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# Real world study of regimen containing bevacizumab as first-line therapy in Chinese patients with advanced non-small cell lung cancer

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**Keywords**
Bevacizumab; chemotherapy; non-small cell lung cancer; progression-free survival; safety.

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## Abstract

**Background:** Large scale randomized controlled trials have demonstrated that the use of bevacizumab in addition to chemotherapy in patients with advanced non-small cell lung cancer (NSCLC) conveys significant survival benefits. We explored the clinical impact of a first-line regimen containing bevacizumab (B+) versus a non-bevacizumab regimen (non-B) in advanced non-squamous NSCLC (NS-NSCLC) patients in a real world setting.

**Methods:** The medical records of patients with advanced NS-NSCLC who received first-line therapy with or without bevacizumab were retrospectively collected. The primary outcome was progression-free survival (PFS), with secondary objectives of objective response rate (ORR), disease control rate (DCR), and safety. Exploratory analysis of *EGFR* and *ALK* status was conducted in subgroup.

**Results:** One hundred and forty-nine patients met the selection criteria: 62 in the B+ and 87 in the non-B group. The baseline characteristics were well balanced. In the overall population, the median PFS was significantly longer in the B+ than in the non-B group (9.7 vs. 7.0 months, hazard ratio [HR] 0.52, 95% confidence interval [CI] 0.30–0.91; $P = 0.0184$). Improved trends in both ORR and DCR were observed in the B+ group. In wild-type patients, the median PFS of the B+ was 11.3 compared to 5.5 months in the non-B group (HR 0.43, 95% CI 0.20–0.91; $P = 0.0234$). In wild type and unknown populations, the median PFS was 11.3 (B+) compared to 6.0 months (non-B) (HR 0.53; 95% CI 0.28–1.02; $P = 0.0520$). The safety profile was acceptable in both groups and no unexpected findings were observed.

**Conclusion:** Our analysis confirmed that a first-line regimen containing bevacizumab showed superior clinical benefits over a non-bevacizumab regimen in Chinese patients with advanced NS-NSCLC in a real world setting.

## Introduction

Non-small cell lung cancer (NSCLC) accounts for over 85% of lung cancer diagnoses and most patients present with advanced stage at the time of diagnosis.[1] Current standard first-line treatment for advanced NSCLC is platinum-based doublet chemotherapy when no targetable alterations, such as *EGFR* mutations or *ALK* or *ROS1* rearrangements, are detected in genomic testing.[2] However, the response rate of chemotherapy regimens is only 15–30%, with high toxicity, and the prognosis for these patients is extremely poor, with five-year survival rates reported at < 5%.[3] Additional therapeutic options are urgently required. Bevacizumab, a recombinant humanized monoclonal antibody that binds VEGF-A and prevents interaction with VEGFR-1 and VEGFR-2 (the primary receptors involved in endothelial cell proliferation and migration),[4] reduces tumor expansion by controlling abnormal growth of blood vessels around the

  

tumor.[5] Several pivotal trials have proven the efficacy of bevacizumab in patients with advanced NSCLC as first-line treatment in combination with platinum-based chemotherapy.[6–9] An Eastern Cooperative Oncology Group (ECOG) randomized controlled trial (E4599) demonstrated that patients treated with bevacizumab–carboplatin–paclitaxel (BCP) had significantly longer median overall survival (OS) than those treated with carboplatin–paclitaxel (CP) alone (12.3 vs. 10.3 months, hazard ratio [HR] 0.79; $P = 0.003$)[6] Similar efficacy was also observed in other pivotal studies, extending OS and progression-free survival (PFS).[10,11] These studies included mainly Caucasian patients. Subsequent subgroup analyses in the Avastin in Lung (AVAiL) and phase IV Safety of Avastin in Lung (SAiL) studies suggested that bevacizumab is also efficacious in Asian populations.[7,8] The randomized, double-blind, multicenter, placebo-controlled, phase III BEYOND trial confirmed higher PFS, OS, and overall response rate (ORR) in the BCP compared to the CP group in a Chinese population.[9] However, these clinical trials were designed for highly selected patients and standardized conditions different from the realities of real-world clinical practice settings. Patients with brain metastases and poor ECOG performance status (PS > 1) were virtually excluded because of the risk of hemorrhage, which inhibits the widespread use of bevacizumab, as 25–30% of patients with NSCLC will ultimately be diagnosed with brain metastases, and this is also often the first site of recurrence in patients initially treated for early-stage disease.[11,12] Thus, there is a lack of real world evidence to illustrate the effectiveness and safety of bevacizumab. Therefore, we retrospectively assessed the real-world outcomes of patients with advanced non-squamous (NS)-NSCLC who received first line regimens with or without bevacizumab at our Cancer Center.

