**GLOSSARY**

**OSMOTIC BLOOD–BRAIN BARRIER (BBB) DISRUPTION**
A technique where the blood–brain barrier is temporarily opened, allowing enhanced delivery and increased dose intensity of chemotherapeutic agents to the tumor site

## EGFR copy number and gefitinib efficacy in advanced NSCLC

Recent research by Cappuzzo *et al*. suggests that the efficacy of gefitinib treatment in advanced non-small-cell lung cancer (NSCLC) is predicted by the patient's epidermal growth factor receptor (*EGFR*) gene copy number. If validated in an ongoing, prospective study, these findings might be useful in selecting patients for therapy.

The researchers obtained tumor specimens from 102 NSCLC patients who were due to undergo gefitinib therapy. Using fluorescence *in situ* hybridization, they determined the *EGFR* copy number for each tumor. EGFR protein expression, *EGFR* mutations and Akt activation status were also analyzed. These factors were then compared with the patients' clinical outcomes.

Around one-third of patients had amplification or high polysomy of the *EGFR* gene, and more than half of the specimens showed high expression of the corresponding protein. Patients displaying either of these characteristics showed significantly better response to treatment, disease control rate, time to progression and survival than seen in patients not displaying increased gene or protein EGFR levels. In a multivariate analysis, a high *EGFR* gene copy remained significantly associated with improved survival, leading Cappuzzo *et al.* to conclude that this might be "an effective molecular predictive marker for gefitinib sensitivity in patients with advanced NSCLC".

**Original article** Cappuzzo F *et al.* (2005) Epidermal growth factor receptor gene and protein and gefitinib sensitivity in non-small-cell lung cancer. *J Natl Cancer Inst* **97:** 643–655

## Penetrating the blood–brain barrier: enhanced chemotherapy for central nervous system tumors

Therapy for brain tumors is challenging, and the majority of these lesions remain ultimately fatal. Delivery of chemotherapeutic agents to the tumor site is impeded by the blood–brain barrier (BBB), and therapeutic success is therefore limited. OSMOTIC BBB DISRUPTION can alleviate this complication, and a modified protocol is the subject of a recent phase II study by Fortin and colleagues from the Centre hospitalier universitaire de Sherbrooke, Quebec.

Between November 1999 and June 2002, 72 patients of median age 44 years (range 8–72 years) with various central nervous system malignancies underwent carotid or vertebral artery catheterization and mannitol infusion to open the BBB, followed by intra-arterial chemotherapy with etoposide and cyclophosphamide and either methotrexate or carboplatin, depending on tumor histology. This single-dose procedure was repeated once every 4 weeks for ≤12 cycles (mean 4.9 cycles). Response to therapy was assessed by monthly CT and MRI scans.

A total of 58% of patients with malignant astrocytomas achieved a complete or partial response to therapy, but only partial responses were noted in anaplastic oligodendroglioma patients (52%). All lymphoma patients responded (42% complete, 58% partial); 70% of those with brain metastases achieved a response, with the remaining 30% in this group exhibiting stable disease. Overall median survival times from treatment initiation were 9.2 months, 13.9 months, and 9.9 months for glioblastomas, anaplastic oligodendrogliomas and metastases, respectively. Overall survival for glioblastomas was 33 months. Based on promising results in the astrocytoma patients, the authors conclude that this single-dose per cycle regimen is a safe and successful modification of the original BBB disruption protocol, and a randomized, phase III trial has been initiated as a result.

**Original article** Fortin D *et al.* (2005) Enhanced chemotherapy delivery by intraarterial infusion and blood-brain barrier disruption in malignant brain tumors. *Cancer* [doi: 10.1002/cncr.21112]

## Oblimersen and gimatecan in the treatment of human melanoma

Bcl-2 is thought to be involved in the resistance of melanoma to chemotherapy, and the down-regulation of this protein has therefore been explored as a therapeutic strategy. De Cesare *et al.* have carried out preclinical studies of an antisense oligonucleotide—oblimersen—that results in the degradation of Bcl-2 messenger RNA. The results have shown that this agent appears to enhance the antitumor efficacy of gimatecan, a novel lipophilic camptothecin.