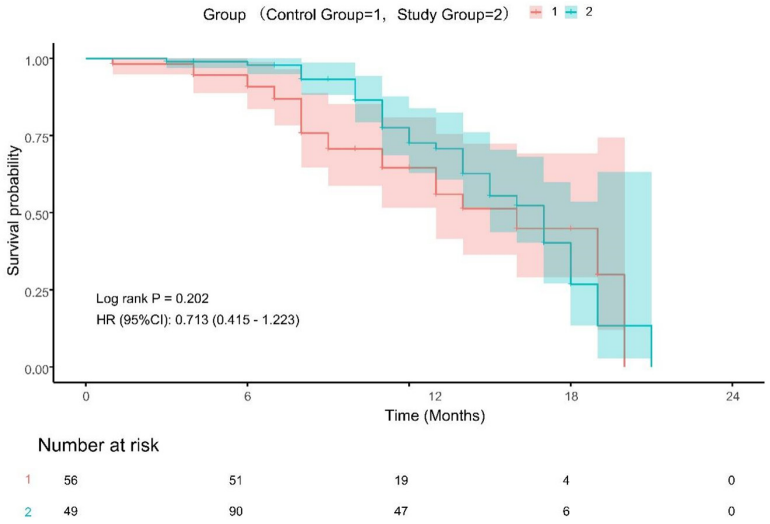

Figure 4. Progression-free survival curves. Note: HR, hazard ratio; CI, confidence interval. The HR and its 95% CI were derived from a univariable Cox regression model. *P*-value was calculated by the log-rank test.

tion. This variability may affect the stability of the therapeutic effect, thus limiting the efficacy of combined therapy [17].

In this study, the study group showed more significant improvement in inflammatory markers, which may be attributed to the multifaceted anti-inflammatory effects of statins. Statins are believed to exert anti-inflammatory effects by inhibiting key inflammatory signaling pathways, thereby reducing the production of pro-inflammatory cytokines (including IL-6 and IL-1β) [18]. In this study, no significant changes were observed in alanine transaminase, aspartate aminotransferase, creatinine levels between the control and study groups before treatment. This is because although atorvastatin is primarily metabolized by the liver, its metabolites exhibit no hepatotoxicity, and only approximately 2% is excreted via the kidneys, exerting minimal impact on renal function. Consequently, the combination therapy did not increase the risk of hepatic or renal injury. Research by Chen et al. [19] indicates that the risk of hepatic and renal impairment is significantly reduced with low-dose statin therapy. In addition, the baseline liver and kidney function of the patients enrolled in this study was good, and the drug metabolism and excretion ability were relatively normal, so there was no significant effect on these functions. However, in clinical practice, it is still recommended to use low-dose initial treatment and strictly monitor changes in liver and kidney function.

Recent studies [20, 21] have shown that excessive proliferation of cancer cells can lead to excessive lipid metabolism in the body, which in turn leads to disorder of lipoprotein levels.

Table 7. Results of univariate and multivariate Cox regression analyses

Project	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Gender				
Male	1.000 (Reference)			
Female	1.370 (0.813-2.310)	0.237		
Age	0.985 (0.923-1.051)	0.645		
Marital status				
Married	1.000 (Reference)			
Unmarried/Divorced/Widowed	0.829 (0.424-1.623)	0.585		
Educational attainment				
Junior secondary school and below	1.000 (Reference)			
Secondary technical/Secondary school	0.467 (0.182-1.200)	0.114		
College degree or above	0.423 (0.140-1.281)	0.128		
Smoking history				
No	1.000 (Reference)			
Yes	0.623 (0.344-1.129)	0.119		
Drinking history				
No	1.000 (Reference)			
Yes	1.053 (0.607-1.827)	0.854		
Pathological type				
Lung cancer	1.000 (Reference)			
Esophageal cancer	0.770 (0.237-2.501)	0.664		
Liver cancer	0.805 (0.192-3.385)	0.768		
Nasopharyngeal carcinoma	1.785 (0.456-6.996)	0.406		
TNM staging				
III	1.000 (Reference)			
IV	1.073 (0.606-1.898)	0.810		
Tumor diameter				
<5 cm	1.000 (Reference)			
≥5 cm	0.857 (0.484-1.515)	0.595		
Number of tumors				
Single	1.000 (Reference)		1.000 (Reference)	
Multiple	0.402 (0.182-0.856)	0.023	0.380 (0.212-0.681)	0.001
Surgical history				
No	1.000 (Reference)			
Yes	0.867 (0.436-1.724)	0.684		
Treatment methods				
Monotherapy immunotherapy	1.000 (Reference)			
Combination therapy	0.888 (0.527-1.497)	0.656		
Child-Pugh classification				
A	1.000 (Reference)			
B	1.033 (0.610-1.748)	0.905		
ECOG-PS score				
≤1 score	1.000 (Reference)		1.000 (Reference)	
2 score	0.395 (0.221-0.707)	0.002	0.395 (0.221-0.707)	0.002
Treatment methods				
Combination statin therapy	1.000 (Reference)			
Without statin therapy	0.711 (0.414-1.220)	0.216		

Note: HR, hazard ratio; CI, confidence interval; TNM, Tumor, Node, Metastasis; ECOG-PS, Eastern Cooperative Oncology Group Performance Status.

