Neoadjuvant immunotherapy followed by surgery with curative intent in 35 patients with advanced NSCLC: the retrospective experiences of a multidisciplinary team

Dongjie Ma[1#], Yuan Xu[1#], Yingzhi Qin[1], Shanqing Li[1], Ji Li[2], Ying Jiang[2], Mengzhao Wang[3], Yan Xu[3], Jing Zhao[3], Minjiang Chen[3], Wuying Cheng[4], Ke Hu[5], Hongsheng Liu[1]

[1]Department of Thoracic Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China; [2]Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China; [3]Department of Respiratory and Critical Care Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China; [4]Department of Nuclear Medicine, Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China; [5]Department of Radiotherapy, Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China

Contributions: (I) Conception and design: H Liu; (II) Administrative support: Y Qin, J Li, Y Jiang, W Cheng, K Hu; (III) Provision of study materials or patients: S Li, M Wang, Y Xu, J Zhao, M Chen; (IV) Collection and assembly of data: D Ma, Y Xu; (V) Data analysis and interpretation: Y Xu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Hongsheng Liu. Department of Thoracic Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Science & Peking Union Medical College, Beijing, China. Email: hongshengliu16@163.com.

Background: In recent years, neoadjuvant immunotherapy combined with chemotherapy has been used to treat locally advanced non-small cell lung cancer (NSCLC); however, no data are available to guide the selection of patients suitable for radical resection. In this paper, we report a clinical mode based on a multidisciplinary team (MDT).

Methods: We retrospectively analyzed the clinical data of patients with advanced NSCLC who were treated in our center between 26 December, 2019 and 1 October, 2021. These cases received an MDT assessment first. Eligible patients then received chemotherapy combined with personalized neoadjuvant immunotherapy. Adverse events were recorded. Chest computed tomography (CT) was performed every other cycle for tumor assessment. Radical resection was subsequently performed for potentially resectable tumors. Intraoperative conditions and surgical complications were recorded. The resected specimens were evaluated to determine the response to neoadjuvant therapy.

Results: The MDT team selected a total of 35 patients (squamous cell carcinoma: n=26, adenocarcinoma: n=8, adenosquamous carcinoma: n=1) for radical resection following neoadjuvant immunotherapy combined with chemotherapy. According to the Response Evaluation Criteria in Solid Tumors (RECIST) findings, 1 patient had complete remission, 27 had partial remission, 6 had progressive disease, and 1 had stable disease. All participants underwent radical resection, including video-assisted thoracoscopic surgery [VATS; 32 (91.4%)], sleeve resection [7 (20.0%)], and multilobar resection [7 (20.0%)]. A total of 17 patients (48.6%) achieved complete pathological remission, and 10 (28.6%) achieved major pathological remission. After surgery, the pathological grade was reduced in 33 patients (94.2%); the RECIST findings were unrelated to postoperative pathological remission (P=0.15).

Conclusions: The MDT mode helps to select suitable patients for radical resection and results in satisfactory pathological remission.

Keywords: Non-small cell lung cancer (NSCLC); neoadjuvant immunotherapy; multidisciplinary team (MDT)

Submitted Feb 22, 2022. Accepted for publication May 20, 2022.

doi: 10.21037/atm-22-2271

View this article at: https://dx.doi.org/10.21037/atm-22-2271

Introduction

Lung cancer is one of the most common malignancies worldwide, and approximately one-third of cases of non-small cell lung cancer (NSCLC) are locally advanced at the time of diagnosis (1). Platinum-based chemotherapy is routinely used to treat advanced or metastatic NSCLC. In recent years, targeted therapy and programmed death-ligand 1 (PD-L1) immune checkpoint inhibitors (ICIs) have transformed the treatment of NSCLC patients. In NSCLC patients receiving neoadjuvant ICI plus chemotherapy were found to have significantly longer event-free survival and a higher percentage of patients with a pathological complete response than chemotherapy alone (2). Accordingly, PD-L1 ICI immunotherapy has become the first-line treatment for most patients with metastatic NSCLC and negative driver genes (3).

Surgical resection following neoadjuvant therapy has become an important treatment for locally advanced NSCLC. In recent years, ICIs have been used as neoadjuvant therapy for these patients; however, no data are available to guide the selection of patients for radical resection. Nowadays there has been an increasing trend for the use of multi-disciplinary teams (MDT) in the management of NSCLC (4,5). Herein we report a clinical mode based on a MDT and had satisfactory patient selection results. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-2271/rc).

