Transcript Details

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Patient-Centered Discussions and Shared Decision-Making in the Management of NSCLC with METex14 Skipping Mutations

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Patient-Centered Discussions and Shared Decision-Making in the Management of NSCLC with METex14 Skipping Mutations” is provided by **AGILE**.

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Dr. Patel:
Hello, I'm Dr. Jyoti Patel from Northwestern Medicine, and I'd like to welcome you to our Patient-Clinician Connection on MET met exon 14 skipping mutations in non-small cell lung cancer.

Therapeutics targeting actionable oncogenic drivers and non-small cell lung cancer have profoundly shifted the treatment landscape. Use of broad molecular profiling ensures that patients receive the appropriate targeted therapy. MET exon 14 skipping mutations are observed in 3% to 4% of all non-small cell lung cancer cases. And we now have 2 drugs approved by regulatory agencies such as the FDA [US Food and Drug Administration] and EMA [European Medicines Agency], to consider for non-small cell lung cancer patients harboring these alterations.

Remember, when discussing treatment options, it's important to align patient and clinician goals. Today, I'll be illustrating my approach to treating MET exon 14 skipping mutations and non-small cell lung cancer through clinical vignettes. Let's get started.

Today, my patient Sally is in my office to discuss initial treatment options for her recently diagnosed non-small cell lung cancer. Sally is 75 years old and has a 25 pack-year history of smoking. She has well-controlled hypertension, and we found that her non-small cell lung cancer is positive for a MET exon skipping mutation. She has good performance status of 1, and on physical exam, she has no lymphadenopathy and decreased breath sounds in her left lung. We were able to complete both blood and tissue NGS [next-generation sequencing] testing, and both showed MET exon 14 skipping mutations. Furthermore, her PD-L1 score was less than 1%.

Dr. Patel:
Hi, Sally, how are you doing today?

Sally:
Overall, I feel okay. But I do have a little shortness of breath, which is stopping me from playing tennis.

Dr. Patel:
I know how much you like tennis, and I'm sorry these symptoms are bothering you. It's been a little bit of a wait, but we did get those tests, we were waiting for, your biomarker results. And we found that you have MET exon 14 skipping mutation. That sounds like alphabet soup, but it's a targetable mutation that's on your cancer cells for which we have FDA-approved therapies.

Sally:
That sounds overwhelming. What does that mean?

Dr. Patel:
MET exon 14 skipping mutations occur in about 3% to 4% of patients with non-small cell lung cancer, predominantly lung adenocarcinoma, but sometimes squamous and sarcomatoid histologic subtypes, and they mostly occur in the absence of other driver mutations. Next-generation sequencing, or NGS testing, enables us to identify specific alterations, such as the MET exon 14 skipping mutation, and to use targeted therapies to more effectively treat our patients.

Let's return to our discussion with Sally to ease her mind about this mutation, and discuss next steps.

Dr. Patel:
I know this seems like a lot. There are currently 2 drugs that we generally use for patients with non-small cell lung cancer, who have a MET exon 14 skipping mutation. The drugs are called capmatinib and tepotinib. Both drugs are MET inhibitors, which are specifically designed to target the MET protein that's on cancerous cells, and not so much on your normal cells. Both drugs have great safety profiles and really good efficacy profiles. While they're similar, there are some distinctions between both drugs, and I'll walk you through this.

Sally:
Is this chemotherapy?

Dr. Patel:
These aren't chemotherapies. These are targeted drugs. These drugs, by blocking the MET pathway, blocks the signaling that drives tumor growth. These are pills that you take every day, at home, either once or twice a day. And that depends on which one we choose.

Sally:
So what are the differences between the two treatments?

Dr. Patel:
The drugs are actually pretty similar and were approved at about the same time. Capmatinib, you take twice a day at home, and tepotinib, you take once a day.

Sally:
I would much prefer a drug that I take only once a day because it's so much easier for me to remember.

