Long-Term Survival of PD-1 Inhibitor Combined with Antiangiogenic Agents in a Patient with Pulmonary Sarcomatoid Carcinoma Complicated with Esophageal Cancer: A Case Report and Literature Review

Shuyue Jiao
Henan Cancer Hospital  https://orcid.org/0000-0003-3910-5590

Xiao Zhang
Henan Cancer Hospital

Ruilin Wang
Henan Cancer Hospital

Hui Zhu
Henan Cancer Hospital

Shaomei Li
Henan Cancer Hospital

Hong Tang (✉ 852261201@qq.com)
Henan Cancer Hospital

Research Article

Keywords: pulmonary sarcomatoid carcinoma, immunotherapy, programmed death-ligand 1, antiangiogenic, case report

Posted Date: December 8th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1113754/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License.  Read Full License
Abstract

Pulmonary sarcomatoid carcinoma (PSC) is a highly aggressive rare subtype of non-small cell lung cancer (NSCLC). PSC is known for its poor prognosis and low sensitivity to conventional treatments such as chemotherapy, radiation, and adjuvant therapies. In recent years, the application of targeted therapy and immunotherapy in this field has made progress. Although programmed cell death 1 (PD-1) inhibitors have been reported to show favorable antitumor effects in PSC patients with high programmed death-ligand 1 (PD-L1) expression, the efficacy of PD-1 inhibitors in combination with antiangiogenic drugs has not been investigated. Here, we report for the first time a case of dual-source cancer with low expression of PD-L1 and microsatellite stability (MSS) which showed continuous response to sintilimab combined with anlotinib as first-line treatment and achieved a long progression free survival (PFS) of 24 months with no serious adverse reactions. This case presents a new therapeutic prospect for PSC and a potential to enhance its prognosis and treatment strategies.

Introduction

Pulmonary sarcomatoid carcinoma (PSC) is a rare subtype of non-small cell lung cancer (NSCLC), defined as poorly differentiated and accounts for 0.1-0.4% of all lung malignancies. PSC patients may benefit from surgery at early stages of the disease; however, most cases are only diagnosed at advanced stages and, therefore, denied the opportunity to undergo surgical treatment. A retrospective analysis of PSC patients (the National Cancer Database (1998-2011)) showed that 48% were stage IV cases with a median OS of 5.4 months, while the median OS was 16.9 months for stage I-II and 5.8 months for stage III patients. A number of retrospective studies have shown that PSCs are highly resistant to first-line chemotherapy agents, and therefore associated with poor prognosis. In recent years, PD-1 inhibitors have gradually become the main treatment for NSCLC, a retrospective study showed that PD-1 inhibitors alone can be beneficial for PSC as second-line or third-line treatment. However, the efficacy of PD-1 inhibitors combined with antiangiogenic agents as first-line treatment for PSC has not been proven.

We herein report for the first time (in accordance with the CARE reporting checklist) a case of dual-source cancer with low expression of PD-L1 and microsatellite stability (MSS) which showed a remarkable continuous response to sintilimab combined with anlotinib as first-line treatment. Our findings bring hope to PSC patients who cannot benefit from traditional treatments.

Case Presentation

A 69-year-old male with a long history of smoking was admitted to our hospital. Chest computed tomography (CT) scan revealed a 39*29mm mass in the left lower lobe and another 31*24mm mass near the hilum in the left lower lobe. The patients showed no obvious symptoms at the initial stage of diagnosis and did not receive any treatments prior to the protocol presented in this report. Chest positron emission tomography - computed tomography (PET-CT) revealed a 43*33mm mass in the left lower lobe and a 21*13mm mass near the hilum in the left lower lobe. CT-guided lung biopsy was conducted. Immunohistochemistry (IHC) analysis of the biopsy samples from the lung lesions revealed spindle cell malignancy of the left lung with necrosis, and sarcomatoid carcinoma was considered (Figure 1a). The final diagnosis was sarcomatoid carcinoma of the lung (cT2N2M0, cstage IIIA, UICC version 8). IHC analysis of lung tumor biopsy samples revealed less than 1% programmed death-ligand 1 (PD-L1) expression on tumor cells (clone 22C3, Dako), mis-match repair (MMR) protein detection suggested microsatellite stability (MSS) (Figure 1b, 1c), with no driver-gene mutations observed. In addition, this patient also had in-situ esophageal squamous cell carcinoma (Figure 4a, 4b). However, due to the poor prognosis of PSC and based on patient's wishes, esophageal squamous cell carcinoma was not treated. Patient's consent and cooperation, and the availability of all necessary tools and technologies created no further challenges during the completion of diagnosis or throughout the treatment.

