The effect of guideline-consistent antiemetic therapy on chemotherapy-induced nausea and vomiting (CINV): the Pan European Emesis Registry (PEER)

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Background: While guidelines for preventing chemotherapy-induced nausea and vomiting (CINV) are widely available, clinical uptake of guidelines remains low. Our objective was to evaluate the effect of guideline-consistent CINV prophylaxis (GCCP) on patient outcomes.

Patients and methods: This prospective, observational multicenter study enrolled chemotherapy-naive adults initiating single-day highly or moderately emetogenic chemotherapy (HEC or MEC) for cancer. Patients completed 6-day daily diaries beginning with cycle 1 for up to three chemotherapy cycles. The primary study end point, complete response (no emesis and no use of rescue therapy) during 120 h after cycle 1 chemotherapy, was compared between GCCP and guideline-inconsistent CINV prophylaxis (GICP) cohorts using multivariate logistic regression, adjusting for potential confounding factors.

Results: In cycle 1 (N = 991), use of GCCP was 55 % and 46 % during acute and delayed phases, respectively, and 29 % for the overall study period (acute plus delayed phases). Complete response was recorded by 172/287 (59.9 %) and 357/704 (50.7 %) patients in GCCP and GICP cohorts, respectively (P = 0.008). The adjusted odds ratio for complete response was 1.43 (95 % confidence interval 1.04–1.97; P = 0.027) for patients receiving GCCP versus GICP.

Conclusion: GCCP reduces the incidence of CINV after single-day HEC and MEC.

Key words: antiemetic therapy, chemotherapy, emesis, guidelines, nausea

introduction

Several evidence-based consensus guidelines for preventing chemotherapy-induced nausea and vomiting (CINV) are published and regularly updated [1–3]. However, studies suggest that the clinical uptake of antiemetic guidelines is often suboptimal, and CINV is a persistent problem for patients receiving chemotherapy [4–8]. Patients who experience CINV may be discouraged from completing their chemotherapy regimen; CINV adversely impacts both quality of life and the ability to carry out the activities of daily living [9–11]. Moreover, patients with emesis may require emergency care or hospitalization, adding to the economic burden of cancer care [12, 13].

In the absence of antiemetic therapy, >90 % of patients receiving highly emetogenic chemotherapy (HEC) and 30 %–90 % receiving moderately emetogenic chemotherapy (MEC) experience CINV. The occurrence of CINV is typically biphasic; thus, recommendations for antiemetic therapy are targeted to prevent CINV in the acute phase, occurring in the first 24 h, and the delayed phase, occurring >24 h after chemotherapy [14–16]. Prevention of CINV from the start of chemotherapy is important, both because delayed emesis is correlated with the presence of acute emesis [17] and because patients who experience CINV in one cycle are more likely to develop anticipatory CINV during subsequent chemotherapy cycles [14].

There are a number of observational studies evaluating the effectiveness of different antiemetic regimens and the optimal means of implementing antiemetic guidelines in practice, but the effect of guideline adherence in preventing CINV has not been systematically studied [18–20]. The primary objective of this prospective observational study was to analyze the proportions of patients with complete response (no emesis and no use of rescue therapy) during the first 120 h after cycle 1 chemotherapy.
HEC or MEC among patients receiving guideline-consistent CINV prophylaxis (GCCP) as compared with guideline-inconsistent CINV prophylaxis (GICP). Our hypothesis was that use of GCCP, as compared with GICP, would result in a greater proportion of patients achieving complete response in the 120 h after the initiation of HEC or MEC. Secondary study objectives were to describe the use of CINV prophylaxis for HEC and MEC in European clinical practice and to describe the experience of nausea and vomiting among patients receiving GCCP or GICP for HEC and MEC.

**patients and methods**

**study design**

This prospective observational study was conducted from September 2009 to June 2010 in eight European countries, including Austria, Belgium, France, Italy, Spain, Sweden, The Netherlands, and UK.

