Supportive Care in Cancer (2024) 32:45
https://doi.org/10.1007/s00520-023-08222-3

SPECIAL SECTION

2023 updated MASCC/ESMO Consensus recommendations: Prevention of nausea and vomiting following moderately emetic risk antineoplastic agents

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Accepted: 1 December 2023

Abstract

Purpose Review the literature to update the MASCC guidelines from 2015 for controlling nausea and vomiting with systemic cancer treatment of moderate emetic potential.

Methods A systematic literature review was completed using Medline, Embase, and Scopus databases. The literature search was done from June 2015 to January 2023 of the management of antiemetic prophylaxis for anticancer therapy of moderate emetic potential.

Results Of 342 papers identified, 19 were relevant to update recommendations about managing antiemetic prophylaxis for systemic cancer treatment regimens of moderate emetic potential. Important practice changing updates include the use of emetic prophylaxis based on a triple combination of neurokinin $(NK)_1$ receptor antagonist, 5-HT_3 receptor antagonist, and steroids for patients undergoing carboplatin (AUC ≥ 5) and women < 50 years of age receiving oxaliplatin-based treatment. A double combination of 5-HT_3 receptor antagonist and steroids remains the recommended prophylaxis for other MEC. Based on the data in the literature, it is recommended that the administration of steroids should be limited to day 1 in moderately emetogenic chemotherapy regimens, due to the demonstration of non-inferiority between the different regimens.

More data is needed on the emetogenicity of new agents at moderate emetogenic risk. Of particular interest would be antiemetic studies with the agents sacituzumab-govitecan and trastuzumab-deruxtecan. Experience to date with these agents indicate an emetogenic potential comparable to carboplatin > AUC 5. Future studies should systematically include patient-related risk assessment in order to define the risk of emesis with MEC beyond the emetogenicity of the chemotherapy and improve the guidelines for new drugs.

Conclusion This antiemetic MASCC-ESMO guideline update includes new recommendations considering individual risk factors and the optimization of supportive anti-emetic treatments.

Keywords Guidelines · Nausea · Vomiting · Chemotherapy · Low emetogenicity · Minimal emetogenicity

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Published online: 20 December 2023

Introduction

The moderately emetogenic anticancer (MEC) agents are a large heterogeneous group in which patients receiving these treatments have a risk of developing emesis in 30 to 90% of cases. This wide range means that prophylaxis recommendations, based on the literature, need to be adapted to the different situations. For example, patients receiving carboplatin are considered to be at the high end of this group, with a higher risk of emesis than other agents in the same group.

This paper reviews the class of MEC agents that entail a risk of nausea and vomiting for 30 to 90% of patients treated, in the absence of prophylaxis [1].

Since the previous 2015 update of the MASCC-ESMO MEC recommendations [2], new anti-cancer drugs have come onto the market, within eight i.v. MEC and fourteen oral agents identified as high-moderate, making it necessary to include them in the table of recommendations for antiemetic prophylaxis [3]. In addition, several questions that had not been resolved due to a lack of data in the literature at the time of the previous MASCC-ESMO recommendations emerged and required a reassessment of the prophylactic proposals.

The primary research question was "In adults with solid cancers or hematological malignancies receiving MEC, what are the best antiemetic treatment combination strategies?". Secondary questions were considered to refine the primary one. These secondary questions were as follows: (1) Are neurokinin $(NK)_1$ receptor antagonists (RAs) required for MEC prophylaxis? (2) Can steroids be administered on day 1 of chemotherapy only? (3) What is the best recommended prophylaxis for acute (0–24 h after chemotherapy) MEC? (4) What is to be recommended for prophylaxis of delayed (24–120 h) MEC? (5) What is to be recommended for prophylaxis of overall (0–120 h) MEC? (6) Is there a place for olanzapine in MEC prophylaxis? (7) Is there a need for prophylaxis of very long delayed MEC (> 5 days)?

