Challenges of Managing Frail and Elderly Patients with Lung Cancer, Part 2: Locally Advanced Non-Small Cell Lung Cancer

with Drs. Paul J. Hesketh & Karen Kelly

Dr. West: Hello, and welcome everyone; my name is Jack West. I'm a Medical Oncologist and the President and CEO of GRACE, the Global Resource for Advancing Cancer Education.

I'm happy to be here with two great colleagues of mine from other parts of the country to talk about challenges of treating elderly and frail patients with lung cancer.

With me today are Dr. Paul Hesketh, who's a Medical Oncologist, and Director of Thoracic Oncology at the Lahey Clinic just outside of Boston in Burlington, Massachusetts; and also Dr. Karen Kelly from Kansas University Medical Center in Kansas City. She is a medical oncologist with an internationally recognized expertise in lung cancer.

Here are the declared conflicts of interest for each of us on the program.

This activity is made possible through an educational grant from OSI Pharmaceuticals, who provided no input into its content.

We're going to cover several cases that highlight the challenges of treating lung cancer in a frail, often elderly patient population.

Let's move on to an elderly patient with locally advanced non small cell. This is an 82-year-old Asian woman with a very significant smoking history; 60 pack years and quit last year. And she noticed that she had lost about 10 pounds over the preceding 3 to 4 months and when she saw her doctor that lead to a chest x-ray and a CT scan that was abnormal. Her performance status was still good, a little limited by shortness of breath, but she didn't have any cough and wasn't coughing up blood.

She goes for walks daily; she can climb stairs perhaps one flight. She lives with a daughter and she has pretty minimal past medical history; essentially just high blood pressure.

She ended up having a chest x-ray and a CT scan that showed a clear PET-avid mass [error here; should have said PET scan rather than CT], again in her right lower lobe. She also has a great deal of nodal involvement; pretty bulky disease in her mediastinum in her mid chest.

She saw a pulmonologist and underwent bronchoscopy and endobronchial ultrasound; and that showed squamous cell, non-small cell from the mass itself, in the primary tumor, and a station 7 node below the carina, the splitting point of the airway -- the main airway. She had a head MRI that didn't show any

evidence of spread to the brain, and so her overall stage was IIIA, with bulky mediastinum disease; and with that extent of disease I would say that our surgeons would not have been at all inclined to consider surgery.

But in somebody who has potentially curable, locally advanced disease, but in this case is 82, how would you approach such a case, Paul? Can we speak from the standpoint of any data, or how would you think about this in terms of concurrent versus sequential, and what kind of chemo regimen you might consider?

Dr. Hesketh: Well, I think the age does factor in our considerations here because again we're not talking about a single modality, but we're talking about potentially using two modalities at once, which we know in any age population is going to be a potentially very toxic therapy that's fraught with difficulties. I think that the problem again is if you look at the studies, I think the data is kind of all over the place and a bit conflicting. I think some studies show that there's an excess of toxicity and a complete lack of any survival benefit using concurrent chemotherapy and radiation versus the single modalities. Others show that perhaps doing it is feasible, and it seems to have benefit. And I think other studies basically show that there is increased toxicity but there is some benefit.

So the studies, unfortunately, are all over the place, and I think that in my own situation, I am concerned if I have a patient who has quite frankly moved beyond 80 years of age. I think that it's not magic, and obviously you still have to look at the individual, but in my own experience, I have found it to be much more challenging to try to give concurrent chemo/radiation to patients who are in their 80s. And I think that in general, as a general rule -- there may be exceptions -- but as a general rule I usually do not give concurrent chemo/radiation to patients that are in their 80s because there's no real good data out there to help support me in that. And based upon my own personal experience, we've run into significant difficulties with some of those patients. So, in general, even though this patient may be interested in aggressive therapy, things that would make me worry about her would be, first of all we don't know about her pulmonary function. She has had an extensive, a significant amount of weight loss greater than probably 5% of her total body weight, and she has an extensive smoking history. So I think I would be very leery in this particular individual of giving a standard kind of concurrent radiation approach.

Dr. West: Karen, what's your approach? Do you give concurrent to patients across the age spectrum, or is there an age where you think that it may be a contraindication?

Dr. Kelly: Well I think that certainly I try not to let age alone make that decision, but I think that when you do get to 80, I do think you have to use more caution.

Now, in the CALGB trial of the weekly Taxol/carbo with radiation vs. the induction followed by the weekly carbo/Taxol with radiation, they did do a subset analysis of looking at a different prognostic group, and when they used factors like weight loss greater than or equal to 5%, or age over 70, performance status 1 or hemoglobin, if you had two or more of those factors, you did very poor in either arm. So just Taxol/carboplatin weekly with radiation, medium survival of nine months versus eighteen if you only had one; and had those ratios up about 1.8

for that poor group, so this patient has not only the age issue I think as Paul pointed out, that weight loss is a significant issue. Her performance status of 1 is in our book good, but it's not zero. I think her smoking history -- I think that this is someone really that I would be hesitant to give concurrent chemo/radiation. And typically sometimes I do refer to a weekly Taxol-carboplatin with radiation, but I would be a little leery of that even in this particular patient.