Methods

Patients

We retrospectively analyzed the clinical data of patients with advanced NSCLC who were treated at Peking Union Medical College Hospital between 26 December, 2019 and 1 October, 2021. The cases received an MDT assessment first. Criteria for inclusion in the MDT assessment were as follows: age of at least 18 years; NSCLC confirmed with fibreoptic bronchoscopy or biopsy; clinical stage II–IV [based on chest computed tomography (CT), brain magnetic resonance imaging (MRI), bone scan, abdominal CT, or whole-body positron emission tomography (PET)/CT and categorized according to the 8th edition of the tumor-node-metastasis (TNM) staging system of the American Joint Committee on Cancer (6)]; tumors that were unresectable or potentially resectable but not suitable for immediate surgery; no variation in specific driver genes, including epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK); no prior cancer treatment; Eastern Cooperative Oncology Group (ECOG) score 0–2; and no organ dysfunction. The exclusion criteria were as follows: immunodeficiency; on-going systemic immunosuppressive therapy; active autoimmune or infectious disease; or other malignancies. The MDT included physicians from the departments of thoracic surgery, respiratory and critical care medicine, pathology, radiology, nuclear medicine, and radiotherapy. Each specialist had more than 15 years of clinical experience.

Clinical mode

This retrospective study was approved by the Ethics Committee of Peking Union Medical College Hospital (No. S-K2062) and conducted in accordance with the Declaration of Helsinki (as revised in 2013). Eligible patients signed the informed consent form before receiving chemotherapy combined with personalized neoadjuvant immunotherapy, as determined by the MDT. Any adverse reaction from the start of treatment to 1 month after the end of treatment was recorded as an adverse event. Chest CT was performed every other cycle for tumor assessment, and the results were classified according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (7), as complete remission (CR), partial remission (PR), stable disease (SD), or progressive disease (PD). After neoadjuvant therapy was administered, the MDT identified patients for radical resection based on following criteria: (I) PR or CR with the possibility of radical resection (i.e., no signs of tumor invasion of any major vessel or the diaphragm, heart, trachea, or carina); or (II) SD or PD regarded as pseudo-progression or potentially resectable.

The operation was performed by a team of experienced thoracic surgeons. Intraoperative exploration was performed to assess adhesions, fibrosis, and tumor invasion of blood vessels. Radical resection was subsequently performed for resectable tumors and included lobectomy, multilobar resection, or pneumonectomy combined with systemic hilar and mediastinal lymph node dissection. Intraoperative conditions and postoperative complications were recorded. Surgical complications were evaluated and recorded according to the criteria defined by the Society of Thoracic Surgeons' and the European Society of Thoracic Surgeons' general thoracic surgery databases (8). The resected specimens were evaluated by 2 pathologists

Table 1 Clinical characteristics of the total cohort

Characteristic	Values
Gender, n (%)	
Male	27 (77.1)
Female	8 (22.9)
Median age [range], years	63 [46–76]
Preoperative stage, n (%)	
IIB	2 (5.7)
IIIA	20 (57.1)
IIIB	12 (34.3)
IIIC	1 (2.9)
Histology, n (%)	
Squamous cell carcinoma	26 (74.3)
Adenocarcinoma	8 (22.9)
Adenosquamous carcinoma	1 (2.9)
Smoking history (smoking index), n (%)	
Non-smokers	6 (17.1)
≤400	6 (17.1)
401–799	6 (17.1)
≥800	17 (48.6)
Resected lobe, n (%)	
RUL	9 (25.7)
RML	1 (2.9)
RLL	5 (14.3)
LUL	10 (28.6)
LLL	3 (8.6)
RML + RLL	7 (20.0)

RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.

from the lung cancer team to determine the response to neoadjuvant therapy. Any discrepancy was reconciled via discussion.

Statistical analysis

Major pathological remission (MPR) was defined as ≤10% of remaining viable tumor cells on postoperative pathological examination, and complete pathological remission (CPR) was defined as tumor regression without residual tumor on pathological examination (9,10). Chi-square test was used to compare differences between groups. A two-sided P<0.05 was considered statistically significant. Statistical analyses were performed using SPSS 22.0 software (IBM Corp., Armonk, NY, USA).

