ANTICANCER RESEARCH *39*: 897-902 (2019)
doi:10.21873/anticanres.13191

Neoadjuvant Tyrosine Kinase Inhibition in Locally-advanced Non-small Cell Lung Cancer: Two Cases and a Brief Literature Review

ANISH B. PARIKH[1], LINDSAY HAMMONS[2] and JORGE E. GOMEZ[1]

[1]*Tisch Cancer Institute, Division of Hematology/Oncology, Icahn School of Medicine at Mount Sinai, New York, NY, U.S.A.;*
[2]*Department of Internal Medicine, Mount Sinai Beth Israel, New York, NY, U.S.A.*

Abstract. *Background: Despite their remarkable efficacy in metastatic non-small cell lung cancer (NSCLC), EGFR- and ALK-targeted therapies have not been shown to confer any survival benefit in stage III disease, even in subsets of patients with driver mutations. Case Studies: Here, two patients with unresectable stage III NSCLC carrying mutations in the ALK (case 1) and EGFR (case 2) genes are presented. Treatment of the patient carrying an ALK mutation with an ALK inhibitor and the patient carrying an EGFR mutation with an EGFR inhibitor resulted in dramatic and durable responses. Conclusion: These cases demonstrated that ALK or EGFR mutation-positive stage III NSCLC patients can be treated with the corresponding inhibitors. They also highlight the urgent need for prospective data to assess their potential efficacy in order to improve patient outcomes.*

Despite several important advances in screening and treatment in the past decade, lung cancer remains one of the most common and lethal malignancies worldwide. In the United States, there are an estimated 234,000 new cases each year, with over 154,000 related deaths annually (1). Non-small cell lung cancer (NSCLC) comprises 80-85% of all lung cancer diagnoses (2).

The management of locally-advanced (stage III) NSCLC remains a controversial topic, despite ongoing efforts to elucidate the optimal treatment approach. Among the primary reasons for this lack of consensus are the clinical heterogeneity of stage III disease as well as continued evolution in diagnostics, staging systems, and clinical trial definitions. The current standard of care for unresectable stage III NSCLC is concurrent chemotherapy and thoracic radiation, followed by consolidation immunotherapy with durvalumab for those who respond to treatment (3, 4). Sequential chemotherapy and radiation can be used in patients who are unable to tolerate concurrent treatment.

The use of tyrosine kinase inhibitors (TKIs) that target common driver mutations involving the epidermal growth factor receptor (*EGFR*) has previously been studied in locally-advanced disease with disappointing results. Indeed, phase 3 studies have failed to show any significant benefit from the use of EGFR inhibitors in unresectable stage III NSCLC, even in subsets of patients with known activating *EGFR* mutations (5, 6). Recently reported interim results from the ADJUVANT trial, which evaluated adjuvant gefitinib *versus* chemotherapy in resected stage I-IIIA NSCLC, did show a benefit in progression-free survival (PFS) in patients with *EGFR* mutations, however overall survival (OS) data are not available yet (7). Parallel attempts to evaluate the use of TKIs targeting anaplastic lymphoma kinase (*ALK*) translocations in this setting have similarly failed to demonstrate any meaningful survival benefit (8-10).

Consequently, there is no proven role for EGFR or ALK inhibitors in locally-advanced NSCLC, even in patients whose tumors harbor these driver mutations. The RTOG 1306 trial attempted to clarify this issue in a prospective manner by randomizing unresectable stage III patients with *EGFR* or *ALK* mutations to 12 weeks of induction therapy with a corresponding TKI followed by concurrent chemoradiation *versus* chemoradiation alone (11). However, this trial was terminated after 5 years due to poor accrual, perhaps because of low molecular testing rates in patients with non-metastatic disease. To our knowledge, there are only four case reports of using TKIs as neoadjuvant or

Correspondence to: Anish B. Parikh, MD, Tisch Cancer Institute, Division of Hematology/Medical Oncology, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1079, New York, NY 10029-6574, U.S.A. Tel: +1 2122414705, Fax: +1 2122412684, e-mail: anish.parikh@mountsinai.org, ORCID: 0000-0002-7322-6372

Key Words: Locally-advanced non-small cell lung cancer, NSCLC, tyrosine kinase inhibitor, TKI, neoadjuvant, induction, EGFR, ALK.

induction therapy in stage III disease, which reflects the tremendous paucity of data regarding therapy of these patients (12-14).

