Current Problems in Cancer 43 (2019) 344–353

Contents lists available at ScienceDirect

Current Problems in Cancer

journal homepage: www.elsevier.com/locate/cpcancer

The compliance with antiemetic guidelines of Turkish medical oncologists. A survey study of Turkish Oncology Group

Murat Araz[a,*], Mustafa Karaagac[b], Levent Korkmaz[b], Ismail Beypinar[a], Mukremin Uysal[a]

[a] *Department of Medical Oncology, Afyon Kocatepe University Faculty of Medicine, Afyon, Turkey*
[b] *Department of Medical Oncology, Necmettin Erbakan University Meram Faculty of Medicine, Konya, Turkey*

ABSTRACT

Purpose: We aimed to investigate the compliance of Turkish Medical Oncologists to antiemetic guidelines for treatment of acute and delayed chemotherapy-induced nausea and vomiting (CINV) in patients receiving high (HEC), moderate (MEC), and low (LEC) emetogenic chemotherapy.
Method: A covering electronic mail letter with an online questionnaire link was sent to e-mail and mobile application groups including all 599 members of the Turkish Society of Medical Oncology in January 2018. The online survey has consisted of twelve questions.
Results: Questionnaire form was responded by 146 of Turkish Medical Oncologists. The most of the participants were following up more than one antiemetic guideline (53%). While compliance with the antiemetic guidelines was higher in acute CINV prophylaxis for HEC and MEC, it was significantly lower in the delayed CINV treatment of HEC and LEC. The highest and lowest compliance rate was found in the prophylaxis of acute and delayed CINV of HEC (92% and 15%, respectively). The incidence of noncompliance for delayed CINV in HEC was statistically significantly higher in those who worked for $\leq$ five years in an oncology department, under 39 years of age, and non-academicians ($p = 0.004$, $p = 0.042$, $p = 0.005$, respectively).
Conclusions: Noncompliance with the antiemetic guidelines is continue to be a big problem in Turkish Medical Oncologists. The use of standardized antiemetic protocols in chemotherapy order forms or a computerized decision-support system is now seen as a better tool to enhance compliance with the guidelines.

Abbreviations: HEC, high emetogenic chemotherapy; MEC, moderate emetogenic chemotherapy; LEC, low emetogenic chemotherapy; CINV, chemotherapy induced nause and vomiting; 5HT3RA, 5-hydroxytryptamine type 3 receptors antagonist.

* Correspondence to: Afyon Kocatepe University Faculty of Medicine, Department of Medical Oncology, Afyon - Turkey.
E-mail address: zaratarum@yahoo.com (M. Araz).

https://doi.org/10.1016/j.currproblcancer.2018.09.002
0147-0272/

A R T I C L E I N F O

Keywords: Antiemetic guidelines; Chemotherapy-induced nausea and vomiting; Compliance; Oncologist

Introduction

Chemotherapy-induced nausea and vomiting (CINV) remain an important side effect that has a negative impact on quality of life.[1] Also, CINV escalates the cost of cancer therapy and can pose an economic burden via increasing apply to emergency services and unexpected hospitalizations. Furthermore, unpleasant experiences with the treatment may cause refusal of potentially curative treatment.[2]

Guidelines allow clinicians to quickly access existing evidence-based recommendations, including international expert consensus panels.[3] Many doctors believe that the use of guidelines is a good educational tool and contributes to improving the quality of patient care and improving clinical outcomes despite some limitations.[4] In last decade, consensus guidelines for antiemetic therapy have been published and regularly updated in the Europe (European Society of Medical Oncology [ESMO]/Multinational Association of Supportive Care in Cancer [MASCC]) and in the United States of America (USA) (American Society of Clinical Oncology [ASCO] and National Comprehensive Cancer Network [NCCN]). The recommendations of the ESMO/MASCC, ASCO, and NCCN antiemetic guidelines are often similar, although with some minor differences.[3]

The results of the Pan European Emesis Registry (PEER)[5] and INSPIRE[6] studies have shown that compliance with antiemetic guidelines reduces the incidence of CINV. Noncompliance with antiemetic guidelines seems to lead to inadequate (undertreatment) or excessive (overtreatment) use of antiemetic drugs for acute or delayed CINV, both of which result in increased financial burden.[4-6] Nonetheless, antiemetic guidelines are generally not followed, and 30%-50% of cancer patients do not receive the appropriate antiemetic prophylaxis.[7] Besides, the results of previous studies indicate that it is more difficult than expected to improve compliance with the guidelines.[8]

There is lack of studies which show the compatibility of Turkish oncologists with antiemetic guidelines in the literature. For the first time, we have set up this study to investigate the compliance of Turkish medical oncologists to antiemetic guidelines for acute and delayed CINV in patients receiving high, moderate, and low emetogenic chemotherapy.

