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OFFICE perspectives

Seizing Opportunities to Enhance the Care of Chemotherapy-Induced Nausea and Vomiting

A CE/CME Activity

Overview

By reviewing case presentations, **Lee Schwartzberg, MD,** and **Sally Yowell Barbour, PharmD,** discuss best practices in classifying patients at risk for chemotherapy-induced nausea and vomiting (CINV), minimizing CINV risk in patients, and collaborating with other health care professionals on preventive and management strategies.

Case Presentations:

Faculty

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CE/CME Information

Target Audience
This activity was developed for oncologists, hematologists/oncologists, oncology pharmacists, and other health care professionals who care for patients at risk for chemotherapy-induced nausea and vomiting (CINV).

Learning Objectives
At the conclusion of this activity, participants should be better able to:

- Classify patients with regard to their risk for CINV
- Select appropriate pharmacologic interventions to minimize CINV in at-risk patients
- Identify opportunities to collaborate with other health care professionals in the prevention and management of CINV

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This activity was originally released in October 2016 and is eligible for credit through October 2017.

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1 Case 1: Management of Highly Emetogenic Chemotherapy

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Dr. Barbour: Good afternoon and welcome. Dr. Schwartzberg and I would like to welcome everyone, all the participants to this CE opportunity entitled "Office Perspectives: Seizing Opportunities to Enhance the Care of Chemotherapy-Induced Nausea and Vomiting." My name is Sally Barbour. I'm the director of oncology, pharmacy and a clinical pharmacist practitioner here at Duke University Hospital and Cancer Center. Dr. Schwartzberg, would you like to introduce yourself?

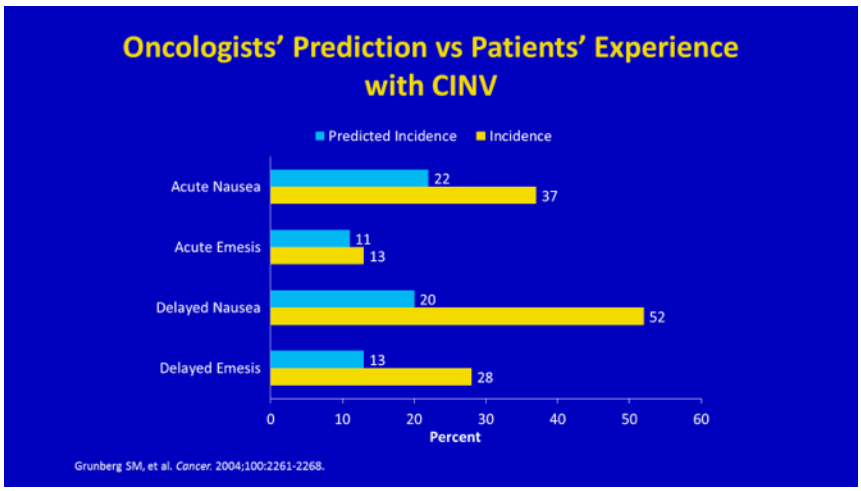
Dr. Schwartzberg: Yes. Thank you, Sally. I'm Lee Schwartzberg, a professor of medicine and executive director of the West Cancer Center and the division chief for the University of Tennessee Health Science Center Hematology Oncology Division.

Dr. Barbour: I'd like to just start by briefly going over the learning objectives today. Dr. Schwartzberg and I are going to be discussing 2 cases and, in our discussion of these cases, we'll be classifying the risks that put patients at risk for chemotherapy-induced nausea and vomiting. We'll be discussing the various interventions that we have available and how we utilize them to try to minimize this risk, and discuss how health care practitioners, including pharmacists, collaborate together to prevent and manage chemotherapy-induced nausea and vomiting.

As many of you probably know, chemotherapy-induced nausea and vomiting is a significant concern for patients who are undergoing chemotherapy, despite the many advances that have been made over the past several years and, really, what those advances have offered us is a great improvement, primarily in vomiting. Where we really see our continued challenges is in the area of nausea. It's just a much harder symptom to treat than vomiting at this point.

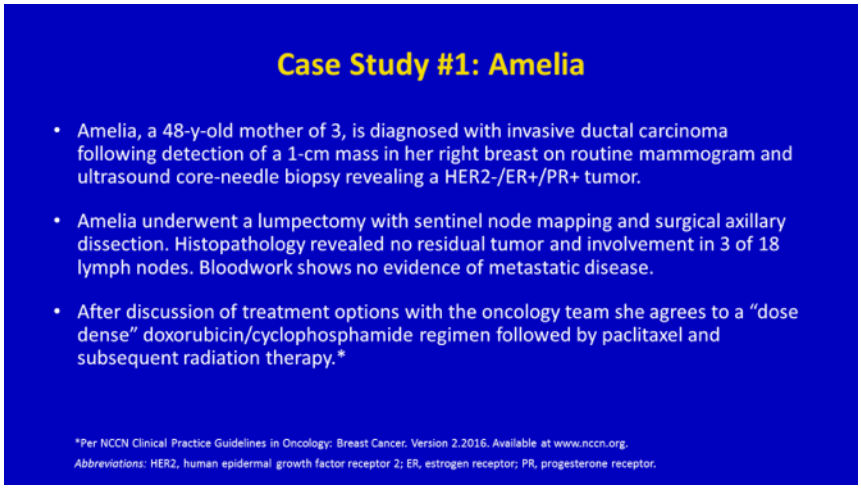
Chemotherapy-induced nausea and vomiting, if it isn't managed well or it is uncontrolled, can still lead to some complications.

Again, because we control vomiting much better, maybe not some of the more severe ones that we heard about in school, but patients can still end up dehydrating, they can choose to no longer want to receive chemotherapy if they're having a really bad experience with nausea and vomiting. They can end up with electrolyte imbalances. Both dehydration and the need for electrolyte supplementation can certainly necessitate them either coming back to the clinic or getting admitted to the hospital, and it affects their abilities to carry on their daily functions and spending time with their family and just generally feeling pretty miserable.



