Evaluation of NK1 antagonists for emesis prevention in oxaliplatin chemo: SENRI trial

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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-HT3 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-HT3 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-HT3 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."

More information: References:

1 Abstract O-0001 'A phase III trial of aprepitant in colorectal cancer patients receiving oxaliplatin-based chemotherapy (SENRI Trial)' will be presented by Junichi Nishimura during Session I: Opening, Selected Abstracts, and Keynote Lecture on Wednesday 1 July, 14:15.

2 Nishimura J, Satoh T, Fukunaga M, Takemoto H, Nakata K, Ide Y, Fukuzaki T, Kudo T, Miyake Y, Yasui M, Morita S, Sakai D, Uemura M, Hata T,Takemasa I, Mizushima T, Ohno Y, Yamamoto H, Sekimoto M, Nezu R, Doki Y, Mori M; Multi-center Clinical Study Group of Osaka, Colorectal Cancer Treatment Group (MCSGO). Combination antiemetic therapy with aprepitant/fosaprepitant in patients with colorectal cancer receiving oxaliplatin-based chemotherapy (SENRI trial): A multicentre, randomised, controlled phase 3 trial. Eur J Cancer.

2015 Jul;51(10):1274-1282. DOI: 10.1016/j.ejca.2015.03.024. Epub 2015 Apr 24.

3 Fosaprepitant is a prodrug of aprepitant.

4 Hesketh PJ, Wright O, Rosati G, Russo M, Levin J, Lane S, Moiseyenko V, Dube P, Kopp M, Makhson A. Single-dose intravenous casopitant in combination with ondansetron and dexamethasone for the prevention of oxaliplatin-induced nausea and vomiting: a multicenter, randomized, double-blind, active-controlled, two arm, parallel group study. Support Care Cancer. 2012 Jul;20(7):1471-1478. DOI: 10.1007/s00520-011-1235-4. Epub 2011 Aug 7.

5 Rapoport BL, Weinstein C, Camacho ES, Khanani SA, Beckford-Brathwaite E, Kevill L, Vallejos W, Liang LW, Noga SJ. A phase III, randomized, double-blind study of single-dose intravenous fosaprepitant in preventing chemotherapy-induced nausea and vomiting associated with moderately emetogenic chemotherapy. J Clin Oncol. 2015;33 (suppl; abstr 9629).