Herein, we describe two recent cases with mutation-positive unresectable stage III NSCLC, treated with an ALK inhibitor (Case 1) and an EGFR inhibitor (Case 2). Treatment resulted in dramatic clinical and radiographic responses. In both instances, this non-standard approach was selected only after extensive discussion with each patient regarding standard treatment options and the potential risks of employing a non-standard treatment strategy.

Case 1

A 49-year-old female former smoker initially presented in March 2014 with several months of progressive dyspnea, cough, and neck pain. Imaging showed a right upper lobe lung mass as well as bulky hilar, mediastinal, and supraclavicular lymphadenopathy, all hypermetabolic in nature. Brain imaging was normal. Biopsies of the lung and supraclavicular masses showed lung adenocarcinoma. Interphase fluorescence *in situ* hybridization (FISH) testing revealed that 16% of cells were positive for an atypical *ALK* gene rearrangement, though no fusion partner was reported. According to the most current edition of the American Joint Committee on Cancer (AJCC) staging manual at that time (7th ed), her disease was characterized as stage IIIB (T1N3M0) and was therefore considered inoperable (15).

The patient was deemed unlikely to be able to tolerate concurrent chemoradiation given the large size of the radiation field required and the associated toxicities. Thus, a sequential approach, with systemic induction therapy preceding local radiation therapy, was recommended. Her induction regimen consisted of cisplatin plus pemetrexed, to which concurrent ALK inhibition using 250 mg crizotinib twice daily was added in order to maximize chances of a response given the extent of her disease. Repetition of the imaging after 2 cycles showed marked improvement, as seen in Figure 1. This coincided with a dramatic clinical improvement, and so she chose to stop crizotinib given the lack of any clear clinical guidelines in this situation. She then began thoracic radiation therapy and continued with cisplatin and pemetrexed. She completed 4 cycles of chemotherapy and 60 Gy of radiation without major issues aside from mild dehydration and diarrhea, and then chose to resume crizotinib thereafter. Imaging around this time confirmed a sustained complete response to therapy, which was maintained for over 4 years on serial follow-up studies. She then developed multiple renal cysts and worsening diarrhea so she was switched to a next-generation ALK inhibitor, alectinib. She is now approaching 5 years since her diagnosis and continues to have no evidence of disease on imaging.

Case 2

A 55-year-old female never-smoker initially presented in July 2017 with several months of persistent cough. Imaging showed a large left lower lobe mass with hilar and mediastinal lymphadenopathy, all hypermetabolic in nature. Brain imaging was normal. Biopsies of the lung and mediastinal masses showed lung adenocarcinoma, and molecular analysis revealed an *EGFR* exon 19 deletion. According to the AJCC 8th edition staging manual, her disease was characterized as stage IIIC (T3N3M0) and was therefore considered inoperable (16).

As in Case 1, the patient was deemed unlikely to be able to tolerate concurrent chemoradiation due to the extent of her disease, and so a sequential approach was again recommended. Given her *EGFR* mutation, a second-generation EGFR TKI (afatinib 40 mg daily) was administered as an induction agent prior to chemoradiation, after an extensive discussion regarding this non-standard strategy. This medication was well tolerated, associated only with self-limited grade I diarrhea and rash. The patient remained on afatinib for 4 months with dramatic symptomatic improvement. Repetition of the imaging showed near complete anatomic and metabolic response, as seen in Figure 2. Again, given the lack of clear clinical guidelines in this situation, the patient chose to stop afatinib treatment and continue with concurrent chemoradiation, with 4 cycles of cisplatin and pemetrexed being given during thoracic radiation treatment to a total of 60 Gy. Two months after completing chemoradiation, she unfortunately presented with new-onset seizures and was found to have multiple brain metastases. She was started on steroids and anti-epileptics in the hospital and afatinib was resumed with good clinical and radiographic response on continued follow-up. She is now approaching 2 years since her diagnosis.