One of our continued challenges in the area of chemotherapy-induced nausea and vomiting, it's really one of the other objectives of this program, is just to educate and to continue to make people aware—aware of the challenges and aware of what we have available. One of the things you can see on this graph here, is a survey that was done several years ago but, for better or worse, I think it's still true, is that one of our challenges is a lack of awareness or discordance. You can see on this graph that often, as health care practitioners, we think people are doing better, we predict they're doing better than they really are and, as you can see in this graph here, really nausea is where, again, we see most of this discrepancy.

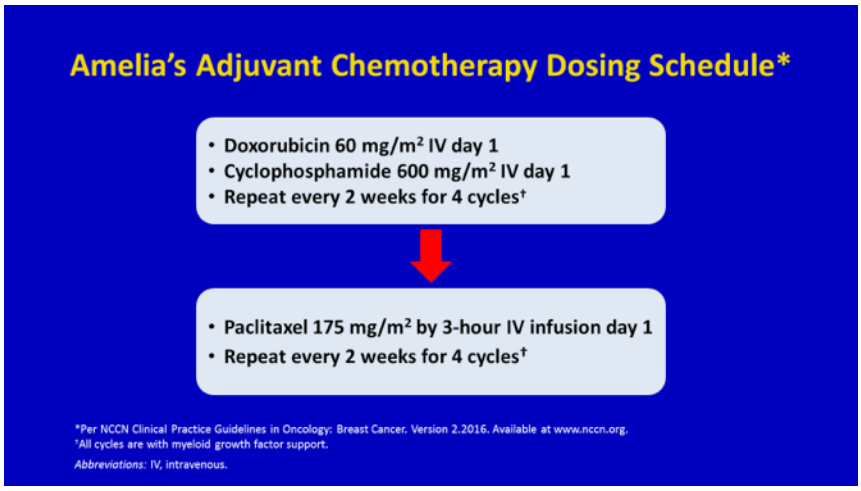
Dr. Schwartzberg, with that brief introduction, I'll ask for you to present our first case.

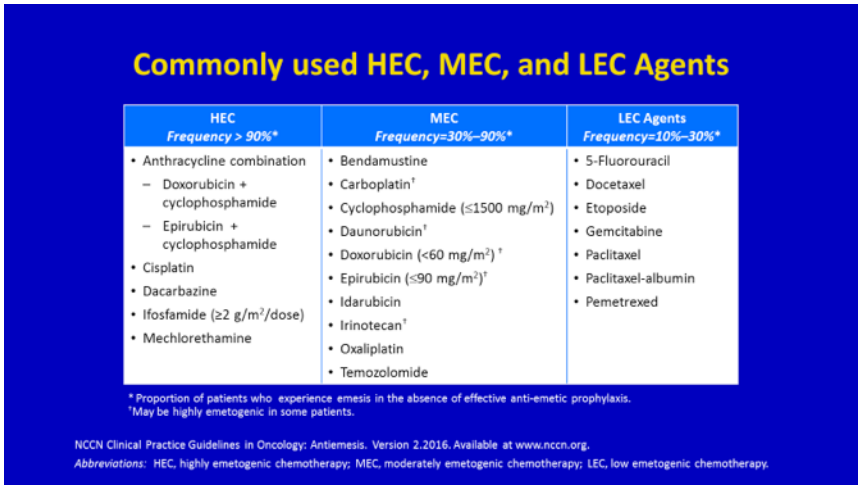


Dr. Schwartzberg: Sure. Thank you, Sally. Our first case is Amelia, a 48-year-old mother of 3, who was diagnosed with invasive ductal cancer after a 1 centimeter mass was found on mammogram and she had a biopsy which showed this cancer, which was estrogen receptor positive and HER2 negative. Amelia underwent a lumpectomy, a sentinel lymph node biopsy, and axillary dissection. Her pathology showed no residual tumor in the breast, interestingly, but she had 3 of 18 lymph nodes positive. After discussion of treatment options with the oncology team, she agreed to a recommended dose-dense doxorubicin-cyclophosphamide regimen, followed by paclitaxel and then radiation therapy to her breast.

Her regimen is shown on the slide. She will receive standard dose doxorubicin at 60 mg/m^2 and cyclophosphamide at 600 mg/m^2 on day 1 and that would be 4 cycles of therapy repeated every 2 weeks with growth factor support. Then she would receive paclitaxel at 175 mg/m^2 every 2 weeks for 4 cycles. That's a standard dose-dense regimen.

If we look here, on this slide, we can see that we characterize all chemotherapy based on the degree of emetogenicity, or the chance that a patient would get sick in the absence of having any prophylactic medication against the nausea and vomiting. The development of this kind of criteria and tiering the drugs that we use now, a couple of decades ago really set the stage for what kind of prevention we needed to use and the relative intensity of the preventive therapy we need to give in terms of antiemetics.





We break it out into 3 groups, as shown here: highly emetogenic chemotherapy, which basically means, in the absence of any effective drugs, almost everyone will get sick from the chemotherapy. You can see that in this particular instance the combination of anthracycline and cyclophosphamide is considered a highly emetogenic chemotherapy. That's a change from a few years ago, so for people who haven't looked at this in a while, we need to emphasize that the AC regimen, still very commonly used, as in this patient, is very emetogenic and patients should receive appropriate antiemetic therapy, which we'll talk about.

In addition, the other drug that we use frequently, which is in the emetogenic range, is cisplatin. Cisplatin, at any dose, is essentially highly emetogenic. This is important to keep in mind. Then, a few other drugs that are also called highly emetogenic drugs, either by themselves or in combination with other drugs.

When we make decisions, Sally, about chemotherapy, what's the make up of the ideal team? How do you look at this? Particularly, can you focus on the role of the pharmacist in the team in making decisions both about chemo and around antiemetics?

Dr. Barbour: Yeah. I think the first place to start is to emphasize the multidisciplinary team which I had mentioned previously, including the provider, nurse practitioners, PAs, pharmacists, nurses, I think all of those people are very important. Ultimately, it really starts with the patient. When we're starting someone on chemotherapy, the first person that we obviously talk to is the patient, looking at what chemotherapy are they getting, what are their risk factors, which we'll talk a little bit more about. What are their expectations? What have they heard, so that we can dispel any rumors and really understand where they are when we're going to be starting them on chemotherapy.

