

Lenvatinib in Combination with PD-1 Blockades as Re-Challenging Treatment for Patients with Metastatic Soft Tissue Sarcoma Following TKI Treatment Failure: A Retrospective Study

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Background: Previous research has demonstrated the effectiveness of lenvatinib and programmed death-1 (PD-1) blockades in the treatment of sarcoma. However, there is limited information regarding the efficacy and safety of combining lenvatinib with PD-1 blockades as a re-challenge therapy in patients with metastatic soft tissue sarcoma (STS) following prior treatment failure with tyrosine kinase inhibitors (TKIs).

Methods: Between October 2019 and September 2024, 28 patients with metastatic STS who received rechallenge treatment with lenvatinib in combination with PD-1 blockades following progression on prior TKI treatment were included in this retrospective analysis. The primary endpoint was progression-free survival (PFS). Secondary endpoints included objective response rate (ORR), clinical benefit rate (CBR), overall survival (OS), and safety.

Results: Of the 28 patients, ORR and CBR were 0 and 64.3%, respectively. The median duration of follow-up was 26 months (range, 13.2–38.8). The median PFS was 4.8 months (95% CI: 2.7–6.9), while the median OS was 23 months (95% CI: 16.5–29.5). Approximately 96.4% of patients experienced adverse events of grade 1 or higher. Grade 3 adverse events were reported in 5 patients, accounting for 17.9%.

Conclusion: Our findings indicate that patients with metastatic STS may potentially benefit from the combination of lenvatinib and PD-1 blockades following the failure of prior TKI therapy. The combination of lenvatinib and PD-1 blockade therapy showed encouraging survival results in patients with metastatic STS, with an acceptable and manageable safety profile.

Keywords: metastatic soft tissue sarcoma, tyrosine kinase inhibitor, lenvatinib, PD-1 blockades, rechallenge

Introduction

Soft tissue sarcoma (STS) is a collection of rare mesenchymal tumors representing approximately 1% of adult malignancies and encompasses more than 70 distinct histological subtypes.^{1,2} Surgery remains the standard primary treatment for most patients with localized soft tissue sarcoma.³ However, despite comprehensive management, approximately 25% of patients diagnosed with high-risk soft tissue sarcomas subsequently develop metastatic disease.⁴ Patients with metastatic disease are generally treated with anthracycline-based chemotherapy, which typically results in a poor median progression-free survival of 4.2 months.^{5–7} Currently, therapeutic options for patients with metastatic soft tissue

sarcomas who experience disease progression after first-line chemotherapy are quite limited.^{8–10} Therefore, the development of innovative treatment approaches is essential to improve the prognosis for patients with soft tissue sarcoma.

For patients with metastatic soft tissue sarcomas that fail to benefit from surgical or chemotherapeutic interventions, tyrosine kinase inhibitors (TKIs) have emerged as a significant treatment option.^{11,12} An increasing number of TKIs have demonstrated favorable clinical efficacy in patients with specific histological subtypes of advanced soft tissue sarcoma.¹³ However, the development of drug resistance is a common challenge during TKIs therapy, and the limited number of treatment options available to overcome such resistance has negatively impacted the overall survival of sarcoma patients.¹⁴ Currently, no validated treatments exist outside of clinical trial settings. Recent literature reports indicate that rechallenge with multi-targeted TKIs may be a viable approach for patients with advanced tumors who have exhausted approved second-line or subsequent treatment options.^{15,16} However, their use in sarcoma patients is currently limited to clinical trials or off-label applications.

Lenvatinib is an orally administered tyrosine kinase inhibitor that selectively targets PDGFR- α , VEGFRs 1–3, RET, FGFRs 1–4, and KIT.¹⁷ An increasing body of research indicates that rechallenging with lenvatinib may serve as a viable treatment option for selected patients with advanced malignancies, including sarcoma.^{18–20} A Phase I dose-escalation studies have demonstrated disease stabilization in some patients with leiomyosarcoma treated with lenvatinib.²¹ A Phase Ib/II clinical study evaluating the combination of lenvatinib and eribulin was conducted in patients with leiomyosarcoma and liposarcoma.²² The study reported an objective response rate of 19% in the leiomyosarcoma cohort and 20% in the liposarcoma cohort, with a median progression-free survival of 8.56 months.