# Methods

## Data source and study population

The medical data of patients who visited the Cancer Hospital, Chinese Academy of Medical Sciences from July 2009 to December 2016 were collected. Eligible patients were required to be newly diagnosed with stage IIIB or IV cancer based on the American Joint Committee on Cancer 7th Edition Cancer Staging Manual with histologically or cytologically confirmed NS-NSCLC. Study subjects were classified into two mutually exclusive groups according to their first-line regimen: bevacizumab-containing (B+) and non-bevacizumab (non-B). A total of 149 patients were included in this study.

## Assessment

The primary outcome was progression-free survival (PFS), with secondary objectives of ORR, disease control rate (DCR), and treatment-induced toxicities in patients with NS-NSCLC. Exploratory analysis of *EGFR* and *ALK* status was conducted in subgroup.

Disease response to treatment was assessed according to Response Evaluation Criteria in Solid Tumors. PFS was defined as the duration from the start of treatment until disease progression or death from any cause. DCR was defined as complete response (CR), partial response (PR), or stable disease (SD) ≥ 6 weeks, while ORR was defined as CR or PR. In subgroup analysis, the wild-type subgroup refers to *EGFR* negative/*ALK* negative, *EGFR* negative/*ALK* unknown, and *EGFR* unknown/ALK negative populations. Wild type and unknown subgroups were defined as *EGFR* negative/*ALK* negative, *EGFR* negative/*ALK* unknown, *EGFR* unknown/ALK negative, and *EGFR* unknown/*ALK* unknown populations. Adverse events (AEs) were recorded according to Common Terminology Criteria for Adverse Events version 4.0. Other baseline clinical variables included age, gender, ECOG PS, smoking history, histology, disease stage, *EGFR* status, *ALK* status, brain metastasis, and concomitant chemotherapy.

## Statistics analysis

The distribution of patients' baseline demographic/clinical characteristics (age, gender, ECOG status, smoking status, histology, disease stage, *EGFR*/*ALK* status, brain metastasis) and treatment patterns were described using frequency analysis. Chi-square and Fisher's exact tests were used for categorical variables and a *t*-test for continuous variables to assess the difference between the two treatment groups at baseline. The Kaplan–Meier method was applied to obtain the distribution function for PFS. A log-rank test was used to evaluate the difference between the two groups. Cox regression was used to explore the potential predictors for PFS and results from both univariate and multivariate models are reported. ORR and DCR were compared using chi-square or Fisher's exact tests. All analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA) and alpha = 0.05 was used as a significance level in all statistical testing.

# Results

## Patients and characteristics

From July 2009 to December 2016, 149 patients with advanced NS-NSCLC administered first-line therapy with or without bevacizumab at our hospital were retrospectively reviewed. All 149 patients met the selection criteria:

 

62 in the B+ and 87 in the non-B group. Chemotherapy was the standard treatment in both groups: 57 patients in the B+ and 71 in the non-B group. All other patients were treated with *EGFR*/*ALK* tyrosine kinase inhibitors (TKIs). Most of the patients administered concomitant chemotherapy were treated with doublet-chemotherapy (55/62 and 66/87 in B+ and non-B groups, respectively). An evaluation of efficacy was possible in 60 and 77 patients in the B + and non-B groups, respectively. Baseline characteristics of study population are shown in Table 1, including age, gender, ECOG status, smoking status, histology, disease stage, *EGFR*/*ALK* status, and brain metastasis.

