Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/managing-egfr-mutated-mnsclc-data-recommendations/56306/

Released: 07/16/2026
Valid until: 07/16/2027
Time needed to complete: 60 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Novel Strategies for Managing EGFR-mutated mNSCLC: Expert Insights into the Latest Data and Recommendations

Announcer:
Welcome to CME on ReachMD. This activity, titled “Novel Strategies for Managing EGFR-mutated mNSCLC: Expert Insights into the Latest Data and Recommendations” is provided by Cornerstone Medical Education and the American Academy of CME.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. May:
Did you know that lung cancer is the leading cause of cancer incidence and death worldwide, with an estimated 2.5 million new lung cancer cases and 1.8 million lung cancer deaths occurring annually? In 2026 in the United States alone, it is estimated that almost 230,000 people will be diagnosed with lung cancer, and it remains the leading cause of cancer death. Of these, EGFR-positive lung cancer accounts for approximately 10 to 15% of all non-small cell lung cancers in the United States.

This is CME on ReachMD, and I'm Dr. Alexandria May. Joining me to discuss new strategies for treating EGFR-mutated non-small cell lung cancer is Dr. Helena Yu. She's a thoracic medical oncologist at Memorial Sloan Kettering Cancer Center in New York. Dr. Yu, thanks for being here today.

Dr. Yu:
Dr. May, it's my absolute pleasure. Happy to be here.

Dr. May:
And later in the program, we will be joined by Dr. Victoria Sherry, a thoracic oncology nurse practitioner at the Abramson Cancer Center at Penn Medicine in Philadelphia. Dr. Sherry, we are looking forward to speaking with you today.

For some background, the treatment landscape for EGFR-mutated non-small cell lung cancer has been rapidly changing with recent approvals of amivantamab and lazertinib, chemotherapy combinations with amivantamab and osimertinib, and the emerging subcutaneous formulation of amivantamab. But these advances have also expanded the need to monitor for potential toxicities and have created new educational needs among care teams.

Dr. Yu, before we dive into our discussion of treatments, let's start at the beginning. Why do biomarkers matter? And why is testing for biomarkers so important in non-small cell lung cancer?

Dr. Yu:
Yes, I want to agree with you. I think that the standard of care for EGFR-mutant lung cancer, both in the first- and second-line setting, have changed dramatically in the last 3 years. But absolutely, I think going back to the beginning is really biomarkers.

There are two main types of biomarkers that we utilize in non-small cell lung cancer. The first being molecular biomarkers. So we look for gene mutations in genes that are important for oncogenesis and actually have very important treatment implications as well. The way that we look for these gene alterations is actually through something called next-generation sequencing typically, which is a platform test that really tests for all of the different genes that are relevant in non-small cell lung cancer, and those include EGFR, as you mentioned,

© 2026 ReachMD

but also KRAS, which is another common mutation, and then other rare alterations like ALK and MET and ROS1 and RET and HER2, BRAF, among others.

And just to state that this next-generation sequencing can occur on tumor tissue directly after a biopsy or a surgery but also can be done on a liquid biopsy where we look for cell-free DNA that is from the tumor.

The other type of biomarker that we utilize are based on protein expression from the cancer cell, and these are done on a tumor tissue biopsy. And then the most important one that we look for now is something called PD-L1 expression. And this is detected using immunohistochemistry, where we look for this protein staining on the cell surface, and we calculate what percentage of the cells have expression and how strong the expression is. And it's about 2/3 to 3/4 that will have some degree of PD-L1 expression in terms of non-small cell lung cancers, and about 1/4 or so will have high PD-L1 expression, and then there's about 1/4 that do not have any PD-L1 expression. And this PD-L1 expression becomes important when we determine whether immune checkpoints should be given with other therapy, like chemotherapy, or given alone.

When we think of biomarkers, 20 years ago we really did not have any sense of different mutations that are present in lung cancer, and now I'm sure many of you have seen those kind of mutation pies where they segment lung cancer into different oncogene subsets. As was mentioned, EGFR is probably the most common and certainly the most common targetable oncogene we see in lung cancer, and then KRAS follows second at about 25%.

There really has been a molecular revolution where we really have multiple, more than 10 targeted therapy indications where there are certain genes, including EGFR alterations, both common EGFR mutations as well as uncommon, and exon 20 insertion mutations, KRAS, ALK, ROS1, BRAF and NTRK, MET exon 14, RET, HER2, NRG1 fusions, that have these targeted therapies that we utilize. And most of these targeted therapies are utilized actually in the first-line setting, and I would say it's more rare, really limited to KRAS-altered lung cancer, where we use some of the targeted therapies after chemotherapy or immunotherapy.

