PRESS RELEASE
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SENRI trial opens window to evaluate NK1 antagonists for emesis prevention in oxaliplatin chemotherapy

BARCELONA-LUGANO, 1 July 2015 – The SENRI trial has opened the window to evaluate NK1 antagonists for emesis prevention in patients taking oxaliplatin chemotherapy, antiemetics expert and ESMO spokesperson Fausto Roila said, putting into perspective the results of a Japanese study presented today at the ESMO 17th World Congress on Gastrointestinal Cancer 2015 in Barcelona.

Roila’s comments came as the SENRI Trial results were presented including a new gender analysis (1),(2). He said: “Until now we said that NK1 antagonists have no role in the prevention of emesis in oxaliplatin chemotherapy, classified as having a moderate emetogenic risk only.”

The multicentre, open label, randomised phase III SENRI Trial evaluated the NK1 antagonist aprepitant for the prevention of nausea and vomiting induced by oxaliplatin-based chemotherapy in Japanese patients with colorectal cancer. Patients were randomised 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 (3)) in the first course. All patients were treated with aprepitant/fosaprepitant in the second course. The primary endpoint was the rate of patients with no emesis. The results presented today also include a new analysis of the potential effect of gender on treatment response.

The trial enrolled 413 patients from 25 centres in Japan. Significantly more patients in the aprepitant group achieved no vomiting overall and in the delayed phase than those in the control group. Rates of overall complete response were lower in women compared to men in both the control and aprepitant groups. In women the rates of no nausea and complete protection were significantly higher in the aprepitant group compared to the control group.

“We found that the three-drug combination antiemetic therapy of aprepitant, a 5-HT₃ receptor antagonist and dexamethasone significantly increased the inhibition rate of vomiting and nausea,”
said lead study author Junichi Nishimura, assistant professor at Osaka University in Japan. “The inhibition rate was especially clear in females. This three-drug combination might be a good antiemetic treatment option for oxaliplatin-based chemotherapy in patients with colorectal cancer.”

Standard prophylaxis for the prevention of acute emesis is a 5-HT\textsubscript{3} receptor antagonist plus dexamethasone, and for delayed emesis is corticosteroids. The only previous randomised trial evaluating the addition of an NK1 antagonist to prevent oxaliplatin induced emesis found no benefit.(4)

“Unfortunately the two studies gave different results,” said Roila, who is one of the chairs of the Multinational Association of Supportive Care in Cancer (MASCC) and ESMO Antiemetic Guidelines Committee and director of the Medical Oncology Division, Santa Maria Hospital in Terni, Italy. “My opinion is that because we have contrasting results we need to await new data from other studies before we can conclude whether or not NK1 antagonists can be added to a 5-HT\textsubscript{3} receptor antagonist plus dexamethasone in patients treated with oxaliplatin-based chemotherapy.”

A study evaluating fosaprepitant for the prevention of emesis in moderately emetogenic chemotherapy including oxaliplatin found that it increased complete protection above ondansetron plus dexamethasone alone.(5) Roila said: “We need a subgroup analysis in patients receiving oxaliplatin-based chemotherapy to evaluate the efficacy of fosaprepitant versus placebo when both are combined with a 5-HT\textsubscript{3} antagonist and dexamethasone.”

Commenting on the new gender analysis from the SENRI Trial presented today, Roila said: “Women generally experience more chemotherapy induced emesis than men. The addition of aprepitant induced an increase of overall complete response both in males and in females, from 64\% to 78\% in females and from 81\% to 90\% in males.”

He concluded: “The findings of the SENRI Trial have important implications because they raise the possibility that NK1 antagonists may prevent emesis in patients treated with oxaliplatin-based chemotherapy. Oxaliplatin is a widely used antineoplastic drug both as adjuvant treatment for colorectal cancer and for the metastatic diseases of many cancers of the gastrointestinal tract, the pancreas and the biliary tract.”
A phase III trial of aprepitant in colorectal cancer patients receiving oxaliplatin-based chemotherapy (SENRI Trial)

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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.
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