Immune checkpoint inhibitors (ICIs) targeting programmed death-1 (PD-1) have demonstrated notable success in the treatment of solid tumours, leading to further investigation into their potential role in sarcoma management.²³ The specific efficacy of immunotherapy has been observed in certain selected histological subtypes. PD-1 blockades have demonstrated promising results in cases of alveolar soft part sarcoma (ASPS), undifferentiated pleomorphic sarcomas, malignant rhabdoid tumours, and angiosarcoma.²⁴ A systematic review and meta-analysis of clinical trials evaluating ICIs for soft tissue sarcomas indicates that, with ICI monotherapy, the overall objective response rate (ORR) was 16%, and the disease control rate (DCR) was 64%. Compared to monotherapy, combination treatment demonstrates improved efficacy, particularly when incorporating PD-1 blockades and TKIs, which achieves an objective response rate of 28%.²⁵ This indicates that immune checkpoint inhibitors, particularly when combined with tyrosine kinase inhibitors, offer significant therapeutic benefits in the treatment of soft tissue sarcomas.

Preclinical studies using murine tumor models demonstrated that pretreatment with lenvatinib reduces the presence of immunosuppressive tumor-associated macrophages, enhances the activation of cytotoxic T cells, stimulates interferon- γ signaling, and exhibits synergistic effects when combined with PD-1 inhibition.^{26,27} Recent clinical trials assessing the combination of lenvatinib and PD-1 blockades have demonstrated sustained responses in patients with sarcoma.²⁸ This study identified evidence of activity for lenvatinib and pembrolizumab in synovial sarcoma, MPNST, and osteosarcoma. The overall response rate was 15.2%. Treatment-related adverse events of any grade were observed in 98% of patients, with 57% experiencing Grade 3 or higher events. However, the data concerning the use of lenvatinib in combination with PD-1 blockades for patients with soft tissue sarcoma who have experienced failure of TKI therapy remains limited, and there is insufficient information regarding its effects on patient outcomes, particularly in real-world clinical practice. This retrospective study aims to evaluate real-world experiences with reinitiating lenvatinib in combination with PD-1 blockades in patients with metastatic soft tissue sarcoma following the failure of prior tyrosine kinase inhibitor therapies.

Patients and Methods

Patients and Study Design

This retrospective, single-center study was conducted in a real-world clinical setting to assess the efficacy and safety of lenvatinib in combination with PD-1 blockades in patients with soft tissue sarcoma who have experienced progression following TKIs therapy between October 2019 and September 2024. The inclusion criteria were as follows: (1) histologically-confirmed STS; (2) metastatic tumor lesions unsuitable for curative treatment; (3) at least one measurable lesion in accordance with RECIST 1.1 criteria; (4) A minimum of one treatment cycle with lenvatinib in combination

with PD-1 blockades, following the failure of initial tyrosine kinase inhibitor therapy. Patients were excluded from the study if they received treatment with lenvatinib in combination with PD-1 blockades alongside other concurrent therapies, or if their medical records were incomplete. We reviewed patients' treatment histories within our hospital's electronic medical records system to identify individuals who meet the inclusion criteria and to exclude those who meet the exclusion criteria.

This study was conducted in accordance with the Declaration of Helsinki and complies with all applicable legal and ethical data protection standards. Ethical approval for this study was obtained from the Ethics Board at Sun Yat-sen University Cancer Center. The ethics review committee granted an exemption from obtaining informed consent from the patients.