Material and methods

Participants

In January 2018, an electronic questionnaire was sent to e-mail, WhatsApp, and telegram groups covering 599 members of Turkish Medical Oncology Association. The electronic questionnaire link was sent a total of 3 times for a month, at most once a week. Participation in this survey was voluntary. No promotions or gifts were given to increase participation in the survey.

Survey

The questionnaire was established via Google Forms and included 12 questions which were divided into 2 groups and mandatory to answer. The first group, consisted of 6 questions which were used to determine the information of participants' age, gender, duration of medical oncology practice (including training of fellowship years), primary practice location, academic status (professor/associate professor/assistant professor and the others like staff/specialist physician and fellow) and which antiemetic guidelines (ESMO/MASCC, ASCO, and NCCN) they prefer. The

Table 1
Recommendations of antiemetic guidelines for acute and delayed CINV.

	Phases	NCCN[9]	ASCO[10]	MASCC/ESMO[1]
HEC	Acute phase (day 1)	5HT3RA + NK-1 + Dex	5HT3RA + NK-1 + Dex	5HT3RA + NK-1 + Dex
	Delayed phase (day 2–4)	Dex + NK-1	Dex + NK-1	Only NK-1 or Dex or Dex + NK-1 or NK-1 +DOP
MEC	Acute phase (day 1)	5HT3RA + Dex or 5HT3RA +NK-1 +Dex	5HT3RA + Dex	5HT3RA + Dex
	Delayed phase (day 2–4)	Only Dex or 5HT3RA or NK-1 ± Dex (if aprepitant was given day one)	Dex	No routine prophylaxis (Dex can be considered)
LEC	Acute phase (day 1)	5HT3RA or Dex or DOP	Dex	5HT3RA or Dex or DOP
	Delayed phase (day 2–4)	No routine prophylaxis	No routine prophylaxis	No routine prophylaxis

Dex, Dexamethasone; DOP, Dopamine receptor Antagonist (Metoclopramide); 5HT3RA, 5-hydroxytryptamine type 3 (5-HT3) receptors antagonist; NK-1, Neurokinin-1 receptor antagonist.

second group consisted of the other 6 questions that aim to find out which antiemetic drugs are preferred by Turkish medical oncologists for acute and delayed CINV in patients who have received high (HEC), moderate (MEC) and low emetogenic chemotherapy (LEC) for the first cycle. The whole of the questionnaire form is accessible in Supply Appendix.

Antiemetic guidelines and recommendations

The recommendations (Table 1) in the MASCC/ESMO Antiemetic Guideline 2016,[1] NCCN Antiemesis Guideline Version 2.2017,[9] and ASCO 2016 Antiemetics Guideline[10] were used to make a comparison between the recommendations of the antiemetic guidelines and the answers given to our questionnaire.

Emetogenic effects of chemotherapy regimens have been classified as 4-level: high emetogenic chemotherapy (HEC, emetic risk > 90%), moderate emetogenic chemotherapy (MEC, emetic risk 30%-90%), low emetogenic chemotherapy (LEC, emetic risk 10%-30%), and minimal emetogenic chemotherapy (emetic risk <10%)[1]. CINV is typically occurred in the first 24 hours after chemotherapy (acute phase) and 24-120 hour after chemotherapy (delayed phase).

Statistics

Statistical analyses were performed using SPSS Version 20.0 software for Windows (SPSS, Chicago, IL). Mean ± standard deviation, median, and percentage (%) values were determined by standard descriptive statistics. The chi-square test was used for comparing the categorical data; the effect of age, gender, duration of working in the oncology department, and being an academician. Values of P <0.05 were considered statistically significant. While analyzing the compliance to guidelines of participants who were following many guidelines, we accepted the answer as compatible, if any of the guidelines that a participant specified as following includes a recommendation of this participant's choices.

This survey study was approved by the local ethics committee at Afyon Kocatepe University Faculty of Medicine and carried out in accordance with the Declaration of Helsinki principles and all relevant regulations.

