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ORIGINAL RESEARCH

Lenvatinib Monotherapy Versus Lenvatinib in Combination with PD-1 Blockades as Re-Challenging Treatment for Patients with Metastatic Osteosarcoma: A Real-World Study

Guohui Song[1,2,*], Qinglian Tang[1,2,*], Jinchang Lu[1,2,*], Huaiyuan Xu[1,2], Anqi Wang[1,2], Chuangzhong Deng[1,2], Hao Wu[1,2], Jinxin Hu[1,2], Xiaojun Zhu[1,2], Jin Wang[1,2]

[1]Department of Musculoskeletal Oncology, Sun Yat-Sen University Cancer Center, Guangzhou, 510060, People's Republic of China; [2]State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, Guangzhou, 510060, People's Republic of China

*These authors contributed equally to this work

Correspondence: Jin Wang; Xiaojun Zhu, Department of Musculoskeletal Oncology, Sun Yat-Sen University Cancer Center 651 Dongfeng East Road, Yuexiu District, Guangzhou, 510060, People's Republic of China, Tel +86-20-87340519, Email wangjinr@sysucc.org.cn; zhuxj@sysucc.org.cn

Purpose: To explore the efficacy and safety of lenvatinib, either as a monotherapy or in combination with programmed death-1 (PD-1) blockades, as re-challenging treatment in patients with metastatic osteosarcoma following treatment failure with previous tyrosine kinase inhibitors (TKIs).

Patients and Methods: We retrospectively reviewed the data of 26 patients with metastatic osteosarcoma who received rechallenge treatment with lenvatinib monotherapy or lenvatinib plus PD-1 blockades after failure of the initial TKI treatment from January 2020 to June 2024 in our center. The primary endpoint was progression-free survival (PFS). Secondary endpoints included objective response rate (ORR), clinical benefit rate (CBR), and safety.

Results: Of the 26 patients, ORR and CBR were 11.5% and 61.5%, respectively. The median duration of follow-up was 15 months (range, 4.3–25.6) with a median PFS of 7.2 months (95% CI: 1.9–12.5). A total of 14 patients received lenvatinib as a monotherapy, and 12 received a combination therapy of lenvatinib and PD-1 blockade. No significant differences were observed in ORR (0 vs 25%) and CBR (57.1 vs 66.7%) between the two groups. Additionally, the combination cohort exhibited a significantly longer PFS compared to the monotherapy cohort (8.6 [95% CI: 5.0–12.1] vs 4.0 months [95% CI: 1.0–7.0], $p = 0.022$). 96.2% of patients experienced grade 1 or more adverse events (AEs). Grade 3 adverse events occurred in 6 (23.1%) patients. The safety profiles of the lenvatinib and PD-1 blockade combination group were found to be comparable to those of the lenvatinib monotherapy group.

Conclusion: Our data indicated that patients with metastatic osteosarcoma could potentially benefit from lenvatinib rechallenge after progress with initial TKI treatment. The combination of lenvatinib and PD-1 blockade therapy demonstrated promising survival outcomes in patients with metastatic osteosarcoma, accompanied by a manageable toxicity profile.

Keywords: metastatic osteosarcoma, tyrosine kinase inhibitor, lenvatinib, PD-1 blockades, rechallenge

Introduction

Osteosarcoma (OS) is the most prevalent primary malignant tumor of the bone. It primarily affects children and adolescents, with an additional peak in incidence observed in adults over the age of 50.[1] The current treatment regimen for osteosarcoma includes a combination of surgical intervention and intensive multi-agent chemotherapy. Since the introduction of chemotherapy, the five-year survival rate for OS patients has increased to approximately 60–75%. However, it is crucial to recognize that 30–35% of patients with osteosarcoma experience pulmonary metastasis and relapse, which are linked to considerably poorer outcomes.[2] The treatment options available for patients with metastatic osteosarcoma who experience

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disease progression following first-line chemotherapy are currently limited. The effectiveness of second-line chemotherapy in osteosarcoma is linked to an expected PFS rate of only 12% over a four-month period.[3] This situation contributes to an overall five-year survival rate of approximately 20% in patients with metastatic osteosarcoma. Therefore, there is an urgent need for the development of new therapeutic strategies to enhance patient outcomes.

