

Systemic Therapy of Lung Cancer: Chemotherapy (Video Transcript)

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Featuring:

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I'm Philip Hoffman. I'm in the Section of Hematology/Oncology in the Department of Medicine. I'm a medical oncologist. I think it's important to mention that you're hearing this evening from a surgeon, a radiation oncologist, and myself. And we don't work in a vacuum. We actually work reasonably well together as a team.

Most patients with lung cancer do require more than one modality of therapy as part of their overall treatment plan. We have conference every Wednesday morning where all of the groups get together and discuss patients that are under our care, who are being evaluated, so that we can get everybody's input in formulating a plan.

The other thing I want to mention, we have a special unexpected guest who'll be following me on the podium so stay tuned.

So I'm going to be talking about systematic therapy of lung cancer. My two preceding colleagues have spoken about local therapies of lung cancer. Surgery is a local form of therapy, because it treats what you're working on, and radiation is another local form, because it treats what you're aiming it at.

Systemic therapy indicates there's a medication going throughout the body trying to kill tumor cells, stop tumor cell growth wherever this medication encounters them. Now the usual method of systematic therapy in lung cancer certainly is chemotherapy. But we also have and I'll mention these what are called, small molecule inhibitors and Ng Genesis inhibitors. Ng Genesis is the method by which tumors make their small blood vessels and there are drugs now, which are aimed at that small blood vessel formation.

It's worth noting that in some other cancers, systematic therapies may include other types, such as breast and prostate cancer. And where we use hormonal therapy very commonly. They're pills generally, sometimes injections, but again they are drugs that go throughout the body to try to affect tumor cells. And finally, in a few situations we use immune modulators like interleukins and interferon in the treatment of some other types of cancers.

Now monoclonal antibodies--another form of systematic therapy--is directed against tumors, cells are very widely used in lymphoma, the drug rituxan, in particular in breast cancer the drug Herceptin, and in some patients with colon cancer namely Erbitux or cetuximab, they're just being evaluated in the treatment of lung cancer, and again cetuximab or Erbitux is the example that is now being at least tested in the management of lung cancer.

Now we use chemotherapy in lung cancer in a variety of ways. We can use adjuvant chemotherapy. Adjuvant implies that it's added on to something else. So adjuvant chemotherapy may be given for several months after surgery or radiation therapy with the idea that if there has been microscopic tumor cells spread that that's the best time to try to kill those cells and not allow them over time to develop into more overt metastases. So patients often think of it as a preventive therapy, because it's an effort to prevent recurrence.

Now we now very often use it in patients with non-small cell lung cancer after surgery, particularly in patients who have larger stage one cancers and stage two and stage three cancers. And we use several courses of chemotherapy usually using either cisplatin or carboplatin and the common regimens are cisplatin and vinorelbine or carboplatin paclitaxel. And there has been recent studies that suggest that this chemotherapy can increase the five year survival rate by as much as 10 or 12% in certain patient groups.

So there certainly is a role now for chemotherapy after surgery, particularly in that setting. We sometimes use it as neoadjuvant. Neoadjuvant implies that it's added on, but added on at the beginning. Neo means new, so it's added on. So it's given for a few months or months prior to the local therapy of surgery or radiation. And this is sometimes used for example in patients with stage three disease. Meaning that their tumor is locally advanced within the chest. The purpose of this therapy is to get systematic therapy into the patient early to try to address any microscopic spread that has occurred. As well as to try to shrink the tumor itself that's within the chest, because it may allow for an easier surgical approach. And it certainly may allow for an easier radiation approach, because if you could shrink the tumor early, the radiation oncologist has a smaller tumor volume to focus on and therefore, a smaller amount of normal lung tissue that might get radiated. So there's some potential value if we have effective neoadjuvant therapy. And as I say, this is commonly used in patients with stage three disease.

Now certainly we use chemotherapy very commonly in the treatment of advanced disease. And in this situation it's given in the hopes of shrinking tumors, inducing a period of remission and prolonging survival. In stage three patients, chemotherapy before or during radiation therapy has clearly been shown in many studies to improve the rate of remission and the duration of remission and survival prospects and even a cure rate for patients compared to having radiation by itself.

So chemotherapy clearly does add on. And when it's possible, we try to give it simultaneously with radiation. Sometimes that's too risky and we'll give it in a sequence. In stage four disease where there has been spread of tumor to other parts of the body, chemotherapy has been shown to improve symptoms, reduce pain, induce partial remissions, and to prolong survival in patients who are sufficiently well to receive it.

In non-small cell lung cancer, which is the majority of patients we see, chemotherapy usually is a two-drug regimen. It's usually a platin drug either cisplatin or carboplatin and a second drug. And the second drug is either Taxol, Taxotere, gemcitabine, or Navelbine. Now there are--if

a patient has first-line chemotherapy and then fails or if they fail to respond to the initial therapy-- there are several drugs that are proven as second line therapy for non-small cell. And one of them is quite new, Alimta or pemetrexed, and Taxotere, or docetaxel has been around for some time.