Due to the high resistance of PSC to conventional first-line chemotherapy and the absence of target gene mutations, the patient received sintilimab (200mg/ body weight, once in every 21 days) in combination with anlotinib (12mg, once daily for 14 days followed by 7 days off). No changes in therapeutic protocol were introduced throughout the course of treatment.

After two cycles of treatment, CT results started to show significant reduction in the size of lung lesions. CT, MRI, and other examinations were performed regularly throughout the treatment to evaluate the changes. The best curative effect observed was partial response (PR), and after 24 months of treatment, a significant reduction in size was observed in both lung lesions (lower left
lung mass was reduced from 43*33mm to 13*8mm and the hilar mass was reduced from 21*13mm to 13*6mm). Improvements in the esophageal lesions were also observed (Figure 2, 3, 4c).

There were no serious adverse reactions observed during the treatment or sever discomfort/symptoms reported by the patient. As of the writing of this report, patient's progression free survival (PFS) was 24 months. In view of the good treatment effect and tolerable adverse reactions in the treatment process, the patient was very satisfied with the treatment, had a good compliance and continuously expressed his satisfaction and gratitude to the doctor.

All performed procedures which involved human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

**Discussion**

PSC is a rare type of NSCLC that contains sarcomatoid cells or sarcomatoid differentiation. According to the 2015 World Health Organization (WHO) classification, PSC can be divided into five subgroups: pleomorphic carcinoma (PC), spindle cell carcinoma (SCC), giant cell carcinoma (GCC) carcinosarcoma, and pulmonary blastoma\[^{6}\]. PSC patients are mostly middle-aged or elderly men who smoke, with no specific clinical symptoms. Most patients develop metastases at early stages and cannot be operated on, which leads to poor prognosis. In an analysis of clinical characteristics of 38 patients with PSC, median survival was 21 months, and 1-year, 3-year, and 5-year survival rates were 68.4%, 31.6%, and 18.4%, respectively\[^{7}\]. The 5-year survival rate was extremely low compared to other types of NSCLC.

Advanced PSC patients are highly resistant to first-line chemotherapy. A retrospective study showed that median PFS and median overall survival (OS) were 2.7 and 4.3 months respectively for PSC patients treated with first-line chemotherapeutic drugs\[^{8}\]. How to improve the prognosis of PSC patients is a difficult problem. At present, a variety of gene mutations have been found in PSC patients, of which EGFR, TP53, KRAS, ALK and MET are the most common. Lococo et al. analyzed mutations in 49 PSC patients and found that 39 (80%) patients had at least one mutation, and that patients with PSC mutations had a shorter survival compared to those without mutations\[^{9}\]. Another analysis showed that of 33 PSC patients, 72% had at least one genetic mutation, 58% had TP53 mutations, and 30% had KRAS mutations\[^{10}\]. Such findings can be used as a reference for targeted therapy. It has been reported that afatinib combined with crizotinib could lead to partial remission in PSC patients\[^{11}\]. Unfortunately, retrospective studies have shown that the majority of Chinese population cannot benefit from EGFR-TKI drugs due to low EGFR mutation rates. There are only few reports of the use of targeted drugs for other targets in PSC patients; therefore, the efficacy of targeted therapy in PSC patients is still largely unknown.

