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/intracranial-activity-of-ros1-tkis/18157/

Released: 03/01/2024
Valid until: 03/01/2025
Time needed to complete: 1h 17m

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

Intracranial Activity of ROS1 TKIs

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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

Dr. Aggarwal:
Hello and welcome. I'm Dr. Charu Aggarwal, I'm a Leslye Heisler Associate Professor for Lung Cancer Excellence at University of Pennsylvania's Abramson Cancer Center. Today, we'll talk about intracranial activity of ROS1 TKIs.

This is important because when you think about gene fusions such as ALK, one of the things as a lung cancer specialist that I immediately worry about is brain metastases. Well, we know that it remains a clear problem that leads to morbidity in our patients. Patients with ROS1 non-small cell lung cancer do have a predilection that may be higher than other oncogene-driven cancers to develop brain mets. Research has shown that this may not be as high as some of the subsets seen with ALK-positive lung cancer but recognizing that any cancer that's driven by a fusion may still be a little bit higher risk, making this a clinically important unmet need in the management of these patients.

We talked a little bit about different treatment options. We have options such as crizotinib, entrectinib, and repotrectinib; all listed as preferred first-line treatment options. However, having said that, if brain metastases are going to be an issue that we want to manage well, I think it's important to recognize that we should be focusing on drugs that have intracranial penetration. When we look across activity of different ROS1 TKIs, two things are very clear; trials have included both subsets of patients that may be treatment naïve, as well as previously treated with other ROS1 TKIs, and secondly, that these trials have included patients with and without baseline metastases. While this leads to heterogeneity of patient populations, it actually gives us a lot of information that we can glean from and learn from as we apply to our patients. For example, with a drug such as repotrectinib that has recently been approved and included as our first-line option, we see intracranial activity that's present both in previously treated as well as treatment-naïve patients. With a drug such as repotrectinib, we can expect an intracranial overall response rate of about 89% amongst patients who may have had baseline brain metastases and were treatment naïve. This is similar to a drug such as entrectinib, which may have slightly numerically lower intracranial activity of about 80%. But both of these are vastly different from what we would see with a drug such as crizotinib or ceritinib, which may have very little to no activity in the CNS; therefore, preferentially making the later-generation TKIs slightly more attractive option, recognizing that brain mets can be clearly a morbidity concern for our patients.

There are other drugs in development such as taletrectinib, which also promise intracranial activity, they're currently not approved. And I think we can look at them in terms of future development. Lorlatinib, which is a drug that has been approved for ALK-positive non-small cell lung cancer may also have activity in ROS1 non-small cell lung cancer, and the overall response rate, as well as intracranial overall response rate matches what we see in the ALK subsets.

When we look at the data from repotrectinib, it's very intriguing to see that there is responses, as I mentioned before, up to 89% in treatment naïve. However, if a patient had brain metastases, let's say, on a previous therapy, and then was initiated on repotrectinib, we

can see from clinical trial results that we can see an intracranial overall response rate of about 38%, which is not trivial. This means that we can avoid Gamma Knife, we can avoid radiation, as well as some of the crippling effects that can occur with radiation therapy.

Development of new brain metastases in TKI-naïve as well as pretreated patients without baseline metastases has also been demonstrated to be lower in patients who begin therapy with repotrectinib. And I think this is the promise of both precision therapy, as well as therapies that are highly active and brain penetrant.

So, in summary, brain metastases really remain an area of therapeutic need for our patients with ROS1 rearranged non-small cell lung cancer. Deep and durable intracranial activity has been demonstrated in both ROS1 TKI treatment-naïve and pretreated patients with newer ROS1 TKIs. Entrectinib, lorlatinib, and repotrectinib are recommended for patients with ROS1 rearranged lung cancer that present with brain metastases.

Thank you for watching.

Announcer:
You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, LLC. and is part of our MinuteCE curriculum.

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