Targeting TROP-2 in treatment-resistant non-small cell lung cancer harboring the *KRAS* G12C mutation and TROP-2 upregulation: A case report

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Abstract. Non-small cell lung cancer (NSCLC) with v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog gene (*KRAS*) mutations is one of the most aggressive and refractory tumors. Trophoblast cell-surface antigen 2 (TROP-2) is a recognized marker of poor prognosis in NSCLC. Several clinical trials targeting TROP-2 and *KRAS* mutations have established novel possibilities for the treatment of patients with NSCLC. However, the results remain unsatisfactory, likely due to the heterogeneity of tumor cells and the presence of diverse co-mutations. No consensus has been reached regarding the treatment of patients with concurrent TROP-2 upregulation and *KRAS* mutations. The present report describes the case of a patient diagnosed with lung adenocarcinoma who presented with a *KRAS* G12C mutation, TROP-2 upregulation and widespread treatment-resistant disease. The patient subsequently benefited from a novel antibody-drug conjugate targeting human TROP-2 as second-line treatment following first lines of therapy. Follow-up computed tomography imaging over a 34-month treatment period demonstrated partial remission (42% reduction based on Response Evaluation Criteria in Solid Tumors version 1.1) without serious adverse events. Currently, therapeutic options for patients with recurrent NSCLC exhibiting simultaneous TROP-2 upregulation and *KRAS* mutation are limited. Targeting TROP-2 may represent a novel therapeutic approach for patients with NSCLC, particularly those with chemo-radioresistant disease.

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Abbreviations: *KRAS*, v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog gene; NSCLC, non-small cell lung cancer; LUAD, lung adenocarcinoma; TROP-2, trophoblast cell-surface antigen 2; ADC, antibody-drug conjugate; CT, computed tomography

Key words: TROP-2, NSCLC, ADC, treatment resistance, *KRAS* G12C mutation

Introduction

Mutations in the v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog gene *(KRAS)* are important genetic testing indicators for advanced-stage non-small cell lung cancer (NSCLC), occurring in 8-10% of Asian patients with lung adenocarcinoma (LUAD) (1). Approximately half of *KRAS*-mutated NSCLCs display co-occurring genomic alterations, mainly in cyclin dependent kinase inhibitor 2A, *PI3KA*, *TP53*, *AKT1*, serine/threonine kinase 11 (*STK11*), kelch like ECH associated protein 1 (*KEAP1*) and *BRAF* (2), which are associated with an invasive phenotype, resistance to chemoradiotherapy and poorer clinical outcomes (3). Advancements in targeting the mutant KRAS G12C protein in LUAD include the development of sotorasib (AMG 510) and adagrasib (MRTX849), which have shown promising results (4,5); however, current clinical guidelines still recommend *KRAS* G12C inhibitors as second-line treatments (6).

Trophoblast cell-surface antigen 2 (TROP-2) has potential as a novel therapeutic target in lung cancer (7). High TROP-2 expression has been observed in several human tumors, including lung, colorectal and breast cancer, and is a negative prognostic factor in solid cancers (8-10). TROP-2 upregulation has been detected in 60% of squamous lung cell carcinomas, 40-60% of adenocarcinomas and 20% of high-grade pulmonary neuroendocrine neoplasms (11,12). TROP-2 may be considered a useful marker of poor cancer prognosis (13). TROP-2-targeted antibody-drug conjugates (ADCs) have demonstrated efficacy in clinical trials of multiple types of solid cancer , such as advanced urothelial cancer and breast cancer (14,15).

The current understanding and effective treatment of lung cancer harboring *KRAS* mutation and TROP-2 upregulation remain inadequate, and NSCLCs with both the *KRAS* G12C mutation and TROP-2 upregulation have not, to the best of our knowledge, been reported.

The present report describes a patient with advanced LUAD who achieved favorable therapeutic outcomes with

TROP-2-targeted ADC therapy following resistance to radiotherapy, chemotherapy and immunotherapy, without serious adverse reactions.

Case report

A 65-year-old man, a smoker with a past medical history of coronary artery disease and hypertension, presented to Huangshi Hospital of Chinese Traditional Medicine (Huangshi, China) in February 2022 with intermittent chest tightness and pain lasting 2 weeks. The patient was transferred to Hubei Cancer Hospital (Wuhan, China) in March 2022.

The chest computed tomography (CT) revealed a primary malignancy in the middle lobe of the right lung (~6.7x5.7 cm) (Fig. 1A), accompanied by a small amount of obstructive inflammation; multiple enlarged lymph nodes in mediastinal groups 2, 4 and 7, and in the right pulmonary hilum; and multiple metastases in both lungs and bilateral pleura (largest measuring ~2.7x1.7 cm) (Fig. 1B). No evidence of metastasis was found elsewhere in the body. Adenocarcinoma was diagnosed by CT-guided needle biopsy in March 2022 (Fig. 1C).

