GLOSSARY

VEGF
Vascular endothelial growth factor; a soluble factor that stimulates vascular permeability and blood vessel growth

consisted of three cycles of cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) followed by involved-field radiotherapy.

After a median length of follow-up of 7.7 years, the chemotherapy-alone group had significantly higher rates of event-free and overall survival compared with the rates in the CHOP plus radiotherapy group. The estimated 5-year event-free survival rate was 82% (95% CI 78–87%) in the ACVBP group and 74% (95% CI 69–78%) in those receiving chemoradiotherapy. The 5-year estimated rates of overall survival were 90% (95% CI 87–93%) with chemotherapy alone and 81% (95% CI 77–86%) with chemoradiotherapy. Multivariate analysis revealed that the differences in event-free and overall survival rates between the two groups were unaffected by prognostic factors such as tumor stage and burden. The authors conclude that ACVBP is a preferable treatment to CHOP plus radiotherapy for patients aged below 61 years with low-risk, localized lymphoma.

Original article Reyes F *et al.* (2005) ACVBP versus CHOP plus radiotherapy for localized aggressive lymphoma. *N Engl J Med* **352:** 1197–1205

A new role for sirolimus: regression of Kaposi's sarcoma in kidney-transplant recipients

Immunosuppression is thought to be important in the natural history of Kaposi's sarcoma, and the disease is 500 times more prevalent in patients who have received a solid-organ transplant than in the general population. In such patients, the skin lesions associated with Kaposi's sarcoma can be controlled by reducing immunosuppressive therapy, but this increases the risk of graft rejection.

The immunosuppressive drug sirolimus (rapamycin) is reported to inhibit tumorigenesis by suppressing VEGF expression and disrupting the Akt–p70S6 signaling pathway; therefore, this compound has therapeutic potential for immunosuppression-related malignancies. Stallone and co-workers have recently investigated the antineoplastic properties of sirolimus in kidney-transplant recipients with Kaposi's sarcoma.

Between October 2001 and March 2004, 15 kidney-graft recipients (mean age 48.7 years) on identical immunosuppressive drug regimens were enrolled in the study. All patients were HIV negative. Immunosuppressive therapy was changed from cyclosporine, mycophenolate mofetil and prednisone to sirolimus and prednisone when Kaposi's sarcoma was diagnosed. Biopsies of lesions and normal skin were taken at diagnosis and analyzed for VEGF, Flk-1/KDR protein, phosphorylated Akt and p70S6 kinase, which were all found to be present in significantly higher levels in Kaposi's sarcoma cells than in normal skin cells. After 3 months of sirolimus therapy, cutaneous lesions were undetectable in all patients. Biopsies taken from the site of the original lesion, 6 months after sirolimus therapy was initiated, confirmed that all patients had attained clinical remission of Kaposi's sarcoma with no incidents of graft rejection. The authors conclude that sirolimus is effective in treating Kaposi's sarcoma in kidney-transplant patients, while maintaining an immunosuppressive effect.

Original article Stallone G *et al.* (2005) Sirolimus for Kaposi's sarcoma in renal-transplant recipients. *N Engl J Med* **352:** 1317–1323

Glioblastoma treatment with temozolomide plus radiotherapy

Glioblastoma is a relatively common primary malignant tumor in adults, with an incidence of ~6/100,000 each year. After diagnosis, most patients survive much less than 2 years. Current treatment regimens consist of tumor resection and subsequent radiotherapy; standard chemotherapy regimens have had limited success, but there is some evidence that a combination of radiotherapy and chemotherapy is effective.

Chemotherapeutic alkylation of tumor DNA increases the rate of tumor-cell death. In order to maintain their ability to multiply, tumor cells use DNA-repair enzymes that remove the alkyl groups. Inactivation of the genes that encode DNA-repair enzymes improves the chemotherapeutic effect, as do frequent cycles of alkylation and repair, which result in depletion of the repair enzymes. Frequent administration of most chemotherapy agents is limited by the adverse events they induce.

Temozolomide is an alkylating agent that has been shown to be effective and safe in small