Results

Questionnaire form for CINV treatment was answered by 146 Turkish Medical Oncologists. The number of participants was about one-fourth of the Turkish Medical Oncologists and was

Table 2
Descriptive statistics.

Groups	n (%) of participants
Age (Median (min-max))	39 (30–62)
Gender	
Male	87 (%60)
Female	59 (%40)
Duration of working in the oncology department	
1–5 years	53 (%36)
6–10 years	56 (%39)
10–15 years	18 (%12)
15–20 years	12 (%8)
>20 years	7 (%5)
Guideline choices	
Only one guideline*	60 (%41)
Many guidelines*	77 (%53)
Not following any guideline	9 (%6)

* Any of international guidelines, NCCN, ESMO/MASCC, ASCO.

Table 3
The ratio of compliance with the guidelines and antiemetic choices of participants.

	HEC n (%)		MEC n (%)		LEC n (%)	
	Acute phase	Delayed phase	Acute phase	Delayed phase	Acute phase	Delayed phase
5HT3RA+ dex+ apr	134 (92)	38 (26)	9 (6)	-	-	-
5HT3RA + dex	3 (2)	11 (7)	104 (71)	14 (10)	36 (25)	-
5HT3RA + apr	9 (6)	45 (31)	-	-	-	-
5HT3RA + met	-	-	16 (11)	28 (19)	9 (6)	5 (3)
Dexa + met	-	-	5 (4)	10 (7)	13 (9)	3 (2)
Dexa + apr	-	19 (13)	-	-	-	-
5HT3RA	-	-	-	73 (50)	45 (31)	36 (25)
Dex	-	-	-	11 (7)	5 (3)	2 (1)
Met	-	-	-	8 (6)	17 (12)	44 (30)
Others*	-	33 (23)	12 (8)	-	-	-
Not preferring	-	-	-	2 (1)	21 (14)	56 (39)
Compliance	125 (92)	21 (15)	106 (73)	77 (56)	65 (47)	54 (39)
Noncompliance	12 (8)	116 (85)	31 (21)	60 (44)	72 (53)	83 (61)

Dex, Dexamethasone; DOP, Dopamine receptor Antagonist (Metoclopramide=met); 5HT3RA, 5-hydroxytryptamine type 3 (5-HT3) receptors antagonist; NK-1, Neurokinin-1 receptor antagonist (aprepitant=apr).
* Undetermined drug combinations in our survey.

large enough to sample the medical oncologists in our country. The mean age of the participants was 39 years (range: 30-62), and 60 % were male. Regarding working time, the largest group of participants was 6-10 years, and 39% of the participants were in this group. Table 2 shows the characteristics of the participants.

Most of the participants were applying more than 1 antiemetic guideline (n = 77, 53%). Nine (6%) medical oncologists were not following any antiemetic guideline. Therefore, compliance analysis was performed in the rest 137 medical oncologists. In all groups (HEC, MEC, and LEC), the rate of guideline compliance for acute phase antiemetic prophylaxis for HEC and MEC was higher and acceptable, while the rate of guideline compliance for delayed phase antiemetic prophylaxis for HEC and LEC was significantly lower (Table 3).

The majority of the participants (n = 125, 92%) were found to be in compliance with the guidelines for acute phase antiemetic prophylaxis for HEC. Conversely, we found a sizeable statistical difference in compliance with the guidelines for delayed phase antiemetic prophylaxis for HEC. A 116 (85%) participants were incompatible with guidelines. None of the parameters of age, gender, being an academician, and duration of working in the oncology department affected the rate of guideline compliance for acute phase antiemetic prophylaxis for HEC. However, aca-

Tablo 4
Oncologists characteristics and their responses to the survey.

