



INFECTIOUS DISEASES NEWS AND VIEWS*

Discovery of gene that controls hepatitis C virus replication

A study in mice (1) has identified a gene, called protein kinase R (PKR), that plays an important role in controlling HCV replication and mediating interferon-induced antiviral response. This discovery will help researchers understand why the six HCV genotypes respond differently to interferon treatment.

REFERENCES

1. Chang KS, et al. J Virol 2006;80(15):7364-7374.

Very early viral response predicts sustained virological response in HIV/HCV co-infected patients

Mira and coworkers (1) have concluded in a large Spanish study that very early viral response (i.e. undetectable serum HCV-RNA determination at week 4) to treatment with pegylated-interferon and ribavirin is a reliable predictor of sustained virological response in HCV/HIV co-infected patients.

In another study O'Shea and coworkers (2) found a positive predictive value at week 4 of 94% among HCV mono-infected patients and 92% for HCV/HIV co-infected patients.

According to these studies, assessment of very early viral response can guide optimal treatment duration. Patients showing response at week 4 should be supported to complete

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full-dose therapy especially HCV/HIV co-infected patients.

REFERENCES

1. Mira JM, et al. Conference on retroviruses and opportunistic infections. February 25-28, 2007.
2. O'Shea D, et al. Conference on retroviruses and opportunistic infections. February 25-28, 2007.

Antibiotics and *clostridium difficile*-associated diarrhea

In a prospective study of 150 patients, Zar and coworkers (1) compared vancomycin and metronidazole orally and then stratified results based on severity of disease. A score of points was considered severe disease; 2 points were given for endoscopic evidence of pseudomembranous colitis. The primary outcomes assessed were cure, treatment failure, and relapse. Overall, cure was 84% in the metronidazole group and 97% in the vancomycin group (p=0.006). No statistically significant differences were seen in those with mild disease (90% vs 98%) (p=0.36), but vancomycin was superior in those with severe disease (76% vs 97%) (p=0.02). No differences in relapse were observed between the two groups (14% vs 7%) (p=0.27).

In many centers, metronidazole is used as a first line therapy for *clostridium difficile* colitis, and the results of this study suggest this is an appropriate practice. However, these results suggest a more rapid shift from metronidazole to vancomycin if the patient did not rapidly improve. Although not statistically significant, relapse was twice as likely in the metronidazole group.

REFERENCES

1. Zar FA, *et al.* Clin Infect Dis 2007, 45:302-307.

Statins block HCV

In a Japanese study, Ikeda and coworkers (1) showed that statins, typically used as anti-cholesterol medications, can block the replication of hepatitis C virus, apparently by inhibiting certain proteins required for such replication. When combined with interferon, all except pravastatin blocked HCV-RNA replication more effectively than when used alone. Statins` anti-HCV activity was unrelated to cytotoxicity or direct HMC-CoA inhibition.

REFERENCES

1. Ikeda M, *et al.* Hepatology 2006;44:117-125.

CPG 10101 in patients with chronic hepatitis C virus

(McHutchison J, *et al.* Hepatology 2007, 46:1341-49)

McHutchinson and colleagues have recently reported on the efficacy of one of the new class of immunomodulatory drugs so called CPG 10101 (Actilon) from Coley Pharmaceutical Group Inc., Wellesley, MA in patients with chronic hepatitis C (1). Such new molecular entity arising as a result of expending scientific knowledge of the importance of B cell and plasmacytoid dendritic cell (pDC) Toll-like receptor 9 (TLR9) stimulation as mechanism of HCV antiviral effect.

In this reported placebo-controlled phase 1b study, 60 patients with chronic HCV, both naïve and treatment experienced, were treated with placebo or 1 of 7 varying dose or dosing frequency regimens of CPG 10101 for 4 weeks. Dose-dependent cytokine induction was observed in the subjects receiving CPG 10101, including significant increases in interferon alpha levels. HCV-RNA levels were decrease in dose-dependent pattern and the overall HCV-RNA response for CPG 10101

appeared to be similar for that previously reported for pegylated interferon monotherapy. The data indicate that CPG 10101 has HCV antiviral activity across a range of doses and is generally well-tolerated. The authors of the study concluded by suggesting that «The data support further clinical studies of CPG 10101 for treating chronic HCV infection».

Reference

1. McHutchison J, *et al.* Phase 1B, randomized, double-blind, dose-escalation trial of CPG 0101 in patients with chronic hepatitis C virus. Hepatology 2007, 46:1341-49.

Screening for *Helicobacter pylori* infection in developing countries: Highlights on WGO-OMGE Practice Guideline.

(Hunt RH, *et al.* World Gastroenterol News 2006; 2: 22-29)

Helicobacter pylori (*H. pylori*) infection in developing countries is an important public-health problem. The high prevalence of the infection in some developing countries, which may reach up to 90%, requires the development of public-health interventions. The WGO-OMGE practice guideline on *H. pylori* in developing countries has recently been reported by an international review team from 16 countries (1). The debate about screening for *H. pylori* infection as part of a periodic health examination in growing in importance in some developed countries. The potential for a screening program is of particular interest and importance in countries with a high incidence of gastric cancer. «The question of whether *H. pylori* infection should be sought out and eradicated in people who do not present with symptoms is an important one. Detection when there are no symptoms is especially important in developing countries in which there is a high incidence of gastric cancer. Most consensus statements, guidelines, and reviews have focused on the treatment of

patients who present with a clinical problem. But is this cost-effective?», as reported by the review team. A systematic review by the team identified 12 nested prospective case-control studies and meta-analyses, which suggested that *H. pylori* is associated with an increase in the odds ratio of developing non-cardia gastric cancer of 5.9 (95% CI, 3.4 to 10.3). These are not interventional studies, and it is not known with confidence whether eradication of *H. pylori* infection reduces the risk of gastric cancer.

Screening populations for *H. pylori* infection and treatment of those infected may lead to a reduction in the incidence of gastric cancer. More research is needed to evaluate the efficacy of *H. pylori* eradication in preventing gastric cancer and gastric lymphoma in the general population before decisions can be taken on whether or not screening for *H. pylori* in countries with a high incidence of gastric cancer will be cost-effective (1). Community screening and eradication of *H. pylori* infection is feasible in the general population and can

lead to significant reductions in the numbers of patients who consult for dyspepsia with symptoms two years after treatment. However, these benefits have to be balanced against the costs of eradication treatment, so that a targeted eradication strategy in dyspeptic patients may be preferable (1).

Vaccination with a treatment vaccine is probably the only strategy that would make a decisive difference in the prevalence and incidence worldwide. However, such a vaccine is still not available, and one short-term approach would therefore be to follow the same strategies as for developed countries. Provided that resources allow it, a test-and-treat strategy is preferable for those at risk for peptic ulcer disease or gastric cancer or for those with serious symptoms of dyspepsia and indigestion.

Reference

1. Hunt RH, et al. WGO-OMGE practice guideline highlights: *Helicobacter pylori* in developing countries. World Gastroenterol News 2006; 2: 22-29.