GLOSSARY

AMSTERDAM CRITERIA

The criteria developed by the International Collaborative Group in Amsterdam in 1990, to define hereditary nonpolyposis colorectal cancer

MICROSATELLITE SEQUENCES

Short repetitive DNA sequences, usually of 1–4 nucleotides, which can be used as markers for genetic linkage studies

SUMMIT

Study of Uncontrolled Multiple Myeloma managed with proteasome Inhibition Therapy

CREST

Clinical Response and Efficacy Study of bortezomib in the Treatment of relapsing multiple myeloma

New molecular links with hereditary colorectal cancer?

Early studies describing the cancer now known as hereditary nonpolyposis colorectal cancer suggested that this cancer type is genetically transmitted and could be molecularly defined. Further work showed, however, that a subgroup of patients who met the AMSTERDAM CRITERIA had neither the instability in their MICROSATELLITE SEQUENCES nor the germline mutations in particular DNA-repair genes to lead to that suggestion. To better define this subgroup, Mueller-Koch and co-workers compared the clinical features of patients whose tumors did or did not have DNA-repair gene mutations and high levels of microsatellite instability.

Of the 41 families studied, 25 (106 patients) had truncating mutations in DNA-repair genes ('positive'), and 16 (71 patients) had no mutations in these genes and no identified instability, but fulfilled the Amsterdam criteria ('negative'). The median age of cancer onset was earlier in positive families for both all tumors and colorectal tumors. The positive group had a higher incidence of extracolorectal tumors and a greater proportion of colorectal tumors that were near the splenic flexure. Adenomas were less common than carcinomas in the positive group, suggesting that progression to malignant tumors is faster in these patients.

These findings have implications for surveillance programs generally and for the frequency of monitoring. Cancer research should focus on defining the germline mutations that are associated with the development of this cancer type in the negative subset of patients.

Kate Matthews

Original article Mueller-Koch Y *et al.* (2005) Hereditary non-polyposis colorectal cancer: clinical and molecular evidence for a new entity of hereditary colorectal cancer. *Gut* 54: 1733–1740

Bortezomib-induced thrombocytopenia is transient in patients with multiple myeloma

A multicenter team from the US reports on the frequency of and risk factors for thrombocytopenia in patients receiving bortezomib for relapsed or refractory multiple myeloma. The data, from the SUMMIT and CREST phase II trial cohorts, suggest that the mechanism of

bortezomib-induced thrombocytopenia varies from that of other cytotoxic agents and should be managed differently.

The study population comprised 228 patients whose previous treatment with first-line chemotherapy or at least two previous regimens of chemotherapy, as part of the CREST or SUMMIT studies respectively, had failed. Patients received up to 8 cycles of treatment. Bortezomib (1.3 mg/m²) was administered twice weekly for the first 2 weeks of each 3-week cycle. Platelet count and serum M-protein were measured at baseline, and platelet counts were monitored throughout treatment.

Grade 3/4 thrombocytopenia was experienced by 30% of patients, and incidence was inversely related to baseline platelet count. Multivariate analysis revealed that low baseline platelet count, high baseline M-protein concentration, and number of prior regimens, were significant predictors of grade 3/4 thrombocytopenia ($P < 0.001$, $P = 0.032$ and $P = 0.007$, respectively). All patients had an approximately 60% reduction in platelet count from baseline to nadir, although concentrations generally followed a cyclic pattern, decreasing during bortezomib therapy but returning to baseline values during the breaks in treatment. The authors did not observe any evidence of cumulative toxicity and validated their data using a murine model, which indicated that megakaryocytes are not permanently affected by bortezomib.

The authors recommend that platelet transfusion should be used in preference to reduction of therapy in patients with bortezomib-induced thrombocytopenia.

Alexandra King

Original article Lonial S *et al.* (2005) Risk factors and kinetics of thrombocytopenia associated with bortezomib for relapsed, refractory multiple myeloma. *Blood* 106: 3777–3784

Akt activation leads to poor prognosis in postoperative breast cancer patients

Activation of the serine/threonine kinase Akt interferes with apoptosis, promotes resistance to chemotherapy and hormone therapy, and has an important role in cancer progression. Tokunaga *et al.* investigated the association between activated (phosphorylated) Akt and hormone receptor expression and