Original Article

Short-term outcomes of neoadjuvant sintilimab with chemotherapy in stage III non-small cell lung cancer: a case series

Bo-Shi Fan[1#], Xing-Tong Wang[2#], Shou-Yin Di[1], Jia-Hua Zhao[1], Si-Yu Chen[1], Shao-Hua Zhou[1], Cai-Ying Yue[1], Wei-An Song[1], Tai-Qian Gong[1]

[1]Department of Thoracic Surgery, the Sixth Medical Center of Chinese PLA General Hospital, Beijing, China; [2]Senior Department of Burn & Plastic Surgery, the Forth Medical Center of Chinese PLA General Hospital, Beijing, China

Contributions: (I) Conception and design: BS Fan, TQ Gong, WA Song; (II) Administrative support: XT Wang; (III) Provision of study materials or patients: WA Song, TQ Gong, SH Zhou, CY Yue; (IV) Collection and assembly of data: SY Di, SY Chen; (V) Data analysis and interpretation: BS Fan; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Tai-Qian Gong. Department of Thoracic Surgery, the Sixth Medical Center of Chinese PLA General Hospital, Beijing 100048, China. Email: gongtq_thoracic@163.com; Wei-An Song. Department of Thoracic Surgery, the Sixth Medical Center of Chinese PLA General Hospital, Beijing 100048, China. Email: songweian186@126.com.

Background: Neoadjuvant chemoimmunotherapy seems to be a promising treatment option for stage III non-small cell lung cancer (NSCLC). Sintilimab, as a programmed death receptor-1 inhibitor, has exhibited a fine performance in treating NSCLC. However, the efficiency of sintilimab combined with chemotherapy for stage IIIA/IIIB NSCLC remains inconclusive. The purpose of this study was to share our experience on sintilimab in neoadjuvant chemoimmunotherapy for stage III NSCLC.

Methods: This study retrospectively reviewed patients who received surgical resection following 1–3 cycles of neoadjuvant sintilimab (200 mg) with chemotherapy for stage III NSCLC between June 2020 and March 2022 in our center. Patients characteristics, surgical factors, surgery-related complications 30 days postoperatively, and treatment-related adverse events (TRAEs) before surgery were recorded through reviewing medical record data and telephone follow-up.

Results: A total of eight patients were enrolled, including six cases of squamous cell carcinoma and two cases of adenocarcinoma. All of the patients received 1–3 cycles of neoadjuvant therapy. There were no treatment-related surgical delays. All patients underwent lobectomy, among which two underwent sleeve lobectomy and one received bronchoplasty. Five patients underwent open thoracotomy. Fibrosis of the primary tumor and lymph nodes was observed in all the cases. There were no surgery-related complications > grade 2 at 30 days postoperatively. According to the radiographic findings, one patient had stable disease and all of the others achieved a partial response. The median of maximum standardized uptake value change from baseline was a 52.75% reduction (range, 37.2–68.8%). Five patients achieved a major pathological response. R0 resection was achieved in all eight cases. One grade 4 event was observed. Neutropenia was the most common TRAE > grade 2 (3/8). There were no cases of treatment discontinuation or dose reduction due to TRAEs.

Conclusions: The current study found that neoadjuvant sintilimab plus chemotherapy bring a high rate of major pathological response and acceptable TRAEs. Even though it increased the difficulties of surgery, there is still no evidence suggesting that it will brings additional surgical death. We believe that neoadjuvant sintilimab plus chemotherapy might be feasible for stage III NSCLC.

Keywords: Neoadjuvant; non-small cell lung cancer (NSCLC); programmed cell death 1 inhibitor (PD-1 inhibitor); sintilimab; case series

© Translational Cancer Research. All rights reserved.

Submitted Apr 07, 2022. Accepted for publication Jun 20, 2022.
doi: 10.21037/tcr-22-1194
View this article at: https://dx.doi.org/10.21037/tcr-22-1194

Introduction

Stage III non-small cell lung cancer (NSCLC) accounts for approximately 40% of newly diagnosed NSCLC cases (1). Due to the specificity of lymph node metastasis, there are considerable differences in the clinical treatment and prognosis of stage III NSCLC. It is difficult to achieve ideal treatment outcomes by only relying on surgery since there is a high risk of recurrence and metastasis postoperatively (2). Numerous studies have confirmed the effectiveness of neoadjuvant therapy in the treatment of stage III NSCLC (3). However, most of the previous neoadjuvant regimens for stage III NSCLC involved chemotherapy or chemoradiotherapy (3); a considerable portion of patients are not sensitive to chemotherapy or combined chemoradiotherapy, and some patients even suffered disease progression.

