PostScript

LETTERS

Authors' reply

We appreciate the interest given to our article (*Gut* 2005;54:1536-40) by Bhuiyan and Mencias Vera¹ as well as by Gillen and McColl.² Both letters requested individual scores for atrophy and intestinal metaplasia at baseline and at 12 years of follow-up. Table 1 shows the scores.

We wish to emphasise that the histopathology score (table 1, fig 1 in the original article) was based on the global diagnosis and reflects the grade of atrophy and dysplasia, and the type and extent of intestinal metaplasia. The inflammatory infiltrate was not part of this histopathology score. Therefore, the resolution of the inflammatory infiltrate does not explain the fall in the average histopathology score. Acute and chronic inflammatory scores were classified separately in the antrum and the corpus according to the updated Sydney System in an ordinal scale (0-3). Figure 2 in the original article shows the average values in the antrum over time (*Gut* 2005;54:1536-40).

Objective evidence of the regression of gastric atrophy was reported by our group in a previous report.³ We showed, in a subset of patients of the same cohort, that subjects cured of *Helicobacter pylori* infection after 6 years of follow-up showed a major reduction of atrophy indices in the antrum, evaluated by strict morphometric techniques.

As our trial was based on precancerous end points, the size and duration in this study are insufficient to assess results on the basis of gastric cancer as an end point. Therefore, comparisons of results among studies with different end points should be made with caution.

Finally, we apologise for the error that Gillen and McColl brought to our attention, which does not affect any of our conclusions. The correct number of subjects with intestinal metaplasia at baseline who were *Helicobacter pylori* negative at 12 years is 37/182 or 20% (instead of 70/182).

We hope these clarifications help in the interpretation of our findings and conclusions.

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Competing interests: None.

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Treatment of patients with lamivudine-resistant and adefovir dipivoxil-resistant chronic hepatitis B virus infection: is tenofovir the answer?

We read with great interest the article by Yeon *et al.* reporting resistance rates to adefovir dipivoxil (ADV) in 25% of patients with lamivudine-resistant hepatitis B virus (HBV) after 24 months of ADV treatment (*Gut* 2006;55:1488-95). How should we deal with these new important data on ADV resistance? The acyclic nucleotide analogue tenofovir disoproxil fumarate (TDF) was recently shown to be effective in patients with lamivudine-resistant HBV, with incomplete virological response to ADV.¹ However, little is known about the efficacy of TDF in patients with lamivudine-resistant and ADV-resistant HBV as described by Yeon *et al.*

We report data on six male patients (median age 48 years, range 34-64 years), who have been treated with TDF for at least 6 months. Five out of six patients were hepatitis B e (Hbe) antigen negative, and documented cirrhosis (Child-Pugh stage A) was present in two of

them. Earlier treatments included lamivudine (median treatment duration 45 months, range 16-72 months), followed by ADV (median treatment duration 24 months, range 11-45). ADV resistance was suspected when virological breakthrough (HBV DNA $\geq 4 \log_{10}$ copies/ml; COBAS TaqMan, Roche, Grenzach-Whylen, Germany; lower limit of quantification 1.85 $\log_{10}$ copies/ml) occurred. In four of six patients, the typical HBV polymerase mutations rtA181V, rtA181T or rtN236T were shown (table 1). At that time, HBV DNA considerably increased in all patients (median HBV DNA 7.64, range 5.57-8.64, $\log_{10}$ copies/ml), and alanine aminotransferase (ALT) levels (median 183 IU/L, range 34-358 IU/L) were elevated in five of six patients. None of these patients had evidence of hepatic decompensation. Subsequently, treatment with ADV was stopped and TDF (300 mg/day) was started. Patients were followed after 4, 12 and 24 weeks. At 12 and 24 weeks, ALT level considerably decreased in all five patients with raised level at baseline. Moreover, four of six patients had ALT level within the normal range at week 24. After 24 weeks of TDF treatment, the median HBV DNA decline was 4.24 $\log_{10}$ copies/ml (range 3.27-4.87), and none of the patients had evidence of resistance (table 1). No side effects occurred during treatment with TDF.

Taken together, we showed that TDF is highly effective in patients with lamivudine-resistant and ADV-resistant chronic HBV. TDF leads to a rapid virological response and normalisation of ALT levels in most patients. The efficacy of TDF in lamivudine-resistant and ADV-resistant HBV strains seems comparable to that in lamivudine-resistant HBV. In the latter patients, van Bömmel *et al.* found a mean decline HBV DNA of 5.2 $\log_{10}$ copies/ml after 24 weeks of treatment,² which is in accordance with our data.

The rapid antiviral effect of TDF makes it an attractive salvage treatment for patients with lamivudine-resistant and ADV-resistant chronic HBV, especially for those with decompensated chronic liver disease.³ Moreover, recent studies strongly suggest that TDF may be the treatment of choice in patients co-infected with HIV and HBV.^{4,5} However, prospective studies in patients with chronic HBV are needed to assess the long-term antiviral efficacy and the potential for emergence of TDF resistance.

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doi: 10.1136/gut.2006.108928

Competing interests: None.

References

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Table 1 Histopathology scores at baseline and at 12 years of follow-up in patients treated and free of *Helicobacter pylori* infection at 12 years

Diagnosis at baseline	Histopathology score, mean (95% CI)	
	Baseline	12 years
Atrophy	3.57 (3.54 to 3.60)	1.87 (1.44 to 2.29)
Intestinal metaplasia	4.46 (4.43 to 4.50)	3.83 (3.56 to 4.10)
Total	3.77 (3.68 to 3.86)	3.18 (3.10 to 3.26)