Chairman's Introduction

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Since the early days of H₂-receptor blockade, pioneered by Sir James Black with ci-metidine, research into new drugs for the treatment of peptic ulcer disease has led to the ultimate in the targeted control of gastric acid secretion with acid pump inhibitors, such as omeprazole, which now approach the concept of Ehrlich's magic bullet.

As it has become possible to achieve a greater and more prolonged control of acid secretion, concerns have been raised over the possible consequences of treatment. Issues such as rebound acid secretion, hypergastrinaemia, bacterial overgrowth and enteric infection, and the theoretical risk of carcino-genesis have all attracted attention. These issues have been investigated by scientists from both academia and industry, who have often joined forces to solve the problems using the best scientific methods available.

Clinicians who have had the opportunity to use omeprazole in clinical practice have been able to see its dramatic benefits, especially in patients with gastro-oesophageal reflux disease, refractory duodenal or gastric ulcer and hypersecretory states such as Zol-linger-Ellison syndrome. For the first time

since those early days with cimetidine, clinicians have seen patients, especially those with gastro-oesophageal reflux disease, proclaiming their appreciation of pain relief in dramatic terms, and this has raised the question of how long to continue treatment with omeprazole.

Concerns over prolonged treatment with omeprazole have arisen as a result of the long-term safety issues initially raised by the finding of gastric enterochromaffin-like (ECL) cell carcinoids in rat toxicology studies. More recently, in a letter to the Lancet (17 February 1990), Burlinson et al. [1] published a report suggesting that omeprazole might have the potential for genotoxicity. The issue of gastric ECL cell carcinoids and hypergastrinaemia stimulated a series of scientific studies in rats to unravel the relationship between effective acid control, increased gastrin levels and ECL cell hyper-plasia. These studies are published, are in press, or have been submitted to peer-reviewed journals.

The sequence of events which results from a lifetime of profound acid inhibition, achieved by a variety of surgical or pharmaco-

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logical methods, can lead to gastric ECL cell hyperplasia in rats and the development of gastric ECL cell carcinoids in some animals. Studies have shown, however, that such drug-induced gastric ECL cell carcinoids are not the result of acid suppression by any one drug or class of drugs.

But what of genotoxicity? In the Burlinson experiment [2], a newly developed in vivo method was used to determine the amount of unscheduled DNA synthesis as a measure of possible drug-

induced DNA damage in the rat gastric mucosa. Although this method is highly controversial, it was concluded from this experiment that 'for omeprazole a geno-toxic mechanism of action cannot be discounted'.

The symposium on which this proceedings is based was organized to give scientists and clinicians a chance to hear the other side of this controversial issue. This important meeting drew together a distinguished faculty of independent authorities in the field, as well as scientific and medical personnel from AB Astra. The faculty was charged with addressing three principal areas: (1) the role of gas-trin as a trophic hormone, and its part in the development of gastric ECL cell hyperplasia

and gastric ECL cell carcinoids in rats, (2) the current understanding of scheduled and unscheduled DNA synthesis and repair in relation to data from various laboratories, and (3) current clinical studies, drug safety and future developments with omeprazole.

This supplement reports on the proceedings of a meeting held in London in April 1990. I hope that the information it contains will enable readers to evaluate the scientific validity of current studies in this field with objectivity.

References

Burlinson B, Morriss SH, Gatehouse DG, Tweats DJ: Genotoxicity studies of gastric acid inhibiting drugs. *Lancet* 1990;335:419-420.

Burlinson B: An in vivo unscheduled DNA (UDS) assay in the rat gastric mucosa: Preliminary development. *Carcinogenesis* 1989;10:1425-1428.