Next-generation sequencing performed in Huangshi Hospital of Chinese Traditional Medicine revealed a *KRAS* G12C mutation and a programmed cell death ligand 1 (PD-L1) tumor proportion score of <1%, without other co-mutations. The patient was diagnosed with right LUAD with multiple metastases to both lungs [stage IV, cT2N0M1 according to TNM Classification and Union for International Cancer Control (16)] harboring a *KRAS* G12C mutation.

For patients with advanced NSCLC harboring *KRAS* mutations, first-line therapy consists of platinum-based dual-drug chemotherapy combined with antivascular treatment or immunotherapy (17). The current patient received chemotherapy (cisplatin/pemetrexed) every 3 weeks for four cycles combined with immunotherapy (camrelizumab). Cisplatin (25 mg/m^2) was administered for 3 days, and intravenous pemetrexed (500 mg/m^2) and camrelizumab (200 mg) were administered on day 1 of each cycle from March 2022 to June 2022. The patient did not receive immune maintenance therapy due to financial constraints. Evaluation indicated partial responseon CT scan after the fourth treatment cycle (Fig. 1D and E) based on the Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) (18). Due to gastrointestinal adverse effects, the patient refused to continue chemotherapy beyond June 2022.

The addition of thoracic radiotherapy in patients with advanced NSCLC can improve overall survival (OS) (19). To consolidate the curative effect, chest radiotherapy was proposed in July 2022 (gross tumor volume, 60 Gy/30 F; planning target volume, 54 Gy/30 F). Follow-up CT scans were performed every 6 weeks after radiotherapy. The patient did not receive antitumor treatment after September 2022 and suffered disease progression in February 2023 (half a year later).

Malignant pleural effusion and tumor growth were observed (Fig. 1D-F). Sotorasib and adagrasib have been approved as second-line therapies for adults with NSCLC harboring the *KRAS* G12C mutation (20). The patient could not access *KRAS* G12C inhibitors due to financial hardship and was counselled for enrolment in a phase II clinical trial (KLUS Pharma, Inc., program no. KL264-01; trial ID NCT04152499) involving the TROP-2 ADC SKB264. Standard methods were used for immunohistochemistry (performed at the Central Laboratory of MEDx Translational Medicine Co., Ltd.) and the evaluation of TROP-2 expression using the H-score. TROP-2 expression was observed under the microscope by a pathologist after staining and was evaluated according to the coloring ratio and depth. The H-score was interpreted as follows: 0 (negative), no membrane staining of arbitrary strength; 1+ (weakly positive), tumor cells exhibit weak cell membrane staining; 2+ (moderately positive), tumor cells exhibit moderate membrane staining; and 3+ (strongly positive), tumor cells exhibit strong membrane staining. H-score=[1x (% cells 1+) + 2x (% cells 2+) + 3x (% cells 3+)] x100. TROP-2 expression was defined as: Weakly positive, H-score ≤100; moderately positive, H-score ≤200; and strongly positive, H-score ≤300. Finally, TROP-2 upregulation was confirmed at the 2+ level by immunohistochemistry (Fig. 2). The patient was administered SKB264 (10 mg/kg, day 1 of 14-day cycles) beginning in March 2023. The first follow-up CT scan was performed within 3 months of treatment initiation and is ongoing.

At the time of writing this report, the clinical response of the patient has persisted for 34 months (January 2026) after treatment initiation. The patient suffered disease progression in February 2023 after first-line treatment (without antitumor treatment from September 2022). There was a 42% reduction in tumor size from the baseline (February 2023), as measured based on RECIST 1.1 (Fig. 3). The therapeutic course is shown in Fig. 4. The patient experienced Grade I anemia (21) in March 2023 without obvious symptoms of ischemia, such as dizziness or fatigue, and intermittently took oral iron supplements. In addition, the patient experienced intermittent Grade I decreased appetite after June 2023 and received appropriate nutritional supplementation. No other serious adverse events were observed.

Discussion

The present case highlights the clinical potential of ADCs targeting TROP-2 in NSCLC harboring a *KRAS* G12C mutation. TROP-2 upregulation was detected, and the patient with the *KRAS* G12C mutation was enrolled in a phase II clinical trial. *KRAS* inhibitors were not selected due to financial reasons. After multiline therapy, the patient benefited from a novel ADC targeting TROP-2 (SKB264). The patient responded well to SKB264 treatment and achieved good outcomes. Follow-up CT imaging showed a 42% reduction in target lesions over 34 months and no serious adverse events were observed. The survival of the patient exceeded expectations based on published clinical trial data (22), providing novel insights into potential strategies for the treatment of NSCLC with *KRAS* G12C mutations.