The rapid development of immunotherapy in recent years has changed the direction of tumor therapy. A retrospective study suggested that PD-L1 expression in PSC patients was higher than that in NSCLC patients, with a significant immune infiltration\[^{12}\]. The expression of PD-L1 in tumor tissues has become a common and preferable biomarker for predicting the efficacy of immunotherapy. The high expression of PD-L1 provides a biological basis for immunotherapy. In a report of 5 patients with advanced PSC, the response rate after immunotherapy was 80%, the median OS was between 14 and 33 months, and one patient was fully responsive\[^{13}\]. In multiple case reports, first-line immunotherapy has resulted in a variety of benefits for patients with PSC(Table 1). Registration trials of immunotherapy for PSC patients are also listed in this article (Table 2). However, in our case, PD-L1 expression was negative (TPS < 1%). In a retrospective study of 37 PSC patients treated with nivolumab as second or third line, the ORR and OS were 0% and 1.84 months in patients with negative PD-L1 expression, respectively\[^{5}\]. Considering the high resistance of PSC patients to first-line chemotherapy, the absence of EGFR, ALK and other genes’ mutations, the low expression of PD-L1, and the characteristics of MSS, we believe that the application and benefits of PD-1 inhibitor monotherapy would be limited in this case. Therefore, we adopted the treatment strategy of combination therapy to fit the specific needs of this patient.
# Table 1
Case reports of first-line treatment for pulmonary sarcomatoid carcinoma.

| First author(year)            | Number of patients | Pathological diagnosis(staging) | PD-L1 expression       | Treatment regimen                  | PFS, months | OS, months |
|-------------------------------|--------------------|---------------------------------|------------------------|------------------------------------|-------------|------------|
| Yoko Matsumoto (2017)²⁴      | 1                  | PPC, IIIB                       | PD-L1 (+), >50%        | pembrolizumab                      | 2.5+        | NA         |
| Tozuka (2018)²⁵              | 1                  | PPC, IV                         | PD-L1 (+), >50%        | pembrolizumab                      | 5           | NA         |
| Xiaofeng Li (2018)²⁶         | 1                  | PSC, IV                         | NA                     | apatinib                           | 14+         | NA         |
| Hirokazu Tokuyasu (2019)²⁷   | 1                  | PPC, IV                         | PD-L1 (+), 100%        | pembrolizumab                      | 17+         | NA         |
| Vineeth Sukrithan (2019)¹³   | 5                  | PSC                             | PD-L1 (+), >75%        | pembrolizumab                      | 11+-29+     | 14+-33+    |
| Federica D’Antonio (2019)²⁸  | 1                  | PSC, IV                         | PD-L1 (+), >50%        | pembrolizumab                      | 3           | NA         |
| Emanuela Cimpeanu (2020)²⁹   | 1                  | PSC, IIIA                       | PD-L1 (+), >50%        | pembrolizumab                      | 14+         | NA         |
| Feng-Wei Kong (2020)³⁰       | 3                  | PSC, III-IV                     | PD-L1 (+)              | nab-paclitaxel+ carboplatin+ apatinib | 6+,6+,7     | NA         |
| Fengwei Kong (2020)³¹        | 1                  | PSC, IIIB                       | PD-L1 (+)              | camrelizumab + doxorubicin         | 20+         | NA         |
| Hirokazu Taniguchi (2021)²²  | 1                  | PSC, IIIB                       | PD-L1 (+), 1%          | Pembrolizumab+ carboplatin+ pemetrexed | 3           | NA         |

OS=overall survival, PFS=progression-free survival, PSC=pulmonary sarcomatoid carcinoma, PPC=pulmonary pleomorphic carcinoma
### Table 2
The registered trials of immunotherapy therapy for PSC patients

| Identifier     | Year | Study design | Regimen                                      | Estimated enrollment | Treatment lines | Primary endpoint | Status         | Country        |
|----------------|------|--------------|----------------------------------------------|----------------------|-----------------|------------------|----------------|----------------|
| NCT02834013    | 2016 | Single-arm   | Nivolumab and Ipilimumab or nivolumab monotherapy | 818                  | 2nd line and beyond | ORR              | Recruiting     | America        |
| NCT03022500    | 2017 | Single-arm, phase II study | Durvalumab+ Tremelimumab | 18                  | 1st line and beyond | Response rate | Active, not recruiting | South Korea   |
| NCT04224337    | 2020 | Single-arm, phase II study | Durvalumab+ Doxorubicin+ ifosfamide | 34                  | 1st line and beyond | Response rate | Recruiting     | South Korea   |
| ChiCTR2000031478| 2020 | Single-arm, phase II study | Camrelizumab + Albumin-Paclitaxel and carboplatin | 15                  | 2nd line | ORR, DCR, PFS | Recruiting     | China          |
| NCT04725448    | 2021 | Single-arm, phase II study | Toripalimab + Bevacizumab, Nab-Paclitaxel + Carboplatin | 27                  | 1st line | PFS            | Recruiting     | China          |

ORR=objective response rate, DCR=disease control rate, PFS=progression-free survival.