Groups		Acute phase n(%)			Delayed phase n(%)		
		Compliance	Noncompliance	*P*	Compliance	Noncompliance	*P*
HEC	**Gender**						
	Male	5 (9)	50 (91)		11 (13)	71 (87)	
	Female	7 (8)	75 (92)	0.571	10 (18)	45 (82)	0.300
	Duration[†]						
	1-5 years	7 (14)	42 (86)		2 (4)	47 (96)	
	>5 years	5 (6)	83 (94)	0.084	19 (22)	69 (78)	**0.004**
	Age						
	<39	8 (12)	58 (88)		6 (9)	60 (91)	
	≥39	4 (6)	67 (96)	0.149	15 (21)	56 (79)	**0.042**
	Academician[*]						
	Yes	69 (95)	4 (5)		17 (23)	56 (77)	
	No	56 (87)	8 (13)	0.126	4 (6)	60 (94)	**0.005**
MEC	**Gender**						
	Male	60 (73)	22 (27)		55 (67)	27 (33)	
	Female	46 (84)	9 (16)	0.109	22 (40)	33 (60)	**0.003**
	Duration						
	1–5 years	35 (71)	14 (29)		28 (57)	21 (43)	
	>5 years	71 (81)	17 (19)	0.152	49 (56)	39 (44)	0.507
	Age						
	<39	48 (73)	18 (27)		37 (56)	29 (44)	
	≥39	58 (82)	13 (18)	0.147	40 (56)	31 (44)	0.555
	Academician						
	Yes	60 (82)	13 (18)		37 (51)	36 (49)	
	No	46 (72)	18 (28)	0.108	40 (63)	24 (37)	0.111
LEC	**Gender**						
	Male	39 (48)	43 (52)		32 (39)	50 (61)	
	Female	26 (47)	29 (53)	0.556	22 (40)	33 (60)	0.524
	Duration						
	1–5 years	23 (47)	26 (53)		19 (39)	30 (61)	
	>5 years	42 (48)	46 (52)	0.536	35 (40)	53 (60)	0.529
	Age						
	<39	34 (52)	32 (48)		25 (38)	41 (62)	
	≥39	31 (44)	40 (56)	0.227	29 (41)	42 (59)	0.429
	Academician						
	Yes	35 (48)	38 (52)		29 (40)	44 (60)	
	No	30 (47)	34 (53)	0.519	25 (40)	39 (60)	0.535

[*] Academician group includes professors, associate professors, and assistant professors.
[†] Duration of working in the oncology department.

demicians, oncologists who had been in an oncology department for over 5 years and older participants were more likely to be in compliance with the guidelines for delayed phase antiemetic prophylaxis for HEC and these were statistically significant ($P = 0.005$, $P = 0.004$, $P = 0.042$, respectively; Table 4).

The compliance with the guidelines for acute and delayed phase antiemetic prophylaxis for MEC was found to be 73% (n = 106) and 56% (n = 77) of the participants, respectively. None of the parameters of age, gender, being an academician, and duration of working in the oncology department affected the rate of guideline compliance for acute phase antiemetic prophylaxis for MEC. However, only male participants were more likely to be in compliance with the guidelines for delayed phase antiemetic prophylaxis for MEC, and this was statistically significant ($P = 0.003$). (Table 4)

The compliance with the guidelines for both acute and delayed phase antiemetic prophylaxis for LEC was found to be 47% (n = 65) of the participants. None of the parameters of age, gender, being an academician, and duration of working in the oncology department affected the rate of guideline compliance for both acute and delayed phase antiemetic prophylaxis for LEC (Table 4).

Discussion

In this study, we have shown that Turkish Medical Oncologists have higher compliance with the guidelines for prophylaxis of acute CINV in patients who receive HEC and MEC (92% and 73%, respectively), but lower in patients who receive LEC (47%). Noncompliance with antiemetic guidelines for prophylaxis of delayed CINV was the highest in patients receiving HEC (85%) and the lowest in patients receiving MEC (44%). Continued use of 5HT3RA for the treatment of delayed CINV in HEC patients was the leading cause of incompatibility with guidelines. The main reason for noncompliance with delayed CINV guidelines for MEC was the use of metoclopramide by oncologists in combination with 5HT3RA or dexamethasone, although none of the 3 antiemetic guidelines[1,9,10] suggested a dual antiemetic combination. Oncologists preferred to use 5HT3RA (25%) or metoclopramide (30%) alone in the treatment of delayed CINV for LEC, although none of these guidelines were recommended at all.

