

## Chemotherapy can replace or delay radiotherapy in pediatric intracranial ependymoma

Radiotherapy is an effective treatment for childhood intracranial ependymoma (IE), but its use in patients younger than 5 years of age is associated with damage to the central nervous system and an increased risk of a second malignancy. A study by Grundy *et al.* has examined the role of chemotherapy in children with IE.

The study enrolled 89 children with IE aged 3 years or younger at diagnosis who had not received prior drug or radiation treatment. Following surgery, the children received alternating cycles of myelosuppressive and non-myelosuppressive chemotherapy for 1 year. Among the 80 patients without metastatic disease, 50 progressed; 34 received radiotherapy for this progression. The 5-year cumulative incidence rate of freedom from radiotherapy in those patients without metastatic disease was 42%. The 3-year and 5-year event-free survival rates for these patients were 47.6% and 41.8%, respectively. The overall 3-year and 5-year survival rates for nonmetastatic patients were 79.3% and 63.4%, respectively. Complete resection did not result in a better outcome, and overall and event-free survival did not differ according to age at diagnosis, site of disease or histological grade. The median time to progression was 1.6 years. The post-chemotherapy 5-year overall survival rates for the patients who received the highest ( $n=23$ ) and lowest ( $n=32$ ) relative dose intensity of chemotherapy were 76% and 52%, respectively.

This study shows that radiotherapy can be delayed or avoided in children with IE without compromising survival, when these patients are treated with chemotherapy.

**Original article** Grundy RG *et al.* (2007) Primary postoperative chemotherapy without radiotherapy for intracranial ependymoma in children: the UKCCSG/SIOP prospective study. *Lancet Oncol* 8: 696–705

## Potential therapy for Ph1-ALL and CML tumors unresponsive to imatinib and/or dasatinib

Patients with blast crisis chronic myelogenous leukemia (CML) or adult acute lymphoblastic leukemias that express the *BCR-ABL* oncogene (Ph1-ALL) have a poor prognosis. CML typically

starts with an indolent chronic phase followed by an aggressive myeloid or lymphoid blast crisis phase, which is dependent on the constitutive kinase activity of the *BCR-ABL* oncoprotein.

Imatinib, a *BCR-ABL* kinase inhibitor, shows excellent therapeutic efficacy in chronic-phase CML patients, but most patients with more-advanced CML or ALL do not show long-term response, or develop resistance, to imatinib and to the new generation of kinase inhibitors. Alternative treatments strategies are, therefore, required. Neviani *et al.* recently reported that a crucial point in blast transformation of CML is the loss of protein phosphatase 2A (PP2A) activity; they have subsequently investigated the therapeutic potential of the PP2A activator FTY720 (fingolimod) by use of *BCR-ABL*-transformed hematopoietic cell lines, primary bone marrow progenitors from chronic phase and blast crisis CML and Ph1-ALL patients sensitive and resistant to imatinib and/or dasatinib, and mouse models of these leukemias.

The study revealed that FTY720 induces cell death and reduces clonogenicity in myeloid and lymphoid cell lines and patient-derived progenitors that were either sensitive or resistant to imatinib and/or dasatinib, but it had no adverse effects on normal bone marrow progenitor cell growth and survival. Furthermore, pharmacological doses of FTY720 markedly suppressed the *in vivo* leukemogenesis driven by the wild-type and dasatinib-resistant T315I *BCR-ABL* oncogene kinases, without any observed toxicity in control animals. The authors conclude that rescuing PP2A tumor suppressor activity could be of great therapeutic relevance in patients with advanced-phase ALL or CML who are unresponsive to imatinib and/or dasatinib.

**Original article** Neviani P *et al.* (2007) FTY720, a new alternative for treating blast crisis chronic myelogenous leukemia and Philadelphia chromosome-positive acute lymphocytic leukemia. *J Clin Invest* 117: 2408–2421

## IgE levels correlate with survival in patients with multiple myeloma

Serum levels of polyclonal IgG, IgA and IgM are usually decreased in patients with multiple myeloma (MM); however, little is known about the prognostic significance of polyclonal levels of IgE in these patients. Matta *et al.* have recently reported data on IgE levels in patients with MM