Transcript Details

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Investigator Perspectives on Treating Patients in a Ph2 NSCLC Trial

ReachMD Announcer:
Welcome to *Project Oncology* on ReachMD. This medical industry feature, titled "Investigator Perspectives on Treating Patients in the Phase 2 LUMINOSITY Trial," is sponsored by AbbVie US Medical Affairs. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is *Project Oncology* on ReachMD, and I'm your host Dr. Jennifer Caudle. Joining me today to discuss the key findings from the LUMINOSITY trial studying a treatment for non-small cell lung cancer are Drs. Jonathan Goldman and Ross Camidge.

Dr. Goldman is a Professor of Medicine at UCLA in the Hematology/Oncology Division as well as the Director of Clinical Trials in Thoracic Oncology at UCLA Medical Center in Santa Monica, California.

Dr. Goldman, thank you for being here today.

Dr. Goldman:
It's a pleasure to be here.

Dr. Caudle:
Also with us is Dr. Ross Camidge who is the Joyce Zeff Chair in Lung Cancer Research at the University of Colorado as well as the Director of Thoracic Oncology at the University of Colorado Cancer Center in Aurora. Dr. Camidge, we're happy to have you with us today.

Dr. Camidge:
Well, thanks for having me on the program.

Dr. Caudle:
Of course. Before we get into LUMINOSITY, let's take a moment to review the indication and select important safety information for telisotuzumab vedotin-tllv.

ReachMD Announcer:

INDICATION

- Telisotuzumab vedotin-tllv is indicated for the treatment of adult patients with locally advanced or metastatic, non-squamous non-small cell lung cancer (NSCLC) with high c-Met protein overexpression [≥50% of tumor cells with strong (3+) staining], as determined by an FDA-approved test, who have received a prior systemic therapy.
- This indication is approved under accelerated approval based on overall response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

SELECT IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Peripheral neuropathy, interstitial lung disease/pneumonitis, ocular surface disorders, infusion-related reactions, and embryo-fetal toxicity.

Adverse Reactions

- Serious adverse reactions occurred in 35% of patients. The most common adverse reactions (≥20%) were peripheral neuropathy, fatigue, decreased appetite, and peripheral edema.
- The most common Grade 3 or 4 laboratory abnormalities (≥2%) were decreased lymphocytes, increased glucose, increased alanine aminotransferase, increased gamma glutamyl transferase, decreased phosphorus, decreased sodium, decreased hemoglobin, and decreased calcium.

Please see full Important Safety Information at the end of this video.

Dr. Caudle:
So now that we've heard that important safety information, let's begin our discussion with some background. As an investigator in LUMINOSITY, Dr. Goldman, can you tell us about the rationale behind the trial?

Dr. Goldman:
Yes, I'd be happy to. We know that alterations in the *MET* gene and the c-Met protein's function can affect cell proliferation, survival, and angiogenesis.[1,2]

In non-small cell lung cancer, MET can be dysregulated in a few ways, such as, c-MET protein overexpression, MET gene amplification, and MET exon 14 skipping mutations. These MET aberrations are associated with a poor prognosis, and they aren't mutually exclusive. Tumors may exhibit some overlap between these MET aberrations. Due to their role in carcinogenesis and cancer progression, MET aberrations are emerging as biomarkers.[3]

High c-MET protein overexpression is seen in about 14% of patients with EGFR wild-type non-squamous non-small cell lung cancer. That's about 1 in 7 patients. So there's a lot of interest in more targeted approaches for tumors with this characteristic.[3]

Dr. Caudle:
I see. Now, Dr. Camidge, you were also involved in this trial. Could you walk us through the design of the LUMINOSITY trial?

Dr. Camidge:
Absolutely. So LUMINOSITY studied telisotuzumab vedotin-tllv, also known as Teliso-V which is a first-in-class c-MET protein–directed antibody-drug conjugate.[3]

It's made up of a monoclonal antibody—telisotuzumab—that's conjugated to a cytotoxic payload—monomethyl auristatin E, or MMAE—using a cleavable linker. MMAE is a microtubule inhibitor that prevents tubulin polymerization, effectively blocking mitosis and leading to tumor cell death. Telisotuzumab vedotin-tllv targets c-Met protein to deliver this payload to cells.[3]