Discussion

The remarkable efficacy of EGFR and ALK inhibitors in metastatic NSCLC has transformed the treatment of this disease and has helped to usher in the era of precision medicine in oncology (12, 17-23). Despite this degree of clinical activity, these agents have yet to show any convincing survival benefit in randomized clinical trials (RCTs) evaluating their use in earlier stages of disease. Indeed, there is little-to-no evidence to support the use of these therapies in the stage III setting, despite the widely held belief that patients with unresectable stage III NSCLC are likely to already have micro-metastatic disease (24, 25). Furthermore, previous attempts to study this issue in a rationally-designed prospective RCT (RTOG 1306) were unfortunately hindered by poor accrual, ultimately leading to trial termination. This represents a glaring knowledge gap in

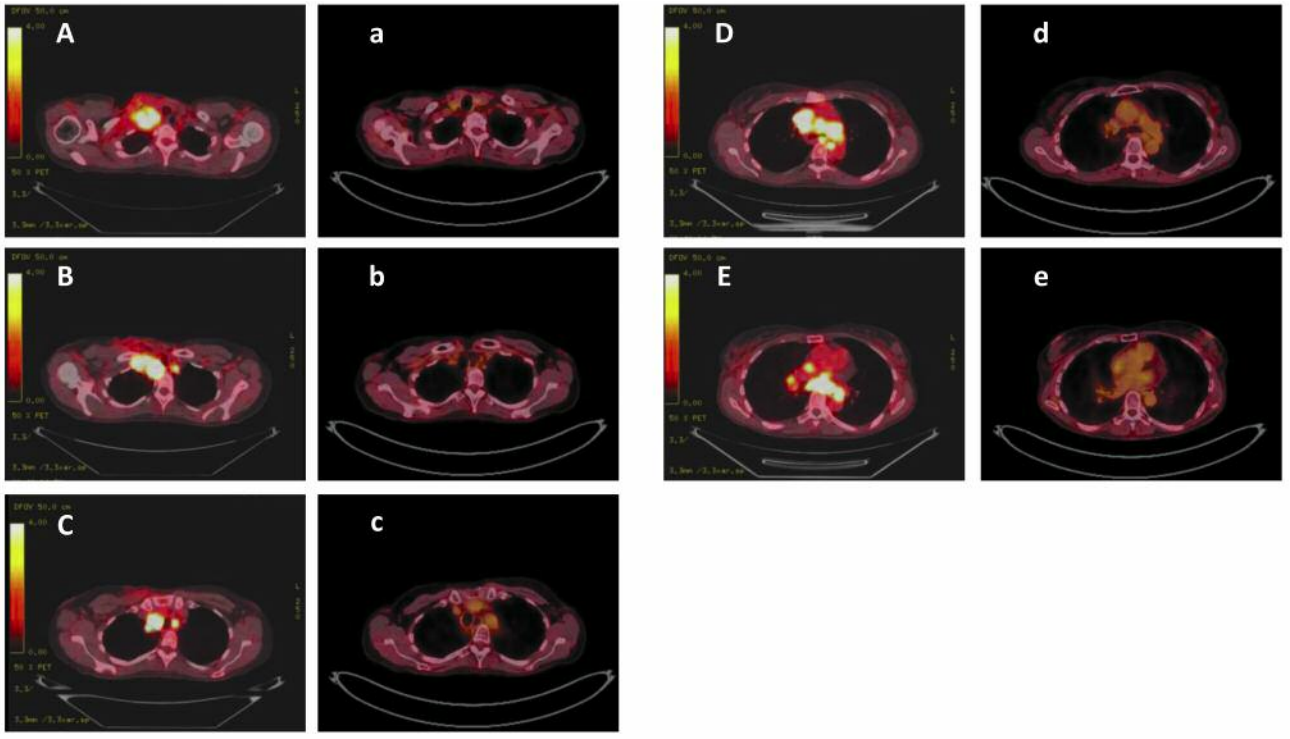

Figure 1. *Comparison of pre-therapy (A, B, C, D, E) and post-therapy (a, b, c, d, e) positron emission tomography (PET) scans for the patient in Case 1, who was treated with crizotinib plus 2 cycles of cisplatin/pemetrexed in the 6-week interval.*

