

Challenging Cases in Lung Cancer: Unresectable Stage IIIB NSCLC and Consolidation Therapy

Dr. West:

Hello and welcome. My name is Dr. Jack West, and I'm a medical oncologist and the Founder and CEO of GRACE, the Global Resource for Advancing Cancer Education. Our program today is made possible through generous support from the LUNGeivity Foundation.

This is part of a series of podcasts covering challenging clinical cases in lung cancer that don't have a clear correct answer for the best treatment based on the evidence, and they therefore require our best judgment as experts consider the options and the merits of one approach over another.

The same series of cases was discussed with multiple experts in the field of lung cancer from several different institutions to provide a better sense of where there is consensus and where there is still a wide range of treatment styles that might all be considered appropriate.

Each podcast starts with a brief thumbnail of a case presentation and then discussion from a live program done with Dr. Robert Doebele, Assistant Professor of Medical Oncology at the University of Colorado Medical Center in Denver, and Dr. Jyoti Patel, Associate Professor of Medical Oncology at the Feinberg School of Medicine at Northwestern University in Chicago.

The discussions will then continue with commentary by the several other clinical experts, including:

- Dr. Suresh Ramalingam, from Winship Cancer Center, Emory University in Atlanta, GA,
- Dr. Jonathan Goldman, from Premier Oncology in Santa Monica, CA.
- Dr. Julie Brahmer, from Sydney Kimmel Cancer Center at Johns Hopkins University, in Baltimore, MD
- Dr. Heather Wakelee, from Stanford University Cancer Center in Palo Alto, CA
- Dr. Karen Reckamp, from City of Hope Cancer Center in Duarte, CA

Right. Moving on, we'll turn to unresectable disease. This is a 59 year old woman with an excellent performance status. She has unresectable Stage IIIB non-small cell lung cancer, poorly differentiated with some features of adenocarcinoma. She starts on a course of cisplatin and etoposide for two cycles along with radiation therapy to a definitive dose of 64 grey. At the end of that, she's tolerated it well. She undergoes a repeat CT scan that shows a partial response but some residual findings that are ambiguous, as is often the case.

It's not clear whether this is responding disease, which may be dying and non-viable scar tissue, or whether there is viable cancer within that. Her performance status is good, and she's interested in the chemo or some other systemic therapy at this point, but really open minded to the question.

So I'll turn to you, Jyoti, about whether you would recommend any consolidation therapy? Any further treatment after she's completed a couple of cycles of good systemic therapy with concurrent radiation?

Dr. Patel:

This is such a common scenario, and it's so difficult because we generally, or I at least, generally do a CT scan about four weeks after patients finish chemotherapy and radiation. I sort of set that CT up with telling patients that this is not to assess response, because we know that we continue to see a response at three to four months out. But this is really to look for toxicity. We get that CT scan and often the nodes are smaller, but they certainly haven't gone away and they are difficult to interpret.

I especially don't know what to do if someone brings a PET scan to me from another institution or another oncologist, because that will even cloud the picture more. Are we seeing necrosis or are we seeing a recurring tumor? I don't know. If patients are feeling well and they've done quite well with chemo-radiation, my bias has been to continue with consolidation therapy. So I generally give an additional two cycles or cisplatin/etoposide.

Several years ago I would've given docetaxel, but we have good data from Nasser Hanna and his Hoosier Oncology Group study that this doesn't improve survival, and patients get into toxicity. I'm not sure if that's because of some of the pneumonitis issues, certainly we saw a lot more neutropenia in those patients, who didn't have growth factor support. I tend to do more cisplatin/etoposide again: I'll just do two more cycles. By the time you're done with that, patients have gotten a hefty dose of cisplatin: 400 milligrams total (per meter squared). By that time, they are generally willing to stop. I have not changed therapy very often. So if patients are getting cisplatin/etoposide before we know the JMIG trial, which is a phase III trial looking at cisplatin and pemetrexed followed by more pemetrexed versus cisplatin/etoposide. In that trial, the FDA actually mandated different regimens, cisplatin/vinorelbine, or carboplatin/taxol. I haven't done that as much, but I think that would be reasonable as well.

Dr. West:

Bob, what are your thoughts here?

Dr. Doebele:

I would echo what Jyoti is saying in that, first of all, I try to educate the patients from the beginning that the scans that we do after therapy are not going to inform us on whether we've gotten a long term control of the disease. It can tell us whether it's failed, but it rarely tells us if we succeed. Only time will tell us that. That is something that is difficult. If you tell patients up front, it helps to ease the anxiety later. I would agree that I only do CT scans early and reserve PET/CTs to evaluate findings that may be related to both on their own or other distant recurrence because PET/CTs are very difficult and can be misleading in both directions with both false-positive and false-negative changes in the PET activity after chemo-radiation. So I try to avoid that unless I'm looking for something outside the radiation field.

The HOG data has given me pause in consolidation chemo, also along with the CALGB, where there was not a significantly different outcome in patients who received additional rounds of a different chemotherapy, granted. So, carboplatin/ paclitaxel. I'm not convinced that additional cycles of chemotherapy before or after are going to improve outcomes.

So I would most often do two round of cisplatin/etoposide with chemo-radiation. I'm open to doing more cycles. But I'm not sure that the evidence supports a necessarily better outcome.

Dr. West:

That's an uneasy time I think for all of us, because we don't have evidence of more being better but it's hard to sit tight with just two cycles and knowing that the risk of reoccurrence is very significant, but we just don't have evidence to show that we can make that better by giving more. And we have the potential to make things worse by having toxicity more than efficacy. Yet, we're still left using largely judgment, I think.

