Welcome to Yale Cancer Answers with your host, doctor Anees Chagpar.

Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it's a conversation about lung cancer with Doctor Anne Chiang.

Doctor Chiang is an associate professor in medical oncology at the Yale School of Medicine where Doctor Chagpar is a professor of surgical oncology.

Let’s start at the beginning.

I think a lot of people know about lung cancer, but this whole differentiation between small cell, non small cell tell us a little bit more about that. What exactly is the difference?

How many people are affected by each? And why should we care?

I think that the basics about lung cancer are that they form in the lung. There’s mainly two different types, small cell, that underneath the microscope the pathologist looks at the cells and they’re very small and round and blue,
and everything else which is non small cell.
The small cell kind is typically a little bit more aggressive.
It grows more quickly.
It tends to spread.
There are different types that I typically tell my patients are like chocolate, vanilla and pistachio.
There is adenocarcinoma, squamous cell carcinoma, and other types.
They look a little bit different underneath the microscope, and sometimes there are molecular markers that can help us to understand a particular subtype that might be responsive to taking a pill, for example, instead of IV medication.
Of all of these types the first question is which type are the most common.
You say the small cells are a little bit more aggressive than the non small cells and even within that there’s a whole bunch of different types.
What type is most common?
What’s the distribution in terms of these cancers?
The most common type is
non small cell and pretty much 80-85% of lung cancer is non small cell and then 15-20% is small cell and so we know that smoking is related to lung cancer, but are there specific risk factors for getting each of these different types, or is it kind of all just a mishmash and which type you get is luck of the draw? Smoking is definitely a risk factor for both non small cell and small cell. That being said, there are folks who are never smokers, a small population of never smokers or light smokers who may develop mutations in specific genes called EGFR or ALK ROS1. Some of these mutations are called oncogenes and these mutations tend to lead to lung cancer. A specific kind and because it’s not sort of the same as the lung cancer that comes from smoking where repeated exposure and inflammation to carcinogens caused lung cancer, those patients with, for example, a mutation in EGFR can actually be treated with a targeted therapy that targets EGFR, and that, as I said before, is often in the shape of a pill that you can take daily.
So it’s really important when you’re diagnosed with lung cancer to understand the pathology and specifically the molecular pathology. That means the kinds of mutations that might be available. Especially if you’ve never smoked, or if you have a very light history or remote history of smoking. For the people who have never smoked or have a very light history of smoking, are they more likely to get one type of lung cancer in terms of small cell versus non small cell than others? And these mutations that I spoke of are more common in non small cell and those folks who are light or never smokers are more likely to develop non small cell lung cancer than small cell lung cancer. Typically it has rarely happened that I’ve seen patients who never smoked develop small cell cancer, but typically there is a history of smoking.
You mentioned earlier that small cell were more aggressive. Tell us about the prognosis. So it sounds to me like if you’re going to have a choice you would prefer to have a non small cell lung cancer. But how bad is one versus the other? I think that the key thing to know for both is that there have really been a lot of advances such that we’ve actually seen improvements in the outcomes for both non small cell and small cell. And this was just published last year in the New England Journal of Medicine that the incidence of both these and the outcomes of both these types of cancers are improving. So I think that’s a really important message to know. The other aspect of how you’re going to do with this particular cancer has to do with staging, and that just means the geography of where the cancer is in your body when you’re diagnosed with it. If you have tumors that are just in the lung or have migrated into very nearby lymph nodes, then you maybe have a stage one
or stage two cancer. You may be eligible for a local treatment like surgery or radiation in combination with chemotherapy to really try to remove that tumor, and that’s when you have the best prognosis, regardless if it’s non small cell or small cell. Overall, folks with non small cell do a little bit better. But again, having lung cancer, it’s definitely a treatable disease. If you have stage four cancer, which means that you’ve had disease that has traveled outside of the lung to a different organ such as the liver or the brain or your bones, then we take a different approach, which is then we need to use systemic therapy. That means something that gets into your bloodstream because every single cancer cell anywhere needs to have a blood supply and therefore administering chemotherapy, or more recently, all these advances in immunotherapy that way those therapeutic drugs can reach all of the cells that are in your body,
wherever they may be.