Abnormal lipid metabolism can be seen in all kinds of malignant tumor patients, and the levels of TC, LDL-C and HDL-C are often lower than those of healthy people [22]. In this study, TC and LDL-C levels decreased post-treatment in the study group compared to pre-treatment levels, reflecting the lipid-lowering effect of the medication. This suggests that in combination therapy, attention should be paid to the potential risks arising from the combined effects of tumor-related lipid metabolism disorders and the lipid-lowering effects of drugs. Nevertheless, lipid fluctuations in the study group remained within normal ranges, indicating that atorvastatin exerted its hypolipidemic effects without significantly disrupting patients' baseline lipid homeostasis, thereby supporting the safety profile of combined therapy. Moreover, the study group in this study exhibited more pronounced reductions in AFP and CEA levels post-intervention, which may indirectly reflect the potential adjuvant anti-tumor activity of statins. Statins competitively inhibit HMG-CoA reductase, thereby blocking the mevalonate pathway and leading to depletion of downstream metabolites such as isopentenyl pyrophosphate and farnesyl pyrophosphate. These metabolites are essential for the post-translational modification of a variety of key signaling proteins, which play a decisive role in maintaining tumor cell proliferation, survival, invasion and metastasis. Blocking this pathway can directly induce cancer cell cycle arrest, promote apoptosis and weaken invasion ability [23, 24]. Kamal et al. [25] confirmed that statins have pro-apoptotic effects in breast cancer and may improve the prognosis of patients with esophageal cancer [26]. Atorvastatin combined with camrelizumab synergistically enhances the anti-tumor efficacy through the above mechanism, thereby improving the level of tumor markers.

The study group and the control group did not show a statistically significant difference in the incidence of adverse reactions and events. When elevations in CK, CK-MB, transaminases, cTnI, and proBNP reached ≤2.5 ULN, there was also no statistically significant difference in CK and transaminase improvement between the discontinuation group and the continuation group. This result is consistent with the study by Kostine et al. [27], indicating that ICIs combined with statins did not increase additional toxicity. Follow-up results indicated that the median PFS in the study group exceeded that of the control group, consistent with the findings of Chiang et al. [28]. However, this difference did not reach statistical significance. With regard to the mechanism of action, statins may slightly improve PFS in patients with immunotherapy through two possible pathways: first, by inhibiting the mevalonate pathway to reduce the key metabolites required for tumor cell proliferation, thereby indirectly inhibiting tumor growth [29]; second, by regulating the function of immune cells in the tumor microenvironment to enhance T-cell-mediated antitumor activity [30]. However, these effects are ancillary and cannot replace the anti-tumor efficacy of the immunotherapy drugs themselves. Consequently, their contribution to PFS prolongation is limited, yielding only modest improvements upon the baseline treatment.

The findings of this study indicate that multiple tumors and an ECOG-PS score of 2 constitute risk factors for PFS in elderly cancer patients. This aligns with multiple studies, confirming the close association of tumor number and ECOG-PS score with cancer prognosis [31, 32]. However, tumor diameter showed no difference between the two groups in this study, differing from previous research [33], which may be related to the characteristics of the included sample. While combined statin therapy was associated with improved PFS, it failed to meet criteria for independent protective factors, further confirming its adjunctive role. Research indicates that statins have no significant impact on the overall prognosis of bladder or lung cancer [34], a finding consistent with the results of the present study. This finding also suggests that in clinical practice, one cannot expect statin combination therapy to compensate for core prognostic disadvantages such as high tumor burden or poor performance status. Optimizing immunotherapy regimens and controlling tumor progression must remain the primary objectives.

This study has certain limitations. It is a single-center retrospective analysis, with case inclusion dependent on the completeness of medical records. It does not cover other types or doses of statins, and geographical restrictions limit its representativeness. The follow-up period was too brief to adequately assess overall

survival or long-term adverse reactions. Constrained by the hospital's testing capabilities, no detailed analysis of lipid control status was conducted. Furthermore, pre-specified stratified analyses were not performed across all cancer types. The sample size and distribution characteristics of cases also limited the feasibility of conducting interaction effect analyses. Future studies should consider expanding sample sizes, incorporating more detailed lipid parameters, and refining cancer subgroups. Comparisons of efficacy and safety between different statins, extended follow-up periods, and deeper mechanistic investigations are warranted to enhance the reliability of conclusions. For ethical and clinical practice considerations, probucol was used as a lipid-lowering treatment for patients with dyslipidemia who were allergic to statins in the control group. Probucol itself has lipid-lowering properties, and may have anti-inflammatory and antioxidant effects. These characteristics may become confounding factors that affect the evaluation of the efficacy of statins alone. Future studies need to establish a control group that does not use lipid-lowering drugs at all to clarify the mechanism of statins in immunotherapy more clearly. Finally, the sample size limited in-depth subgroup analyses based on high-risk factors such as age stratification, smoking status, and different cardiovascular comorbidities. Future prospective studies should incorporate larger sample sizes and pre-specify subgroup analyses targeting these key influencing factors. This would enable more precise identification of populations likely to benefit from combined therapy, or those requiring cautious use, thereby advancing individualized treatment decision-making.

Conclusion

During the immunotherapy with camrelizumab in elderly cancer patients, the combined use of atorvastatin shows good safety characteristics. It may bring potential clinical benefits by reducing the level of tumor markers and improving the quality of life, thus prolonging the PFS. By improving the quality of life and regulating the internal environment of the body, the combination supports elderly patients to complete immunotherapy steadily, which neither affects the main treatment effect nor increases the risk. However, statins have limited and only auxiliary effects on improving PFS, and cannot replace precise anti-cancer treatment for the tumor itself. Clinical application should be individualized according to the patient's blood lipid level, basic cardiovascular disease and other related factors.

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Disclosure of conflict of interest

None.

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