Tyrosine kinase inhibitors (TKIs) have revolutionized cancer treatment in recent years, and has become the main therapeutic alternative for patients with refractory sarcoma that fail to benefit from surgery or chemotherapy. Several TKIs, such as anlotinib, apatinib, regorafenib, pazopanib, sorafenib, cabozantinib, and sunitinib, have demonstrated both preclinical and clinical efficacy in the treatment of osteosarcoma.[4] These agents have been associated with an extension of PFS in patients experiencing progressive relapsed osteosarcoma, with median PFS reported between 3.4 and 6.7 months.[5] Nevertheless, some patients develop resistance to TKI therapy after initial remission and there are currently no validated treatment options beyond clinical trials. Therefore, treatment of osteosarcoma after failure of initial TKI therapy remains a considerable therapeutic challenge. Recent literature reports suggested that multi-targeted TKIs rechallenge can be a successful approach for individuals with advanced tumors who have no approved second-line or later treatment options, although their availability for sarcoma is limited to the clinical trials or "off-label".[6,7]

Lenvatinib, an orally administered inhibitor of various receptor tyrosine kinases including PDGFR-α, VEGFRs 1–3, RET, FGFRs 1–4, and KIT signaling pathways, has demonstrated efficacy in suppressing tumor growth, inhibiting angiogenesis, and modulating immune responses in a variety of cancer types.[8] A growing body of small retrospective studies and case reports indicates that lenvatinib rechallenge may be an efficacious strategy for select patients with advanced malignancies.[6,9] Lenvatinib is the latest medication added to the treatment options for tyrosine kinase inhibitors trialed in osteosarcoma. A Phase I/II study evaluating single-agent lenvatinib in 31 children and young adults with osteosarcoma has demonstrated a response rate of 6.7% and a median progression-free survival of 3 months.[10] Another study involving 35 patients with relapsed osteosarcoma examined the combination of lenvatinib with etoposide and ifosfamide, which resulted in a PFS of 51% at 4 months.[11] Preclinical studies utilizing murine tumor models indicated that pretreatment with lenvatinib reduced the presence of immunosuppressive tumor-associated macrophages and enhanced the infiltration of CD8+T cells, and activates NK cells. This resulted in a notably improved antitumor response compared to anti–PD-1 treatment alone.[12] Recent clinical trials evaluating the combination of lenvatinib and PD-1 blockade have shown encouraging antitumor activity in patients with advanced tumors, including osteosarcoma.[13,14] However, data regarding the use of lenvatinib rechallenge, with or without PD-1 blockades in patients with metastatic osteosarcoma remains unclear and little is known about its impact on patients' outcome, especially in the real-world setting.[5,6,8,15]

This retrospective study aims to summarize the real-world experiences of rechallenging patients with metastatic osteosarcoma using lenvatinib, either as monotherapy or in combination with PD-1 blockade, following the failure of previous TKI treatments. The objective is to evaluate the efficacy of lenvatinib and explore potential treatment options for this patient population.

Patients and Methods

Patients and Study Design

This study was a retrospective, single-center analysis conducted in a real-world setting to evaluate the efficacy and safety of lenvatinib, both as a monotherapy and in combination with PD-1 blockade, in patients diagnosed with metastatic osteosarcoma between January 2020 and June 2024. Ethical approval for this study was granted by the Ethics Board at Sun Yat-sen University Cancer Center. Informed consent from patients was exempted by the ethical review board. To safeguard patient privacy and maintain data confidentiality, all collected information is securely stored within an encrypted database. Access to this data is restricted to authorized personnel only. This study was conducted in alignment with the Declaration of Helsinki and adheres to rigorous legal and ethical standards for data protection.