Now just to move to the side for a minute and mention small-cell lung cell cancer. Small cell represents about 15 or 20% of patients with lung cancer, and in this situation, chemotherapy is certainly the mainstay of therapy for those patients. We have very high remission rates and very rapid remission, so that patients can have very dramatic shrinkage of tumors on their scans within a matter of a few weeks sometimes.

Most commonly we use Cisplatin and etoposide or carboplatin and etoposide. There's been some interest in another regiment of Cisplatin and irinotecan recently. Radiation therapy is routinely used in patients with limited stage disease, where the tumor is confined in the chest. And because the brain is a very common place for spread of lung cancer, of small cell lung cancer particularly, patients who have limited disease are also commonly given radiation to the brain in a preventive way in the thought that there may be microscopic spread there to try to get rid of early.

Now there are some new areas of interest in drugs approved. The targeted molecules, the first one that was approved was Iressa or gefitinib, that is now pretty much been supplanted by Tarceva. Iressa is actually not even available anymore. And Tarceva was clearly shown to be superior to it. And these are drugs that work by inhibiting a particular step in the growth of tumor cells, the epidermal growth factor TK receptor.

Now the drug cetuximab, Erbitux is also directed against that same target. In this case it's a molecule antibody that's directed against and that's currently in trials. Erbitux is the drug that put Martha Stewart in jail. It had nothing to do with the drug, it just had to do with some I guess financial shenanigans, alleged shenanigans.

Now Tarceva is approved now for the second line treatment of advanced non-small cell lung cancer. So along with Alimta and Taxotere. Now the thing about Tarceva is that the response rate overall is fairly low. But some are actually – many of the patients who do respond to it respond quite dramatically and for long periods of time. So it's really very heartening when we see patients who've responded well to this. Because they can get really excellent results. We just wish that the percentage of patients who got the excellent results was higher. Tarceva is generally pretty mild in terms of its ill effects. There's often diarrhea, there's usually a rash, and very rarely a lung toxicity. It's also one of the more expensive drugs out there. If you have to pay cash for it it's something on the order of \$3,500.00 dollars for a month's supply. So it's really pretty wild.

Now, patients who appear most prone to benefit from a Tarceva course, we're trying to work out the molecular reasons for this. But women, patients with adenocarcinoma, particularly the bronchial alveolar carcinoma, which is a relatively uncommon sub-type. Never smokers and patients of Asian descent seem to be particularly likely to respond to this drug. But in the studies that have been done that put the drug on the map, patients of all stripes responded. Men, women, smokers, non-smokers, all the various sub-types. But if we encounter an Asian woman never smoker with bronchial alveolar carcinoma, we're ready to give them Tarceva, because they're the most prone to benefit. And occasionally we do encounter such a patient.

Other areas of interest the so called VEGF inhibitors or vascular endothelial growth factor

inhibitors, these are the ones that affect the blood vessel formation in tumors. The drug Avastin or Bevacizumab is currently FDA approved in the treatment of colon cancer. And is being evaluated in a variety of other settings. And just a few weeks ago was approved for the treatment of advanced non-small cell lung cancer in conjunction with chemotherapy based on a large trial that showed that patients who got chemotherapy plus Avastin had a two month better overall outlook then those who got chemotherapy alone.

It's not a free ride however. Because, as you might guess, when you're using a drug that affects blood vessel formation, bleeding and clotting might be the risks involved. And in fact, they are. And so, bleeding is especially a problem in lung cancer patients, particularly those that have tumors that are rather centrally located in the chest and are more prone to cause bleeding. So we're very wary about using the drug in patients who have tumors of that nature. And there are a lot of clinical trials under way to see how best we should be using this drug.

Chemotherapy is a systemic form of treatment. It goes throughout the body, normal cells are going to be exposed to it as well. And so, that's why there are side effects. So we have side effects that could be sort-of characterized in terms of their severity. We have the annoying ones: nausea and vomiting, which is largely not a huge problem any more. It's much less common because of better anti-nausea drugs that we have and the current drugs that we use routinely are less prone to cause severe nausea. That said, there's still many patients who experience significant nausea, but it's a lot less then it used to be. But fatigue is common, there may be mouth sores temporarily, and diarrhea.

The more serious ill effects relate to infection risk. Particularly when the white blood cells are temporarily reduced. And occasionally platelets may be seriously reduced and have bleeding risk. Occasionally these infections can be life threatening, but that's fortunately rare.