Treatment

All patients underwent a minimum of one treatment cycle combining lenvatinib with PD-1 blockades. The initial dose of lenvatinib was prescribed based on patient body weight: patients weighing less than 60 kg received 8 mg once daily, while those weighing more than 60 kg received 12 mg once daily. The discontinuation, suspension, and dosage modifications of lenvatinib were permissible in response to disease progression or the occurrence of adverse events. Simultaneously, PD-1 blockades, including camrelizumab (Jiangsu Hengrui Pharmaceutical Co., Ltd.) and sintilimab (Innovent Biopharmaceuticals (Suzhou) Co., Ltd), were administered intravenously at a dose of 200 mg every three weeks. Both sintilimab and camrelizumab have been approved and launched in China. As domestically produced PD-1 inhibitors, they are extensively utilised in immunotherapy for a range of tumours.^{29–32} Both medications are included under medical insurance coverage. Each patient received one of these two medications, with the selection made by the clinician based on medication availability and the patient's overall condition. Only two patients received sintilimab, while the remaining 26 patients were treated with camrelizumab. Treatment was continued until disease progression, development of unacceptable toxicity, or patient or physician decision to discontinue.

Treatment Evaluation

Treatment response was evaluated in accordance with the Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1, utilizing CT or MRI imaging every two treatment cycles or as clinically indicated. The primary endpoint was PFS, defined as the duration from the initiation of lenvatinib in combination with PD-1 blockades therapy to the occurrence of disease progression or death from any cause. Secondary endpoints included ORR, CBR, OS, and safety. The ORR was determined by summing the rates of confirmed CR and PR. A minimum duration of six weeks is required to be classified as SD. The CBR was defined as the proportion of patients achieving complete response, partial response, or stable disease. OS is defined as the duration from the initiation of lenvatinib combined with PD-1 blockades to the time of death from any cause. Safety assessments were conducted by AEs using the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.3.

Statistical Analysis

The GraphPad Prism version 8.0 and SPSS software (version 26.0) were used for statistical analysis. The Kaplan–Meier method was employed to generate the PFS and OS curves. Univariate analyses were conducted using Cox proportional hazards regression models. Statistical significance was defined as a p-value less than 0.05. Results were expressed as hazard ratios (HR) with 95% confidence intervals (CI).

Results

Patient Characteristics

As detailed in [Table 1](#), a total of 28 eligible patients with metastatic STS were enrolled between October 2019 and September 2024, with a median age of 46 years (range: 16 to 72 years). Of the patients, 14 (50%) identified as male, and 13 patients (46.4%) had an Eastern Cooperative Oncology Group (ECOG) performance status score ranging from 0 to 1. There were five patients diagnosed with malignant peripheral nerve sheath tumor (MPNST), five with alveolar soft part

Table 1 Baseline Characteristics of All Patients

Characteristics	N=28
Age (years)	
Median	46
Range	16-72
Sex	
Male	14(50%)
Female	14(50%)
ECOG performance status	
0–1	13(46.4%)
≥2	15(53.6%)
Histology	
Malignant peripheral nerve sheath tumor	5(17.9%)
Alveolar soft part sarcoma	5(17.9%)
Fibrosarcoma	3(10.7%)
Synovial sarcoma	2(7.1%)
Dedifferentiated liposarcoma	2(7.1%)
Clear cell sarcoma	2(7.1%)
Undifferentiated pleomorphic sarcoma	2(7.1%)
Leiomyosarcoma	1(3.6%)
Desmoplastic small round cell tumor	1(3.6%)
Alveolar rhabdomyosarcoma	1(3.6%)
Epithelioid sarcoma	1(3.6%)
Angiosarcoma	1(3.6%)
Unclassified sarcoma	2(7.1%)
Surgery history	
Yes	28(100%)
No	0
Distant metastases	
Lung only	6(21.4%)
Multiple organs	22(78.6%)
Radiotherapy history	
Yes	8(28.6%)
No	20(71.4%)

(Continued)

Table 1 (Continued).