**patients**

Male and female outpatients (aged ≥ 18 years) who were chemotherapy naive and scheduled to receive at least two cycles of single-day HEC or MEC were eligible for inclusion in the study. Intended treatment of cancer was with a minimum of any one of the following agents: cisplatin, cyclophosphamide, dacarbazine, oxaliplatin, carboplatin, doxorubicin, epirubicin, irinotecan, oral temozolomide, oral vinorelbine. Patients were excluded from the study if they received chronic systemic corticosteroid therapy, concurrent abdominal or pelvic radiation therapy, or HEC or MEC within 120 h (5 days) after day 1 chemotherapy administration. Other key exclusion criteria were the presence of brain metastases or vomiting in the 24 h before chemotherapy.

**procedures**

The study was approved by the local ethics committee at each site, and patients gave written informed consent. Adult patients initiating HEC or MEC were recruited consecutively at study sites (hospital, community, and private oncology clinics). Patients completed 6-day daily diaries beginning on the day of single-day chemotherapy and for one to three chemotherapy cycles. The study was designed specifically to avoid influencing treatment decisions or inducing any study-specific investigations.

Electronic data capture forms were used to record demographic and clinical data from source documents, including patient diaries, and to complete investigator site questionnaires. Study sites anonymized any clinical data from source documents, including patient diaries, and to prevent identification of individual patients. Definitions of nausea and vomiting were based on the MASCC 2006 guidelines [22].

**outcome assessments**

The primary study end point of complete response was defined as no emesis and no use of rescue therapy to relieve symptoms of nausea or vomiting. No emesis was defined as no vomiting (expulsion of stomach contents through mouth) and no retching (nonproductive attempts to vomit). Distinct emesis episodes were separated by the absence of vomiting and retching for at least 1 min. No nausea was defined as nausea scored as < 5 on the VAS. No CINV was defined as no emesis and no nausea. Rescue medication was defined as any medication taken in addition to prophylactic treatment for control of nausea or vomiting. Secondary

<table>
<thead>
<tr>
<th>Chemotherapy</th>
<th>Acute phase (day 1) GCCP</th>
<th>Delayed phase (days 2–4) GCCP</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEC</td>
<td>Corticosteroid + NK1-RA + 5HT3-RA&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Corticosteroid days 2–4 + NK1-RA days 2–3</td>
</tr>
<tr>
<td>Female AC</td>
<td>Corticosteroid + NK1-RA + 5HT3-RA&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Corticosteroid +/or NK1-RA days 2–3&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>MEC</td>
<td>Corticosteroid + 5HT3-RA&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Corticosteroid +/or 5HT3-RA days 2–3&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>All 5HT3-RA were considered equivalent and interchangeable. Oral and i.v. formulations of corticosteroid, 5HT3-RA, and NK1-RA were considered equivalent and interchangeable.

<sup>b</sup>Palonosetron on day 1 was considered to provide prophylaxis on days 2–3 for MEC.

<sup>c</sup>The study GCCP definition differs from MASCC 2006 guidelines in the delayed phase for female AC and MEC by permitting use of both listed agents (+/or instead of or).

AC, anthracycline plus cyclophosphamide; HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy; NK1-RA, neurokinin-1 receptor antagonist; 5HT3-RA, 5-hydroxytryptamine-3 receptor antagonist.
antiemetic therapy

Antiemetic therapies prescribed for cycle 1 of single-day chemotherapy are summarized in online Supplemental Table S1 (available at Annals of Oncology online) for the acute and delayed phases according to guideline consistency. The use of GCCP varied substantially between acute and delayed phases and among the three categories of chemotherapy emetogenicity (Figure 1). Of the emetic risk categories, HEC represented a higher proportion of GICP than GCCP (23.9 % versus 7.3 % ), while MEC was a higher proportion of GCCP than GICP (46.3 % versus 29.3 % ; see Table 2). Guideline consistency was highest overall (acute and delayed phases) for patients receiving MEC and higher in the acute than the delayed phase for patients who received HEC or MEC. For female AC, guideline consistency was higher in the delayed than the acute phase, in