Specifically, in terms of the pharmacist, the pharmacists have, depending on their role, different roles. The pharmacist might be involved, even at the early stage when they're looking at what agents a practice or an institution is going to have on their formulary. While there are many 5-HT_3 antagonists available and now there are multiple NK_1 antagonists available, what is the one that you're going to have available at your institution? Pharmacists are involved at that back-end part of the decision process but, in the clinic and in the practice setting, our pharmacists are involved, again, in educating patients, making sure that patients are receiving appropriate antiemetic prophylaxis for whatever their chemotherapy regimen is.

In this example, we have pharmacists that are in our clinic that are working side by side with physicians like yourself, and nurse practitioners, physician assistants, so we're very much involved in discussing patients' antiemetics with them and, again, making sure, not only that they're prescribed, but that they can afford them, that they're able to pick them up. If they've already gotten the medicines, we verify, making sure that they've got them and they understand how to take them, making sure that, if there are any drug interactions, especially these days it's not uncommon when we all have these electronic medical records, there's a frequent notification of QTC interactions a lot of these days with our antiemetics and really trying to help address that for patients who are on other medications that might interact.

Then, for pharmacists that are involved in the processing of the orders, again, it's not only, obviously, reviewing the chemotherapy, but again, making sure those patients, if they're getting a specific regimen, are getting the appropriate antiemetic prophylaxis. It's really a multitude of steps, where a pharmacist has the potential to be involved, but again, I think the important thing is making sure that it's a multidisciplinary process and that all are involved. We have pharmacists that are also involved in follow-up. I know in a lot of places nurses are doing that. I don't think it really matters who. I think we're all quite capable of doing it but I think following up with patients to see how they did after chemotherapy is a very important thing to do, as well, because if we find out that they're not doing well, the next day we can make some changes to what we already prescribed. That's how we do it here.

How about in your practice? Do you have pharmacists or how is this approached in your practice?

Dr. Schwartzberg: Yeah, we do have pharmacists and I agree completely with everything you said. Depending on the practice setting, either you'll use the pharmacist for educator or there will be a nurse educator. Same thing for follow-up. I think pharmacists can play that role tremendously and we are the designees that can do that.

I just want to emphasize what you said. The education of the patient, first of all, dispelling the rumors that everyone has to get sick, which, as you mentioned, we're still seeing in the popular media that chemotherapy equals getting sick and throwing up, that's not true, as we know and that we have good efficacious drugs to help do that—that's what we're talking about. Then, secondly though, to make sure that the patient knows to call if they do have a problem and that we're going to follow up with them. The pharmacist's role in terms of the drug interactions, as you mentioned, is getting more and more critical with everything that we do because we're using polypharmacy, both in terms of the antiemetic drugs, in terms of the chemotherapy, many patients now are on additional oral medications, all of which, as we've learned more, can interact with each other and there can be metabolic changes. That role, which is really specific to the pharmacist, is crucial and ever more important in my own practice and, I think, everyone's practice.

Let me ask you: what kind of patient risk factors should we consider? How do you think about that when you're making the decision with your multidisciplinary team on what antiemetic regimen a patient should have?

Dr. Barbour: Again, we start with the patient. We're lucky we have an electronic medical record so all of our treatment plans are built and they have the appropriate… At our institution we base our antiemetics off the NCCN guidelines but we have all of those built in so we start with that and knowing that we have the minimal recommended antiemetics included in a particular regimen. Then, you talk to the patient.

In this particular case, if Amelia was being treated at our institution, again, number one: what's the chemotherapy? Making sure that the antiemetic prophylaxis matches the chemotherapy, but then looking at the other risk factors: she's a female. We know that being a female increases your risk of chemotherapy-induced nausea and vomiting. Age. She's 48. We know that younger patients—roughly less than 50—that they have an increased risk. Asking the patient did they have issues with nausea when they were pregnant, whether they have motion sickness. If we have someone who has had chemotherapy before, asking "Did you have issues with your chemotherapy? How did you do with your chemotherapy? What worked for you? What didn't work for you?" Looking at those risk factors. Alcohol intake, that's another one. We know that patients that have a significant history of alcohol intake actually do better.

Looking at those different risk factors are ones that we would use to try to see if we needed to increase our standard or somehow make a change in what our standard antiemetic prophylaxis regimen would be.

How about you? Do you all incorporate those risk factors in any different way?

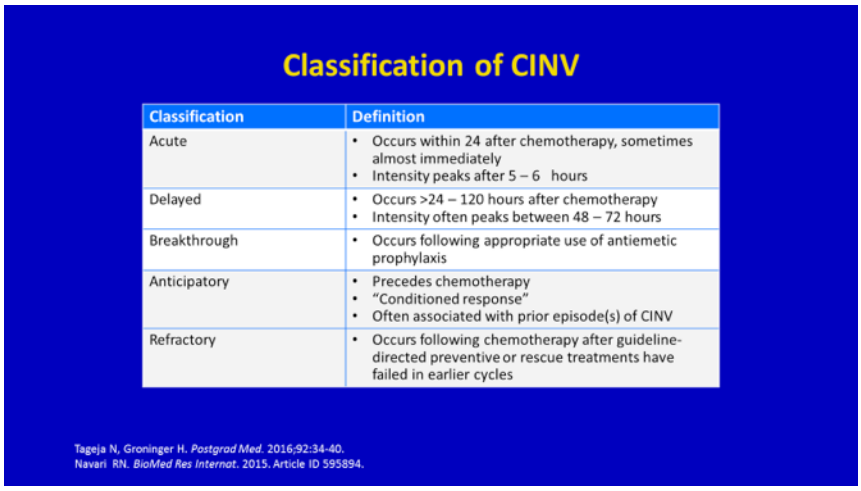
Dr. Schwartzberg: No. I agree with you completely. I find that they're particularly useful in that broad range of moderately emetogenic chemotherapy where a number of drugs are found that we use commonly, like the other platinums like carboplatin, oxaliplatin and irinotecan. Those are drugs that have a fairly broad range of likelihood of emesis and we lump them together, although, by definition, they have a 30% to 90% range, so that's a very wide range and, I think, in that particular instance, for many of those drugs that are in the intermediate range, that the patient risk factors play a big role in determining the degree of antiemetic prophylaxis we're going to use.