Characteristics	N=28
Treatment lines of prior chemotherapy	
0	5(17.9%)
1	11(39.3%)
≥2	12(42.8%)
Immunotherapy history	
Yes	23(82.1%)
No	5(17.9%)
No. of prior TKIs	
1	18(64.3%)
2	9(32.1%)
3	1(3.6%)
Reason for prior TKI treatment discontinuation	
Progression	26(92.8%)
Toxicity	1(3.6%)
Other/unknown	1(3.6%)

Note: Data were expressed as n (%).

Abbreviations: ECOG, Eastern Cooperative Oncology Group; TKI, tyrosine kinase inhibitor.

sarcoma (ASPS), three with fibrosarcoma (FS), two with synovial sarcoma (SS), two with dedifferentiated liposarcoma (DDLp), two with clear cell sarcoma (CCS), two with undifferentiated pleomorphic sarcoma (UPS), and seven patients with other subtypes. All patients displayed metastatic lesions, with 6 patients (21.4%) presenting with isolated lung metastasis and 22 patients (78.6%) exhibiting metastases involving multiple organs. Prior to initiating TKI therapy, 23 patients (82.1%) had received first-line chemotherapy, and 12 patients (42.8%) had undergone a minimum of two lines of chemotherapy. 23 patients (82.1%) had received immunotherapy, including three patients who had previously undergone combined treatment with TKI and immunotherapy. Prior to initiating combination therapy with lenvatinib and PD-1 blockades, all patients had previously undergone initial TKIs treatment, including anlotinib, apatinib, and pazopanib, with 9 patients having received two or more different types of TKI therapies.

Efficacy

As of the data cutoff date, the median follow-up duration for all patients was 26 months (range: 13.2–38.8), with no patients lost to follow-up. Although none of the 28 patients achieved complete or partial responses, 18 patients maintained stable disease, resulting in a clinical benefit rate of 64.3% (five patients with ASPS, three patients with MPNST, two patients with FS, one patient with SS, one patient with DDLp, one patient with CCS, one patient with UPS, one patient with desmoplastic small round cell tumor (DSRCT), one patient with angiosarcoma (AS) (Table 2). The median PFS was 4.8 months (95% CI: 2.7–6.9), while the median OS was 23 months (95% CI: 16.5–29.5) (Figures 1 and 2). Univariate analysis was conducted to evaluate the relationship between clinical variables (including gender, age, ECOG performance status, primary site, sites of metastasis, prior radiotherapy, prior immunotherapy, and previous TKI categories) and patient outcomes within the entire cohort of 28 patients. The univariable analysis results indicated that the aforementioned variables did not have a significant impact on the progression-free survival of the combined treatment (Table 3).

Table 2 Responses of Lenvatinib and PD-I Blockade Combination Therapy

	Total (n=28)	MPNST (n=5)	ASPS (n=5)	FS (n=3)	SS (n=2)	DDLPS (n=2)	CCS (n=2)	UPS (n=2)	LMS (n=1)	DSRCT (n=1)	ARMS (n=1)	ES (n=1)	AS (n=1)	Others (n=2)
CR	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PR	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SD	18(64.3%)	3(60.0%)	5(100.0%)	2(66.7%)	1(50.0%)	1(50.0%)	1(50.0%)	1(50.0%)	0	1(100.0%)	0	0	1(100.0%)	2(100.0%)
PD	10(35.7%)	2(40.0%)	0	1(33.3%)	1(50.0%)	1(50.0%)	1(50.0%)	1(50.0%)	1(100.0%)	0	1(100.0%)	1(100.0%)	0	0
ORR	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CBR	64.3%	60.0%	100.0%	66.7%	50.0%	50.0%	50.0%	50.0%	0	100.0%	0	0	100.0%	100.0%

Note: Data were expressed as n (%).

