

**Getting a grip on the guidelines:
understanding antiemetic usage and barriers to adherence**

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I will discuss the environment of the patients and the improvement, the knowledge of guidelines, and why it is important to have this knowledge.

Disclosures

These are my disclosures.

Question 1

I will first start with all the questions.

The first one is, are you familiar with the antiemetic guidelines, and do you use them?

The response number (1) is, yes, I am familiar with the guidelines, and I use them.

Number (2) is, yes, I am familiar with the guidelines, but I don't use them. Why? We will discuss at the end of the session.

Number (3) is, no, I am not familiar with the guidelines, and it is why you attend this session, so you are in the right place at the right time.

Number (4) is, I do not need the guidelines because I make my own decisions—why not?

Number (5) is, I am not familiar with the guidelines, but I am keen to be informed, and it is why you are here also.

You vote, and the answer is for 50% of you, yes, I am familiar with guidelines and you use them, and for the other ones, I am sure that at the end of the session, we will be 100% of us to say, yes, I am familiar with the guidelines and I will use them.

Patient case: Jeanette

We move forward to the patient case. Jeanette—a perfect name from France. She is a French woman. She is 54 years old. She is married and has 2 daughters. She has no comorbidities. She smokes. No morning sickness. She sleeps well. She has no medication use, no anxiety.

She has a lung cancer with an early stage, with a resection margin R0. Decision for adjuvant therapy with cisplatin and vinorelbine for 4 cycles.

The proposition by the multidisciplinary team for supportive care in cancer proposed NK1 receptor antagonist, plus setron, plus steroid regimen.

Question 2

What is your advice?

She will receive this triple association regimen.

Do you agree with this because it is consistent with the MASCC/ESMO guidelines?

Do you agree because it is consistent with ASCO guidelines?

Do you agree because it is consistent with my local/your local guidelines?

You disagree because NK1 inhibitors are not necessary for this indication?

You disagree because you follow your local guidelines?

You agree with both (1) and (2) – I mean MASCC/ESMO guidelines and ASCO guidelines?

Patient case: Mauricette

The next case is Mauricette. Mauricette is a Swiss woman. She is 68 years old. She is married with 1 daughter and has 3 granddaughters.

Her symptoms include postpartum blues following pregnancies, nausea, bad mood, insomnia, and anxiety with chemotherapy.

She consumes alcohol daily.

She has a diagnosis of ovarian cancer with peritoneal carcinosis, BRCA-negative.

She will receive a chemotherapy regimen with carboplatin and paclitaxel for 6 cycles, and she will receive because of the proposition of the multidisciplinary team for supportive care in cancer, a double association with setron plus steroids.

Question 3

What is your opinion?

Do you agree because it is consistent with MASCC/ESMO guidelines?

Do you agree because it is consistent with your local guidelines?

Number (3) is you disagree, and you follow your local guidelines.

You disagree. It is not consistent with MASCC/ESMO guidelines?

You disagree. NK₁ inhibitors are necessary for this indication?

Both (4) and (5)?

The answer is—the majority is you say both (4) and (5), so you disagree. It is not consistent. You are right, because we have to use a triple association for patients under carboplatin with NK₁ inhibitors, plus setron, plus steroid.

ANTIEMETIC GUIDELINES: MASCC/ESMO

ACUTE Nausea and Vomiting: SUMMARY

Why would I say that? We have today very perfect guidelines published by the MASCC/ESMO, as you can see on that slide.

This is the summary of the acute setting, and we have to use for patients with HEC—highly emetogenic chemotherapy, cisplatin-based or AC adriamycin-cyclophosphamide-based. The triple association of setron, plus dexamethasone, plus NK₁ inhibitors is exactly the same for carboplatin regimen.

For the patients on the MEC, except carboplatin we only have to use the association with setron plus dexamethasone. For patients with low emetogenic chemotherapy, you can choose a setron, or dexamethasone, or dopamine-receptor antagonist, and for minimal emesis, no routine prophylaxis.

ANTIEMETIC GUIDELINES: MASCC/ESMO

DELAYED Nausea and Vomiting: SUMMARY

I move forward to the delayed phase. For the delayed phase, you have here the summary.

For HEC, you don't choose anything else than dexamethasone, expect the use of aprepitant, and if you use aprepitant you can decide dexamethasone or metoclopramide.

For patients under AC regimen, you don't use dexamethasone, but you can have the choice between dexamethasone or aprepitant if you use it in the acute phase.

For carboplatin regimen, you don't have to use anything except aprepitant if you have used aprepitant 125 mg at day 1, and for patients with oxaliplatin, anthracycline alone, or cyclophosphamide alone, dexamethasone can be considered. You don't use anything as routine prophylaxis for other patients under moderate, low, and minimal emetic risk.

Are we following the guidelines, ...and why?

Are we following the guidelines, and why are we following them?

