

## Letter to the Editor

## Is membranous location of EGFR or EGFRvIII immunostaining associated with good prognosis in renal cell carcinoma?

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Sir,

We read with great interest the published article by Kallio *et al* (2003) in the British Journal of Cancer on the association between the location of EGFR immunostaining and overall survival in renal cell carcinoma (RCC) patients. In this paper, the authors have reported that overall survival was significantly longer ( $P=0.004$ ) in patients with prominent membranous EGFR expression compared to patients with either EGFR-negative tumours or tumours with predominantly cytoplasmic EGFR staining (Kallio *et al*, 2003). This is an important finding, as the expression of membranous EGFR has often been associated with a poor prognosis in cancer patients (Lager *et al*, 1994; Moch *et al*, 1997), while other studies have found either no association between EGFR expression and prognosis (Hofmockel *et al*, 1997) or more recently an association between the expression of cytoplasmic EGFR and poor prognosis in RCC patients (Langner *et al*, 2004).

To our knowledge, the paper by Kallio *et al* is the first paper to describe an association between prominent membranous EGFR immunostaining and longer overall survival in RCC patients.

However, there is a conflicting statement in the Materials and Methods section of the paper by Kallio *et al* that prevents us from accepting their conclusion and the authors need to clarify/rectify accordingly. In the immunohistochemical staining section of the Materials and Methods, Kallio *et al* stated the use of a polyclonal rabbit anti-EGFR variant III antibody (EGFRvIII) for EGFR immunostaining. The EGFRvIII is a ligand-independent, constitutively active and mutated form of EGFR (Pederson *et al*, 2001). Did the author use the rabbit anti-EGFRvIII antibody in their study and if so does it crossreact with the EGFR? Could Kallio *et al* clarify/rectify whether the prominent membranous EGFRvIII immunostaining in that study was associated with a good prognosis in patients with RCC? While no clear association has been found between the expression of the EGFR and response to the EGFR inhibitors in cancer patients, including patients with RCC, the expression of membranous EGFR and/or EGFRvIII in RCC patients would, however, make them an ideal target for therapy with the anti-EGFR antibodies (Modjtahedi *et al*, 2003; Dawson *et al*, 2004; Rowinsky *et al*, 2004; Dancey, 2004). We would appreciate clarification from Kallio *et al*.

## REFERENCES

- Dancey JE (2004) Epidermal growth factor receptor and epidermal growth factor receptor therapies in renal cell carcinoma: do we need a better mouse trap? *J Clin Oncol* 22: 2975–2977
- Dawson NA, Guo C, Zak R, Dorsey B, Smoot J, Wong J, Hussain A (2004) A phase II trial of gefitinib (Iressa, ZD1839) in stage IV and recurrent renal cell carcinoma. *Clin Cancer Res* 10: 7812–7819
- Hofmockel G, Riess S, Bassukas ID, Dammrich J (1997) Epidermal growth factor family and renal cell carcinoma: expression and prognostic impact. *Eur Urol* 31: 478–484
- Kallio JP, Hirvikoski P, Helin H, Kellokumpu-Lehtinen P, Luukkaala T, Tammela TL, Martikainen PM (2003) Membranous location of EGFR immunostaining is associated with good prognosis in renal cell carcinoma. *Br J Cancer* 89: 1266–1269
- Lager DJ, Slagel DD, Palechek PL (1994) The expression of epidermal growth factor receptor and transforming growth factor alpha in renal cell carcinoma. *Mod Pathol* 7: 544–548
- Langner C, Ratschek M, Rehak P, Schips L, Zigeuner R (2004) Are heterogenous results of EGFR immunoreactivity in renal cell carcinoma related to non-standardised criteria for staining evaluation? *J Clin Pathol* 57: 773–775
- Moch H, Sauter G, Buchholz N, Gasser TC, Bubendorf L, Waldman FM, Mihatsch MJ (1997) Epidermal growth factor receptor expression is associated with rapid tumor cell proliferation in renal cell carcinoma. *Hum Pathol* 28: 1255–1259
- Modjtahedi H, Moscatello DK, Box G, Green M, Shotton C, Lamb DJ, Reynolds LJ, Wong AL, Dean C, Thomas H, Eccles S (2003) Targeting of cells expressing wild type EGFR and type-III mutant EGFR (EGFRvIII) by anti-EGFR mAbs ICR62: a two pronged attack for tumour therapy. *Int J cancer* 105(2): 273–280
- Pederson MW, Meltorn M, Damstrup L, Polsen HS (2001) The type III epidermal growth factor receptor mutation. Biological significance and potential target for anti-cancer therapy. *Ann Oncol* 12: 745–760
- Rowinsky EK, Schwartz GH, Gollob JA, Thompson JA, Vogelzang NJ, Figlin R, Bukowski R, Haas N, Lockbaum P, Li YP, Arends R, Foon KA, Schwab G, Dutcher J (2004) Safety, pharmacokinetics, and activity of ABX-EGF, a fully human ant-epidermal growth factor receptor monoclonal antibody in patients with metastatic renal cell cancer. *J Clin Oncol* 22: 3003–3015

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