After a discussion, the authors decided to focus on five main specific topics:

- Carboplatin—dose-dependent recommendations
- Oxaliplatin—patient demographic risk factors
- Other MEC antineoplastic agents
- Steroid-sparing regimens
- Olanzapine in MEC

In this systematic review, the recent literature was analyzed in order to update the previous MASCC guidelines of 2016 for controlling nausea and vomiting with systemic cancer treatment of moderate emetic potential [2].

Methods

A systematic literature review from June 1, 2015, through January 31, 2023, was done following the PRISMA guidelines for reporting [4].

The literature search used the Medline, Embase, and Scopus databases. Each database was searched individually using the platform listed in the previous items. We did not search any study registries and did not contact representatives from the manufacturers of antiemetics, corresponding or first authors of included trials. Many experts (including corresponding and/or first authors of included trials) were, however, available as members of the MASCC/ESMO 2023 Antiemetic Guideline Update Consensus Committee.

We did a systematic review based on the list of moderate emetic agents and included new and old agents, in the search strategy from the previous guideline including the new agents identified for this update [2, 5].

An overview of intravenous (classified as moderate) and oral (classified as high/moderate) anticancer agents is given in Table 1.

Search concepts were specific antiemetic agents (aprepitant, fosaprepitant, netupitant, fosnetupitant, rolapitant, ondansetron, granisetron, palonosetron, ramosetron, dexamethasone, methylprednisolone, prednisone, steroid, metoclopramide, domperidone, metopimazine, prochlorperazine, olanzapine, amisulpride) and moderately emetogenic chemotherapy regimens (amivantamab, dinutuximab, fam-trastuzumab deruxtecan, lurbinectedin, sacituzumab govitecan, trabectedin, oxaliplatin, carboplatin, ifosfamide, irinotecan, azacitidine, cytarabine, doxorubicin, epirubicin, daunorubicin, idarubicin, bendamustine, alemtuzumab). The search limited to randomized controlled trials (RCTs), systematic reviews, and meta-analyses. Filters restricted papers to humans and English language publications. It was decided to limit the work to adults 19 + years as pediatrics guidelines update were already performed by the POGO group (Pediatric Oncology Group of Ontario) (https://www.pogo.ca/wp-content/uloads/2023/01/4.3-Antiemetics.pdf).

The keywords used for the strategy of literature review, used the name of the anticancer drug (X) followed by the antiemetics selected by families:

- X AND aprepitant OR netupitant OR rolapitant OR fosaprepitant OR fosnetupitant OR neurokinin antagonist.
- X AND ondansetron OR granisetron OR palonosetron OR ramosetron OR serotonin antagonist.
- X AND dexamethasone or methylprednisolone or prednisolone or steroid.
- X AND metoclopramide OR domperidone OR metopimazine OR prochlorperazine OR olanzapine OR amisulpride OR dopamine antagonist.

Table 1 Emetogenic potential of intravenous (moderate) and oral (high/moderate) antineoplastic agents

Moderate	Alemtuzumab	Idarubicin
	Arsenic trioxide	Ifosfamide
	Azacitidine	Irinotecan
	Bendamustine	Irinotecan peg-liposomal
	Busulfan	Lurbinectedin
	Carboplatin*	Naxitamab
	Clofarabine	Oxaliplatin
	Cyclophosphamide < 1500 mg/m^2	Romidepsin
	Cytarabine > 1000 mg/m^2	Sacituzumab-govitecan**
	Cytarabine/daunorubicin liposomal	Temozolomide[a]
	Daunorubicin	Thiotepa[b]
	Dinutuximab beta	Trabectedin
	Doxorubicin	Trastuzumab-deruxtecan**
	Epirubicin	
High/moderate***	Abemaciclib	Lenvatinib
	Adagrasib	Lomustine
	Avapritinib	Midostaurin
	Bosutinib	Mobocertinib
	Cabozantinib	Niraparib
	Ceritinib	Olaparib
	Crizotinib	Procarbazine
	Cyclophosphamide	Ribociclib
	Enasidenib	Rucaparib
	Fedratinib	Selinexor**
	Hexamethylmelamine	Temozolomide
	Imatinib	Vinorelbine

[a]No direct evidence found for temozolomide IV; as all sources indicate a similar safety profile of oral temozolomide, the classification was based on oral temozolomide