Recently, several studies preliminary reported the safety and effectiveness of neoadjuvant chemoimmunotherapy for stage III NSCLC (4-6). One study reported that atezolizumab [a programmed cell death 1 ligand 1 (PD-L1) inhibitor] plus chemotherapy before surgery may be feasible for resectable stage IB–IIIA NSCLC (7). Furthermore, a phase 2 trial supported the potential value of the neoadjuvant nivolumab with chemotherapy for the treatment of resectable stage IIIA NSCLC (8). Similarly, a phase 2 trial from China suggested a neoadjuvant chemoimmunotherapy regimen for stage IIIA NSCLC and T3–4N2 IIIB NSCLC (9). Some other studies that explore the efficiency of the neoadjuvant chemoimmunotherapy on stage IIIA/B NSCLC are ongoing (10). However, there is currently no definitive conclusion on the feasibility of neoadjuvant chemoimmunotherapy for stage III NSCLC (5,6,11,12).

Sintilimab, as a PD-1 inhibitor from China, is reportedly tolerable for patients and has achieved a 40.5% major pathological response (MPR) rate in neoadjuvant therapy for stage IA–IIIB NSCLC (13). Recently, two phase 2 trials reported its safety and feasibility when combined with chemotherapy for resectable stage IIIA/IIIB NSCLC (14,15). However, the number of cases enrolled in these two studies was small and more cases are essential to better identify the efficiency of sintilimab combined with on stage III NSCLC. In this study, we similarly shared our experience on sintilimab in neoadjuvant chemoimmunotherapy for stage III NSCLC. We present the following article in accordance with the STROBE and AME Case Series reporting checklists (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1194/rc).

Methods

Study design

This is a single-center clinical retrospective study conducted in the Sixth Medical Center of Chinese PLA General Hospital. All consecutive stage III NSCLC patients who received surgery after neoadjuvant chemoimmunotherapy between June 2020 and March 2022 were screened. Patients were enrolled according to the following criteria: (I) those with pathologically confirmed clinical IIIa–IIIc NSCLC at the time of diagnosis (5,16); (II) cases in which neoadjuvant sintilimab plus chemotherapy was administered; and (III) patients lacking positive mutation of the corresponding driven-gene for lung adenocarcinoma (AD). Patients receiving only neoadjuvant immunotherapy were not included. This retrospective study was approved by the medical ethics committee of the Sixth Medical Center of Chinese PLA General Hospital (No. HZKY-PJ-2022-9), and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The informed consent for this retrospective research was waived.

Data collection

The patients' clinical data, including gender, age, neoadjuvant chemoimmunotherapy strategy, clinical stage at diagnosis and post neoadjuvant chemoimmunotherapy, surgical procedure, intra-operative blood loss, interval between neoadjuvant chemoimmunotherapy and surgery, operation time, complications, intensive care unit (ICU) stay, and final pathological diagnosis, were collected by reviewing the medical record. Mortality and surgery-related complications ≥ grade 2 according to the Clavien-Dindo classification system were recorded for 30 days after surgery (17). Pulmonary air leakage is defined as air

© Translational Cancer Research. All rights reserved.