KRAS is one of the most frequently mutated oncogenes in solid tumors. *KRAS* mutations occur in 20-30% of lung cancers, with the G12C variant accounting for 35-45% of these (23,24). Although the prevalence is lower in Asian populations (25), nearly 3% of Chinese patients with NSCLC harbor the *KRAS* G12C mutation (26), with a higher incidence in male smokers (27). Approximately half of NSCLCs with *KRAS* mutations display co-occurring genomic alterations (mainly in

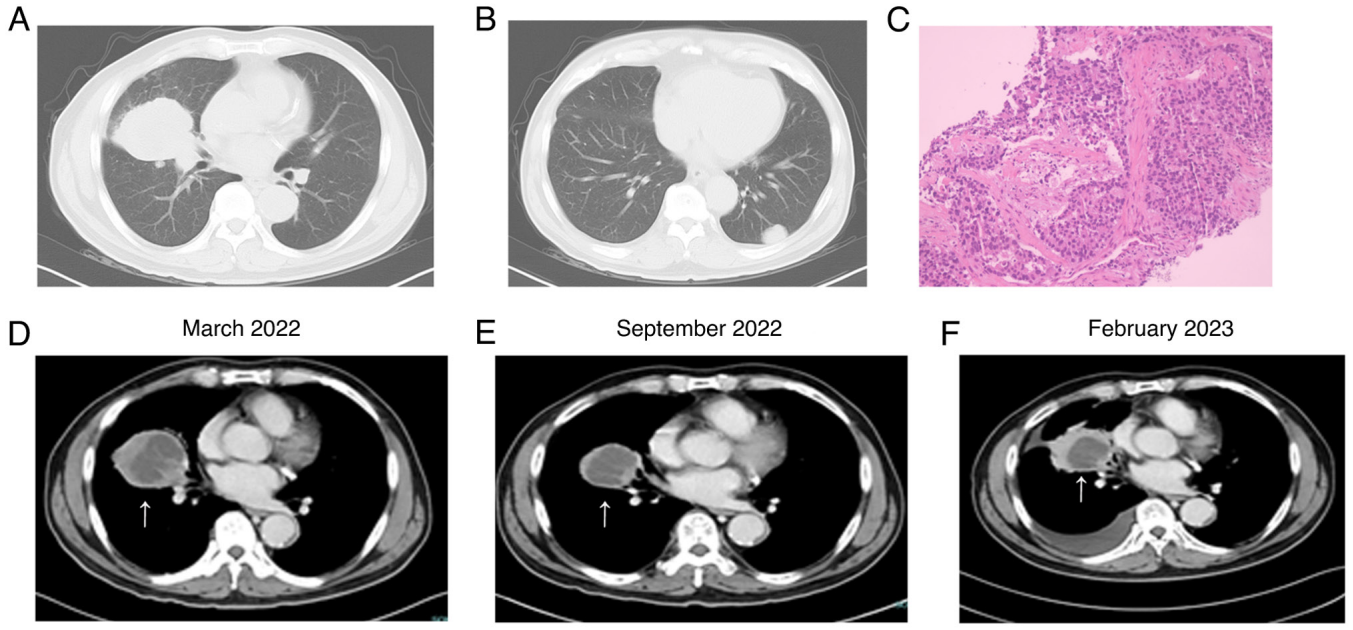

Figure 1. CT images and pathological results of lung cancer. (A) Primary malignancy in the middle lobe of the right lung; (B) metastases in bilateral pleura; and (C) adenocarcinoma. CT scan (D) at baseline (March 2022), (E) after chemoradiation (September 2022) and (F) during follow-up (February 2023). The arrows indicate the primary tumor. CT, computed tomography.