To obtain more robust data, specific eligibility criteria were carefully implemented to ensure an accurate assessment of the efficacy and safety of lenvatinib, either as a monotherapy or in combination with PD-1 blockades, for patients with metastatic osteosarcoma. The inclusion criteria comprised patients with histologically confirmed high grade osteosarcoma, metastatic tumor lesions that were not suitable for curative treatment, at least one evaluable lesion as defined by

RECIST 1.1, history of surgical interventions, previous chemotherapy failure, and those who had received a minimum of one cycle of lenvatinib, either as a monotherapy or in combination with PD-1 blockades, following the failure of initial tyrosine kinase inhibitor therapy. Patients were excluded from the study if they received a combination of heterogeneous therapies or had incomplete medical data. We conducted a review of the treatment history of patients using our hospital's medical records system to identify individuals who fulfilled the inclusion criteria, while excluding those who met the exclusion criteria. The gathered data comprised patient demographics, diagnosis information, treatment methods, follow-up outcomes, and any complications or side effects encountered. A total of 26 patients with a history of treated metastatic osteosarcoma were deemed eligible for inclusion in this study. Patients were categorized into two groups: the monotherapy group, which included those receiving lenvatinib as a monotherapy, and the combination group, which comprised patients treated with lenvatinib in conjunction with a PD-1 blockade.

Treatment

The initial dosage of lenvatinib was determined according to the patient's body weight: individuals weighing less than 60 kg were administered 8 mg once daily, whereas those weighing more than 60 kg received 12 mg once daily. Additionally, the discontinuation, suspension, and dosage adjustments of lenvatinib were allowable in response to disease progression or the occurrence of adverse events.

The decision to administer PD-1 blockades was made by physicians following a comprehensive assessment of the patient's condition. The PD-1 blockades, including camrelizumab (Jiangsu Hengrui Pharmaceutical Co., Ltd)., tislelizumab (BeiGene, Ltd)., and sintilimab (Innovent Biopharmaceuticals (Suzhou) Co., Ltd)., were administered via intravenous infusion at a dosage of 200 mg every three weeks.

Treatment Evaluation

Criteria for assessing treatment response were based on the Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1. CT assessment of lung lesions was conducted prior to and following the administration of lenvatinib, along with CT or MRI evaluations of target lesions in other anatomical locations. CT or MRI images were reviewed and interpreted by qualified radiologists and surgeons who were not informed of the clinical outcomes. Target lesion assessments were conducted every two treatment cycles or as necessary, particularly in instances where the patient's condition showed signs of deterioration. The primary endpoint was the PFS, which was calculated by tracking all patients starting lenvatinib treatment until they reached disease progression or death from any cause. Secondary endpoints included ORR, CBR, OS, and safety. The outcomes of ORR, CBR, PFS, and OS were further analyzed in patient subgroups to assess the efficacy of lenvatinib monotherapy compared to the combination of lenvatinib and PD-1 blockade therapy. ORR was calculated by adding the rates of confirmed complete response (CR) and partial response (PR). At least 6 weeks are required for stable disease (SD). Clinical benefit rate (CBR) was defined as the percentage of patients who had complete response, partial response, or stable disease. The overall survival (OS) refers to the time from lenvatinib initiation to death from any cause. Safety was evaluated by AEs utilizing the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.3.

Statistical Analysis

Continuous variables were represented by the mean and standard deviation for normally distributed data, or by the median and interquartile range for skewed distributed data. Categorical variables were presented as counts and percentages. Between-group comparisons of normally distributed continuous variables were conducted using Student's *t*-test, while skewed continuous variables were assessed using the Mann–Whitney *U*-test. Comparisons of categorical variables between groups were analyzed using Chi-square tests or Fisher's exact tests as appropriate. OS and PFS were estimated using the Kaplan-Meier method, and curves were compared using a Log rank test. A two-sided $p<0.05$ was considered statistically significant. Results were presented in hazard ratio (HR) with a 95% confidence interval (CI). The SPSS software (version 26.0) was used for statistical analysis.