[b]Classification refers to individual evidence from pediatric trials

*Emetic potential appears to be at the high end of the moderate category

**Emetic potential appears to be at the high end of the moderate category, most closely resembling that of carboplatin

***Classified emetic potential of oral agents based upon a full course of therapy and not a single dose within the first cycle

The publications identified were divided into four subgroups to analyze topics related more specifically to serotonin (5-HT)$_3$ receptor antagonists, NK$_1$ receptor antagonists, dopamine receptor antagonists (focusing the multireceptor targeting agent, olanzapine) and steroids. All references were reviewed in duplicate and independently by two members of the assigned working group (chair and co-chair), in order to mitigate the risk of bias and identify the relevant papers for the review. All authors then met and analyzed the content of the publications identified to enable recommendations to be made.

Results

A total of 342 publications were screened. Among these, 41 were identified by the chair and co-chair as relevant for the update (Fig. 1) and divided in the four subgroups:

- MEC AND NK$_1$-RAs, 23 references
- MEC AND steroids, 8 references
- MEC AND olanzapine, 9 references (no other dopamine-receptor antagonist references qualified)
- MEC AND 5-HT$_3$-RAs, 1 reference

After review by all authors, 19 references were judged relevant and finally selected for the guidelines update to enable the answers to the prespecified questions (Fig. 1).

Recommendations herein were reviewed by all 34 members of the Guideline Update Committee and approved with minor changes.

Data are very limited as concerns prophylaxis of nausea and vomiting in patients treated with oral agents and consequently no precise recommendations can be given. In general, only on demand antiemetics are recommended.