Dr. Barbour: I would agree. Again, just referring back to Amelia, what type of nausea and vomiting do you think that she might experience with this regimen?

Dr. Schwartzberg: One thing that's good to keep in mind is the different classifications of chemotherapy-induced nausea and vomiting. These are used in clinical trials but they're also very useful in a clinical framework because it mirrors the way that the drugs actually act.

Many drugs actually have a biphasic response in terms of causing nausea and vomiting, sometimes in the early time after the treatment and, really, the classic drug here is cisplatin, which has a peak very early, within the first couple of hours of delivering it, and then a second peak a few days later. Other drugs have different responses but, generally, we know that the risk from chemotherapy for developing nausea and vomiting occurs within the first 5 days or so after chemotherapy. Once you get out beyond that time, really, the clinician needs to think about, potentially, other sources. Although, occasionally, patients will still have a prolonged effect. Especially if it's been severe in the first few days.

We define the acute phase as in that first day after chemotherapy. We've conquered that, as you alluded to before, for the most part. We have much, much less nausea and vomiting, particularly vomiting in that first day, which is what everyone with cisplatin used to have before we had effective regimens, including 5-HT_3 receptor antagonists, the first drugs that we had.



Then, the delayed time is really after that first day through the end of around 5 days. That first 5-day period, acute into late, is what's at risk and that's how the clinical trials are set up and it's a bit of an artificial distinction, but it's a good framework to use.

The other kinds of nausea and vomiting we see are breakthrough. Breakthrough is what happens if you get nausea and vomiting, if you have to take a medication because you're nauseated enough during those 5 days or, if you do actually have emesis, that's considered breakthrough because you should be getting the effective drugs as prevention during that period of time.

Then we have a category called "refractory." Refractory means we've tried the effective drugs, we've given the right regimen, and yet patients are still getting sick. We're trying to eliminate refractory CINV but, occasionally, even today, we see that.

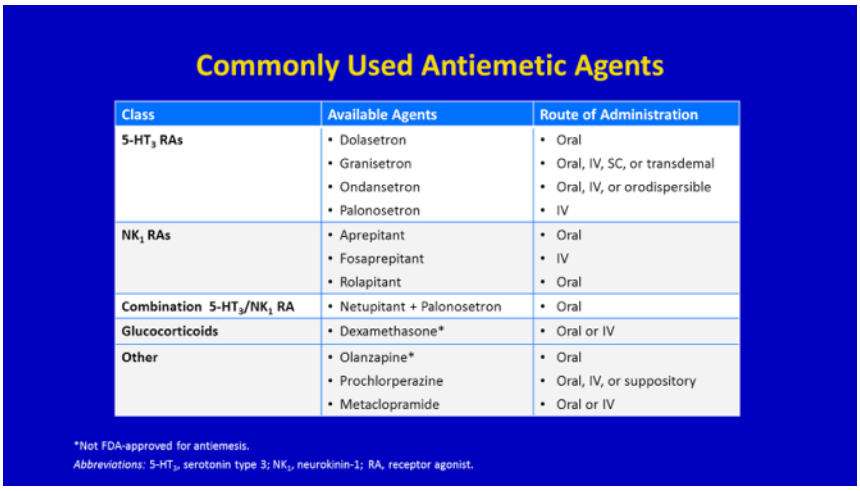
Finally, we have the category called "anticipatory nausea and vomiting." This is a little different. This is really a Pavlovian type of response and, typically, we see it in patients who we didn't control well the first time they got chemotherapy, which is why we need to emphasize that giving the right antiemetic regimen as per guidelines, from day one of the first chemotherapy, is so important. Because, if you do that, the vast majority of people will not have anticipatory nausea. Anticipatory nausea, though, is very characteristic. The patient walks into the clinic or the hospital and immediately has this response which is an anticipatory, a psychological response but, still, very, very physically real, that they get nauseated and there are triggers.

We treat that a little differently. Patients can use anxiolytics, like lorazepam for example, or other anxiolytics, before they come to the clinic, which sometimes helps, or in addition to the antiemetics that are given as part of the regular regimen, to help anticipatory nausea. The best approach, though, is to prevent it.

Dr. Barbour: Again, back to Amelia, what is going to be our goal? I think we know our goal is to not have her be sick, but what would you say is the goal and how would you manage Amelia and her chemotherapy in terms of nausea and vomiting prevention?

Dr. Schwartzberg: Our goal for everyone, our ultimate goal, is no one should get sick, no one should get nauseated and no one should have vomiting with chemotherapy. We're not there yet, but we get better, and over the last few years, with the development of newer drugs and with the combinations that we have now, the majority of our patients, even with the most highly emetogenic chemotherapy, can succeed and not have that happen.

We want to use the correct antiemetic regimen for the appropriate type of chemotherapy. We have a group of commonly used antiemetic agents and we basically look at this as 4 classes of drugs. The standard, foundational drug, is what's called the 5-HT_3 receptor antagonist. Those are serotonin antagonists. They tend to work predominately in the gut where there are serotonin receptors and noxious substances, whether they come in orally or they come in through intravenously, are affected in that way, both in the gut and in the central nervous system.



Commonly Used Antiemetic Agents

Class	Available Agents	Route of Administration
5-HT_3 RAs	• Dolasetron • Granisetron • Ondansetron • Palonosetron	• Oral • Oral, IV, SC, or transdemal • Oral, IV, or orodispersible • IV
NK_1 RAs	• Aprepitant • Fosaprepitant • Rolapitant	• Oral • IV • Oral
Combination 5-HT_3/NK_1 RA	• Netupitant + Palonosetron	• Oral
Glucocorticoids	• Dexamethasone*	• Oral or IV
Other	• Olanzapine* • Prochlorperazine • Metaclopramide	• Oral • Oral, IV, or suppository • Oral or IV

*Not FDA-approved for antiemesis.
Abbreviations: 5-HT_3, serotonin type 3; NK_1, neurokinin-1; RA, receptor agonist.