Table 1 Characteristics of 8 cases before surgery

Case	Gender	Age, years	Histology	c-stage[a]	PD-L1 TPS	Neoadjuvant chemoimmunotherapy regimen
1	Male	63	SCC	T3N2M0, IIIb	–	Albumin-bound paclitaxel 400 g d1 + cisplatin 60 mg d1–d2 + sintilimab 200 mg d2, 2 cycles
2	Male	77	SCC	T4N2M0, IIIb	–	Albumin-bound paclitaxel 300 g d1 + carboplatin 60 mg d1 + sintilimab 200 mg d2, 2 cycles
3	Female	40	SCC	T4N3M0, IIIc	–	Albumin-bound paclitaxel 300 g d1 + cisplatin 60 mg d1, 30 mg d2–d3 + sintilimab 200 mg d3, 3 cycles
4	Male	72	SCC	T3N2M0, IIIb	–	Paclitaxel liposome 240 mg d1 + cisplatin 120 mg d1 + sintilimab 200 mg d2, 2 cycles
5	Male	70	SCC	T2bN2M0, IIIb	–	Albumin-bound paclitaxel 400 mg d1 + cisplatin 30 mg d1–d3 + sintilimab 200 mg d5, 1 cycle
6	Male	65	SCC	T3N2M0, IIIb	–	Paclitaxel liposome 210 mg d1 + cisplatin 60 mg d1–d2 + sintilimab 200 mg d2, 2 cycles
7	Male	65	AD	T4N2M0, IIIb	<1%	Pemetrexed disodium 0.8 g d1 + lobaplatin 50 mg d1 + sintilimab 200 mg d2, 2 cycles
8	Male	67	AD	T1bN2M0, IIIa	90%	Pemetrexed disodium 0.95 g d1 + cisplatin 50 mg d1–d3 + sintilimab 200 mg d2, 2 cycles

[a], c-stage, clinical stage at the time of first diagnosis, according to the 8th edition of TNM staging system. –, not detected; AD, adenocarcinoma; PD-L1, programmed cell death ligand 1; SCC, squamous cell carcinoma; TNM, tumor node metastasis; TPS, tissue polypeptide specific antigen.

leak that persists for more than 5 days postoperatively. Neoadjuvant chemoimmunotherapy-related adverse events [treatment-related adverse events (TRAEs)] before surgery that occurred in more than two cases or were > grade 2 were recorded here. TRAEs were measured according to the National Cancer Institute Common Terminology Criteria for Adverse Eversion 5.0 (CTCAE5.0) (18). Telephone follow-up was performed per 3 weeks during the entire treatment period. All of the operations were performed by WA Song and TQ Gong (the corresponding authors), who are highly experienced thoracic surgeons.

Radiographic and pathological assessment

A radiographic positron emission tomography (PET)-computed tomography (CT) or CT was performed before surgery to analyze the radiographic response according to Response Evaluation Criteria in Solid Tumours (RECIST) 1.1 (19). Pathological analysis was performed by a pathologist according to the Cottrell methods. Briefly, tumor samples <6 cm were analyzed entirely; however, for those >6 cm, more than one section/cm from the maximum dimension was analyzed. MPR was defined as ≤10% of viable residual tumor in samples (20).

Statistical analysis

Data processing was carried out using SPSS 21.0 (IBM Corp., Armonk, NY, USA). Descriptive analysis was performed using statistics including the median with range, specific value, and frequency with percentage.

Results

Patients characteristics

The characteristics of the enrolled patients are listed in *Table 1*. Nine patients who received neoadjuvant chemoimmunotherapy were screened between July 2020 and March 2022, and eight patients were eventually enrolled. One patient was excluded because of an indefinite pathological type. None of the included patients refused surgery after neoadjuvant treatment.

The included cohort comprised one female and seven males, with a median age of 66 years (range, 40–77 years). Six patients had squamous cell carcinoma (SCC) and two had AD. Five patients were stage IIIb, two were stage IIIa, and one was stage IIIc at the time of diagnosis. The neoadjuvant chemotherapy regimens for SCC and AD were paclitaxel plus platinum and pemetrexed

© Translational Cancer Research. All rights reserved.

Table 2 Surgical factors

Case	Interval[a] (days)	Surgical procedure	Fibrosis of primary tumor and lymph nodes	Operation time (minutes)	Intraoperative blood loss (mL)	Intraoperative blood transfusion	Postoperative complications	ICU stay (days)	Postoperative hospital stay (days)
1	28	(Open) sleeve LUL + LND	Y	140	100	–	–	–	8
2	30	(Open) sleeve RUL + LND	Y	375	500	Y	–	1	7
3	29	(Open) RUML + LND	Y	370	200	–	Pulmonary air leakage	–	14
4	28	(VATS) RUL + LND	Y	320	100	–	Atrial fibrillation atrial	–	5
5	29	(VATS) LLL + BP + LND	Y	240	100	–	–	1	9
6	29	(Open) RUML + LND	Y	165	200	–	–	–	5
7	25	(Open) LUL + LND	Y	190	800	Y	Atrial fibrillation atrial	–	12
8	32	(VATS) LUL + LND	Y	245	100	–	–	–	5