In general, tumor growth and metastasis are dependent on neovascularization, and hypoxic-driven vascular endothelial growth factor (VEGF) is a major regulator of angiogenesis. The response to immunotherapy is associated with the immune invasion of tumor microenvironment (TME). However, VEGF blocks T cells infiltration by down-regulating lymphocytes, interferes with T cells functions, promotes myeloid-derived suppressor cell (MDSCs), induces proliferation and differentiation of regulatory T cells (Tregs), and inhibits maturation of dendritic cells (DCs) precursors, which lead to immunosuppression of the TME. Anti-angiogenic drugs can reverse the immunosuppressive effect caused by VEGF, and also normalize the tumor vascular system and promote the delivery of T cells and other immune effector molecules. On the other hand, ICIs can normalize the tumor vascular system and increase the infiltration and killing function of effector T cells by activating them. In addition, vascular normalization can improve the efficiency of drug delivery. This combination therapy form is being explored in multiple solid tumors.

Impower150 is the first phase III study of the combination of immunotherapy and anti-angiogenic agents in NSCLC. In all patients, the combination group (atezolizumab + bevacizumab + carboplatin + paclitaxel, ABCP) showed significant improvement in PFS and OS, with median PFS of 8.4 months and median OS of 19.5 months compared to 6.8 months, and 14.7 months in (bevacizumab + carboplatin + paclitaxel, BCP) group, respectively. Based on the research results of IMPower150, ABCP four-drug combination has become the first-line treatment recommendation for non-squamous NSCLC in the National Comprehensive Cancer Network guidelines of the United States. In the JVDF clinical trial, ramucirumab combined with pembrolizumab treated NSCLC with a median PFS of 9.7 months. Meanwhile, at the 2019 World Lung Cancer Congress, Professor Baohui Han reported the efficacy of...
sintilimab combined with anlotinib as first-line treatment of advanced NSCLC with negative driver genes, with an objective response rate (ORR) of 72.7%, a disease control rate (DCR) of 100%, and a median PFS of 15 months [21]. This treatment regimen has shown good results in NSCLC patients, but its application in PSC has not been reported, and, therefore, improving the prognosis of PSC is still a challenge. At this year's ASCO meeting, the IMbrave150 study published the results of first-line treatment of patients with hepatocellular carcinoma (HCC) with atezolizumab combined with bevacizumab, the median OS was 19.2 months for all patients and 24.0 months for the Chinese subpopulation[22]. In the REGONIVO study, the combination of regorafenib and nivolumab overcame the disadvantage of immunotherapy in MSS type tumors [23]. Previously, MSS-type tumors have been at a disadvantage to benefit from immunotherapy. The successful finding of REGONIVO study is believed to be that regorafenib, by blocking multiple targets, can influence immune-related mechanisms and reverse anti-tumor immune activities. Similarly, anlotinib, as a novel multi-target antiangiogenic agent, has long been approved as a third-line treatment for NSCLC. Despite the low expression of PD-L1 and the characteristics of MSS, our patient still benefited from this combination therapy. The patient's PFS reached 24 months and the esophageal lesion was improved, which far exceeded the benefits previously reported in PSC patients. Our findings present this combination therapy as a potential treatment for advanced PSC patients with negative driver-gene mutations. However, since this is the first investigation of this combination therapy in PSC, and due the inclusion of only one case in this report, future studies with larger sample sizes are needed to investigate the feasibility and efficacy of this scheme.

Combining immunotherapy with antiangiogenic agents as anti-tumor therapeutic strategy has enhanced patients’ survival in a variety of solid tumors. However, a further investigation of best drug combinations, doses, and treatment plans are still encouraged. A further consideration of improvements to increase efficacy, yet reduce toxicity and tolerance in patients is also needed in future studies. In addition, no biomarker has been found that can accurately predict the efficacy of such therapeutic combination. Such problems should be addressed and investigated to improve the application of the combination of immunotherapy and anti-angiogenic drugs.

