# Comparative study between the clinical effect of palonosetron and granisetron as antiemetic therapy for patients receiving highly emetogenic chemotherapy

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## Abstract

*Background:*
Chemotherapy induced nausea and vomiting (CINV) is considered the main fear for both oncologists and patients. It affects quality of life dramatically, especially the food intake and nutritional status. This can be clearly observed in highly emetogenic chemotherapy (HEC) such as AC protocol in breast cancer patients or cisplatin based regimens in other types of cancer.

*Objectives:*
The aim of this study was to evaluate the antiemetic efficacy of palonosetron (PALO) over granisetron (GRA) in combination dexamethasone for multiple high emetogenic risk (HER) anticancer agents especially in chemotherapy regimens in breast cancer and Cisplatin based regimens.

*Methods:*
All patients received dexamethasone in combination with the 5-HT3 receptor antagonist. Clinical and biochemical characteristics of patients were recorded, and blood samples were drawn to monitor serum substance P and serotonin in correlation with chemotherapy induced nausea and vomiting (CINV). MASCC antiemetic tool in acute phase (0hr-24hr) and delayed phase (24hr-120hr) was used to evaluate patient`s outcomes in both phases after each chemotherapy cycle.

*Results:*
In PALO group, only 5% of patients showed acute nausea and vomiting, whereas 29.3% of patients showed acute vomiting and 74.6% showed acute nausea in GRA group (p<0.0001).
For delayed CINV, 5.8% of patients showed delayed vomiting and 24.5% showed delayed nausea in PALO group, while 69.5 % patients showed delayed emesis and 91.4 % patients showed delayed nausea in GRA group (p<0.0001). Adverse events of both antiemetic drugs (PALO and GRA) were mostly mild to moderate, with quite low rates among the two groups.

*Conclusion:*
Palonosetron in combination with dexamethasone is more effective than granisetron and dexamethasone combination against both acute and delayed emesis induced by highly emetogenic cisplatin-based chemotherapy and highly emetogenic combination of cyclophosphamide and anthracyclines (AC).

## Introduction

Chemotherapeutic and patient characteristics are among the contributing factors, with the specific chemotherapeutic agent and dose administered probably the most significant risk factors for CINV. Agents with the highest emetogenic potential result in emesis during the first 24 h post-chemotherapy (acute CINV) in well over 90% of patients without anti-emetic prophylaxis.

Patient characteristics that increase the risk of CINV include female gender, younger age, previous exposure to chemotherapy, history of alcohol abstention, and presence of nausea and vomiting with prior chemotherapy.

Poor control of acute CINV is an established predictor for delayed CINV that typically peaks in severity between day 2 and day 4 post-chemotherapy, depending on the emetogenic profile of the agent(s) used.

Because 5-HT3 receptors are important neurotransmitters involved in CINV, drugs that inhibit these receptors are commonly used in clinical practice.

Among the various types of available anti-emetic agents, 5-HT3 receptor antagonists have become established as the cornerstone of therapy for prevention of CINV, due to their proven efficacy and low incidence of side effects compared with alternatives. This study is performed to compare the clinical outcome and the efficacy of two 5-HT3 receptor antagonists in preventing and management of CINV. This might be due to unique pharmacokinetic properties of palonosetron as a second generation 5-HT3 receptor antagonists such as prolonged half life and more allosteric binding sites in comparison with granisetron.

## Methodology

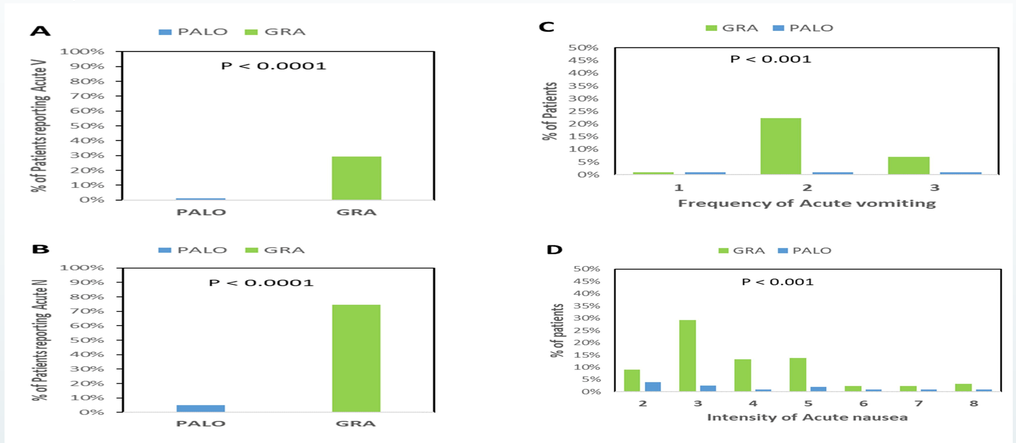
Open-label randomized trial was carried out including 115 patients receiving at least 4 courses of highly emetogenic chemotherapy regimens. All patients received dexamethasone in combination with the seretonin receptor antagonist. Clinical and biochemical characteristics of patients were recorded, and blood samples were drawn to monitor serum substance P (SP) and serotonin ( 5-HT3) in correlation with chemotherapy induced nausea and vomiting (CINV) using commercially available ELISA kits. Besides, (MASCC) antiemetic tool in acute phase (0 hr-24 hrs) and delayed phase (24 hr-120 hrs) was used to evaluate patients` outcomes in both phases after each chemotherapy cycle.

