

World Journal of *Clinical Cases*

World J Clin Cases 2022 June 16; 10(17): 5518-5933



MINIREVIEWS

- 5518** Occult hepatitis B — the result of the host immune response interaction with different genomic expressions of the virus
Gherlan GS
- 5531** Pulmonary complications of portal hypertension: The overlooked decompensation
Craciun R, Mocan T, Procopet B, Nemes A, Tefas C, Sparchez M, Mocan LP, Sparchez Z
- 5541** Ethical review of off-label drugs during the COVID-19 pandemic
Li QY, Lv Y, An ZY, Dai NN, Hong X, Zhang Y, Liang LJ

ORIGINAL ARTICLE

Case Control Study

- 5551** Gut peptide changes in patients with obstructive jaundice undergoing biliary drainage: A prospective case control study
Pavić T, Pelajić S, Blažević N, Kralj D, Milošević M, Mikolasevic I, Lerotic I, Hrabar D

Retrospective Cohort Study

- 5566** Longitudinal assessment of liver stiffness by transient elastography for chronic hepatitis C patients
Mezina A, Krishnan A, Woreta TA, Rubenstein KB, Watson E, Chen PH, Rodriguez-Watson C

Retrospective Study

- 5577** Clinical evaluation of prone position ventilation in the treatment of acute respiratory distress syndrome induced by sepsis
Xia WH, Yang CL, Chen Z, Ouyang CH, Ouyang GQ, Li QG
- 5586** Three-dimensional arterial spin labeling and diffusion kurtosis imaging in evaluating perfusion and infarct area size in acute cerebral ischemia
Jiang YY, Zhong ZL, Zuo M
- 5595** Intrathecal methotrexate in combination with systemic chemotherapy in glioblastoma patients with leptomeningeal dissemination: A retrospective analysis
Kang X, Chen F, Yang SB, Wang YL, Qian ZH, Li Y, Lin H, Li P, Peng YC, Wang XM, Li WB
- 5606** Hepatic epithelioid hemangioendothelioma: Clinical characteristics, diagnosis, treatment, and prognosis
Zhao M, Yin F
- 5620** Difference between type 2 gastroesophageal varices and isolated fundic varices in clinical profiles and portosystemic collaterals
Song YH, Xiang HY, Si KK, Wang ZH, Zhang Y, Liu C, Xu KS, Li X

- 5634** Assessment of incidental focal colorectal uptake by analysis of fluorine-18 fluorodeoxyglucose positron emission tomography parameters

Lee H, Hwang KH, Kwon KA

Observational Study

- 5646** "Zero ischemia" laparoscopic partial nephrectomy by high-power GreenLight laser enucleation for renal carcinoma: A single-center experience

Zhang XM, Xu JD, Lv JM, Pan XW, Cao JW, Chu J, Cui XG

- 5655** High Eckardt score and previous treatment were associated with poor postperoral endoscopic myotomy pain control: A retrospective study

Chen WN, Xu YL, Zhang XG

- 5667** Higher volume growth rate is associated with development of worrisome features in patients with branch duct-intraductal papillary mucinous neoplasms

Innocenti T, Danti G, Lynch EN, Dragoni G, Gottin M, Fedeli F, Palatresi D, Biagini MR, Milani S, Miele V, Galli A

Prospective Study

- 5680** Application of a new anatomic hook-rod-pedicle screw system in young patients with lumbar spondylolysis: A pilot study

Li DM, Li YC, Jiang W, Peng BG

META-ANALYSIS

- 5690** Systematic review of Yougui pills combined with levothyroxine sodium in the treatment of hypothyroidism

Liu XP, Zhou YN, Tan CE

CASE REPORT

- 5702** Allogeneic stem cell transplantation-A curative treatment for paroxysmal nocturnal hemoglobinuria with PIGT mutation: A case report

Schenone L, Notarantonio AB, Latger-Cannard V, Fremeaux-Bacchi V, De Carvalho-Bittencourt M, Rubio MT, Muller M, D'Aveni M

- 5708** Gray zone lymphoma effectively treated with cyclophosphamide, doxorubicin, vincristine, prednisolone, and rituximab chemotherapy: A case report

Hojo N, Nagasaki M, Mihara Y

- 5717** Diagnosis of spontaneous isolated superior mesenteric artery dissection with ultrasound: A case report

Zhang Y, Zhou JY, Liu J, Bai C

- 5723** Adrenocorticotrophic hormone-secreting pancreatic neuroendocrine carcinoma with multiple organ infections and widespread thrombosis: A case report

Yoshihara A, Nishihama K, Inoue C, Okano Y, Eguchi K, Tanaka S, Maki K, Fridman D'Alessandro V, Takeshita A, Yasuma T, Uemura M, Suzuki T, Gabazza EC, Yano Y

- 5732** Management of the palato-radicular groove with a periodontal regenerative procedure and prosthodontic treatment: A case report

