

## Significantly decreased BMD in noncirrhotic patients with chronic HCV infection

The association between osteoporosis and cirrhosis is well known; however, the prevalence of osteoporosis and the effects of antiviral treatments on bone metabolism of noncirrhotic patients with chronic hepatitis C (CHC) are unclear. A prospective study by Hofmann *et al.* investigated bone mineral density (BMD) and bone metabolism in 30 consecutive noncirrhotic patients with CHC who received antiviral therapy with pegylated interferon  $\alpha$ 2a and ribavirin. BMD and levels of the serum bone metabolism markers osteocalcin and procollagen type I C-terminal propeptide were measured at baseline, after 48 weeks of therapy, and after 24 weeks of follow-up.

At baseline, 43% of patients had osteopenia and 13% had osteoporosis. By the end of treatment, BMD at the hip and lumbar spine had significantly increased in 75% and 83% of patients, respectively. BMD declined after cessation of treatment, but remained above baseline values in patients with a sustained virological response. By contrast, BMD returned to baseline values in patients who had virologically relapsed at the 24-week follow-up. Levels of osteocalcin and procollagen type I C-terminal propeptide revealed a decrease in bone turnover during treatment.

This study demonstrates that a substantial proportion of patients with CHC who do not have established cirrhosis do have low BMD. The response of BMD and bone metabolism markers to antiviral therapy suggests that the treatment and/or the virus directly modulates bone metabolism.

**Original article** Hofmann WP *et al.* (2008) Prospective study of bone mineral density and metabolism in patients with chronic hepatitis C during pegylated interferon alpha and ribavirin therapy. *J Viral Hepat* 15: 790–796

## Mutations in KRAS render cetuximab therapy for advanced CRC ineffective

Therapy with cetuximab, a monoclonal antibody against the epidermal growth factor receptor, improves outcomes in patients who have chemotherapy-unresponsive colorectal

cancer (CRC). However, the presence of mutations in *KRAS*, a gene involved in the receptor's signaling, has been reported to affect cetuximab efficacy.

Karapetis *et al.* analyzed *KRAS* sequences in tumor samples from 394 of the 572 patients enrolled in the phase III, CO.17, randomized trial of cetuximab plus supportive care versus supportive care alone in patients with chemotherapy-unresponsive CRC. Among patients with *KRAS* mutations (42% of the sample), median survival was not significantly different in patients on cetuximab plus supportive care, and those on supportive care alone (4.5 months vs 4.6 months). Among patients with wild-type *KRAS* alleles, median survival was 9.5 months in the cetuximab plus supportive care group, and 4.8 months in the supportive care group ( $P < 0.001$ ). Analogous trends were observed in data on progression-free survival—the time between randomization and the first objective evidence of disease progression or death from any cause. Among patients on supportive care alone, no significant difference was recorded in median survival or median progression-free survival between supportive-care-only patients with wild-type *KRAS* and patients with mutated *KRAS* (4.8 months vs 4.6 months and 1.9 months vs 1.8 months).

Given the relatively high price of cetuximab, probing for *KRAS* mutations could be a cost-effective way to identify patients with chemotherapy-resistant CRC who would benefit from this therapy.

**Original article** Karapetis CS *et al.* (2008) K-ras mutations and benefit from cetuximab in advanced colorectal cancer. *N Engl J Med* 359: 1757–1765

## Bile-duct injury malpractice litigation: poor agreement among experts

Bile-duct injury (BDI), a common complication of laparoscopic cholecystectomy, is one of the most common grounds for malpractice litigation. Judges and/or juries who lack medical training decide whether malpractice has occurred and, therefore, the testimonies of expert witnesses are of considerable importance.

The inter-rater agreement of expert witnesses in deciding whether surgical negligence