our current understanding of stage III NSCLC and thus embodies a key lingering question in the management of this complicated disease. Our experience, described above, helps highlight the fact that these agents can have clinically meaningful activity in this setting, despite the lack of a strong evidence base, and should therefore continue to be studied to assess for potential efficacy.

In this report, patients with high-volume stage III disease with targetable mutations who were deemed unable to tolerate concurrent chemoradiation based on their disease burden are presented. Current standard-of-care guidelines in these situations would suggest a sequential approach to delivering chemotherapy and radiation. However, it has been well-established that this approach leads to significant reductions in response rate as well as in median and long-term overall survival when compared to the concurrent approach (26, 27). After extensive discussion with these patients, an unconventional approach of using the respective TKI up-front was chosen, as opposed to saving it for an overt metastatic recurrence in the future. This strategy was employed in hope of achieving a response significant enough to allow the patients to proceed with concurrent therapy, which remains the standard and most optimal definitive management in this situation. It is very important to note, as alluded to earlier, that this approach was fraught with uncertainty as it remains unclear how to actually integrate the use of these agents into the complicated treatment protocols for stage III NSCLC.

Fortunately, our patients experienced dramatic responses which allowed them to complete concurrent therapy in a timely manner. Importantly, although radiographic benefit was confirmed by imaging after 6 weeks of crizotinib (Case 1) and after 4 months of afatinib (Case 2), the onset of clinical benefit in terms of symptomatic improvement occurred quickly, in the range of 1-2 weeks in each case. Both cases also demonstrated the potential durability of these responses. The patient carrying an *ALK* mutation remained on crizotinib for over 4 years with no evidence of disease, and was only switched to another agent when she developed multiple renal cysts, a known though rare side effect of crizotinib (28). The patient carrying an *EGFR* mutation unfortunately developed brain metastases 2 months after completing chemoradiation while still off afatinib, which again highlights the fact that the optimal integration of TKIs with conventional treatment in this setting remains unclear. Fortunately, however, her intracranial disease remained responsive to afatinib upon resumption of this agent and she is now doing well. Ultimately, these medications were

