ISSN 2689-8268 | Volume 4

American Journal of Surgery and Clinical Case Reports

Research Article Open Access

# Clinical Analysis and Survival of 83 Patients with Pulmonary Sarcomatoid Carcinoma

**Hailin Liu[1,4*], Qi Li[2,4,6], Juan Pang[2,4,6], Yue Li[1,4], Zhenfa Zhang[1,4], Chenguang Li[1,4], Tingting Qin[2,5] and Changli Wang[1,4]**

[1]Department of Lung Cancer, Tianjin Medical University Cancer Institute and Hospital

[2]Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer

[3]Key Laboratory of Cancer Prevention and Therapy, Tianjin

[4]Tianjin's Clinical Research Center for Cancer

[5]Department of Thoracic Oncology, Tianjin Lung Cancer Center, Tianjin Cancer Institute and Hospital

[6]Department of Pathology, Tianjin Medical University Cancer Institute and Hospital

**[*]Corresponding author:**

Tingting Qin and Changli Wang,
Lung cancer center laboratory, 3/F, block C,
Huan-hu-xi Road, He-xi District, Tianjin 300060,
China, E-mail:shadowzlyy@163.com and
wangchangli@tjmuch.com

Received: 06 Apr 2022
Accepted: 02 May 2022
Published: 07 May 2022
J Short Name: AJSCCR

**Keywords:**

Pulmonary sarcomatoid carcinoma; EGFR mutations; Kras mutations; Tumor markers



**Citation:**

Tingting Qin and Changli Wang. Clinical Analysis and Survival of 83 Patients with Pulmonary Sarcomatoid Carcinoma. Ame J Surg Clin Case Rep. 2022; 4(13): 1-7

## 1. Abstract

Pulmonary sarcomatoid carcinoma (PSC) is a rare type of lung cancer. The objective was to collect data on the clinical characteristics, EGFR mutations, KRAS mutations, tumor markers and prognosis of patients with PSC. Eighty-three patients with PSC and 83 patients with ordinary non-small cell lung cancer (NSCLC) who were treated at the Tianjin Medical University Cancer Institute and Hospital between 2008 and 2017 underwent EGFR and Kras mutation testing. We collected data on patient sex, age, smoking history, tumor size, TNM stage, immunohistochemical results, pathohistological subtype, and survival. Of the 83 PSC patients included in this study, All of the patients underwent mutations testing, Tumor markers, including Tissue Polypeptide Specific Antigen(TSPA), Squamous Cell Carcinoma antigen(SCC), Neuron Specific Enolase (NSE), and Carcinoma Embryonic Antigen (CEA). Pulmonary sarcomatoid carcinoma is more uncommon and aggressive than ordinary non-small cell lung cancer. Smoking history is a relevant factor associated with EGFR mutations in both patients with PSC and ordinary NSCLC. In patients with ordinary NSCLC, sex and subtype were relevant factors ($p<0.0001$). TNM stage was a prognostic factor for survival, and the tumor markers TSPA, SCC, NSE, CA199 and CEA were also prognostic factors for survival. Early detection and early diagnosis are the best methods for PSC patients. Nonsmoking PSC patients with EGFR mutations may benefit from targeted therapy, and PSC patients with low levels of tumor markers have a good prognosis.

## 2. Introduction

Pulmonary sarcomatoid carcinoma (PSC) is a type of non-small cell lung cancer that includes five subtypes: pleomorphic carcinoma, spindle cell carcinoma, giant cell carcinoma, carcinosarcoma, and pulmonary blastoma [1]. Among lung cancers, PSC has a low incidence and a high degree of malignancy. Recent population-based studies in the United States revealed that 0.4% of patients with lung cancer had PSC, and in Korea, 2.35% of patients with NSCLC who underwent curative surgery had PSC [2,3]. For this reason, PSC has been rarely studied, and patients with PSC have aggressive clinical characteristics and inferior survival outcomes relative to those with other subtypes of NSCLC [4]. Regarding clinical characteristics, PSC patients often present with nonspecific symptoms, including chest discomfort, chest pain, and coughing [5]. Patients with PSC have inferior survival outcomes, and effective treatments are lacking. PSC belongs to non-small-cell lung cancer (NSCLC), and patients with ordinary NSCLC and EGFR mutations can benefit from epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs). EGFR-TKIs include FDA-approved gefitinib, erlotinib, and afatinib [6]. The recent use of targeted drugs has led to improvements in the treatment of non-small cell lung cancer, but there are no studies on whether patients with PSC can benefit from targeted therapy. Our study aimed to identify factors related to EGFR mutations in PSC patients to further guide targeted therapy. We describe 83 patients with PSC and 83 with adenocarcinoma and squamous carcinoma who were treat-