In a single-center European study from Switzerland, Burmeister et al[8] showed that adherence to ESMO/MASCC 2008 recommendations for prophylaxis of CINV was below expected. The rate of adherence to ESMO/MASCC was 61% for overall prophylaxis of acute CINV, and the rate of nonadherence was 89% for delayed CINV. Overuse of 5HT3RAs for prophylaxis of acute CINV in patients receiving LEC and overuse of 5HT3RAs for prophylaxis of delayed CINV in patients receiving HEC and MEC were the most important reasons of noncompliance. Whereas, 5HT3RAs have been admitted ineffective or minimally effective on delayed emesis. When assessing patient-related factors and MASCC guideline compliance, they found that older age, solid tumor type, and inpatient treatment were associated with better compliance. In the univariate analysis, while LEC and MEC potentially predicted nonadherence guideline but, the emetogenic potential was not determined an independent factor of adherence in the multivariate analysis. Unlike Burmeister and colleagues who have investigated patient-related factors in compliance with the guidelines, in our study we focused on clinician-related factors, such as gender, age, academic status, and time spent in the profession. In our study, the incidence of noncompliance with antiemetic guidelines for delayed CINV in HEC recipients was found to be statistically significantly higher in those who worked for ≤5 years in an oncology department, under 39 years of age, and nonacademicians ($P = 0.004$, $P = 0.042$, $P = 0.005$, respectively). Incompatibility with antiemetic guidelines for delayed CINV in MEC recipients was statistically significantly lower ($P = 0.003$) only among male medical oncologists. We did not find any statistically significant difference between prophylaxis for acute CINV of HEC, MEC, and LEC and delayed CINV treatment of LEC, regarding age, gender, academic status, and time spent in the profession.

In the last decade, 2 large, multicenter, prospective observational studies which conducted to investigate the compliance with antiemetic guidelines in patients receiving HEC and MEC were published. PEER study that performed by Aapro et al[5] was conducted in 8 European countries, including Austria, Belgium, France, Italy, Spain, Sweden, the Netherlands, and the United Kingdom. In this study, a total of 991 patients receiving single-day MEC and HEC were admitted, and female AC was classified as a new group. The rate of adherence with the MASCC 2006 antiemetic guideline was determined 55% in acute CINV and 46% in delayed CINV. Of the emetic risk categories, Guideline consistency rate in acute CINV for patients receiving MEC was the highest (91%), unlike our study, while Guideline consistency rate in delayed phase for patients receiving HEC was the lowest (12%) similar to our study. The main reasons of nonadherence with the guidelines for HEC were the nonuse of NK-1 inhibitor for the acute CINV (51.8 %) and the nonuse of corticosteroid for the delayed phase. The most common reason (29.6%) of incompatibility with the guideline for female AC and MEC was that 5HT3RA was not used for delayed phase. Routine prophylaxis in the MASCC 2016 antiemetic guideline[1] is not recommended, although 5HT3RA was recommended for the delayed phase in patients receiving MEC in the MASCC 2006 antiemetic guideline. The results of this European study showed that the complete response rates for CINV were higher (59.9% vs 50.7%, $P < 0.008$) in patients treated with compliance to the MASCC antiemetic guidelines and that increasing adherence to the guidelines reduced financial burden related with CINV.

In the INSPIRE study, Gilmore et al[6] were investigating compliance with the NCCN antiemetic guidelines (v2.2011) for after first cycle HEC and MEC in the United States. A total of 1295 patients were admitted to this study from 4 different cancer center. Compliance with the guideline was 29% in patients receiving HEC, and the primary cause of noncompliance with the guideline was the nonuse of corticosteroid for the delayed phase. If corticosteroid were used for delayed CINV, the rate of compliance with the guideline for patients receiving HEC would increase from 28.7% to 89.8%. Compliance with the guideline was higher (73%) for patients receiving MEC than HEC and the main reason for nonadherence with the guideline was the nonuse of NK-1 inhibitors for prophylaxis of acute CINV. If NK-1 inhibitor were prescribed, the rate of compliance with the guideline for patients receiving MEC would increase from 73.1% to 97.8 %. However, The NCCN guideline v2.2017[9] recommends that NK-1 inhibitor have to be used for selected patients who have additional risk factors or for patients who have not responded to prior treatment. It should not be routinely used, just as it does in the NCCN guidelines v2.2017,[9] ASCO 2016,[10] and MASCC 2016[1] antiemetic guidelines. In this American study, compliance with the NCCN guidelines has been shown to significantly improve the response rates of CINV prophylaxis, as in the European (PEER) study. These 2 large prospective studies[5,6] have shown a statistically significant improvement of approximately 10% in the complete response for CINV.

