Almonertinib as a neoadjuvant therapy for patients with a superior pulmonary sulcus tumor with activated EGFR mutation: A case report

KAI KANG*, ZHIXIAO JIANG*, JINDAN KAI, SI CHEN and FEI XIONG

Department of Thoracic Surgery, Hubei Cancer Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei 430079, P.R. China

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Abstract. A superior pulmonary sulcus tumor, also known as a Pancoast tumor, invades tissues or organs at the entrance of the thorax, such as the brachial plexus, upper ribs, vertebrae, subclavian vessels and stellate ganglia. Induction concurrent chemoradiotherapy followed by radical surgical resection is the preferred treatment. The present study reported the case of a 52-year-old male who presented at Hubei Cancer Hospital, Tongji Medical College (Wuhan, Hubei) with left chest pain and an abnormal chest computed tomography scan showing a mass of 81x43 mm in the left upper chest wall that invaded the first, second and third anterior ribs. Biopsy of the mass showed stage cT4N0M0, IIIA, poorly differentiated adenocarcinoma and epidermal growth factor receptor+. The patient was treated by induction chemotherapy and targeted therapy, which was followed by surgical resection of the left upper lobe and the affected chest wall via the transmanubrial approach. The targeted therapy with almonertinib was continued postoperatively. To date, no disease recurrence has been detected during the 4 months follow-up.

Correspondence to: Professor Jindan Kai or Ms. Si Chen, Department of Thoracic Surgery, Hubei Cancer Hospital, Tongji Medical College, Huazhong University of Science and Technology, 116 Zhuodaoquan South Road, Hongshan, Wuhan, Hubei 430079, P.R. China
E-mail: casine1018@163.com
E-mail: 530013454@qq.com

*Contributed equally

Abbreviations: CT, computed tomography; NSCLC, non-small cell lung cancer; EGFR, epidermal growth factor receptor

Key words: superior pulmonary sulcus tumor, epidermal growth factor receptor, targeted therapy, almonertinib

Introduction

It is almost 100 years since Dr Henry Pancoast first described the clinical and radiographic findings associated with superior sulcus tumors (1), which were later named after the author. Superior sulcus tumors are a relatively rare subtype of non-small cell lung cancer (NSCLC), accounting for <5% of all bronchogenic carcinomas. This tumor occurs in the apex of the upper lobe of the lung and often involves the first rib, brachial plexus, subclavian vessels, sympathetic chain, stellate ganglion or vertebrae. Clinically, a superior sulcus tumor consists of a constellation of characteristic symptoms, including arm and shoulder pain or Horner's syndrome (2,3).

In the 1930s to 1950s, superior sulcus tumors of the lung were considered inoperable and incurable and radiation therapy was predominantly used to alleviate the condition. In the 1950s, Chardack and MacCallum (4) reported the first successful surgical resection and postoperative radiotherapy for upper sulcus tumors; the patient was alive and disease-free 5 years later. In 1956, Shaw introduced a new treatment model: Preoperative radiotherapy combined with radical resection surgery. Patients receiving this treatment achieved good results (5) and within 40 years, bimodal therapy (radiotherapy plus surgery) became the standard treatment method for upper sulcus tumors (6). However, survival did not significantly improve with this treatment and the 5-year overall survival remained ~30%. Since the 1990s, increasing experience and research data in combination therapy has led to the introduction of radical surgical resection after induced chemoradiotherapy as a new treatment standard for superior sulcus tumors, with significantly improved results (7-14).

The present study reported a patient with an epidermal growth factor receptor (EGFR)-mutated superior sulcus tumor who underwent surgical resection following neoadjuvant targeted therapy and achieved good curative effect, with no recurrence to date during follow-up.

Case Report

A 52-year-old male patient was from a rural area and had a history of smoking and alcohol consumption. In the past month, he had repeatedly experienced left chest pain, which he was

able to bear most of the time, so he did not go to the hospital; occasionally, he needed to take painkillers to alleviate pain symptoms. The left chest pain had gradually worsened over the previous week, accompanied by persistent left shoulder pain. This pain prevented the patient placing their left thoracic back and shoulders on the back of a chair and the surface of a bed. Therefore, the patient sought medical treatment at the Songzi People's Hospital (Jingzhou, China) in November 2021 and the doctor prescribed non-steroidal anti-inflammatory drugs for pain relief; however, these drugs did not relieve the left chest and shoulder pain. Simultaneously, chest computed tomography (CT) examination revealed a lump in the left lung of the patient. As the exact diagnosis was unclear, the patient visited the thoracic surgery clinic of Huazhong University of Science and Technology Tongji Medical College Affiliated Hubei Cancer Hospital (Wuhan, China) in November 2021.