Results

Patient Characteristics

A total of 26 eligible patients were enrolled in this study. The median age of the participants was 18 years, with an age range of 12 to 51 years. Among the patients, 20 (76.9%) were male, and 12 patients (46.2%) had an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 to 1. All patients presented with metastatic lesions, with 20 patients (76.9%) exhibiting single lung metastasis and 6 patients (23.1%) demonstrating multiple organ metastasis. Prior to receiving TKI treatment, all patients underwent first-line chemotherapy, with six patients having received at least two lines of chemotherapy. Before the commencement of lenvatinib treatment, 14 patients (53.8%) had received immunotherapy. Among the 26 patients, 14 (53.8%) were administered lenvatinib as a monotherapy, while 12 (46.2%) received a combination therapy of lenvatinib and PD-1 blockade. Within the cohort receiving combination therapy, the PD-1 agents utilized included camrelizumab in 10 patients (83.4%), tislelizumab in 1 patient (8.3%), and sintilimab in 1 patient (8.3%). The baseline characteristics of the two patient groups are presented in Table 1. The groups were well balanced for baseline characteristics.

Table 1 Baseline Characteristics of All Patients

	Total (n=26)	**Monotherapy Group (n=14)**	**Combination Group (n=12)**	***P* value**
Age (years)				–
Median	18	17	21	
Range	12–51	12–51	12–45	
Sex				1
Male	20 (76.9)	11(78.6)	9(75.0)	
Female	6(23.1)	3(21.4)	3(25.0)	
ECOG performance status				0.716
0–1	12(46.2)	6(42.9)	6(50.0)	
≥2	14(53.8)	8(57.1)	6(50.0)	
Primary tumor site				0.789
femur	16(61.5)	8(57.1)	8(66.6)	
tibia	5(19.2)	3(21.4)	2(16.7)	
humerus	4(15.4)	2(14.2)	2(16.7)	
fibula	1(3.9)	1(7.1)	0(0)	
Distant metastases				0.652
Lung only	20 (76.9)	10(71.4)	10(83.3)	
Multiple organs	6(23.1)	4(28.6)	2(16.7)	
Radiotherapy history				1
Yes	2(7.7)	1(7.1)	1(8.3)	
No	24(92.3)	13(92.9)	11(91.7)	

(*Continued*)

Table 1 (Continued).

	Total (n=26)	Monotherapy Group (n=14)	Combination Group (n=12)	*P* value
Treatment lines of prior chemotherapy				0.365
1	20 (76.9)	12(85.7)	8(66.7)	
≥2	6(23.1)	2(14.3)	4(33.3)	
Immunotherapy history				0.671
Yes	14(53.8)	7(50)	7(58.3)	
No	12(46.2)	7(50)	5(41.7)	
Prior TKI				0.701
Anlotinib	16(61.5)	8(57.1)	8(66.7)	
Apatinib	10(38.5)	6(42.9)	4(33.3)	
Reason for prior TKI treatment discontinuation				0.791
Progression or death	20(76.9)	10(71.4)	10(83.4)	
Toxicity	2(7.7)	1(7.1)	1(8.3)	
Other/unknown	4(15.4)	3(21.5)	1(8.3)	

Note: Data were expressed as n (%).
Abbreviations: ECOG, Eastern Cooperative Oncology Group; TKI, tyrosine kinase inhibitor.

Efficacy of Initial TKI Therapy

Before the initiation of lenvatinib treatment, all patients had undergone prior therapy with a tyrosine kinase inhibitor (TKI). Specifically, anlotinib was administered to 61.5% of the patients, while apatinib was given to 38.5%. No patients achieved a complete response. One patient treated with anlotinib experienced a partial response, and 15 patients exhibited stable disease, resulting in a clinical benefit rate of 61.5% (Table 2). The estimated median PFS from the commencement of initial TKI therapy was 5 months (95% CI: 1.3–8.7), with patients receiving anlotinib demonstrating comparable median PFS to those treated with apatinib (5.0[95% CI: 1.1–8.9] vs 4.0[95% CI: 0.0–11.4]months, $p = 0.271$) (Figure 1). The reasons for discontinuing initial TKI treatment were as follows: disease progression (n=20, 76.9%), adverse events (n=2, 7.7%), and other/unknown reasons (n=4, 15.4%).