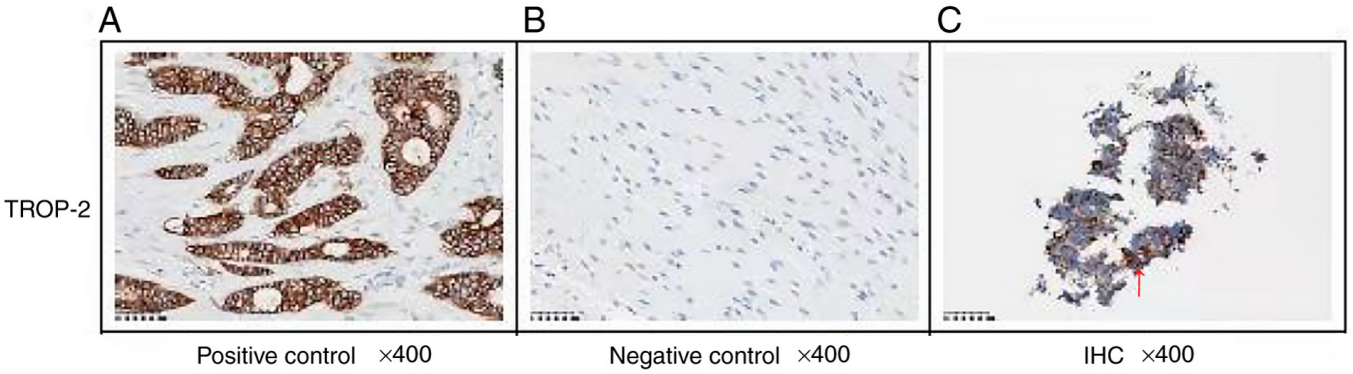

Figure 2. TROP-2 expression was observed in tumors using IHC staining. (A) Positive control. (B) Negative control. (C) TROP-2 expression in the current case. The arrow indicates TROP-2 expression in tumor tissue. Magnification, x400. IHC, immunohistochemistry; TROP-2, trophoblast cell-surface antigen 2. Positive control, TROP-2 (+++); Negative control, TROP-2 (-).

TP53, *STK11* and *KEAP1*). The co-occurring genomic mutations may be associated with an invasive phenotype, resistance to chemoradiotherapy and a worse clinical outcome (28). Based on existing mechanistic study, TROP-2 is involved in the regulation of several tumor signaling pathways, including the PI3K-AKT, B-Raf-ERK, Wnt/β-catenin and other pathways (29). Genes such as *TP53*, *STK11* and *KEAP1* are also directly or indirectly implicated. Although abnormal expression of these genes often suggests poor prognosis or resistance to current treatment models, targeting of TROP-2 could serve a multi-pronged role in therapy (30). In addition, genes such as *STK11*, *KEAP1* and *TP53*, as well as biomarkers such as PD-L1 and tumor mutation burden, are currently widely reported for predicting the efficacy of immunotherapy (31). However, to the best of our knowledge, whether these co-mutations or biomarkers will impact the efficacy of ADCs is still unknown. This remains a key issue that needs to be addressed when ADC drugs are widely used in clinical practice, both now and in the future.

The National Comprehensive Cancer Network guidelines (V3. 2022) recommend platinum-based chemotherapy, with or without immunotherapy, as the first-line treatment for metastatic NSCLC with *KRAS* mutations (32). Notably, *KRAS* mutations may upregulate PD-L1 expression, contributing to immune resistance (30,33), reducing $CD8^+$ T cell infiltration and lowering tumor mutational burden factors that contribute to reduced benefit from immune checkpoint inhibitors (34). However, to the best of our knowledge, no differences have been observed between the outcomes of patients treated with immunotherapy or immunotherapy plus chemotherapy, with and without *KRAS* mutations. A retrospective analysis of the KEYNOTE-042 trial suggests that immune checkpoint inhibitors may improve the prognosis of *KRAS*-mutant NSCLC (35). According to the Flatiron database, patients with *KRAS*