The patient was unable to rest flat on the ward bed upon admission and the pain was grade 4 (Pain was scored on a 0-10 numerical rating scale, ranging from 0 (no pain) to 10 (worst pain imaginable) or categorized (none, mild, moderate, severe or very severe/horrible). (15-17), with a Nutritional Risk Screening 2002 (NRS2002) score of 2 (The NRS2002 system evaluates patients based on their nutritional status and disease severity, and gives a total score of 0-6 based on whether they are absent, mild, moderate, or severe) (18). The patient had no family history of oncologic diseases. A CT scan revealed an 81x43 mm mass of the left upper chest wall, which invaded the first, second and third anterior ribs (Figs. 1 and 2A). Considering that the patient's mass was located at the left lung apex, compression of the mass itself onto the left brachial plexus might have been the cause of the severe pain. Consequently, a powerful opioid analgesic drug (morphine; initial dose 20 mg q12 h) was administered to the patient for pain relief. After maintaining the initial dose for 12 days, in order to achieve superior pain relief, the patient's daily dose of morphine was increased to 30 mg q12 h and continued to be used for ~1 month thereafter. Upon admission on November 23, 2021, blood routine and biochemical examination revealed the following: a white blood cell count of 21.2 (normal range: 4-10x10^9/l), a platelet count of 440 (normal range: 100-300x10^9/l), hemoglobin of 133 (normal range: 110-170 g/l) and carbon dioxide binding capacity 20.6 (normal range: 21-31 mmol/l). Tumor marker results showed cancer antigen 125 180 U/ml (normal range, <35 U/ml), cytokeratin 19 fragment (CYFRA 21-1) 16.79 ng/ml (normal range, <3.3 ng/ml), neuroson-specific enolase 17.53 ng/ml (normal range, 0-16.3 ng/ml), carcinoembryonic antigen 7.43 ng/ml (normal range, <5 ng/ml) and SCC 1.61 ng/ml (normal range, <2.7 ng/ml). Positron emission tomography CT revealed intense high metabolism of the mass, with a size of 83x49 mm, an 18F-fluorodeoxyglucose standard uptake value maximum of 13.75 and involvement of the left 1-3 ribs and the upper lobe of the left lung. Needle biopsy of the mass showed poorly differentiated adenocarcinoma; therefore, the patient was diagnosed with stage cT4N2M0, IIIA lung cancer and TNM classification was performed according to the criteria of the 8th edition staging of the TNM classification (19). The mutation of EGFR was detected by DNA sequencing. DNA sequencing was performed using reverse transcription-polymerase chain reaction, which was carried out by the Pathology Department of Hubei Cancer Hospital. The AmoyDx EGFR 29 Mutations Detection Kit (Amoy Diagnostics Co., Ltd.) was used. The AmoyDx EGFR 29 Mutations Detection Kit is a real-time PCR assay for qualitative detection of 29 somatic mutation in exons 18, 19, 20 and 21 of EGFR gene in human genomic DNA extracted from formalin-fixed paraffin-embedded tumor tissue. The kit adopts amplification refractory mutation system technology which comprises specific primers and fluorescent probes to detect gene mutations in reverse transcription PCR assay. During the nucleic acid amplification, the targeted mutant DNA is matched with the bases at the 3' end of the primer, amplified selectively and efficiently, then the mutant amplicon is detected by fluorescent probes labeled with fluorescein amidite. Where the wild-type DNA cannot be matched with specific primers, no amplification occurs. The kit is composed of EGFR Reaction Mix strips, EGFR Enzyme Mix (contains Taq DNA polymerase for PCR amplification and uracil-N-glycosylase which works at room temperature to prevent PCR amplicon carryover contamination) and EGFR Positive Control. The thermocycling conditions are shown in Table I. The results showed that there were exon 21 L858R and exon 20 T790M point mutations in EGFR.

Table I. Cycling parameters.

Stage	Cycles	Temperature	Time	Data collection
1	1	95˚C	5 min	/
		95˚C	25 sec	/
2	15	64˚C	20 sec	/
		72˚C	20 sec	/
		93˚C	25 sec	/
3	31	60˚C	35 sec	FAM and HEX/VIC
		72˚C	20 sec	/

FAM, fluorescein amidite.