**Table 1. Demographic and clinical characteristics of the two groups of patients receiving either Palonosetron or Granisetron.**

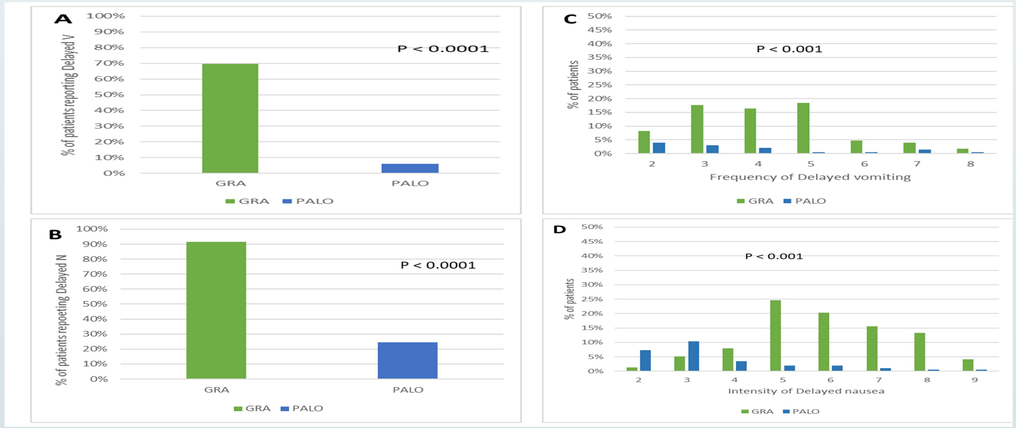
| | Palonosetron group | Granisetron group | P-value |
|---|---|---|---|
| Number of patients | 51 | 64 | |
| Chemotherapy protocols | AC 52.9%<br>CISPLATIN 47.1% | AC 59.3%<br>CISPLATIN 40.6% | |
| Age in years (mean± SD) | 47.49 ± 9.22 | 49.88 ± 8.96 | 0.164 |
| ALT (U/L ) | 32.48 ±13.7 | 33.59 ± 19.05 | 0.7280 |
| Absolute neutrophil count (*10³/uL) | 4.32 ± 2.49 | 4.08 ± 1.72 | 0.551 |
| AST (U/L) | 31.05 ± 13.48 | 31.09 ± 15.09 | 0.988 |
| Haemoglobin ( g/dL ) | 11.52 ± 1.21 | 11.7 ± 1.13 | 0.415 |
| Platelet count (*10³/uL) | 277.36 ± 74.94 | 294.91 ± 81.71 | 0.238 |
| Serum creatinine (mg/dL) | 0.72 ± 0.24 | 0.71 ± 0.2 | 0.84 |
| Total bilirubin (mg/dL) | 0.48 ± 0.35 | 0.46 ± 0.22 | 0.654 |
| Total leucocytes count (*10³/uL) | 7.1 ± 3.4373 | 6.61 ± 1.88 | 0.325 |

## Results

As shown below in **Fig.A and B** for PALO group, only 5% of patients showed acute nausea and vomiting, whereas 29.3% of patients showed acute vomiting and 74.6% showed acute nausea in GRA group (p<0.0001) figures 1 and 2.While in **Fig.C and D** for PALO groups only 5% of patients reported acute nausea and vomiting in different degrees while in GRA group 22% of patients showed acute vomiting and more than 29% reported acute nausea (p<0.0001).




For delayed CINV in **Fig. A and B** 5.8% of patients showed delayed vomiting and 24.5% showed delayed nausea in PALO group, while 69.5 % patients showed delayed emesis and 91.4 % patients showed delayed nausea in GRA group (p<0.0001). When we look at **Fig. C and D** we can find that only 4% of patients in PALO group reported delayed vomiting while 18.4% in GRA group showed the same event , also 10.36% of patients in PALO group showed delayed nausea versus 24.6 % in GRA group (P<0.0001)




## Conclusion

Our study demonstrates palonosetron in combination with dexamethasone is more effective than granisetron and dexamethasone combination against both acute and delayed emesis induced by highly emetogenic cisplatin-based chemotherapy and highly emetogenic combination of cyclophosphamide and anthracyclines (AC).So , we can recommend palonosetron plus dexamethasone as an effective combination in prophylaxis and treatment of CINV in both acute and delayed phase. Beside all previous, these results comply with many clinical trials performed in this approach and also MASCC and ESMO clinical practice guidelines update 2016.

In conclusion, both vomiting and nausea in the first week after chemotherapy remain a significant medical problem and more effort should be made by medical team members especially clinical pharmacy individuals in monitoring of therapy effectiveness and help other health care providers to achieve suitable and reliable care plan.

## References

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