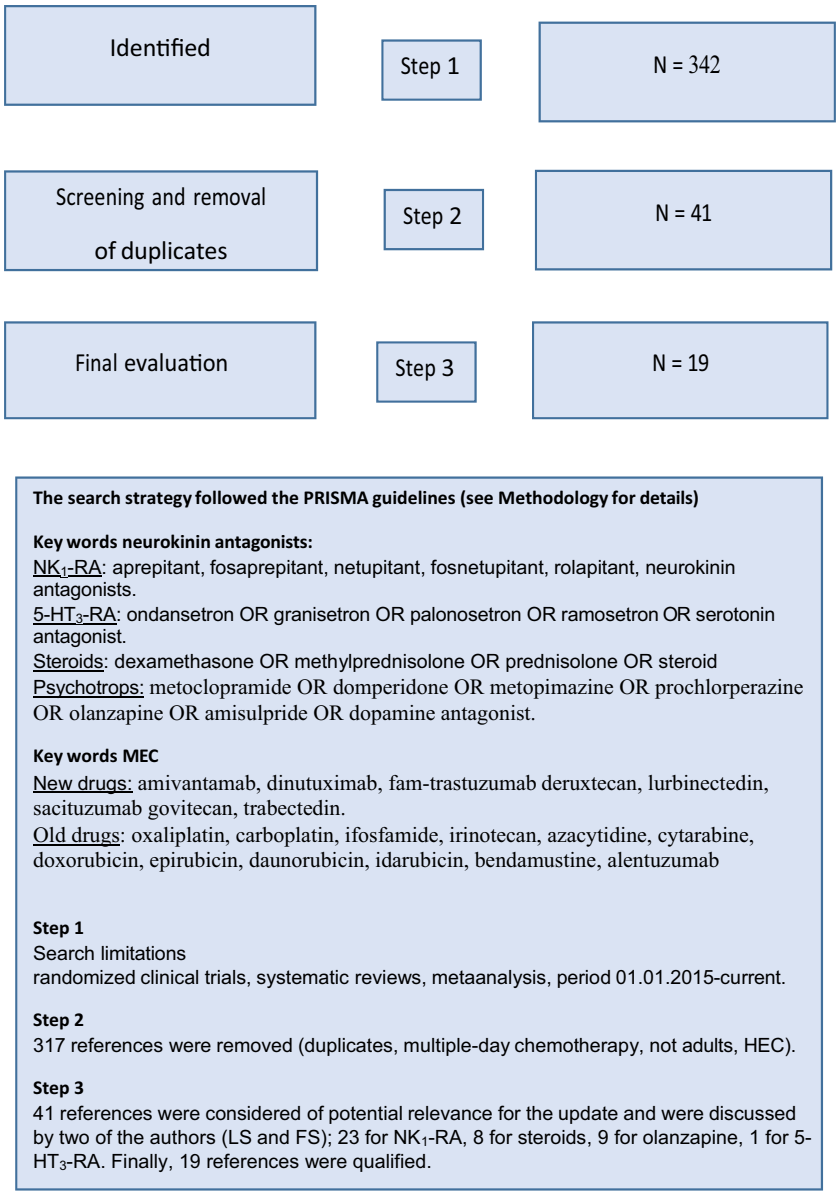

Fig. 1 PRISMA flow diagram

Carboplatin—dose-dependent recommendations

Antiemetic regimens were specifically assessed in two double-blinded RCT and two meta-analyses. A sub-group analysis of a large RCT (1349 HEC and MEC patients) assessed the efficacy of an NK_1-RA versus placebo in association with dexamethasone (DEX) 20 mg orally D1 and a 5-HT_3-RA (oral granisetron 2 mg administered once daily on days 1–3), in patients receiving carboplatin) [6]. Of the 1332 patients who composed the intent-to-treat population, 401 received a first course of chemotherapy with a carboplatin-based regimen and were randomized in the NK_1-RA cohort ($n=192$) or the placebo cohort ($n=209$). In patients of this cohort, the triplet regimen NK_1-RA significantly improved complete response (CP) rates from 64.6 to 80.2% in the overall phase ($P<0.001$) and 82.3% vs 65.6% ($P<0.001$) in the delayed phase. No significant difference was seen in the acute phase.

A total of 324 patients were evaluated in a multicenter, placebo-controlled, double-blind, randomized study studying the addition of aprepitant to the antiemetic regimen in patients receiving a carboplatin-paclitaxel combination regimen for a gynecologic cancer [7]. All the patients received DEX 20 mg i.v. day 1 and a 5-HT_3-RA (granisetron 1 mg or ondansetron 4 mg) orally day 1. The primary endpoint assessed hypersensitivity reaction (HSR) to paclitaxel, but secondary endpoints analyzed antiemetic efficacy (complete response, no vomiting and no nausea). Antiemetic efficacy as documented by the complete response rate was significantly higher in the group with aprepitant compared to the placebo group (61.6% versus 47.3%, $p=0.0073$).

Sixteen trials (3848 patients) were identified in a systematic review with the intent to assess the use of NK_1-RA in MEC non-AC regimen in which nine studies (1790 patients) received a carboplatin regimen [8]. The OR for achieving an overall CR was 1.96 (95% CI 1.57–2.45; $p < 0.00001$) in favor of the NK_1-RA containing regimen.

A meta-analysis reviewed ten trials (2928 patients) for the efficacy of a triple regimen containing an NK_1-RA versus a double regimen (DEX + a 5-HT_3-RA) in patients receiving MEC. For the 1668 carboplatin-based chemotherapy patients, the triple regimen with an NK_1-RA showed significant better CR (RR, 1.22; 95% CI, 1.14–1.32; $p < 0.001$) in the overall phase compared with the DEX + 5-HT_3-RA regimen [9].

All of these data presented in the study used a standard dose of every 3-week carboplatin with a dosage clearly identified as AUC ≥ 5. No data were available in our systematic review for patients receiving a lower carboplatin dose (AUC < 5).

On the basis of the consistent findings presented above, it is recommended to use a three-drug regimen including single doses of a 5-HT_3-RA, DEX, and an NK_1-RA (aprepitant, fosaprepitant, fosnetupitant, netupitant, or rolapitant), given before chemotherapy for patients receiving carboplatin AUC ≥ 5.

There is no data to recommend the use of an NK_1-RA for carboplatin AUC < 5 (I, A).