ed at the Tianjin Medical University Cancer Institute and Hospital between 2008 and 2017 and underwent EGFR mutation testing. Clinical characteristics, factors related to EGFR mutations, patient survival, and prognostic factors of this disease were reviewed.

## 3. Materials and Methods

**3.1. Patient Data**: The data on 83 patients with PSC and 83 patients with ordinary NSCLC who were treated at the Tianjin Medical University Cancer Institute and Hospital between 2008 and 2017 were analyzed, and all of the patients were tested for EGFR mutations. Pathological diagnoses were made after surgical resection (61/83) and endobronchial biopsy (22/83). There were 53 cases of pleomorphic carcinoma, 3 cases of carcinosarcoma, 8 cases of giant cell carcinoma, 2 cases of pulmonary blastoma, and 17 cases of spindle cell carcinoma. There were 33 males and 12 females aged 40~79 years. Clinical characteristics, factors related to EGFR mutations, patient survival, and prognostic factors of this disease were considered.

**3.1. EGFR Mutations were Detected**: EGFR mutations were detected in both patients with PSC and patients with ordinary NSCLC. Researchers found, in agreement with previous studies [7-9], that EGFR mutations were associated with smoking history, sex and subtype in patients with ordinary NSCLC. However, in our study, EGFR mutations were associated only with smoking history in PSC patients, as shown in table 2 (P=0.002).

**3.2. Biomarkers were Detected in PSC Patients**: Tumor markers, including TSPA, SCC, NSE, and CEA, were tested in PSC patients, and the correlations between survival and these biomarkers were studied.

**3.3. DNA Extraction**: DNA was extracted using a QIAamp FFPE DNA Extraction Kit (Qiagen, Germany 56404). After the histopathology wax block was sliced and 10 slices were placed in Eppendorf tubes, xylene was added to the tubes and incubated in a 70°C water bath for 10 minutes. The tubes were centrifuged at 14000 rpm for 1 minute, and xylene was added twice. A suitable amount of alcohol was added to elute xylene in a 70°C water bath for 10 minutes, and the tubes were centrifuged at 14000 rpm for 1 minute. The residual ethanol from xylene removal was evaporated at 70°C for 5 min to save time), and necrotic tissue was resected after the specimen was thoroughly dry. Cracking buffer (200 μL) and proteinase K (60 μL, 200 μg/mL) were added to the tubes before they were incubated in a 56°C water bath overnight. Following this step, tubes were centrifuged for 10 min at 14000 rpm, and the supernatant was absorbed. The supernatant (120 μl) was placed into a RocheLC 20, and the concentration of DNA was tested on a Nano Drop. The supernatant from the harvested DNA sample conformed to the standards OD260/OD280=1.8±0.2 and OD260/OD230 ≥1.7, and the concentration was between 20~50 ng/μL.

**3.4. Polymerase Chain Reaction (PCR) Amplification**: The EGFR mutation status was analyzed with a human EGFR gene mutation detection kit (TB004, China) following the manufacturer's instructions on a LightCycler® 480II (Roche, Switzerland) in our certified laboratory. The experiment involved a negative control (NC) and a positive control (PC). The FAM and HEX channels were amplified in PC and had a Ct value ≤28 but were not amplified in the NC, and then the experiment proceeded. The PCR conditions were as follows: initial melting at 95°C for 10 min; 40 cycles of melting at 95°C for 15 s and annealing at 60°C for 60 s. The signals were collected, and real-time quantitative PCR was performed.