During the period of examination following admission, the painkillers were effective, allowing the patient to briefly rest flat on the ward bed. The patient was offered targeted therapy (almonertinib; 110 mg qd) from the second neoadjuvant cycle. After 6 weeks of almonertinib targeted therapy, the patient's chest pain was significantly relieved, the tumor marker CYFRA 21-1 was 3.33 ng/ml, markedly lower than that before treatment and other lung adenocarcinoma-related tumor markers had decreased to normal ranges (Fig. 3). In addition, the blood routine test results reached normal standards: white blood cell count was 4.3 (normal range: 4-10x10^9/l), platelet count was 268 (normal range: 100-300x10^9/l) and hemoglobin was 109 (normal range: 110-170 g/l). Chest enhanced CT showed significant tumor regression compared to the chest CT results on November 22, 2021; the target lesion diameter was reduced by 36.75% (Fig. 2B). According to the Response Evaluation Criteria in Solid Tumors (RECIST) methodology, the efficacy evaluation was partial response (PR). The clinical stage reduced to stage IIB (T3N0M0) (19).

The patient underwent a thoracotomy on February 23, 2022. A combined incision of the anterolateral incision and the superior median sternotomy was used and tumor-free margins

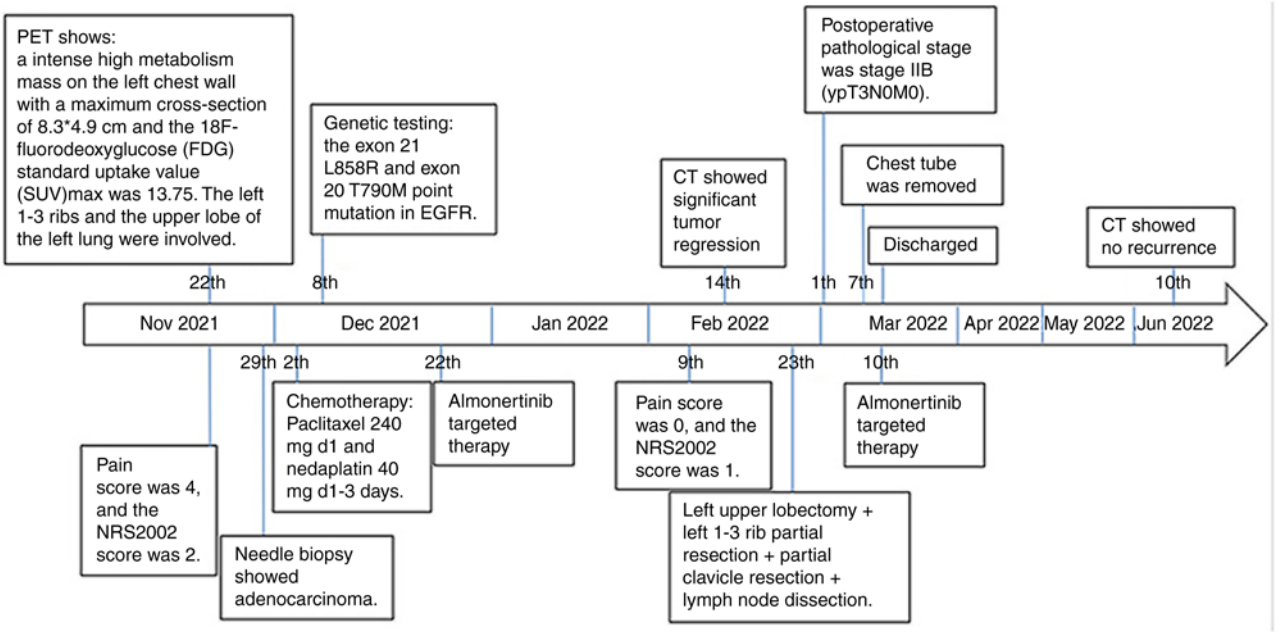


Figure 1. Timeline of clinical diagnosis and treatment process for a patient with EGFR-mutated superior sulcus tumor. EGFR, epidermal growth factor receptor; PET, positron emission tomography; CT, computed tomography.

