Meet The Professors:

Oncologist and Nurse Investigators Consult on Challenging Cases of Actual Patients

Proceedings from a Four-Part Satellite Symposia Series Hosted in Conjunction with the 2010 Oncology Nursing Society Annual Congress

LUNG CANCER

INTERVIEW OF ANN CULKIN, RN, OCN BY AVIVA ASNIS-ALIBOZEK, PA-C, MPAS

EGFR TARGETED THERAPY IN NSCLC

MS ASNIS-ALIBOZEK: The first question asks about your approach to the use of erlotinib for patients with NSCLC.

MS CULKIN: We use erlotinib in the event that the patient's diagnostic molecular pathology has revealed that they have an exon deletion. Only in that setting – if they test positive for an EGFR mutation – do we recommend erlotinib.

MS ASNIS-ALIBOZEK: More specifically, do you administer erlotinib as front-line therapy, or do you generally use chemotherapy and then deliver erlotinib maintenance?

MS CULKIN: We have used it both ways. What we have found most beneficial is starting it up front as first-line therapy. In the event that they have an acquired resistance or the patient experiences disease progression, then we never stop the erlotinib. We would just add chemotherapy to the mix.

MS ASNIS-ALIBOZEK: So in answer to another question, the only situation in which you would utilize erlotinib in the maintenance setting is for patients who harbor a mutation?

MS CULKIN: That's correct. There is evidence that for patients who don't have a mutation, the likelihood of erlotinib providing a benefit is less than one percent.

MS ASNIS-ALIBOZEK: Can you explain why patients with EGFR mutated non-small cell lung cancer who are responding to erlotinib suddenly develop resistance?

MS CULKIN: We have not been able to figure that out. What we are looking at is rebiopsying those patients to study the molecular pathology of the tumor. We are also identifying additional mutations. For instance, T790M is a common mutation found in patients who experience disease progression while on erlotinib therapy.

MS ASNIS-ALIBOZEK: Will patients subsequently respond to any other targeted therapy after that?

MS CULKIN: Currently, there are no approved second-line EGFR TKI inhibitor therapies available.

MS ASNIS-ALIBOZEK: Next, would you compare for our audience members the two first-generation EGFR inhibitors gefitinib and erlotinib?

MS CULKIN: Gefitinib was actually the first identified targeted therapy available in the United States. However, it is no longer available in the US based on favorable clinical trial results for erlotinib, though the agents were not compared head to head in the US. Gefitinib is still available in Europe.

MS ASNIS-ALIBOZEK: One question was whether you expect gefitinib to return as a treatment option in the US.

MS CULKIN: There are several ongoing clinical trials, so my answer would be, yes, there's hope for the future of gefitinib in the United States.

MS ASNIS-ALIBOZEK: Can you give any advice to physicians on educating both patients and other medical professionals in terms of making EGFR testing standard practice?

MS CULKIN: I'd have to quote Dr Love, "The issue is the tissue." It's all about obtaining a biopsy – so at the time of diagnosis, when patients are going for biopsy, to get enough tissue that can be studied for both a diagnosis of a cancer as well as evaluating the molecular pathology of the cancer. Traditionally, we

have been accustomed to fine needle aspirations or bronchial washings, which give you enough for a diagnosis, but that's not enough tissue to really look at the molecular profile of the tumor.

So core biopsy should definitely be the recommended standard of practice for obtaining tissue and making accurate diagnosis.

EGFR MUTATIONS AND ERCC1 TESTING AS PREDICTORS OF RESPONSE TO CHEMOTHERAPY

MS ASNIS-ALIBOZEK: Our next question is, what specifically about EGFR testing is clinically important?

MS CULKIN: If the molecular pathology indicates a patient has an EGFR mutation, then that opens your possibilities to more treatment options, particularly those of targeted therapy of first-line treatment.

MS ASNIS-ALIBOZEK: In your practice, are all patients tested for the EGFR mutation?

MS CULKIN: At Memorial Sloan-Kettering, have what we call "reflex testing." At the time of surgery or biopsy, any patient with adenocarcinoma automatically has a tumor specimen sent directly to molecular pathology. It is part of the standard of care.

MS ASNIS-ALIBOZEK: Does EGFR testing impact the use of cetuximab?

MS CULKIN: It does not. EGFR testing does not impact the use of cetuximab.

MS ASNIS-ALIBOZEK: So EGFR mutations have not been shown to predict the benefit of cetuximab, similar to the way that they predict a benefit of erlotinib in lung cancer?