## Clinical outcomes

The median follow-up duration was 10.7 months. In the overall population, the median PFS was significantly longer in the B+ than in the non-B group: 9.7 versus 7.0 months ($P$ = 0.0184) (Fig 1). Although the differences in ORR and DCR were not statistically significant, both measurements were higher in the B+ group (63.33% vs. 51.95% for ORR, $P$ = 0.1818; and 93.33% vs. 85.71% for DCR, $P$ = 0.1565). Similar trends were observed in all subgroup analyses. In the wild-type subgroup, the median PFS in the B+ group was 11.3 compared to 5.5 months in the non-B group ($P$ = 0.0234) (Fig 2). ORR and DCR in the B+ and non-B groups were 55.17% vs. 38.24% ($P$ = 0.1788) and 96.55% vs. 79.41% ($P$ = 0.0598), respectively. The median PFS in the population with wild type and unknown *EGFR*/*ALK* status was 11.3 (B+) compared to 6.0 months (non-B) ($P$ = 0.0520) (Fig 3). The ORR and DCR in the two groups were 56.10% vs. 46.30% ($P$ = 0.3440) and 92.68% vs. 83.33% ($P$ = 0.1743), respectively.

**Table 1** Baseline characteristics of NS-NSCLC patients at first-line therapy ($n$ = 149)

| | No. of patients (%) | | | |
|---|---|---|---|---|
| Characteristics | All $n$ = 149 | B+ $n$ = 62 | Non-B $n$ = 87 | $P$ |
| Age, years | | | | 0.2885 |
| Median | 53.0 | 54.0 | 53.0 | |
| Mean | 53.1 | 54.2 | 52.4 | |
| Range | 25–75 | 30–73 | 25–75 | |
| Gender | | | | 0.9924 |
| Male | 101 (67.8) | 42 (67.7) | 59 (67.8) | |
| Female | 48 (32.2) | 20 (32.3) | 28 (32.2) | |
| ECOG PS† | | | | 0.5282 |
| 0 | 45 (30.41) | 22 (35.48) | 23 (26.74) | |
| 1 | 100 (67.57) | 39 (62.90) | 61 (70.93) | |
| 2 | 3 (2.03) | 1 (1.61) | 2 (2.33) | |
| Smoking status‡ | | | | 0.2402 |
| Non-smoker | 65 (45.1) | 31 (50.8) | 34 (41.0) | |
| Former/current smoker | 79 (54.9) | 30 (49.2) | 49 (59.0) | |
| Histology | | | | 0.4928 |
| Adenocarcinoma | 134 (89.9) | 57 (91.9) | 77 (88.5) | |
| Others | 15 (10.1) | 5 (8.1) | 10 (11.5) | |
| Disease stage | | | | 0.1476 |
| IIIB | 19 (12.8) | 5 (8.1) | 14 (16.15) | |
| IV | 130 (89.3) | 57 (91.9) | 73 (83.9) | |
| Driver mutation test§ | | | | |
| *EGFR* positive | 35 | 16 | 19 | 0.7775 |
| *ALK* positive | 14 | 4 | 10 | 0.1886 |
| Brain metastasis | 22 | 8 | 14 | 0.5886 |
| Concomitant chemotherapy | | | | 0.1693 |
| Non | 21 (14.09) | 5 (8.06) | 16 (18.39) | |
| Mono-chemotherapy | 7 (4.70) | 2 (3.23) | 5 (5.75) | |
| Pemetrexed-based | 2 | 1 | 1 | |
| Paclitaxel-based | 0 | 0 | 0 | |
| Doublet-chemotherapy | 121 (81.21) | 55 (88.71) | 66 (75.86) | |
| Pemetrexed-based | 88 | 46 | 42 | |
| Paclitaxel-based | 9 | 3 | 6 | |

†Data of one patient was missing. ‡Data of five patients were missing. §Both *EGFR* and *ALK* positive: 2. ECOG PS, Eastern Cooperative Oncology Group performance status; NS-NSCLC, non-squamous non-small cell lung cancer.

