

## Letter to the Editor

# Reply: K-Ras: a prognostic factor for survival in non-small cell lung cancer

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British Journal of Cancer (2006) 94, 1549. doi:10.1038/sj.bjc.6603113 www.bjcancer.com

Published online 25 April 2006

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Sir,

We would like to thank Gianluigi Ferreti and his colleagues for their interest in our systematic review.

In their letter, Ferreti *et al.* interrogated on the prognostic role of Ras in NSCLC. They cited seven studies with apparent conflicting results. Some comments have to be made. First, we discussed in our articles the controversial results of the literature relative to biological prognostic factors, justifying the need for meta-analyses, as we reported with K-Ras (Mascaux *et al.*, 2005) and other biomarkers previously such as p53, bcl2, VEGF, Neu, Ki-67 or EGFR.

Secondly, we have some concerns with the studies cited by Ferreti *et al.* Some of these articles were not included in our systematic review for the following reasons:

- no prognostic analysis (Ferreti *et al.*, 2000);
- no survival prognostic analysis but assessment of the predictive role of K-Ras for response to chemotherapy (Eberhard *et al.*, 2005; Winton *et al.*, 2005);

- assessment of K-Ras mutation on resected tumours after induction chemotherapy (Broermann *et al.*, 2002);
- publication after the deadline for the selection of the studies to be included in the meta-analysis (Zhu *et al.*, 2004).

The last two studies that Ferreti *et al.* commented (Moldvay *et al.*, 2000; Schiller *et al.*, 2001) were included in our systematic review and were aggregated with the 26 other evaluable studies for meta-analysis.

In conclusion, our systematic review showed that K-Ras is a potential prognostic factor for survival in lung cancer according to the literature published on this topic till end of 2003. The predictive role of K-Ras for response to chemotherapy and the impact of K-Ras mutation on survival in patients receiving induction chemotherapy before surgery were not the subjects of our meta-analysis and need further investigations.

## REFERENCES

- Broermann P, Junker K, Brandt BH, Heinecke A, Freitag L, Klinke F, Berdel WE, Thomas M (2002) Trimodality treatment in Stage III nonsmall cell lung carcinoma: prognostic impact of K-ras mutations after neoadjuvant therapy. *Cancer* 94: 2055-2062
- Eberhard DA, Johnson BE, Amler LC, Goddard AD, Heldens SL, Herbst RS, Ince WL, Janne PA, Januario T, Johnson DH, Klein P, Miller VA, Ostland MA, Ramies DA, Sebisano D, Stinson JA, Zhang YR, Seshagiri S, Hillan KJ (2005) Mutations in the epidermal growth factor receptor and in KRAS are predictive and prognostic indicators in patients with non-small-cell lung cancer treated with chemotherapy alone and in combination with erlotinib. *J Clin Oncol* 23: 5900-5909
- Ferreti G, Curigliano G, Pastorino U, Cittadini A, Flamini G, Calabro MG, De PT, Orlando L, Mandala M, Colleoni M, Spaggiari L, Granone PL, Pagliari G, de BF, Fazio N, Goldhirsch A (2000) Detection by denaturing gradient gel electrophoresis of tumor-specific mutations in biopsies and relative bronchoalveolar lavage fluid from resectable non-small cell lung cancer. *Clin Cancer Res* 6: 2393-2400
- Mascaux C, Iannino N, Martin B, Paesmans M, Berghmans T, Dusart M, Haller A, Lothaire P, Meert AP, Noel S, Lafitte JJ, Sculier JP (2005) The role of RAS oncogene in survival of patients with lung cancer: a systematic review of the literature with meta-analysis. *Br J Cancer* 92: 131-139
- Moldvay J, Scheid P, Wild P, Nabil K, Siat J, Borrelly J, Marie B, Farre G, Labib T, Pottier G, Sesboue R, Bronner C, Vignaud JM, Martinet Y, Martinet N (2000) Predictive survival markers in patients with surgically resected non-small cell lung carcinoma. *Clin Cancer Res* 6: 1125-1134
- Schiller JH, Adak S, Feins RH, Keller SM, Fry WA, Livingston RB, Hammond ME, Wolf B, Sabatini L, Jett J, Kohman L, Johnson DH (2001) Lack of prognostic significance of p53 and K-ras mutations in primary resected non-small-cell lung cancer on E4592: a Laboratory Ancillary Study on an Eastern Cooperative Oncology Group Prospective Randomized Trial of Postoperative Adjuvant Therapy. *J Clin Oncol* 19: 448-457
- Winton T, Livingston R, Johnson D, Rigas J, Johnston M, Butts C, Cormier Y, Goss G, Inculter R, Vallieres E, Fry W, Bethune D, Ayoub J, Ding K, Seymour L, Graham B, Tsao MS, Gandara D, Kesler K, Demmy T, Shepherd F (2005) Vinorelbine plus cisplatin vs observation in resected non-small-cell lung cancer. *N Engl J Med* 352: 2589-2597
- Zhu CQ, Blackhall FH, Pintilie M, Iyengar P, Liu N, Ho J, Chomiak T, Lau D, Winton T, Shepherd FA, Tsao MS (2004) Skp2 gene copy number aberrations are common in non-small cell lung carcinoma, and its overexpression in tumors with ras mutation is a poor prognostic marker. *Clin Cancer Res* 10: 1984-1991

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