Table 2. Patient demographic and clinical characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>GCCP (N = 287)</th>
<th>GICP (N = 704)</th>
<th>Overall (N = 991)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>57.1 (11.7)</td>
<td>56.6 (11.2)</td>
<td>56.7 (11.4)</td>
<td>0.542</td>
</tr>
<tr>
<td>Female</td>
<td>225 (78.4)</td>
<td>497 (70.6)</td>
<td>722 (72.9)</td>
<td>0.012</td>
</tr>
<tr>
<td>Primary cancer diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>157 (54.7)</td>
<td>368 (52.3)</td>
<td>525 (53.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Colorectal</td>
<td>47 (16.4)</td>
<td>79 (11.2)</td>
<td>126 (12.7)</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>21 (7.3)</td>
<td>90 (12.8)</td>
<td>111 (11.2)</td>
<td></td>
</tr>
<tr>
<td>Ovarian</td>
<td>20 (7.0)</td>
<td>31 (4.4)</td>
<td>51 (5.1)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>42 (14.6)</td>
<td>136 (19.3)</td>
<td>178 (18.0)</td>
<td></td>
</tr>
<tr>
<td>Metastatic disease</td>
<td>65 (22.6)</td>
<td>228 (32.4)</td>
<td>293 (29.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>History of nausea or vomiting (≥10 drinks per week)</td>
<td>22 (7.8)</td>
<td>83 (12.0)</td>
<td>105 (10.8)</td>
<td>0.056</td>
</tr>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy emetic risk category</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HEC</td>
<td>21 (7.3)</td>
<td>168 (23.9)</td>
<td>189 (19.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Female AC</td>
<td>133 (46.3)</td>
<td>330 (46.9)</td>
<td>463 (46.7)</td>
<td></td>
</tr>
<tr>
<td>MEC</td>
<td>133 (46.3)</td>
<td>206 (29.3)</td>
<td>339 (34.2)</td>
<td></td>
</tr>
<tr>
<td>Pre-chemotherapy diary question responses (0–100 VAS), mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-chemotherapy anxiety</td>
<td></td>
<td></td>
<td></td>
<td>0.037</td>
</tr>
<tr>
<td>Expectation of nausea</td>
<td></td>
<td></td>
<td></td>
<td>0.020</td>
</tr>
</tbody>
</table>

Values represent number (%) of patients unless otherwise noted.

*aChi-square test for categorical values; t test for continuous variables for the comparisons between GCCP and GICP cohorts.

*bMeasured during the 24-h period before start of chemotherapy.

AC, anthracycline plus cyclophosphamide; CINV, chemotherapy-induced nausea and vomiting; GCCP, guideline-consistent CINV prophylaxis; GICP, guideline-inconsistent CINV prophylaxis; HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy; VAS, visual analogue scale for nausea or vomiting.

**Table 2 summarizes demographic and clinical characteristics for patients included in the analyses for cycle 1. Patients ranged in age from 19 to 84 years, with mean age of 57 years in both cohorts. Almost three quarters of patients were women, with a significantly greater proportion of women in the GCCP cohort, and 99 % of patients were white. Breast cancer was the most common diagnosis. Overall, one-fifth of patients received HEC, almost half were women who received anthracycline plus cyclophosphamide (female AC), and the remaining patients (34 % ) received MEC (see Table 2).

**Figure 1. Prevalence of guideline-consistent CINV prophylaxis (GCCP) for cycle 1 single-day chemotherapy, by emetogenicity of chemotherapy and for the total study population. For the overall study period, patient assignment to the GCCP cohort was based on guideline consistency during both acute and delayed phases (0–120 h post-chemotherapy). AC, anthracycline plus cyclophosphamide; HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy.