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

The first answer is please go to this publication. The effect of guideline-consistent antiemetic therapy on chemotherapy-induced nausea and vomiting. It was the PEER study published by many great leaders involved the setting of nausea and vomiting, such as Matti Apro, Mario Dicato, Alexander Molassiotis, and Fausto Roila, for example.

Follow-up on the impact of guideline adherence

As you can see on that slide, there is a real huge impact on the follow-up or the non-follow-up of the guidelines.

If we follow the guidelines correctly, there is an impact in terms of complete response, and it is a significant result between consistent or inconsistent use of guidelines.

What does it mean in the daily practice? It means that if you are an oncologist, you will receive more patients in a visit and you will have more of your patients at the Emergency Department with a significant result comparing the two cohorts.

Therefore, please, use the guidelines, and, first, you have to get the knowledge, the perfect knowledge of these guidelines.

The perceptual gap: perception vs reality

We don't use guidelines probably because there is a gap of perception between what we think and how the patient really lives with the chemotherapy, the anticancer treatment.

You can see that there is a gap specifically in the nausea and vomiting setting comparing patient reports and clinician reports, with a higher grade for the response of patients.

Nausea and vomiting with chemotherapy are underestimated

We have this very old study by Steven Grunberg. Steven Grunberg has published those results, and they are very important because you can see that in the acute phase we have the same perception with our patients between nurses and physicians, but what appears is that in the delayed phase, a 30% gap will appear between patients' living and the physicians' perception.

Therefore, you can see that this is really important to focus on the delayed phase because it is a time when the patient went back home and is alone with some of his medications and doesn't know what to do.

Utilisation of guideline-recommended antiemetic agents in practice: ONS survey

The use of guideline-recommended antiemetic agents in practice, I want to present to you the one result of the Clark-Snow study. Rebecca Clark-Snow was one of the leaders in antiemetics and involved in the MASCC workshop.

You can see that for the HEC, 90% of us don't use NK₁ inhibitors as primary prophylaxis, and you can see that in day 2 and beyond, 80% of patients will receive setrons. We know that we have to use NK₁ inhibitors at day 1. We don't have to use setrons at day 2 and beyond.

What about MEC? In the MEC setting, you can see that many patients will receive setron plus steroids. Only 23% of them will receive NK₁ inhibitors. We know that 100% of our patients have to receive setron plus steroids, and in the carboplatin setting, they will have to receive an NK₁ inhibitor associated with the 2 other drugs.

Awareness and use of antiemetic guidelines: survey among European oncology nurses

The awareness and the use of antiemetic guidelines—this is a European survey presented by Pascale Dielenseger from Gustave Roussy Hospital in France.

It is a very interesting study because we can see that nurses are really familiar with the guidelines—46% of them with ASCO guidelines, 40% of them with MASCC guidelines, NCCN, and others, but 41% with individual guidelines.

What are the guidelines used? The guidelines used are first of all, individual guidelines, and you can see that the barriers interfering with the implementation of the guidelines is, first, physician preference. So, you have many nurses involved in supportive care, involved in the nausea and vomiting fight, and they cannot do anything because of our interference in our guidelines.

Once again, we have to get the knowledge of the international guidelines validated, published, and we have to use them.

Evaluation of NK₁ RA use in the EU5: emetic risk in patients receiving chemotherapy

If we move to the results in Europe in 5 Western countries—France, the UK, Germany, Spain, and Italy—you can see that the emetic risk category based on the MASCC-ESMO level score is for HEC, 26% of patients, for MEC, 40% of patients, and for LEC, 34%.

NK1 RA usage in common chemotherapy settings: acute phase

The results are about the NK1 inhibitors used in common chemotherapy in the acute phase, an increase of the use of NK1 inhibitors in the carboplatin setting.

Moving from 14% to 23% is very good because we will be in 10 years confident with the guidelines, with the current guidelines, but you can see that in the cisplatin and AC regimen, we only have around 40% of patients receiving NK1 inhibitors. We should prescribe NK1 inhibitors to 100% of our patients, so we are missing for 60% of them.

Physicians' perception on emetic risk and NK1 RA use

What is our perception? The gap is probably the perception of the physicians, of the prescribers of the antiemetic prophylaxis.

What is the physicians' perception on emetic risk and the NK1 inhibitor use? You can see that if you ask the physicians, they consider for 40% of them that cisplatin plus pemetrexed is not a high emetogenic chemotherapy.

We know that cisplatin will put this regimen in the high emetogenic chemotherapy class.

You can see that it is the same for cisplatin/gemcitabine, and if we move to carboplatin, it is exactly the same. We consider for the majority of us that carboplatin is not a HEC. No, it is not a HEC, it is a MEC, but it is a MEC that needs to get a prophylaxis with the triple association, as well as the highly emetogenic chemotherapy regimen.

Emetogenicity of common chemotherapy agents is underestimated

What about the emetogenicity of common chemotherapy agents and the underestimation? If you consider that cisplatin plus pemetrexed is not a HEC, so you don't deliver the right drug, you don't deliver the triple association, and what is presented in that study, it means that only 80% of us will prescribe it if we consider this regimen with cisplatin as HEC, and only 34% of us will prescribe NK1 inhibitors if we consider not as a HEC.