And I think a question that should be asked, and that has been asked, is why do we care? Why is it important to look for these biomarkers? And that's really because if a patient has a biomarker within their tumor, if we give them biomarker-directed therapy, their survival improves. And so it really is important for us to test for these different gene mutations because it allows for a different array of therapies to be available. And these targeted therapies are generally far more effective than our standard chemotherapy and immunotherapy for these subsets.

And in terms of timing, it's always the most ideal to be able to look for these gene mutations prior to initiation of first-line therapy because it is so important to start on the right treatment that we really would like to have those results back before we initiate treatment. Of course, there are rare instances where patients need treatment right away, and in that setting I actually often start chemotherapy alone, wait for those mutation test results, and then I can either pivot to targeted therapy or add on immunotherapy, but not limit myself by starting a full treatment up front that it'll be hard to segue to something else.

When we think about this biomarker testing, the other question is, who should we be testing? And I think the answer is changing, but I would say lately it really should be all patients with non-small cell lung cancer. I think we traditionally used to say adenocarcinomas, and maybe we would even label some phenotype, a certain phenotype, never smokers, but really we've come to realize that these gene mutations can occur in all patients with or without a smoking history. And really, so for all of those histologies, adenocarcinoma, large cell, poorly differentiated carcinoma, squamous cell carcinoma, we really should be considering biomarker testing, including PD-L1.

I mentioned, how do we test for these biomarkers? I think it's pretty well established now that we do use these comprehensive multi-gene platform tests, and these are commercial assays that are commonly used but they test for multiple genes, often hundreds of genes, with one sample. I think previously, before we had a whole lot of different oncogenes, when we just had EGFR and ALK and, say, ROS1, there was a lot of piecemeal testing where we would test for each gene separately, but I think that may not always be cost-effective, and it certainly is not always tissue-effective, right, where we do oftentimes run out of tissue. And so doing one test on the tissue that would really look for all of those genes really is typical.

As I mentioned, there are two different ways to do this next-generation sequencing testing. We can do it on the tumor tissue, or we can do it on circulating tumor DNA that we can identify and collect in plasma. I think both have advantages and disadvantages, and often they're done collectively or concurrently, right? I think that there's additive data we get from both. Of course, the tissue biopsy is the gold standard. You often get more tumor DNA, so you're able to do the test. It is more invasive, where, of course, it takes a biopsy to obtain that tumor tissue, and oftentimes the turnaround time for these tissue-based sequencing assays is longer.

Liquid biopsies are convenient. Obviously, it's a blood draw, and that blood is sent out. The turnaround time is often quicker, where you can get results in maybe 1 to 2 weeks compared to 2 to 3 weeks with the tumor tissue biopsy. But there is a question of false negatives,

© 2026 ReachMD

where if you find a mutation on a liquid biopsy, it is almost certainly a true mutation, but if you find no mutations on the liquid biopsy, that might be a false negative, and if you were able to assay or test the tumor tissue, you might find a mutation.

There have been studies that have compared liquid and tumor tissue biopsies and really showed that there is, of course, concordance between tissue and liquid biopsies, but that they can be additive to one another, where there are definitely a larger number of mutations that are tested and identified on both assays. But I would say that there are some mutations that are only found in the tumor tissue, and actually there's a portion of mutations that may only be found in the plasma. And so I do think that to get the most comprehensive answer in terms of if there is a mutation within the tumor, if possible the goal would be to send both.

And a lot of our consensus guidelines, including NCCN, ESMO, ASCO, and IASLC, do say that these can be done, but either sequentially, but it's reasonable to do these tests concurrently to really have the highest yield of an answer.

Dr. May:
Now that we understand that a subset of lung tumors are dependent on oncogenic driver mutations for growth and proliferation, what do the latest guidelines recommend for biomarker testing in non-small cell lung cancer?

Dr. Yu:
So, yes, this is a great question. So, the guidelines really recommend either concurrent or sequential biomarker testing. I think all of the guidelines are quite consistent, and these include the NCCN guidelines, ESMO, ASCO, and IASLC, where they often say that the testing is complementary, and obviously they are additive to one another, and to reduce turnaround time and increase yields, it makes sense to do both.

I also think some of the other guidelines have different language where they state that it could be considered sequentially as well, but I think the key is sending off something, and if the test is non-diagnostic or negative, maybe at the very least sending off the other assay, because really we do want to be certain about a mutation—to understand if a mutation is present or not.

And as I mentioned, concurrent NGS testing really does increase detection rates, where the majority of mutations are identified by both assays, but there are definite unique alterations that are found in the solid tumor, and there's probably more there, and then a small portion that are only detected in the ctDNA. And there was different tests that looked at this, and I would say that the detection rates between tumor tissue and plasma are different also between different tumor types as well, where perhaps with breast cancer there might be a greater detection in the ctDNA, but then other tumors, like non-small cell lung cancer, colorectal cancer, where we're finding more of the mutations in the tumor tissue or in both.