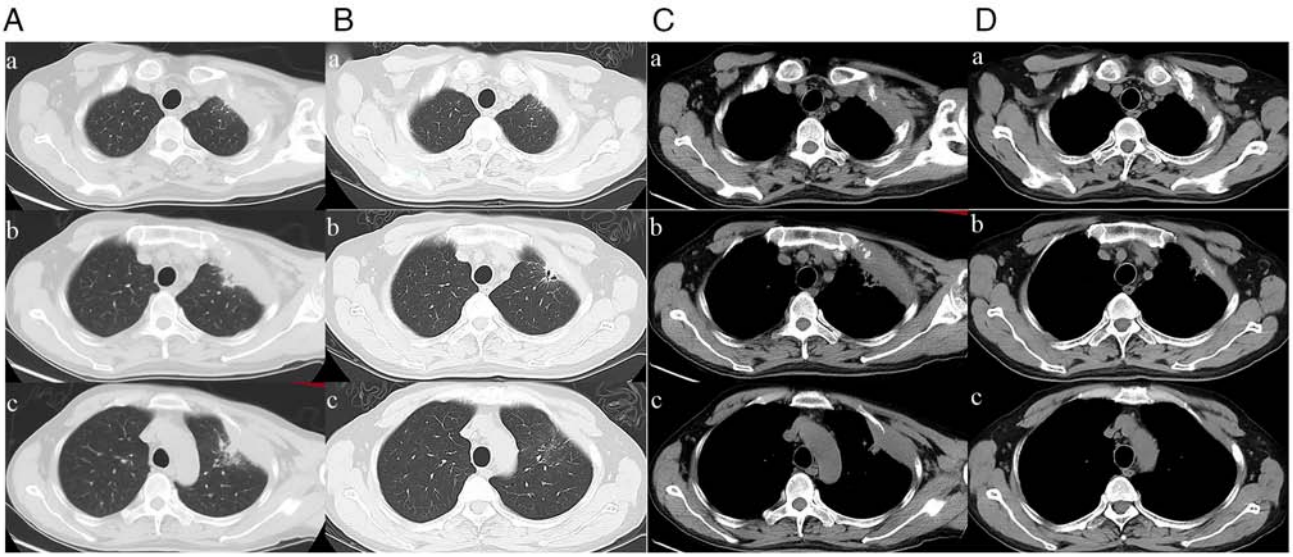
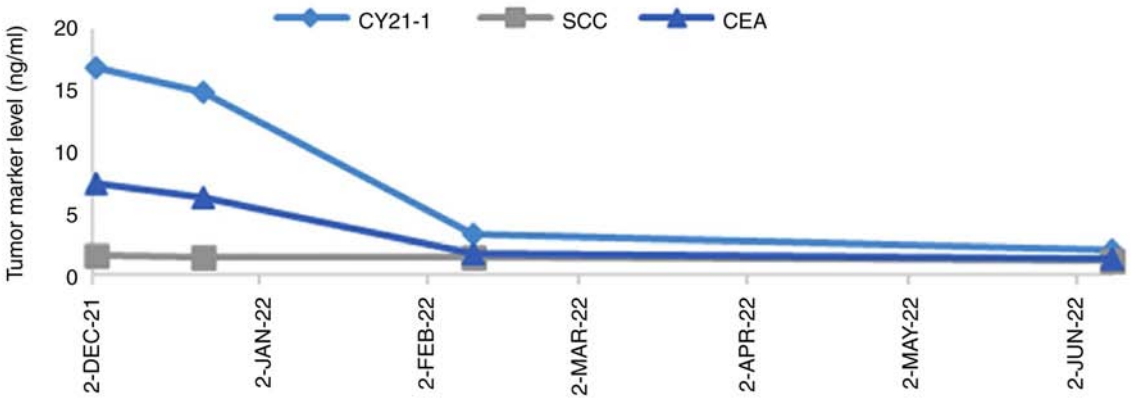


Figure 2. (A) Chest CT (pulmonary window) showed a mass in the left upper chest wall invading the (a) first, (b) second and (c) third anterior ribs. (B) On the pulmonary window, the tumor invading the (a) first, (b) second and (c) third anterior ribs was smaller after one cycle of chemotherapy plus targeted therapy, compared with the initial untreated tumor. (C) Chest CT (mediastinum window) showed a mass in the left upper chest wall invading the (a) first, (b) second and (c) third anterior ribs. (D) On the mediastinum window, the tumor invading the (a) first, (b) second and (c) third anterior ribs was smaller after one cycle of chemotherapy plus targeted therapy, compared with the initial untreated tumor. CT, computed tomography.

obtained in a section of the chest wall (ribs 1, 2 and 3), which included 1-3 parts of the anterior rib and a segment of the clavicle. Next, a lobectomy and systematic lymph node dissection was performed according to the surgical treatment principle of lung cancer. Finally, the chest wall was reconstructed with artificial mesh after placing a chest tube. The whole operation took 5 h and the intraoperative bleeding totaled ~600 ml.