It is the same for carboplatin, and it is the same for the AC regimen.

NERO study: evaluation of antiemetic usage across Eastern Europe

What about the NERO study? We were in the West of Europe. We are moving to the East of Europe. The NERO study is a multicentre, noninterventional prospective study to assess the impact of adherence to antiemetic guidelines in patients receiving repeated cycles of either HEC and MEC; the primary outcome is the complete response.

The secondary outcome will be the effect on quality of life.

European countries/centres involved in NERO

You can see on that map the different centres involved in this interesting study with Austria, Bulgaria, Czech Republic, Hungary, Poland, Romania, and Slovakia. The number of patients currently involved is above 700, with more than 80 clinical sites open.

What about patient-related characteristics?

What about patient-related characteristics?

Why do patients not report nausea and/or vomiting?

First, why do patients not report nausea and/or vomiting? It was a publication by Cheryl Vidall presented 3 years ago at a MASCC meeting in Copenhagen, and the first answer by physicians, nurses, and patients is “I accept that nausea and/or vomiting is a normal side effect of chemotherapy/radiotherapy that has to be tolerated.”

My answer is no. We don't have to agree with that answer. We have to fight against nausea and vomiting. It is not normal. For patients, we have to focus on quality of life, on daily living, on daughters, on eating, and not on nausea and vomiting. Therefore, we have to use the right drug at the right place for the right patient to avoid any nausea and vomiting.

The development of a prediction tool to identify cancer patients at high risk for chemotherapy-induced nausea and vomiting

It is because what was published was this very, very terrific paper by Dranitsaris and other leaders to develop a prediction tool to assess the individual risk of our patients in terms of nausea and vomiting.

Risk scoring algorithm of for \geq grade 2 CINV in cancer patients receiving chemotherapy

This is the risk table. The risk scoring is written, and you can see that the impact of patient risk factors is, first, age, with point 1. A patient expects to have CINV. Patients slept less than 7 hours the night before chemotherapy, so remember, one of the first questions about sleeping before chemotherapy. The history of morning sickness. The level of emetogenicity of the chemotherapy regimen and the prescription at home that the patients have available. The nausea and vomiting in the previous cycle, and what about the second cycle, the third cycle, etc.?

Adapting the antiemetic regimen to patient characteristics

There is a cut-off at 16, and then we can have this editorial that I published in the same issue of *Annals of Oncology* is that maybe in the future we can upgrade our patients from MEC to HEC, or from HEC to a very HEC regimen, and then maybe add a new drug. If

you start with an association with setron plus steroid, then if the patient has several risk factors you can add the NK₁ inhibitors whenever the patient has LEC or MEC, and if the patient has a HEC following the MASCC/ESMO guidelines you have to prescribe a triple association NK₁ inhibitor, plus setron, plus steroid. If the patient has several characteristics you may upgrade this risk and then add the olanzapine or another antiemetic to the triple association.

CINV Risk Assessment

What is proposed in this very, very good application, and please move to the website to try it. You can use it in your daily practice face to face with your patients, to assess the risk score of your patients.

Just type www.riskcinv.org, and then you have these risk factors.

Patient case: Jeannette

If we move back to our clinical cases, the first one is Jeannette, the French woman who is 54 years old. She is young. She is married with 2 daughters. She has no comorbidities. She smokes. She has no morning sickness. She sleeps well. She has no medication use. She has no anxiety. She has lung cancer with an adjuvant therapy with cisplatin regimen, and she will receive triple association NK₁ inhibitors, plus a setron, plus a steroid regimen.

Jeannette

What we can see on the website is that this chemotherapy is at a high emetogenic level, and we have to prescribe the triple association NK₁ inhibitors, plus setron, plus corticosteroids, and it is not necessary to add another antiemetic.

Patient case: Mauricette

The last case is Mauricette, the Swiss woman. She is 68 years old. She is married with a daughter and granddaughters. The symptoms include postpartum blues, nausea, bad mood, insomnia, anxiety with chemotherapy. She consumes alcohol daily. The diagnosis is an ovarian cancer and she will receive carboplatin regimen.

Therefore, the proposition was an association, a double association of setron plus steroid. The answer, when you put the risk factors in the website is a high level of emesis, and you have to prescribe triple association NK₁ inhibitors, plus steroid, plus setron, and you can add another antiemetic. Therefore, a quadruple association.

Mauricette

This is what it means when you use this risk tool. You can see that it is very interesting because you don't just focus on the level of emetogenicity. You use today the level of emetogenicity of the chemotherapy regimen, but also you use the patient's characteristics.

“Supportive care makes excellent cancer care possible”

I conclude on that sentence by Dorothy Keefe and by the MASCC. This is our message: supportive care makes excellent cancer care possible. Thank you very much.

[Ends]