# Palonosetron Plus 1-Day Dexamethasone for the Prevention of Nausea and Vomiting Due to Moderately Emetogenic Chemotherapy: Effect of Established Risk Factors on Treatment Outcome in a Phase III Trial

Luigi Celio, MD; Angela Denaro, MD; Francesco Agustoni, MD; and Emilio Bajetta, MD


## ABSTRACT

**Background:** The non-inferiority of palonosetron plus 1-day versus 3-day dexamethasone in preventing chemotherapy-induced nausea and vomiting (CINV) due to moderately emetogenic chemotherapy (MEC) has been previously demonstrated.

**Objective:** The objectives of this prespecified post hoc analysis were to demonstrate the non-inferiority hypothesis in an adjusted model for known risk factors (age, gender, alcohol consumption, and type of MEC [anthracycline plus cyclophosphamide (AC)–based versus other MEC]) for CINV and to explore the impact on antiemetic outcome of these risk factors.

**Methods:** Chemonaive patients (n = 324) with solid tumors were randomized to receive palonosetron 0.25 mg IV plus dexamethasone 8 mg IV on day 1 of chemotherapy or the same regimen followed by oral dexamethasone 8 mg on days 2 and 3. The primary end point was complete response (CR, no emesis and no rescue antiemetics) during the 5-day study period. A modified intention-to-treat approach was used for multivariable analysis.

**Results:** Non-inferiority of the 1-day regimen was confirmed even after adjusting for risk factors (risk difference −4.4%, 95% CI −14.1% to 5.4%; $P = .381$). Only age less than 50 years ($P = .044$) independently predicted a poor outcome of antiemetic treatment. However, most of the younger patients were women (1-day regimen 81.8%, 3-day regimen 88.4%) who underwent AC-based chemotherapy (1-day regimen 61.1%, 3-day regimen 71.0%). There were no significant between-treatment differences in the CR rate according to risk factors.

**Conclusion:** This analysis confirmed that the 1-day regimen provides a valid treatment option for prevention of CINV in delayed, non-AC-based MEC.


Chemotherapy-induced nausea and vomiting (CINV) is associated with the most distressing symptoms experienced by cancer patients.[1] Guiding principles in the management of CINV include not only selecting antiemetic potency to match the emetogenic potential of the chemotherapy regimen but also scheduling antiemetics throughout the full period of risk, which can continue for at least 2–3 days after the last dose of highly or moderately emetogenic chemotherapy (MEC).[2] In spite of the limited knowledge regarding the potential for delayed emesis of many moderately emetogenic agents, corticosteroids such as dexamethasone are recommended by current treatment guidelines as maintenance therapy in the prevention of delayed CINV.[3,4] However, many physicians are reluctant to prescribe multiple-day corticosteroids and prophylactic dexamethasone for delayed emesis after MEC since it can induce moderate to severe adverse effects that may have substantial impact on the quality of life.[5]

Author Affiliations: Department of Medical Oncology, Fondazione IRCCS "Istituto Nazionale Tumori," Milan, Italy.

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A. Denaro's present address is: Centro Sociale Oncologico, Via Della Pietà 19, 34129 Trieste, Italy.

E. Bajetta's present address is: Istituto di Oncologia, Policlinico di Monza, Via Amati 111, 20052 Monza, Italy.

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Corresponding Author: Luigi Celio, MD, Department of Medical Oncology, Fondazione IRCCS "Istituto Nazionale Tumori," Via Venezian 1, 20133 Milan, Italy; telephone: +39 0223902597; fax: +39 0223902149; e-mail: luigi.celio@istitutotumori.mi.it

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Palonosetron (Aloxi®), a second-generation serotonin (5-$HT_3$) receptor antagonist, is now used in routine clinical practice[6] and is the only 5-$HT_3$ receptor antagonist approved by the US Food and Drug Administration for the prevention of acute and delayed nausea and vomiting after MEC. In a randomized, phase III trial involving patients receiving common MEC regimens, it was recently demonstrated that antiemetic prophylaxis including palonosetron plus single-dose dexamethasone provides complete protection against CINV that is non-inferior to that of palonosetron plus dexamethasone for 3 days.[7]

In addition to the type of chemotherapeutic agent, there are numerous patient-related factors that are known to affect the risk of developing CINV. For example, patients under the age of 50 years are at highest risk of CINV, and women are more likely to experience CINV with less effective control despite prophylaxis with antiemetics.[8] Patients with a history of light or no alcohol consumption may also face an increased incidence of nausea and vomiting.[8] The purpose of the present analysis was to use a multivariable model to verify whether the non-inferiority hypothesis of a dexamethasone-sparing regimen can be demonstrated even after adjustment for known risk factors for developing CINV. A secondary objective was to assess the impact of the risk factors studied on antiemetic outcome.