We have several different agents which are available as 5-HT_3 receptor antagonists: ondansetron, granisetron, dolasetron, and palonosetron. These can either be given orally in some cases or intravenously.

We have NK_1 receptor antagonists, that's the second class. These target another receptor, predominately in the brain, and they're responsible, particularly, for delayed nausea and vomiting. There's a good combination and a synergistic effect between the 5-HT_3 antagonists, which are particularly good for acute nausea and vomiting, and the NK_1 antagonists which are good for delayed, and using those together is also frequently very useful.

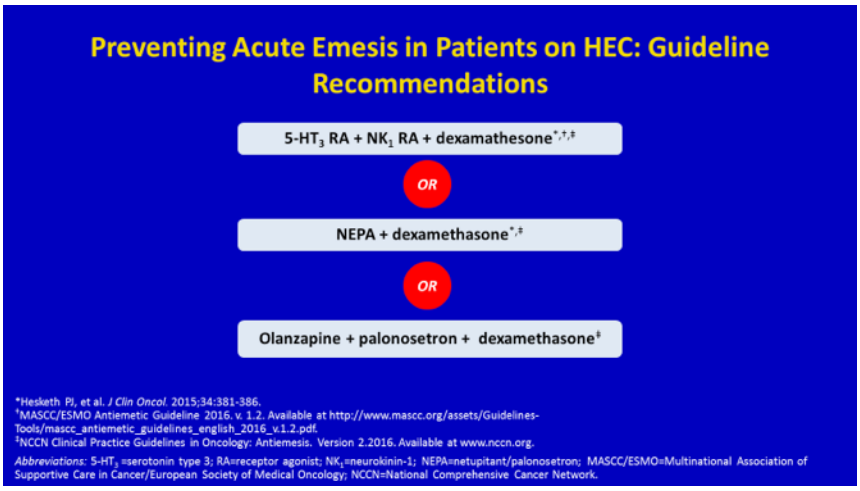
We have several different drugs there. We have aprepitant, which is an oral form; fosaprepitant, which is the same drug in an IV form; and we have rolapitant, a newer oral NK_1 antagonist that's recently become available. Then, we have a combination which is a fixed dose in 1 capsule of the 5-HT_3 and the NK_1 together, which is netupitant and palonosetron (NEPA). Netupitant is a new NK_1 antagonist with the second generation 5-HT_3 receptor antagonist, palonosetron, in a fixed dose in an oral capsule.

Then the third class of agent is glucocorticoids, which we usually use dexamethasone. Dexamethasone has a somewhat pleiotropic effect on multiple receptors in both the gut and the brain and adds to the actions of other specific receptor antagonists.

Finally, we have another group of drugs which are the atypical drugs: atypical antipsychotics. A major one that we use is olanzapine. It's a very old drug but it is a drug that actually hits multiple receptors in the brain and has been shown to add to the other 3 types of antiemetics that we have.

Dr. Barbour: What would you recommend be used for Amelia? What would be her guideline-recommended antiemetic regimen?

Dr. Schwartzberg: For highly emetogenic chemotherapy, or "HEC," we recommend a 3-drug combination and this is very important. The intensity of the antiemetic regimen sort of mirrors the intensity of the chemotherapy as it relates to the potential for nausea and vomiting.



The 3 drugs we would use would be a 5-HT_3, an NK_1, and a glucocorticoid—usually dexamethasone. That regimen can be given as 3 separate drugs, or it can be given as the combination of NEPA and dexamethasone, or other trials have actually switched out the NK_1 for olanzapine, the drug I mentioned, and olanzapine plus a 5-HT_3 receptor antagonist and dexamethasone is another alternative. Any one of those 3 options provides the most highly effective prophylaxis against CINV for highly-emetogenic chemotherapy.

Dr. Barbour: Given any of these regimens that might be utilized in the acute setting, is there any difference for how you manage the delayed setting in terms of how you would prevent emesis in the delayed setting as opposed to the acute setting?

Dr. Schwartzberg: What we just talked about, importantly, is what to give before the chemotherapy so that triplet regimen is given typically 30 minutes to an hour before the chemotherapy so the drugs are in the system of the patient before they get the chemotherapy and the toxic effects which affect those receptors. That is very good therapy.

Now, in the guidelines, there is a recommendation also for additional therapy in the delayed phase, on days 2 and 3, during that period of highest risk. It varies, depending on what you pick as your primary antiemetic prophylaxis. If you're giving aprepitant, which is an oral and it's short acting, you have to give that on days 2 and 3. For highly emetogenic chemotherapy, most guidelines recommend continuing the dexamethasone for 2 to 3 days afterwards because you get an additional effect there. If one uses a short-acting 5-HT_3 receptor antagonist like ondansetron or granisetron, you could continue that in days 2 and 3. If one gives palonosetron, which is a long-acting, second-generation agent, there is no need to give an additional 5-HT_3 receptor antagonist for the delayed phase because the drug remains in the system over the whole period of risk.

It varies and, in those cases, it's really good for the practice to consult the guidelines and to build into their care plans, or to their pathways, what to do for the delayed phase.

I want to just mention, before we go on to the next case, that AC is a highly emetogenic regimen. For paclitaxel, in this particular case that we presented, the antiemetic regimen would not need to be as intense. In fact, actually, paclitaxel has a lower risk of antiemesis so we wouldn't continue for this regimen, the triplet, throughout the entire course.

Whenever you're changing drugs it's important to consult what the degrees of emetogenicity is, layered on by the patient risk factors, and then make a decision.