Abbreviations: PR, partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate; CBR, clinical benefit rate; MPNST, Malignant peripheral nerve sheath tumor; ASPS, Alveolar soft part sarcoma; FS, Fibrosarcoma; SS, Synovial sarcoma; DDLPS, Dedifferentiated liposarcoma; CCS, Clear cell sarcoma; UPS, Undifferentiated pleomorphic sarcoma; LMS, Leiomyosarcoma; DSRCT, Desmoplastic small round cell tumor; ARMS, Alveolar rhabdomyosarcoma; ES, Epithelioid sarcoma; AS, angiosarcoma; Others, Unclassified sarcoma.

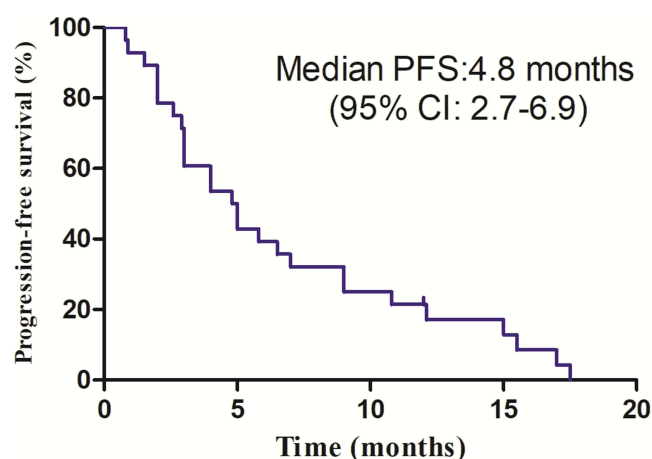


Figure 1 Kaplan-Meier estimates of progression-free survival for all the 28 patients with metastatic STS.

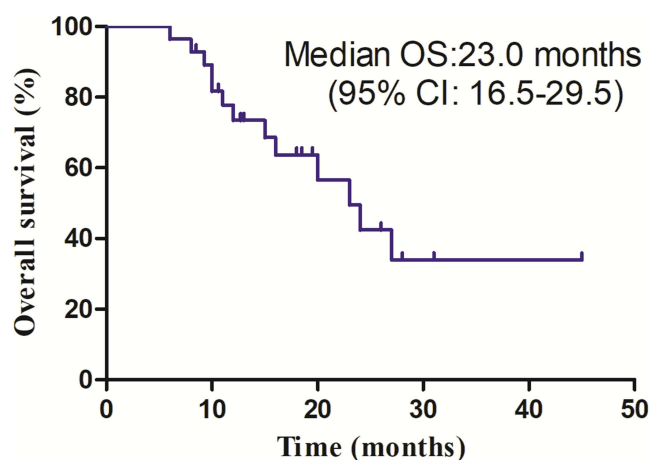


Figure 2 Kaplan-Meier estimates of overall survival for all the 28 patients with metastatic STS.

Safety

All 28 patients were included in the safety analysis, and the observed toxicities are detailed in Table 4. A total of 27 out of 28 patients (96.4%) experienced adverse events of grade 1 or higher. Treatment-related adverse events resulted in dose reductions for 5 patients (17.9%), treatment suspension for 3 patients (10.7%), and permanent discontinuation of therapy for 2 patients (7.1%). The TRAEs of grade 1–2 that occurred in more than 20% of patients were hypertension (12, 42.9%), proteinuria (12, 42.9%), fatigue (11, 39.3%), hand-foot syndrome (10, 35.7%), hypothyroidism (10, 35.7%), diarrhea (7, 25%), elevated gamma glutamyltransferase (8, 28.6%), AST increased (8, 28.6%), and nausea or vomiting (7, 25%). No grade 4 TRAEs were observed; however, 5 patients (17.9%) experienced grade 3 TRAEs, including hypertension (2 patients, 7.1%), diarrhea (1 patient, 3.6%), pneumothorax (1 patient, 3.6%), and immune-related pneumonia (1 patient, 3.6%).