Ling DH, Shi WP, Wang YH, Lai DP, Zhang YZ

- 5741** Combined thoracic paravertebral block and interscalene brachial plexus block for modified radical mastectomy: A case report
Hu ZT, Sun G, Wang ST, Li K
- 5748** Chondromyxoid fibroma of the cervical spine: A case report
Li C, Li S, Hu W
- 5756** Preterm neonate with a large congenital hemangioma on maxillofacial site causing thrombocytopenia and heart failure: A case report
Ren N, Jin CS, Zhao XQ, Gao WH, Gao YX, Wang Y, Zhang YF
- 5764** Simultaneous multiple primary malignancies diagnosed by endoscopic ultrasound-guided fine-needle aspiration: A case report
Yang J, Zeng Y, Zhang JW
- 5770** Neuroendocrine tumour of the descending part of the duodenum complicated with schwannoma: A case report
Zhang L, Zhang C, Feng SY, Ma PP, Zhang S, Wang QQ
- 5776** Massive hemothorax following internal jugular vein catheterization under ultrasound guidance: A case report
Kang H, Cho SY, Suk EH, Ju W, Choi JY
- 5783** Unilateral adrenal tuberculosis whose computed tomography imaging characteristics mimic a malignant tumor: A case report
Liu H, Tang TJ, An ZM, Yu YR
- 5789** Modified membrane fixation technique in a severe continuous horizontal bone defect: A case report
Wang LH, Ruan Y, Zhao WY, Chen JP, Yang F
- 5798** Surgical repair of an emergent giant hepatic aneurysm with an abdominal aortic dissection: A case report
Wen X, Yao ZY, Zhang Q, Wei W, Chen XY, Huang B
- 5805** Heterotopic ossification beneath the upper abdominal incision after radical gastrectomy: Two case reports
Zhang X, Xia PT, Ma YC, Dai Y, Wang YL
- 5810** Non-alcoholic Wernicke encephalopathy in an esophageal cancer patient receiving radiotherapy: A case report
Zhang Y, Wang L, Jiang J, Chen WY
- 5816** New approach for the treatment of vertical root fracture of teeth: A case report and review of literature
Zhong X, Yan P, Fan W
- 5825** Ultrasound-guided microwave ablation as a palliative treatment for mycosis fungoides eyelid involvement: A case report
Chen YW, Yang HZ, Zhao SS, Zhang Z, Chen ZM, Feng HH, An MH, Wang KK, Duan R, Chen BD
- 5833** Pulp revascularization on an adult mandibular right second premolar: A case report
Yang YQ, Wu BL, Zeng JK, Jiang C, Chen M

- 5841** Barrett's esophagus in a patient with bulimia nervosa: A case report
Gouda A, El-Kassas M
- 5846** Spontaneous gallbladder perforation and colon fistula in hypertriglyceridemia-related severe acute pancreatitis: A case report
Wang QP, Chen YJ, Sun MX, Dai JY, Cao J, Xu Q, Zhang GN, Zhang SY
- 5854** Beware of gastric tube in esophagectomy after gastric radiotherapy: A case report
Yurttas C, Wichmann D, Gani C, Bongers MN, Singer S, Thiel C, Koenigsrainer A, Thiel K
- 5861** Transition from minimal change disease to focal segmental glomerulosclerosis related to occupational exposure: A case report
Tang L, Cai Z, Wang SX, Zhao WJ
- 5869** Lung adenocarcinoma metastasis to paranasal sinus: A case report
Li WJ, Xue HX, You JQ, Chao CJ
- 5877** Follicular lymphoma presenting like marginal zone lymphoma: A case report
Peng HY, Xiu YJ, Chen WH, Gu QL, Du X
- 5884** Primary renal small cell carcinoma: A case report
Xie K, Li XY, Liao BJ, Wu SC, Chen WM
- 5893** Gitelman syndrome: A case report
Chen SY, Jie N
- 5899** High-frame-rate contrast-enhanced ultrasound findings of liver metastasis of duodenal gastrointestinal stromal tumor: A case report and literature review
Chen JH, Huang Y
- 5910** Tumor-like disorder of the brachial plexus region in a patient with hemophilia: A case report
Guo EQ, Yang XD, Lu HR
- 5916** Response to dacomitinib in advanced non-small-cell lung cancer harboring the rare delE709_T710insD mutation: A case report
Xu F, Xia ML, Pan HY, Pan JW, Shen YH
- 5923** Loss of human epidermal receptor-2 in human epidermal receptor-2+ breast cancer after neoadjuvant treatment: A case report
Yu J, Li NL

LETTER TO THE EDITOR

- 5929** Repetitive transcranial magnetic stimulation for post-traumatic stress disorder: Lights and shadows
Concerto C, Lanza G, Fiscaro F, Pennisi M, Rodolico A, Torrisi G, Bella R, Aguglia E

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Raden Andri Primadhi, MD, PhD, Assistant Professor, Surgeon, Department of Orthopaedics and Traumatology, Universitas Padjadjaran Medical School, Hasan Sadikin Hospital, Bandung 40161, Indonesia. randri@unpad.ac.id

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The WJCC is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for WJCC as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The WJCC's CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Hua-Ge Yin, Production Department Director: Xiang Li, Editorial Office Director: Jin-Lai Wang.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

June 16, 2022

COPYRIGHT

© 2022 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Response to dacomitinib in advanced non-small-cell lung cancer harboring the rare delE709_T710insD mutation: A case report

Fei Xu, Meng-Ling Xia, Hui-Yun Pan, Jiong-Wei Pan, Yi-Hong Shen

Specialty type: Medicine, research and experimental

Provenance and peer review:

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): A

Grade B (Very good): B

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

P-Reviewer: Covantsev S, Russia; Suravajhala PN, India

Received: January 22, 2022

Peer-review started: January 22, 2022

First decision: March 16, 2022

Revised: March 21, 2022

Accepted: April 9, 2022

Article in press: April 9, 2022

Published online: June 16, 2022



Fei Xu, Meng-Ling Xia, Yi-Hong Shen, Department of Respiratory Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310000, Zhejiang Province, China

Hui-Yun Pan, Department of Day Care Ward, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310000, Zhejiang Province, China

Jiong-Wei Pan, Department of Respiratory Diseases, Lishui City People's Hospital, Lishui 323000, Zhejiang Province, China

Corresponding author: Yi-Hong Shen, MD, Chief Doctor, Department of Respiratory Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, No. 79 Qingchun Road, Hangzhou 310000, Zhejiang Province, China. drsyh@zju.edu.cn

Abstract

BACKGROUND

Tyrosine kinase inhibitors (TKI) have been the standard first-line therapy for advanced non-small cell lung cancer (NSCLC) of epidermal growth factor receptor (*EGFR*) sensitive mutations. Uncommon *EGFR* mutations are increasingly reported with the development of next-generation sequencing. However, their sensitivity to TKIs is variable with limited clinical evidence.

CASE SUMMARY

Here, we report a patient with the rare delE709_T710insD mutation, who showed the favorable efficacy of dacomitinib and achieved a partial response with a progression-free survival of 7.0 mo.

CONCLUSION

To our knowledge, this is the first report displaying the clinical efficacy of dacomitinib for patients with delE709_T710insD, which may help to provide alternatives in non-classical variant NSCLC patients. Further studies are warranted to make the optimal choice of *EGFR*-TKI for rare mutations.

Key Words: Next-generation sequencing; DelE709_T710insD; Non-small-cell lung cancer; Dacomitinib; Uncommon *EGFR* mutation; Case report

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: DelE709_T710insD is an extremely rare complex in-frame deletion mutation in exon 18 and accounts for only 0.11% of epidermal growth factor receptor mutations. The development of next-generation sequencing enabled the more identification of rare variants. Our case is the first report describing the clinical efficacy of dacomitinib for delE709_T710insD and achieved a progression-free survival of 7.0 mo. More patients with the rare variants may benefit from dacomitinib targeted therapy based on our study.

Citation: Xu F, Xia ML, Pan HY, Pan JW, Shen YH. Response to dacomitinib in advanced non-small-cell lung cancer harboring the rare delE709_T710insD mutation: A case report. *World J Clin Cases* 2022; 10(17): 5916-5922

URL: <https://www.wjgnet.com/2307-8960/full/v10/i17/5916.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v10.i17.5916>

INTRODUCTION

Among non-small-cell lung cancer (NSCLC) patients with epidermal growth factor receptor (*EGFR*) mutations, the most common mutations are exon 19 deletions and exon 21 L858R point mutations, accounting for 80%-90% of all *EGFR* mutations[1]. With the development of next-generation sequencing (NGS), more rare or atypical mutations, such as *EGFR* exon 20 and exon 18, have been identified, but their responses to TKIs have been variable and less investigated.

Mutations in *EGFR* exon 18, including point mutations and deletion-insertion mutations, were observed in approximately 4% of patients with *EGFR* mutations[2]. DelE709_T710insD is a rare complex in-frame deletion mutation in exon 18 and accounts for only 0.11% of *EGFR* mutations (33/31015) according to the Catalog of Somatic Mutations in Cancer (COSMIC) v.94 database[3]. Evidence regarding its response to available *EGFR*-TKIs is limited.

Here, we present a patient with advanced lung adenocarcinoma harboring the rare *EGFR* delE709_T710insD mutation who responded well to the second-generation *EGFR* TKI dacomitinib.

CASE PRESENTATION

Chief complaints

A 56-year-old female patient presented with right chest discomfort for 3 mo.

History of present illness

Chest computed tomography (CT) revealed a 1.9 cm × 2.1 cm mass in the anterior segment of the right upper lobe and multiple nodules in the bilateral lungs, accompanied by right pleural effusion. Moreover, the right hilar, mediastinal, and paratracheal lymph nodes (LNs) were found to be enlarged.

History of past illness

The patient had no history of any other diseases.

Personal and family history

The patient was free of any known congenital disease.