Dr. Patel:

One thing to bring up with this case though is, this is a patient with an adenocarcinoma. One of her greatest risks of reoccurrence is in her brain. And so, I think a few years ago there was feeling that maybe these patients should get prophylactic cranial irradiation. There's been a study that's presented that's negative. That it's under accrued. My sense, my feeling is that patients should not get PCI in this situation. But I don't think it's a completely closed question.

Dr. Suresh Ramalingam, Winship Cancer Center, Emory University, Atlanta, GA:

I think the SWOG (*sic*) study that looked at consolidation docetaxel clearly showed that giving 3 cycles of docetaxel in the post-chemo/RT setting did not lead to a favorable outcome – that has really changed my view of how I approach consolidation therapy. For patients who get initial treatment with cis/etoposide and radiation, that alone remains the standard of care. There is no clear proof that giving two more cycles of either same cis/etoposide or any other chemotherapy or a targeted therapy actually results in improved survival. For this particular patient, with the regimen she got, I think this is adequate therapy.

She is still at high likelihood of having recurrent disease, but there is no evidence that doing something more is going to alter that.

If a patient receives the carboplatin/paclitaxel chemosensitizing regimen with radiation, those patients I am inclined to give them two cycles of systemic doses of carboplatin/paclitaxel in the consolidation setting, as was done in the major studies with this particular regimen.

So that's my approach to stage IIIB disease after completion of chemo/radiation.

Dr. West

And I presume you're not especially inclined to pursue prophylactic cranial irradiation in this setting?

Dr. Ramalingam

No, we do not routinely do prophylactic cranial irradiation. I am aware of the RTOG trial that was reported last year that suggested, even though the trial was closed for slow accrual, there were some trends that indicated benefit, but clearly this an area where we don't have good evidence to give this to all patients.

Dr. Jonathan Goldman, Premier Oncology, Santa Monica, CA:

As you know there's no evidence that anything further would improve her outcome. But, from lower risk disease we think that at least four cycles of chemo is necessary. I guess probably the only thing that is clear is that docetaxol as a switch, or Taxotere, doesn't make a significant benefit. In the end, I usually give two more cycles of the same chemotherapy.

Dr. West:

Even though we don't have evidence, it still doesn't sit well with most of us.

Dr. Goldman:

Right. Because we know that the metastatic disease is a significant issue, micrometastatic disease more specifically. We don't think we could give her enough chemo for that.

Dr. Julie Brahmer, Sydney Kimmel Cancer Center, Johns Hopkins University, Baltimore, MD:

Good question. If there is a question of residual disease, I usually will consider consolidation chemotherapy and I'll still stick with the cisplatin and either combine that with Taxotere or even potentially Alimta or even gemcitabine, depending on the patient and what subtype of tumor that they have. If there is really no evidence of residual disease, I don't. So, again the most recent studies say cisplatin/etoposide/radiation, you're done with the treatment and you should do just as well as compared with just chemotherapy afterwards. But I don't think anybody has really looked at the cisplatin regimes after the radiation with the cisplatin and etoposide.

Dr. West:

I think it's hard, because it's not like we've achieved such phenomenal results. So it's hard to rest on our laurels here, and I don't think anyone is really satisfied with that yet we don't have evidence for anything beyond it.

Dr. Brahmer:

Right and it's a long conversation that you have with the patient about the potential risk of the chemotherapy afterwards versus trying to get some type of benefit.

Dr. West:

Do you think the additional systemic therapy raises the risk of pneumonitis?

Dr. Brahmer:

Yes it does. A lot of the chemotherapy that we have can cause pneumonitis on its own. Then on top of radiation it might increase that chance. We just don't have a whole lot of information about that. So that's why we pick the regimens pretty carefully.

Dr. Heather Wakelee, Stanford University Cancer Center, Palo Alto, CA:

I tend to give one or two more cycles of the same, of the cis-etoposide. I'll change the regime a little. I won't give the 50/50 of the Cis. I'll switch over to 75 on day one and then switch over the etoposide.

Dr. West:

Ok. Obviously, nobody has good data on this, but nobody is very happy stopping with two cycles.

Dr. Wakelee:

Right. There is some, but I'm not one of them.

Dr. Karen Reckamp, City of Hope Cancer Center, Duarte, CA

So generally, it depends on how she's feeling right now. Generally for patients that can tolerate the full cisplatin/etoposide the SWOG dosing of cisplatin and etoposide, I'm assuming that was weekly cisplatin for two weeks and one week of etoposide. So it's full dose and they get the two cycles. I tend not to give any more therapy based on the questionable efficacy of adding docetaxel after.

If I'm giving weekly carbo/Taxol, which would be the other regimen I use more frequently, then I would tend to give a consolidation -- two courses or three courses of chemo following, because they haven't received full doses of chemo. But if they get the full cisplatin/etoposide, I tend not to unless they really had no toxicities, which is pretty rare.

Dr. West:

Do you tend to favor the weekly carbo/paclitaxel based on a sense that it's essentially an equivalent outcome or just the feasibility of getting patients through this aggressive approach?

Dr. Reckamp:

I favor cisplatin/etoposide because again I think there is benefit to giving full-dose chemo while you're giving radiation because I think you're attacking micrometastatic disease and preventing metastatic disease from happening. But I think it's difficult to tolerate. So, if a person has more co-morbidities or poor performance status, I will tend to use the weekly carbo/Taxol, or questionable renal functioning. So that you can withhold a dose and it's a little more easy to give.

For curative intent, I still prefer to use cisplatin/etoposide.

Dr. West:

I hope that the program was helpful, and we'd also like to again thank the folks from LUNGeVity Foundation for their partnership on this program.