[a], interval between target therapy and operation. –, no; Y, yes; BP, bronchoplasty; ICU, intensive care unit; LLL, left lower lobectomy; LND, lymph node dissection; LUL, left upper lobectomy; Open, open surgery; RUL, right upper lobectomy; RUML, right upper and middle lobectomy; VATS, video-assisted thoracoscopic surgery.

plus platinum, respectively. All of the patients received 1–3 cycles. Radiological assessment was performed following the completion of neoadjuvant chemotherapy. The PD-L1 tissue polypeptide specific antigen (TPS) was negative and 90% in the two AD cases, respectively. PD-L1 TPS was not detected in the SCC cases.

Surgery and outcomes

The surgical factors are displayed in *Table 2*. All eight patients received surgery and the median time from the end of neoadjuvant chemoimmunotherapy to surgery was 29 days (range, 25–32 days). No neoadjuvant chemoimmunotherapy-related surgical delays occurred. The median operation time was 242.5 min (range, 140–375 min). All of the patients underwent lobectomy, among which two underwent sleeve lobectomy and one received bronchoplasty. Five patients underwent open thoracotomy while the others underwent single-port video-assisted thoracoscopic surgery. Fibrosis of primary tumor and lymph nodes was observed in all of the patients (100%). Two patients suffered intraoperative bleeding requiring blood transfusion. Three patients suffered grade 2 surgical complications, including two cases of atrial fibrillation and one case of pulmonary air leakage. The median postoperative hospital stay was 7.5 days (range, 5–14 days). The surgical mortality rate at 30 days postoperatively was 0%.

Radiographic findings and pathological response

The radiographic and pathological responses are recorded in *Table 3*. According to the radiographic findings, seven (87.5%) patients achieved a partial response, one had stable disease, and no one achieved a complete response or had progressive disease during the neoadjuvant treatment. The median sum of lesion diameter change from baseline was a 38.2% reduction (range, 30.0–63.6%) and the median of maximum standardized uptake value (SUVmax) change from baseline was a 52.75% reduction (range, 37.2–68.8%). The SUVmax change from the baseline of four patients was missing.

As for the pathological response, five (62.5%) cases achieved a MPR and no achieved a pathologic complete

© Translational Cancer Research. All rights reserved.

Table 3 Radiographic and pathological assessment

Case	SLD change from baseline, %	SUVmax change from baseline, %	y-stage	Therapeutic effect[a]	Histology[b]	P-stage	Pathological response
1	–68.0	NA	T1cN2M0, IIIa	PR	SCC	T2bN0M0, IIA	15–20% tumor residue
2	–36.6	–41.4	T4N2M0, IIIb	PR	SCC	T2N2M0, IIIB	MPR (5% tumor residue)
3	–37.5	–37.2	T3N2M0, IIIb	PR	SCC	T2aN2M0, IIIA	15–20% tumor residue
4	–63.6	NA	T2aN2M0, IIIa	PR	SCC	T2aN0M0, IB	MPR (5% tumor residue)
5	–38.8	NA	T1cN2M0, IIIa	PR	SCC	T0N2M0	MPR[c]
6	–30.0	–68.3	T3N2M0, IIIb	SD	SCC	T3N0M0, IIA	MPR (<10% tumor residue)
7	–49.4	–68.8	T3N2M0, IIIb	PR	AD	T1aN0M0, IA	MPR (<10% tumor residue)
8	–33.3	NA	T1bN2M0, IIIa	PR	AD	T1aN2M0, IIIA	15–20% tumor residue

[a], therapeutic effect of preoperative treatment according to radiologic response; [b], histology post-surgery; [c], for the fifth case, the primary tumor achieved PCR, but the lymph node of lower lung ligament was positive. y-stage, clinical stage after neoadjuvant chemoimmunotherapy; P-stage, pathological stage; AD, adenocarcinoma; MPR, major pathological response; NA, not available; PCR, pathologic complete response; PR, partial response; SCC, squamous cell carcinoma; SD, stable disease; SLD, sum of lesion diameter; SUVmax, maximum standardized uptake value.