Physical examination

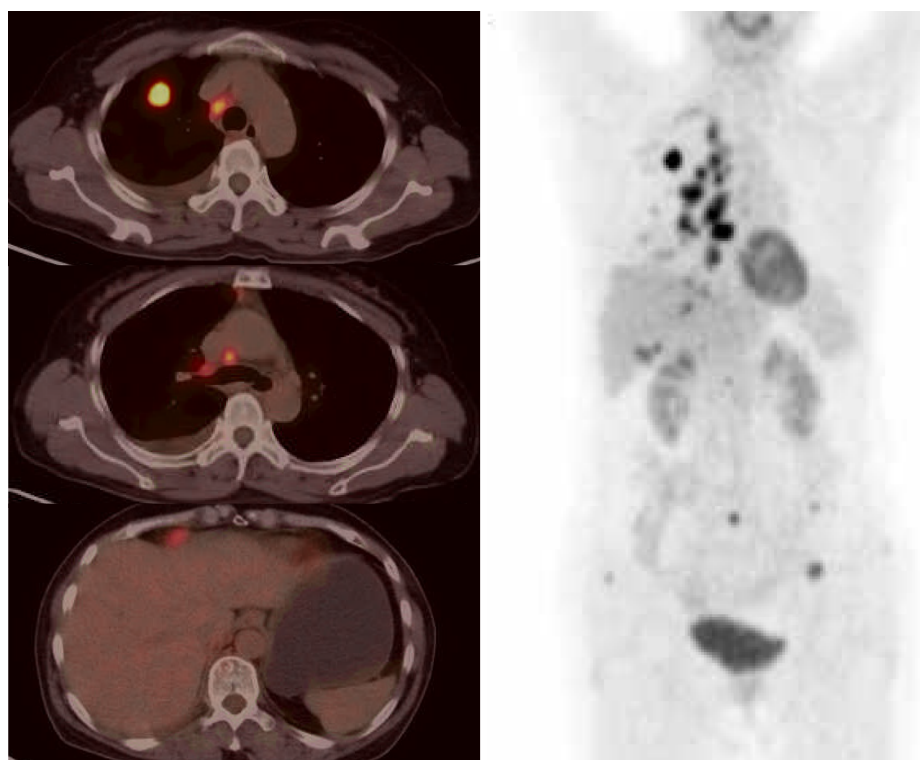
The right supraclavicular painless lymph node was palpated in the size of a soybean.

Laboratory examinations

The laboratory test data revealed that the serum carcinoembryonic antigen level was 279.6 ng/mL.

Imaging examinations

A positron emission tomography (PET) scan showed increased fluorodeoxyglucose (FDG) uptake in the right upper lobe mass, multiple pulmonary and subpleural nodules, and right supraclavicular, mediastinal, and right hilar lymph nodes. PET also indicated hypermetabolic nodules with low density in segment 6 of the liver and anterolateral area of the liver capsule, along with multiple bone destruction changes and high FDG uptake in T7 and T8 vertebral bodies and appendages, L5 spinous processes, and bilateral iliac bones (Figure 1). Magnetic resonance imaging of the brain was negative.



DOI: 10.12998/wjcc.v10.i17.5916 Copyright ©The Author(s) 2022.

Figure 1 Positron emission tomography scans at presentation.

MULTIDISCIPLINARY EXPERT CONSULTATION

She subsequently underwent ultrasound-guided needle biopsy of the right supraclavicular lymph node and right closed thoracic drainage. Endobronchial ultrasound-transbronchial needle aspiration (EBUS-TBNA) was performed on LN 7 and 11R. Cancer cells were found both in the pleural effusion and clavicular lymph nodes. Pathological results of LN 11R were identified pulmonary adenocarcinoma, with P40 (-), CK7 (+), TTF-1 (+), Napsin A (+), CK5/6 (-), ALK Ventana (-), ALK-Negative (-) through immunohistochemistry (IHC). Genetic testing was performed on cell block samples from pleural effusion by polymerase chain reaction (PCR). Routine molecular genetic testing, including mutation of *EGFR*, *KRAS*, *NRAS*, *BRAF*, *HER2*, *MET*, and *PIK3CA*, and fusion of *ALK*, *RET*, and *ROS1*, were all negative. **Supplementary material** listed all gene and mutation sites of the PCR diagnostic kits.

FINAL DIAGNOSIS

Based on this, the patient was identified as "driver gene-negative" right lung adenocarcinoma, cT1cN3M1c (TNM 8th Edition), stage IVB.

TREATMENT

The patient then started chemotherapy with pemetrexed plus carboplatin and bevacizumab in September 2020. A CT scan after 2 cycles showed a reduction in the mass in the right upper lobe, but disease progression was observed in February 2021. The progression-free survival¹ (PFS¹) is 5 mo, and the best response was reduced stable disease based on Response Evaluation Criteria in Solid Tumors (RECIST) criteria. To seek more effective and potential treatment, CT-guided transthoracic lung biopsy was taken from the right upper lobe as her family demanded. A 12-gene NGS panel (Shanghai Yikon Genomics Inc. China) for lung cancer revealed the *EGFR* Del18 (delE709_T710insD) mutation. However, there are no recommended targeted drugs for this rare mutation. Dacomitinib 30 mg/d was administered as the second-line treatment, starting in February 2021.