## PATIENTS AND METHODS

### Study Design

This was a post hoc analysis of a randomized, multicenter, phase III trial to test the non-inferiority of a 1-day dexamethasone regimen compared with a 3-day regimen in the prevention of acute and delayed CINV after a broad range of MEC. The study was coordinated by the Italian Trials in Medical Oncology (ITMO) group and approved by the institutional review board of each participating site. All patients gave written informed consent to participate in the study. Detailed descriptions of the design as well as the primary efficacy and tolerability results have been reported elsewhere.[7]

### Study Population

Patients eligible for the study were adults with a confirmed solid tumor and receiving chemotherapy for the first time with intravenous agents classified as moderately emetogenic according to the modified Hesketh chemotherapy classification given as a single dose on study day 1.[9] Additional chemotherapeutic agents of Hesketh emetogenic level ≤2 were also permitted between days 1 and 5 of the study. All patients had an adequate Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2. Regardless of assignment to either study arm, all patients received a single intravenous dose of palonosetron (0.25 mg) as a bolus given 30 minutes before initiation of chemotherapy on day 1. Administration of prophylactic dexamethasone (8 mg intravenously) within 15 minutes before chemotherapy initiation on day 1 was also required. Patients were randomly assigned to one of two delayed antiemetic regimens: no additional dexamethasone (1-day regimen) or dexamethasone (8 mg orally) on days 2 and 3 (3-day regimen). After chemotherapy, rescue medication including dexamethasone and/or metoclopramide for treatment of nausea and vomiting was permitted on an as-needed basis.

### Assessments and Statistical Analysis

Patients made daily entries in their diary for 5 days after chemotherapy initiation to record emetic events in the previous 24 hours, use of rescue medication, and maximum nausea experienced in the previous 24 hours, assessed by a four-point categorical Likert scale (0, none; 1, mild; 2, moderate; 3, severe). The study coordinator (the ITMO group) managed the data and performed the analyses, and investigators had access to the data. The primary efficacy end point was complete response (CR, defined as no emetic episodes and no rescue antiemetics) during the overall 5-day study period.

An analysis of the phase III trial according to established risk factors for CINV was prespecified. The modified intention-to-treat analysis included all patients who received study medication and completed the follow-up period (days 1–5 after chemotherapy initiation) without any major protocol deviation. The post hoc analysis was conducted only on the primary end point of CR rate during the overall 5-day study period. The impact on CR of the 1-day regimen and on a number of known risk factors for CINV, including age (<50 and ≥50 years), gender, and alcohol consumption (never and regularly), was investigated. Since anthracycline plus cyclophosphamide (AC)–based chemotherapy is considered to be more emetogenic than other moderately emetogenic agents, the type of MEC regimen (AC-based and non-AC MEC) as a risk factor was also included in the analysis.[10] Other possible risk factors, including history of motion sickness, significant emesis during a past pregnancy, and extreme anxiety, were not assessed due to the lack of relevant data. Comparisons were also made between treatment groups within each prespecified risk factor for the secondary end point of no nausea in the overall study period.

First-order interactions between antiemetic regimen and risk factors, included one by one into the statistical model, were tested using a generalized linear model implemented with binomial distribution and identity link function (non-canonical link function). The model effects were treatment, risk factor, and the treatment-by-risk factor interaction term. Multivariable analysis was carried out using a generalized linear model with the previously defined parameterization (ie, binomial distribution and identity link function) and with the treatment and all prespecified risk factors as covariates. Results were reported as risk differences (RDs) with associated 95% confidence intervals (CIs) and two-tailed *P* values. The identity link function was adopted to estimate RD instead of the usual odds ratio. RD allowed a straightforward comparison between the unadjusted (univariable) and adjusted (multi-