Dr. West: At our institution we have been really been disinclined to pursue a concurrent approach beyond about 79-80, and there aren't any hard and fast rules, but there is an escalating concern about it. Even in younger patients concurrent chemo radiation we know that there is a lot of potential toxicity and even death from our treatment. It's never trivial to do this kind of approach, multi-modality, in stage III in fit patients and younger patients; and I think there's certainly a lot more potential to run aground as you run up the age and performance status issues, and we just don't have good data to address that, because the studies really haven't been done.

I don't know if you have any standard regimen that you generally pursue in either poor performance status or the very elderly, or is it a completely individualized approach based on the person in front of you? Paul?

Dr. Hesketh: I think it's individualized. And I think that in this particular patient, I think you could make a case to start with a chemotherapy regimen, and in terms of what regimen to consider, the patient has a squamous cell histology so you'd be inclined to consider a gemcitabine inclusion, but if there's the potential that you're going to move on to radiation in sequential fashion, I think I'd be a little leery of starting with gemcitabine. So I think a regimen that probably would be reasonable would be a carboplatin with paclitaxel regimen to start. See how the patient tolerates that, if they have reasonable tolerance, and seem to have some reasonable benefit, then I might consider consolidating with radiation therapy in sequential fashion. It would entirely depend on how they do with that initial treatment. I definitely will individualize based upon what I think the patient is likely to tolerate.

So if the renal function is not bad and at the other end organ function is not bad, I think a carboplatin with paclitaxel regimen might be a reasonable way to start in this particular individual.

Dr. West: Karen, I believe you use cisplatin and etoposide for your best performance for patients, but not for everybody probably.

Dr. Kelly: No again, I do use Taxol-carboplatin in this particular situation, but I do want to bring up a point.

I think that one could also, and I struggle with this, about whether you should give the chemo first or the radiation first. I was looking back to see if she was symptomatic in her chest, and I'm not seeing that she was. Sometimes when patients are symptomatic in their chest, I'll do the radiation first and then do the chemotherapy, to help the symptoms like cough, hemoptysis, pain, now she doesn't have that, so I think certainly starting with chemotherapy is reasonable. But one could think about starting with radiation.

Dr. West: And that's actually been my general inclination, certainly from treating symptoms but also that in fact when you look historically, radiation was the first cornerstone and then the chemo was added on. I kind of think of it in terms of what would be the more important modality to try to get in here. I think that a patient with bulky locally advanced disease may get more benefit from the radiation than the chemotherapy frankly.

Dr. Hesketh: That's a reasonable approach certainly. Particularly if the patient has any symptoms or if you think they're likely to get into trouble with an impending airway obstruction or some issue or certainly any degree of hemoptysis, then you know you're going to get more bang for your buck locally with the radiotherapy, as opposed to systemic treatment.

Dr. West: And then there's a lot of open questions about the potential role of consolidation therapy after somebody gets through chemo and radiation, and if she were to come to you for a second opinion after she had received weekly carboplatin and paclitaxel with radiation, and she navigated through that and still had a pretty good performance status; would you be inclined to recommend additional chemotherapy, or would you be happy with what she had received? Paul?

Dr. Hesketh: Well I think to be honest with you, if I got through that and she had a full course of radiotherapy and got the concurrent chemotherapy, I mean that's a yeoman's job to be able to do that, and as you know right know the data that's out there is not strongly supportive of consolidative chemotherapy after receiving concurrent chemo radiation. I think we all feel somewhat inadequate, however, when we often just give perhaps two cycles of chemotherapy if it's the cisplatin/etoposide regimen or weekly chemotherapy if we're using carbloplatin/paclitaxel. I think most of us feel like, "is that all there is and should we be doing something more?" I've certainly done that on a case by case basis. I think I might in this situation maybe pushing my luck if I got the person through both chemotherapy and concurrent radiation based upon the data where it is and based upon the patient's age and some concerns about toxicity, I think I might just say "Congratulations! We've done a great job here and we're going to follow you very closely."

Dr. West: Karen, what are your thoughts?

Dr. Kelly: I do think that we don't really have sufficient data at this time to say that consolidation therapy is warranted, and I do try to stick with just the chemo/radiation, but it is individualized. And the other thing that I try to utilize to help me and guide me, because of course you do worry a lot about these patients, is what does their PET scan or CT/PET look like two months later? I think it would still be reasonable to do consolidation therapy. So I do take that into consideration, and what their scans look like and how they're feeling, and if they're still symptomatic, then I think that I probably would recommend further treatment if they're still having symptoms. So I think the point is that it's very individualized, and I try to use other tools to help me at lease feel confident in further recommendations.