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Introduction

Giorgio Cocconi

IN THIS SYMPOSIUM many aspects of the problems of nausea and vomiting associated with cytotoxic chemotherapy were covered. The attitudes of patients and medical professionals to treatment, behavioural interventions and psychological aspects of care as well as data on treatment with granisetron were reported.

Granisetron is a recently developed 5-HT_3 receptor antagonist which is now available for the treatment of nausea and vomiting induced by emetogenic anticancer agents. Nausea and vomiting are among the most disturbing adverse effects associated with chemotherapy and the patients' quality of life can be significantly impaired by these symptoms. Moreover, some patients may even refuse further administration or continuation of possibly curative chemotherapy programmes due to these distressing adverse effects.

The recognition of the strong antiemetic activity of high-dose metoclopramide has radically altered our approach to prevention and to treatment of nausea and vomiting induced by anticancer agents. The development of such antiemetics has made cytotoxic chemotherapy more acceptable and improved the quality of life of the patient. High-dose metoclopramide was important not only because it improved quality of life, but also because research into its mode of action led to the discovery that at high doses its antidopaminergic activity was not sufficient to explain its efficacy. Ultimately this has led to the discovery of 5-HT_3 receptor antagonists and the subsequent development of specific inhibitors.

Granisetron, one of the first drugs in this new class of antiemetic agents, is a potent, highly selective antagonist of 5-HT_3 receptors. In the ferret, low doses of granisetron in prophylaxis or interventional use, could prevent emesis induced by cisplatin, combinations of cytotoxic drugs and whole body irradiation. In healthy volunteers, granisetron was well tolerated, constipation being the only persistent adverse event. The elimination half life of granisetron is approximately 3-6 h with a wide inter-patient variation. The prolonged antiemetic activity is not related to elimination half life and probably results from a potent pharmacodynamic inhibitory effect on 5-HT_3 receptors. Plasma concentrations are dose related.

Placebo-controlled studies have confirmed the potent antiemetic activity of granisetron when given prophylactically. Moreover, its efficacy as an interventional agent for rapid control of emesis experienced by patients receiving placebo has been demonstrated.

The prime objectives of this symposium were to update the already impressive available data and to add information from new studies, most of which have been undertaken to assess the role of granisetron in routine clinical care. Specific presentations were devoted to the establishment of the optimal dose of intravenous granisetron in an attempt to indicate whether this drug is preferable to conventional combinations. Additional information concerning the maintenance of granisetron efficacy in repeat-cycle chemotherapy, and to assess whether granisetron or conventional emetics should be used in fractionated chemotherapy were also presented. The potential indications for oral granisetron were also discussed.

Granisetron is one of several 5-HT_3 receptor antagonists and it is highly probable that within a few years the medical literature will be flooded with information concerning several drugs of this same class. Against this background it is important to try to define pharmacological differences that will help differentiate and distinguish this expanding group of 5-HT_3 antagonists in the clinical setting. Indeed, the title of one of the presentations given here "Are all 5-HT_3 receptor antagonists the same?" would appear suitably timed to address this question as far as granisetron is concerned.

Correspondence to: G.Cocconi
G. Cocconi is at the Ospedale Regionale, Parma, Italy.