**Table 1**

Baseline Characteristics by Treatment Group

| VARIABLE | 1-DAY REGIMEN[a] (n = 163), n (%) | 3-DAY REGIMEN[b] (n = 161), n (%) | *P* |
|---|---|---|---|
| Gender | | | .279 |
| Women | 101 (62.0) | 109 (67.7) | |
| Men | 62 (38.0) | 52 (32.3) | |
| Age (years) | | | .954 |
| <50 | 44 (27.0) | 43 (26.7) | |
| ≥50 | 119 (73.0) | 118 (73.3) | |
| Alcohol consumption | | | .838 |
| Never | 98 (60.1) | 95 (59.0) | |
| Regularly[c] | 65 (39.9) | 66 (41.0) | |
| Metastatic disease | 67 (41.1) | 49 (30.4) | .045 |
| Primary tumor | | | .481 |
| Breast | 63 (38.6) | 76 (47.2) | |
| Colorectal | 65 (39.9) | 54 (33.5) | |
| Lung | 15 (9.20) | 13 (8.1) | |
| Other | 20 (12.3) | 18 (11.2) | |
| MEC regimen[d] | | | .698 |
| AC-based[e] | 53 (32.5) | 59 (36.6) | |
| Oxaliplatin-based | 63 (38.6) | 52 (32.3) | |
| Carboplatin-based | 20 (12.3) | 17 (10.6) | |
| Irinotecan-based | 13 (8.0) | 16 (9.9) | |
| Other | 14 (8.6) | 17 (10.6) | |

*P* values calculated by two-sided chi-squared test.

[a] Patients who received palonosetron plus dexamethasone on day 1 before chemotherapy initiation.

[b] Patients who received palonosetron plus dexamethasone on day 1 and continued with dexamethasone on days 2 and 3.

[c] One to two glasses of wine per day.

[d] Moderately emetogenic chemotherapy.

[e] Anthracycline plus cyclophosphamide–based chemotherapy.

**Table 2**

Unadjusted Risk Differences of Achieving Complete Response (No Emesis and No Rescue Antiemetics) in the Overall 5-Day Study Period among 324 Patients

| VARIABLE (COMPARISON) | RISK DIFFERENCE[a] (%) | 95% CI[b] | *P* |
|---|---|---|---|
| Antiemetic prophylaxis (1-day vs 3-day regimen)[c] | −3.3 | (−13.4 to 6.8) | .520 |
| Age (<50 vs ≥50 years) | 16.7 | (4.8–28.5) | .006 |
| Gender (female vs male) | 14.7 | (4.7–24.7) | .004 |
| Alcohol consumption (never vs regularly)[d] | 10.6 | (0.5–20.6) | .039 |
| Type of MEC regimen[e] (AC-based vs non-AC MEC)[f] | 12.8 | (2.0–23.6) | .020 |

[a] Risk difference was obtained through a generalized linear model with treatment and risk factors as covariates. A risk difference larger than 0 indicates a decreased probability of achieving complete response.

[b] 95% confidence interval.

[c] Patients received palonosetron plus dexamethasone on day 1 either with or without dexamethasone on days 2 and 3.

[d] One to two glasses of wine per day.

[e] Moderately emetogenic chemotherapy.

[f] Anthracycline plus cyclophosphamide–based chemotherapy.

variable) two-sided 95% CI of the between-group difference in CR to antiemetic treatment for testing the non-inferiority hypothesis of the 1-day regimen (preset threshold of a −15% difference between groups).[7]

Fisher's exact test was used to compare proportions of the other categorical variables. These secondary analyses were evaluated in an explorative or descriptive manner, and therefore, no adjustment for multiplicity was applied. All *P* values were two-sided, and $P < .05$ was considered statistically significant. All statistical analyses were performed using SAS software (version 9.1; SAS Institute, Cary, NC).

## RESULTS

The total sample consisted of 324 patients with a median age of 57.5 years, about two-thirds of whom were women (Table 1). The proportion of patients with the prespecified risk factors for CINV was balanced between treatment arms. All but one of the patients had an excellent performance status (ECOG score of 0 or 1); 36% had distant metastases, and 35% received AC-based chemotherapy.

