Trial watch

A DOUBLE HIT

A Phase I/II safety and immunogenicity evaluation trial of trastuzumab combined with ERBB2 vaccination in patients with metastatic breast cancer has recently been published.

Twenty-two patients with stage IV, ERBB2-positive breast cancer who were being treated with trastuzumab were vaccinated with an ERBB2 peptide-based vaccine that stimulates $CD4^+$ T helper cells. These cells should enter the tumour and, through interactions with antigen-presenting cells, enable the activation of cytotoxic T cells that bind ERBB2 and other tumour antigens. Monthly vaccinations were administered intradermally for the first 6 months of the trial. The response of T cells to the vaccine was monitored using interferon-γ-linked immunosorbent spot assay. Although most patients had pre-existing T cell responses to ERBB2 and other breast cancer antigens, these were boosted and prolonged by the vaccine. Epitope spreading in the form of response to additional tumour-related antigens was also evident.

Trastuzumab is known to affect heart function, and 15% of patients on this trial experienced a decline in left ventricular ejection volume. However, this was asymptomatic and the combined treatment was well tolerated overall and seems safe.

ORIGINAL RESEARCH PAPER Disis, M. L. *et al.* Concurrent trastuzumab and HER2/neu-specific vaccination in patients with metastatic breast cancer. *J. Clin. Oncol.* **27,** 4685–4692 (2009)

LIGANDS COULD BE KEY

There is good evidence that response to the epidermal growth factor receptor (EGFR) inhibitor cetuximab in patients with colorectal cancer is dependent on the tumour having wild-type *KRAS*. However, identifying which of these patients will respond well to cetuximab is not currently possible. On the basis of initial findings, Bart Jacobs and colleagues examined the mRNA levels of the EGFR ligands amphiregulin (AREG) and epiregulin (EREG) in tumour samples to see whether these ligands can predict outcome.

mRNA expression levels and *KRAS* mutation status were analysed in 220 formalin-fixed, paraffin-embedded colorectal tumour samples from patients with chemorefractory metastatic colorectal cancer treated with irinotecan and cetuximab. Response to treatment was assessed using Response Evaluation Criteria In Solid Tumours. In patients with tumours that were wild-type for *KRAS*, expression levels of *EREG* and *AREG* mRNA were predictive of outcome — EREG overall survival (OS) hazard ratio (HR) was 0.42 (95% confidence interval (CI) 0.28–0.63, $p<0.001$) and AREG OS HR was 0.40 (95% CI 0.27–0.64, $p<0.001$).

Therefore, high levels of *EREG* or *AREG* mRNA could be used in concert with *KRAS* status to predict response to cetuximab in colorectal cancer. However, some patients with low levels of expression also responded, as did one patient with mutant *KRAS*, indicating that additional markers are needed to improve predictive ability.

ORIGINAL RESEARCH PAPER Jacobs, B. *et al.* Amphiregulin and epiregulin mRNA expression in primary tumours predicts outcome in metstatic colorectal cancer treated with cetuximab. *J. Clin. Oncol.* 8 Sep 2009 (doi:10.1200/JCO.2008.21.3744)