MEC and higher in the acute than the delayed phase for patients who received HEC or MEC. For female AC, guideline consistency was higher in the delayed than the acute phase, in

results

patients

A total of 1128 eligible patients were enrolled from 52 study sites; of these, 991 (87.9 % ), 888 (78.7 % ), and 769 (68.2 % ) patients received single-day chemotherapy and completed diaries for chemotherapy cycles 1, 2, and 3, respectively. The remaining 137 patients were excluded from study because they did not complete the cycle 1 diary (n = 26), or they received HEC or MEC within 120 h after initiation of cycle 1 chemotherapy (primary end point), as well as other CINV outcomes, including no emesis, no nausea, and no CINV. The models included GCCP/GICP as a binary variable and other relevant demographic and clinical variables. Multivariate Poisson regression was used to compare the count of health care visits due to CINV in cycle 1 between the GCCP and GICP cohorts. Statistical significance was assessed at the two-sided 0.05 level.

The study was planned to have 80 % power to detect a 10-percentage point between-group difference (α = 0.05, two-sided) in complete response with 300 assessable patients in the GCCP cohort and 900 patients in the GICP cohort, assuming a 55 % complete response in the guideline-consistent group and a 45 % complete response in the guideline-inconsistent group.

statistical analyses

Patient characteristics and study end points were summarized using descriptive statistics. Categorical and continuous variables were compared between GCCP and GICP cohorts using Pearson’s χ² test and Student’s t test, respectively. Multivariate logistic regressions were used to compare proportions of patients (GCCP versus GICP) achieving complete response during the study period of 120 h after initiation of cycle 1 chemotherapy (primary end point), as well as other CINV outcomes, including no emesis, no nausea, and no CINV. The models included GCCP/GICP as a binary variable and other relevant demographic and clinical variables. Multivariate Poisson regression was used to compare the count of health care visits due to CINV in cycle 1 between the GCCP and GICP cohorts. Statistical significance was assessed at the two-sided 0.05 level.

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antiemetic agents included any antiemetic other than the three primary classes of antiemetic agents (corticosteroids, neurokinin-1 receptor antagonists [NK1-RAs], and 5-hydroxytryptamine-3 receptor antagonists [5-HT3-RAs]).

objective articles

Original articles

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Figure 1. Prevalence of guideline-consistent CINV prophylaxis (GCCP) for cycle 1 single-day chemotherapy, by emetogenicity of chemotherapy and for the total study population. For the overall study period, patient assignment to the GCCP cohort was based on guideline consistency during both acute and delayed phases (0–120 h post-chemotherapy). AC, anthracycline plus cyclophosphamide; HEC, highly emetogenic chemotherapy; MEC, moderately emetogenic chemotherapy.
part, because we included as GCCP the prescription of corticosteroid and/or (rather than ‘or’) NK1-RA.

The reasons for guideline inconsistency within the GICP group varied across emetogenic risk group (see online supplementalTable S2, available at Annals of Oncology online). For HEC GICP patients, non-prescribing of corticosteroid (delayed phase, range from 16.1 % to 38.7 %) and NK1-RA (acute phase, 51.8 %) were the most common reasons for guideline inconsistency. For female AC and MEC, the primary reasons for guideline inconsistent prescribing were non-prescribing of NK1-RA use (acute phase, 7 %) and corticosteroid and/or 5HT3-RA (delayed phase, 6.3 % to 29.6 %), respectively.

Secondary antiemetic therapies were prescribed to 29 % of patients overall with no significant difference between GCCP and GICP cohorts (31.0 % versus 28.1 %, \( P = 0.364 \); online Supplemental Table S3, available at Annals of Oncology online). Of the secondary antiemetic therapies, benzodiazepines were prescribed significantly more frequently in the GCCP cohort (10.5 % versus 1.0 %, \( P < 0.001 \)) and benzamides, in the GICP cohort (13.2 % versus 24.4 %, \( P < 0.001 \)). The overall use of complementary therapies, most commonly herbal supplements or special foods (e.g. ginger, fennel seeds) to prevent or manage vomiting or nausea, was similar in the two cohorts (16.7 % versus 18.3 %, \( P = 0.55 \)).