Oxaliplatin—patient demographic risk factors

Four hundred thirteen patients, enrolled in the SENRI trial, received an oxaliplatin-based regimen for colorectal cancer (neoadjuvant, adjuvant or recurrent-metastatic disease) and were randomized to antiemetic prophylaxis with a triple drug regimen including an NK_1-RA or a double drug regimen (DEX + a 5-HT_3-RA) [10]. Patients randomized to aprepitant/fosaprepitant also received i.v. DEX 6 mg on day 1 and oral DEX 2 mg twice daily on days 2 and 3. Patients in the control group received a 5-HT_3-RA and DEX 9.9 mg i.v. day 1 followed by oral DEX (4 mg) twice daily on days 2 and 3. There was no difference in the characteristics of patients by age (> or < 60) or gender (male or female) between the two groups. The aprepitant group had significantly higher rates of complete response overall (85.0% versus 74.3%; $p = 0.01$).

An unplanned analysis identified risk factors for emesis and the differences in efficacy between antiemetic regimens in the previous study [11]. In women, the rate of no nausea, no vomiting, and total control (no nausea, no emesis, no rescue medication) was higher in the aprepitant group than in the control group. The benefit of triple antiemetic therapy was higher in the female cohort compared to males. The complete response rate increased from 65.3 to 78.1% in women receiving aprepitant, compared with 80.2 to 89.5% in men.

A total of 248 women were enrolled in a RCT to assess the prophylactic efficacy of a triple drug combination (NK_1-RA + 5-HT_3-RA and DEX) in young women (age ≤ 50 years) [12]. Patients receiving FOLFOX or FOLFIRI for a gastrointestinal cancer were randomized in the ratio 1:1 to intervention or control. Patients in the control group received placebo (day 1 through day 3), palonosetron 0.25 mg i.v., and DEX 12 mg orally 30 min before initiation of chemotherapy, while patients in the intervention group received aprepitant (125 mg orally on day 1 and 80 mg orally each morning of days 2 and 3) and palonosetron, 0.25 mg i.v. with DEX 6 mg orally on day 1. The primary efficacy endpoint was reached in the modified intention-to-treat population, with a CR rate of 87.0% in the NK_1-RA group compared to 66.7% in the placebo group in the overall phase ($P < 0.001$). Results were also significantly superior in the acute and delayed phases. A subgroup analysis of patients in the oxaliplatin-based FOLFOX regimen, demonstrated a CR rate in the overall phase significantly higher in the NK_1-RA vs placebo group (89.8% versus 66.3%; $P < 0.001$). The results were not statistically significant in the irinotecan-based FOLFIRI regimen group.

Based on the above studies, a two-drug regimen including single doses of a 5-HT_3-RA and DEX, given before chemotherapy is recommended for patients receiving oxaliplatin.

Addition of an NK_1-RA (aprepitant, fosaprepitant, netupitant, fosnetupitant, or rolapitant) is suggested for oxaliplatin CINV prophylaxis in women aged < 50 years old.

There is no evidence that an NK_1-RA should be routinely used as first line in women > 50 years old (III, B).

It should be noted that the European Medicines Agency has withdrawn marketing authorization for rolapitant. It remains available in the USA as an oral agent.

Other MEC antineoplastic agents

In the 21 selected RCT, meta-analysis, or systematic review publications, none revealed significant data to change the previous recommendation for other MEC antineoplastic agents than carboplatin- and oxaliplatin-based regimens.

No data were available on new anticancer drugs. New treatments considered as MEC should then receive the same prophylaxis as other MEC. Exceptions may be the new agents sacituzumab-govitecan and trastuzumab-deruxtecan which appear to have an emetogenic potential comparable to carboplatin, at the high end of the moderate category. While prospective studies are needed it is suggested to prevent emesis as for carboplatin AUC ≥ 5.

However, in the absence of clinical trials evaluating antiemetic approaches for these agents, definitive antiemetic prophylaxis recommendations cannot be made at this time.

A two-drug regimen including single doses of a 5-HT_3-RA and DEX, given before chemotherapy, is recommended for patients receiving other MEC (II, C).