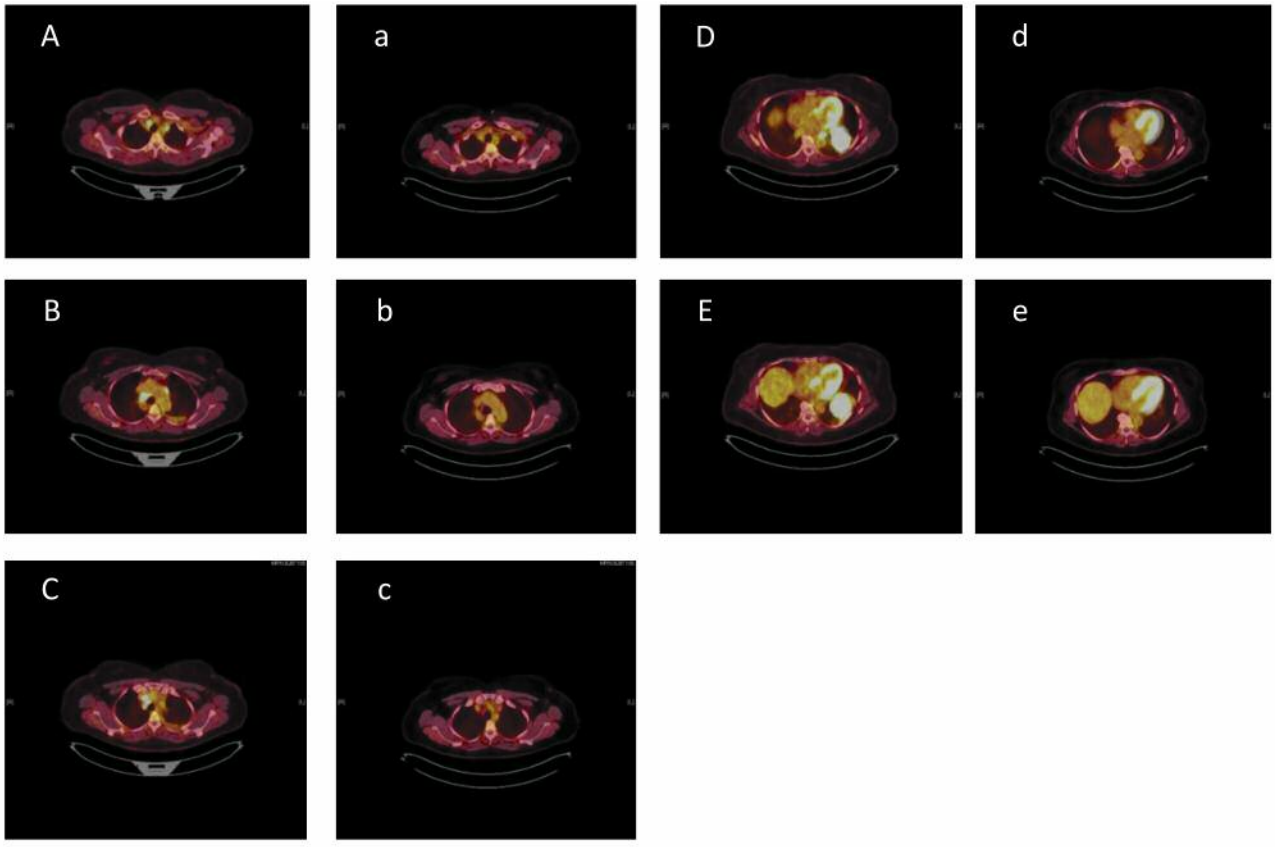

Figure 2. *Comparison of pre-therapy (A, B, C, D, E) and post-therapy (a, b, c, d, e) positron emission tomography (PET) scans for the patient in Case 2, who was treated with afatinib monotherapy in the 4-month interval.*

tolerated well in the induction setting, both when used concomitantly with chemotherapy (as in Case 1) and when given as monotherapy (as in Case 2). This is an especially important point given the high toxicity rates associated with concurrent chemoradiation reported in clinical trials (5, 29).

Conclusion

Despite many attempts to expand the indications for targeted therapies in NSCLC, these highly selective and effective tyrosine kinase inhibitors remain approved only in the metastatic setting. Though there has not yet been any convincing data supporting the use of such agents for unresectable stage III disease, even in patients with relevant driver mutations, the cases described above demonstrate their efficacy and tolerability. Our experience suggests that these agents may be a potential option for induction therapy in patients who cannot tolerate concurrent chemoradiation, and highlights the ongoing and unmet need for prospective data in order to improve patient outcomes.

Authors' Contributions

Study Conception (ABP, JEG); Chart Review (ABP, LH); Image Collection/Preparation (ABP, LH); Literature Review (ABP, LH); Manuscript Preparation (ABP, LH, JEG); Manuscript Submission (ABP); Manuscript Revision (ABP).

Conflicts of Interest

The Authors declare that they have no conflicts of interest or relevant disclosures to make.

Acknowledgements

The Authors would like to thank the patients described in these cases for their support in this endeavor.

References

1 Siegel RL, Miller KD and Jemal A: Cancer statistics. CA Cancer J Clin *68(1)*: 7-30, 2018. PMID: 29313949, DOI: 10.3322/caac.21442

2 Dela Cruz CS, Tanoue LT and Matthay RA: Lung cancer: Epidemiology, etiology, and prevention. Clin Chest Med *32(4)*: 605-644, 2011. PMID: 22054876, DOI: 10.1016/j.ccm.2011.09.001

3 Rosenzweig KE and Gomez JE: Concurrent chemotherapy and radiation therapy for inoperable locally advanced non-small-cell lung cancer. J Clin Oncol *35(1)*: 6-10, 2017. PMID: 27870565, DOI: 10.1200/JCO.2016.69.9678