**3.5. Statistical data Analysis**: The SPSS 23.0 statistical software package was used. The Kaplan-Meier method was used to analyze the data and draw the survival curve, and the log-rank test was used to determine prognostic factors in the univariate analysis. The enumeration data were analyzed with the x2 test, Differences were considered statistically significant when the P value was less than 0.05.

## 4. Results

**4.1. Patient Characteristics and Demographics**: Eighty-three PSC patients were studied. The clinicopathological characteristics of the 83 PSC patients are shown in Table 1. The patients' ages ranged from 40 to 79 years, and the median age was 62 years. In this study, 61 males and 22 females were analyzed. The median survival period was 13 months (range from 1-110 months). Fifty-nine patients were smokers, and 24 were nonsmokers. There were 53 cases of pleomorphic carcinoma, 3 cases of carcinosarcoma, 8 cases of giant cell carcinoma, 2 cases of pulmonary blastoma, and 17 cases of spindle cell carcinoma. Tumors were staged according to the eighth edition of the TNM staging system. The tumors ranged in size from 1 cm to 18 cm. We divided tumors into two size groups: T1+T2 and T3+T4. Distant metastases were present in 38 patients at the initial diagnosis. The overall staging was 30 cases of stage IV, 22 cases of stage III, 18 cases of stage II and 19 cases of stage I (Table 1). The median survival time was also statistically analyzed, as shown in Table 1. There were statistically significant associations between T stage, distant metastases and TNM with survival time, with p values of 0.008, less than 0.001, and less than 0.001.

**4.2. EGFR Mutations in Patients with PSC and Ordinary NSCLC**: Eighty-three patients with ordinary NSCLC and 83 with PSC were analyzed in our study. All patients underwent EGFR mutation testing. As shown in table 2 and table 3, smoking history, sex and subtype were associated with EGFR mutations, and there were statistically significant differences in patients with ordinary NSCLC. However, only smoking history was associated with EGFR mutations in PSC patients. Specifically 20/83 patients with ordinary NSCLC had EGFR mutations; on the other hand, 8/83 patients with PSC had EGFR mutations, which was significantly lower.

| Characteristic | Patients ( % ) | Median survival time (months) | 95% CI | P Value |
|---|---|---|---|---|
| Age | | | | 0.239 |
| ≤60 | 35 ( 42% ) | 20 | 3.77-36.23 | |
| > 60 | 48 ( 58% ) | 11 | 7.61-14.40 | |
| Smoking history | | | | 0.183 |
| Yes | 59 ( 71% ) | 18 | 9.39-26.60 | |
| No | 24 ( 29% ) | 7 | 0.99-13.00 | |
| Sex | | | | 0.254 |
| Male | 61 ( 73% ) | 18 | 9.25-26.75 | |
| Female | 22 ( 27% ) | 10 | 4.64-15.36 | |
| TNM ( biopsy result ) | | | | < 0.0001 |
| I | 19 ( 23% ) | 60 | 24.50-95.4 | |
| II | 18 ( 22% ) | 27 | 14.52-39.47 | |
| III | 22 ( 27% ) | 12 | 1.65-22.34 | |
| IV | 24 ( 28% ) | 4 | 1.31-6.68 | |
| Subtype | | | | 0.597 |
| Pleomorphic carcinoma | 53(65.2%) | 18 | 9.08-26.92 | |
| Carcinosarcoma | 3(4.5%) | 3 | | |
| Giant cell carcinoma | 8(9.0%) | 10 | 2.61-17.39 | |
| Pulmonary blastoma | 2(2.2%) | 10 | | |
| Spindle cell carcinoma | 17(19.1%) | 12 | 0.0001-27.55 | |
| Distant metastases | | | | < 0.0001 |
| M0 | 45 ( 49.4% ) | 43 | 9.75-76.25 | |
| M1 | 38 ( 50.6% ) | 6 | 3.58-8.42 | |
| T stage | | | | 0.008 |
| T1+T2 | 41 ( 49% ) | 23 | 16.73-29.27 | |
| T3+T4 | 42 ( 51% ) | 8 | 4.37-11.63 | |
| Kras mutation | 14 | 4 | 0.33-7.67 | 0.008 |
| Kras wild type | 69 | 18 | 9.86-26.14 | |