Table 4 Neoadjuvant TRAEs[a]

Patients (n=8)	Grade 1–2	Grade 3	Grade 4
Anemia	7	–	–
Neutropenia	3	2	1
Thrombocytopenia	3	–	–
Alopecia [grades 1, 2]	7 [3, 4]	–	–
Arthralgia	2	–	–
Diarrhea	–	1	–
Asthenia	6	1	–
Nausea	4	2	–
Pruritus	4	1	–
Rash	4	–	–
Peripheral neuritis	2	–	–
Hypothyroidism	2	–	–
Constipation	2	–	–

[a], TRAEs that occurred in more than two cases or > grade 2 were recorded here. Grade 1: alopecia <50%; grade 2: alopecia >50%. –, no. TRAEs, treatment-related adverse events.

response (PCR). Among these patients, the primary tumor of one case reached PCR, but the left pulmonary ligament lymph node was positive, so we classified it as MPR. The other three patients who did not reach MPR also obtained a 10–20% tumor residue. The pathological assessment showed that R0 resection was achieved in all eight included patients (100%).

Neoadjuvant TRAEs

The TRAEs caused by neoadjuvant chemoimmunotherapy are shown in *Table 4*. Alopecia, anemia, and asthenia tied for the top three TRAEs of any grade, which occurred in seven of eight patients, followed by neutropenia (6/8) and nausea (6/8), pruritus (5/8), and rash (4/8). Neutropenia was the most frequent TRAE > grade 2 (3/8), followed by nausea (2/8). One grade 4 event was observed and no deaths occurred. No neoadjuvant treatment delays or drug dose reductions occurred because of TRAEs.

Discussion

Our results preliminarily showed that neoadjuvant chemoimmunotherapy with sintilimab plus chemotherapy was well tolerated and the TRAEs were acceptable. The high pathological response rate suggested that sintilimab with chemotherapy is promising and worthy of further study in neoadjuvant chemoimmunotherapy for stage III NSCLC.

Since long-term survival data requires a longer period of time to obtain and MPR is closely related to the prognosis of patients who receive neoadjuvant therapy, MPR is now considered an important method to evaluate the effect of

© Translational Cancer Research. All rights reserved.

neoadjuvant therapy (21). In this study, the MPR rate was 62.5%, which demonstrates the ideal effect of neoadjuvant sintilimab plus chemotherapy. This MPR rate is consistent with that reported by Sun *et al.* (62.5%) and is higher than that reported by Zhang *et al.* (43.3%) (14,15). The PCR rates reported by Sun *et al.* and Zhang *et al.* reached 31% and 20%, respectively, whereas none of the patients in our study reached PCR (14,15). This inconsistency can be explained by the different chemotherapy regimens and cycles. In our study, the proportion of patients who received one, two, and three cycles of treatment before surgery was 12.5%, 75%, and 12.5%, respectively, compared with 0%, 35%, and 65% in Sun *et al.* and 2%, 72%, and 20% in Zhang *et al.* (14,15). In addition, 6% of the patients in Zhang *et al.* received four cycles of treatment (14). More cycles seem to improve the efficacy of neoadjuvant chemoimmunotherapy.

In this study, we found that the sum of lesion diameter had an at least 30% reduction in the MPR group, which was consistent with previous studies (13,15). Regarding the relationship between PET-SUVmax and the postoperative pathological response, Zhao *et al.* found that the decline in the SUVmax was more extensive in the MPR/PCR groups compared to the non-MPR group (9). Similarly, all of the SUVmax values had a large reduction in the MPR group in our study. This suggested that the extent of SUVmax reduction might play a role in predicting the pathological response. Meanwhile, the cut-off value of SUV reduction between MPR and non-MPR requires further research (22). Tao *et al.* investigated the role of PET-CT in predicting MPR in lung cancer and found that all cases with a ΔSULpeak% <–30.0% (SUL: standardized uptake value corrected for lean body mass) achieved MPR. However, SUL is not commonly used in clinics (22).

