

if there was no response to treatment after 4 weeks. Blood tests were carried out at weeks 4, 8, and 12, and patients were asked to assess fatigue levels based on a four-point scale (0–3; 3 being the most severe) at baseline, week 4, and the end of follow-up.

A response to therapy was observed in 72% of patients, 16.9% of whom required dose escalation. The response rate was higher in patients with baseline Hb levels <10 g/dl (74.4%) than in those with Hb levels ≥10 g/dl (68.8%). Patients with lower Hb levels at baseline also received more blood transfusions (62.5%). The percentage of responsive patients reporting fatigue scores of 2 or 3 decreased from 93.3 at the initiation of treatment to 38.3 at the end of follow-up. The authors conclude that darbepoetin alfa is effective at controlling the symptoms of chemotherapy-related anemia, and further evaluation of this agent in larger phase II and III studies is recommended.

Alexandra King

**Original article** Bartsch R *et al.* (2005) Darbepoetin  $\alpha$  as treatment for anemia in patients receiving chemotherapy: a single-center experience. *Anticancer Drugs* 16: 617–620

## The origins of multifocal papillary thyroid tumors

Multifocal papillary thyroid tumors are associated with an increased risk of persistent local disease and regional recurrence after treatment, as well as with lymph-node and distant metastases. A recent study by Shattuck *et al.* investigated the origins of such multiple distinct

thyroid tumor foci, using X-chromosome inactivation.

The researchers assessed DNA from tumor samples taken from 10 women who had undergone thyroidectomy to treat papillary thyroid carcinoma and who had multiple distinct tumor foci. All women were heterozygous for a polymorphism in the *HUMARA* (X-linked human androgen receptor) gene, and a polymerase chain reaction assay based on this gene was used to compare the patterns of monoclonal X-chromosome inactivation in tumor foci samples.

On comparison of the configurations of X-chromosome inactivation for each patient's individual tumor foci, 5 of the 10 patients showed discordant patterns between discrete foci, indicating that the tumors had independent origins. The remaining five patients showed identical monoclonal configurations in each of either two or three tumor foci, suggesting that the individual foci could have either a shared or a separate clonal origin.

In conclusion, the authors note that when surgery is used to treat multifocal papillary thyroid cancer, any thyroid tissue remaining post-surgery might either contain or be likely to develop further cancer foci that could become recurrences. Their results imply a strong predisposition to the development of new thyroid cancers in such patients, and therefore provide a biological rationale that supports bilateral thyroidectomy and radioablation of the remaining tissue.

Christine Kyme

**Original article** Shattuck TM *et al.* (2005) Independent clonal origins of distinct tumor foci in multifocal papillary thyroid carcinoma. *N Engl J Med* 352: 2406–2412