Postoperative histopathological examination was carried out by the Pathology Department of Hubei Cancer Hospital, and the pathological results were moderately differentiated and invasive adenocarcinoma in the left upper lobe of the lung [large area of inflammatory and fibrotic components (83%), ~15% of tumor cells and 2% of tumor cell necrosis], with visceral pleural invasion (PL3+) and rib invasion. The lymph nodes and cutting edge were negative, that is, R0 resection. The pathological stage was ypT3N0M0, IIB (19).

The patient had postoperative chylous pleural effusion and recovered after receiving total parenteral nutrition therapy for 3 days without any serious in-hospital complications. The chest tube was removed on postoperative day 12



	2-Dec-21	22-Dec-21	10-Feb-22	8-Jun-22
CY21-1	16.79	14.75	3.33	2.05
SCC	1.61	1.45	1.44	1.2
CEA	7.43	6.34	1.7	1.27

Figure 3. The evolution of lung adenocarcinoma-related tumor markers during treatment. CYFRA21-1, cytokeratin 19 fragment; SCCAg, serum squamous cell carcinoma antigen; CEA, carcinoembryonic antigen.

and the patient was discharged 15 days after surgery. The targeted therapy with almonertinib was continued postoperatively. No disease recurrence has been detected during one year of follow-up.

Discussion

It is not satisfactory to treat superior sulcus tumors with a single form of treatment. Preoperative irradiation, which aims to shrink tumors, appears to improve tumor resectability and yields satisfactory palliative results when combined with surgical resection. In 1961, Shaw *et al* (5) first described the advantages of preoperative radiotherapy for superior sulcus tumors.

Since the 1990s, concurrent chemoradiotherapy combined with surgery has been applied to the treatment of superior sulcus tumors and a series of studies have confirmed the effectiveness of this method of treatment (10,12,20,21). The principle of adding concurrent chemotherapy on a base of preoperative radiotherapy is adding systemic treatment on a base of local treatment to control occult systemic disease and limit the risk of distant relapse (10). Induction concurrent chemoradiotherapy followed by radical surgical resection has become the current standard of care in patients with superior sulcus tumors.

The clinical stage of our patient was T4N0M0 and the radiotherapy plan could not be implemented because of the patient's pain and inability to lie down. Therefore, paclitaxel combined with platinum-based chemotherapy was administered and genetic testing performed. Considering the efficacy of chemotherapy for resectable NSCLC, the 5-year survival benefit is only 5-6% (22-24). Subsequently, targeted therapy was administered after learning of the EGFR gene mutation. After 4-8 weeks of treatment, imaging showed that this patient had a good response to treatment, with significant tumor volume reduction. This may indicate an efficacy advantage of almonertinib in the neoadjuvant phase of therapy. Likewise, the EMERGING-CTONG 1103 study (25) revealed that there is a tendency toward an improved overall response rate, lymph node step-down, major pathological response and R0 resection rate with the neoadjuvant erlotinib, in comparison with a neoadjuvant chemotherapy for patients who suffered from EGFRm NSCLC and chronic progression-free survival to a great extent. According to the indications from case reports and other reported clinical tests, EGFR-tyrosine kinase inhibitor (EGFR-TKI) therapy before surgery can achieve a certain effect for patients with resectable NSCLC (26-36), which indicates that neoadjuvant targeted therapy can also become a clinical option. Based on superior sulcus tumors exhibiting the same biological behavior as other lung cancers (37), we consider that neoadjuvant targeted therapy may be a consideration for superior sulcus tumors.

