

EMERGING TRENDS IN ANTIEMETIC THERAPY FOR THE 21ST CENTURY

In Dr. Paul Hesketh's presentation, sponsored by MGI PHARMA, Inc, he provided an overview of the classification, pathophysiology and risk factors for CINV, as well as a review of treatment guidelines and physician's perceptions vs. the patient's reality of control of CINV with current treatments. He also presented data on two novel, recently approved agents, a second-generation serotonin antagonist, palonosetron (Aloxi™) and an NK₁ antagonist, aprepitant (Emend®).

Palonosetron is a pharmacologically differentiated, selective 5-HT₃ receptor antagonist with a 30-fold higher receptor binding affinity than the other agents in this class. Palonosetron also has an extended plasma half life of approximately 40 hrs vs. 4-8 hrs for the other 5-HT₃ receptor antagonists. Dr Hesketh reviewed the efficacy and safety data from three large (>500 patients), Phase III multi-center, comparative trials previously presented at MASCC 2002/2003 and ASCO 2003. In two trials in patients receiving moderately emetogenic chemotherapy, a greater proportion of palonosetron (Aloxi™)-treated patients had a complete response (no emesis, no rescue medication) than ondansetron or dolasetron-treated patients during the acute (0-24 hrs post-

chemotherapy) and delayed (24-120 hrs) phases. In the 3rd trial, palonosetron resulted in similar response rates to ondansetron in patients receiving highly emetogenic chemotherapy (2/3 pts received concomitant dexamethasone; subset data not shown). Palonosetron was well-tolerated with a similar safety profile to ondansetron and dolasetron.

Aprepitant is the first approved agent in a new class of substance P/NK1 antagonists, known to have a central role in the emetic response. Dr Hesketh reviewed efficacy data from two Phase III trials (JCO, in press; Cancer 2003) comparing triplet therapy of aprepitant, ondansetron, and dexamethasone with standard therapy (ondansetron + dexamethasone). Superior response rates were seen for the aprepitant combination compared with standard therapy in the acute and delayed phases. Aprepitant was well tolerated with a similar safety profile to standard therapy.

In conclusion, Dr. Hesketh acknowledged that marked advances in antiemetic therapy had occurred over the last 15 years; however, a proportion of patients remain suboptimally controlled. These new agents "offer the possibility of the first substantive advances in the management of CINV in over a decade."



Dr. Paul Hesketh

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