4 Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, Yokoi T, Chiappori A, Lee KH, de Wit M, Cho BC, Bourhaba M, Quantin X, Tokito T, Mekhail T, Planchard D, Kim YC, Karapetis CS, Hiret S, Ostoros G, Kubota K, Gray JE, Paz-Ares L, de Castro Carpeño J, Wadsworth C, Melillo G, Jiang H, Huang Y, Dennis PA and Özgüroğlu M: Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. N Engl J Med *377(20)*: 1919-1929, 2017. PMID: 28885881, DOI: 10.1056/NEJMoa1709937

5 Bradley JD, Paulus R, Komaki R, Masters G, Blumenschein G, Schild S, Bogart J, Hu C, Forster K, Magliocco A, Kavadi V, Garces YI, Narayan S, Iyengar P, Robinson C, Wynn RB, Koprowski C, Meng J, Beitler J, Gaur R, Curran W Jr and Choy H: Standard-dose *versus* high-dose conformal radiotherapy with concurrent and consolidation carboplatin plus paclitaxel with or without cetuximab for patients with stage IIIA or IIIB non-small-cell lung cancer (RTOG 0617): A randomised, two-by-two factorial phase 3 study. Lancet Oncol *16(2)*: 187-199, 2015. PMID: 25601342, DOI: 10.1016/S1470-2045(14)71207-0

6 Ready N, Janne PA, Bogart J, DiPetrillo T, Garst J, Graziano S, Gu L, Wang X, Green MR and Vokes EE: Chemoradiotherapy and gefitinib in stage III non-small cell lung cancer with epidermal growth factor receptor and KRAS mutation analysis: Cancer and leukemia group B (CALEB) 30106, a CALGB-stratified phase II trial. J Thorac Oncol *5(9)*: 1382-1390, 2010. PMID: 20686428, DOI: https://doi.org/10.1097/JTO.0b013e3181eba657

7 Wu YL, Zhong W, Wang Q, Xu ST, Mao WM, Wu L, Shen Y, Liu YY, Chen C, Cheng Y, Xu L, Wang J, Fei K, Li XF, Li J, Huang C, Liu ZD, Chen KN, Yan HH and Yang XN: Gefitinib (G) *versus* vinorelbine+cisplatin (VP) as adjuvant treatment in stage II-IIIA (N1-N2) non-small-cell lung cancer (NSCLC) with EGFR-activating mutation (ADJUVANT): A randomized, phase III trial (CTONG 1104). J Clin Oncol *35(15)*: 8500-8500, 2017. DOI: 10.1200/JCO.2017.35.15_suppl.8500

8 Camidge D, Bang Y, Kwak E, Iafrate AJ, Varella-Garcia M, Fox SB, Riely GJ, Solomon B, Ou SH, Kim DW, Salgia R, Fidias P, Engelman JA, Gandhi L, Janne PA, Costa DB, Shapiro GI, Lorusso P, Ruffner K, Stephenson P, Tang Y, Wilner K, Clark JW and Shaw AT: Activity and safety of crizotinib in patients with ALK-positive non-small-cell lung cancer: Updated results from a phase 1 study. Lancet Oncol *13(10)*: 1011-1019, 2012. PMID: 22954507, DOI: 10.1016/S1470-2045(12)70344-3

9 Hida TA, Seto T, Horinouchi H, Maemondo M, Takeda M, Hotta K, Hirai F, Kim YH, Matsumoto S, Ito M, Ayukawa K, Tokushige K, Yonemura M, Mitsudomi T and Nishio M: Phase 2 study of ceritinib in alectinib-pretreated patients with ALK-rearranged metastatic NSCLC in Japan: ASCEND-9. Cancer Sci *109(9)*: 2863-2872, 2018. PMID: 29959808, DOI: 10.1111/ cas.13721