Compared with the efficacy of the pathologic complete response (pCR) obtained after neoadjuvant immunotherapy combined with chemotherapy reported in Tang *et al* (38), our patient still had viable tumor cells after neoadjuvant targeted therapy. However, the small proportion of tumor cells and the large number of inflammatory responses suggest that our neoadjuvant targeted therapy is effective. Furthermore, it is not known whether the patient can achieve superior treatment results or even achieve pCR if the duration of preoperative induction targeted therapy is prolonged (for example, up to 8 weeks). In addition, the timing of surgery after neoadjuvant targeted therapy should be considered because it also may affect the overall oncologic outcomes (31,39). For example, in a retrospective study of patients with stage IIIa NSCLC, after preoperative EGFR-TKI neoadjuvant therapy, 1- and 3-year survival were significantly decreased in the short-delay group compared with

the long-delay group (40). However, there is no unified conclusion on the surgical intervention time of neoadjuvant targeted therapy. We consider that choosing to perform surgical intervention after 2 weeks of drug withdrawal can reduce the impact of drug side effects and increase the safety of surgery.

The present study is the first case report of neoadjuvant targeted therapy for superior sulcus tumors. In this case, almonertinib achieved good efficacy and safety and this has reference significance for guiding perioperative targeted therapy for EGFR-mutated superior sulcus tumors. In summary, the present study provided real-world evidence that neoadjuvant targeted therapy enables patients to achieve surgical R0 resection and obtain superior results. In the future, following confirmation by more studies in this field, neoadjuvant targeted therapy may become a standard treatment option for superior sulcus tumors after neoadjuvant chemoradiotherapy.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

JK and FX conceived and designed the study. SC collected data and images. KK and ZJ wrote the manuscript. KK, SC and JK confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from the patient.

Patient consent for publication

The patient provided written informed consent regarding the publication of the case details and any associated images.

Competing interests

The authors declare that they have no competing interests.

References

1. Nikolaos P, Vasilios L, Efstratios K, Panagiotis A, Christos P, Nikolaos B, Antonios H, Tsakiridis K, Zarogoulidis P, Zarogoulidis K, *et al*: Therapeutic modalities for Pancoast tumors. J Thorac Dis 6 (Suppl 1): S180-S193, 2014.
2. Detterbeck FC: Changes in the treatment of Pancoast tumors. Ann Thorac Surg 75: 1990-1997, 2003.
3. Marulli G, Battistella L, Mammana M, Calabrese F and Rea F: Superior sulcus tumors (Pancoast tumors). Ann Transl Med 4: 239, 2016.
4. Chardack WM and Maccallum JD: Pancoast tumor; five-year survival without recurrence or metastases following radical resection and postoperative irradiation. J Thorac Surg 31: 535-542, 1956.
5. Shaw RR, Paulson DL and Kee JL: Treatment of superior sulcus tumor by irradiation followed by resection. Ann Surg 154: 29-40, 1961.
6. Shaw RR: Pancoast's tumor. Ann Thorac Surg 37: 343-345, 1984.
7. Martínez-Monge R, Herreros J, Aristu JJ, Áramendía JM and Azinovic I: Combined treatment in superior sulcus tumors. Am J Clin Oncol 17: 317-322, 1994.
8. Attar S, Krasna MJ, Sonett JR, Hankins JR, Slawson RG, Suter CM and McLaughlin JS: Superior sulcus (Pancoast) tumor: Experience with 105 patients. Ann Thorac Surg 66: 193-198, 1998.