Now, in terms of the study design, LUMINOSITY was a phase two open-label, single-arm, and multi-cohort clinical trial in two stages. The first stage was designed to identify the population of patients with locally advanced or metastatic non-small cell lung cancer best suited for second line-treatment with telisotuzumab vedotin-tllv monotherapy. Patients who had non-squamous non-small cell lung cancer either with or without EGFR-activating mutations—as well as those with squamous non-small cell lung cancer were enrolled in this stage. The study included patients who had treatment with prior systemic therapy, including no more than one line of prior chemotherapy.[3] c-Met protein overexpression was measured by immunohistochemistry, or IHC, with pre-specified cutoffs for the squamous cohort as well as for c-Met intermediate and c-Met high non-squamous cohorts.[3] The second stage of the study evaluated the efficacy and safety of telisotuzumab vedotin-tllv in patients who met the expansion criteria in stage one.[3]

For today's discussion, we'll go over results for patients who had EGFR-wild-type non-squamous non-small cell lung cancer with high c-Met protein overexpression. In the LUMINOSITY trial, high c-Met protein overexpression was defined as 50 percent or more tumor cells demonstrating strong, or three-plus, staining on archival or recent tissue samples by IHC.[3]

Dr. Caudle:
So with that in mind, Dr. Camidge, what should we know about the efficacy findings?

Dr. Camidge:
The primary endpoint was the overall response as assessed by a blinded independent central review committee, with the duration of response as a secondary endpoint.[3] For the 84 patients with high c-Met protein-overexpressing, non-squamous EGFR wild-type non-small cell lung cancer[3] the overall response rate was 35 percent with a 95 percent confidence interval between 24 and 46 percent[3,4] The median time to response was quick, about 1.4 months for the overall c-Met-overexpression group, ranging between one to 4.2 months.[5] The median duration of response was 7.2 months, with a 95 percent confidence interval between 4.2 and 12 months.[4] We also saw that 59 percent of patients maintained their response for six months or longer, with 21 percent maintaining duration of response for one year or more.[3,4]

Given these results, telisotuzumab vedotin-tllv is now included in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) The NCCN Guidelines® include telisotuzumab vedotin-tllv as a Category 2A recommended option for treating patients with advanced or metastatic non-squamous non-small cell lung cancer as a subsequent therapy and in disease progression. It's specifically recommended for EGFR wild-type tumors with high c-Met protein overexpression.[6]

Dr. Caudle:
Now, let me turn to you, Dr. Goldman. Can you tell us about the safety data from LUMINOSITY?

Dr. Goldman:
Yes, absolutely. The safety population included 168 patients with EGFR wild-type non-squamous non-small cell lung cancer who had c-Met protein overexpression and who had received telisotuzumab vedotin-tllv monotherapy.[3,4]

One of the most common adverse reactions was peripheral neuropathy, which occurred in 51 percent of patients.[4] Ocular surface disorders occurred in 25 percent of patients.[4] Other adverse events included fatigue in 29 percent, decreased appetite and peripheral edema in 22 percent each, and pneumonia in 13 percent.[4]

Dr. Caudle:
So with that efficacy and safety data in mind, Dr. Goldman, what should clinicians know about the FDA approval of telisotuzumab vedotin-tllv?

Dr. Goldman:
In May 2025, the FDA approved telisotuzumab vedotin-tllv for the treatment of adult patients with locally advanced or metastatic EGFR wild-type non-squamous non-small cell lung cancer whose tumors show high c-Met protein overexpression as determined by an FDA-approved test and who have received a prior systemic therapy.[4]

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[4]

In addition, the FDA also authorized the VENTANA SP44 IHC assay as the companion diagnostic to test for c-Met protein expression and identify eligible patients for telisotuzumab vedotin-tllv.[7]

The NCCN Guidelines also added c-Met/MET immunohistochemistry as a Category 2A recommended biomarker test.[6]

So now, with both the therapeutic and the diagnostic approved, we have a path forward to identify and treat patients who have EGFR wild-type non-small cell lung cancer with at least 50 percent of cells showing three-plus c-Met protein staining as detected by IHC.[4,7]

Dr. Caudle:
For those of you who are just tuning in, you're listening to *Project Oncology* on ReachMD. I'm your host Dr. Jennifer Caudle, and today I'm speaking with Drs. Jonathan Goldman and Ross Camidge about the LUMINOSITY trial results on telisotuzumab vedotin-tllv in non-small cell lung cancer.

So Dr. Camidge, given the findings from LUMINOSITY, as well as the FDA approvals, how should we be thinking about testing for c-Met protein overexpression in clinical practice?

Dr. Camidge:
That's really the key question because how and when we test can have a direct impact on patient access to targeted therapies like telisotuzumab vedotin-tllv. In my practice, I think c-Met testing a bit like how we approach PD-L1 testing.