Table 2 shows the RD of achieving CR to antiemetic treatment from the unadjusted (univariable) analysis. Consistent with an age younger than 50 years, female gender, no history of alcohol consumption, and AC-based chemotherapy as risk factors for developing CINV, these factors were all significantly associated with a lower probability of achieving CR to antiemetic treatment in the unadjusted analysis ($P = .006$, $P = .004$, $P = .039$, and $P = .020$ for the four comparisons, respectively). The first-order interactions of overall CR between antiemetic treatment and each risk factor were not statistically significant, confirming that the additivity assumption was adequate ($P = .316$ for treatment-by-age, $P = .512$ for treatment-by-gender, $P = .772$ for treatment-by-alcohol consumption, and $P = .672$ for treatment-by-type of MEC regimen). Table 3 shows the RD of achieving CR to antiemetic treatment from an adjusted (multivariable) analysis for the influences of the risk factors studied. Since the lower boundary of the 95% CI of RD with the 3-day regimen was greater than the preset threshold of −15% difference, non-inferiority of the 1-day regimen was demonstrated even after adjustment for the model covariates. In the adjusted model, only younger age ($P = .044$) was significantly associated with poorer outcome in terms of CR to antiemetic treatment. As compared with older patients, those under the age of 50 years had a probability of achieving complete protection against CINV in the overall 5-day study period that was reduced by approximately 13 percentage points. It should be noted that younger patients represented a subgroup at particularly high risk of developing CINV since most were women (1-day regimen 81.8%, 3-day regimen 88.4%) who underwent AC-based chemotherapy (1-day regimen 61.1%, 3-day regimen 71.0%). In addition, two-thirds of younger patients had no history of alcohol consumption (1-day regimen 72.7%, 3-day regimen 76.7%).

**Table 3**

Adjusted Risk Differences of Achieving Complete Response (No Emesis and No Rescue Antiemetics) in the Overall 5-Day Study Period among 324 Patients

| VARIABLE (COMPARISON) | RISK DIFFERENCE[a] (%) | 95% CI[b] | *P* |
|---|---|---|---|
| Antiemetic prophylaxis (1-day vs 3-day regimen)[c] | −4.4 | (−14.1 to 5.4)[g] | .381 |
| Age (<50 vs ≥50 years) | 12.9 | (0.4–25.5) | .044 |
| Gender (female vs male) | 9.1 | (−3.1 to 21.2) | .144 |
| Alcohol consumption (never vs regularly)[d] | 5.9 | (−4.6 to 16.4) | .270 |
| Type of MEC regimen[e] (AC-based vs non-AC MEC)[f] | 4.2 | (−9.5 to 17.9) | .544 |

[a] Risk difference was obtained through a generalized linear model with treatment and risk factors as covariates. A risk difference larger than 0 indicates a decreased probability of achieving complete response.

[b] 95% confidence interval.

[c] Patients received palonosetron plus dexamethasone on day 1 either with or without dexamethasone on days 2 and 3.

[d] One to two glasses of wine per day.

[e] Moderately emetogenic chemotherapy.

[f] Anthracycline plus cyclophosphamide-based chemotherapy.

[g] Non-inferiority hypothesis of the 1-day regimen was proven as the lower boundary of the 95% CI of risk difference was greater than the preset threshold (−15%).

Figure 1 shows the percentages of patients with CR in the overall 5-day study period by risk factor and treatment group. There was no evidence for significant between-treatment differences in CR rate according to age, gender, alcohol consumption, and type of MEC regimen. However, the rate of overall CR irrespective of treatment group was lower among high-risk patients compared with the response rate among low-risk patients, confirming that each of the prespecified prognostic factors acted as a risk factor in this study. The incremental improvement observed with additional dexamethasone doses (ie, the between-treatment difference) was not statistically significant and of only minimal or modest magnitude in all risk groups. The incremental improvement was of greater magnitude in older patients (6 percentage points for older patients vs 0 percentage points for younger patients), in men (9 percentage points for men vs 2 percentage points for women), in patients with history of alcohol consumption (5 percentage points for drinkers vs 2 percentage points for nondrinkers), and in patients receiving non-AC MEC (4 percentage points for non-AC MEC vs 3 percentage points for AC-based chemotherapy).

The rates of patients with no nausea in the overall 5-day study period by risk factor and treatment group are shown in Table 4. There were no significant differences between treatment groups in the rate of no nausea according to each risk factor studied. However, among patients undergoing AC-based chemotherapy, approximately 15% lower nausea control was observed in the overall time period in patients receiving a single dose of dexamethasone on day 1 compared with the group receiving dexamethasone for 3 days ($P$ = .132). It also should be noted that, in the subgroup of younger patients undergoing AC-based chemotherapy, a between-treatment difference was apparent for nausea control in the overall 5-day study period, which was higher in the 3-day regimen group (59.3%, n = 27) than the 1-day regimen group (36.4%, n = 22) ($P$ = .075). For the overall time period, there was no evidence for a significant difference between treatments in the rate of nausea-free patients among older patients undergoing AC-based chemotherapy (38.7% vs 46.9% in the 1-day regimen [n = 31] and 3-day regimen [n = 32] groups, respectively; $P$ = .613).