**Table 1:** Correlations between basic characteristics and overall survival.

| Characteristic | Patients ( % ) | EGFR Mutations | Wild Type | P Value |
|---|---|---|---|---|
| Age | | | | 0.37 |
| ≤60 | 38 ( 46.8% ) | 8 | 30 | |
| > 60 | 45 ( 53.2% ) | 12 | 33 | |
| Smoking history | | | | < 0.0001 |
| Yes | 54 ( 65.1% ) | 5 | 49 | |
| No | 29 ( 34.9% ) | 15 | 14 | |
| Sex | | | | < 0.0001 |
| Male | 57 ( 68.7% ) | 5 | 52 | |
| Female | 26 ( 32.3% ) | 15 | 11 | |
| TNM ( biopsy result ) | | | | 0.39 |
| I | 29 ( 34.9% ) | 8 | 21 | |
| II | 24 ( 24.1% ) | 3 | 21 | |
| III | 29 ( 34.9% ) | 9 | 20 | |
| IV | 1 ( 1.1% ) | 0 | 1 | |
| Subtype | | | | < 0.0001 |
| Adenocarcinoma | 37(44.6%) | 17 | 20 | |
| Squamous carcinoma | 46(54.4%) | 3 | 43 | |

**Table 2:** Correlations between basic characteristics and EGFR mutations in patients with ordinary NSCLC.

| Characteristic | Patients ( % ) | EGFR Mutations | Wild Type | P Value |
|---|---|---|---|---|
| Age | | | | 0.179 |
| ≤60 | 35 ( 42% ) | 2 | 33 | |
| > 60 | 48 ( 58% ) | 7 | 41 | |
| Smoking history | | | | 0.002 |
| Yes | 59 ( 71% ) | 2 | 57 | |
| No | 24 ( 29% ) | 7 | 17 | |
| Sex | | | | 0.051 |
| Male | 61 ( 73% ) | 4 | 57 | |
| Female | 22 ( 27% ) | 5 | 17 | |
| TNM ( biopsy result ) | | | | 0.126 |
| I | 19 ( 23% ) | 0 | 19 | |
| II | 18 ( 22% ) | 3 | 15 | |
| III | 22 ( 27% ) | 2 | 20 | |
| IV | 24 ( 28% ) | 4 | 20 | |
| Subtype | | | | 0.129 |
| Pleomorphic carcinoma | 53(65.2%) | 4 | 49 | |
| Carcinosarcoma | 3(4.5%) | 1 | 2 | |
| Giant cell carcinoma | 8(9.0%) | 0 | 8 | |
| Pulmonary blastoma | 2(2.2%) | 1 | 1 | |
| Spindle cell carcinoma | 17(19.1%) | 3 | 14 | |
| Distant metastases | | | | 0.164 |
| M0 | 45 ( 49.4% ) | 3 | 42 | |
| M1 | 38 ( 50.6% ) | 6 | 32 | |
| T stage | | | | 0.254 |
| T1+T2 | 41 ( 49% ) | 3 | 38 | |
| T3+T4 | 42 ( 51% ) | 6 | 36 | |

**Table 3:** Correlations between basic characteristics and EGFR mutations in PSC patients.

**4.3. Survival Analysis**: The median survival time of all patients was 13 months (range: 1-110). The 1-year survival rate was 49.40%, and the 2-, 3-, 4-, and 5-year survival rates were 13.25%, 8.43%, 12.05%, and 15.66%, respectively. Univariate analysis showed that OS was not correlated with age, sex, smoking, or subtype ($P>0.05$). Patients with a small T stage, without distant metastasis, and early TNM stage had significantly better OS ($P<0.05$). The KRAS mutation was associated with worse overall survival ($P=0.008$), as shown in Figure 1.

**4.4. High Levels of Tumor Markers Indicate a Poor Prognosis of Patients with PSC**. Tumor markers, including TSPA, SCC, NSE, and CEA, were also tested in PSC patients. High levels of CEA and NSE were significantly associated with poor OS ($P<0.001$, $P=0.013$). On the other hand, TSPA and SCC were not correlated with OS ($P>0.05$), as shown in **Figure 2**.