Results

Patient characteristics

A total of 35 patients underwent radical resection after neoadjuvant immunotherapy combined with chemotherapy. The baseline data are shown in *Table 1*. Among the cases, 27 patients (77.1%) were men, with a median age of 63 years; 29 patients (82.9%) were former smokers, with a median smoking index of 800. Pre-treatment biopsy showed squamous cell carcinoma in 26 patients (74.3%), adenocarcinoma in 8 patients (22.8%), and adenosquamous carcinoma in 1 patient (2.9%). The preoperative stage was stage IIB in 2 patients (5.7%), stage IIIA in 20 patients (57.1%), stage IIIB in 12 patients (34.3%), and stage IIIC in one patient (2.9%).

The patients did not undergo preoperative radiotherapy. Most of the patients [27 (77.1%)] received paclitaxel + cisplatin + pembrolizumab (PC + K). Among the 35 patients, 17 (48.6%) received 3 cycles of treatment, 14 (40.0%) received 4 cycles of treatment, and 2 (5.7%) received 5 cycles of treatment. The median neoadjuvant treatment time was 67 days. The median time to surgery (TTS) was 39 days. There's no relationship between the number of cycles administered and the clinical stage (P=0.15, Chi-square test, Table S1).

Neoadjuvant therapy response

A total of 6 patients (17.1%) had immune-related adverse events (irAEs) or treatment-related adverse events (TRAEs), including post-chemotherapy bone marrow suppression (n=1), rash (n=1), immune-related thyroiditis (n=1), arrhythmia (n=1), and limb numbness (n=2). No immune-related pneumonia or myocarditis was observed. No patient discontinued immunotherapy or received steroid therapy due to grade 3–4 adverse reactions. No patient's surgery was delayed due to any TRAE.

After neoadjuvant therapy, imaging evaluations showed CR in 1 case (2.9%), PR in 27 cases (77.1%), SD in 6 cases (17.1%), and PD in 1 case (3.2%). *Table 2* shows the decrease in the pathological grade for each individual

patient. In 1 case, the imaging showed that the tumor had shrunk, but the N2 lymph nodes were enlarged. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) confirmed an inflammatory response in the lymph nodes, which supported the determination of PR. The maximum cross-sectional area of the tumor was reduced a median of 61.6% (range, –0.2% to 100%). The pathological grade of the lymph nodes was reduced in 10 of the 27 patients (37.0%) who underwent an initial assessment of lymph node metastasis.

All cases underwent radical resection after neoadjuvant therapy; treatments included thoracoscopic surgery [32 (91.4%); no conversion to thoracotomy], thoracotomy [3 (8.6%)], sleeve resection [7 (20.0%)], and multilobar resection [7 (20.0%)]. No patient underwent pneumonectomy or required perioperative blood transfusion. There were 4 cases (11.4%) who had complete pleural adhesions, and 21 cases (60%) had partial pleural adhesions. Postoperative complications included atrial fibrillation [2 (5.7%)] and poor lung recruitment [1 (2.9%)].

Postoperative pathological examination

Postoperative pathological examination showed that the pathological grade was reduced in 33 cases (94.2%), including 96.3% of the patients with squamous cell carcinoma (26/27). The pathological grade of the lymph nodes was reduced in 24 of the 27 patients (88.9%) who underwent an initial assessment of lymph node metastasis. The changes in TNM staging and lymph node staging are shown in *Table 2* (for each patient) and *Figure 1*. A total of 17 cases (48.6%) achieved CPR, and 10 cases (28.6%) achieved MPR. In the remaining 8 non-MPR patients, the pathological grade was reduced in 6 cases and remained unchanged in 2 cases. Imaging remission was unrelated to postoperative pathological remission (P=0.15, Chi-square test, Table S2), which indicates that the imaging-based RECIST assessment did not reflect the actual tumour response. The patient who was classified as PD (according to RECIST) showed MPR on the postoperative pathological examination, indicating that preoperative imaging-based "progression" was pseudo-progression.

