ABSTRACT

Introduction
Ondansetron (OND) became available more than 20 years ago, representing the first 5HT3 receptor antagonist (5HT3 RA) in oncology. Palonosetron (PALO) and aprepitant (AP) for prevention of Chemotherapy-induced Nausea and Vomiting (CINV) were introduced approximately 10 years ago. Along with dexamethasone (Dex), these antiemetics have become standard-of-care. Yet, how well do they work in current oncology care in preventing CINV?

Objectives
Determine CINV incidence in patients receiving antiemetics prior to emetogenic chemotherapy (CT).

Methods
In order to develop Bayesian single nucleotide polymorphism networks predicting strategies to identify at-risk, chemo-naïve patients who, based on new antiemetics are needed to reduce the incidence and impact of this common and troubling side effect of cancer treatment. In particular, new agents

Results
Three hundred fifty-seven patients received combination CT: doxorubicin/cyclophosphamide-based (AC) [N=110], oxaliplatin-based (OX) [N=72], other moderately emetogenic chemotherapy (MEC) [N=175]. Median age was 54 years, 82% female. PALO-based regimens constituted 89% of antiemetics; 28% received 5HT3 RA+Dex+AP. Overall, 62% reported CINV: 36% had moderate to severe nausea, 11% had vomiting. For AC, 71% reported CINV. For 5HT3 RA+Dex+AP, 36% reported moderate to severe nausea; 10% had vomiting. MEC and OX regimens had CINV rates similar to the overall group.

Conclusion
Despite multiple-class antiemetic use, CINV burden remains significant for patients receiving emetogenic CT. Newer agents and strategies to identify at-risk, chemo-naïve patients are needed to reduce the impact of CINV.

BACKGROUND

• Control rates for CINV have improved significantly over the past 2 decades with multimodal antiemetic combinations becoming standard-of-care for patients receiving highly emetogenic chemotherapy (HEC) and moderately emetogenic chemotherapy (MEC). We were interested in the population-based effectiveness of currently available and guideline-based antiemetic prophylaxis, including the use of novel agents such as:
  - Palonosetron, a molecularly differentiated 5HT3 receptor antagonist that binds to the 5HT3 receptor and subsequently causes internalization of the receptor with secondary NK1, signaling effects
  - Aprepitant or the intravenous formulation fosaprepitant, NK1 receptor blockers that when used in combination with a 5HT3 receptor antagonist and dexamethasone improved the control rates of CINV in patients receiving cisplatin-based highly emetogenic chemotherapy regimens and AC-based regimens
  - Except for clinical trials, population-based outcomes for symptom assessment are being routinely captured by a minority of oncology practices in the United States. One such practice that does so, the West Clinic, has been using the PCM©, a validated, patient-reported outcomes assessment instrument, for more than a decade. The PCM affords a glimpse into current patient experiences with symptoms due to chemotherapy, including CINV.

METHODS

• Patients were enrolled if they had a diagnosis of breast, colorectal, non-small cell lung (NSCLC), or ovarian cancer and either received or were scheduled to receive at least 3 cycles of chemotherapy, including:
  - AC-based (AC)
  - Oxaliplatin-based (OX)
  - Cisplatin-based (CIS)
  - Other MEC regimen (MEC)
  - Other low emetogenic chemotherapy or minimal regimens (OTH)
  - Demographics for the AC, OX, and MEC regimen categories are displayed in Table 1

• Antiemetic use is summarized by chemotherapy category (Figure 1)

• PCM was used to evaluate side effects with a 0-10 point scale. CINV severity was determined based on the maximum severity over the first 3 cycles where 0=None, 1-3=Mild, 4-7= Moderate, and 8-10=Severe. The severity rate is summarized by chemotherapy category and antiemetic regimen used (Figure 2)

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• Rate of moderate-to-severe CINV continued to be high even with recommended antiemetic regimens
  - 46% of those receiving 5HT3+Dex+NK1 for AC-based regimens
  - Greater than 30% of those receiving 5HT3+Dex for MEC-based regimens

CONCLUSIONS

• Despite decades of antiemetic advances and the use of multiple drug classes, a significant number of patients undergoing chemotherapy still suffer from moderate-to-severe CINV in today’s oncology practice

• As a result, new antiemetics are needed to reduce the incidence and impact of this common and troubling side effect of cancer treatment. In particular, new agents are needed to manage nausea, which remains a difficult clinical challenge

• New strategies are also needed to identify chemo-naïve patients who, based on their genomic profile, are at particular risk of developing CINV so that action can be taken in advance of therapy. Research in this area of personalized medicine is ongoing

REFERENCES