Well, it’s certainly good news that lung cancer, which is something that I think a lot of people fear, is becoming a treatable disease and that there are all of these advances. But first something that you said really struck a chord with me and has been the case with a lot of cancers and that is the earlier you find it, the lower the stage, the more treatable it is. So if you have a stage one lung cancer that’s more treatable than a stage four lung cancer, and I was wondering if you could talk a little bit about advances that have been made in terms of screening that have helped us to find these lung cancers earlier?

Screening is a hot topic now because the US Preventive Services Task Force just issued a different recommendation or it altered their recommendation on screening for lung cancer. So previously, if you were aged 55 or older, or you had a 30 pack year history of smoking and that means smoking one pack per day for roughly 30 years, then you would be eligible for a low dose
CT scan because you had a higher risk of lung cancer and being able to have a screening CT scan allows us to pick up things when they’re very small and you don’t have any symptoms and often help us to detect lung cancers when they are in a very early stage. So recently in March the US Preventive Services Task Force changed that recommendation to drop the age to 50 and for the pack year history to 20. So the idea being, let’s expand the population of people that are being screened. I think that our insurers are catching up with that but the recommendations have changed and I think that that’s going to be very positive in terms of again being able to detect lung cancers in earlier stages where they might be able to undergo local therapy such as surgery or focused radiation. So important for people to get screened because there are so many advances in terms of treatment. Just one clarifying question though, and the other thing that a lot of people have now done, especially because we’ve seen
advances in things like smoking cessation is to quit smoking. So let’s suppose that you have a 20-25 or thirty pack year history of smoking, but you just quit.

You made it a New Year’s resolution and you quit maybe a year ago, maybe six months ago.

Are you still eligible for screening? Should you still be screened even though now you’re officially a non smoker or a former smoker?

Yes, if you have a history of smoking that’s 25 pack years, even if it was ten years ago, you can still be eligible for this screening.

I think it’s a really important message to folks that wherever you are in your course of stopping smoking and it’s certainly one of the hardest things to do, it’s always important to realize that stopping or quitting smoking is going to help you and help your lungs.

It’s going to help your overall health and you’re going to do better than if you continue to smoke. There is data that even for folks who have smoked a lot over the course and maybe even 2 packs per day.
We certainly had in our society a number of years where everybody smoked and that was really sort of run of the mill, so I think that it’s really important that wherever you are, if you’re a one pack a day smoker, 2 pack a day or you smoke a couple of cigarettes a week, I think that stopping smoking can really help you and we do have a smoking cessation clinic here at Yale that’s incredibly successful. There have been so many advances that I can’t even keep track.

It was just the patch and the lozenge. And now there’s so many different options to help people stop and being able to do some of this through Televist consultation either through video or phone, can allow people to access this kind of help and support to really improve their health.