MS CULKIN: That's correct. Yes.

MS ASNIS-ALIBOZEK: Next, can you explain what ERCC1 is and how it is used in lung cancer?

MS CULKIN: ERCC1 is an immunohistochemistry diagnostic test that may determine the effectiveness of cisplatin in treatment of NSCLC. This diagnostic test is currently under FDA review.

We do not use it at Memorial, however, because it has not yet been approved as a diagnostic therapy to recommend intervention.

MANAGEMENT OF ERLOTINIB-INDUCED SKIN RASH

MS ASNIS-ALIBOZEK: Several audience members asked, is the skin rash with EGFR TKIs preventable?

MS CULKIN: No, it is a side effect of the medication. We utilize prophylactic treatment, which is a little bit different than preventative treatment. At the initiation of erlotinib therapy, we recommend that patients have an extensive teaching session where they learn about their skin and the importance of maintaining their skin. We teach patients about moisturizing the skin, because the first side effect of erlotinib is dry skin.

We also describe the potential rash that patients may experience with erlotinib therapy. The rash can occur between days 10 to 113 on treatment, presents itself as a pustular-looking rash, and usually starts on the face. If untreated, it can then spread throughout your body. Prophylactic treatments include administering antibiotics, typically one from the tetracycline family, such as minocycline or doxycycline.

MS ASNIS-ALIBOZEK: In addition, do you prescribe those treatments prophylactically before the rash, or do you give them as soon as the rash starts?

MS CULKIN: In our practice, we prescribe antibiotics as soon as a patient presents with rash. Dr Mario Lacouture is a big proponent of administering prophylactic prescriptions at the time of therapy initiation. Data from his STEPP trial were published last year, utilizing this approach for patients with metastatic colorectal cancer receiving panitumumab. This approach has not been studied directly for patients receiving erlotinib.

One of the main reasons we do not prescribe prophylactic antibiotics in our practice is we want to hear from patients if they get rash. We want to have them describe the rash, and we want to offer intervention. We ask if they are indeed taking the drug one hour before eating or two hours after eating. Are they compliant in the dosing of the drug? So there's a double-back checklist, if you will, to ensure patient adherence. Based on their symptoms, we intervene. After we assess and grade the rash, patients begin oral antibiotics and also receive one of a number of topical creams to treat the rash.

Another facet we are on the lookout for is superimposed skin infections. So we're very concerned about patients with diabetes or patients who are receiving other medications that can cause rash. That's another aspect we will review with the patient if they develop rash.

PATIENT EDUCATION ABOUT SMOKING CESSATION

MS ASNIS-ALIBOZEK: A lot of questions arose about dealing with patients who are both receiving treatment and still smoking. What is your approach here?

MS CULKIN: We always ask patients at initial assessment and at every visit about their smoking history, even in the never smoker and the former smoker. If a patient continues to smoke, we offer them smoking cessation.

Many patients have already been through a smoking cessation program, not specifically at Memorial Sloan-Kettering but in the community or even online. But it's always offered to support patients to stop smoking, and we do inform patients that they will live longer if they stop smoking.

PSYCHOSOCIAL SUPPORT FOR PATIENTS WITH NEWLY DIAGNOSED LUNG CANCER

MS ASNIS-ALIBOZEK: Can you give our audience an example of what you tell patients who are diagnosed with lung cancer, even though they are nonsmokers and may have never been exposed to smoke?

MS CULKIN: We perform an extensive history and discuss their genetic heritage and possible exposures they may have encountered, particularly that to second-hand smoke and radon, although we can never clearly tell them that that is the cause of their lung cancer.

There's so much of a psychosocial support for people in understanding how they got this disease because of its association with smoking. It's difficult to come to that place of understanding for the never smoker. More than 20,000 people will be diagnosed with lung cancer this year who've never smoked.

MS ASNIS-ALIBOZEK: Another audience member asked whether you discuss some of the new research relating to somatic mutations when you're getting into that discussion.

MS CULKIN: We do. The pendulum is now swinging, in that every patient with lung cancer, whether they've smoked or not, should be tested for an EGFR mutation because of the recent IPASS data. Also, in retrospective tissue analysis you see that former smokers, even limited smokers, people who smoked in college and then haven't smoked in 30 years, can potentially have the mutation.

HYPERTROPHIC PULMONARY OSTEOARTHROPATHY (HPOA)

MS ASNIS-ALIBOZEK: The next viewer question relates to HPOA. What are its specific signs and symptoms?