Now we often combine chemotherapy with radiation in patients with stage three disease-- locally advanced disease. And because of that, some normal lung tissue and the esophagus, which sits in the back of the chest, can be significantly affected by the treatment. And we're taking advantage of the fact that the drugs sensitize the cancer cells to the effects of the radiation and that's good. But the normal cells also get sensitized by the effects of the radiation, particularly the esophagus. And so, we sometimes encounter significant breathing difficulties and swallowing difficulties. And occasionally we have serious problems with hydration and nutrition, and patients may need a lot of extra support to get through it.

So what's coming up? Well, the current trials and some of the new trials mainly use chemotherapy in conjunction with a targeted drug or an Ng genesis inhibitor, something like that. I think we're past the point of adding a third and a fourth chemotherapy drug in terms of how much extra benefit we're going to accomplish. A lot of clinical research under way to figure out what are the targets in the cancer cell that can then be used as a way to figure out what we should be attacking these targets with. So if we can learn more about the targets we can try to better create drugs, produce drugs.

There's been a lot of progress in the last ten years. We have better drugs, better tolerated drugs, but we certainly are far from where we want to be. And clinical trials, patient participation in clinical trials, is really the key to moving forward and you know fortunately patients are often quite willing to participate in clinical trials and be part of the answer, as well as we hope be getting up-to-

date therapy. So I'll stop here and I'll entertain some questions before I introduce their surprise guest.

Q: From the floor no microphone.

.... Well, it really is a function of the trials that were done of the drugs. If they were done as a first line and it was shown to be useful they would – the drug company might go for FDA approval for that purpose. It sort of depends on, you know, where it was tested and how it was tested. We're not locked into that situation. However, I mean the drugs that are approved for second line are now being looked at quite a lot in first line trials, too. And then it might later get an extended approval for a different indication.

Q: From the floor no microphone.

.... Yes. Well, the question was – yeah, the question was there was a notice in the paper yesterday or the day before that the University of Chicago was awarded a \$20 million dollar grant from the Ludwig Foundation for cancer research purposes. And how might that money be spent?

But I believe that this is actually going to be sort of an institute with specific goals in mind. I'm not sure how the money – it was – I know that they quoted Dr. Weichselbaum, who's the chairman of radiation oncology. And I think he's probably involved in organizing the approach. But I actually don't know the details. I wasn't involved in it.

Q: From the floor no microphone.

.... Right. That's true. The goal of it, the main focus of the research is metastasis. How do cancers spread and what might be done to reduce that? So what I assume is going to happen is that certain scientists will be recruited to study this. And again, it's some sort of an institute would likely be organized to do that. There are like six of them around the country that were funded.

Q: From the floor no microphone.

.... All right, the question is, are there second line drugs for small cell? There's one drug that's specifically approved second line for small cell namely, topotecan. There are other drugs, which we commonly use second line, which do sometimes have useful activity. They don't happen to be specifically approved for that. And there are drugs that are being tested in that setting, you know, for future use.

Q: From the floor no microphone.

.... Well, the question was could some of that Ludwig money be used for mesothelioma research? I have no control of this money. So I don't really know what the charge was for it. There's already a fair amount of money I know in mesothelioma research. But I actually don't know the answer to that.

Q: From the floor no microphone.

.... Okay, we have a guest this evening from – we have two visitors from – who drove up from Springfield today representing the Illinois Emergency Management Agency, regarding the Radon Program there. And I'd like to introduce Cindy who's just going to talk to us briefly about efforts in the state government regarding Radon eradication. Radon is bad, right?

CINDY S. Patrick Daniels and I are with the Illinois Emergency Management Agency. We were invited by the American Lung Association, and we're here just to let you know if you don't

that while it's clear that smoking is the number one cause of lung cancer, radon is the number two leading cause of lung cancer. And we have information about radon. If you don't know what radon is, radon is a radioactive gas that's naturally occurring that comes from uranium in the soil. And radon can enter your home through any opening between the slab and the soil. And like I said, it comes from uranium. Uranium starts out as a solid, radium is a solid and the radium then _____ to radon, which is the gas you literally breathe the radon in and the radon out. And products from radon can affect the lung cells.

But what we have is a lot of information about radon, and we're also in the process right now of actually giving away free test kits. And we're thrilled to be working with the Lung Association to share these test kits with citizens of Illinois. So we've got a couple of brochures for you. And we've got them sitting on the back table and we also have coupons. And if you're interested in getting a free test kit just fill out that information and you can either send it to us or else we also have an 800 number, if you don't want to fill out the information we'll be glad to get the test kits to you and you can test your home and see what your radon level is. Does anybody have any questions?

Q: From the floor no microphone.

.... Yes, it's 1-800-325-1245. We also have a Web site. And our Web site is also listed on these brochures. Thank you very much for allowing us — oh, and the Web site is:

<http://www.radon.illinois.gov/>

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<http://www.uchospitals.edu/specialties/cancer/lung/index.html>

To request an appointment with a University of Chicago Medical Center physician, visit our Web site at www.uchospitals.edu or call toll-free, 1-888-UCH-0200.

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