Title

Long-Term Survival of a Patient With Late-Stage Non-Small Cell Lung Cancer.

Journal

Federal practitioner : for the health care professionals of the VA, DoD, and PHS, 33(Suppl 5)

Authors

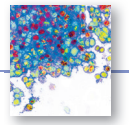
Allan-Blitz, Lao-Tzu

Hashemi, Leila

Publication Date

2016-08-01

Peer reviewed



Long-Term Survival of a Patient With Late-Stage Non-Small Cell Lung Cancer

Lao-Tzu Allan-Blitz; and Leila Hashemi, MD

After not responding to chemotherapy and monoclonal antibody therapy, a patient with late-stage non-small cell lung cancer benefited from treatment with erlotinib.

Lung cancer is the leading cause of cancer death in the world, with non-small cell lung cancer (NSCLC) a significant component of those deaths.[1,2] Treatments for advanced-stage NSCLC, however, are limited. Erlotinib, a small-molecule tyrosine kinase inhibitor of epidermal growth factor receptor (EGFR), has aided in advancing NSCLC therapy. Erlotinib has been shown to increase survival by 2 months compared with placebo in a phase 3, randomized controlled trial when used as second- or third-line therapy.[3] The authors present a case of a man surviving almost 8 years with late-stage NSCLC on treatment with erlotinib at the VA West Los Angeles Medical Center (WLAMC).

CASE REPORT

Mr. J is a 59-year-old man with a medical history of hepatitis C. He smoked 2 packs of cigarettes a day for 25 years and quit in 2003. He also had a known history of IV drug use. He was unaware of his family history because he was adopted, but his twin sister, who has no known medical problems, is also a smoker. In 2005, when Mr. J was evaluated for treatment options of long-standing hepatitis C with liver ultrasound, a large, irregular right adrenal mass was found, measuring 6.4 x 3.5 cm. A subsequent positron emission tomography (PET) scan identified a lung nodule measuring 3.8 x 3.6 x 3.3 cm. A biopsy guided by computed tomography (CT) showed NSCLC. Subsequently, metastases to the liver and adrenal glands were noted, and Mr. J was started on chemotherapy. He received 4 cycles of carboplatin 725 mg and gemcitabine 2,000 mg as well as a thoracotomy and left upper lung wedge resection in December 2005. His pain was controlled with slow-release morphine 15 mg 2 times per day and oxycodone 5 mg and acetaminophen 325 mg 4 times per day as needed for breakthrough pain.

In 2006, after 4 cycles of chemotherapy, the size of the adrenal mass and the lung mass had decreased; however, he developed new abdominal pain. A CT scan showed new intrahepatic and extrahepatic biliary dilatation and worsening pancreatic function. He could not tolerate the recommended endoscopic ultrasound and left WLAMC, later presenting to an outside hospital for his abdominal pain.

At the outside hospital, 2 masses that were surgically removed from the head of the pancreas were confirmed to be EGFR-positive NSCLC, and he was given 4 cycles of cisplatin and irinotecan at unknown doses. The only adverse effects (AEs) Mr. J reported during this period were nausea and vomiting immediately after chemotherapy. He failed to respond to this treatment and was started on bevacizumab, also at an unknown dose. The patient again did not respond and was transitioned to erlotinib 150 mg daily. The patient showed remarkable response, with lesions decreasing in size.

The patient returned to the WLAMC with multiple ulcerated lesions on his face, chest, back, and extremities and hair loss, which he reported all began within weeks of starting erlotinib. Later, he also developed trichomegaly, also presumed to be a consequence of erlotinib.

Mr. Allan-Blitz is a medical student and **Dr. Hashemi** is an assistant professor of clinical medicine at the David Geffen School of Medicine, University of California Los Angeles. Dr. Hashemi is also a physician at the VA Greater Los Angeles Healthcare System in California.

Despite these AEs, erlotinib was continued at the same dose, given his impressive response to this treatment, the absence of response to other therapy, and the patient's insistence on continuing the medication.