Discussion

Neoadjuvant immunotherapy causes the primary tumor to shrink, reduces the tumor stage, and increases the likelihood of radical resection after neoadjuvant therapy (11). It works by inducing antigens that produce a strong and durable anti-tumor T cell immune response. Immunotherapy works synergistically with chemotherapy: chemotherapy inhibits the proliferation of tumor cells, while immunotherapy enhances the anti-tumor immune response, thereby extending progression-free survival and overall survival (12,13). Several ICIs are being investigated as neoadjuvant therapies in Phase 3 clinical trials. They are being combined with chemotherapy to treat NSCLC (11). Studies have shown that neoadjuvant immunotherapy is effective for reducing lesions, increasing access to surgery, and improving survival. In the Lung Cancer Mutation Consortium (LCMC3) study (ClinicalTrials.gov number: NCT02927301), a total of 101 patients received neoadjuvant immunotherapy; the MPR rate was 19%, and that of CPR was 5% (11,14). In this real-world study, we retrospectively analyzed the clinical data of 35 patients and found that with the MDT model, the maximum cross-sectional area of the tumor was reduced by 61.6% (median; based on imaging), the pathological grade was reduced in 94.2% of cases, and the pathological grade of the lymph nodes was reduced in 85.7% of cases. These data indicate that neoadjuvant immunotherapy is effective for advanced NSCLC.

In this study, all cases had advanced NSCLC. The MDT selected patients for (radical) resection based on tumor shrinkage, improvement in the pathological grade of the lymph nodes, and tumor resectability. All cases underwent radical resection, with a CPR rate of 48.6% and an MPR rate of 28.6%, indicating that the MDT model is advantageous for patient selection.

For patient selection, tumor shrinkage may be a better indicator than improvement in the pathological grade of lymph nodes. In this study, the tumor was reduced by an average of 66% in MPR and CPR patients, which was significantly higher than the tumor reduction in non-MPR patients (46%), suggesting that tumor shrinkage was a more reliable indicator for patient selection. Moreover, the preoperative N staging (ycN) was N1–N3 in 57.7% 15/26) of the MPR and CPR cases, similar to that of the non-MPR patients (55.6%, 5/9), suggesting that lymph node grade is a limited indicator for patient selection, possibly due to immunotherapy-induced reactive hyperplasia, such as granuloma and fibrosis (15). It should be noted that in 1 case, the N2 lymph nodes were larger after neoadjuvant therapy; however, EBUS-TBNA confirmed pseudo-progression, providing further evidence that lymph nodes cannot accurately reflect treatment response.

In the Checkmate816 study, the CPR rate was 24%

Table 2 TNM and N stage of the total cohort

c-TNM	yc-TNM	yp-TNM	RECIST evaluation	Pathologic response	C-N	yp-N
IIB	IA	CPR	PR	CPR	0	0
IIB	IIB	CPR	PR	CPR	1	0
IIIA	IA	CPR	PR	CPR	0	0
IIIA	IIA	IIIA	SD	MPR not achieved	0	2
IIIA	IIIA	CPR	PR	CPR	0	0
IIIA	IIIA	CPR	PR	CPR	0	0
IIIA	IIIA	IIB	SD	MPR not achieved	0	0
IIIA	IIIA	IA	PR	MPR not achieved	0	0
IIIA	IIIA	IIB	PR	MPR	0	1
IIIA	IIB	IIB	PR	CPR	1	1
IIIA	IIIA	CPR	PR	CPR	1	0
IIIA	IIIA	CPR	PR	CPR	1	0
IIIA	IIIA	CPR	PR	CPR	1	0
IIIA	IIIA	IIA	SD	CPR	1	0
IIIA	CR	CPR	CR	CPR	2	0
IIIA	IA	IA3	PR	MPR not achieved	2	0
IIIA	IB	IIIA	SD	MPR not achieved	2	2
IIIA	IIA	IIIA	PR	MPR not achieved	2	2
IIIA	IIIA	CPR	PR	CPR	2	0
IIIA	IIIA	IA	PR	MPR	2	0
IIIA	IIIA	IA	PR	MPR	2	0
IIIA	IIIA	IB	PR	MPR	2	0
IIIB	IB	CPR	PR	CPR	2	0
IIIB	IB	IIB	PR	MPR not achieved	2	1
IIIB	IIIA	CPR	PR	CPR	2	0
IIIB	IIIA	IIA	PR	MPR	2	0
IIIB	IIIA	IIB	PR	CPR	2	1
IIIB	IIIB	CPR	PR	CPR	2	0
IIIB	IIIB	CPR	SD	CPR	2	0
IIIB	IIIB	IA	SD	MPR	2	0
IIIB	IIIB	IIB	PR	MPR not achieved	2	1
IIIB	IIB	IA	PR	MPR	3	0
IIIB	IIB	IB	PD	MPR	3	0
IIIB	IIIA	IIIA	PR	MPR	3	2
IIIC	IIIA	IA	PR	MPR	3	0

TNM, tumor-node-metastasis; RECIST, Response Evaluation Criteria in Solid Tumors; CR, complete remission; CPR, complete pathological remission; PR, partial response; SD, stable disease; PD, progressive disease; MPR, major pathological remission.