We also evaluated the impact of sintilimab plus chemotherapy on surgery. We found that after neoadjuvant treatment, the primary lesions and lymph nodes had different degrees of fibrosis and adhesion with surrounding tissues, regardless of whether or not the patients achieved MPR. We considered that neoadjuvant sintilimab plus chemotherapy increases the difficulty of surgery. Thoracotomy, bronchoplasty, and sleeve resection are often needed, all of which will increase the risk of intraoperative bleeding and postoperative complications, including air leakage and arrhythmia. This is similar to the findings of Sun *et al.* and Zhang *et al.* (14,15). However, it is uncertain whether immunotherapy or chemotherapy is the main factor affecting the increased surgical difficulty. There is still no evidence suggesting that neoadjuvant chemoimmunotherapy increases the risk of surgical death (7,12,14,15).

In this study, the TRAEs of neoadjuvant sintilimab combined with chemotherapy were acceptable. The results showed that alopecia, nausea, asthenia, and neutropenia were the main TRAEs in our study and most of the TRAEs were grade 1–2. TRAEs > grade 2 were observed in 62.5% of patients, which is higher than that reported in previous studies. However, all of the patients with TRAEs > grade 2 recovered after short-term treatment. The most common TRAE > grade 2 in our research was neutropenia, which is similar to the findings of Sun *et al.*, whereas Zhang *et al.* reported that hyperglycemia was the most common (14,15). Immune pneumonia is an important complication caused by immunotherapy (23); severe immune pneumonia will lead to death. Both Sun *et al.* and Zhang *et al.* reported the occurrence of severe pneumonia (14,15). However, no cases of severe pneumonia occurred in our study.

The limitations of our research are as follows: (I) this is a retrospective study; (II) the number of included cases is small, so it is impossible to perform further subgroup analysis, including by pathological type, gene mutation, PD-L1 score, and other factors, on the curative effect; (III) there was no control group; and (IV) the follow-up time was short. However, we believe that neoadjuvant sintilimab plus chemotherapy might be a promising therapeutic option for patients with locally advanced NSCLC.

Conclusions

Our results suggested that neoadjuvant sintilimab plus chemotherapy might be feasible for stage III NSCLC since it had a high MPR rate and acceptable TRAEs. However, long-term survival data and randomized controlled studies of neoadjuvant chemotherapy, chemoimmunotherapy, and immunotherapy are still needed.

Acknowledgments

Funding: This work was supported by the National Natural Science Foundation of China (Grant. 8190243).

Footnote

Reporting Checklist: The authors have completed the STROBE and AME Case Series reporting checklists. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1194/rc

© Translational Cancer Research. All rights reserved.

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1194/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1194/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 retrospective study was approved by the medical ethics committee of the Sixth Medical Center of Chinese PLA General Hospital (No. HZKY-PJ-2022-9), and was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The informed consent for this retrospective research was waived.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