Dr. Patel:
There are 2 MET inhibitors that have been approved by regulatory agencies such as the FDA and EMA, for the treatment of non-small cell lung cancer with MET exon 14 skipping mutations. Their efficacy data is quite similar and many times the choice comes down to patient preference or access.

In the 2 trials that have led to approval of capmatinib and tepotinib patients were treated with either drug until progression or toxicity. In the GEOMETRY trial, which enrolled 97 patients and treated them with capmatinib, the response rate was 41% in previously treated patients versus 68% in patients who were treatment naïve.

On the VISION trial, 99 patients were treated with tepotinib. In previously treated patients, the response rate was 46%. For treatment-naïve patients, the response rate was 56%. In both trials, the median duration of response was between 9.7 months and 11.1 months. Disease control rates on capmatinib were 83.5%. On tepotinib, the disease control rate was 65.7%. Median progression-free survival treatment with capmatinib was 5.4 months. It was 8.5 months on the VISION trial with tepotinib.

The dosing between capmatinib and tepotinib is different. Capmatinib comes in 2 strengths of tablets, 150 mg and 200 mg, and the starting dose is 400 mg or 2 tablets twice daily. It can be taken regardless of food consumption and may cause some photosensitivity reactions. So patients should be counseled to limit direct ultraviolet exposure or wear sunscreen or protective clothing.

Tepotinib comes in 225-mg tablets. It must be taken with food, and 2 tablets are given once daily.

When thinking about selecting the appropriate treatment, it's important to discuss potential toxicities, as these are often important in deciding a patient's preference. Let's watch as I discuss these with Sally.

Dr. Patel:
Given your active lifestyle, I think that makes really good sense. So the drug that we would choose for you then is tepotinib.

Sally:
Should I be concerned about any side effects?

Dr. Patel:

Overall, these medications are really well tolerated. Nausea can be common, but generally, we can make interventions to decrease it. Most people develop something called lower extremity edema. So that's swelling in your legs. If that happens, you call my office, and there are interventions we can make, either with adding different medications or giving you things that you can do at home to decrease the effect of this.

Some uncommon, but serious side effects include inflammation in your lungs, something called interstitial lung disease. If that happens, you'll develop shortness of breath, you'll call my office right away, and we'll discontinue the medication as we work you up. Another serious side effect can be toxicity to the liver or hepatotoxicity. We usually monitor this by checking blood work on you periodically while you're on the drug.

Sally:
Once I start this medication, when will I start to feel better?

Dr. Patel:
Generally, people feel better once they start taking this drug within several weeks. We know from our studies that patients say that there's an improvement in their cough, shortness of breath, and chest pain as soon as a month after starting this intervention. We generally see you within 3 weeks of starting the drug, and then end up doing a CT scan 6 to 8 weeks after you've initiated the drug to track your progress.

Sally:
Thank you for answering my questions, Dr. Patel.

Dr. Patel:
A common toxicity with MET inhibitors and is class specific is peripheral edema that can affect our patient's quality of life. This can be managed by decreasing the dose or holding the drug until the peripheral edema is improved. Other serious toxicities with MET inhibitors include interstitial lung disease, or pneumonitis. When this happens, we need to immediately withhold the drug and permanently discontinue. Also, patients can experience hepatotoxicity, so we need to monitor liver function tests and withhold, reduce, or permanently discontinue, depending on the severity of the toxicity. Patient-reported outcomes show the impact of treatment with tepotinib on quality of life. There was an improvement in cough, dyspnea, and chest pain, an improvement in quality of life after 6 weeks of therapy on tepotinib.

I think the model presented in these vignettes can be adapted to address the many scenarios we face daily in our medical practices when discussing the diagnosis of and treatment for MET exon 14 skipping mutations in non-small cell lung cancer. When prescribing MET inhibitors for these patients, it's important to apply shared decision-making with the consideration of patient preference and potential advantages as well as challenges in treatment adherence to maximize efficacy.

Thank you for joining me for our Patient-Clinician Connection vignettes on shared decision-making in the management of non-small cell lung cancer with MET exon 14 skipping mutations.

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