Dr. May:
Dr. Yu, thank you for that very thorough explanation of why NGS testing is so important for patients with non-small cell lung cancer. Can you walk us through a specific driver mutation that affects between 10 and 15% of patients with non-small cell lung cancer, the epidermal growth factor receptor, or EGFR for short?

Dr. Yu:
Absolutely. So, as I mentioned, the EGFR mutation is the most common identified mutation within non-small cell lung cancer that has treatment implications. In the US, the frequency of the EGFR mutation is 15 to 20%, but this is very different globally, where in areas in Asia the frequency of EGFR mutations exceeds 50%. So this is truly a global issue.

When we talk about EGFR mutations, there are parts of the gene that are more relevant and active than others, and so when we think about mutations, they're almost certainly located in the kinase domain of EGFR, and that really is exons 18 through 24, and actually primarily 18 to 21. So almost all of the activating cancer-causing mutations that we see in EGFR are between 18 and 21.

There are two common EGFR mutations that you've certainly heard of before, and that is the EGFR exon 21 L858R mutation and then the EGFR exon 19 deletion. Those two mutations together make up about 80% of EGFR-mutant lung cancers, and then there are other rare mutations, which might be mutations in exon 18, which include E709X or G719X, in 21 like L861Q, or other rare mutations.

And then a different type of mutation that actually is treated altogether different from a management standpoint are exon 20 insertions. They have their own type of mutation. They are a distinct mutation that has different treatment paradigms, but that exon 20 insertions really consist of probably after exon 19 deletions and L858R alterations, are the third largest subgroup of EGFR mutations.

Dr. May:
With that in mind, what does the evidence base for treatments targeting EGFR-mutated non-small cell lung cancer in the first line and beyond currently look like?

Dr. Yu:

© 2026 ReachMD

So this is what I mentioned in the intro, that things are really changing today compared to 5 years ago, or even honestly 2 years ago, the treatment that I offer patients that come into my clinic with a new diagnosis of EGFR-mutant lung cancer.

And so really, over the last 5 years, osimertinib, which is a third-generation EGFR TKI, was established as the best monotherapy for EGFR-mutant lung cancer. And so this is an excellent CNS-penetrant targeted therapy that's oral, that you take once a day. But even with people that have very good responses to osimertinib, disease always at some point progresses, and so there was effort into thinking about how we can amplify or escalate treatment in the first-line setting to improve outcomes.

And the regimens that have been developed, one is called the FLAURA2 regimen, based on the study name FLAURA2, and that's adding platinum-based chemotherapy, largely carboplatin and pemetrexed, to osimertinib in the first-line setting. And this is taking two treatments that we used to give sequentially, where most patients typically got osimertinib in the first-line setting and then got carboplatin/pemetrexed in the second-line setting, but combined them together as first-line treatment.

And then the third regimen is called the MARIPOSA regimen, and that's based on giving amivantamab, which is an EGFR-MET bispecific antibody that can be given intravenously, or actually now in a subcutaneous injection, with lazertinib, a third-generation EGFR inhibitor very similar to osimertinib. And so the thought there is, can we double down on EGFR pathway inhibition? And would that be a more effective strategy than just a monotherapy with an EGFR inhibitor?

So both of those studies of chemotherapy and osimertinib, and amivantamab and lazertinib actually demonstrated progression-free survival benefits, as well as overall survival benefits. And so the time that the disease was controlled and the patient was without progression was significantly longer with the combination, and actually both regimens clearly improved survival. And so with that clear survival benefit, I think that that is what has prompted a lot of us to move forward with combination therapy for most patients.

In terms of safety, they do have very different safety profiles. Of course, chemotherapy is cytotoxic therapy. It can lead to cytopenias, like lowered white blood cell count, lowered red blood cell count, lowered platelets. It can lead to nausea and fatigue, and so those are kind of unique side effects that we are aware of because, of course, we give this chemotherapy frequently. And then osimertinib has kind of the standard dry skin, maybe some diarrhea, some GI upset, and those symptoms are additive.

When we think about MARIPOSA, though, these are different side effects. Amivantamab is an EGFR-MET bispecific antibody and actually has stronger EGFR wild-type toxicities, and so you can see a more significant acneiform rash, including a scalp rash, and you can see diarrhea or nail changes, like paronychia or infections in the nail. And then with the MET-directed side effects, you can see swelling.