Efficacy of Lenvatinib Rechallenge

At the time of data cutoff, the median follow-up period for all patients was 15 months (range, 4.3–25.6), and no patient was lost to follow-up. Out of the 26 patients, none achieved CR, while 3 patients (11.5%) demonstrated PR. Additionally,

Table 2 Responses to Anlotinib or Apatinib According to the RECIST Criteria

	No. of patients	PR No.	SD No.	PD No.	ORR (%)	CBR (%)
Anlotinib	16	1	9	6	6.3	62.5
Apatinib	10	0	6	4	0	60
Total	26	1	15	10	3.8	61.5

Abbreviations: PR, partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate; CBR, clinical benefit rate.

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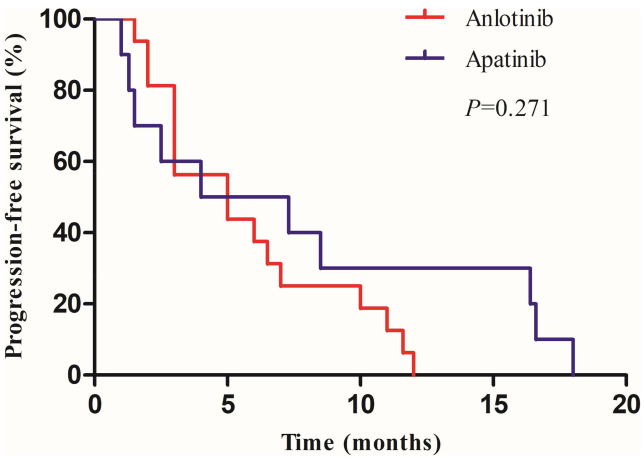

Figure 1 Kaplan-Meier curves illustrating progression-free survival for the anlotinib and apatinib groups.

13 patients (50.0%) experienced SD, and 10 patients (38.5%) had PD. The ORR and CBR were 11.5% and 61.5%, respectively. At the time of the data cutoff, overall survival (OS) data were still developing, with recorded fatalities in a total of 6 patients, representing 23.1%. The median PFS was 7.2 months (95% CI: 1. 9–12.5), while the median OS was not reached.

Of the 14 patients who underwent lenvatinib monotherapy, no patient achieved PR, 8 patients maintained SD, and 6 had PD. The ORR and CBR were 0 and 57.1%, respectively. With regard to the 12 patients who underwent lenvatinib and PD-1 blockade combination therapy, 3 patients achieved PR, 5 patients maintained SD, and 4 had PD. The ORR and CBR were 25% and 66.7%, respectively (Table 3). No statistical difference existed in the ORR and CBR between the two groups. Furthermore, the combination cohort demonstrated a substantially longer median PFS compared to the monotherapy cohort, with durations of 8.6 (95% CI: 5.0–12.2) versus 4.0 (95% CI: 1.0–7.0) months, respectively (p = 0.022) (Figure 2).

Safety

Treatment with lenvatinib was generally well tolerated (Table 4), 25 (96.2%) of 26 patients experienced grade 1 or more AEs. The treatment-related adverse events (TRAEs) caused dose reduction in 4 patients (15.4%), treatment suspension in

Table 3 Responses of Lenvatinib Rechallenge

	Total (n=26)	Monotherapy Group (n=14)	Combination Group (n=12)	P value
CR	0	0	0	
PR	3(11.5)	0	3(25.0)	
SD	13(50.0)	8(57.1)	5(41.7)	
PD	10(38.5)	6(42.9)	4(33.3)	
ORR	3(11.5)	0	3(25.0)	0.085
CBR	16(61.5)	8(57.1)	8(66.7)	0.701

Note: Data were expressed as n (%).
Abbreviations: PR, partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate; CBR, clinical benefit rate.