You want that information early—ideally at the time of diagnosis while still prioritizing first-line biomarker testing—because then you've got the results that you may need after disease progression when tissue might be limited.

What we want to avoid is getting to second-line therapy and discovering, for example, you don't have enough tissue left to test, or that you have to wait for the results, both of which are going to limit access to a treatment that's shown responses in this setting.

Dr. Caudle:
That's important context, thank you for that.

Now, let's switch gears, as I'd like to hear a bit more on how you're managing patients who experience certain adverse reactions while receiving telisotuzumab vedotin-tllv.

So, starting with peripheral neuropathy, Dr. Goldman, what can we learn from LUMINOSITY here?

Dr. Goldman:
So this is why it's important to monitor regularly and intervene early. By following the prescribed guidance to withhold treatment at the first sign of symptoms and resume at a reduced dose once symptoms improve, patients may be able to continue treatment.

We should keep in mind that the MMAE payload used in telisotuzumab vedotin-tllv is a microtubule inhibitor, and agents in this class are known to cause peripheral neuropathy.[8] So it's important to monitor for signs and symptoms of new or worsening peripheral neuropathy, like paresthesia, burning sensation, neuropathic pain, or muscle weakness.[4]

Peripheral neuropathy occurred in just over 1/2 of patients on the LUMINOSITY study. It was more often peripheral sensory neuropathy, which occurred in 45% of patients, with peripheral motor neuropathy occurring in 9%. What's important to note is that the median time to onset was 105 days, or about 3.5 months. What I found particularly interesting is that for the 13% of patients whose peripheral neuropathy led them to discontinue treatment, the median time to discontinuation was 249 days, or about 8 months.[4]

So that is why it's important to monitor regularly and intervene early by following the prescribed guidance to withhold treatment at the first sign of symptoms and resume at a reduced dose. Once symptoms improve, patients may be able to continue treatment. And for patients on telisotuzumab vedotin-tllv who are experiencing these symptoms, one can turn to supportive therapies for this adverse reaction.[4]

Dr. Caudle:
Now let's move over to ocular toxicities, Dr. Goldman. What stood out to you about these events in the study, and how do you typically approach these cases?

Dr. Goldman:
Ocular toxicities occurred in about one-fourth of patients, with blurred vision reported in 15 percent, keratitis in 11 percent, and dry eye in five percent.[4]

Grade Three ocular surface disorders occurred in 1.2 percent of patients. And for patients who develop grade two or higher ocular toxicity, I'd hold telisotuzumab vedotin-tllv and refer to an eye care professional for further examination and management. In some cases, treatment will need to be permanently discontinued.[4]

In my own experience, ocular toxicity with this agent can be mild. I've found that supportive strategies like lubricating and/or steroid eye drops have been useful to manage symptoms such as dry eye.[4]

Dr. Caudle:
I see. Now, we also learned about cases of interstitial lung disease, or ILD, in the review of the LUMINOSITY safety data. Before we close, Dr. Camidge, what do clinicians need to know here?

Dr. Camidge:
You're absolutely right, that's important. We saw that ILD or ILD/pneumonitis occurred in 10 percent of patients in the safety population, including Grade Three events in three percent, Grade Four events in 0.6 percent, and three fatal cases. Seven percent of patients discontinued telisotuzumab vedotin-tllv due to ILD, and the median onset of discontinuation was around 46 days, roughly six weeks into therapy, with a range from 23 to 85 days.[3]

For patients who develop ILD or pneumonitis, I think the biggest takeaway is to catch it early and act on it early. Typically, Grade One is something you see on a scan without symptoms, and Grade Two is when symptoms appear or when you start treatment with steroids.[3]

In practice, some of us might choose to start steroids as soon as we suspect ILD—just based on that Grade One imaging. Our goal is to prevent escalation of ILD.[3] When you intervene earlier—especially at the first sign on imaging—there may be more opportunity to manage the event by withholding telisotuzumab vedotin-tllv and supporting with steroids.[3]

It's still key to monitor for symptoms and signs of ILD/pneumonitis and advise patients to immediately report any symptoms of cough, dyspnea, fever, and new or worsening respiratory symptoms.[3]

So, based on everything we've discussed—from peripheral neuropathy to ocular toxicities to ILD—it's clear to me that proactive monitoring and early intervention are critical to managing adverse reactions with telisotuzumab vedotin-tllv.

Dr. Caudle:
And we'll certainly be watching closely to see how our understanding of telisotuzumab vedotin-tllv in this setting continues to evolve. I'd like to thank my guests, Dr. Jonathan Goldman and Dr. Ross Camidge, for joining me to share insights on treating patients and managing adverse reactions in the LUMINOSITY trial with telisotuzumab vedotin-tllv.