2 Case 2: Management of Moderately Emetogenic Chemotherapy

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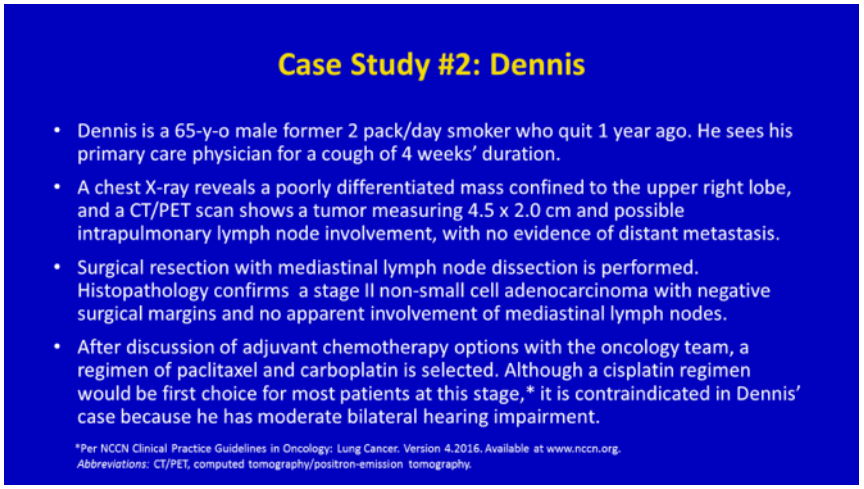
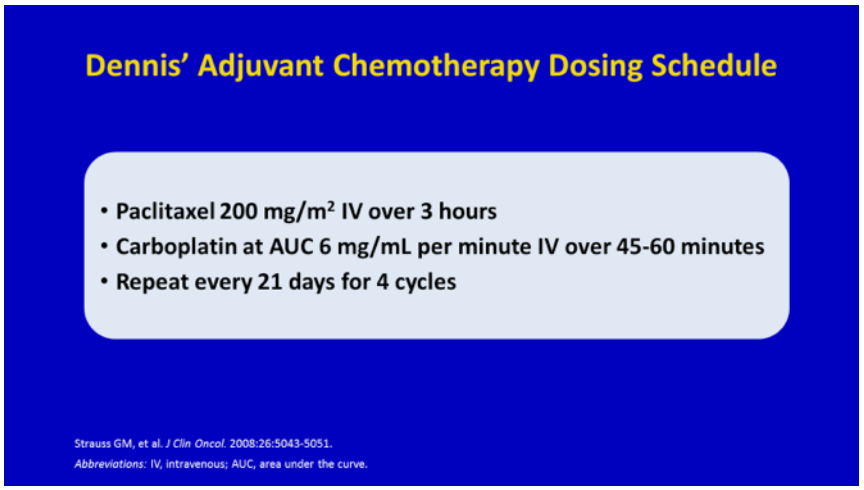
Dr. Barbour: Okay. Our next case is Dennis. Dennis is a 65-year-old male. He's a former 2-pack a day smoker. He quit a year ago. He sees his primary care physician because he's been complaining and experiencing a cough over the past month. A chest X-ray reveals that he has a poorly differentiated mass. It's confined to his upper right lobe and a CT PET scan shows that he has a 4.5 by 2 centimeter tumor and possible intrapulmonary lymph node involvement. He does not have any evidence of distant metastases at this time.



Surgical resection with mediastinal lymph node dissection is performed. His pathology confirms that he has a stage II, non–small cell adenocarcinoma with negative surgical margins and no apparent involvement of his lymph nodes.

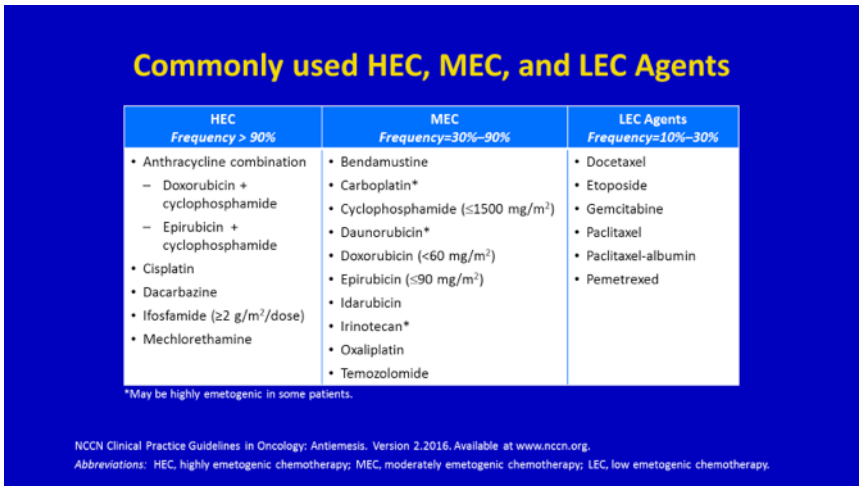
After discussion of adjuvant chemotherapy options with the oncology team, a regimen of carboplatin and paclitaxel is selected. Although a cisplatin regimen would be a first choice for most patients at this stage, it is contraindicated in Dennis because he has moderate bilateral hearing impairment.

Dennis' chemotherapy schedule, again, he's going to be getting paclitaxel at a dose of 200 mg/m^2 that's given every 3 hours and carboplatin at an AUC of 6 mg/mL per minute. This regimen is repeated every 21 days and it's given for 4 cycles. Again, a fairly standard chemotherapy regimen for lung cancer and for many other cancers as well.



Dr. Schwartzberg, given Dennis' chemotherapy regimen of carboplatin and paclitaxel, what is his risk for chemotherapy-induced nausea and vomiting?

Dr. Schwartzberg: We would go back to the chart and look at the individual drugs and, as we talked about already. Paclitaxel is at a low emetogenic risk, but carboplatin is characterized in the NCCN guidelines as in the moderate class. Now, that moderate class, again, is a very broad range which includes between a 30-90% risk of emesis, and we know that carboplatin actually sits at the top of this class, not all that different from cisplatin.