MS CULKIN: HPOA is an inflammatory response, also described as a type of paraneoplastic syndrome, which is a group of symptoms due to substances released by a tumor. It's diagnosed based on symptoms and clinical exam. The signs and symptoms are pain, but pain in the long bones of your body is the usual presentation, and this feeling of a flulike symptom of just achiness and pain. Sometimes joints swell. Some patients have difficulty walking because of the pain.

Blood samples from a number of patients have been evaluated in an attempt to identify some specific marker to potentially explain why some patients develop HPOA.

MS ASNIS-ALIBOZEK: In addition, how frequently does HPOA occur?

MS CULKIN: It's rare. Only a small percentage of patients present with HPOA. It's treated with nonsteroidal anti-inflammatory drugs and treating the cancer. Effective cancer treatment actually treats the HPOA.

MANAGEMENT OF BEVACIZUMAB-ASSOCIATED HYPERTENSION

MS ASNIS-ALIBOZEK: One question that arose was this: In a patient receiving bevacizumab who develops treatment-related hypertension, who should manage the hypertension: a cardiologist or an oncologist?

MS CULKIN: It depends on the patient. In a center like Memorial Sloan-Kettering, where nobody lives in the neighborhood, so to speak, many patients travel in to the center for their treatment. Yet they have internists and cardiologists who they've known for many years prior to meeting an oncologist, so we actually collaborate with them. So there's no exclusive answer. Sometimes the oncologist will take care of the hypertension as well.

That being said, if a patient comes with a prior history of hypertension, we consider that in deciding whether to place the patient on bevacizumab therapy, although an underlying diagnosis of hypertension does not exclude patients from receiving bevacizumab. Their hypertension has to be well controlled with medication and compliance.

If a patient develops hypertension while on bevacizumab, intervention is on an individualized care basis. We either assume the care of hypertension management, or we ask the patient to be followed by their local internist or cardiologist.

MS ASNIS-ALIBOZEK: Would you explain why bevacizumab can cause elevation in blood pressure?

MS CULKIN: Bevacizumab alters the blood flow inside the tumor but also other cells of the body as well. Therefore, hypertension is a potential side effect.

MS ASNIS-ALIBOZEK: Are there any known comorbidities that increase the risk for pulmonary hemorrhage?

MS CULKIN: Patients with squamous cell lung cancer are more at risk for pulmonary hemorrhage if their tumor is centrally located. A central tumor is the description of the location of where the cancer is in the chest, and a central tumor would be closer to the sternum of the body and higher up in the lung. Because squamous cell tumors are more vascular, they have more blood flow going through them.

There are no known comorbidities that increase the risk for pulmonary hemorrhage. If a patient is receiving an agent such as a blood thinner or has a history of prior use of warfarin, that could potentially cause bleeding, but it's not a real comorbid condition for pulmonary hemorrhage.

CONTRAINDICATIONS FOR BEVACIZUMAB USE

MS ASNIS-ALIBOZEK: One of the more basic questions was, which patients are not candidates for bevacizumab?

MS CULKIN: Bevacizumab is contraindicated in patients who've had a prior cardiac event, most recently an MI in the last five years. We do not recommend bevacizumab for patients with stents in their heart or for patients with uncontrolled hypertension.

Bevacizumab is also contraindicated in patients with a diagnosis of adenocarcinoma and a centrally located tumor and in patients who have recently undergone surgery and have an open wound that has not yet healed.

PALLIATIVE CARE FOR PATIENTS WITH LUNG CANCER

MS ASNIS-ALIBOZEK: Many physicians asked specifically how to maintain hope when making a palliative care consult in a patient with lung cancer.

MS CULKIN: Reassurance for the patient and defining best supportive care and/or palliative care are important. We provide the support of a multidisciplinary group to (1) preserve patient dignity and (2) address the patient's symptoms and ensure that they will not suffer from breathlessness and pain, which are the main issues from lung cancer at end of life.

We also address the psychosocial side of the end-of-life trajectory of lung cancer. This can involve a team from specified oncology nurses, perhaps a hospice, in addition to chaplaincy and social work to support the patient and their family at this time.

How do you maintain hope? Hope changes throughout the diagnosis of lung cancer. In the beginning, you hope the scan is going to be okay. When patients are first diagnosed with lung cancer, the hope is that treatment will work. The other part of that hope is that you will live a long time.

So there's hope that is defined throughout the trajectory of the illness. At the end of life, the hope is that you're not alone, that you have achieved all that you wanted to achieve and that you will not suffer at the end of life.