It is important to quit smoking and talk to your doctor or call a quit line to get the help you need. We’re going to take a short break for a medical minute. Please stay tuned to learn more about
small cell lung cancer with my guest
Doctor Anne Chiang.
Funding for Yale Cancer Answers comes from AstraZeneca, working to eliminate cancer as a cause of death. Learn more at astrazeneca-us.com.
It’s estimated that over 240,000 men in the US will be diagnosed with prostate cancer this year, with over 3000 new cases being identified here in Connecticut, one in eight American men will develop prostate cancer in the course of his lifetime. Major advances in the detection and treatment of prostate cancer have dramatically decreased the number of men who die from the disease. Screening can be performed quickly and easily in a physician’s office using two simple tests. A physical exam and a blood test. Clinical trials are currently underway at federally designated Comprehensive cancer centers such as Yale Cancer Center and Smilow Cancer Hospital, where doctors are also using the Artemis machine, which enables targeted biopsies to be performed. More information is available at
You’re listening to Connecticut Public Radio.
Welcome back to Yale Cancer Answers.
This is doctor Anees Chagpar and I’m joined tonight by my guest Doctor Anne Chiang.
We’re discussing recent treatment advances in small cell lung cancer and right before the break you were telling us about the fact that there have been really exciting advances both in small cell as well as in non small cell lung cancer that have really affected outcomes for patients with these diseases.
So tell us more about some of these exciting advances.
I’d love to. This is a really exciting time for lung cancer.
I remember back to when I started at Yale, which was almost 10 years ago, and I put my first patient or one of my first patients on a clinical trial and at that time the standard of care was chemotherapy, and in this case we were looking at treating this patient with immunotherapy and he did extremely well.
And in fact, I saw him a couple of weeks ago and he has been off trial with no treatment for the past eight
years and he is contemplating retirement
and he’s doing just incredibly well.
And that still sends shivers down my spine and I
know that it’s not every single patient
that has that kind of result.
But I think the more that we can learn
through studying and through biology,
through clinical trials,
our aim is really to do the best for
our patients and push that edge as far
as it can go in terms of how they do.
One of the trials that I’m a national
Investigator on spearheading
is a trial called Insigna
and it’s run through our cooperative groups,
that’s groups that
help to do research, clinical
research in the communities.
This trial is open at about
850 centers,
we’re looking for 850 patients to
enroll on this trial and we’re trying
to understand for PD L1 positive or for
patients who have this marker of
PDL one if they are treated with
either immunotherapy upfront or
immunotherapy combined with chemotherapy,
which group will do better
and then with those patients
who are treated with immunotherapy
alone if they progress,
can we then add chemo to the immunotherapy
to sort of boost the immune system?
And at the same time we’re going
to be using the tissue and the
science that we can gather to try to
understand if there are biomarkers or
signatures that can help us understand
which people will benefit and which
people have less of a benefit.
that’s a really exciting trial that is ongoing,
we’re about 40% of the way through on that,
and I think that you know there are
thousands of immunotherapy trials in cancer right now,
but I think this is one that will really help us to understand
what’s the right thing to do
up front.
We talk on this show all the time about immunotherapy.
And it sounds like particularly
giving your anecdotal case with your
patient who’s now nine years out,
it sounds like immunotherapy
really does have a role or a
potential role in lung cancer.
With your trial,
is it open to non small cell lung cancer,
small cell lung cancer, or any lung cancer?
So that trial is open for non small cell
lung cancer and it’s for patients who have
stage four disease and who have a tumor that has a positive marker for PDL 1, which is an important molecule in the signaling for immunotherapy in small cell lung cancer, we have a number of clinical trials also that are available, and I think that the story for small cell is that chemo plus immunotherapy has been approved in the past couple of years. That’s how the landscape of small cell has changed. It was just previously treated with chemotherapy and just in the past couple of years we now treat with chemo, plus immunotherapy. And then the question is what happens after? If that doesn’t work anymore? And I think we have a number of different clinical trials that are available for that, and we’re trying to really understand the biology behind why people respond or why they don’t respond and in small cell it’s typically a tumor where there’s less tissue available to test, and so we’ve put together a really great team here for studying the science that includes...
PhD scientists working on lung cancer as well as myself. And, you know, I think it would be too hard to go into all of the details here, but I think we're going to learn a lot about how we can explore the biology of small cell in order to find out vulnerabilities in order to target this disease. It sounds like you know, across the board in lung cancer, whether you've got small cell or non small cell. It sounds like immunotherapy is increasingly becoming part of the arsenal that your doctor may use to treat your disease. And that really has made a difference now, and is that the case only for people who express PDL one? We've talked on this show before about checkpoint inhibitors like PDL one. So is it the case that people who present with metastatic lung cancer, that they should be having their tumors checked for that marker and then treated with immunotherapy or is immunotherapy something that your doctor may use regardless? For non small cell lung cancer you definitely need to have your tumor checked.
If you have high levels of PDL one so greater than 50% then you may be eligible to be treated with just immunotherapy alone. Otherwise you really need to be treated with a combination of chemo and immunotherapy. For small cell, it is different. There's very little PDL one expression to start with and for the trials that have been done, they've looked at all comers so it doesn’t matter if you have PDL one expression or not because it’s so low anyway, but all of the small cell patients that are diagnosed are treated with chemo plus immuno. It is interesting how that kind of plays out between the two disease types. So tell us a little bit more about other advances that have occurred? Before the break you were telling us about an alphabet soup of markers, things like EGFR and others. ALK, for example. How have these really changed the landscape? Are oncologists using them to kind of target their therapies to personalize things as it were? Great question. So as I was talking about before the break,
if you for example have an EGFR mutation which EGFR stands for epidermal growth factor receptor, I think that the key is that what we found over the years is that if you have a mutation in EGFR directed therapy. In this case, it's a drug called osimertinib and you should do that off the bat if you have stage four disease. If you have stage one disease or stage two disease or you’ve had surgery, there has been a very new advance in the past year and it was led by Doctor Roy Herbst of Yale, our team that basically says that after you have that surgery, you benefit from taking that oral therapy. And I think it’s important also to mention that these trials, such as the ADURO trial, were offered not only in our main academic campus, in New Haven, but also in all of our Smilow care centers across the state. And we have 15 of them,
so we’ve been able to allow patients who are in all parts of the state participate in these types of clinical trials that can really give access to cutting edge drugs or to help to advance science for all patients. And that’s the case across the country, that many of these large trials are offered at academic centers that are offered at community centers and that really people should talk to their doctor because trials, whether they were led by Yale or led by investigators at other centers are often available for patients across the nation. Isn’t that right? Absolutely, and I think that you know, in the past clinical trials you thought, Gee, I will try a clinical trial if everything else has failed and it’s not working for me, so I’m going to try something experimental. Now that paradigm is completely shifted, so it may be that you have your first treatment that you’re going on a clinical trial. And it really is to try and better the outcomes for each of
the recommended treatments that are recommended approaches, standard approaches so that we can push the envelope and really do the best for our patients.