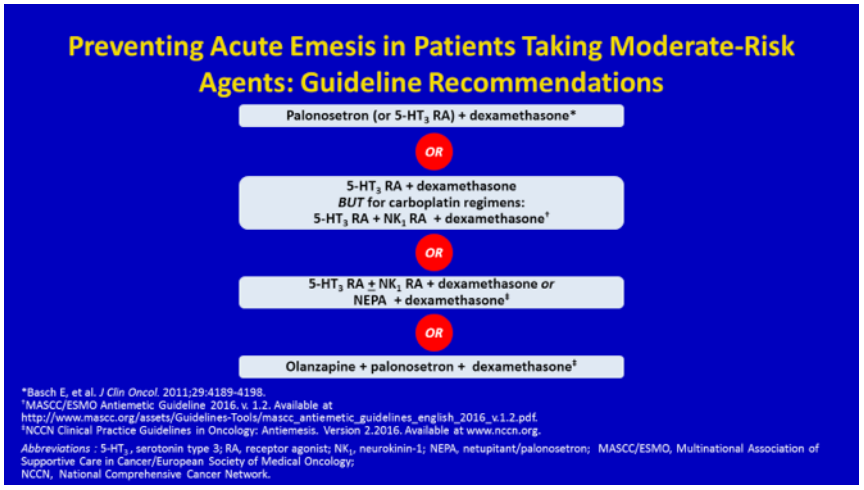
In general, that's the type of patient that we would consider potentially for a 3-drug regimen. The guidelines give latitude here about whether to use a 2-drug antiemetic regimen or a 3-drug antiemetic regimen for carboplatin-containing regimens. Some of the guidelines, like the MASCC/ESMO guidelines have now identified carboplatin as a special category, somewhat analogous to the way AC moved up to highly emetogenic, and that carboplatin should be considered for a more intensive antiemetic regimen like the highly emetogenic chemotherapy drugs.

Dr. Barbour: Other than the carboplatin, what other risk factors might Dennis have that might make you make changes to his antiemetic regimen?

Dr. Schwartzberg: In Dennis' case, as you mentioned, age and gender are very important so he doesn't meet the criteria there to be in the highest risk from patient risk factor perspective. If he had no alcohol use, if he had a history of emesis with other drugs, if he had motion sickness, those would also shade me into considering a more highly emetogenic regimen, although, again, even without these risk factors for carboplatin in particular, I would consider using a 3-drug regimen. I find that the risk factors are particularly good for patients who are maybe in a category just below that, like an oxaliplatin-containing regimen, and the other risk factors are very important to make a decision to start with a more intensive antiemetic regimen.

Dr. Barbour: It sounds like you might have alluded to this already but, specifically, what first line guideline-recommended regimen would you use? One that contains an NK_1 antagonist or have you used perhaps an olanzapine regimen in a patient like this?

Dr. Schwartzberg: Typically, if I'm going to use a 2-drug antiemetic regimen here, as per guideline, I would use palonosetron and dexamethasone and that's because clinical trials have shown that in a doublet regimen, palonosetron and dexamethasone is superior to the first generation 5-HT_3 receptor antagonists and dexamethasone. When you add the NK_1, we don't have information that one 5-HT_3 receptor antagonist is better than the other, we're adding a new class of drug.



Probably I would use a combination and I would still use palonosetron because it's long-acting—palonosetron, an NK_1 antagonist, and dexamethasone in this particular case. However, one could use a NEPA as an alternative. Again, a fixed dose of netupitant and palenosetron. One could use rolapitant or fosaprepitant or aprepitant as the NK_1 antagonist or one could use olanzapine instead of the NK_1.

In my own practice, I'm using olanzapine in 2 instances. One: to add on if a patient does have breakthrough in a previous cycle, even though I've given a 3-drug regimen or, now, with the publication of a randomized trial of 4 drugs vs 3, I think there will be some movement in patients who we think are at very high risk who are receiving AC who are getting a 3-drug regimen. This would be the patient, Sally, that you mentioned. So young, female patients, with a history of hyperemesis in pregnancy or carsickness, those are the patients I'm definitely going to give a 4-drug prophylactic regimen to in the future.

Let's say that Dennis experienced CINV during his first round of chemotherapy, even though we gave a regimen. What would you do in the next round, Sally?

Dr. Barbour: Again, I think we have several different options so it would depend on what we gave in the first round as to how we might change things for subsequent cycles of chemotherapy. Again, I go back to "It's important to talk to the patient." When did they have nausea and vomiting? Was it the day of chemotherapy? Was it 3 days after? Understanding what were they given to take on a scheduled basis and/or on an as-needed basis with his chemotherapy? Did he take it?

Sometimes people just knee-jerk call in a prescription for something. I think it's important to make sure we talk to Dennis or whoever the patient may be and find out exactly what they experience, when they experienced and what drugs they had and whether or not they took them.

If Dennis had been given 5-HT_3 antagonist plus dexamethasone and had delayed emesis despite that, as you sort of alluded to, there are several different options. One: adding an NK_1 antagonist. That's typically what would happen here at our practice. We would add that if we hadn't added it already, looking at if they had taken breakthrough medication and if it had or hadn't worked, making a change there. You alluded to adding olanzapine if an NK_1 antagonist had already been on board, adding a drug.

I think the important thing is to add drugs that have a different mechanism of action. Sometimes folks have a tendency to just want to give more of what they've already given and, usually, the doses that they've been given at we know are doses where they're maximally effective so just giving more doesn't really help. Real important to make sure that you're looking at all the different drugs. The dopamine antagonist, other drugs that are available, that might offer some benefit because they have a different mechanism of action.

I think there's a lot of options. Again, just in this case, if he had just gotten a 5-HT_3 antagonist and dexamethasone we would probably add an NK_1 antagonist. If he had prolonged, delayed emesis, we might extend the dexamethasone a little bit. I think there's a couple of different options.

Dr. Schwartzberg: Great. I agree completely. Can you comment on some of the other kinds of situations that we deal with frequently in our clinics? Multi-day chemotherapy and how do you use antiemetics there? Increasingly we're seeing new oral medications, some of which are at least moderately emetogenic. How should we address these types of patients?