  

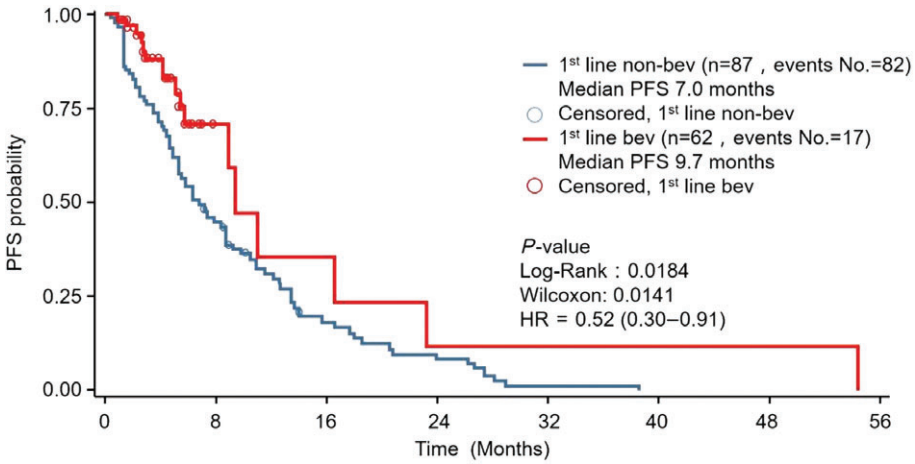


**Figure 1** Progression-free survival (PFS) of B+ versus non-B in the overall population. First-line non-B (*n* = 87, no. of events = 82) median PFS (mPFS) 7.0 months; first-line B+ (*n* = 62, no. of events = 17) mPFS 9.7 months. HR, hazard ratio.

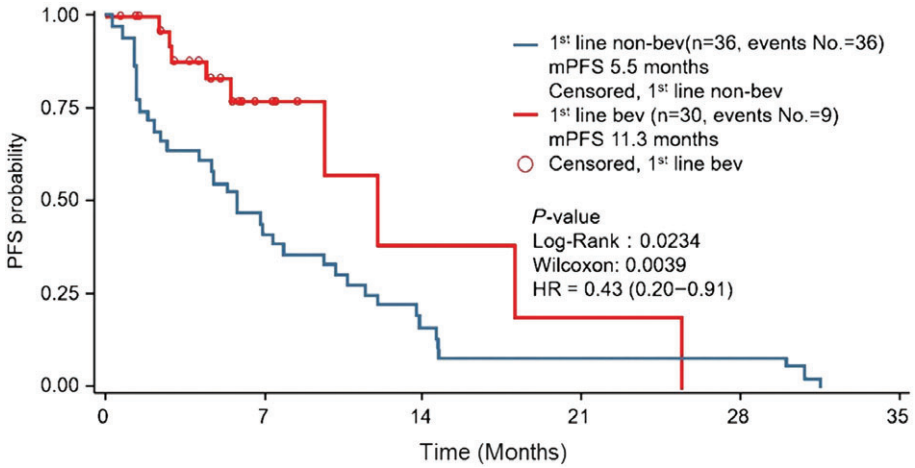


**Figure 2** Progression-free survival (PFS) of B+ versus non-B in the wild type population. First-line non-B (*n* = 36, no. of events = 36) median PFS (mPFS) 5.5 months; first-line B+ (*n* = 30, no. of events = 9) mPFS 11.3 months. HR, hazard ratio.