### CINV events

The percentage of patients with complete response (no emesis or rescue therapy) was significantly higher in the GCCP cohort than in the GICP cohort during both acute and delayed phases as well as overall (during 120 h post-chemotherapy; Table 3). Moreover, the proportions of patients with other desirable CINV outcomes (no emesis, no nausea, and no CINV) were higher in the GCCP than the GICP cohort in all phases, with the differences either being statistically significant or suggesting a strong trend. For all CINV end point results, the differences between GCCP and GICP cohorts were numerically greater in the acute than the delayed phase (see Table 3).

### Table 3. Chemotherapy-induced nausea and vomiting (CINV) outcomes by guideline consistency (GCCP versus GICP) in cycle 1 overall phase: unadjusted and adjusted results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>GCCP</th>
<th>GICP</th>
<th>( P^a )</th>
<th>Multivariate model(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response</td>
<td>172 (59.9)</td>
<td>357 (50.7)</td>
<td>0.008</td>
<td>1.43 (1.04–1.97)</td>
</tr>
<tr>
<td>No emesis</td>
<td>182 (63.4)</td>
<td>412 (58.5)</td>
<td>0.154</td>
<td>1.18 (0.86–1.63)</td>
</tr>
<tr>
<td>No nausea</td>
<td>138 (48.1)</td>
<td>286 (40.6)</td>
<td>0.031</td>
<td>1.37 (0.99–1.90)</td>
</tr>
<tr>
<td>No CINV</td>
<td>122 (42.5)</td>
<td>242 (34.4)</td>
<td>0.016</td>
<td>1.41 (1.01–1.96)</td>
</tr>
</tbody>
</table>

\( ^a \)Chi-square test.

\( ^b \)Model adjusted for age, sex, pre-chemotherapy nausea, pre-chemotherapy anxiety, expectation of nausea, use of primary antiemetic therapy not recommended by guidelines, underdosing of primary antiemetic therapy, and use of secondary antiemetic agents.

GCCP, guideline-consistent CINV prophylaxis; GICP, guideline-inconsistent CINV prophylaxis.

Patients classified as GCCP had 1.43 times the odds of complete response (95 % confidence interval 1.04–1.97; \( P = 0.027 \)) in the overall study period compared with patients receiving GICP, controlling for confounding factors (see Table 3). Similar statistically significant results were observed for the acute and delayed phases, though differences in CINV between the GCCP and GICP groups were larger for the acute than delayed phase (online supplemental Table S4, available at Annals of Oncology online). The results for CINV end points during cycles 2 and 3 supported cycle 1 results (online supplemental Table S5, available at Annals of Oncology online).

The proportions of patients using health care resources during the 5 days after chemotherapy tended to be lower in the GCCP than the GICP cohort (Table 4). Visits to a general practitioner were the most frequent. Compared with those in the GICP cohort, patients in the GCCP cohort had significantly fewer visits to specialists and the emergency room during the 5-day post-chemotherapy period.

### Discussion

Among chemotherapy-naive patients who received HEC or MEC in this large prospective study, the proportion with complete response (no emesis or rescue therapy) during the first 120 h after cycle 1 was significantly higher among those receiving GCCP than those receiving GICP. Overall, almost 10 % more patients receiving GCCP achieved complete response as compared with GICP. An improvement of 10 % in complete response is considered to be a clinically meaningful difference [21]. The beneficial effect of GCCP in promoting complete response persisted after controlling for confounding factors.