**Conclusion**

To our knowledge, this is the first report of sintilimab and anlotinib combined therapy in a patient with PSC. Our findings revealed a long PFS of 24 months with no serious adverse reactions during treatment and showed that such therapeutic combination has synergistic anti-tumor effects. Such findings indicate greater clinical benefits for PSC patients in specific and NSCLC patients in general. Future studies with larger sample-size are still needed to further clarify the benefit and application of this combination in PSC on a larger scale; however, our findings magnify the potential to improve current treatment plans provided to PSC patients.

**Declarations**

**Acknowledgements**

The authors thank the patient for his participation in this study and for the patients' agreement to the publication of the report.

**Availability of data and material**

Not applicable.

**Author Contributions**

Shuyue Jiao and Xiao Zhang drafted the manuscript and the collation of the case. Hong Tang and Hui Zhu critically revised the paper. Ruilin Wang and Shaomei Li participated in the collection and sorting of images and the format editing of the article. All authors contributed toward data analysis, drafting and revising the paper and agree to be accountable for all aspects of the work.

**Funding**

This work was supported by the Natural Science Foundation of Henan Province (No.212300410400).

**Ethics approval**

The case report complies with the current laws of the country in which he was performed.
Informed consent

Informed consent was obtained from the patient.

Consent for publication

The patient declared to consent to the publication of the current paper.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Shum E, Stuart M, Borczuk A, et al. Recent advances in the management of pulmonary sarcomatoid carcinoma[J]. Expert Rev Respir Med, 2016, 10 (4):407-416.DOI:10.1586/17476348.2016.1157475
2. Steuer C, Behera M, Liu Y, et al. Pulmonary Sarcomatoid Carcinoma: An Analysis of the National Cancer Data Base[J]. Clin Lung Cancer, 2017, 18 (3):286-292.DOI:10.1016/j.clc.2016.11.016
3. Ung M, Rouquette I, Filleron T, et al. Characteristics and Clinical Outcomes of Sarcomatoid Carcinoma of the Lung[J]. Clin Lung Cancer, 2016, 17 (5):391-397.DOI:10.1016/j.clc.2016.03.001
4. Vieira T, Girard N, Ung M, et al. Efficacy of first-line chemotherapy in patients with advanced lung sarcomatoid carcinoma[J]. J Thorac Oncol, 2013, 8 (12):1574-7.DOI:10.1097/JTO.0000437008.00554.90
5. Domblides C, Leroy K, Monnet I, et al. Efficacy of Immune Checkpoint Inhibitors in Lung Sarcomatoid Carcinoma[J]. J Thorac Oncol, 2020, 15 (5):860-866.DOI:10.1016/j.jtho.2020.01.014
6. Chen J, He Q, Liu J, et al. CD8+ tumor-infiltrating lymphocytes as a novel prognostic biomarker in lung sarcomatoid carcinoma, a rare subtype of lung cancer[J]. Cancer Manag Res, 2018, 10:3505-3511.DOI:10.2147/CMAR.S169074
7. Li Y, Zhang L, Jiang J, et al. [Clinical Characteristics and Prognostic Analysis of 38 Patients with Pulmonary Sarcomatoid Carcinoma]. Zhongguo Fei Ai Za Zhi, 2015, 18 (9):537-42.DOI:10.3779/j.issn.1009-3419.2015.09.02
8. Sim J K, Chung S M, Choi J H, et al. Clinical and molecular characteristics of pulmonary sarcomatoid carcinoma[J]. Korean J Intern Med, 2018, 33 (4):737-744.DOI:10.3904/kjim.2017.245
9. Lococo F, Gandolfi G, Rossi G, et al. Deep Sequencing Analysis Reveals That KRAS Mutation Is a Marker of Poor Prognosis in Patients with Pulmonary Sarcomatoid Carcinoma[J]. J Thorac Oncol, 2016, 11 (8):1282-1292.DOI:10.1016/j.jtho.2016.04.020
10. Terra S B, Jang J S, Bi L, et al. Molecular characterization of pulmonary sarcomatoid carcinoma: analysis of 33 cases[J]. Mod Pathol, 2016, 29 (8):824-31.DOI:10.1038/modpathol.2016.89
11. He Q, Shi X, Zhu H, et al. A case treated with Crizotinib after secondary MET amplification of a double Rare L747S and G719S EGFR mutation Pulmonary Sarcomatoid Carcinoma[J]. Ann Oncol, 2020, 31 (4):544-546.DOI:10.1016/j.annonc.2020.01.010
12. Vieira T, Antoine M, Hamard C, et al. Sarcomatoid lung carcinomas show high levels of programmed death ligand-1 (PD-L1) and strong immune-cell infiltration by TCD3 cells and macrophages[J]. Lung Cancer, 2016, 98:51-58.DOI:10.1016/j.lungcan.2016.05.013
13. Sukrithan V, Sandler J, Gucalp R, et al. Immune Checkpoint Blockade Is Associated With Durable Responses in Pulmonary Sarcomatoid Carcinoma[J]. Clin Lung Cancer, 2019, 20 (3):e242-e246.DOI:10.1016/j.clc.2018.12.013
14. Bouzin C, Broquet A, De Vrieze J, et al. Effects of vascular endothelial growth factor on the lymphocyte-endothelium interactions: identification of caveolin-1 and nitric oxide as control points of endothelial cell anergy[J]. J Immunol, 2007, 178 (3):1505-11.DOI:10.4049/jimmunol.178.3.1505
15. Manegold C, Dingemans A C, Gray J E, et al. The Potential of Combined Immunotherapy and Antiangiogenesis for the Synergistic Treatment of Advanced NSCLC[J]. J Thorac Oncol, 2017, 12 (2):194-207.DOI:10.1016/j.jtho.2016.10.003
16. Terme M, Pernot S, Marcheteau E, et al. VEGFA-VEGFR pathway blockade inhibits tumor-induced regulatory T-cell proliferation in colorectal cancer[J]. Cancer Res, 2013, 73 (2):539-49.DOI:10.1158/0008-5472.CAN-12-2325
17. Missiaen R, Mazzone M, Bergers G. The reciprocal function and regulation of tumor vessels and immune cells offers new therapeutic opportunities in cancer[J]. Semin Cancer Biol, 2018, 52 (Pt 2):107-116. DOI:10.1016/j.semcancer.2018.06.002