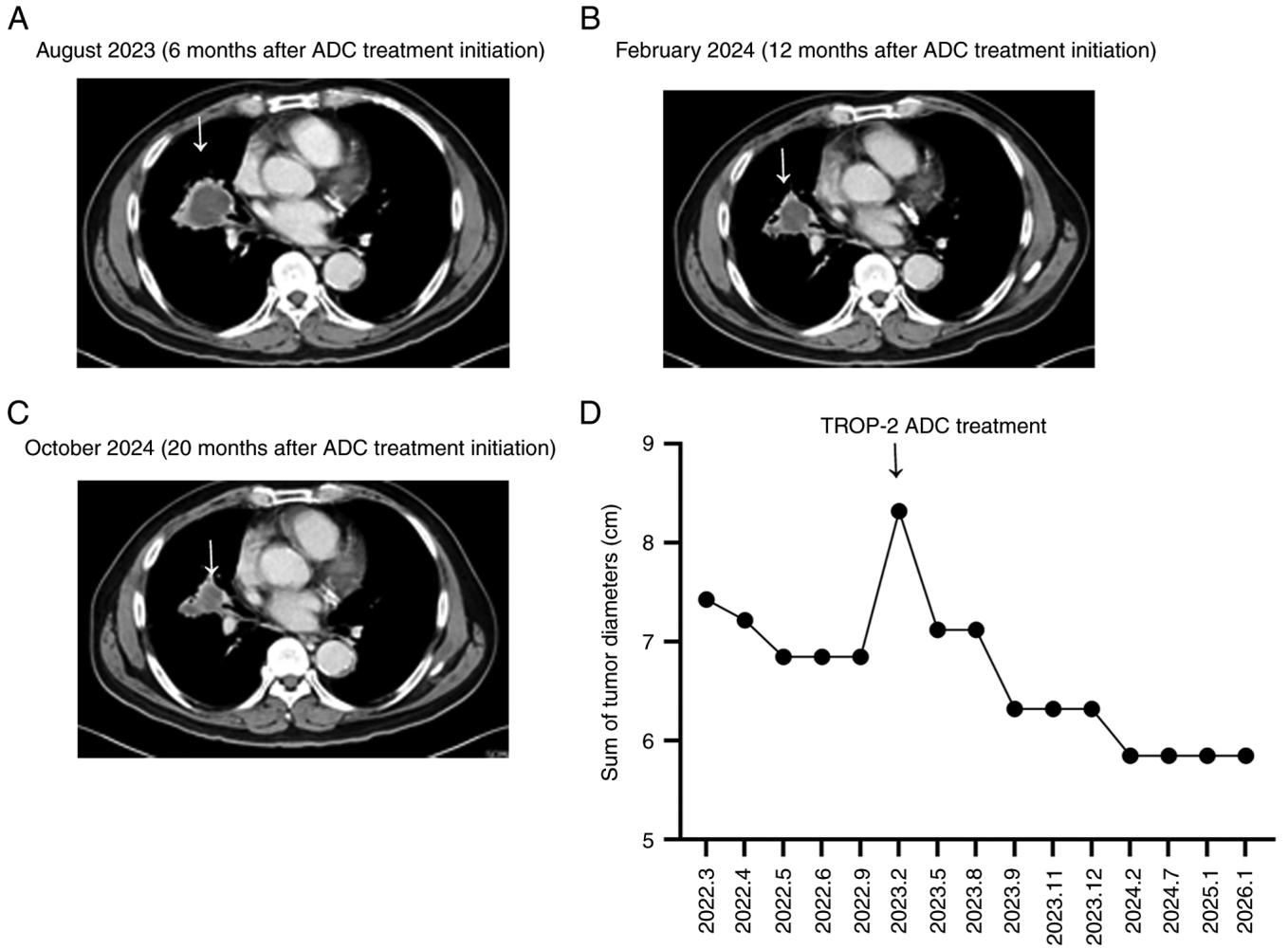

Figure 3. CT images of lung cancer. CT scan (A) after treatment with TROP-2 ADC for 6 months (August 2023), (B) after 12 months (February 2024) and (C) after 20 months (October 2024). Arrows indicate the primary tumor. (D) Changes in tumor size during ADC treatment. CT, computed tomography; TROP-2, trophoblast cell-surface antigen 2; ADC, antibody-drug conjugate.

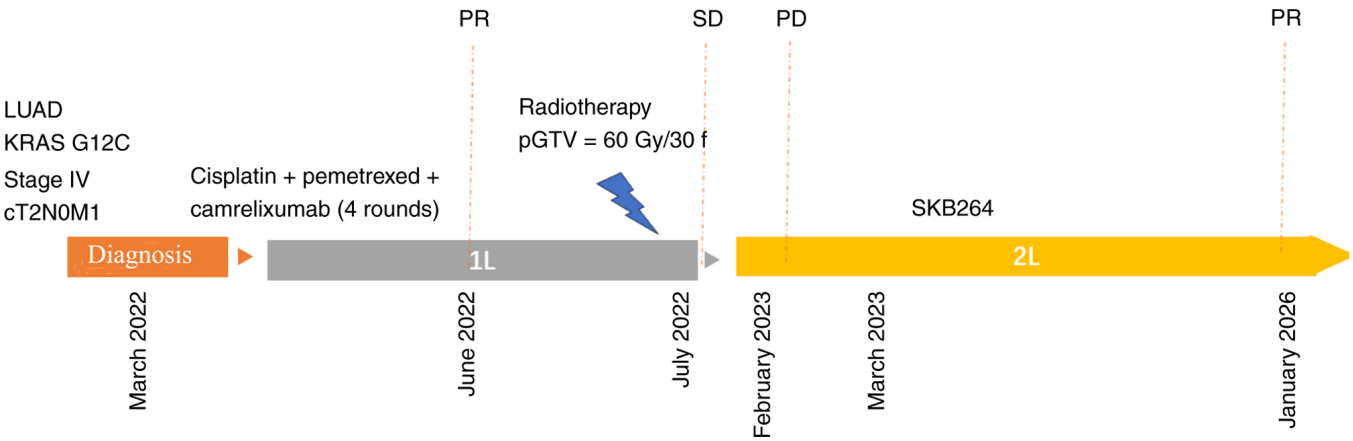

Figure 4. Timeline summarizing the case diagnosis and treatment pathway. KRAS, v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog gene; LUAD, lung adenocarcinoma; PR, partial response; PD, progressive disease; SD, stable disease; PGTV, planning gross tumor volume; 1L, first-line; 2L, second-line.

mutations can benefit from immunotherapy or chemoimmunotherapy; however, those with wild-type tend to benefit from combination therapy (36).