So I think different side effects, and really it becomes a discussion that we have with our patients to decide what's best for a given patient. And I think it really is weighing toxicity—additive toxicity with these combination regimens. What is their quality of life being maintained on these treatments, since these first-line treatments are given over a long period of time, and then also thinking about kind of what their values are.

And the challenging part of this is no one person is the same, and no one cancer is the same. And so even with a diagnosis of EGFR-mutant lung cancer the treatment course or the disease course can be very different, so it really becomes an individualized decision as to what to choose.

Dr. May:
For those just joining in, you're listening to CME on ReachMD. I'm Dr. Alexandria May, and today I'm speaking with Dr. Helena Yu about novel strategies for treating EGFR-mutated metastatic non-small cell lung cancer.

Now, I'd like to invite Dr. Victoria Sherry to join our conversation.

Dr. Sherry:
Hi, welcome. Very excited to be here today.

Dr. May:
We've been talking about the importance of comprehensive next-generation sequencing in non-small cell lung cancer and options for targeted treatment, but now I'd like to shift our focus to treatment planning for EGFR-mutated non-small cell lung cancer and management of the treatment-related adverse events associated with these therapies.

We learned earlier about the evidence base for targeted treatments in the first line and beyond for EGFR-mutated non-small cell lung cancer. So, Dr. Yu, can you explain how you select and individualize treatments for these patients?

Dr. Yu:
Yeah, this is a really great question, and I'm sure, as Vicki can attest, our new visit consultations really take much longer for EGFR-

© 2026 ReachMD

mutant lung cancer because we really do want to very carefully go over these different therapies and really kind of match the right treatment to the right patient.

As I mentioned, there really are three main treatments that we typically utilize. There are other approved agents, but in terms of what is category 1 and preferred, it really is osimertinib monotherapy, osimertinib, carboplatin, and pemetrexed, or amivantamab and lazertinib. So those are the three regimens that I discuss with my patients.

I think that some patients come into our first visit and have very clear ideas. They've done their research and have an idea of what they want, and for some people, of course, they're starting at like square one and really need and would like a healthcare provider to help guide their treatment.

I would say that right now the minority of patients will get single-agent osimertinib. I think with the clear survival benefit of both FLAURA2 and MARIPOSA and the fact that about 1/3 of patients will not get second-line therapy, it really is important to use our very best treatments in the first-line setting. But if a patient says to me they absolutely don't want any chemotherapy, they would not like an injection or a shot, and really want to take a pill and are focused on that, of course, that's a patient where we would proceed with single-agent osimertinib.

And then I think if people have very sort of positive or good-risk features, and that might be an exon 19 deletion, a very low burden of disease that's intrathoracic only, so only present in the lung, and does not have a concurrent TP53 mutation or an RB mutation, and again doesn't have disease outside the lung, and maybe we know it's slow growing because we've observed it over time, that's someone that I might think about single-agent osimertinib.

But really anyone else, any high-risk features, in particular if you have brain metastases, I really am discussing combination therapy. And when you think about high-risk features, which include different sites of disease like liver and central nervous system, types of mutations like L858R or uncommon mutations, co-mutations like P53 or RB, almost everyone has one of these high-risk features. Greater than 80% of lung cancers do, and so really, in my opinion, you're discussing combination therapy for the majority of your patients.

Dr. May:
So, Dr. Yu, could you speak a little bit about how long patients stay on this medication and what the next steps are after that?

Dr. Yu:
Yeah, that's a great question. I mentioned that these targeted therapies are very effective, and they are, but there always is a time where, for most patients, the disease ends up progressing. For osimertinib monotherapy, that is about a year and a half, and for osimertinib and chemotherapy or amivantamab and lazertinib, that's more like 26 to 28 months. But at some point we start to see evidence of disease progression.

I think in some instances we see something called oligoprogression, where the majority of the disease remains stable and controlled, but there might be one site of disease that starts to grow. And if that's the case, we try to utilize local therapy. And so that often is radiation therapy, but it can be ablation or surgery in some instances, where we treat and address the growing area of disease, and that allows patients to stay on the same treatment that they've been on that's controlling the rest of the disease. I'd say that is applicable about 1/3 to 1/4 of the time, where that is something that we can do, and we can do that even multiple times to really prolong the time somebody's on first-line treatment.

But if someone has clear evidence of growth, if it's multisite, so multiple areas growing, or if they're symptomatic from their progression, then we need to do something different. And so the first thing that I try to do is biopsy the disease. If there is an accessible area of growing disease, I'll send them for a tumor tissue biopsy and then often send off a liquid biopsy as well.