Of note, after his transition to the outside hospital, Mr. J and his family paid all his medical expenses because he had no insurance. His family was very supportive, and the patient described their motivation and support as paramount in his receiving treatment.

In 2008, Mr. J presented to a dermatologist and was treated with cleocin solution. Although this helped to control his symptoms, the rash persisted. As a complication of these lesions, he also experienced several superinfections for which he was treated with cephalexin. At this same time, a PET scan showed no evidence of disease. He presented to the pain service for persistent chest wall pain around the surgical site, and his pain regimen was changed to slow-release morphine 200 mg 3 times per day and morphine sulfate solution 20 mg/mL 80 mg every 4 hours for breakthrough pain.

The PET scans, which were repeated every 3 months after Mr. J resumed treatment at WLAMC, showed continued absence of disease. In 2009, when he presented to the hospital with pneumonia, a PET scan showed 2 new areas of tracer uptake measuring 1 cm. His chest wall was irradiated, but radiation therapy was stopped after the biopsy returned benign. In 2015, an annual PET scan showed only evidence of postsurgical changes.

DISCUSSION

The benefits of EGFR therapy have been established for treatment of late-stage NSCLC, but such therapy has limitations. For advanced-stage NSCLC, erlotinib has been shown to improve disease-free progression by 2.7 to 3.25 months and overall survival by 6.7 to 7.9 months.[4-6] However, 1-year survival estimates remain as low as 35.0 to 37.7%,[5,6] and its utility as first-line therapy has been questioned; randomized control trials have shown EGFR therapy to be of benefit only as second- or third-line therapy, when used with platinum-based chemotherapeutics.[3,4] The few reports of complete response, however, have not included a definition of duration of survival.[5,6]

Occasionally, there have been reports of patients surviving for significantly longer periods, including 1 report of a patient who survived with complete remission for 2 years.[7] In another case report, a patient experienced partial remission for more than 1 year with erlotinib as a third-line therapy.[8] Although several reports indicated prolonged survival with erlotinib, or induction of complete remission of metastasis, survival has not been longer than 2 years.[9-12]

Important considerations for use of erlotinib are factors that predict a positive treatment response, including female sex, no previous exposure to tobacco, Asian origin, and adenocarcinoma on histologic examination.[3,13] Mr. J did not meet any of these criteria. Interestingly, one study examining characteristics predictive of a positive response to erlotinib did not show that EGFR gene mutations were associated with response, although other studies have shown this to be a significant predictor of response.[3,14,15]

In this patient, his impressive response to erlotinib was most likely augmented by the presence of the EGFR mutation. Additionally, some reports indicate that pretreatment with platinum-based therapy can induce genetic changes resulting in EGFR mutations, thus enabling the benefit of erlotinib.[10] Given that his biopsy results were not tested for the EGFR mutation prior to initiating carboplatin, this is a possibility.

Other factors specific to Mr. J that may have influenced his response to therapy include his personal wealth, which may have given him direct access to physicians outside the VA. His family support also may have motivated him to pursue and continue treatment, thus augmenting his survival. This support likely contributed in large part to his continuing erlotinib therapy despite the severe rash, hair loss, and trichomegaly. Other AEs associated with long-term erlotinib therapy include folliculitis, diarrhea, fatigue, and paronychia,although Mr. J did not experience these.[16]

CONCLUSION

Mr. J continues to follow up regularly at WLAMC. To the authors' knowledge, this patient's 8 year survival is the longest length of survival for any patient with NSCLC on erlotinib therapy. While the therapeutic benefits of erlotinib as a second-line therapy have been shown, EGFR therapy may be more effective than previously thought. Further research is needed to fully understand the benefits of erlotinib. ●

Author disclosures

The authors report no actual or potential conflicts of interest with regard to this article.