Discussion

For the majority of soft tissue sarcoma subtypes, palliative anthracycline-based chemotherapy, alone or in combination with other cytotoxic agents, is currently considered the standard first-line treatment for patients with advanced or metastatic disease. However, not all patients with advanced or metastatic soft tissue sarcoma respond to conventional chemotherapy.⁵ In these instances, TKIs therapy are becoming an increasingly important treatment option, especially for

Table 3 Univariate Analyses of Factors Associated with PFS and OS

Characteristic	Category	PFS		OS	
		HR (95% CI)	P	HR (95% CI)	P
Gender	Male vs. female	1.51(0.69–3.28)	0.300	2.13(0.69–6.60)	0.188
Age	< 46 vs. ≥46 years	0.85(0.38–1.87)	0.679	1.37(0.42–4.47)	0.598
ECOG performance status	0–1 vs. 2–3	1.27(0.58–2.79)	0.541	1.01(0.34–3.02)	0.985
Primary site	Limbs vs. trunks	0.61(0.27–1.39)	0.241	0.87(0.29–2.62)	0.803
Metastasis organs	Single vs. multiple organs	0.63(0.25–1.60)	0.331	5.36(0.69–41.56)	0.108
Prior radiotherapy	Yes vs. no	0.76(0.30–1.93)	0.571	1.87(0.41–8.49)	0.418
Prior immunotherapy	Yes vs. no	0.89(0.33–2.41)	0.824	1.19(0.32–4.35)	0.797
Previous TKI categories	I vs. 2–3	1.81(0.71–4.57)	0.213	1.22(0.40–3.69)	0.729

Abbreviations: PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group.

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

	Any Grade	Grade 1/2	Grade 3
Hypertension	14(50.0)	12(42.9)	2(7.1)
Proteinuria	12(42.9)	12(42.9)	0
Fatigue	11(39.3)	11(39.3)	0
Hand-foot syndrome	10(35.7)	10(35.7)	0
Hypothyroidism	10(35.7)	10(35.7)	0
Diarrhea	8(28.6)	7(25.0)	1(3.6)
Elevated gamma glutamyltransferase	8(28.6)	8(28.6)	0
AST increased	8(28.6)	8(28.6)	0
Nausea or vomiting	7(25.0)	7(25.0)	0
Pneumothorax	4(14.3)	3(10.7)	1(3.6)
Haematuria	3(10.7)	3(10.7)	0
Immune-related pneumonia	2(7.2)	1(3.6)	1(3.6)

Note: Data were expressed as n (%).

patients who are resistant to or have not experienced satisfactory outcomes with conventional chemotherapy.¹⁰ Pazopanib has shown effectiveness in extending progression-free survival in patients with metastatic non-adipocytic soft tissue sarcoma following prior standard chemotherapy, with median PFS of 4.6 months.³³ It is the first TKI that is approved for the treatment of patients with advanced soft tissue sarcoma who have undergone prior chemotherapy. Additionally, anlotinib has received approval in China for the treatment of patients with refractory advanced soft tissue sarcoma, demonstrating a median PFS of 5.6 months.³⁴ However, the subsequent treatment after the failure of TKIs remains quite challenging.

Recent studies indicate that re-challenging with multi-targeted tyrosine kinase inhibitors can serve as an effective treatment approach for patients with sarcomas. A randomized Phase II trial showed that regorafenib has modest activity

in the treatment of patients with metastatic non-adipocytic soft tissue sarcoma who have received prior chemotherapy and pazopanib.³⁵ The observed median progression-free survival was 2.1 months. A retrospective study revealed that the median PFS for patients with advanced soft tissue sarcoma undergoing multi-targeted TKI rechallenge therapy was 3.3 months.³⁶ The immunomodulatory properties of anti-angiogenic agents indicate that combining anti-angiogenic therapy with immunotherapy may constitute an effective approach for the treatment of sarcomas.^{37,38} In this study, we observed that following failure of initial TKI therapy, 64.3% of patients with metastatic STS experienced clinical benefit from treatment with lenvatinib combined with PD-1 blockades. The median PFS was 4.8 months, and the median OS was 23 months. Based on these findings, reinitiating treatment with lenvatinib in combination with PD-1 blockades may offer a beneficial approach in managing refractory soft tissue sarcoma. To the best of our knowledge, this represents the first documented report assessing the potential efficacy of rechallenge with lenvatinib and PD-1 blockades in metastatic soft tissue sarcoma patients following the development of resistance to initial TKI therapy.