10 Gainor J, Tan D, De Pas T, Solomon BJ, Ahmad A, Lazzari C, de Marinis F, Spitaleri G, Schultz K, Friboulet L, Yeap BY, Engelman JA and Shaw AT: Progression-free and overall survival in ALK-positive NSCLC patients treated with sequential crizotinib and ceritinib. Clin Cancer Res *21(12)*: 2745-2752, 2015. PMID: 25724526, DOI: 10.1158/1078-0432.CCR-14-3009

11 Govindan R: Erlotinib hydrochloride or crizotinib and chemoradiation therapy in treating patients with stage III non-small cell lung cancer, 2018. Identification No. NCT01822496. Retrieved from https://clinicaltrials.gov/ct2/show/NCT01822496.

12 Solomon BJ, Mok T, Kim DW, Wu YL, Nakagawa K, Mekhail T, Felip E, Cappuzzo F, Paolini J, Usari T, Iyer S, Reisman A, Wilner KD, Tursi J and Blackhall F: First-line crizotinib *versus* chemotherapy in ALK-positive lung cancer. N Engl J Med *371*: 2167-2177, 2014. PMID: 26466011, DOI: 10.1056/NEJMx150034

13 Kappers I, Klomp HM, Burgers JA, Van Zandwijk N, Haas RLM and van Pel R: Neoadjuvant (induction) erlotinib response in stage IIIA non–small-cell lung cancer. J Clin Oncol *26(25)*: 4205-4207, 2008. PMID: 18757336, DOI: 10.1200/JCO.2008.16.3709

14 Griesinger F, Lueers AC, Falk M, Conradi I, Reinhardt M, Kluge A, Willborn K, Prenzel R, Scriba DC, Henke R, Eberhardt W, Hallas C and Tiemann M: Intercalated TKI and chemotherapy induction in EGFR mt+ NSCLC stage IIIA and IIIB: report of 3 cases with complete pathologic remission in mediastinal lymph nodes. Pneumologie *70(S 01)*: 2016. DOI: 10.1055/s-0036-1572236

15 Edge SB and Compton CC: The American Joint Committee on Cancer: The 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Onc *17(6)*: 1471-1474, 2010. PMID: 20180029, DOI: 10.1245/s10434-010-0985-4

16 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds.): AJCC Cancer Staging Manual, 8th Ed. New York: Springer; 2017.

17 Wu YL, Zhou C, Liam CK, Wu G, Liu X, Zhong Z, Lu S, Cheng Y, Han B, Chen L, Huang C, Qin S, Zhu Y, Pan H, Liang H, Li E, Jiang G, How SH, Fernando MC, Zhang Y, Xia F and Zuo Y: First-line erlotinib *versus* gemcitabine/cisplatin in patients with advanced EGFR mutation-positive non-small-cell lung cancer: Analyses from the phase III, randomized, open-label, ENSURE study. Ann Oncol *26(9)*: 1883-1889, 2015. PMID: 26105600, DOI: 10.1093/annonc/mdv270

18 Mok TS, Wu YL, Thongprasert S, Yang CH, Chu DT, Saijo N, Sunpaweravong P, Han B, Margono B, Ichinose Y, Nishiwaki Y, Ohe Y, Yang JJ, Chewaskulyong B, Jiang H, Duffield EL, Watkins CL, Armour AA and Fukuoka M: Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. N Engl J Med *361*: 947-957, 2009. PMID: 19692680, DOI: 10.1056/NEJMoa0810699

19 Sequist LV, Yang J.C., Yamamoto N, O'Byrne K, Hirsh V, Mok T, Geater SL, Orlov S, Tsai CM, Boyer M, Su WC, Bennouna J, Kato T, Gorbunova V, Lee KH, Shah R, Massey D, Zazulina V, Shahidi M and Schuler M: Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations. J Clin Oncol *31(27)*: 3327-34, 2013. PMID: 23816960, DOI: 10.1200/JCO.2012.44.2806

20 Peters S, Camidge DR, Shaw AT, Gadgeel S, Ahn JS, Kim DW, Ou S, Perol M, Dziadziuszko R, Rosell R, Zeaiter A, Mitry E,