Table 1 Studies of epidermal growth factor receptor-tyrosine kinase inhibitors response for delE709_T710insD

Ref.	Patient No.	Gender	Age (yr)	Smoking	Stage	Histologic type	TKI used/line	Response	PFS (m)	OS (m)
Wu <i>et al</i> [7], 2011	1	F	61	No	IV	AD	Gefitinib/NA	SD	5.1	22.7
	2	M	65	Yes	IV	AD	Gefitinib/NA	PD	0.9	11.1
Ackerman <i>et al</i> [9], 2012	3	F	88	No	IV	AD	Erlotinib/1 st	PR	6	NA
Kobayashi <i>et al</i> [19], 2015	4	M	63	NA	IV	AD	Erlotinib/3 rd	SD	NA	NA
							Afatinib/4 th	PR	NA	
Wu <i>et al</i> [6], 2016	5	F	57	No	IV	AD	Gefitinib/NA	PD	0.6	24.1
	6	M	79	Yes	IV	AD	Gefitinib/NA	SD	6.2	6.2
	7	M	68	Yes	IV	AD	Gefitinib/NA	PD	2.3	29.5
Klughammer <i>et al</i> [10], 2016	8	F	50	No	III/IV	NSCLC	Erlotinib/2 nd	PD	1.3	1.7
Ibrahim <i>et al</i> [13], 2017	9	F	52	No	IV	AD	Afatinib/1 st	PR	NA	NA
An <i>et al</i> [14], 2019	10	M	56	No	IV	AD	Afatinib/2 nd	PR	11	More than 21
Iwamoto <i>et al</i> [15], 2019	11	F	56	No	IV	AD	Afatinib/6 th	PR	7	NA
D'Haene <i>et al</i> [16], 2019	12	F	57	No	III	AD	Afatinib/2 nd	PR	12	36
Martin <i>et al</i> [11], 2019	13	M	60	No	IV	AD	Erlotinib/NA	PD	1	3
Isaksson <i>et al</i> [12], 2020	14	NA	NA	NA	IV	NA	Erlotinib/1 st	PD	8	NA
Sousa <i>et al</i> [8], 2020	15	F	66	Yes	IV	AD	Gefitinib/1 st	PD	3	24
	16	F	46	Yes	II	AD	Erlotinib/2 nd	PD	4	26
	17	F	57	No	IV	AD	Erlotinib/2 nd	PD	3	18
Wei <i>et al</i> [17], 2021	18	F	70	No	II	NSCLC	Afatinib/1 st	PR	23	On going
Jelli <i>et al</i> [18], 2021	19	F	57	No	IV	AD	Afatinib/1 st	CR	17 (On going)	17 (On going)
Xu <i>et al</i> , 2021 (this case)	20	F	56	No	IV	AD	Dacomitinib/2 nd	PR	7	On going

F: Female; M: Male; NA: Data not-available; PFS: Progression-free survival; OS: Overall survival; TKI: Tyrosine kinase inhibitor; AD: Lung adenocarcinoma; NSCLC: Non-small cell lung cancer; PR: Partial response; SD: Stable disease; PD: Progression disease.

OUTCOME AND FOLLOW-UP

A CT scan revealed that the primary lesion significantly decreased in size after 2 mo, and a partial response (PR) was achieved (Figure 2). There were no significant adverse effects of dacomitinib therapy. Nevertheless, recent CT showed that the mass of the right upper lobe grew larger, which met the RECIST criteria for progressive disease (PD) after 7.0 mo of dacomitinib treatment.

DISCUSSION

EGFR mutations are observed in up to 50% of Asian non-small-cell lung cancer (NSCLC) patients and approximately 10%-20% of non-Asian patients. *EGFR*-TKIs have become the standard first-line treatment for *EGFR* sensitizing mutations (del18 and L858R) NSCLC based on Phase III trials *vs* platinum-based doublet chemotherapy[4], which has revolutionized the management of *EGFR*-mutated NSCLC. Uncommon mutations or less frequent alterations involving exons 18 and 20 in *EGFR* account for 10-20% of all *EGFR* mutations in NSCLC. Individuals with uncommon *EGFR* mutations seem to be a