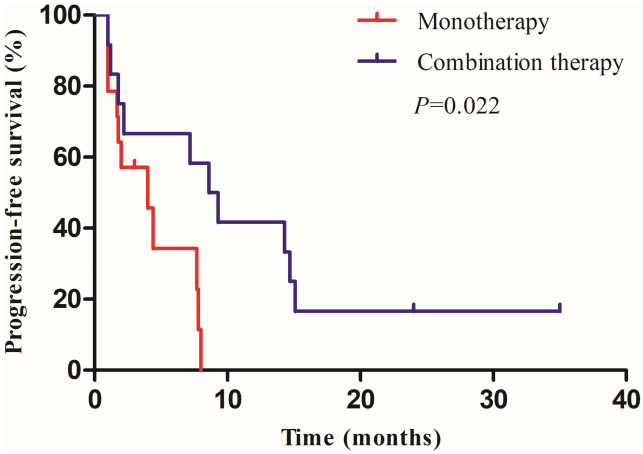

Figure 2 Kaplan-Meier curves illustrating progression-free survival for the groups receiving lenvatinib monotherapy and the combination therapy of lenvatinib with PD-1 blockades.

1 patients (3.8%), and permanent termination of treatment in 1 patients (3.8%). The TRAEs of grade 1–2 that occurred in more than 20% of patients were fatigue (14, 53.8%), hypertension (9, 34.6%), proteinuria (8, 30.8%), hand-foot syndrome (8, 30.8%), diarrhea (7, 26.9%), and nausea or vomiting (6, 23.1%). The grade 3 AEs were not frequent following hypertension (4, 15.4%), pneumothorax (1, 3.8%), and immune-related pneumonia (1, 3.8%). The safety profiles of the lenvatinib and PD-1 blockade combination group were found to be comparable to those of the lenvatinib monotherapy group. No drug-related deaths or Grade 4 AEs were observed among the patients.

Table 4 Summary of Treatment-Related Adverse Events in All Patients

	Total(n=26)			Monotherapy Group (n=14)			Combination Group (n=12)		
	Any Grade	Grade1/2	Grade3	Any Grade	Grade1/2	Grade3	Any Grade	Grade1/2	Grade3
Fatigue	14(53.8)	14(53.8)	0	8(57.1)	8(57.1)	0	6(50.0)	6(50.0)	0
Hypertension	13(50.0)	9(34.6)	4(15.4)	6(42.8)	5(35.7)	1(7.1)	7(58.3)	4(33.3)	3(33.3)
Proteinuria	8(30.8)	8(30.8)	0	3(21.4)	3(21.4)	0	5(41.7)	5(41.7)	0
Hand-foot syndrome	8(30.8)	8(30.8)	0	4(28.6)	4(28.6)	0	4(33.3)	4(33.3)	0
Diarrhea	7(26.9)	7(26.9)	0	4(28.6)	4(28.6)	0	3(25)	3(25)	0
Nausea or vomiting	6(23.1)	6(23.1)	0	3(21.4)	3(21.4)	0	3(25.0)	3(25.0)	0
Hypothyroidism	5(19.2)	5(19.2)	0	3(21.4)	3(21.4)	0	2(16.7)	2(16.7)	0
Elevated gamma glutamyltransferase	3(11.5)	3(11.5)	0	2(14.3)	2(14.3)	0	1(8.3)	1(8.3)	0
AST increased	2(7.7)	2(7.7)	0	1(7.1)	1(7.1)	0	1(8.3)	1(8.3)	0
Haematuria	1(3.8)	1(3.8)	0	0	0	0	1(8.3)	1(8.3)	0
pneumothorax	1(3.8)	0	1(3.8)	0	0	0	1(8.3)	0	1(8.3)
Immune-related pneumonia	1(3.8)	0	1(3.8)	0	0	0	1(8.3)	0	1(8.3)

Note: Data were expressed as n (%).

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Discussion

In recent years, an increased number of literatures have reported the efficacy of TKIs rechallenge treatment in patients with solid tumors.[16–19] A randomized Phase II trial assessed the efficacy and safety of regorafenib in patients with metastatic non-adipocytic STS who were previously treated with both chemotherapy and pazopanib, and observed a significant PFS benefit of regorafenib compared with placebo (m-PFS 2.1 versus 1.1 months, respectively).[20] A retrospective study also suggested that multi-targeted TKI rechallenge may offer potential clinical benefits for advanced soft tissue sarcoma patients previously treated with TKIs, with a median PFS of 3.3 months and a median OS of 11.7 months.[7] In this study, we found that after the failure of initial TKI treatment, 61.5% of patients with metastatic osteosarcoma could still achieve clinical benefit from the treatment with lenvatinib (monotherapy and combination therapy), with a median PFS of 7.2 months. As a result of these findings, rechallenge with TKIs may prove valuable in the management of refractory osteosarcoma. To the best of our knowledge, this is the first report evaluating potential treatment options involving rechallenge with lenvatinib for metastatic osteosarcoma patients after the development of refractoriness to initial TKI treatment.