18. Long J, Hu Z, Xue H, et al. Vascular endothelial growth factor (VEGF) impairs the motility and immune function of human mature dendritic cells through the VEGF receptor 2-RhoA-cofilin1 pathway[J]. Cancer Sci, 2019, 110 (8):2357-2367. DOI:10.1111/cas.14091

19. Socinski M A, Nishio M, Jotte R M, et al. IMpower150 Final Overall Survival Analyses for Atezolizumab Plus Bevacizumab and Chemotherapy in First-Line Metastatic Nonsquamous NSCLC[J]. J Thorac Oncol, 2021. DOI:10.1016/j.jtho.2021.07.009

20. Herbst R S, Arkenau H T, Santana-Davila R, et al. Ramucirumab plus pembrolizumab in patients with previously treated advanced non-small-cell lung cancer, gastro-oesophageal cancer, or urothelial carcinomas (JVDF): a multicohort, non-randomised, open-label, phase 1a/b trial[J]. Lancet Oncol, 2019, 20 (8):1109-1123. DOI:10.1016/S1470-2045(19)30458-9

21. Chu T, Zhong R, Zhong H, et al. Phase 1b Study of Sintilimab Plus Anlotinib as First-line Therapy in Patients With Advanced NSCLC[J]. J Thorac Oncol, 2021, 16 (4):643-652. DOI:10.1016/j.jtho.2020.11.026

22. Singh A, Beechinor R J, Huynh J C, et al. Immunotherapy Updates in Advanced Hepatocellular Carcinoma[J]. Cancers (Basel), 2021, 13 (9). DOI:10.3390/cancers13092164

23. Matsumoto Y, Miura T, Horiuchi H, et al. The Successful Treatment of Pulmonary Pleomorphic Carcinoma with Pembrolizumab: A Case Report[J]. Case Rep Oncol, 2017, 10 (2):752-757. DOI:10.1159/000479552