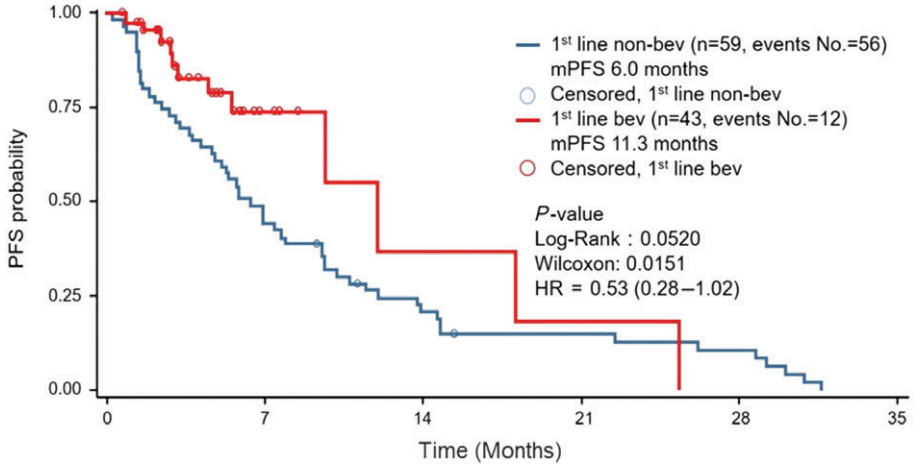


**Figure 3** Progression-free survival (PFS) of B+ versus non-B in the wild type and unknown population. First-line non-B (*n* = 59, no. of events = 56) median PFS (mPFS) 6.0 months; first-line B+ (*n* = 43, no. of events = 12) mPFS 11.3 months. HR, hazard ratio.

In patients with brain metastases, progression was observed in two patients (2/8, 25.00%) in the B+ and 11 (11/14, 78.57%) in the non-B group. ORR and DCR were 50.00% and 100.00% in the B+ compared to 76.92% and 92.31% in the non-B group. In patients with an ECOG PS of 1–2, the median PFS in B+ was 9.7 months, which was significantly longer than in the non-B group at 6.0 months ($P$ = 0.0023) (Fig 4). There were similar trends

 

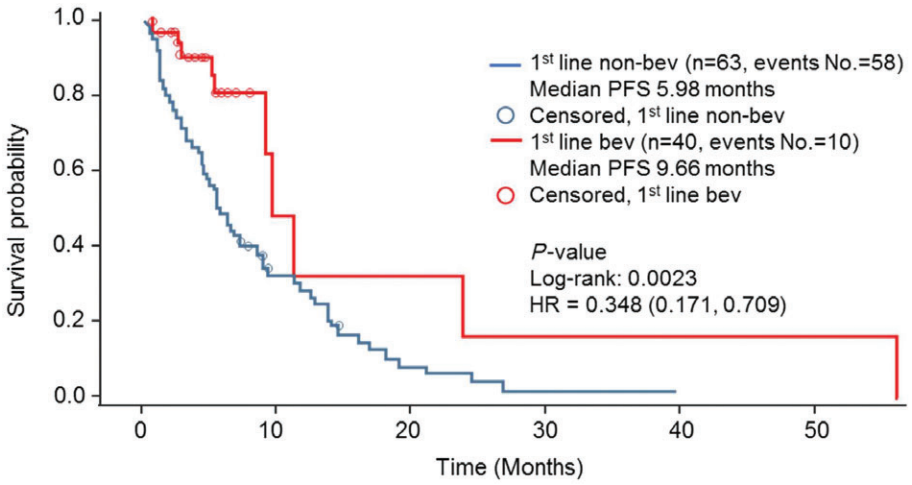


**Figure 4** Progression-free survival (PFS) of B+ versus non-B in patients with Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 1–2. First-line non-B ($n$ = 63, no. of events = 58) median PFS (mPFS) 5.98 months; first-line B+ ($n$ = 40, no. of events = 10) mPFS 9.66 months. HR, hazard ratio.

in ORR and DCR (57.98% vs. 53.70% for ORR, $P$ = 0.6905; and 92.11% vs. 81.48% for DCR, $P$ = 0.1498). Overall survival (OS) was not reached.

The results of Cox regression are reported in Table 2. In the univariate model, first-line bevacizumab use was associated with better PFS (HR 0.52; $P$ = 0.0205) and this association remained stable after adjusting for gender, age, *EGFR*/*ALK* status, smoking status, and concomitant pemetrexed use (HR 0.48; $P$ = 0.0217). Tables 3 and 4 show the results of treatment response and survival analysis.

## Safety

Safety analysis was conducted in the whole population. The most common AEs were myelosuppression and gastrointestinal disorders in both groups. Grade 3/4 AEs were acceptable, with 16/62 (25.8%) in the B+ and 23/87 (26.4%) in the non-B group, including leukopenia, neutropenia, thrombocytopenia, anemia, anorexia, and increased

gamma-glutamyl transferase. No AEs appeared to increase after bevacizumab administration. Specific AEs in the B+ group included bleeding with epistaxis (2/62, 3.2%) and hypertension (1/62, 1.6%). No drug-related deaths or unexpected safety issues were observed in the study. Table 5 shows the AEs in both groups.