The reason I'd like to do the tumor tissue biopsy is one thing that we're ruling out is something called histologic transformation. So about 15% of the time, when a tumor and a patient start osimertinib, they have an adenocarcinoma, but after the time of disease progression, sometimes these cancers can transform and become a small cell lung cancer or a pure squamous cell lung cancer. And this is really important to identify because there are specific chemotherapy treatments that are needed for these new histologies, and really, a tumor tissue biopsy is the only way to identify this histologic transformation.

Besides transformation, I would bucket new things into two different categories. First of all, new acquired alterations are actually quite rare; probably only about 20% of cases we see this. But there can be new on-target resistance, and so this might be in addition to, say, the EGFR exon 19 deletion, there might be a new EGFR mutation. A common one is one called C797S. That is the exact location on the EGFR gene that osimertinib binds to. So having a mutation there, it's called a gatekeeper mutation, really prevents osimertinib from binding to the cancer cell, and so then that can lead to resistance.

© 2026 ReachMD

Sometimes the other category are what we call off-target resistance mechanisms, and these are new mutations, and they can be something like MET amplification or new KRAS mutation. And these mutations lead to activation of parallel or downstream signaling, so it just allows the tumor to signal through these other pathways and continue downstream activation.

And rarely for instance, for someone that has a MET amplification, sometimes we can add in something like a MET inhibitor to the osimertinib and utilize that for treatment.

About half the time we're not able to identify a single gene alteration that drives resistance, and that's when we're thinking about more general treatments. Over the past several years, for EGFR-mutant lung cancer, we have had several approvals for non-biomarker-directed later-line treatment. So one option for these patients is the MARIPOSA-2 regimen, which is carboplatin/pemetrexed with amivantamab, that EGFR/MET bispecific antibody. This is relevant for patients who maybe got osimertinib first line without chemotherapy, or may have gotten the FLAURA2 regimen of chemotherapy and osimertinib, but maybe discontinued, like, the chemotherapy over a year ago, and you want to retry the platinum-based chemotherapy.

Another new approval that was just approved last year is datopotamab deruxtecan. This is a TROP2-directed antibody-drug conjugate, so this is a hybrid between a targeted antibody that has a chemotherapy payload. And this has specifically been approved for EGFR-mutant lung cancer after chemotherapy and after targeted therapy. So this would be something that could work for the majority of patients after first-line treatment.

Dr. May:
Now, turning to you, Dr. Sherry, we've heard a bit from Dr. Yu about the toxicities associated with combination treatment strategies. What should we know about managing these toxicities?

Dr. Sherry:
Sure. So I'll start off with probably one of the most important safety considerations with amivantamab, which is infusion-related reactions. About 63% of patients experience reactions—infusion-related reactions, so they're definitely common, especially with the first dose.

When I first started giving amivantamab, about, I would say, 100% of my patients had infusion-related reactions. So whenever I consented them in clinic, I would tell them to expect a reaction. And these reactions can be anywhere from very mild facial flushing, all the way to anaphylaxis, where you're calling a rapid response and sending them to the ED.

So to reduce these infusion-related reactions, amivantamab, the first dose is split over two days, so they come in the first day, they get 350 mg, and the second day they get 700 mg. And again, in my experience, once they react on day 1, they do not react again. So I always reassure my patients, because it's incredibly scary when they're going through these reactions, that if they do have one on day 1, that day 2 should be much better, because I've had a few patients, and I'm sure Dr. Yu can attest to this, that after they react on day 1, they do not even want to come back in for their day 2 infusion.

So, can we prevent these infusion-related reactions? So there was a trial called the SKIPPirr trial that looked to reduce infusion-related reactions through prophylaxis. And prior to the trial, we would give premeds just the day of treatment. So since this trial, now we are giving dexamethasone 8 mg twice a day 2 days before treatment, and it showed that this reduced IRRs from 67% to 22%, which is a huge reduction.

And then comes along amivantamab not only comes in IV but also in sub-Q. And so there was a PALOMA trial that was designed to really validate the sub-Q formulation and to address these limitations. And so what the trial found was that sub-Q ami delivers equivalent drug exposure and efficacy when compared to IV, with a markedly better safety profile, actually, which is nice. So the infusion-related reaction rate was only 16% with the sub-Q compared to 67% with the IV amivantamab. And it's nice because that split dose could be eliminated.

The administration of sub-Q was under 10 minutes versus 2 hours for IV, so the saved chair time, not only for the institution but especially for the patient.

And then something to think about as nurses, that when we're giving this amivantamab, we want to make sure that we confirm that the patient took their dex premed. If for some reason they did not, it is okay. We are still giving them premedications, but you'll be more alert that these patients might react or have a higher reaction if they did not take their SKIPPirr trial premed like they should have.

Always verify weight. Ami is weight-based, so if they're under 80 kg they get 1050 mg. If they're greater than 80, they get 1400 mg.