There was a consistent benefit of GCCP across CINV end points, and the results for cycles 2 and 3 were consistent with those for cycle 1. Guideline consistency in the acute phase of cycle 1 was highly significant in reducing CINV, including nausea, in the acute phase: in multivariate analyses, adjusted odds ratios for absence of CINV were significantly higher for the GCCP cohort. The benefits of GCCP tended to be less pronounced in the delayed phase, although the odds ratio for

### Table 4. Health care visits to manage CINV over 5 days after initiation of chemotherapy—cycle 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>GCCP</th>
<th>GICP</th>
<th>Multivariate model(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate ratio (95 % CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP visit</td>
<td>7 (2.4)(^a)</td>
<td>29 (4.1)</td>
<td>0.68 (0.45–1.02)</td>
</tr>
<tr>
<td>Specialist visit</td>
<td>3 (1.1)</td>
<td>11 (1.6)</td>
<td>0.51 (0.34–0.79)</td>
</tr>
<tr>
<td>ER visit</td>
<td>4 (1.4)</td>
<td>12 (1.7)</td>
<td>0.57 (0.38–0.84)</td>
</tr>
<tr>
<td>Hospital days</td>
<td>5 (1.7)</td>
<td>10 (1.4)</td>
<td>1.22 (0.79–1.86)</td>
</tr>
</tbody>
</table>

\( ^a \)Values represent total number of visits (normalized to number of visits per 100 patients).

\( ^b \)P values derived from Poisson regression models, accounting for overdispersion, adjusting for the same set of confounding factors as those applied in the multivariate analyses depicted in Table 3.

CINV, chemotherapy-induced nausea and vomiting; ER, emergency room; GCCP, guideline-consistent CINV prophylaxis; GICP, guideline-inconsistent CINV prophylaxis; GP, general practitioner.
the primary end point, complete response, was significantly greater in the GCCP cohort. These findings parallel published observations that, in routine practice, nausea and delayed symptoms remain the most challenging to manage [11, 23–26].

The use of GCCP was relatively low overall (29 %) and lowest (11 %) for patients in the highest emetogenic risk category, most commonly because of the less than optimal use of NK1-RAs and corticosteroids, particularly out to day 4.

Patients receiving GCCP had significantly fewer specialist and emergency room visits to manage CINV over the 5 days after chemotherapy than those receiving GICP and marginally nonsignificantly fewer general practice visits (P = 0.06). While the absolute numbers of hospital days and clinic and emergency visits due to CINV were not large, the differences between cohorts could have important economic and clinical implications considering the many patients treated with multiple cycles of HEC and MEC regimens on an annual basis throughout Europe.

This large prospective study has enabled us to examine antiemetic prescribing patterns across a range of European countries and oncology centers. The sample size, consisting of nearly 1000 assessable patients treated with MEC or HEC, provides a robust evaluation of the benefits of guideline-consistent prophylaxis of CINV, including the newest antiemetic therapies, aprepitant and palonosetron. As a result, the study results will generalize well to current Western European clinical practice.

A weakness of the study is that the GCCP classification was based on CINV prophylaxis as prescribed for oral agents, rather than on actual use by patients. Therefore, patients who failed to adhere to the prescribed regimen would have been misclassified, likely leading to an underestimation of the differences between GCCP and GICP. Moreover, we cannot rule out the possibility of omissions or errors by patients in the diaries. Other study weaknesses include those common to observational studies, namely, cohort assignment based on physician prescribing rather than randomization, resulting in baseline differences between study cohorts and potential confounding by indication. The use of multivariate logistic regression addresses the latter limitation; however, statistically significant differences could occur due to chance.

Comparisons with previous studies on the prevalence and effect of guideline consistency are complicated by differing guidelines, definitions of consistency, time periods, locations, and patient populations. Adherence to guidelines in earlier single-center studies in the United States and Europe was reportedly better for the acute than the delayed phase [4, 5, 8], consistent with our findings for the total study population. Similarly, earlier studies that evaluated the effect of guideline implementation reported better antiemetic outcomes as guideline adherence increased; these were smaller single-center studies based in the United States before the availability of aprepitant and palonosetron [5, 19, 20].