The reason for noncompliance with antiemetic guidelines is often seen as overtreatment and sometimes inadequate treatment of acute or delayed CINV.[4] The issue of compliance with these guidelines is not limited to antiemetic therapy alone, but there are similar problems with the use of guidelines in other medical areas.[7]

Despite the need for more investigation, current studies have shown that adherence to the guidelines is much lower than expected and guidelines are not followed at the same level by doctors in different countries.[11] An important question arising from these studies is how to improve the adherence to the guideline. Because, higher adherence to antiemetic guidelines is associated with better control of CINV and lower financial burden.[4-7] Passive dissemination of training materials is not sufficient alone for increasing compliance.[7,8] Although all medical oncologists in the study of Burmeister et al had already received at least 1 board-certified from the ESMO exam, adherence to guidelines was not high. In an earlier study, Roila et al[12] performed a prospective trial at 103 Italian cancer centers to investigate the effectiveness of ''educational outreach visit" and "audit and feedback" strategies on the antiemetic guideline of MASCC for the prophylaxis of CINV. The combination of these 2 strategies increased the improper prescribing of a 5HT3RA for the prophylaxis of LEC induced acute CINV (from 47.7% to 65.7%, $P < 0.0001$) while showing a positive effect on guideline-based prescribing of antiemetic drugs for acute and delayed CINV induced by HEC and MEC. Alternatively, education by a local opinion leader or a program of in-house education and dissemination of guidelines or diaries of emetic response after chemotherapy and patients' feedback have only had a temporary impact on improving adherence with antiemetic guidelines[4].

Only Affronti et al[13] found that a combination of standardized order-sets containing the accurate antiemetic dose and frequency and audit-feedback strategy was an effective method and significantly increased the compliance with guidelines from 58% to 90% and the rates of complete response to 75% for acute and 84% for delayed CINV in patients with glioma.

Conclusion

Although nearly all of them were following at least an antiemetic guideline, noncompliance with the antiemetic guidelines continues to be a big problem in Turkish Medical Oncologists. Our study and earlier studies showed that exclusively passive dissemination of training materials is not sufficient to improve the rate of compliance with the guidelines. The use of standardized antiemetic protocols in chemotherapy order forms or a computerized decision-support system is now seen as a better tool to enhance compliance with the guidelines.

Conflict of Interest

None of the authors has any potential financial conflict of interest related to this manuscript.

Acknowledgment

We thank for their support to the Turkish Society of Medical Oncology and Turkish Oncology Group (TOG).

Appendix

Survey Questions

Question-1 How old are you?
Question-2 What is your sex?
Question-3 Which hospital are you working for?

- Public University Hospital
- Education and Research Hospital
- State Hospital
- Private Hospital
- Others

Question-4 How long have you been working in Medical Oncology (including fellowship duration)?

- 1-5 years
- 6-10 years
- 11-15 years
- 16-20 years
- >20 years

Question-5 What is your academic status?

- Professor
- Associate Professor
- Assistant Professor
- Specialist
- Fellow

Question-6 Which antiemetic guidelines are you following?

- NCCN
- ASCO
- MASCC/ESMO
- None
- Others (antiemetic guideline of a local clinic)

Question-7 Which antiemetic drugs do you prefer for prophylaxis of acute CINV in patients who received one daily HEC in the first cycle?

- 5HT3RA and dexamethasone and aprepitant
- 5HT3RA and dexamethasone
- 5HT3RA and aprepitant
- Dexamethasone and metoclopramide
- Only 5HT3RA

- Only dexamethasone
- Only metoclopramide
- Other

Question-8 Which antiemetic drugs do you prefer for prophylaxis of delayed CINV in patients who received one daily HEC in the first cycle?

- 5HT3RA and dexamethasone and aprepitant
- 5HT3RA and dexamethasone
- 5HT3RA and aprepitant
- Aprepitant and dexamethasone
- Dexamethasone and metoclopramide
- Only 5HT3RA
- Only dexamethasone
- Only aprepitant
- Other

Question-9 Which antiemetic drugs do you prefer for prophylaxis of acute CINV in patients who received one daily MEC in the first cycle?

- 5HT3RA and dexamethasone and aprepitant
- 5HT3RA and dexamethasone
- 5HT3RA and metoclopramide
- Dexamethasone and metoclopramide
- Only 5HT3RA
- Only dexamethasone
- Only metoclopramide
- Other

Question-10 Which antiemetic drugs do you prefer for prophylaxis of delayed CINV in patients who received one daily MEC in the first cycle?