**Table 2** Cox regression for PFS

| | Crude | | Adjusted | |
|---|---|---|---|---|
| Characteristics | HR | *P* | HR | *P* |
| Male | 0.83 | 0.4231 | 0.53 | 0.0563 |
| Age group (≤ 65) | 0.77 | 0.5251 | 0.57 | 0.2039 |
| Wild type | 1.29 | 0.285 | 1.33 | 0.1946 |
| First-line bevacizumab use | 0.52 | 0.0205 | 0.48 | 0.0217 |
| Smoker | 1.24 | 0.3116 | 1.55 | 0.1423 |
| Pemetrexed use | 1.31 | 0.1937 | 1.38 | 0.1629 |

HR, hazard ratio; PFS, progression-free survival.

## Discussion

The primary end point of this study was to assess the efficacy of first-line bevacizumab in a real world population of patients with NS-NSCLC. The study findings confirm the efficacy of bevacizumab with a manageable safety profile, support the use of bevacizumab in first-line treatment, and establish the relevance of findings of randomized phase III (E4599, AVAiL)[6,7] and phase IV (SAiL and Aries) studies.[8,13]

We explored the clinical impact of first-line therapy with (B+) or without (non-B) bevacizumab for patients with advanced NS-NSCLC in a real world setting. The baseline characteristics were well balanced, including patients with brain metastasis and ECOG PS > 1. In the overall population, the median PFS was significantly longer in the B+ than in the non-B group (9.7 vs. 7.0 months, HR 0.52, 95% CI 0.30–0.91; $P$ = 0.0184). The PFS in our study (9.7 months) was comparable to findings observed in previous Asian subpopulation analyses, including the BEYOND trial[9] (9.2 months), the AVAiL East Asian subgroup[7] (8.2 months), and the SAiL East Asian population,[14] which reported a median time to progression of 8.3 months, with further subgroup analysis of Chinese patients demonstrating a median time to progression of 8.8 months.[8] In multivariate analysis, there was no distinction in PFS when stratified by gender, age, smoking history, or *EGFR*/*ALK* gene status. Improved trends in both ORR and DCR were observed in the B+ group, with ORRs of 63.33% vs. 51.95% ($P$ = 0.1818) and DCRs of 93.33% vs. 85.71% ($P$ = 0.1565), respectively. The higher ORR and DCR in both groups in our study may have occurred because 8.06% and 18.39% of B+ and non-B group

  

**Table 3** ORR and DCR in overall population, wild-type patients, wild-type and unknown patients, patients with brain metastasis and patients with ECOG PS 1–2

| | | No. of patients (%) | | |
|---|---|---|---|---|
| Type of patients | Index | B+ *n* = 62 | non-B *n* = 87 | *P** |
| Overall population | ORR | 38/60 (63.33) | 40/77 (51.95) | 0.1818 |
| | DCR | 56/60 (93.33) | 66/77 (85.71) | 0.1565 |
| Wild-type patients | ORR | 16/29 (55.17) | 13/34 (38.24) | 0.1788 |
| | DCR | 28/29 (96.55) | 27/34 (79.41) | 0.0598** |
| Wild type and unknown patients | ORR | 23/41 (56.10) | 25/54 (46.30) | 0.3440 |
| | DCR | 38/41 (92.68) | 45/54 (83.33) | 0.1743 |
| Brain metastasis | ORR | 4/8 (50.00) | 10/13 (76.92) | 0.3458 |
| | DCR | 8/8 (100.00) | 12/13 (92.31) | 1.0000 |
| ECOG PS 1–2 | ORR | 22/38 (57.89) | 29/54 (53.70) | 0.6905 |
| | DCR | 35/38 (92.11) | 44/54 (81.48) | 0.1498 |

*Chi-square test used, unless specified. **Fisher's exact test. DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; ORR, overall response rate; PFS, progression-free survival.