The emetogenicity of chemotherapy is accepted as the most important risk factor for CINV and is used to guide selection of antiemetic therapy [14]. Our findings provide support for the use of GCCP to reduce the incidence of CINV after cycle 1 HEC, female AC, and MEC. The low prevalence of GCCP in the highest emetogenic risk regimens (11 % for HEC) may reflect economic constraints of hospitals and government payers considering the higher costs of branded-only antiemetic therapies. Nonetheless, this is an area especially needing improvement, and providing appropriate CINV prophylaxis to the subgroups of patients at highest risk of CINV will likely have the greatest impact on improving patient outcomes.

Comprehensive and long-term efforts consisting of efficient education, training, and monitoring of all individuals involved are needed to achieve better adherence to antiemetic guidelines [6, 7]. Key components of successful prior multifaceted strategies to improve guideline adherence include educational outreach visits by opinion leaders [18, 20], the use of standardized antiemetic protocols included in chemotherapy order forms [19], providing feedback to clinicians on the extent and severity of patient CINV outcomes [5], and clinical interventions by pharmacists in the event of inappropriate antiemetic orders [20].

Our study results indicate that there is a significant benefit of guideline-consistent antiemetic therapy across a range of CINV end points in the acute and delayed phases and overall. The incidence of CINV was relatively high, and the prevalence of GCCP relatively low, for the overall study period. Trends favored the GCCP group for lower health care resource use secondary to CINV. The results of this observational study highlight the need to improve the transferability to clinical practice of antiemetic research. Studies are needed to explore the barriers to guideline use for clinicians and to test the effects of different strategies to enhance their use of guidelines. Strategies targeting patients receiving HEC or females receiving AC regimens, where adherence is lower and outcomes poorer are recommended. Education on guideline recommendations for corticosteroids (primarily delayed phase) and NK1-RA (overall phase) within these subgroups is also recommended. Better communication and implementation of antiemetic guidelines must be considered as a means to reduce the burden of CINV.

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MA holds no shares in any drug company or in mutual funds investing exclusively in pharma; he has received study grants, honoraria for consultancy, and/or is on the speaker bureau of Abraxis, Amgen, AstraZeneca, Bayer Schering, Bristol-Myers, Celgene, Cephalon, GSK, Helsinn, Hospira, Johnson and Johnson Ortho Biotech, Merck, MSD, Novartis, Pfizer, Pierre-Fabre, Roche, Sandoz, Schering, sanofi-aventis, Vifor.
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References


Appendix

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Daily skin care habits and the risk of skin eruptions and symptoms in cancer patients

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Background: Cancer patients are at high risk for skin problems because rapidly proliferating skin cells are susceptible to anticancer therapies. However, the effects of daily skin care habits on development of skin problems in cancer patients have rarely been studied.

Patients and methods: We conducted a survey of daily skin care habits and the presence of skin problems in 866 cancer patients.

Results: Hot water bath >1 h significantly increased the risk of definite eruptions [odds ratio (OR) 4.09] and the risk of itching or pain on the skin (OR 1.73). Diligent use of moisturizers did not decrease the risk of definite eruptions and symptoms, and daily bathing, scrubbing off the skin while bathing, and sun protection did not influence the risk of definite eruptions and symptoms. Subgroup analysis of 183 breast cancer patients showed results similar to the total results, including that hot water bath >1 h significantly increased the risk of definite eruptions (OR 3.41).

Conclusions: Being a cross-sectional study, our study could not prove causality. However, at the present stage of knowledge, avoidance of hot water baths of protracted duration should be first emphasized in patient education to prevent skin problems in cancer patients.

Key words: bath, cancer, eruptions, itching, moisturizer, skin care habits

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