A phase III trial of aprepitant in colorectal cancer patients receiving oxaliplatin-based chemotherapy (SENRI Trial)

J. Nishimura¹, T. Satoh¹, M. Fukunaga², H. Takemoto³, K. Nakata⁴, Y. Ide⁵, T. Fukuzaki⁶, T. Kudo⁷, Y. Miyake⁷, M. Yasu⁸, S. Morita⁹, D. Sakai⁹, M. Uemura⁵, T. Hata⁸, I. Takemasa¹, T. Mizushima¹, Y. Ohno¹, H. Yamamoto¹, M. Sekimoto¹⁰, R. Nezu⁸, Y. Doki¹, M. Mori¹

¹Osaka University Graduate School of Medicine, Suita, Japan
²Hyogo Prefectural Nishinomiya Hospital, Nishinomiya, Japan
³Kinki Central Hospital of the Mutual Aid Association of Public School Teachers, Itami, Japan
⁴Sakai City Hospital, Sakai, Japan
⁵Yao Municipal Hospital, Yao, Japan
⁶Sasekai Senri Hospital, Suita, Japan
⁷Nishinomiya Municipal Central Hospital, Dept of Surgery, Nishinomiya, Japan
⁸Kazukura City Hospital, Kazukura, Japan
⁹Toyonaka Municipal Hospital, Toyonaka, Japan
¹⁰National Hospital Organization, Osaka National Hospital, Osaka, Japan

Introduction: The oral neurokinin-1 antagonist aprepitant is recommended in several guidelines for preventing chemotherapy-induced nausea & vomiting (CINV) due to highly emetogenic cancer chemotherapy. In recent guidelines, FOLFOX and XELOX therapies are classified as having moderate emetogenic risk. However, in the phase III study of oxaliplatin-based chemotherapy in patients with metastatic colorectal cancer, the rates of nausea and vomiting ranged from 60.5% to 73.7% and 47.2% to 44.2%, respectively. It is very important to control and minimize nausea and vomiting to enable continuation of cancer chemotherapy. In this study, we conducted a multicenter, randomized phase III study to evaluate the usefulness of the combined use of aprepitant in colorectal cancer patients treated with oxaliplatin.

Methods: In this multicenter, open-label, randomized, phase 3 trial, we recruited patients with colorectal cancer who underwent an oxaliplatin-based chemotherapy. Patients were centrally randomized in a 1:1 ratio to the control group (5-HT3-receptor antagonist + dexamethasone) or aprepitant group (5-HT3-receptor antagonist + dexamethasone + aprepitant or fosaprepitant) in the first course. All patients were treated with aprepitant/fosaprepitant therapy in the second course. The primary endpoint was the rate of patients with no emesis. We also analyzed the potential effect of gender on treatment response.

Results: A total of 413 patients entered this clinical trial from 25 centers in Japan. Significantly more patients in the aprepitant group achieved no vomiting overall and delayed phase than those in the control group (95.7% vs. 83.6% and 95.7% vs. 84.7%, respectively). There was no significant difference in adverse events between the groups. In the control group, 64% of women had overall complete response compared with 81% of men. In the aprepitant group, 78% of women had overall complete response compared with 90% of men. In women, the rates of no nausea and complete protection were significantly higher in the aprepitant group compared with the control group.

Conclusion: In colorectal cancer patients receiving oxaliplatin-based chemotherapy, the aprepitant therapy during chemotherapy improved antiemetic control compared with the control therapy. The addition of aprepitant might be more effective in female gender.