24. Fukuoka S, Hara H, Takahashi N, et al. Regorafenib Plus Nivolumab in Patients With Advanced Gastric or Colorectal Cancer: An Open-Label, Dose-Escalation, and Dose-Expansion Phase Ib Trial (REGONIVO, EPOC1603)[J]. J Clin Oncol, 2020, 38 (18):2053-2061. DOI:10.1200/JCO.19.03296

25. Tozuka T, Sugano T, Noro R, et al. Pembrolizumab-induced agranulocytosis in a pulmonary pleomorphic carcinoma patient who developed interstitial lung disease and ocular myasthenia gravis[J]. Oxf Med Case Reports, 2018, 2018 (11):omy094. DOI:10.1093/omcr/omy094

26. Li X, He Y, Zhu J, et al. Apatinib-based targeted therapy against pulmonary sarcomatoid carcinoma: a case report and literature review[J]. Oncotarget, 2018, 9 (72):33734-33738. DOI:10.18632/oncotarget.25989

27. Tokuyasu H, Ishikawa S, Sakai H, et al. Single pembrolizumab treatment causing profound durable response in a patient with pulmonary pleomorphic carcinoma[J]. Respir Med Case Rep, 2019, 28:100879. DOI:10.1016/j.rmcr.2019.100879

28. D’Antonio F, De Sanctis R, Bolengo I, et al. Pulmonary sarcomatoid carcinoma presenting both ALK rearrangement and PD-L1 high positivity: A case report on the therapeutic regimen[J]. Medicine (Baltimore), 2019, 98 (32):e16754. DOI:10.1097/MD.0000000000016754

29. Cimpeanu E, Ahmed J, Zafar W, et al. Pembrolizumab - emerging treatment of pulmonary sarcomatoid carcinoma: A case report[J]. World J Clin Cases, 2020, 8 (1):97-102. DOI:10.12998/wjcc.v8.i1.97

30. Kong F, Wang W, Liu L, et al. First-line albumin-bound paclitaxel/carboplatin plus apatinib in advanced pulmonary sarcomatoid carcinoma: A case series and review of the literature[J]. Medicine (Baltimore), 2020, 99 (23):e20667. DOI:10.1097/MD.00000000000120667

31. Kong F, Wang W, Gong L, et al. Anti-PD-1 antibody camrelizumab plus doxorubicin showed durable response in pulmonary sarcomatoid carcinoma: Case report and literature review[J]. J Clin Pharm Ther, 2020, 45 (6):1489-1496. DOI:10.1111/jcpt.13234

32. Taniguchi H, Takemoto S, Ozasa M, et al. Remarkable response to pembrolizumab with platinum-doublet in PD-L1-low pulmonary sarcomatoid carcinoma: A case report[J]. Thorac Cancer, 2021, 12 (7):1126-1130. DOI:10.1111/1759-7714.13890

Figures
Figure 1

Pathological analysis of the specimen from primary lung cancer site taken from a patient with pulmonary sarcomatoid carcinoma. (a) Hematoxylin and eosin stain, 100×. (b) Immunohistochemical examination showed that less than 1% of the tumor cells expressed PD-L1, 200×. (c) Immunohistochemical examination showed MSS, 400×.

Figure 2

Patient's treatment time-line and changes in chest computed tomography scan of the lung during the course of treatment.
Figure 3

Chest positron emission tomography - computed tomography. (a) Before treatment, an fluorodeoxyglucose-avid 43*33mm mass in the lower left lung with the maximum standardized uptake value of 10.6, and an fluorodeoxyglucose-avid 21*13mm mass near the hilum of the lower left lung with the maximum standardized uptake value of 7.4. (b) After 24 months of treatment with sintilimab combined with anlotinib, the tumor in the lower left lung was 13*8mm with the maximum standardized uptake value of 3.3, and the hilar mass in the lower left lung was 13*6mm with the maximum standardized uptake value of 4.0.

Figure 4
Esophageal squamous cell carcinoma in situ. (a) In the upper esophagus. (b) At cardia. (c) Improvements observed in esophageal lesions.