## DISCUSSION

We have recently demonstrated that in patients treated with a single dose of the long-acting 5-$HT_3$ receptor antagonist palonosetron on day 1, reducing the total dose of dexamethasone is not associated with significant loss of antiemetic control during the 5-day period after single-day MEC.[7] The prespecified post hoc analysis described here yielded two findings of interest: (1) the non-inferiority hypothesis of palonosetron plus 1-day dexamethasone could be confirmed in an adjusted model for the influences of established risk factors for CINV and (2) age younger than 50 years, a strong risk factor, was an independent predictor for poorer outcome in terms of CR to antiemetic treatment.

Although some patients are at higher risk for developing CINV, treatment guidelines do not take into account numerous patient-related factors that can negatively impact response to antiemetic treatment.[11] The finding that the non-inferiority of the dexamethasone-sparing regimen was confirmed even after adjustment for age, gender, alcohol consumption, and type of MEC regimen (AC-based and non-AC MEC) is consistent with the primary analysis of this data set, in which overall CR rates were 67.5% for patients administered dexamethasone only on day 1 and 71.1% for those also administered dexamethasone on days 2 and 3 (between-group difference −3.6%, 95% CI −13.5 to 6.3).[7] Additionally, these results keep the generalizability of the trial findings at a maximum.

In an exploratory analysis of the impact on antiemetic response of age, gender, and alcohol consumption, additional dexamethasone doses led to no or only minimal incremental improvements in the overall CR rate for the high-risk groups. As expected, older age, male gender, and history of alcohol consumption were associated with higher CR rates to antiemetic treatment; but the incremental improvements among low-risk patients taking additional dexamethasone doses were of only modest magnitude. Therefore, despite the fact that the original trial was not designed to address whether or not the 1-day regimen should be pursued according to risk factors for CINV, it seems unlikely that the dexamethasone-sparing regimen may adversely affect the impact on antiemetic response of the patient-related risk factors studied. Based on published data, dexamethasone may potentially add less benefit to the intrinsically more active 5-$HT_3$ receptor antagonist palonosetron.[6]