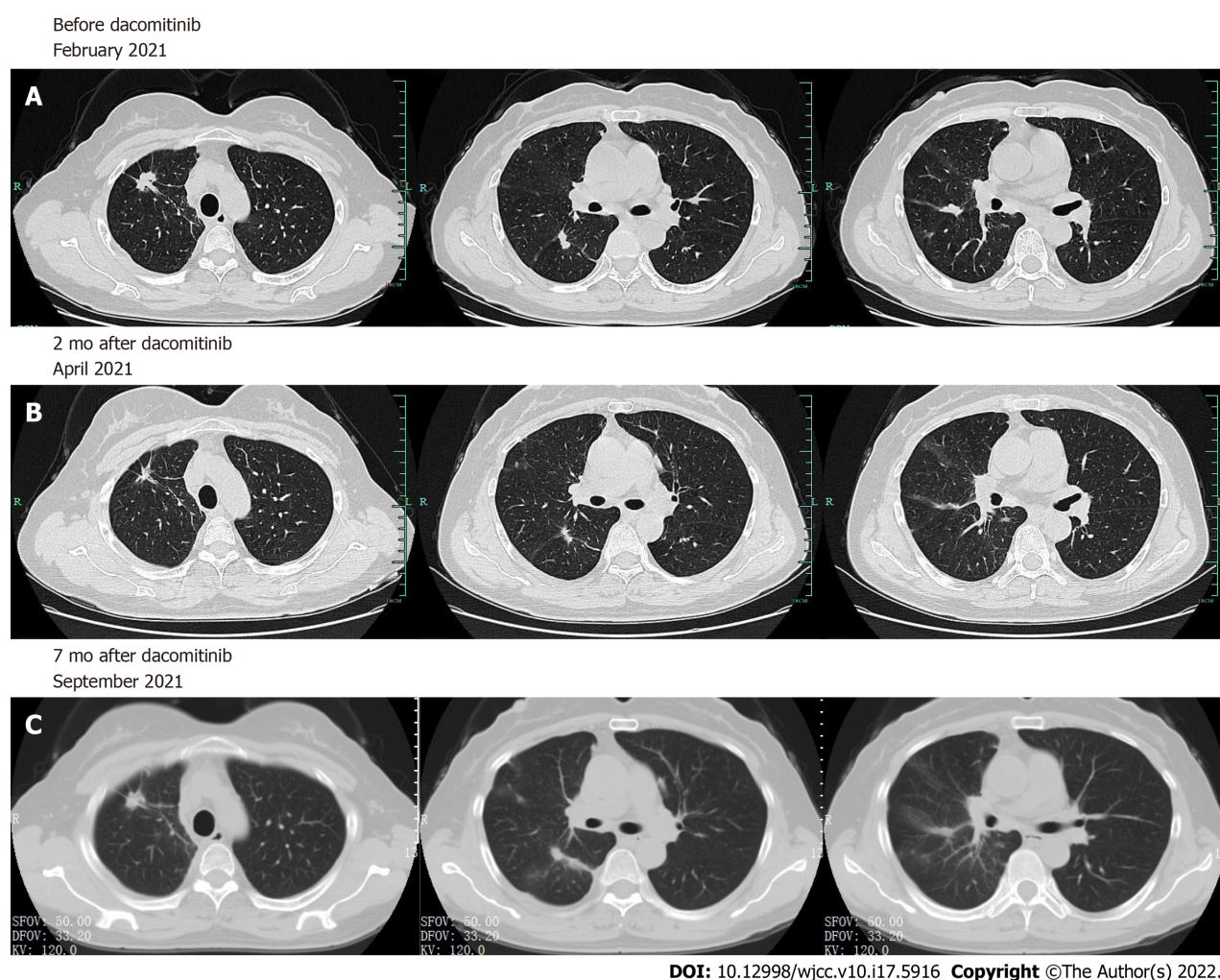


Figure 2 Chest computed tomography scans. A: Chest computed tomography scans before (A) and after dacomitinib therapy; B and C: The patient achieved partial response 2 mo after the initiation of dacomitinib therapy and progressed at 7 mo later.

heterogeneous group exhibiting differential sensitivity to *EGFR* inhibitors, but clinical evidence is scarce [5].

Studies on the delE709_T710insD mutation and its response to *EGFR*-TKIs, including gefitinib, erlotinib, and afatinib, have been reported sporadically in recent years (Table 1). Wu JY *et al* [6] reported that the prevalence of delE709_T710insD is 0.16% (5/3146) in *EGFR* mutations. Six gefitinib-treated patients harboring delE709_T710insD were nonresponders, with a median PFS of 2.65 mo [6-8]. Erlotinib was administered in previous case reports [8-12], which also seemed to be a frustrated treatment for delE709_T710insD. One had a PR, 5 had PD, and the response rate was only 25% (1/6). Afatinib was proven to be effective for such rare variants [13-18]. Among the 6 patients receiving afatinib, one achieved a complete response (CR), and 5 achieved a PR. More significantly, 1 patient with E709_T710delinsD mutations showed a survival benefit of afatinib after erlotinib treatment failed [19]. The overall response rate of afatinib for delE709_T710insD was 100% (7/7). According to the analysis by Rubiera-Pebe R *et al* [20], the median PFS comparison between first-generation TKIs and afatinib for patients with delE709_T710insD is 3.1 mo *vs* 7.0 mo, respectively. *In vitro*, a study by Kobayashi Y *et al* [19] investigated the sensitivities of exon 18 mutations to various *EGFR*-TKIs and suggested that second-generation *EGFR*i have broader inhibitory profiles than other TKIs for rare mutations.

Like afatinib, dacomitinib is a second-generation pan-HER inhibitor that irreversibly binds to all three kinase-active members of the ErbB family (*HER1/EGFR*, *HER2*, and *HER4*), leading to more efficient *EGFR* inhibition. The efficacy of dacomitinib on patients acquiring Ex18 G719A as later-line therapy has been reported by Morita A *et al* [21]. In addition, dacomitinib *in vitro* has an IC_{50} =29 nM for Ba/F3 cells expressing exon 18 delE709_T710insD [19], indicating the potential activity of this nonclassical mutation. The results of a phase 3 trial of dacomitinib (NCT01774721, ARCHER 1050) indicated that first-line dacomitinib significantly improved PFS and OS *vs* gefitinib, and the adverse events were manageable [22]. Based on these findings, dacomitinib seemed to be a promising candidate for *EGFR*-positive advanced NSCLC, including less common mutations. However, limited clinical data have shown the effect of dacomitinib on rare mutations.

CONCLUSION

In our study, we reported that a patient with *EGFR* delE709_T710insD achieved PR after the initiation of dacomitinib, with a PFS2 of 7 mo. To the best of our knowledge, this is the first report describing the clinical efficacy of dacomitinib for *EGFR* delE709_T710insD. The efficacy of dacomitinib on rare mutations needs to be evaluated *in vivo* or *in vitro* by further studies. In addition, appropriate genetic diagnosis methodologies will provide patients with more opportunities for targeted therapy. Our report may help to provide new treatment options for NSCLC patients with nonclassical variants.