9. Barnes JB, Johnson SB, Dahiya RS, Temes RT, Herman TS and Thomas CR Jr: Concomitant weekly cisplatin and thoracic radiotherapy for Pancoast tumors of the lung: Pilot experience of the San Antonio cancer institute. Am J Clin Oncol 25: 90-92, 2002.
10. Rusch VW, Giroux DJ, Kraut MJ, Crowley J, Hazuka M, Winton T, Johnson DH, Shulman L, Shepherd F, Deschamps C, *et al*: Induction chemoradiation and surgical resection for superior sulcus non-small-cell lung carcinomas: Long-term results of Southwest oncology group trial 9416 (Intergroup Trial 0160). J Clin Oncol 25: 313-318, 2007.
11. Pourel N, Santelmo N, Naafa N, Serre A, Hilgers W, Mineur L, Molinari N and Reboul F: Concurrent cisplatin/etoposide plus 3D-conformal radiotherapy followed by surgery for stage IIB (superior sulcus T3N0)/III non-small cell lung cancer yields a high rate of pathological complete response. Eur J Cardiothorac Surg 33: 829-836, 2008.
12. Kunitoh H, Kato H, Tsuboi M, Shibata T, Asamura H, Ichinose Y, Katakami N, Nagai K, Mitsudomi T, Matsumura A, *et al*: Phase II trial of preoperative chemoradiotherapy followed by surgical resection in patients with superior sulcus non-small-cell lung cancers: Report of Japan clinical oncology group trial 9806. J Clin Oncol 26: 644-649, 2008.
13. Kappers I, Belderbos JS, Burgers JA, van Zandwijk N, Groen HJ and Klomp HM: Non-small cell lung carcinoma of the superior sulcus: Favourable outcomes of combined modality treatment in carefully selected patients. Lung Cancer 59: 385-390, 2008.
14. Albain KS, Rusch VW, Crowley JJ, Rice TW, Turrisi AT III, Weick JK, Lonchyna VA, Presant CA, McKenna RJ and Gandara DR: Concurrent cisplatin/etoposide plus chest radiotherapy followed by surgery for stages IIIA (N2) and IIIB non-small-cell lung cancer: Mature results of Southwest oncology group phase II study 8805. J Clin Oncol 13: 1880-1892, 1995.
15. Jensen MP and Karoly P: Self-report scales and procedures for assessing pain in adults. In: Turk DC, Melzack R (eds). Handbook of Pain Assessment, 2nd edn. Guilford Publications: New York: pp 15-34, 2001.
16. Kang Y and Demiris G: Self-report pain assessment tools for cognitively intact older adults: Integrative review. Int J Older People Nurs 13: e12170, 2018.
17. Simmons SF, Schnelle JF, Saraf AA, Coelho CC, Jacobsen JM, Kripalani S, Bell S, Mixon A and Vasilevskis EE: Pain and satisfaction with pain management among older patients during the transition from acute to skilled nursing care. Gerontologist 56: 1138-1145, 2016.
18. Kondrup J, Rasmussen HH, Hamberg O and Stanga Z; Ad Hoc ESPEN Working Group: Nutritional risk screening (NRS 2002): A new method based on an analysis of controlled clinical trials. Clin Nutr 22: 321-336, 2003.
19. Detterbeck FC, Boffa DJ, Kim AW and Tanoue LT: The eighth edition lung cancer stage classification. Chest 151: 193-203, 2017.
20. Felip E and Rosell R: New strategies in the treatment of resectable non-small cell lung cancer. Expert Rev Anticancer Ther 1: 224-228, 2001.
21. Waseda R, Klikovits T, Hoda MA, Hoetzenecker K, Bertoglio P, Dieckmann K, Zöchbauer-Müller S, Pirker R, Prosch H, Döme B and Klepetko W: Trimodality therapy for Pancoast tumors: T4 is not a contraindication to radical surgery. J Surg Oncol 116: 227-235, 2017.
22. Roth JA, Fossella F, Komaki R, Ryan MB, Putnam JB Jr, Lee JS, Dhingra H, De Caro L, Chasen M and McGavran M: A randomized trial comparing perioperative chemotherapy and surgery with surgery alone in resectable stage IIIA non-small-cell lung cancer. J Natl Cancer Inst 86: 673-680, 1994.