Dr. Goldman and Dr. Camidge, it was great speaking with you both today.

Dr. Goldman:
Thanks for this discussion.

Dr. Camidge:
Thanks for having me.

Dr. Caudle:
Now, let's take a moment to hear more important safety information on telisotuzumab vedotin-tllv.

ReachMD Announcer:

TELISOTUZUMAB VEDOTIN-TLLV IMPORTANT SAFETY CONSIDERATIONS

Warnings & Precautions

- **Peripheral neuropathy:** Telisotuzumab vedotin-tllv can cause peripheral neuropathy. In the safety population, peripheral neuropathy occurred in 51% of patients (Grade 3, 11%); this included peripheral sensory neuropathy (45%) and peripheral motor neuropathy (9%). Peripheral neuropathy led to treatment discontinuation in 13% of patients. Monitor patients for signs and symptoms of new or worsening peripheral neuropathy such as hypoesthesia, hyperesthesia, paresthesia, a burning sensation, neuropathic pain, or muscle weakness. Withhold, reduce the dose, or permanently discontinue telisotuzumab vedotin-tllv based on severity.
- **Interstitial lung disease (ILD)/pneumonitis:** Telisotuzumab vedotin-tllv can cause severe, life-threatening, or fatal ILD/pneumonitis. In the safety population, ILD/pneumonitis occurred in 10% of patients (Grade 3, 3%; Grade 4, 0.6%) and there were 3 fatal cases. ILD/pneumonitis led to permanent discontinuation in 7% of patients. Advise patients to immediately report cough, dyspnea, fever, and/or any new or worsening respiratory symptoms. Monitor patients for signs and symptoms of ILD/pneumonitis. Withhold or permanently discontinue telisotuzumab vedotin-tllv based on severity.
- **Ocular surface disorders:** Telisotuzumab vedotin-tllv can cause ocular surface disorders including blurred vision, visual impairment, keratitis, and dry eye. In the safety population, ocular surface disorders occurred in 25% of patients. The most common ocular surface disorders were blurred vision (15%), keratitis (11%), and dry eye (5%). Grade 3 reactions occurred in 1.2% of patients [blurred vision (1.2%) and keratitis (0.6%)]. Monitor patients during treatment. Withhold telisotuzumab vedotin-tllv and refer patients to an eye care professional for an ophthalmic exam and treatment for patients who develop Grade ≥2 ocular toxicity. Withhold or permanently discontinue treatment based on severity.
- **Infusion-related reactions (IRR):** Telisotuzumab vedotin-tllv can cause IRR; signs and symptoms of IRR include dyspnea, flushing, chills, nausea, chest discomfort, and hypotension. In the safety population, IRR occurred in 3% of patients, including Grade 3 in 1.2% and Grade 4 in 0.6%. IRR led to permanent treatment discontinuation in 0.6% of patients. Monitor patients for signs and symptoms of infusion reactions. Withhold, reduce infusion rate, or permanently discontinue telisotuzumab vedotin-tllv based on severity. For patients who experience IRR, administer premedications prior to subsequent infusions.
- **Embryo-fetal toxicity:** Telisotuzumab vedotin-tllv can cause fetal harm when administered to pregnant women. Advise patients of potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 2 months after the last dose. Advise male patients to use effective contraception during treatment and for 4 month after the last dose.

Adverse Reactions

- Serious adverse reactions occurred in 35% of patients. The most common adverse reactions (≥20%) were peripheral neuropathy, fatigue, decreased appetite, and peripheral edema.
- The most common Grade 3/4 lab abnormalities (≥2%) were decreased lymphocytes, increased glucose, increased alanine aminotransferase, increased gamma glutamyl transferase, decreased phosphorus, decreased sodium, decreased hemoglobin and decreased calcium.

Drug Interactions

- Concomitant use of strong CYP3A inhibitors may increase AUC of MMAE. Monitor for adverse reactions.

Specific Populations

- **Severe or Moderate Hepatic impairment:** Avoid use of telisotuzumab vedotin-tllv.
- **Lactation:** Advise not to breastfeed.
- **Infertility:** May impair fertility.

Review full prescribing information for additional information at www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110 or go to abbviemedinfo.com.

This medical industry feature was sponsored by AbbVie US Medical Affairs. If you missed any part of this discussion or to find other episodes in this series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge.

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ABBV-US-02205-MC Version 1.0 Approved November 2025