And in terms of these targeted therapies, whether it’s a drug that’s targeting an EGFR, whether it’s a drug targeting ALK or whatever, this is across the board. Is that right between small cell and non small cell?

And so the question that I have is if that is the case then for everyone who has lung cancer it sounds like they should have their tumor profiled with regards to all of these mutations so that their doctor can better inform what might be the therapy that works best for them. Is that right?

So the the mutations that I talked about EGFR and so forth are really much more common in non small cells. So we do as a matter of fact test all of our non small cell samples and look for these mutations. For small cell it’s a little bit different. We don’t have typically mutations in EGFR or ALK,
0:27:22.09 → 0:27:23.954 specifically for small cell.
0:27:23.954 → 0:27:26.248 However, because we still think
0:27:26.248 → 0:27:28.99 that it’s important to test for
0:27:29.083 → 0:27:31.879 those and typically not up front,
0:27:31.88 → 0:27:35.135 in other words, when you’re first diagnosed,
0:27:35.14 → 0:27:37.93 but if you are treated with
0:27:37.93 → 0:27:39.325 chemo and immunotherapy,
0:27:39.33 → 0:27:42.64 and perhaps it typically works very
0:27:42.64 → 0:27:46.492 well in 80 to 90% of the cases
0:27:46.492 → 0:27:50.16 you have a very good response
0:27:50.16 → 0:27:52.864 but that disease may come back when
0:27:52.864 → 0:27:55.467 you have stage four disease,
0:27:55.47 → 0:27:57.678 it’s typically not something that you’re
0:27:57.678 → 0:28:00.085 going to cure because you
0:28:00.085 → 0:28:02.122 don’t have the option of cutting out
0:28:02.182 → 0:28:04.317 or radiating every microscopic cell.
0:28:04.32 → 0:28:06.09 So if the disease regrows,
0:28:06.09 → 0:28:07.506 if and when,
0:28:07.506 → 0:28:09.248 unfortunately,
0:28:09.248 → 0:28:11.733 the disease regrows,
0:28:11.733 → 0:28:13.393 we want to have options and
0:28:13.393 → 0:28:16.277 really develop more tools is
0:28:16.277 → 0:28:18.122 what I tell my patients to be
0:28:18.13 → 0:28:20.32 and that’s why we
0:28:20.32 → 0:28:22.872 do work so much with clinical
0:28:22.872 → 0:28:25.442 trials and feel that that’s
0:28:25.442 → 0:28:27.787 incredibly important to be able to
0:28:27.787 → 0:28:29.837 advance outcomes for our patients.
0:28:29.84 → 0:28:30.57 Doctor Ann Chiang
0:28:30.57 → 0:28:33.083 is an associate professor and medical
oncologist at the Yale School of Medicine. If you have questions, the address is cancer answers at yale.edu and past editions of the program are available in audio and written form at yalecancercenter.org. We hope you’ll join us next week to learn more about the fight against cancer. Here on Connecticut public radio. Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital and AstraZeneca.