When compared to their respective monotherapies, the combination of lenvatinib and PD-1 inhibitors demonstrated enhanced antitumor activity, leading to higher objective response rates and significant improvements in survival outcomes for patients with solid tumors.³⁹ Previous studies have provided preliminary evidence suggesting the potential benefits of combining lenvatinib with PD-1 inhibitors in patients with advanced STS. A case report documents tumor regression following treatment with pembrolizumab and lenvatinib in a patient with recurrent leiomyosarcoma.⁴⁰ Sujana Movva et al subsequently documented the effectiveness of combining lenvatinib with pembrolizumab in patients with sarcoma in a prospective, open-label, single-institution, non-randomized study.²⁸ Participants in the study had not received any previous treatment with TKIs or immunomodulatory agents. This study identified evidence of activity for lenvatinib and pembrolizumab in synovial sarcoma, MPNST, and osteosarcoma. In the UPS and MPNST/synovial cohorts, the best overall response rates at 27 weeks were 25% and 30%, respectively. Additional responses were observed in angiosarcoma and UPS. The overall response rate was 15.2%. The median PFS varied from 9.8 weeks in the LMS cohort to 34 weeks in the vascular cohort. In our study, none of the 28 patients achieved complete or partial responses; however, 18 patients demonstrated stable disease. The median PFS was 4.8 months, while the median OS was 23 months. The reduction in ORR may be attributable to multiple factors. First, in our study, all patients had previously experienced failure with TKIs therapy prior to receiving lenvatinib and PD-1 blockades, and 80% of the cohort had also undergone immunotherapy with PD-1 blockades. Second, in the present study, patients with diminished performance status were included; notably, those with an ECOG score of 2 or higher comprised 53.6% of the study population. Third, the initial dosage of lenvatinib in our study was set at a lower level, determined based on the patient's body weight: either 8 mg or 12 mg once daily. Finally, our study encompassed a broader range of histological subtypes, including five cases of ASPS and 3 cases of fibrosarcoma. The antitumour efficacy of TKI rechallenge remains poorly understood. One potential explanation is the variation in targets and affinities among multi-targeted TKIs.

The occurrence of adverse events observed in our study was noteworthy; however, the majority of these events were manageable, consistent with previously reported data for the combination. A systematic review has confirmed the safety and efficacy of pembrolizumab in combination with lenvatinib for patients with advanced solid tumors.³⁹ The combination therapy has demonstrated greater effectiveness compared to pembrolizumab or lenvatinib monotherapy across multiple cancer types, with manageable adverse effects.

The present study has some limitations. First, this study is retrospective and involves a limited sample size, which may introduce selection bias. Additionally, this study does not include a control group, which limits the ability to directly compare the efficacy of lenvatinib combined with PD-1 blockades to that of each monotherapy individually. Nonetheless, this study remains a valuable reference for future research.

Conclusion

Our findings indicate that patients with metastatic STS may potentially benefit from the combination of lenvatinib and PD-1 blockades following the failure of prior TKI therapy. The effectiveness of this combination treatment in STS patients with resistance to TKI therapies warrants further investigation through larger cohort studies.

Data Sharing Statement

The data that support the findings of this study are available on request from the corresponding author Jin Wang (wangjinr@sysucc.org.cn). The data are not publicly available due to privacy or ethical restrictions.

Patient Consent and Ethics Approval

The need for patient informed consent was waived 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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