And this is something that I didn't know until recently. You need to use a peripheral line for IV amivantamab for weeks 1 and 2, and this is to again reduce the infusion-related reaction risk. You can use a central line for all subsequent weeks. So, yeah, it's interesting

© 2026 ReachMD

because most of our patients have ports, but they do need to get stuck peripherally for weeks 1 and 2.

And then during the infusion, you want to watch for infusion-related reaction signs and symptoms. So we're looking for chills, dyspnea, flushing, fever, nausea, chest discomfort. We can go hypotension, vomiting. Like I said, it can be anywhere from very mild to very severe, such as anaphylaxis. And the median onset to a reaction is about 1 hour.

For grade 1 and 2 infusion-related reaction, we want to interrupt the infusion immediately. You monitor the symptoms until they resolve, and then you can resume at 50% of the infusion rate at which the reaction occurred. So if no additional symptoms after 30 minutes, the rate can be escalated. For a grade 3, you interrupt the infusion, administer supportive care meds, and then you can resume at a 50% rate once the symptoms have resolved. And grade 4 or any grade event of anaphylaxis, of course, is a permanent discontinuation.

So now to probably dermatologic adverse events which are among the most common associated with EGFR inhibitors. It can affect up to 90% of patients. It can range from anywhere from dry skin, dry eyes, to that classic acneiform rash and nail infections. And these dermatologic adverse events can really impact a patient's quality of life. Most of the regimens that we use in lung cancer, you don't lose your hair. You can look—I want to say I'm putting this in quotes—but you can look normal on the outside, although I know people don't feel normal on the inside. But a rash is a very physical symptom, and it sort of lets everyone know that they have cancer. So proactively educating our patients can really help reduce these side effects.

So, what can we do to help these dermatologic side effects is keeping the skin moisturized. These patients' skin, that their skin gets really, really dry, like alligator flaky dry skin. So use a moisturizer. I always say something mild, hypoallergenic, paba-free, Cetaphil, CeraVe, Eucerin. They're all good moisturizers. I always also tell my patients to get something in a tub rather than a pump, something they can—tubs are usually thicker, like a thicker emollient—and that to use, and much better. They want to avoid hot water, avoid the sun, and avoid heat. So, wearing long clothes, shirts, and a wide-brim hat. You want to wash your face with a gentle cleanser, such as Cetaphil or CeraVe. And then I am more of a reactive practitioner rather than a proactive practitioner, so I educate my patients about all of these, about the dermatologic side effects and really all of the side effects. But I tell them to notify me if they develop any symptoms, and then I start to prescribe stuff. I'm a mentality of less is best. But there are studies that do show that being proactive rather than reactive can be helpful too, especially in some of these combination medications.

So, triamcinolone cream 0.5% is great. Patients can put it on twice a day. So they wash their face, they put on triamcinolone cream, and then they put their lotion on top. Clindamycin gel, we use this to treat acne in teenagers, so we just tell our patients to use it on their pustules. They should not rub it over their entire face; it can be really drying. And then there's two antibiotics, minocycline and doxycycline, that they can take. And again, I reserve this for more of a grade 2 rash, or if my patient's complaining that they don't like the rash, no matter what grade it is, I will prescribe minocycline or doxycycline. I prefer minocycline just because doxycycline is photosensitive, and if patients are out in the sun in the summer, minocycline is a little bit easier.

And then patients also develop these, like a folliculitis on their scalp. They can use Head & Shoulders shampoo, keeping their scalp moisturized. I have my patients put clindamycin gel onto the pustules onto their scalp too to help them. So education is really key, and whether you're proactive or reactive letting your patients know that they're likely to develop these symptoms, and then we do have a whole arsenal of medications and a whole routine that we can give them to help them.

One thing I want to touch on, which is really important when we're talking about these adverse events, is grading these adverse events. And so we use the CTCAE, or the Common Terminology Criteria for Adverse Events, when grading adverse events, and it goes from a grade 1, which is usually mild, grade 2 moderate, grade 3 severe, grade 4 life-threatening, and then grade 5 is death. And when you're writing your notes or documenting these adverse events, make sure you grade them. It's really important. It lets the provider know exactly—anyone who picks up your note or looks at your note can know exactly what you are thinking. I also always encourage to take pictures and to put the pictures in as well.

And then some other dermatologic side effects. We have paronychia. This is probably my biggest struggle to manage. It's inflammation of the nail bed, and it really can be functionally debilitating. So, unlike that acneiform rash, which appears usually within 2 weeks, paronychia develops around 4 to 8 weeks, so it's a later side effect of treatment, and it tends to be chronic and progressive if it's not managed proactively.