Disclaimer

The opinions expressed herein are those of the authors and

do not necessarily reflect those of Federal Practitioner, *Frontline Medical Communications Inc., the U.S. Government, or any of its agencies. This article may discuss unlabeled or investigational use of certain drugs. Please review complete prescribing information for specific drugs or drug combinations—including indications, contraindications, warnings, and adverse effects—before administering pharmacologic therapy to patients.*

REFERENCES

1. Ridge CA, McErlean AM, Ginsberg MS. Epidemiology of lung cancer. *Semin Intervent Radiol.* 2013;30(2):93-98.
2. Gridelli C, Bareschino MA, Schettino C, Rossi A, Maione P, Ciardiello F. Erlotinib in non-small cell lung cancer treatment: current status and future development. *Oncologist.* 2007;12(7):840-849.
3. Shepherd FA, Pereira JR, Ciuleanu T, et al; National Cancer Institute of Canada Clinical Trials Group. Erlotinib in previously treated non–small-cell lung cancer. *N Engl J Med.* 2005;353(2):123-132.
4. Smith J. Erlotinib: small-molecule targeted therapy in the treatment of non-small-cell lung cancer. *Clin Ther.* 2005;27(10):1513-1534.
5. Boyer M, Horwood K, Pavlakis N, et al. Efficacy of erlotinib in patients with advanced non-small-cell lung cancer (NSCLC): analysis of the Australian subpopulation of the TRUST study. *Asia Pac J Clin Oncol.* 2012;8(3):248-254.
6. Reck M, van Zandwijk N, Gridelli C, et al. Erlotinib in advanced non-small cell lung cancer: efficacy and safety findings of the global phase IV Tarceva Lung Cancer Survival Treatment study. *J Thorac Oncol.* 2010;5(10):1616-1622.
7. Vitale MG, Riccardi F, Mocerino C, et al. Erlotinib-induced complete response in a patient with epidermal growth factor receptor wild-type lung adenocarcinoma after chemotherapy failure: a case report. *J Med Case Rep.* 2014;8:102.
8. Duchnowska R, Siemiatkowska A, Grala B, Smoter M. Long-term remission after erlotinib therapy in an elderly patient with advanced non-small-cell lung cancer. Case report and conclusions for clinical practice [in Polish]. *Pneumonol Alergol Pol.* 2008;76(6):451-455.
9. Lai CSL, Boshoff C, Falzon M, Lee SM. Complete response to erlotinib treatment in brain metastases from recurrent NSCLC. *Thorax.* 2006;61(1):91.
10. Karam I, Melosky B. Response to second-line erlotinib in an EGFR mutation-negative patient with non-small-cell lung cancer: make no assumptions. *Curr Oncol.* 2012;19(1):42-46.
11. Kobayashi T, Koizumi T, Agatsuma T, et al. A phase II trial of erlotinib in patients with EGFR wild-type advanced non-small-cell lung cancer. *Cancer Chemother Pharmacol.* 2012;69(5):1241-1246.
12. Gridelli C, Maione P, Galetta D, et al. Three cases of long-lasting tumor control with erlotinib after progression with gefitinib in advanced non-small cell lung cancer. *J Thorac Oncol.* 2007;2(8):758-761.
13. Fukuoka M, Yano S, Giaccone G, et al. Multi-institutional randomized phase II trial of gefitinib for previously treated patients with advanced non-small-cell lung cancer (The IDEAL 1 Trial) [corrected]. *J Clin Oncol.* 2003;21(12):2237-2246.
14. Tsao MS, Sakurada A, Cutz JC, et al. Erlotinib in lung cancer—molecular and clinical predictors of outcome. *N Engl J Med.* 2005;353(2):133-144.
15. Sequist LV, Bell DW, Lynch TJ, Haber DA. Molecular predictors of response to epidermal growth factor receptor antagonists in non-small-cell lung cancer. *J Clin Oncol.* 2007;25(5):587-595.
16. Becker A, van Wijk A, Smit EF, Postmus PE. Side-effects of long-term administration of erlotinib in patients with non-small cell lung cancer. *J Thorac Oncol.* 2010;5(9):1477-1480.