The current patient experienced disease progression within ~1 year of first-line chemoimmunotherapy, which is in line with the estimated poor prognosis for *KRAS* G12C mutation in patients with NSCLC. First-line chemoimmunotherapy for metastatic NSCLC with *KRAS* G12C mutation results in a median progression-free survival (PFS) and OS of 7.9 and 18.1 months, respectively (37).

Drugs targeting *KRAS* G12C have been shown to prolong the survival of patients with metastatic disease. The multicenter phase I/II open-label CodeBreaK 100 trial reported that the disease control rate (DCR) and objective response rate (ORR) of sotorasib in patients with advanced and metastatic NSCLC were 38.1 and 32.2%, respectively, with tolerable toxicity (38). Compared with docetaxel, sotorasib extended the median PFS time by 1 month (5.6 vs. 4.5 months) (39), and received approval as the first *KRAS* G12C inhibitor by the United States Food and Drug Administration in May 2021 for the treatment of advanced NSCLC. Similarly, in the KRYSTAL-12 study, adagrasib achieved a longer median PFS time in patients with pretreated *KRAS* G12C-mutated NSCLC than chemotherapy (5.5 vs. 3.8 months; hazard ratio, 0.58; P<0.0001). Additionally, adagrasib demonstrated intracranial efficacy in patients with brain metastases, with an ORR more than twice that in the docetaxel group (24 vs. 11%) (40). Adagrasib (trade name, Krazati) was approved in the European Union on January 10, 2024, as a treatment for pretreated patients with *KRAS* G12C-mutated NSCLC (41). NCT05005234, a registered phase II clinical study led by Professor Wu Yilong, demonstrated the safety and efficacy of fluzelese monotherapy in the treatment of advanced *KRAS* G12C-mutant NSCLC. Fluzelese exhibited a DCR of 90% (95% CI, 84-95%), ORR of 49% (95% CI, 40-59%) and 12-month durable response rate of 54% (95% CI, 38-67%) (42). Multiple phase III clinical trials (Table I) are currently underway to assess the effectiveness of drugs against *KRAS* G12C-mutant NSCLC. Despite advances, the prognosis of patients with *KRAS* G12C mutations remains poor. The development of novel treatment models is particularly important for improving patient prognosis.

ADCs have emerged as promising therapies, combining targeted monoclonal antibodies with cytotoxic agents to enhance tumor-specific drug delivery and minimize systemic toxicity (43). TROP-2, a type I transmembrane glycoprotein, is upregulated in several malignancies (44). Although its upregulation mechanism is not fully understood, its role in cancer cell proliferation, invasion and metastasis is well documented (10,45). To the best of our knowledge, no research has explored the direct relationship between TROP-2 and *KRAS G12C*. TROP-2 mainly promotes the growth, proliferation and metastasis of tumor cells by regulating various cellular signaling pathways, including the calcium ion, MAPK/ERK and PI3K/AKT signaling pathways (27). The association between *KRAS* mutations and TROP-2 expression has only been reported in colorectal and pancreatic cancer (46). TROP-2 expression is generally upregulated in patients with *KRAS* mutations compared with those with wild-type *KRAS*, suggesting the therapeutic potential of targeting TROP-2 in advanced tumors with *KRAS* mutations (45).

TROP-2 activates MAPK signaling, ERK1/2 phosphorylation and transcription factor activator protein 1, and may drive epithelial-mesenchymal transition through podoplanin (47). TROP-2 upregulation is associated with poorer differentiation, increased lymph node metastasis and worse survival across multiple cancer types, including NSCLC, gastric cancer and ovarian cancer (48-50). High TROP-2 expression in NSCLC has been associated with shorter survival, making it a compelling therapeutic target.

Several TROP-2-directed ADCs have demonstrated clinical potential. Trodelvy (sacituzumab govitecan-hziy) is an ADC developed by Gilead Sciences, Inc., in the United States. The results of the IMMU-132-01 study showed reduced diameters in tumors from different histological sources after gosatuzumab treatment, confirming that TROP-2 is a broad target for various solid tumors (51). According to the latest released follow-up data, Trodelvy exhibited antitumor activity and manageable safety in patients with SCLC in the extensive stage (TROPiCS-03 study) (52). Dato-DXd, an ADC combining a TROP-2 IgG1 monoclonal antibody and a Topo I inhibitor (DXd), inhibited NSCLC growth in xenograft models (53), and improved PFS compared with chemotherapy (4.4 vs. 3.7 months) in the TROPION Lung 01 study. A benefit was seen across a range of TROP-2 expression levels, although heterogeneity, downregulation or structural changes may contribute to resistance (54). Other clinical trials (Table II) are currently underway to assess the effectiveness of TROP-2 ADCs in NSCLC.