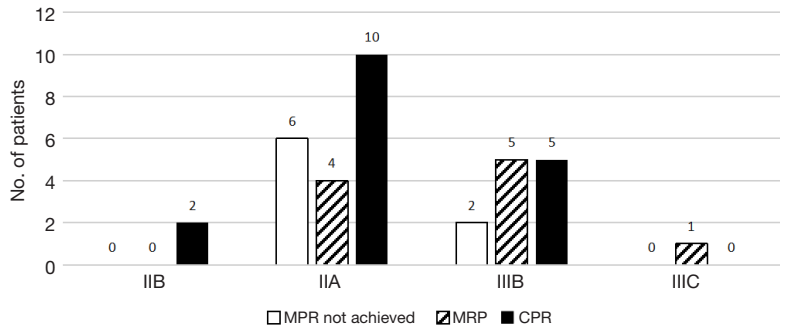

Figure 1 Pathological response and p-TNM stage of the total cohort. MPR, major pathological remission; CPR, complete pathological remission; TNM, tumor-node-metastasis.

in patients who received nivolumab combined with chemotherapy before surgery (2). In a meta-analysis of 252 patients, the CPR rate with neoadjuvant immunotherapy was 11.76% (16). In both studies, the CPR rate was significantly lower than in our study, a difference that may be related to the strict MDT criteria applied. In the present study, among the 6 cases with PR and 1 case with PD (per RECIST), 2 cases achieved CPR, and 2 cases achieved MPR for an overall response rate of 42.9%, suggesting that PD and SD patients may undergo surgery. Furthermore, this study showed that imaging remission was related to postoperative pathological remission; this association may be immune-related because of the significant infiltration of lymphocytes and macrophages and their involvement in mediating tumor necrosis and fibrous tissue repair, which results in an underestimation of tumor shrinkage on imaging. Therefore, we believe that the imaging-based RECIST criteria may be excessively strict. Some researchers have proposed the use of liquid biopsy [e.g., circulating tumor DNA (ctDNA) (17), cell-free DNA (cfDNA) (18), tumour mutational burden (TMB) (11), or immune microenvironment (19)] for preoperative assessment or the use of the PET Response Criteria in Solid Tumors (PERCIST) in place of RECIST (20); however, the supporting evidence is not yet strong enough. Uprety *et al.* showed that PD-L1 expression was not effective for predicting pathological response (21). Until further evidence is available, we recommend that PD and SD patients be carefully evaluated, and surgical exploration may be considered for potentially resectable cases.

Surgeons are concerned about the impact of neoadjuvant therapy on the difficulty of surgery. In the present study, 24 cases (68.5%) had complete or partial pleural adhesions. Specifically, 4 cases (11.4%) had complete pleural adhesions, which increased the difficulty of surgery. This issue is related to the presence of neoadjuvant therapy-induced tissue adhesions. In addition, significantly swollen and merged lymph nodes made it difficult to expose the hilar structure and perform systemic lymph node dissection. Shi *et al.* reported that after neoadjuvant immunotherapy, adhesions, bleeding, vascular invasion, difficult-to-separate fibrotic tissues, and lymph node enlargement increase the difficulty of surgery (22). Nevertheless, in this study, all patients underwent radical resection, and only 3 cases (8.6%) required thoracotomy, without conversion to thoracotomy or pneumonectomy; this indicates that the difficulty of surgery is controllable, which may attributable to a good MDT-based assessment of resectability and good surgical techniques. Jiang *et al.* analyzed the operating time, blood loss, and conversion rate in 31 patients who underwent surgery after neoadjuvant immunotherapy and concluded that neoadjuvant immunotherapy did not significantly increase the difficulty of surgery (23).