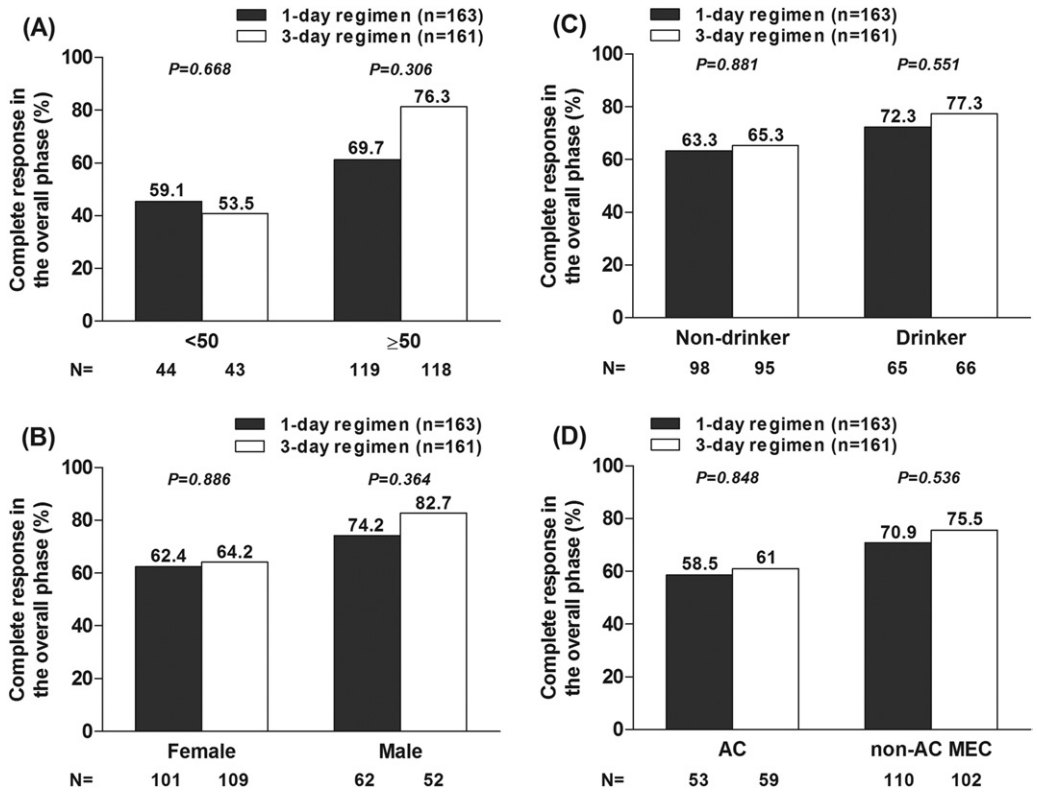


**Figure 1** Percentage of Patients with Complete Response (No Emesis and No Rescue Antiemetics) in the Overall 5-Day Study Period by Treatment Group

Patients were stratified by (A) age, (B) gender, (C) alcohol consumption, and (D) type of MEC regimen. The 1-day regimen consisted of palonosetron plus dexamethasone on day 1 before initiation of chemotherapy; the 3-day regimen consisted of the same regimen on day 1 with dexamethasone administered alone on days 2 and 3. AC = anthracycline plus cyclophosphamide; MEC = moderately emetogenic chemotherapy.

The management of delayed CINV continues to represent a clinical challenge for clinicians caring for cancer patients since few agents have proven efficacy.[12] For the prevention of CINV in patients receiving MEC other than AC-based chemotherapy, current National Comprehensive Cancer Network (NCCN) guidelines recommend a double regimen consisting of a 5-$HT_3$ receptor antagonist plus dexamethasone before chemotherapy, followed by dexamethasone or a 5-$HT_3$ receptor antagonist on subsequent days.[3] The NCCN guidelines also recommend the addition of the neurokinin-1 receptor antagonist aprepitant when the clinician feels that the emetic risk is high enough to warrant more aggressive prophylaxis. Of note, the recently updated MASCC/ESMO (Multinational Association of Supportive Care in Cancer and European Society for Medical Oncology) guidelines recommend antiemetic therapy consisting of palonosetron plus dexamethasone before non-AC MEC, followed by dexamethasone on days 2 and 3.[4] However, in a survey to detect potential corticosteroid-related adverse events, 60 patients receiving oral dexamethasone for prevention of delayed emesis following MEC reported moderate to severe side effects with insomnia (45%), indigestion/epigastric discomfort (27%), agitation (27%), increased appetite (19%), weight gain (16%), and acne (15%) in the week following chemotherapy.[5] Therefore, there is a definite interest in the possibility of reducing dexamethasone in certain clinical situations and/or in subsets of patients.[13]

Herein, we attempted to determine whether the dexamethasone-sparing regimen provided suboptimal control of CINV in patients receiving MEC. Consistent with published data, age younger than 50 years was also an independent predictor for a lower probability of achieving CR to antiemetic treatment in this study.[8] The finding that female gender, no history of alcohol consumption, and AC-based chemotherapy were not significantly associated with CR to antiemetic treatment in an adjusted analysis is likely due to the relatively small sample size. Nevertheless, another plausible explanation is that these risk factors were unimportant predictors in this study because of interaction with age. Most younger patients had additional risk factors for developing CINV because women accounted for the majority of younger patients in each treatment group (1-day regimen 81.8%, 3-day regimen 88.4%) and more than half of the younger women in either group underwent AC-based chemotherapy (1-day regimen 61.1%, 3-day regimen 71.0%). It is now well known that women who receive AC-based chemotherapy are at a particularly high risk of developing CINV, but at the time the trial in the present analysis was planned, the AC-based regimens were considered as MEC.[10] In an exploratory analysis, additional