Several questions remain unanswered. A phase III clinical trial (EVOKE-01 study) failed to show that Trodelvy was more effective than docetaxel as a second-line treatment for NSCLC (55). It is critical to identify the population that could benefit from TROP-2 ADC treatment. Based on analysis of previous research, patients with EGFR mutations may benefit more from TROP-2 ADC treatment after failure of first-line TKI therapy (56). In addition, patients who do not respond to anti-PD-L1 have also been shown to benefit from TROP-2 ADC therapy (22). Therefore, the role of ADCs in lung cancer should be comprehensively re-examined. In particular, efficacy-predictive biomarkers are required. Positivity for TROP-2 calculated using quantitative continuous scoring effectively predicted outcomes after Dato-DXd treatment in the TROPION Lung 01 study (57). High TROP-2 expression may have contributed to the survival benefits in the current patient. Whether *KRAS* G12C affects the efficacy of TROP-2 ADC therapy in patients requires further study. Although the EVOKE-01 clinical study evaluated data from 14 cases with *KRAS* G12C mutations, the design did not include subgroup analysis (55). Research on the association between TROP-2 and the activation mechanism of *KRAS* mutations is still limited. However, from the results of the aforementioned clinical and basic studies that have been published, it can be roughly inferred that upregulation of TROP-2 likely serves an important role in the occurrence and development of *KRAS*-mutant solid tumors, including NSCLC.

The present case suggests that TROP-2-targeted ADCs may represent a viable therapeutic option for patients with *KRAS* G12C-mutant NSCLC, particularly when standard treatments are not feasible or effective. Given the generally poor prognosis and resistance-prone nature of current targeted therapies, TROP-2-directed strategies may offer a novel avenue for improving outcomes. Similarly, the SKB264-II-08 clinical trial suggested that the TROP-2 ADC regimen produced an ORR of 40%, a DCR of 81%, a median PFS time of 6.2 months and a median OS time of 21.8 months (56). This is worse than that recorded for the patient in the present case report. We speculate that patients with *KRAS* G12C combined with high expression of TROP-2 may form the group benefiting from TROP-ADC. However, due to the small number of patients in this category,

Table I. Ongoing phase III trials investigating patients with KRAS G12C-mutant lung cancer (https://clinicaltrials.gov/; accessed on January 30, 2025).

Clinical trial ID	Phase	Setting	Total patients, n	Treatment arms	Primary endpoint
NCT06300177	III	KRAS G12C mutation-positive locally advanced or metastatic NSCLC after prior standard therapy failure	522	D-1553 vs. docetaxel	PFS
CT06497556	III	Pretreated KRAS G12C mutation-positive advanced or metastatic NSCLC	320	Divarasib vs. sotorasib/ adagrasib	PFS
NCT04685135	III	Pretreated KRAS G12C mutation-positive NSCLC patients	453	MRTX849 vs. docetaxel	PFS
NCT02152631	III	Patients with stage IV NSCLC with a detectable KRAS mutation who have progressed after platinum-based chemotherapy	453	Abemaciclib vs. erlotinib	OS
NCT05132075	III	Locally advanced or metastatic KRAS G12C-mutant NSCLC	95	JDQ443 vs. docetaxel	PFS
NCT06345729	III	KRAS G12C-mutant, metastatic NSCLC with PD-L1 TPS ≥50%	600	MK-1084 + pembrolizumab vs. pembrolizumab	PFS
NCT04613596	II/III	Advanced NSCLC with KRAS G12C mutation	806	II: Adagrasib + pembrolizumab III: Adagrasib + pembrolizumab vs. pembrolizumab	II: ORR III: PFS OS
NCT06416410	III	Advanced non-squamous NSCLC with KRAS p.G12C mutation	392	JAB-21822 + JAB-3312 vs. tislelizumab + pemetrexed + carboplatin	PFS
NCT01933932	III	Locally advanced or metastatic NSCLC (stage IIIb-IV)	510	Selumetinib + docetaxel vs. placebo + docetaxel	PFS
NCT06119581	III	NSCLC with KRAS G12C mutation	1,016	LY3537982 + standard therapy vs. standard therapy	TEAE, PFS
NCT05920356	III	Stage IV or advanced stage IIIB/C non-squamous NSCLC, negative for PD-L1 and positive for KRAS p.G12C	750	Sotorasib + platinum doublet chemotherapy vs. pembrolizumab + platinum doublet chemotherapy	PFS
NCT06335355	III	Patients with advanced or metastatic NSCLC with STK11/KEAP1/KRAS mutations	401	Adebrelimab + SHR-8068 + pemetrexed + carboplatin/ camrelizumab + pemetrexed + carboplatin vs. adebrelimab + pemetrexed + carboplatin	ORR, PFS
NCT06008093	III	Patients with metastatic NSCLC with non-squamous histology who have mutations and/or co-mutations in STK11, KEAP1 or KRAS	280	Durvalumab + tremelimumab + chemotherapy vs. pembrolizumab + chemotherapy	OS
NCT04303780	III	Patients with NSCLC with KRAS p.G12c mutation	345	AMG 510 vs. docetaxel	PFS