Things that you can have your patients do to help minimize or prevent these—I don't even know if we can really prevent them, but they can maybe minimize them. So the patients should soak their fingernails or toenails in a 3:1 concentration of warm water and vinegar or bleach. So 15 minutes on, 15 minutes off. They dry their fingernails or toenails, and then they should apply mupirocin ointment to the area and try to keep it open to air, although almost 100% of my patients come into the clinic with Band-Aids on because they're constantly banging their fingers, and their fingers are bleeding. You should prescribe a 4% chlorhexidine rinse or wash that they use twice a day to wash their nails with. Timolol eye drops have been effective too. They apply one to two drops on the affected nail twice a

© 2026 ReachMD

day. And then for fissures, you can tell them to wash the area real good with soap and water and then apply super glue or liquid bandage.

And then always, I always get dermatology, podiatry, or surgery involved fairly early. Paronychia, like I said, I have a really difficult time managing it. It does get progressive, and the problem is that the regimen that I just went over with you, it's time consuming. I mean, some of these patients have a really good quality of life on treatment, and they're out and about, so if I'm telling them to soak several minutes a day, and they're putting lotion, they're putting lotion, and they're putting chlorhexidine and eye drops, it can be really time consuming, and most of my patients end up just quitting it and doing nothing because it's just too much, or they'll just do one thing and not everything.

So one thing that I found out was that I had a patient that had really bad paronychia and couldn't touch her hair, her scalp, and she loved to hang out with her grandkids, and she was very, very active, but it was just that her nails were incredibly painful, and her toenails. I was at a conference, an EGFR conference for caregivers and patients, and I was talking about side effects, and afterwards a patient grabbed me and said, “You know, I had all of my nails removed for my paronychia, and it was incredibly helpful. They grew back, and I never had any pain since then.” And so I said this to my patient, and yes, it was definitely a hard pitch, but she ended up getting two of her nails done because she was like, “There's nothing else I can do, and I should really—let's, let's try this. It's worth it.” And it turned out to be very successful for her. So she had two nails removed. They grew back. It takes about 3 months. She had no pain. She came into clinic. She was banging them on the counter and tapping them. She had absolutely no pain. And then she went on to have her other five nails and four toenails removed too, and all have been very successful. So, I always like to share that story because I struggle so incredibly with managing paronychia.

So, they came up with a study called the COCOON study that showed that adding proactive skin and GI support to amivantamab significantly reduced treatment-related side effects without really compromising efficacy.

So it's sort of very similar to the regimen that I described to you, but it's proactive, and right away when you start someone on ami/laz, they're started on minocycline or doxycycline twice a day prophylactically. They're put on clindamycin lotion to the scalp. They are given the chlorhexidine washes that they start for their nails, and that they're supposed to use a ceramide-based moisturizer daily for 12 months.

And then another thing to think about when you're dealing with these EGFR inhibitor dermatologic toxicities is the timing of them. And so the toxicities really follow a characteristic temporal sequence with different skin manifestations sort of emerging at predictable intervals during treatment. So that papulopustular acneiform rash that I talked about, that's the earliest and most common toxicity, with a median onset about 7 to 10 days after treatment. And it presents as an inflammatory folliculitis. It's sort of concentrated in those seborrheic areas, like the face, the scalp, the upper chest, and back. It does spare the periorbital region, the palms, and the soles. And then the rash peaks in severity around 2 to 4 weeks and then gradually subsides.

Then dry skin can occur, and that starts about 1 to 3 months into treatment, and this can be diffuse, and it could look like eczema, like dermatitis a little bit. This is where we see our skin fissures on the fingertips and heels, which are a consequence of the dry skin.

And then the paronychia that I mentioned before, I did say it's a late effect, and it usually occurs months into treatment, and we can see edema in the nail folds and sometimes pyogenic granuloma-like lesions within the nails too, and we see this particularly with our second-generation EGFR TKIs and amivantamab.

Also, we see trichomegaly, which is that abnormally long, thick, and curled eyelashes, or hypertrichosis, which is excessive hair growth anywhere on the body, and we often see this on the face with females, and that also occurs like several months after treatment has begun.

And the dermatologic toxicities, they follow like a cyclical and overlapping pattern rather than just a simple sort of linear progression, and it's important to know this pattern because as skin problems develop, they change over time, and our treatment approach must change too because of the cyclical pattern that they go through.

So as you know, EGFR is a protein on cells, and it normally does two jobs: it helps skin grow, and it helps skin repair itself. So it really keeps inflammation in check. So when an EGFR inhibitor blocks this protein, the skin loses both of those protective functions, and it kind of sets off this chain reaction of problems that can unfold over weeks to months. Which is the cycle is inflammation damages the skin barrier, and then a damaged barrier lets harmful bacteria colonize, and then the bacteria can cause infection, and then more inflammation causes more barrier damage, and then that cycle repeats.