FOOTNOTES

Author contributions: Shen YH initiated the case report and supervised the entire study; Xu F collected patient data, performed a literature review and wrote the manuscript; Xia ML obtained and analyzed the next-generation sequencing results; Pan HY reviewed the histological pathological examination of the biopsy; Pan JW was involved in patient follow-up after discharge; all authors read and approved the final manuscript.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: China

ORCID number: Fei Xu 0000-0003-4200-1485; Meng-Ling Xia 0000-0002-0182-7400; Hui-Yun Pan 0000-0002-2536-5773; Jiong-Wei Pan 0000-0002-4077-2561; Yi-Hong Shen 0000-0002-7815-9973.

S-Editor: Wang LL

L-Editor: A

P-Editor: Wang LL

REFERENCES

- 1 Han B, Tjulandin S, Hagiwara K, Normanno N, Wulandari L, Laktionov K, Hudoyo A, He Y, Zhang YP, Wang MZ, Liu CY, Ratcliffe M, McCormack R, Reck M. *EGFR* mutation prevalence in Asia-Pacific and Russian patients with advanced NSCLC of adenocarcinoma and non-adenocarcinoma histology: The IGNITE study. *Lung Cancer* 2017; **113**: 37-44 [PMID: 29110846 DOI: 10.1016/j.lungcan.2017.08.021]
- 2 Cheng C, Wang R, Li Y, Pan Y, Zhang Y, Li H, Zheng D, Zheng S, Shen X, Sun Y, Chen H. *EGFR* Exon 18 Mutations in East Asian Patients with Lung Adenocarcinomas: A Comprehensive Investigation of Prevalence, Clinicopathologic Characteristics and Prognosis. *Sci Rep* 2015; **5**: 13959 [PMID: 26354324 DOI: 10.1038/srep13959]
- 3 **Atalogue of Somatic Mutations in Cancer**, release version 94. [cited 20 January 2022]. Available from: <https://cancer.sanger.ac.uk/cosmic>
- 4 Hsu WH, Yang JC, Mok TS, Loong HH. Overview of current systemic management of *EGFR*-mutant NSCLC. *Ann Oncol* 2018; **29**: i3-i9 [PMID: 29462253 DOI: 10.1093/annonc/mdx702]
- 5 Russo A, Franchina T, Ricciardi G, Battaglia A, Picciotto M, Adamo V. Heterogeneous Responses to Epidermal Growth Factor Receptor (*EGFR*) Tyrosine Kinase Inhibitors (TKIs) in Patients with Uncommon *EGFR* Mutations: New Insights and Future Perspectives in this Complex Clinical Scenario. *Int J Mol Sci* 2019; **20** [PMID: 30901844 DOI: 10.3390/ijms20061431]
- 6 Wu JY, Shih JY. Effectiveness of tyrosine kinase inhibitors on uncommon E709X epidermal growth factor receptor mutations in non-small-cell lung cancer. *Onco Targets Ther* 2016; **9**: 6137-6145 [PMID: 27785061 DOI: 10.2147/OTT.S118071]
- 7 Wu JY, Yu CJ, Chang YC, Yang CH, Shih JY, Yang PC. Effectiveness of tyrosine kinase inhibitors on "uncommon" epidermal growth factor receptor mutations of unknown clinical significance in non-small cell lung cancer. *Clin Cancer Res* 2011; **17**: 3812-3821 [PMID: 21531810 DOI: 10.1158/1078-0432.CCR-10-3408]
- 8 Sousa AC, Silveira C, Janeiro A, Malveiro S, Oliveira AR, Felizardo M, Nogueira F, Teixeira E, Martins J, Carmo-Fonseca M. Detection of rare and novel *EGFR* mutations in NSCLC patients: Implications for treatment-decision. *Lung Cancer*