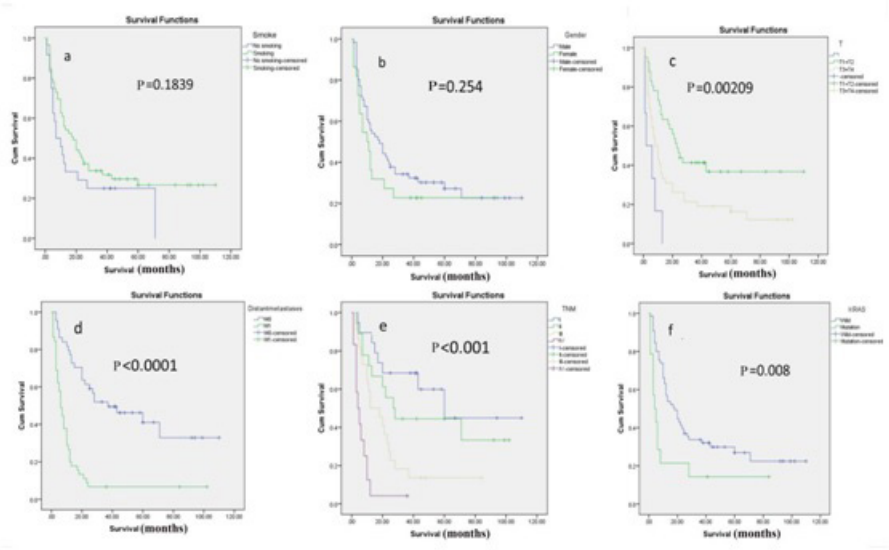


**Figure 1:** Kaplan–Meier survival curves of 83 patients. (a) There was no difference in survival between patients who smoked and did not smoke (P=0.1839). (b) There was no difference in survival between males and females (P=0.254). (c) Patients with T1 + T2 tumors had significantly better survival than patients with T3 +T4 tumors (P = 0.00209). (d) The presence of distant metastases significantly affected survival (P <0.0001). (e) Survival was significantly affected by tumor stage (P <0.0001). (f) Patients with Kras mutations experienced poor survival (P=0.008).

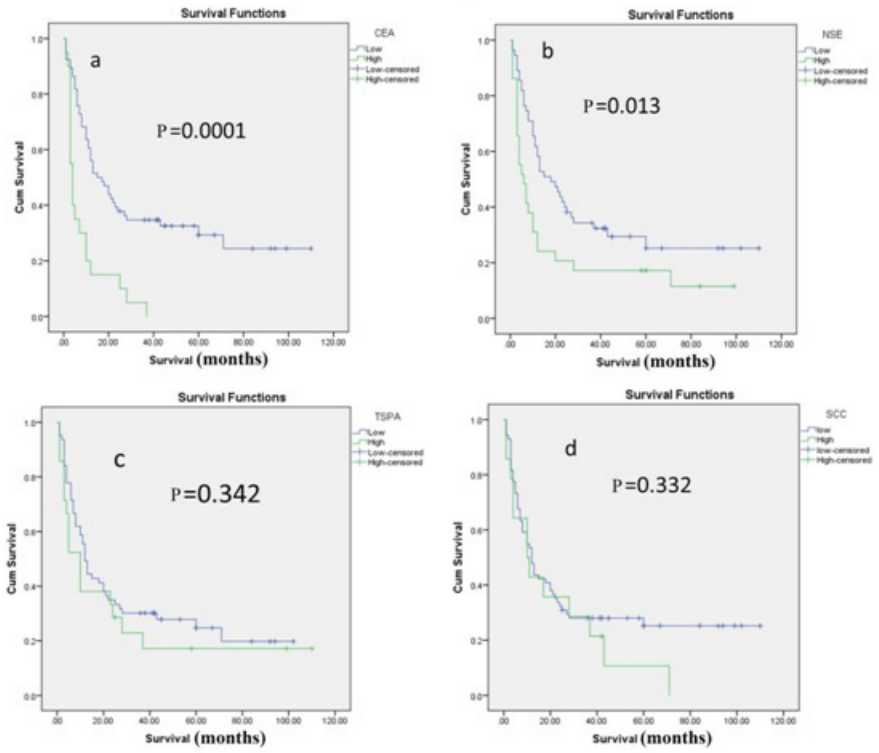


**Figure 2.** High levels of tumor markers indicate a poor prognosis. a) Correlation between the level of CEA and OS. b) Correlation between the level of NSE and OS. c) Correlation between the level of TSPA and OS. d) Correlation between the level of SCC and OS.