Steroid-sparing regimens

In a randomized controlled open label study, 320 chemotherapy-naïve patients receiving a first-line regimen of mFOLFOX6 (oxaliplatin, leucovorin, and 5-fluorouracil) were randomized in a 1:1 ratio to aprepitant 125 mg orally on day 1, 80 mg daily on days 2–3 or to DEX 10 mg i.v. on day 1, followed by 5 mg daily on days 2 and 3. Both groups in addition received palonosetron 0.25 mg i.v. on day 1 [13]. The overall (0–120 h) complete response rate was superior in the aprepitant (+palonosetron) arm compared to the DEX (+palonosetron) arm (88.8% versus 74.2%, $p=0.0010$) and also in the delayed (25–120 h) phase (90.6% versus 75.5%, $p<0.0001$). No significant difference was found in the acute phase.

A large meta-analysis including 4534 patients (17 trials) compared the antiemetic efficacy of 3 days of DEX combined with an NK_1-RA (3-DEX + NK_1-RA) to 1 day of DEX also combined with an NK_1RA (1-DEX + NK_1-RA). Complete response rate in the delayed phase was used as the primary endpoint [14]. There was no significant difference between the two cohorts with an absolute risk difference of 9% (95% CI, − 2.3 to 21.1).

Another large systematic review including 1194 patients (5 RCT) assessed the complete response rate in the overall phase (day 1 through 5) in chemotherapy-naïve adult patients undergoing either MEC or an anthracycline plus cyclophosphamide (AC)–containing regimen [15]. The non-inferiority margin was set at − 8.0%. The non-inferiority of the DEX-sparing regimen (1 day versus 3 days) was demonstrated with a risk difference between the two cohorts at − 1.5% (95% CI, − 7.1% to 4.0%). No significant difference was highlighted between the different chemotherapy regimens (AC vs MEC).

In a randomized, controlled phase III, open label study, non-inferiority was assessed between two regimens of DEX prophylaxis; DEX day 1 only versus DEX day 1 through day 3 [16]. Each of the 305 patients enrolled in the trial received palonosetron (0.75 mg, i.v.) and DEX (9.9 mg i.v.) prior to MEC. Patients in the 3-day DEX regimen received DEX 8 mg (i.v. or p.o.) on days 2–3. The primary endpoint was the overall complete response rate (0–120 h), and the non-inferiority margin was set at − 15%. Non-inferiority was reached with a 2.5% difference (95% confidence interval (CI): − 7.8–12.8%; $p=0.0004$).

Two phase II, randomized, controlled trials (including 82 and 109 patients, respectively) investigated a DEX-sparing regimen in patients receiving carboplatin (AUC5 or AUC6). In the AUC5 carboplatin regimen study [17], all patients received DEX 20 mg i.v. on day 1 associated with palonosetron 0.75 mg i.v. Patients in the non-sparing group received oral DEX 8 mg daily, days 2 and 3. The primary endpoint (CR in the delayed phase) was not statistically significantly different between the two groups (3-day group, 76.9% [30/39]; 1-day group 69.8% [30/43]; $p=0.4652$).

In the AUC6 carboplatin regimen study [18], patients were treated for a gynecologic cancer with a standard paclitaxel-carboplatin (PC) regimen or a dose dense regimen PC regimen. All patients received palonosetron at 0.75 mg i.v. day 1 and were randomized to additional antiemetic therapy with 1 day of DEX versus 3 days of DEX. Complete response in the overall phase (0–120 h) was the primary end-point. CR was observed in 67.9% (95% CI, 53.7–80.1) of patients in the 3-day DEX arm, and 60.7% (95% CI, 46.8–73.5) of patients in the 1-day DEX arm.

Based on these trials, it is recommended that no steroid (or other antiemetic) should be routinely administered after day 1 MEC administration (II, B).

No steroid (or other antiemetic) should be routinely administered after day 1 carboplatin administration (II, B).

No steroid (or other antiemetic) should be routinely administered after day 1 oxaliplatin administration (II, B).

Olanzapine in MEC

A single study was reviewed out of nine screened in order to define the place of olanzapine (OLZ) in MEC antiemetic prophylaxis [19].