Golding S, Balas B, Noe J, Morcos P and Mok T: Alectinib *versus* crizotinib in untreated ALK-positive non-small-cell lung cancer. N Engl J Med *377(9)*: 829-838, 2017. PMID: 28586279, DOI: 10.1056/NEJMoa1704795

21 Kaburagi T, Kiyoshima M, Nawa T, Ichimura H, Saito T, Hayashihara K, Yamada H, Satoh H, Endo T, Inage Y, Saito K, Inagaki M, Hizawa N, Sato Y, Ishikawa H, Sakai M, Kamiyama K, Kikuchi N, Nakamura H, Furukawa K, Kodama T, Yamashita T, Nomura A and Yoshida S: Acquired EGFR T790M mutation after relapse following EGFR-TKI therapy: a population-based multi-institutional study. Anticancer Res *38(5)*: 3145-3150, 2018. PMID: 29715155, DOI: 10.21873/anticanres.12577

22 Miyazaki K, Tamura T, Kaburagi T, Saito K, Inagaki M, Yamashita T, Ichimura H, Nawa T, Endo T, Hayashihara K, Kimura M, Kurishima K, Nakamura H, Furukawa K, Kikuchi N, Satoh H and Hizawa N: Real clinical practice of using afatinib therapy in NSCLC patients with an acquired EGFR T790M mutation. Anticancer Res *38(9)*: 5409-5415, 2018. PMID: 30194196, DOI: 10.21873/anticanres.12871

23 Millett RL, Elkon JM and Tabbara IA: Review: directed therapies in anaplastic lymphoma kinase-rearranged Non-small cell lung cancer. Anticancer Res *38(9)*: 4969-4975, 2018. PMID: 30194140, DOI: 10.21873/anticanres.12815

24 Socinski MA and Rosenman JG: Chemotherapeutic issues in the management of unresectable stage III non-small cell lung cancer. Semin Oncol *32*: S18-S24, 2005. PMID 16015532

25 NSCLC Meta-analysis Collaborative Group: Preoperative chemotherapy for non-small-cell lung cancer: A systematic review and meta-analysis of individual participant data. Lancet *383*: 1561-1571, 2014. PMID: 24576776, DOI: 10.1016/S0140-6736(13)62159-5

26 Curran WJ Jr., Paulus R, Langer CJ, Komaki R, Lee JS, Hauser S, Movsas B, Wasserman T, Rosenthal SA, Gore E, Machtay M, Sause W and Cox JD: Sequential *vs*. concurrent chemoradiation for stage III non-small cell lung cancer: Randomized phase III trial RTOG 9410. J Natl Cancer Inst *103(19)*: 1452-1460, 2011. PMID: 21903745, DOI: 10.1093/jnci/djr325

27 Furuse K, Fukuoka M, Kawahara M, Nishikawa H, Takada Y, Kudoh S, Katagami N and Ariyoshi Y: Phase III study of concurrent *versus* sequential thoracic radiotherapy in combination with mitomycin, vindesine, and cisplatin in unresectable stage III non-small-cell lung cancer. J Clin Oncol *17(9)*: 2692-2699, 1999. PMID: 10561343, DOI: 10.1200/JCO.1999.17.9.2692

28 Lin YT, Wang YF, Yang JC, Yu CJ, Wu SG, Shih JY and Yang PC: Development of renal cysts after crizotinib treatment in advanced ALK-positive non-small-cell lung cancer. J Thorac Oncol *9(11)*: 1720-1725, 2014. PMID: 25436806, DOI: 10.1097/JTO.0000000000000326

29 Albain KS, Crowley JJ, Turrisi AT 3rd, Gandara DR, Farrar WB, Clark JI, Beasley KR and Livingston RB: Concurrent cisplatin, etoposide, and chest radiotherapy in pathologic stage IIIB non-small-cell lung cancer: A southwest oncology group phase II study, SWOG 9019. J Clin Oncol *20(16)*: 3454-3460, 2002. PMID: 12177106, DOI: 10.1200/JCO.2002.03.055

Received December 17, 2019
Revised January 5, 2019
Accepted January 7, 2019