1. Botticella A, Levy A, Le Pechoux C. Stage III NSCLC in Low- and Middle-Income Countries: Where Are We in 2021? J Thorac Oncol 2021;16:1605-6.
2. Evison M; AstraZeneca UK Limited. The current treatment landscape in the UK for stage III NSCLC. Br J Cancer 2020;123:3-9.
3. Watanabe SI, Nakagawa K, Suzuki K, et al. Neoadjuvant and adjuvant therapy for Stage III non-small cell lung cancer. Jpn J Clin Oncol 2017;47:1112-8.
4. Mielgo-Rubio X, Montemuiño S, Jiménez U, et al. Management of Resectable Stage III-N2 Non-Small-Cell Lung Cancer (NSCLC) in the Age of Immunotherapy. Cancers (Basel) 2021;13:4811.
5. Uprety D, Mandrekar SJ, Wigle D, et al. Neoadjuvant Immunotherapy for NSCLC: Current Concepts and Future Approaches. J Thorac Oncol 2020;15:1281-97.
6. Roller JF, Veeramachaneni NK, Zhang J. Exploring the Evolving Scope of Neoadjuvant Immunotherapy in NSCLC. Cancers (Basel) 2022;14:741.
7. West H, McCleod M, Hussein M, et al. Atezolizumab in combination with carboplatin plus nab-paclitaxel chemotherapy compared with chemotherapy alone as first-line treatment for metastatic non-squamous non-small-cell lung cancer (IMpower130): a multicentre, randomised, open-label, phase 3 trial. Lancet Oncol 2019;20:924-37.
8. Provencio M, Nadal E, Insa A, et al. Neoadjuvant chemotherapy and nivolumab in resectable non-small-cell lung cancer (NADIM): an open-label, multicentre, single-arm, phase 2 trial. Lancet Oncol 2020;21:1413-22.
9. Zhao ZR, Yang CP, Chen S, et al. Phase 2 trial of neoadjuvant toripalimab with chemotherapy for resectable stage III non-small-cell lung cancer. Oncoimmunology 2021;10:1996000.
10. Zhao Z, Gao Y, Xue Q, et al. Safety and Efficacy of Neoadjuvant Immune Checkpoint Inhibitor Therapy in Patients with Resectable Non-small-Cell Lung Cancer: A Systematic Review. Target Oncol 2021;16:425-34.
11. Ettinger DS, Wood DE, Aisner DL, et al. NCCN Guidelines Insights: Non-Small Cell Lung Cancer, Version 2.2021. J Natl Compr Canc Netw 2021;19:254-66.
12. Gutierrez-Sainz L, Cruz-Castellanos P, Higuera O, et al. Neoadjuvant Chemoimmunotherapy in Patients with Resectable Non-small Cell Lung Cancer. Curr Treat Options Oncol 2021;22:91.
13. Gao S, Li N, Gao S, et al. Neoadjuvant PD-1 inhibitor (Sintilimab) in NSCLC. J Thorac Oncol 2020;15:816-26.
14. Zhang P, Dai J, Sun F, et al. Neoadjuvant Sintilimab and Chemotherapy for Resectable Stage IIIA Non-Small Cell Lung Cancer. Ann Thorac Surg 2022. [Epub ahead of print]. doi: 10.1016/j.athoracsur.2022.01.039.
15. Sun C, Liu Y, Zhang P, et al. Interim analysis of the efficiency and safety of neoadjuvant PD-1 inhibitor (sintilimab) combined with chemotherapy (nab-paclitaxel and carboplatin) in potentially resectable stage IIIA/IIIB non-small cell lung cancer: a single-arm, phase 2 trial. J Cancer Res Clin Oncol 2022. [Epub ahead of print]. doi: 10.1007/s00432-021-03896-w.
16. Chansky K, Detterbeck FC, Nicholson AG, et al. The IASLC Lung Cancer Staging Project: External Validation of the Revision of the TNM Stage Groupings in the Eighth Edition of the TNM Classification of Lung Cancer. J Thorac Oncol 2017;12:1109-21.
17. Li P, Lai Y, Zhou K, et al. Analysis of Postoperative Complications and Risk Factors of Patients with Lung Cancer through Clavien-Dindo Classification. Zhongguo

© Translational Cancer Research. All rights reserved.

Fei Ai Za Zhi 2017;20:264-71.
18. Freites-Martinez A, Santana N, Arias-Santiago S, et al. Using the Common Terminology Criteria for Adverse Events (CTCAE - Version 5.0) to Evaluate the Severity of Adverse Events of Anticancer Therapies. Actas Dermosifiliogr (Engl Ed) 2021;112:90-2.
19. 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.
20. Cottrell TR, Thompson ED, Forde PM, et al. Pathologic features of response to neoadjuvant anti-PD-1 in resected non-small-cell lung carcinoma: a proposal for quantitative immune-related pathologic response criteria (irPRC). Ann Oncol 2018;29:1853-60.
21. Blakely CM, McCoach CE. Role of MPR as an Early Signal for Efficacy in Neoadjuvant Studies. Clin Cancer Res 2020;26:3499-500.
22. Tao X, Li N, Wu N, et al. The efficiency of 18F-FDG PET-CT for predicting the major pathologic response to the neoadjuvant PD-1 blockade in resectable non-small cell lung cancer. Eur J Nucl Med Mol Imaging 2020;47:1209-19.
23. Friedman CF, Proverbs-Singh TA, Postow MA. Treatment of the Immune-Related Adverse Effects of Immune Checkpoint Inhibitors: A Review. JAMA Oncol 2016;2:1346-53.

Cite this article as: Fan BS, Wang XT, Di SY, Zhao JH, Chen SY, Zhou SH, Yue CY, Song WA, Gong TQ. Short-term outcomes of neoadjuvant sintilimab with chemotherapy in stage III non-small cell lung cancer: a case series. Transl Cancer Res 2022;11(6):1697-1704. doi: 10.21037/tcr-22-1194

© Translational Cancer Research. All rights reserved.