In this randomized open-label study, 81 patients received palonosetron, DEX, and OLZ before start of chemotherapy and were randomized to either OLZ 10 mg as a single oral dose days 2–3 or OLZ 10 mg + DEX 4 mg days 2–3 or DEX 8 mg daily days 2–3 for delayed emesis protection. The primary endpoint was total control (no vomiting, no rescue treatment + no nausea) on days 2–5. No significant difference was found between the three cohorts.

There is no evidence supporting the use of OLZ as primary prophylaxis following MEC (II, C).

A summary of the recommendations for MEC are presented in Table 2.

Discussion

The major changes introduced in this guideline update are to consider triple association of an NK_1-RA combined with a 5-HT_3-RA and DEX on day 1 for patients receiving a carboplatin-based regimen and for females below 50 years of age, receiving an oxaliplatin-based regimen.

The evidence to use this triple antiemetic regimen was clearly demonstrated for patients receiving carboplatin at a dose AUC > 5 with a classic 3-week schedule. No data were available in our systematic review to recommend the use of a triple regimen in patients receiving lower doses of carboplatin.

Table 2 2023 updated MASCC-ESMO recommendations moderate emetic risk chemotherapy

Question	Recommendation	Level of evidence	Grade of recommendation
Carboplatin—dose dependent	A three-drug regimen including single doses of a 5-HT_3-RA, DEX, and NK_1-RA (aprepitant, fosaprepitant, fosnetupitant, netupitant, or rolapitant), given before chemotherapy, is recommended for patients receiving carboplatin AUC ≥ 5 There is no data to support using an NK_1-RA for carboplatin AUC < 5	I	A
Oxaliplatin—risk factor dependent	A two-drug regimen including single doses of a 5-HT_3-RA, and DEX, given before chemotherapy, is recommended for patients receiving oxaliplatin Addition of an NK_1-RA (aprepitant, fosaprepitant, netupitant, fosnetupitant, or rolapitant) is suggested for oxaliplatin CINV prophylaxis in women age < 50 years old There is no evidence that an NK_1-RA should be routinely used as first line in women > 50 years old	III	B
Other MEC*	A two-drug regimen including single doses of a 5-HT_3-RA and DEX, given before chemotherapy, is recommended	II	C
Steroid-sparing regimens	No steroid (or other antiemetic) should be routinely administered after day 1 MEC administration	II	B
Olanzapine	There is no evidence to use OLZ as primary prophylaxis in the MEC population	II	C

*The emetic potential of sacituzumab-govitecan and trastuzumab-deruxtecan appears to be at the high end of the moderate category, most closely resembling that of carboplatin. While prospective studies are needed it is suggested to prevent emesis as for carboplatin AUC > 5

Several randomized controlled trials evaluated adding an NK_1-RA in patients receiving oxaliplatin. A triple antiemetic prophylaxis demonstrates a significant impact in young women without superior efficacy in other situations (male and older female).

The 2022 NCCN guidelines proposes three different options including the triple association of 5-HT_3-RA + DEX + NK_1-RA [20]. The ASCO guidelines for adults treated with moderate-emetic-risk antineoplastic agents (excluding carboplatin AUC ≥ 4 mg/mL/min, but including oxaliplatin) recommend a 2-drug combination of a 5-HT_3-RA and DEX. In oxaliplatin-based regimens, ASCO recommends that a steroid should be offered for two additional days [21].

The Takemoto et al. [11] and Wang et al. [12] studies specifically evaluated the impact related to risk factors and in a young women specific cohort with benefit favoring the NK_1-RA addition in younger women treated with oxaliplatin.

Lack of evidence excluded any recommendation for adding an NK_1-RA outside of the defined younger women population, but this MASCC-ESMO guidelines' update is practice changing with the upgrading of prophylaxis in women < 50 years of age.

Further trials are needed to investigate if other populations treated with an oxaliplatin-based regimens or other MEC including new drugs such as antibody drug conjugates (e.g., sacituzumab-govitecan or trastuzumab-deruxtecan defined as MEC agents) could benefit form addition of an NK_1-RA.

The question of sparing steroids after day 1 administration is heavily debated, due to the adverse events of multiple-day steroids, but we only discovered a poor level of rigorous clinical trials limiting the ability to adopt a strong statement.