## 5. Discussion

Pulmonary sarcomatoid carcinoma (PSC) is a very rare and aggressive type of non-small cell lung cancer with a very poor prognosis. The disease is highly prevalent in men and smokers (approximately 71% of patients were smokers, and 73% of patients were men), similar to previous reports by Linping Gu [10] and Junna Hou [11]. The most common types are pleomorphic carcinoma (up to 65.2%), followed by spindle cell carcinoma (up to 19.1%). Other studies also demonstrated that pleomorphic carcinoma was the most common subtype. These results may be due to a pathologic definition of pleomorphic carcinoma that encompasses a very wide range of cellular components [12]. The median survival time of all patients was 13 months (range: 1-110). The 1-year survival rate was 49.40%, and the 2-, 3-, 4-, and 5-year survival rates were 13.25%, 8.43%, 12.05%, and 15.66%, respectively. The result is similar to that reported by Kunlatida Maneenil [13]. Multivariate

analysis of the prognostic factors for survival in our study revealed that the main factors affecting prognosis were T stage, M stage, TNM stage and Kras mutations. These results were similar to those of previous studies. Linda Martin et al [14] showed that T stage and N stage were prognostic factors. Lin et al [15] showed that M stage was a prognostic factor, and Mitra Mehrad et al [16] showed that the Kras mutation was a prognostic factor. Many studies have demonstrated that the EGFR pathway, K-RAS pathway, and echinoderm microtubule-associated protein-like 4-anaplastic lymphoma kinase (EML4-ALK) fusion gene play important roles in the pathogenesis of certain lung cancers [17-18], particularly in East Asian countries. In our study, no PSC patients with EGFR mutations were found to benefit from therapy. This may be due to the small number of patients. Specifically, there are fewer PSCs than ordinary NSCLCs, and few PSC patients are tested for EGFR mutations. Unlike in patients with ordinary non-small cell lung cancer, in patients with PSC, smoking was associated with EGFR mutations ($p=0.002$). Tumor markers, including TSPA, SCC, NSE, and CEA, were tested in PSC patients. High levels of CEA and NSE markers predict a poor prognosis. CEA is specific for other tumors, including adenocarcinoma, and is affected by external factors, such as smoking [19]. TSPA, SCC, CEA and NSE are considered nonspecific markers for pulmonary pleomorphic carcinoma [19]. In our study, we found that high levels of CEA and NSE predict a poor prognosis, which means that these two markers are helpful for the early diagnosis of PSC. Early detection and early diagnosis are the best methods for PSC patients. The treatment principle for pulmonary sarcomatoid carcinoma is similar to that for other non-small cell lung cancers [20]. In our study, 55 patients received surgical treatment and chemotherapy, and 27 received conventional chemotherapy. Patients who received surgery lived longer than those who did not. This result could also be explained by the fact that patients who receive surgery have lesions that are detected early and have a better chance of survival. In summary, PSC is a rare, highly malignant lung cancer. In many patients, these tumors are not detected early, leading to poor survival. An accurate and early diagnosis is urgently needed. Unlike patients with ordinary non-small cell lung cancer, patients with PSC do not benefit from targeted therapies, increasing the pressure on the clinic. We urgently need more relevant case reports to complete our work in the future.

## 6. Funding

Thanks to the Science & Technology Development Fund of Tianjin Education Commission for Higher Education [2017KJ201, Tingting Qin].