Dr. Barbour: Those are 2 situations that are probably some of our—in addition to just nausea—some of our bigger challenges because the guidelines might not address them or they address them with limited amount of data to support them. Specifically, with multi-day chemotherapy, still the basic tenets of prevention of nausea and vomiting would prevail here. Making sure that each day of a multi-day chemotherapy, whether it's 3 days or 5 days, that the patient is receiving prophylactic antiemetics that match the emetogenicity of the agent they're given. But, also, what complicates this is that often times, or sometimes, patients are getting chemotherapy drugs that have a delayed emesis component with drugs that might be low emetogenicity but there's delayed on top of it. It's trying to predict and manage the acute, and the delayed, when they're overlapping each other.

Again, making sure that they're receiving antiemetics on the days of chemotherapy that match that risk and really looking at the other risk factors. Really, in this case, it *is* important to look at all the chemotherapy and what days they're getting it and matching it to that. Then, I think, usually, although not all the time, but you're seeing patients, whether they're inpatient or outpatient, you're seeing them every day that they're getting this chemotherapy. I think it goes back to the importance of continual reassessment. If you have a patient that, let's say, is getting cisplatin and cisplatin and etoposide for 5 days, having the infusion nurse check in with them on day 2 and day 3, "Are you having any issues?" so that you can make changes and address it while they're there.

I know that the guidelines address this but they're not specific recommendations and that's because the guidelines are based off of studies that looked at single-day chemotherapy being administered on one day so we just don't have a lot of the data. That's how we approach multi-day chemotherapy.

Oral chemotherapy is another challenge. Obviously there's been a significant growth in the utilization of these agents in a variety of different tumor types. In general, I would say most of them fall into the lower category but, again, there are those that fall into a more moderate and patients do need something prophylactically. It's hard because often times patients are taking these drugs every day, sometimes twice a day.

At least the NCCN guidelines have tried to address and categorize these drugs into 2 categories of low-to-minimal where you could just make sure they have something to use as needed. Then, drugs like crizotinib and some of the other drugs that are more moderately emetogenic. At least, in those instances, we'll have patients take something prophylactically and then sort of see how it goes because sometimes it causes nausea when they begin to take it but then it will sometimes ease off a little bit.

That's been our approach. What are your thoughts on those 2 scenarios?

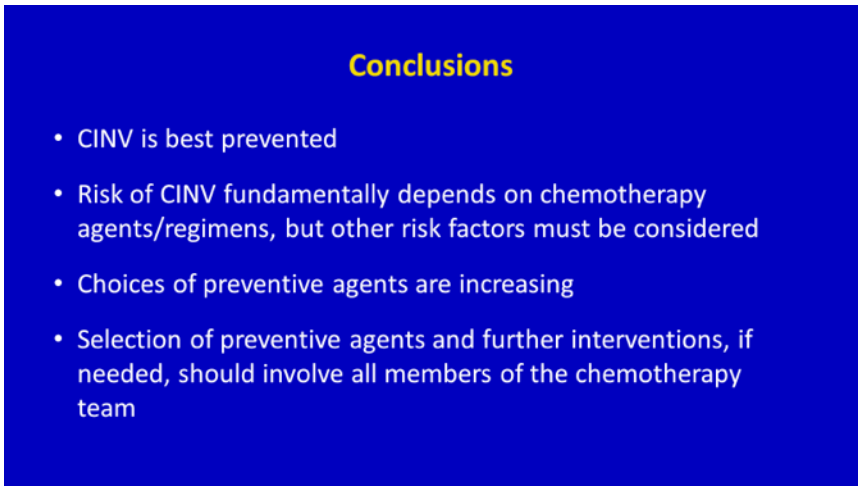
Dr. Schwartzberg: No, I agree. I agree completely and I think the orals still need to be worked out, but you're right, there's only a few drugs that are moderately emetogenic and sometimes giving a 5-HT_3 orally and then to use as needed after the first few days and see what happens I think is exactly the right strategy.

Dr. Barbour: Another scenario: a lot of times patients are also getting concurrent radiation with chemotherapy. Do you have a different approach or what is your approach to manage nausea in patients who might be getting concurrent radiation with their chemotherapy?

Dr. Schwartzberg: This is another area where there's not as much data as we would like. We do know that radiation by itself can be characterized for its emetogenicity based on where you're irradiating. The higher abdominal tends to have a higher risk of getting nausea and vomiting. No surprise because the GI tract is in that. Less so for thoracic radiation and pelvic radiation per se, although pelvic itself still does have a risk. Total body radiation, which is used predominately in bone marrow transplant, has a very high risk of nausea and vomiting. That's sort of the baseline and then, if you add on the chemotherapy, we'd use the same principles as we would for chemotherapy.

In gynecologic patients there is frequently a weekly cisplatin dose added to radiation and those patients may be at extremely high risk, highly emetogenic risk between their radiation and their chemo and there's been some recent work which suggests that a triplet regimen given weekly, NK_1, $5\text{-}HT_3$, and dexamethasone, can help alleviate the chronic nausea and vomiting that occurs over a 5-to-6 week period of combined chemoradiation. We hope to see more around that, but I've gotten more aggressive in my antiemesis approach for patients who are receiving that kind of treatment, because of the data now.

We've had a nice discussion and I think we can wrap up now with a few conclusions. Number one, the most important point: What we'd like to do with CINV is prevent it, not have to treat it and we're talking about giving prophylaxis before the first cycle and every cycle of chemotherapy based on the degree of emetogenicity of the regimen and the patient risk factors.



The choices of preventive agents are increasing. We have new drugs that have been approved over the last couple of years. We have the old stalwarts over the last couple of decades which have fundamentally changed our approach and the chance of a patient getting nausea and vomiting, although it's not always recognized out in the community that we've done much better than we did before.

The selection of preventive agents and any further intervention, if needed, should absolutely involve all members of the team. The multidisciplinary team is the way we treat patients today. Every member has great value in adding to that team. Pharmacists in particular, when it comes to CINV, are invaluable from many dimensions in terms of patient interactions and also helping manage interactions between the drugs that patients take.

I think it's fair to say we're optimistic that we're making progress, year over year now, in terms of preventing CINV and our ultimate goal is, hopefully, at hand.

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