**Table 4**

Analysis by Risk Factor and Treatment Group of the Rates of Nausea-Free Patients in the Overall 5-Day Study Period among 324 Patients

| | NAUSEA-FREE PATIENTS | | | |
|---|---|---|---|---|
| | 1-DAY REGIMEN,[a] n (%) | 3-DAY REGIMEN,[b] n (%) | RISK DIFFERENCE[c] (95% CI) (%) | *P* |
| Age | | | | |
| <50 years | 22/44 (50) | 20/43 (46.5) | 3.5 (−17.5 to 24.5) | .831 |
| ≥50 years | 63/119 (52.9) | 71/118 (60.2) | −7.2 (−19.8 to 5.1) | .295 |
| Gender | | | | |
| Female | 48/101 (47.5) | 55/109 (50.5) | −2.9 (−16.5 to 10.6) | .681 |
| Male | 37/62 (59.7) | 36/52 (69.2) | −9.5 (−27.2 to 8.1) | .331 |
| Alcohol consumption | | | | |
| Never | 50/98 (51) | 50/95 (52.6) | −1.6 (−15.7 to 12.5) | .886 |
| Regularly[d] | 35/65 (53.8) | 41/66 (62.1) | −8.3 (−25.2 to 8.6) | .379 |
| Type of MEC regimen[e] | | | | |
| AC-based[f] | 20/53 (37.7) | 31/59 (52.5) | −14.8 (−33.3 to 3.7) | .132 |
| Non-AC MEC | 65/110 (59.1) | 60/102 (58.8) | 0.3 (−12.9 to 13.5) | 1.0 |

[a] Patients who received palonosetron plus dexamethasone on day 1 before chemotherapy initiation.
[b] Patients who received palonosetron plus dexamethasone on day 1 and continued with dexamethasone on days 2 and 3.
[c] 1-day minus 3-day regimen with 95% confidence interval obtained using normal approximation of binomial data.
[d] One to two glasses of wine per day.
[e] Moderately emetogenic chemotherapy.
[f] Anthracycline plus cyclophosphamide-based chemotherapy.

dexamethasone doses had only minimal impact on the CR rate in the overall study period for patients receiving AC-based chemotherapy (1-day regimen 58.5%, 3-day regimen 61%). This finding is consistent with the results of a double-blind phase III trial recently reported by Aapro et al,[14] who demonstrated the non-inferiority of palonosetron plus 1-day dexamethasone versus 3-day dexamethasone in the 5-day study period among chemotherapy-naive women receiving AC-based chemotherapy (CR 53.6% vs 53.7% in the 1-day and 3-day regimens, respectively). In spite of this, female patients receiving additional dexamethasone doses experienced less emesis on day 3 than the group receiving a single dose of dexamethasone (97% vs 89%, $P = .004$). We also found that, within the AC subgroup, the 3-day regimen appeared to be significantly more efficacious in the delayed phase in comparison with the 1-day regimen (CR 75% vs 56%).[7] On the basis of both literature data and the baseline characteristics of younger patients in our study, it is reasonable to suggest that the dexamethasone-sparing regimen may represent a suboptimal treatment option especially in younger women who are scheduled to receive a highly emetogenic combination of AC. For the prevention of CINV due to AC-based chemotherapy, guidelines recommend a triple regimen consisting of a 5-$HT_3$ receptor antagonist plus dexamethasone and aprepitant before chemotherapy, followed by aprepitant on days 2 and 3.[3,4] Results from a recent phase II study that included 41 patients (40 female) receiving MEC (including AC-based chemotherapy in 90% of cases) indicated that a single-day regimen of palonosetron, dexamethasone, and aprepitant is feasible and effective for protection against acute and delayed vomiting.[15] In the light of this, a single-day three-drug antiemetic regimen should be formally compared to the standard multiday regimen in female patients for the prevention of CINV following AC-based chemotherapy.

## CONCLUSIONS

In a prespecified post hoc analysis, we confirmed the benefits of palonosetron plus 1-day dexamethasone for the prevention of acute and delayed nausea and vomiting due to single-day MEC even after adjusting for the influences of known risk factors for CINV. Younger age was identified as an independent predictor for decreased efficacy of the dexamethasone-sparing regimen. Since this finding may have been negatively biased because of the high number of younger women undergoing AC-based chemotherapy, further research will be needed to better determine which patient populations treated with non-AC MEC may achieve suboptimal antiemetic coverage due to the dexamethasone-sparing regimen. Our findings support the evidence that palonosetron provides the opportunity to reduce the total dexamethasone dose with no significant loss of antiemetic control in delayed non-AC MEC.

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**Conflict of Interest Disclosures:** All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Celio is a paid consultant for Helsinn. All other authors have no conflicts of interest to report.

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