## References

1. M.B. Beasley, E. Brambilla, W.D. Travis, The 2004 World Health Organization classifification of lung tumors, Semin. Roentgenol. 2005; 40: 90-97.
2. Yendamuri S, Caty L, Pine M. Outcomes of sarcomatoid carcinoma of the lung: a Surveillance, Epidemiology, and End Results Database analysis. Surgery. 2012; 152: 397- 402.
3. Park JS, Lee Y, Han J. Clinicopathologic outcomes of curative resection for sarcomatoid carcinoma of the lung. Oncology. 2011; 81: 206-213.
4. Vieira T, Girard N, Ung M. Efficacy of first-line chemotherapy in patients with advanced lung sarcomatoid carcinoma. J Thorac Oncol. 2013; 8: 1574-1577.
5. Franks T J, Galvin J R. Sarcomatoid carcinoma of the lung: histologic criteria and common lesions in the differential diagnosis. Archives of Pathology & Laboratory Medicine. 2010; 134(1): 49-54.
6. Youngjoo Kim, Mihaela Apetri, BeiBei Luo, Jeffrey E Settleman, Karen S Anderson. Differential Effects of Tyrosine Kinase Inhibitors on Normal and Oncogenic EGFR Signaling and Downstream Effectors. Molecular Cancer Research Mcr. 2015; 13(4): 765.
7. Janne, PA, Lee JC. EGFR mutation in lung cancer: correlation with clinical response to gefitinib therapy. Science. 2004; 304(5676): 1497-1500.
8. Ren, R X , Li, J Y , Li, X F , Chen, X. Detection of epidermal growth factor receptor mutations in small specimens of non-small cell lung cancer by amplification refractory mutation system. Tumor. 2012; 32(11).
9. Zhang Y, Wang Q, Han ZG, Shan L. Differences in epidermal growth factor receptor gene mutations and relationship with clinicopathological features in NSCLC between Uygur and Han ethnic groups. Asian Pac J Cancer Prev. 2013; 14(5): 2879-83.
10. Linping Gu, Yunhua Xu, Chen Zhiwei, Pan Yan, Lu Shun. Clinical analysis of 95 cases of pulmonary sarcomatoid carcinoma. Biomedicine & Pharmacotherapy. 2015; 76: 134-40.
11. Hou J, Xing L, Yuan Y. A clinical analysis of 114 cases of sarcomatoid carcinoma of the lung. Clin Exp Med. 2018; 18(4): 555-562.
12. Sim J K , Chung S M , Choi J H. Clinical and molecular characteristics of pulmonary sarcomatoid carcinoma. Korean Journal of Internal Medicine. 2018; 33(4): 737-744.
13. Maneenil K, Xue Z, Liu M. Sarcomatoid Carcinoma of the Lung: The Mayo Clinic Experience in 127 Patients. Clin Lung Cancer. 2018; 19(3): e323-e333.
14. Martin L W, Correa A M , Ordonez N G. Sarcomatoid Carcinoma of the Lung: A Predictor of Poor Prognosis. Annals of Thoracic Surgery. 2007; 84(3): 973-980.
15. Yongbin Lin, Han Yang, Qingqing Cai. Characteristics and Prognostic Analysis of 69 Patients With Pulmonary Sarcomatoid Carcinoma. American journal of clinical oncology. 2016; 39(3): 215-22.

16. Mehrad M, Roy S, Laframboise W A. KRAS Mutation is Predictive of Outcome in Patients with Pulmonary Sarcomatoid Carcinoma. Histopathology. 2018; 73(2).
17. Zhang L, Ma S, Song X. Gefitinib versus placebo as maintenance therapy in patients with locally advanced or metastatic non-small-cell lung cancer (INFORM; C-TONG 0804): a multicentre, double-blind randomised phase 3 trial. Lancet Oncology. 2012; 13(5): 466-475.
18. Yoshida A, Tsuta K, Nakamura H. Comprehensive histologic analysis of ALK-rearranged lung carcinomas. American Journal of Surgical Pathology. 2011; 35(8): 1226-1234.
19. Ito K, Oizumi S, Fukumoto S. Clinical characteristics of pleomorphic carcinoma of the lung. Lung Cancer. 2010; 68 (2): 204-210.
20. Huang S, Shen S , Li X. Pulmonary sarcomatoid carcinoma: a clinicopathologic study and prognostic analysis of 51 cases. World Journal of Surgical Oncology. 2013; 11(1): 252.