The National Comprehensive Cancer Network (NCCN) guidelines have no specific recommendations for the number of cycles of neoadjuvant immunotherapy. In this study, most patients received 3–4 cycles of neoadjuvant therapy with a median treatment time of 67 days due to careful monitoring and prompt and effective treatment of any adverse events by our MDT. The overall response rate was 76.4% (13/17) in cases who received 3 cycles of neoadjuvant immunotherapy and 76.9% (10/13) in those who received 4 cycles of neoadjuvant immunotherapy, suggesting that it is feasible to administer 3–4 cycles of neoadjuvant immunotherapy. There were 2 cases who received 5 cycles of neoadjuvant therapy; both patients were non-PR after 4 cycles of neoadjuvant therapy and thus received an additional cycle of treatment. However,

RECIST assessment still showed PD and SD, and these patients did not achieve MPR after surgery, suggesting that additional cycles of neoadjuvant therapy (beyond 4) may not further improve efficacy.

Increasing evidence demonstrates the long tail effect of immunotherapy. Further research is needed to investigate this effect for neoadjuvant immunotherapy. We deduced that a longer TTS (as appropriate) may further improve the results of neoadjuvant immunotherapy; however, it may also increase the difficulty of surgery. In this study, the median TTS was 39 days. Our observations showed that a longer TTS did not significantly increase the difficulty of surgery (as no conversion to thoracotomy, pneumonectomy or perioperative blood transfusion occurred).

A total of 7 cases in this study underwent sleeve resection, with an overall response rate of 85.7% (6/7), suggesting that sleeve resection may be unnecessary in some cases. For patients who undergo elective sleeve resection, frozen pathology of the surgical margins may be performed, and sleeve resection may be halted if the result is negative. However, additional clinical evidence is needed to support this approach. A total of 7 patients underwent multilobar lobectomy (right upper lobe + right middle lobe) with an overall response rate of 42.9% (3/7), suggesting that this surgical approach is necessary if the right middle bronchus is invaded. No patient underwent pneumonectomy, indicating that the MDT performed well regarding patient selection. Given the uncertainty regarding surgery, patients with central lung cancer should undergo careful evaluation before surgery, including evaluation of tumor imaging and cardiopulmonary function, in order to prepare for pneumonectomy.

This retrospective study has several limitations. The total number of patients who received intended neoadjuvant immunotherapy are not clear as a lack of follow-up, e.g., some patients decided to receive therapy in local centers due to the epidemic of COVID-19 or economic reasons. As a result, the characteristics of patients who finally received surgery is different from other reports. Those who showed poor response to neoadjuvant immunotherapy were also ruled out as they failed to receive surgery. A prospective design and better follow-up are needed in the future work.

Conclusions

This MDT-based model is effective for selecting patients for radical resection and results in satisfactory pathological remission.

Acknowledgments

The authors thank Dr. Alfons Navarro of the Molecular Oncology and Embryology Laboratory, Human Anatomy Unit, Faculty of Medicine and Health Sciences, University of Barcelona, IDIBAPS for the very valuable comments on this manuscript. The authors appreciate the academic support from the AME Thoracic Surgery Collaborative Group.

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-2271/rc

Data Sharing Statement: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-2271/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-2271/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Ethics Committee of Peking Union Medical College Hospital (No. S-K2062) and conducted in accordance with the Declaration of Helsinki (as revised in 2013). All the enrolled patients had signed informed consent.