KRAS, v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog gene; NSCLC, non-small cell lung cancer; PFS, progression-free survival; OS, overall survival; ORR, objective response rate; TEAE, treatment-emergent adverse event; KEAP1, kelch like ECH associated protein 1; PD-L1, programmed death-ligand 1; STK11, serine/threonine kinase 11; TPS, tumor proportion score.

Table II. Ongoing trials involving anti-TROP-2 ADCs in lung cancer (https://clinicaltrials.gov/; accessed on October 30, 2024).

Clinical trial ID	Phase	Setting	N	Treatment arms	Primary endpoint
NCT04152499	I/II	Patients with locally advanced unresectable/metastatic solid tumors who are refractory to available standard therapies	1,300	SKB264	ORR
NCT05941507	II	Patients with advanced solid tumors refractory to the standard of care, or for whom no standard of care exists	300	LCB84 vs. LCB84 + anti-PD-1	ORR, DOR, PFS, OS
NCT05460273 (TROPION-PanTumor02)	I/II	Advanced NSCLC	119	Dato-DXd	ORR
NCT04940325 (ICARUS-LUNG01)	II	Advanced and/or unresectable NSCLC	100	DS-1062a	ORR
NCT06074588 (MK-2870-004)	III	Previously treated NSCLC with EGFR mutations	556	SKB264 vs. docetaxel/pemetrexed	PFS and OS
NCT06480136	II	NSCLC with previously treated	32	SHR-A1921 + adebrelimab	ORR
NCT05609968 (KEYNOTE D46/EVOKE-03)	III	Metastatic NSCLC with PD-L1 TPS ≥50%	614	Pembrolizumab + sacituzumab govitecan vs. pembrolizumab	PFS, OS
NCT05687266 (AVANZAR)	III	Locally advanced or metastatic NSCLC without actionable genomic alterations	1,280	Dato-DXd + durvalumab + carboplatin vs. durvalumab + carboplatin + cisplatin/pemetrexed/paclitaxel	PFS, OS
NCT06431633 (ARIAN)	II	Patients with IB to IIIA and IIIB (N2) NSCLC who did not achieve pCR after neoadjuvant treatment	129	Control vs. zimberelimab vs. sacituzumab govitecan + zimberelimab	DFS

NSCLC, non-small cell lung cancer; PFS, progression-free survival; OS, overall survival; ORR, objective response rate; pCR, pathologic complete response; PD-L1, programmed cell death ligand 1; TPS, tumor proportion score; DOR, duration of response; TROP-2, trophoblast cell-surface antigen 2; ADC, antibody-drug conjugate; DFS, disease-free survival; PD-1, programmed cell death protein 1.

more reports on similar patients are required and this hypothesis will be further explored in future work. As aforementioned, research on TROP-2 in *KRAS*-mutant solid tumors, including lung cancer, is limited. The present case report provides indirect evidence for the association between the two and offers novel insights and ideas for the treatment of patients with advanced NSCLC with *KRAS* mutations and high TROP-2 expression. However, the present case report has some limitations, including the unavailability of clearer TROP-2 immunohistochemistry and raw next-generation sequencing data.

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Availability of data and materials

The TROP-2 immunohistochemistry data generated in the present study may be requested from MEDx Translational Medicine Co. Ltd., due to clinical trial requirements. The next-generation sequencing data generated in the present study are not publicly available since this was performed by Huangshi Hospital of Chinese Traditional Medicine (Huangshi, China). The other data generated in the present study may be requested from the corresponding author.

Authors' contributions

YP conceived and designed the study. LS and XL analyzed the data and wrote the manuscript. YX collected data and images.

All authors have read and approved the final version of the manuscript. YP and LS confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written consent for publication of the images was provided by the patient.

Competing interests

The authors declare that they have no competing interests.

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