A Phase I/II study evaluated the efficacy of single-agent lenvatinib in young adults with osteosarcoma, revealing a median PFS of 3.0 months and an ORR of 6.7% (ITCC-050).[10] In our current analysis, the median PFS for lenvatinib monotherapy remained comparable; however, the ORR was reported as 0%. The increased ORR observed in the ITCC-050 trial is believed to be linked to distinct patient characteristics, particularly as only 12.9% of patients in that study had previously received anti-VEGF therapy. In addition, the ITCC-050 trial enrolled patients with a good performance status, while in the current study, patients with a poor performance status were not excluded. Patients in the study were heavily pre-treated and had already received multiple lines of chemotherapy and TKIs.

It is encouraging that the combination of lenvatinib with PD-1 blockade showed promising antitumour activity with longer PFS than lenvatinib monotherapy in this study (8.6 vs 4.0 months). A unique biological mechanism of action may explain effectiveness of lenvatinib as a combination therapy for various indications. It has been shown in a growing number of preclinical studies that lenvatinib treatment reduces the proportion of monocytes and macrophages, enhances the infiltration of CD8+T cells, and activates NK cells, transforming the naturally immunosuppressive environment of tumors into a condition that boosts the immune system, supporting the use of lenvatinib in combination with immunotherapy.[8,12,21] The inhibition of angiogenesis by lenvatinib results in normalization of tumor vasculature, increasing chemotherapy delivery and uptake.[22] An anti-tumor study using lenvatinib and etoposide and ifosfamide showed promising results in osteosarcoma patients, with m-PFS reported in 8.7 months.[11] These results suggest that lenvatinib combined with immune checkpoint inhibitors or chemotherapy may provide potential clinical value to the management of refractory osteosarcoma.

The occurrence of adverse events (AEs) in our study was relatively high; however, the majority of these events were manageable. The combined therapy did not lead to a significant increase in the incidence or severity of adverse events compared to lenvatinib alone. Additionally, the most frequently observed treatment-related adverse events associated with the combination of lenvatinib and PD-1 blockade included fatigue, hypertension, hand-foot syndrome, diarrhea, proteinuria and hypothyroidism, which align with the established adverse events of each individual agent. The treatments were well tolerated, with no drug-related deaths or 4 AEs. In alignment with our findings, a systematic review has demonstrated that the combination of lenvatinib and pembrolizumab exhibits a comparable safety profile to that of lenvatinib or pembrolizumab when administered individually.[14] Additionally, certain drug-related adverse events may serve as indicators of a positive treatment response in patients with cancer.[23] Therefore, it is important to manage patients experiencing these events appropriately and to encourage them to continue their treatment, as these events may be predictive of their response to therapy.

The present study had several shortcomings. First, most of the data regarding the efficacy and toxicity of rechallenge therapy are based on arbitrary records at the discretion of the primary. Therefore, the variance of the data should be considered. Additionally, the relatively small sample size led to selection bias and the analysis of predictors of efficacy and toxicity of rechallenge therapy was not possible.

Conclusion

Our findings suggest that patients with metastatic osteosarcoma might benefit from lenvatinib rechallenge after prior TKI therapy failed. The combination of lenvatinib and PD-1 blockade therapy demonstrated promising survival outcomes in patients with metastatic osteosarcoma, accompanied by a manageable toxicity profile. However, its specific clinical application strategy, applicable population and anti-tumor mechanism need to be further explored.

Data Sharing Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Patient Consent and Ethics Approval

The need for patient informed consent was waivered due to the retrospective nature of the study, and ethical approval was obtained from the ethics committee of our hospital.

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Disclosure

There is no conflict of interest.

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