**Table 4** PFS in different types of patients

| Types of patients | Treatments | Median PFS (months) | Log-rank *P* |
|---|---|---|---|
| Overall patients | B+ | 9.7 | 0.0184 |
| | Non-B | 7.0 | |
| Wild type patients | B+ | 11.3 | 0.0234 |
| | Non-B | 5.5 | |
| Wild type and unknown patients | B+ | 11.3 | 0.0520 |
| | Non-B | 6.0 | |
| ECOG PS 1–2 | B+ | 9.7 | 0.0023 |
| | Non-B | 6.0 | |

ECOG PS, Eastern Cooperative Oncology Group performance status; PFS, progression-free survival.

patients, respectively, harboring activating mutations in *EGFR*/*ALK* had been treated with EGFR/ALK-TKIs. Several studies have demonstrated a survival benefit in patients with *EGFR* exon19del mutations treated with bevacizumab plus geftinib or erlotinib.[15,16]

Currently, targeted therapies, such as *EGFR* and *ALK* TKIs, are being developed to improve efficacy in selected patients with advanced NSCLC; thus patients with *EGFR*/*ALK* gene mutations are usually administered corresponding targeted therapy as first-line treatment. However, patients without *EGFR*/*ALK* mutations and those with inadequate samples for gene testing may be excluded from EGFR/ALK-TKI therapy, and previous studies have shown no benefit of using bevacizumab plus TKIs in *EGFR*-unselected patients.[17–19] For these patients, chemotherapy is still the primary choice, therefore it is important to find an effective and safe regimen for this population. Thus, we explored the efficacy and safety of bevacizumab use in wild type, and in wild type and unknown populations excluded from targeted therapy. In wild-type patients, the median PFS of the B+ was 11.3 compared to 5.5 months in the non-B group (HR 0.43, 95% CI 0.20–0.91; $P = 0.0234$). In the wild type and unknown population, the median PFS was 11.3 (B+) compared to 6.0 months (non-B) (HR, 0.53; 95% CI, 0.28–1.02; $P = 0.0520$), with a higher ORR and DCR in the B+ group. The results of our subgroup analysis are consistent with results of the BEYOND trial (8.3 vs. 5.6 months of B + CP and Pl + CP groups in *EGFR* wild-type tumors), which identified that therapy containing bevacizumab may present a better choice in patients with *EGFR*/*ALK* gene negative or unknown status.[9]

In addition, previous studies have shown that penetration of cytotoxic agents and humanized monoclonal antibodies to the blood brain barrier is low,[20,21] thus data of efficacy of bevacizumab in patients with brain metastases (BM) is lacking. Our study demonstrated a higher DCR in the B+ group of patients with BM than in the non-B group. The median PFS of BM patients in the B+ group was not reached, and progression was only observed in two patients, which suggests the acceptable efficacy of bevacizumab in NSCLC patients with BM. However, further studies including BM patients are needed. In regard to AEs and tolerability, bevacizumab was used with caution in patients with ECOG PS ≥ 1. A significantly longer median PFS in patients with ECOG PS 1–2 was observed in the B+ group, which suggests bevacizumab has a tolerable safety profile.

 

