

# PostScript

## LETTERS TO THE EDITOR

### Complete response to erlotinib treatment in brain metastases from recurrent NSCLC

We report a case of a 55 year old Chinese female never smoker who presented with a 6 month history of cough in October 2002. In November 2002 she underwent a right middle lobectomy for adenocarcinoma. In June 2003 a CT scan showed recurrences in the mediastinum, pleura, and ribs. In January 2004 she completed six cycles of treatment with gemcitabine and carboplatin and the CT scan following treatment demonstrated a partial response. In June 2004 she developed breathlessness, unsteadiness, dizziness, and weakness involving the right upper limb. A CT scan showed disease recurrence in the chest with multiple lesions in her right lung and precarinal nodes and brain metastases. She received second line therapy with docetaxel and whole brain radiotherapy (20 Gy in five fractions) for brain metastases in July 2004. However, chemotherapy was suspended after two cycles because of life threatening sepsis. A CT scan performed after chemotherapy showed significant disease response in the thorax.

In December 2004 she developed progressively worsening pulmonary and neurological symptoms including dizziness. An MRI scan showed cerebral metastases with lesions in the left and right parietal lobes (fig 1A). She was commenced on third line therapy with erlotinib (Roche, 150 mg daily). Within a week of starting treatment her neurological symptoms resolved and her breathlessness improved. An MRI scan taken 6 weeks after starting erlotinib showed a complete response of brain metastases (fig 1B). Six months after starting treatment she remains clinically well on erlotinib without chest related or neurological symptoms except for a grade 1 skin rash.

The presence of somatic mutation in epidermal growth factor receptor (*EGFR*) gene has been associated with a higher responsiveness to erlotinib.<sup>1,2</sup> We sequenced exons 18–21 of the *EGFR* gene using DNA

extracted from tumour and normal lung tissue obtained at previous resection: the L858R mutation was detected. This point mutation in the activation loop of the kinase domain is linked to erlotinib responses.<sup>1,2</sup>

This is the first case report to show that erlotinib can be used to induce complete remission in brain disease from non-small cell lung cancer (NSCLC). Although gefitinib, another anti-EGFR small molecule, can induce remission of brain secondaries,<sup>3</sup> differences exist in molecule structure and binding profiles of these receptor tyrosine kinase inhibitors.<sup>4</sup> Furthermore, erlotinib treatment is now also associated with a survival benefit in NSCLC.<sup>5</sup> Brain metastases are a significant problem in individuals with NSCLC and, as adjuvant chemotherapy, concurrent chemoradiation and more effective third generation cytotoxic agents are prolonging survival, its rate might increase. Future studies should investigate the efficacy of combined erlotinib and brain irradiation.

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doi: 10.1136/thx.2005.052233

This work was supported in part by the London Lung Cancer Group, London, UK (Registered Charity No. 1074994) which received funding from Roche to support research on erlotinib.

Competing interests: none.

### References

- 1 Pao W, Miller VA. Epidermal growth factor receptor mutations, small-molecule kinase inhibitors, and non-small-cell lung cancer: current knowledge and future directions. *J Clin Oncol* 2005;**23**:2556–68.
- 2 Tsao MS, Sakurada A, Cutz JC, et al. Erlotinib in lung cancer: molecular and clinical predictors of outcome. *N Engl J Med* 2005;**353**:133–44.
- 3 Cappuzzo F, Ardizzoni A, Soto-Parra H, et al. Epidermal growth factor receptor targeted

therapy by ZD 1839 (Iressa) in patients with brain metastases from non-small cell lung cancer (NSCLC). *Lung Cancer* 2003;**41**:227–31.

- 4 Fabian MA, Biggs WH 3rd, Treiber DK, et al. A small molecule-kinase interaction map for clinical kinase inhibitors. *Nat Biotechnol* 2005;**23**:329–36.
- 5 Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al. Erlotinib in previously treated non-small-cell lung cancer. *N Engl J Med* 2005;**353**:123–32.

### Health outcomes following treatment for 6 months with once daily tiotropium compared with twice daily salmeterol in patients with COPD

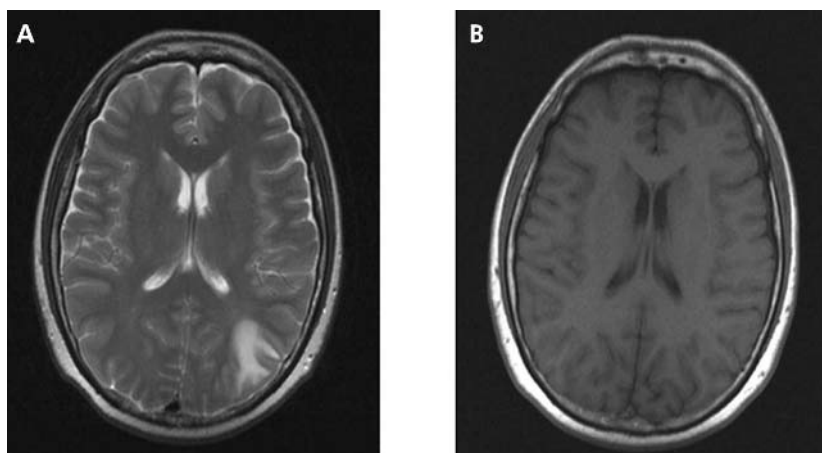
We wish to clarify issues raised by your recent letter regarding the abovementioned paper published in May 2003 in *Thorax* (2003;**58**:399–404). Our intention was to notify the editors and to reference the paper by Donohue *et al* appearing in *Chest*. We believe this is evidenced by our declaring in the cover letter that the data from one of the two trials were under review. However, we wish to apologise that we did not follow this up and did not remember to notify the Editorial Office about the acceptance of the Donohue manuscript in our response to the reviewers. We wish to assure you that it was not our desire to hide this information and we believe in and support the integrity of the scientific review and publication policies of all peer review journals.

Two separate clinical trials were conducted, as mentioned in the paper. Only the trial by Donohue *et al* examined 12 hour spirometry, representing the dosing interval of salmeterol, and constituted the first publication. As the St George's Respiratory Questionnaire and Mahler dyspnoea index were part of both trials, the information was included in the initial report. The absence of including the data that were collected could be perceived negatively. However, as mentioned in the introduction to the paper in *Thorax*, both protocols stated a priori that they would be combined for health outcome end points such as exacerbations and health resource utilisation, which were the focus of the *Thorax* publication. In the analysis section in the *Thorax* paper there is a detailed description of how the health resource utilisation data were analysed, and this is distinct from data presented in the paper by Donohue *et al*. The data in the results section are presented as combined data and therefore include the contribution from the study by Donohue *et al*. The health resource data were not analysed or reported for the individual trials and do not appear in the *Chest* manuscript. The pulmonary function data could only be presented as 3 hour data and were included for completeness as combined data in the *Thorax* manuscript. The focus of the discussion in the *Thorax* paper was on exacerbations and health outcome end points.

We sincerely regret our oversight and will ensure that this does not occur again. We thank you for giving us the opportunity to explain this regrettable omission and proclaim the goodness of our intentions.

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doi: 10.1136/thx.2005.brusascolett



**Figure 1** (A) MRI scan of one peripheral lesion in the right parietal lobe before starting treatment with erlotinib and (B) a repeat scan 6 weeks later indicating complete response of this metastasis.