23. Rosell R, Gómez-Codina J, Camps C, Maestre J, Padille J, Cantó A, Mate JL, Li S, Roig J and Olazábal A: A randomized trial comparing preoperative chemotherapy plus surgery with surgery alone in patients with non-small-cell lung cancer. N Engl J Med 330: 153-158, 1994.
24. Pisters KM, Vallières E, Crowley JJ, Franklin WA, Bunn PA Jr, Ginsberg RJ, Putnam JB Jr, Chansky K and Gandara D: Surgery with or without preoperative paclitaxel and carboplatin in early-stage non-small-cell lung cancer: Southwest oncology group trial S9900, an intergroup, randomized, phase III trial. J Clin Oncol 28: 1843-1849, 2010.
25. Zhong WZ, Chen KN, Chen C, Gu CD, Wang J, Yang XN, Mao WM, Wang Q, Qiao GB, Cheng Y, *et al*: Erlotinib versus gemcitabine plus cisplatin as neoadjuvant treatment of stage IIIA-N2 EGFR-mutant non-small-cell lung cancer (EMERGING-CTONG 1103): A randomized phase II study. J Clin Oncol 37: 2235-2245, 2019.
26. Hishida T, Nagai K, Mitsudomi T, Yokoi K, Kondo H, Horinouchi H, Akiyama H, Nagayasu T and Tsuboi M; Japan Clinical Oncology Group: Salvage surgery for advanced non-small cell lung cancer after response to gefitinib. J Thorac Cardiovasc Surg 140: e69-e71, 2010.
27. Lara-Guerra H, Chung CT, Schwock J, Pintilie M, Hwang DM, Leighl NB, Waddell TK and Tsao MS: Histopathological and immunohistochemical features associated with clinical response to neoadjuvant gefitinib therapy in early stage non-small cell lung cancer. Lung Cancer 76: 235-241, 2012.
28. Schaake EE, Kappers I, Codrington HE, Olmos RA, Teertstra HJ, van Pel R, Burgers JA, van Tinteren H and Klomp HM: Tumor response and toxicity of neoadjuvant erlotinib in patients with early-stage non-small-cell lung cancer. J Clin Oncol 30: 2731-2738, 2012.
29. Zhong W, Yang X, Yan H, Zhang X, Su J, Chen Z, Liao R, Nie Q, Dong S, Zhou Q, *et al*: Phase II study of biomarker-guided neoadjuvant treatment strategy for IIIA-N2 non-small cell lung cancer based on epidermal growth factor receptor mutation status. J Hematol Oncol 8: 54, 2015.
30. Sun L, Guo YJ, Song J, Wang YR, Zhang SL, Huang LT, Zhao JZ, Jing W, Han CB and Ma JT: Neoadjuvant EGFR-TKI therapy for EGFR-mutant NSCLC: A systematic review and pooled analysis of five prospective clinical trials. Front Oncol 10: 586596, 2020.
31. Cansouline X, Lipan B, Sizaret D, Tallet A, Vandier C, Carmier D and Legras A: EGFR-mutant non-small-cell lung cancer at surgical stages: What is the place for tyrosine kinase inhibitors? Cancers (Basel) 14: 2257, 2022.
32. Xiong L, Lou Y, Bai H, Li R, Xia J, Fang W, Zhang J, Han-Zhang H, Lizaso A, Li B, *et al*: Efficacy of erlotinib as neoadjuvant regimen in EGFR-mutant locally advanced non-small cell lung cancer patients. J Int Med Res 48: 300060519887275, 2020.
33. Zhang Y, Fu F, Hu H, Wang S, Li Y, Hu H and Chen H: Gefitinib as neoadjuvant therapy for resectable stage II-IIIA non-small cell lung cancer: A phase II study. J Thorac Cardiovasc Surg 161: 434-442.e2, 2021.
34. Chen WQ, Li P, Wang Q, Zhang YJ, Li HY, Jin XT, Yan S, Kou GF, Cai SL and Liu G: A randomized controlled study of erlotinib versus pemetrexed combined with cisplatin in neoadjuvant therapy of stage A EGFR-mutant lung adenocarcinoma. Zhonghua Zhong Liu Za Zhi 40: 133-137, 2018 (In Chinese).
35. Liu M, Jiang G, He W, Zhang P and Song N: Surgical resection of locally advanced pulmonary adenocarcinoma after gefitinib therapy. Ann Thorac Surg 92: e11-e12, 2011.
36. Feng S, Qiang Z, Wanwan C, Zhaozhun Z, Yuewu X and Shencun F: Case report: Aumolertinib as neoadjuvant therapy for patients with unresectable Stage III non-small cell lung cancer with activated EGFR mutation: Case series. Front Oncol 12: 872225, 2022.
37. Arcasoy SM and Jett JR: Superior pulmonary sulcus tumors and Pancoast's syndrome. N Engl J Med 337: 1370-1376, 1997.
38. Tang WF, Xu W, Huang WZ, Lin GN, Zeng YM, Lin JS, Wu M, Bao H, Peng JW, Jiang HM, *et al*: Pathologic complete response after neoadjuvant tislelizumab and chemotherapy for Pancoast tumor: A case report. Thorac Cancer 12: 1256-1259, 2021.
39. Zhong WZ, Wang Q, Mao WM, Xu ST, Wu L, Wei YC, Liu YY, Chen C, Cheng Y, Yin R, *et al*: Gefitinib versus vinorelbine plus cisplatin as adjuvant treatment for stage II-IIIA (N1-N2) EGFR-mutant NSCLC: Final overall survival analysis of CTONG1104 phase III trial. J Clin Oncol 39: 713-722, 2021.
40. Rice JD, Heidel J, Trivedi JR and van Berkel VH: Optimal surgical timing after neoadjuvant therapy for Stage IIIa non-small cell lung cancer. Ann Thorac Surg 109: 842-847, 2020.