Dr. May:
How important is shared decision-making in the management of EGFR-mutated non-small cell lung cancer? Dr. Sherry, I'll start with

© 2026 ReachMD

you.

Dr. Sherry:
Sure. So shared decision-making, it's really the heart of patient-centered oncology care. We are not making treatment decisions for the patient, but really with the patient. And I always tell my patients that this is a two-way street. We make decisions together, we don't make them for you.

And I think things that we can do to help with shared decision-making is communicating properly and appropriately, and letting them know how to communicate and get in touch with us as well. I prefer always going through the portal or sending messages through the portal. I give them phone numbers, and involving caregivers and loved ones is really important. These patients are completely and utterly overwhelmed during their visits, especially their initial ones, or maybe even at progression. So involving others and for another extra set of eyes and ears is always really important. And another thing I like to do is I like to ask open-ended questions rather than yes/no. So when you're talking about treatment, maybe things like, what worries you the most about treatment? Or what matters to you the most right now? You can get so much more from a patient with asking those kind of questions rather than just yes/no questions.

I'll pass it over to you, Dr. Yu.

Dr. Yu:
Yeah, I think everything that you've said, Vicki, is critical. I think that I see our job as providing information, right? I think obviously we're experts in oncology care, and so giving people the right information of what to expect, what are side effects, what is the efficacy like that's my job to provide. But what they do with that information, obviously it filters through them, right? And I do think that when you said open-ended questions, I think it's really understanding values, right? So everybody has a different life perspective and might have different goals or things that they prioritize.

And so sometimes I just explicitly ask, like, what is your understanding of your disease? And now that this disease is here what are your goals? And that might be "To live as long as possible, and I'm willing to take any treatment to do that." Or it might be "I really want to prioritize my quality of life. I'm willing to take and undergo cancer treatment, but not if my quality of life is not acceptable." Or I have a patient that is a painter, and she says "You can give me any treatment, doc, but I don't want neuropathy because I want to be able to continue to paint." And so I think really individualizing and listening to our patients and kind of working around what their values are, I think is really important.

And then, like you said, Vicki, the discussion, right? I think it's not a one-time discussion, it's an ongoing discussion, right? I think you have it up front when you discuss prognosis and first-line treatment. You have it during kind of every scan and changes that you make. And then, of course, it becomes very important at the end of life too, where you really want to understand when people have limited time left what are their values? What are they prioritizing? Really becomes critical.

Dr. May:
This has been such a great discussion about treatment considerations for EGFR-mutated non-small cell lung cancer. As we wrap up our time together, would each of you provide the audience with some of your key takeaways from our discussion?

Dr. Yu:
Absolutely, I can go first. I think the first thing is that for newly diagnosed stage IV non-small cell lung cancer, biomarker testing is not optional, it's the standard of care. It helps our patients live longer and really matches them with the appropriate therapy. And so this would be next-generation sequencing, as well as PD-L1 IHC testing.

The standard of care for EGFR-mutant non-small cell lung cancer has entered its combination therapy era. And so really, for the majority of patients, because of the PFS and OS benefit with the combination, I am thinking about that for most of my patients, and then considering osimertinib monotherapy or opting out of combination therapy for patients where monotherapy fits their values and quality of life.

And then resistance to therapy is inevitable, but there are new targets. And of course as Vicki has gone over, like, it is a multidisciplinary care team, and nurses and pharmacists are critical to optimizing outcomes because they really are on the front lines helping our patients. You want your patients on the drug, but they need to stay on the drug, and they need to thrive on the drugs. And so having the right support to allow that and to equip our patients for that really is key.

Dr. Sherry:
Thank you, Helena. I'm just going to wrap it up by saying that oncology nurses, you are the front-line defense against treatment-limiting toxicity. So proactive nursing-led interventions, you know, your structured skin toxicity programs, early symptom assessment, patient education—these all have been shown to reduce drug interruptions and improve patients' quality of life, and it keeps them on life-

© 2026 ReachMD

prolonging therapy longer. So keep up the good work.

Dr. May:
That's a great way to round out our discussion, and I want to thank my guests, Dr. Helena Yu and Dr. Victoria Sherry, for helping us better understand our approach to managing EGFR-mutated non-small cell lung cancer. Dr. Yu, Dr. Sherry, it was great speaking with you both today.

Dr. Yu:
It was a pleasure.

Dr. Sherry:
Thank you so much.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Cornerstone Medical Education and the American Academy of CME.

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.

© 2026 ReachMD