In one phase III RCT and one phase II RCT, non-inferiority was tested and significantly reached between two regimens of DEX prophylaxis: DEX day 1 only versus DEX day 1 to day 3 [16, 17]. These results were confirmed in the Okada et al. systematic review [15]. These studies led to our recommendation for sparing steroids after day 1.

The place of olanzapine in MEC could not be defined because of a paucity of data addressing its use in this setting.

These findings (or missing data) are a reminder of the need to carry out further research in order to develop future recommendations, particularly with regard to other patient populations or other anti-cancer drugs. Reassessment before each course of treatment and vigilance with regard to the individual risk factors of each patient are essential if these recommendations are to be applied as effectively as possible, and to avoid any emetic events during the course of treatment for patients undergoing treatment for cancer [21, 22].

Conclusions

These antiemetic guidelines for moderately emetogenic chemotherapy, based on a systematic review of the current literature, have undergone some important changes, particularly with regard to the use of emetic prophylaxis based on a triple combination of NK_1-RA, 5-HT_3-RA and DEX for patients undergoing carboplatin (AUC ≥ 5)

and women < 50 years of age receiving oxaliplatin-based treatment. A double combination of a 5-HT_3-RA and steroids remains the recommended prophylaxis for other MEC. Based on the data in the literature, it has been recommended that steroids be spared after day 1, in MEC regimens, due to the demonstration of non-inferiority in antiemesis control for single-day steroids compared to multi-day regimens.

More data are needed on the emetogenicity of new agents of moderate emetogenic risk. Of particular interest would be antiemetic studies with the agents sacituzumab-govitecan and trastuzumab- deruxtecan. Experience to date with these agents indicate an emetogenic potential comparable to carboplatin in a dose of AUC > 5. Future studies should systematically include patient-related risk assessment in order to define the risk of emesis with MEC beyond the emetogenicity of the chemotherapy and improve the guidelines for new drugs.

Author contribution FS and LS did the literature search. All authors reviewed the selected publications. The initial draft was written by FS, and all authors revised it critically for its intellectual content.

All authors reached agreement on the recommendations, are accountable for the accuracy and integrity of the work, and have approved the final version of the manuscript.

Declarations

Conflict of interest Florian Scotté declares he has received honoraria from Sanofi, Sandoz, Roche, MSD, Prostrakan, Leo Pharma, Janssen, AMGEN, Pierre Fabre Oncologie, Vifor Pharma, Arrow, Pfizer, BMS, Bayer, Thermo Fisher, Pharmanovia, Gilead, Viatris, and Helsinn.
Lee Schwartzberg declares he has received honoraria from Helsinn, GlaxoSmithKline, and Pfizer.
Hirotoshi Iihara declares that he has received personal fees from Taiho, Chugai, Yakult, Astellas, Eli Lilly, Daiichi Sankyo, AstraZeneca, Nippon Kayaku, Ono, and Nippon Boehringer Ingelheim and consulting fees for their institution from Taiho and Eisai outside the submitted work.
Matti Aapro declares the following interests relevant to this manuscript: has received honoraria from Berlin-Chemie, Fosun, Helsinn Healthcare SA, Juniper Biologics, Knight Therapeutics, Mundipharma International Limited, and Vifor Pharma.
Richard Gralla declares the following interests relevant to this manuscript: has received honoraria from Fosun, Helsinn Healthcare SA, Juniper Biologics, Knight Therapeutics, Mundipharma International Limited, and Vifor Pharma.
Paul J Hesketh declares that he has no financial interests.
Karin Jordan reports personal fees as an invited speaker from Amgen, Art Tempi, Helsinn Healthcare SA, Hexal, Med Update GmbH, MSD, Mundipharma, Onkowissen, Esteve, Roche, Shire (Takeda), and Vifor; personal fees for advisory board membership from Amgen, AstraZeneca, BD Solutions, Hexal, Karyopharm, and Voluntis; and personal fees as author for UpToDate.
Ronald Chow declares that he has no financial interests.
Jørn Herrstedt declares he has received honoraria from Pharmathen S.A.
The other authors have no relevant financial or non-financial interests to declare.

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