References

1. Ganti AK, Klein AB, Cotarla I, et al. Update of Incidence, Prevalence, Survival, and Initial Treatment in Patients

With Non-Small Cell Lung Cancer in the US. JAMA Oncol 2021;7:1824-32.
2. Forde PM, Spicer J, Lu S, et al. Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer. N Engl J Med 2022. [Epub ahead of print]. doi: 10.1056/NEJMoa2202170.
3. Friedlaender A, Naidoo J, Banna GL, et al. Role and impact of immune checkpoint inhibitors in neoadjuvant treatment for NSCLC. Cancer Treat Rev 2022;104:102350.
4. Liu H, Song Y. MDT is still important in the treatment of early stage lung cancer. J Thorac Dis 2018;10:S3984-S5.
5. Nelson A, Longo M, Byrne A, et al. Chemotherapy decision-making in advanced lung cancer: a prospective qualitative study. BMJ Support Palliat Care 2020. [Epub ahead of print]. doi: 10.1136/bmjspcare-2020-002395.
6. Goldstraw P, Chansky K, Crowley J, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. J Thorac Oncol 2016;11:39-51.
7. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 2009;45:228-47.
8. Fernandez FG, Falcoz PE, Kozower BD, et al. The Society of Thoracic Surgeons and the European Society of Thoracic Surgeons general thoracic surgery databases: joint standardization of variable definitions and terminology. Ann Thorac Surg 2015;99:368-76.
9. Travis WD, Dacic S, Wistuba I, et al. IASLC Multidisciplinary Recommendations for Pathologic Assessment of Lung Cancer Resection Specimens After Neoadjuvant Therapy. J Thorac Oncol 2020;15:709-40.
10. Hellmann MD, Chaft JE, William WN, Jr., et al. Pathological response after neoadjuvant chemotherapy in resectable non-small-cell lung cancers: proposal for the use of major pathological response as a surrogate endpoint. Lancet Oncol 2014;15:e42-50.
11. Forde PM, Chaft JE, Pardoll DM. Neoadjuvant PD-1 Blockade in Resectable Lung Cancer. N Engl J Med 2018;379:e14.
12. Gandhi L, Rodriguez-Abreu D, Gadgeel S, et al. Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. N Engl J Med 2018;378:2078-92.
13. Reck M, Shankar G, Lee A, et al. Atezolizumab in combination with bevacizumab, paclitaxel and carboplatin for the first-line treatment of patients with metastatic non-squamous non-small cell lung cancer, including patients with EGFR mutations. Expert Rev Respir Med 2020;14:125-36.
14. Forde PM, Chaft JE, Smith KN, et al. Neoadjuvant PD-1 Blockade in Resectable Lung Cancer. N Engl J Med 2018;378:1976-86.
15. Liang H, Yang C, Gonzalez-Rivas D, et al. Sleeve lobectomy after neoadjuvant chemoimmunotherapy/chemotherapy for local advanced non-small cell lung cancer. Transl Lung Cancer Res 2021;10:143-55.
16. Jia XH, Xu H, Geng LY, et al. Efficacy and safety of neoadjuvant immunotherapy in resectable nonsmall cell lung cancer: A meta-analysis. Lung Cancer 2020;147:143-53.
17. Peng M, Huang Q, Yin W, et al. Circulating Tumor DNA as a Prognostic Biomarker in Localized Non-small Cell Lung Cancer. Front Oncol 2020;10:561598.
18. Ma Y, Wang Q, Dong Q, et al. How to differentiate pseudoprogression from true progression in cancer patients treated with immunotherapy. Am J Cancer Res 2019;9:1546-53.
19. Ojlert AK, Halvorsen AR, Nebdal D, et al. The immune microenvironment in non-small cell lung cancer is predictive of prognosis after surgery. Mol Oncol 2019;13:1166-79.
20. Aide N, Hicks RJ, Le Tourneau C, et al. FDG PET/CT for assessing tumour response to immunotherapy : Report on the EANM symposium on immune modulation and recent review of the literature. Eur J Nucl Med Mol Imaging 2019;46:238-50.
21. Uprety D, Mandrekar SJ, Wigle D, et al. Neoadjuvant Immunotherapy for NSCLC: Current Concepts and Future Approaches. J Thorac Oncol 2020;15:1281-97.
22. Shi Y, Li J, Chen M, et al. Sarcoidosis-like reaction after neoadjuvant pembrolizumab combined with chemotherapy mimicking disease progression of NSCLC induced encouraging discovery of pathological complete response. Thorac Cancer 2021;12:3433-6.
23. Jiang L, Huang J, Jiang S, et al. The surgical perspective in neoadjuvant immunotherapy for resectable non-small cell lung cancer. Cancer Immunol Immunother 2021;70:2313-21.

Cite this article as: Ma D, Xu Y, Qin Y, Li S, Li J, Jiang Y, Wang M, Xu Y, Zhao J, Chen M, Cheng W, Hu K, Liu H. Neoadjuvant immunotherapy followed by surgery with curative intent in 35 patients with advanced NSCLC: the retrospective experiences of a multidisciplinary team. Ann Transl Med 2022;10(10):609. doi: 10.21037/atm-22-2271

Supplementary

Table S1 Comparisons between the number of cycles administered and the clinical stage

No. of cycles	2–3 cycles	4–5 cycles
IIB–IIIA	14	8
IIIB–IIIC	5	8

Table S2 Comparisons between RECIST findings and postoperative pathological remission

RECIST findings	Non-MPR	MPR + CPR
CR + PR	5	23
PD + SD	3	4

MPR, major pathological remission; CPR, complete pathological remission; CR, complete remission; PR, partial response; SD, stable disease; PD, progressive disease.

https://dx.doi.org/10.21037/atm-22-2271