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Letter to the Editor Carbonic anhydrase IX expression is more predictive than prognostic in breast cancer

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Sir,

In a recent paper in the *British Journal of Cancer*, Hussain *et al* (2007) found carbonic anhydrase IX expression to be related to a poor prognosis in 144 unselected breast cancer patients. They state: 'CA IX expression may contribute to the identification of patients at greater risk of relapse who should be offered adjuvant treatment while sparing those whose prognosis is already good.'

However, in their patient description, Hussain *et al.* do not give any information concerning whether adjuvant treatment was given to these patients and, if so, which type of treatment. This makes the data difficult to interpret. We have earlier described the interactions of CA IX expression with both adjuvant endocrine and chemotherapy in 253 breast cancer patients (Span *et al* 2003). CA IX is induced by hypoxia inducible factor (HIF)-1, and is

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Hussain SA, Ganesan R, Reynolds G, Gross L, Stevens A, Pastorek J, Murray PG, Perunovic B, Anwar MS, Billingham L, James ND, Spooner D, Poole CJ, Rea DW, Palmer DH (2007) Hypoxia-regulated carbonic anhydrase IX expression is associated with poor survival in patients with invasive breast cancer. Br J Cancer 96: 104-109; doi:10.1038/sj.bjc.6603530 particularly overexpressed in VHL-related clear-cell renal carcinoma. Hypoxia itself is known to be associated with a poor response to radio- and chemotherapy. This indicates that CAIX expression is not prognostic – being associated with disease progression irrespective of treatment – but rather predictive, – predicting which patients will benefit from adjuvant treatment and who will not.

As such, we disagree with the authors' statement that CA IX expression will identify patient who should be offered adjuvant treatment due to a poor prognosis. Rather, more aggressive treatment or alternative treatment modalities might be offered to patients with high CA IX expression in their breast tumours, as the available data indicate that radiotherapy, endocrine and chemotherapy will be less successful for them than for patients with low CA IX expression.

Span PN, Bussink J, Manders P, Beex LVAM, Sweep CGJ (2003) Carbonic anhydrase-9 expression levels and prognosis in human breast cancer: association with treatment outcome. Br J Cancer 89: 271–276; doi:10.1038/sj.bjc.6601122

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