- 5HT3RA and dexamethasone
- 5HT3RA and metoclopramide
- Dexamethasone and metoclopramide
- Only 5HT3RA
- Only dexamethasone
- Only metoclopramide
- I do not use
- Other

Question-11 Which antiemetic drugs do you prefer for prophylaxis of acute CINV in patients who received one daily LEC in the first cycle?

- 5HT3RA and dexamethasone
- 5HT3RA and metoclopramide
- Dexamethasone and metoclopramide
- Only 5HT3RA
- Only dexamethasone
- Only metoclopramide
- I do not use
- Other

Question-12 Which antiemetic drugs do you prefer for prophylaxis of delayed CINV in patients who received one daily LEC in the first cycle?

- 5HT3RA and dexamethasone
- 5HT3RA and metoclopramide

- Dexamethasone and metoclopramide
- Only 5HT3RA
- Only dexamethasone
- Only metoclopramide
- I do not use
- Other

Acute CINV: Occurring within the first 24 hour after chemotherapy
Delayed CINV: Occurring within the 25-120 hour after chemotherapy

❖ Please consider the reimbursement conditions of Turkey while answering the questions 7-12. Because Aprepitant is paid by Turkish government only for in patients who received $\geq$50 mg/m^2 cisplatin or combination of doxorubicin plus cyclophosphamide chemotherapy.

References

1. Roila F. 2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients. *Ann Oncol*. 2016;27:119–133. https://doi.org/10.1093/annonc/mdw270.
2. Carlotto A, Hogsett VL, Maiorini EM, Razulis JG, Sonis ST. The economic burden of toxicities associated with cancer treatment: review of the literature and analysis of nausea and vomiting, diarrhoea, oral mucositis and fatigue. *Pharmaco Econ*. 2013;31:753–766. doi:10.1007/s40273-013-0081-2.
3. Jordan K, Gralla R, Jahn F, Molassiotis A. International antiemetic guidelines on chemotherapy induced nausea and vomiting (CINV): content and implementation in daily routine practice. *Eur J Pharmacol*. 2014;722:197–202. doi:10.1016/j.ejphar.2013.09.073.
4. Grunberg SM. Obstacles to the implementation of antiemetic guidelines. *JNCCN J Natl Comprehensive Cancer Network*. 2009;7:601–605. doi:10.6004/jnccn.2009.0040.
5. Aapro M, et al. The effect of guideline-consistent antiemetic therapy on chemotherapy-induced nausea and vomiting (CINV): the Pan European Emesis Registry (PEER). *Ann Oncol*. 2012;23:1986–1992. doi:10.1093/annonc/mds021.
6. Gilmore JW. Antiemetic guideline consistency and incidence of chemotherapy-induced nausea and vomiting in US community oncology practice: INSPIRE Study. *J Oncol Pract/Am Soc Clin Oncol*. 2014;10(1):68–74. doi:10.1200/JOP.2012.000816.
7. Kaiser R. Antiemetic guidelines: are they being used? *Lancet Oncol*. 2005;6(8):622–625. doi:10.1016/S1470-2045(05)70284-9.
8. Burmeister H, Aebi S, Studer C, Fey MF, Gautschi O. Adherence to ESMO clinical recommendations for prophylaxis of chemotherapy-induced nausea and vomiting. *Support Care Cancer*. 2012;20:141–147. doi:10.1007/s00520-010-1079-3.
9. Berger MJ, et al. NCCN Guidelines Insights: Antiemesis, Version 2.2017. *J Natl Compr Canc Netw*. 2017;15:883–893. doi:10.6004/jnccn.2017.0117.
10. Hesketh PJ. Antiemetics: American Society of Clinical Oncology focused guideline update. *J Clin Oncol*. 2016;34:381–386. doi:10.1200/JCO.2015.64.3635.
11. Navari RM, Aapro M. Antiemetic prophylaxis for chemotherapy-induced nausea and vomiting. *N Engl J Med*. 2016;374:1356–1367. doi:10.1056/NEJMra1515442.
12. Roila F. Transferring scientific evidence to oncological practice: a trial on the impact of three different implementation in strategies on antiemetic prescriptions. *Support Care Cancer*. 2004;12:446–453. doi:10.1007/s00520-003-0553-6.
13. Affronti ML, Schneider SM, Herndon JE, Schlundt S, Friedman HS. Adherence to antiemetic guidelines in patients with malignant glioma: a quality improvement project to translate evidence into practice. *Support Care Cancer.*. 2014;22:1897–1905. doi:10.1007/s00520-014-2136-0.