**Table 5** Adverse events

| Type of AE | AE grade | Total report | B+ | Non-B | *P* |
|---|---|---|---|---|---|
| Total | ≥ 3 | 39 | 16 | 23 | |
| Anemia | 1 | 7 | 2 | 5 | 0.4535 |
| | 2 | 9 | 2 | 7 | |
| | 3 | 3 | 2 | 1 | |
| White blood cell count decreased | 1 | 7 | 4 | 3 | 0.0541 |
| | 2 | 8 | 0 | 8 | |
| | 3 | 12 | 6 | 6 | |
| Neutrophil count decreased | 1 | 12 | 4 | 8 | 0.4550 |
| | 2 | 10 | 4 | 6 | |
| | 3 | 11 | 3 | 8 | |
| | 4 | 2 | 2 | 0 | |
| Platelet count decreased | 1 | 5 | 2 | 3 | 0.3846 |
| | 2 | 4 | 3 | 1 | |
| | 3 | 1 | 1 | 0 | |
| | 4 | 2 | 0 | 2 | |
| Leukomonocyte count decreased | 1 | 1 | 1 | 0 | 0.7138 |
| | 2 | 2 | 1 | 1 | |
| Nausea | 1 | 43 | 19 | 24 | 0.1162 |
| | 2 | 10 | 1 | 9 | |
| Vomiting | 1 | 17 | 7 | 10 | 0.1662 |
| | 2 | 9 | 1 | 8 | |
| Mucositis oral | 1 | 1 | 0 | 1 | 1.0000 |
| | 2 | 2 | 1 | 1 | |
| Loss of appetite | 1 | 46 | 18 | 28 | 0.2206 |
| | 2 | 8 | 1 | 7 | |
| | 3 | 1 | 0 | 1 | |
| Diarrhea | 1 | 2 | 0 | 2 | 0.5108 |
| | 2 | 1 | 0 | 1 | |
| Rash | 1 | 2 | 0 | 2 | 0.7608 |
| | 2 | 2 | 1 | 1 | |
| Constipation | 1 | 4 | 1 | 3 | 0.6413 |
| ALT increased | 1 | 3 | 1 | 2 | 0.7501 |
| | 2 | 1 | 0 | 1 | |
| AST increased | 1 | 2 | 0 | 2 | 0.5108 |
| GGT increased | 1 | 2 | 2 | 0 | 0.1715 |
| | 3 | 1 | 0 | 1 | |
| ALP increased | 1 | 1 | 0 | 1 | 1.0000 |

AE, adverse events; GGT, gamma-glutamyl transferase.

Although pemetrexed plus platinum is the traditional standard regimen for first-line treatment of NS-NSCLC, the concomitant chemotherapy regimens used in previous studies were mainly carboplatin/cisplatin plus paclitaxel, or gemcitabine plus cisplatin.[22,23] Several studies have explored the efficacy of pemetrexed-based chemotherapy plus bevacizumab.[24–26] The PointBreak study was the first to compare pemetrexed/carboplatin plus bevacizumab with paclitaxel/carboplatin plus bevacizumab in patients with advanced NSCLC, and demonstrated a significant difference in PFS between the two arms (6.0 vs. 5.6 months, respectively), but not in OS.[27] In our study, most patients received pemetrexed-based therapy, which reflects real world clinical practice. The improved PFS, ORR, and DCR may be attributed to the use of pemetrexed, but further clinical trials and real world data are required to confirm our results.

The safety profile was acceptable in both groups. The percentage of ≥ grade 3 AEs was 16/62 in the B+ and 23/87 in the non-B groups, illustrating that a regimen containing bevacizumab may not cause further AEs. No unexpected findings were observed. In general, the addition of bevacizumab was well tolerated. Bevacizumab did not increase the incidence of myelosuppression, diarrhea, nausea, vomiting, mucositis, or liver dysfunction relative to chemotherapy or TKI alone. Epistaxis and hypertension have been observed in other clinical trials of bevacizumab.[6–9] These events were also observed in this study, but were minor in severity and did not require discontinuation of bevacizumab. Other mechanism-based AEs observed in clinical trials, including proteinuria, gastrointestinal perforation, and thromboembolic events, were not observed in this study, which may be attributed to good performance status (ECOG PS ≤ 1 accounted for 98.4% and 97.7% in the B+ and non-B groups, respectively).[6–9]

There are a number of advantages of our study. The data used is relatively new, which may reflect current medical practice. We also included elderly patients, and patients with ECOG PS > 1 and BM, which are usually excluded from prospective clinical trials. Nevertheless, our study has several limitations, including its single-center, retrospective design. The higher PFS observed in the B+ group may have resulted from the selection of patients without cardiovascular disease, or less cerebral metastasis. Our sample of patients with ECOG PS 2 was small, and may have influenced our results regarding the tolerability of chemotherapy and bevacizumab.

Based on this retrospective analysis, a regimen containing bevacizumab is an effective first-line strategy for patients with advanced NS-NSCLC, yielding improved PFS, ORR and DCR, particularly in driver gene negative or unknown patients, with tolerable and manageable AEs.

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## Disclosure

No authors report any conflict of interest.

  

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