- 2020; **139**: 35-40 [PMID: [31715539](#) DOI: [10.1016/j.lungcan.2019.10.030](#)]
- 9 **Ackerman A**, Goldstein MA, Kobayashi S, Costa DB. *EGFR* delE709_T710insD: a rare but potentially *EGFR* inhibitor responsive mutation in non-small-cell lung cancer. *J Thorac Oncol* 2012; **7**: e19-e20 [PMID: [22982663](#) DOI: [10.1097/JTO.0b013e3182635ab4](#)]
- 10 **Klughammer B**, Brugger W, Cappuzzo F, Ciuleanu T, Mok T, Reck M, Tan EH, Delmar P, Klingelschmitt G, Yin AY, Spleiss O, Wu L, Shames DS. Examining Treatment Outcomes with Erlotinib in Patients with Advanced Non-Small Cell Lung Cancer Whose Tumors Harbor Uncommon *EGFR* Mutations. *J Thorac Oncol* 2016; **11**: 545-555 [PMID: [26773740](#) DOI: [10.1016/j.jtho.2015.12.107](#)]
- 11 **Martin J**, Lehmann A, Klauschen F, Hummel M, Lenze D, Grohé C, Tessmer A, Gottschalk J, Schmidt B, Pau HW, Witt C, Moegling S, Kromminga R, Jöhrens K. Clinical Impact of Rare and Compound Mutations of Epidermal Growth Factor Receptor in Patients With Non-Small-Cell Lung Cancer. *Clin Lung Cancer* 2019; **20**: 350-362.e4 [PMID: [31175009](#) DOI: [10.1016/j.clcc.2019.04.012](#)]
- 12 **Isaksson S**, Hazem B, Jönsson M, Reuterswärd C, Karlsson A, Griph H, Engleson J, Oskarsdottir G, Öhman R, Holm K, Rosengren F, Annersten K, Jönsson G, Borg Å, Edsjö A, Levén P, Brunnström H, Lindquist KE, Staaf J, Planck M. Clinical Utility of Targeted Sequencing in Lung Cancer: Experience From an Autonomous Swedish Health Care Center. *JTO Clin Res Rep* 2020; **1**: 100013 [PMID: [34589915](#) DOI: [10.1016/j.jtocrr.2020.100013](#)]
- 13 **Ibrahim U**, Saqib A, Atallah JP. *EGFR* exon 18 delE709_T710insD mutated stage IV lung adenocarcinoma with response to afatinib. *Lung Cancer* 2017; **108**: 45-47 [PMID: [28625646](#) DOI: [10.1016/j.lungcan.2017.02.023](#)]
- 14 **An N**, Wang H, Zhu H, Yan W, Jing W, Kong L, Zhang Y, Yu J. Great efficacy of afatinib on a patient with lung adenocarcinoma harboring uncommon *EGFR* delE709_T710insD mutations: a case report. *Onco Targets Ther* 2019; **12**: 7399-7404 [PMID: [31686847](#) DOI: [10.2147/OTT.S221638](#)]
- 15 **Iwamoto Y**, Ichihara E, Hara N, Nakasuka T, Ando C, Umeno T, Hirabae A, Maeda Y, Kiura K. Efficacy of afatinib treatment for lung adenocarcinoma harboring exon 18 delE709_T710insD mutation. *Jpn J Clin Oncol* 2019; **49**: 786-788 [PMID: [31187861](#) DOI: [10.1093/jcco/hyz086](#)]
- 16 **D'Haene N**, Le Mercier M, Salmon I, Mekinda Z, Rummelink M, Berghmans T. SMAD4 Mutation in Small Cell Transformation of Epidermal Growth Factor Receptor Mutated Lung Adenocarcinoma. *Oncologist* 2019; **24**: 9-13 [PMID: [30413663](#) DOI: [10.1634/theoncologist.2018-0016](#)]
- 17 **Wei Y**, Cui Y, Guo Y, Li L, Zeng L. A Lung Adenocarcinoma Patient With a Rare *EGFR* E709_T710delinsD Mutation Showed a Good Response to Afatinib Treatment: A Case Report and Literature Review. *Front Oncol* 2021; **11**: 700345 [PMID: [34178699](#) DOI: [10.3389/fonc.2021.700345](#)]
- 18 **Jelli B**, Taton O, D'Haene N, Rummelink M, Mekinda Z. Complete Response to Afatinib of an *EGFR* Exon 18 delE709_T710insD-Mutated Stage IV Lung Adenocarcinoma. *Eur J Case Rep Intern Med* 2021; **8**: 002749 [PMID: [34527619](#) DOI: [10.12890/2021_002749](#)]
- 19 **Kobayashi Y**, Togashi Y, Yatabe Y, Mizuuchi H, Jangchul P, Kondo C, Shimoji M, Sato K, Suda K, Tomizawa K, Takemoto T, Hida T, Nishio K, Mitsudomi T. *EGFR* Exon 18 Mutations in Lung Cancer: Molecular Predictors of Augmented Sensitivity to Afatinib or Neratinib as Compared with First- or Third-Generation TKIs. *Clin Cancer Res* 2015; **21**: 5305-5313 [PMID: [26206867](#) DOI: [10.1158/1078-0432.ccr-15-1046](#)]
- 20 **Rubiera-Pebe R**, Hicks JK, Tanvetyanon T. Efficacy of tyrosine kinase inhibitors against lung cancer with *EGFR* exon 18 deletion: Case report and pooled analysis. *Cancer Treat Res Commun* 2021; **28**: 100407 [PMID: [34090219](#) DOI: [10.1016/j.ctarc.2021.100407](#)]
- 21 **Morita A**, Hosokawa S, Yamada K, Umeno T, Kano H, Kayatani H, Shiojiri M, Sakugawa M, Bessho A. Dacomitinib as a retreatment for advanced non-small cell lung cancer patient with an uncommon *EGFR* mutation. *Thorac Cancer* 2021; **12**: 1248-1251 [PMID: [33651475](#) DOI: [10.1111/1759-7714.13897](#)]
- 22 **Wu YL**, Cheng Y, Zhou X, Lee KH, Nakagawa K, Niho S, Tsuji F, Linke R, Rosell R, Corral J, Migliorino MR, Pluzanski A, Sbar EI, Wang T, White JL, Nadanaciva S, Sandin R, Mok TS. Dacomitinib vs gefitinib as first-line treatment for patients with *EGFR*-mutation-positive non-small-cell lung cancer (ARCHER 1050): a randomised, open-label, phase 3 trial. *Lancet Oncol* 2017; **18**: 1454-1466 [PMID: [28958502](#) DOI: [10.1016/S1470-2045](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

