

Journal Club Spotlights: Current Advancements in Non-Small Cell Lung Cancer



Editor's Note: This is a transcript of a discussion on July 10, 2026. It has been edited and condensed for clarity. To obtain credit for participation [CLICK HERE](#).

Jamie Chافت: Welcome. I am Dr. Jamie Chافت from Memorial Sloan Kettering Cancer Center. In this accredited webinar, we are going to discuss the article “Selpercatinib in early stage *RET* fusion positive non-small cell lung cancer.” It was published concurrently with the American Society of Clinical Oncology (ASCO) annual meeting in late May [2026] in the *New England Journal of Medicine*, and presented in the plenary session. I am joined today by Dr. Jonathan Goldman from UCLA, who was one of the LIBRETTO-432 trial investigators. Dr. Goldman, welcome. Thank you for joining us, and I would ask you to start with an overview of why this study was created.

Jonathan Goldman: Thank you. It is a pleasure to meet with you and talk to you, as always, and great to speak about this trial. This trial fits within a paradigm of new targeted therapy approaches in the perioperative setting. We know that as we are doing more screening, and patients are getting scans for other reasons, we are diagnosing lung cancer more often at an early stage. Unfortunately, lung cancer still carries a high recurrence risk. So, even stage IB, II, and III, all of them have a meaningful recurrence risk that we would like to do whatever we can to lower that risk. And through a few trials, including the ADAURA and ALINA trials, we showed that *EGFR* therapy or *ALK* targeted therapy reduces recurrences by 75% to 80%. We know that we have several other very targetable mutations with excellent oral agents, and we wanted to demonstrate whether a *RET* therapy, selpercatinib, could similarly and meaningfully improve outcomes for patients after definitive surgery.

Jamie Chافت: Tell me a little bit about *RET* in general. It is rare.

Jonathan Goldman: It is rare. About 2% of lung cancer is characterized by a *RET* fusion. These *KIF5B* or *CCDC6* are some of the more common fusion partners, but there is a long list of possible fusions, and this is one of the well-characterized driving mutations in lung cancer. *RET* is also interesting for being involved in other cancers, thyroid cancers most specifically, but often point mutations, not fusions. There are rare events of other *RET*-driven cancers. I have actually 2 small cell lung cancer patients, and selpercatinib does carry an approval for lung cancer, for thyroid cancer, and a tumor agnostic approval for any solid tumor with a *RET* mutation or fusion.

Jamie Chافت: Right, I think that is really important to point out. We see these *RET* point mutations on next-generation sequencing reports all the time, and they are not biologically

Journal Club Spotlights: Current Advancements in Non-Small Cell Lung Cancer



relevant for lung cancer at least, just the fusions, and those are best picked up on RNA testing when we can get it, right?

Jonathan Goldman: Right, exactly. DNA and RNA gives us our best sensitivity. One of the important points was this trial was a huge screening project, almost 3½ thousand patients were screened in order to identify and enroll 151 patients. You really do have to be thinking about it. I think in the overall picture of non-small cell lung cancer, doing a broad, comprehensive, mutation profiling does make sense to make sure we have the optimal therapy for all our patients.

Jamie Chaff: Right, and before we start any therapy.

Jonathan Goldman: Right.

Jamie Chaff: Tell me about this study. What were the main objectives?

Jonathan Goldman: The main endpoint was event-free survival (EFS) and this was not the same as the other adjuvant therapy trials. They had disease-free survival, but this trial was designed to include patients that got definitive radiation. For them [patients receiving definitive radiation], progression-free survival was felt to be sort of the concept, and for patients that had surgery, it would be disease-free survival. Putting them together was this concept of event-free survival. Ideally, to be confirmed by a biopsy, in that event. These patients were treated with 3 years of therapy, selipencatinib or placebo, followed with imaging. The trial did include brain MRI imaging at each of the CT time points and they were followed for cancer recurrence. We did find that cancer recurrence was more common in the placebo arm.

Jamie Chaff: We will dive briefly into the details of this study. So early-stage *RET* fusion positive stage IB through III, you told us already. Are there any other key inclusion criteria that we should be aware of?

Jonathan Goldman: I think the requirement for definitive therapy. Patients were allowed, but not required, to get chemotherapy. It could be neoadjuvant or adjuvant, or none at all. More than 90% of the stage II and IIIA patients got chemotherapy, mostly in the adjuvant setting. There were 3 patients that also got immunotherapy. That was mostly in the chemo-immunotherapy setting prior to surgery, but we did not collect all of that information, we just have the dates, and so we can put that together, but that was probably before the *RET* fusion was identified in those few cases.

Journal Club Spotlights: Current Advancements in Non-Small Cell Lung Cancer



Jamie Chaff: It is important to note that we do not really think immunotherapy works in this population, and perhaps can even increase the risks of the tyrosine kinase inhibitor (TKI) toxicities later. We need to get this data early.

Jonathan Goldman: Absolutely, that is a very helpful point.

Jamie Chaff: Any key exclusion criteria?

Jonathan Goldman: The patients should have no evidence of cancer recurrence following surgery. We do not have a lot of comorbidity exclusions like we might have with immune therapy, so the main thing is the identification of that *RET* fusion.

Jamie Chaff: You already told us this was a herculean effort in terms of screening. It was a phase 3 multicenter international study with 65 sites in 22 countries. Tell us how the eligible patients were randomized.

Jonathan Goldman: Yes, a huge effort, spanning several years, about 4 years to enroll the patients, and we can talk more about that later. One of the things I think is remarkable about the trial is that the effect size is so big that you can get a positive readout so quickly, and I think that can really help us as we think about doing similar trials in other small groups of patients. The patients were randomized 1:1 to get selpercatinib or placebo.

Jamie Chaff: In the typical weight-based formulation per the label.

Jonathan Goldman: That is right, exactly.

Jamie Chaff: I think one of the most notable things about the study was prespecified crossover, right? Patients who progressed could cross over to selpercatinib, right?

Jonathan Goldman: Yes, absolutely. There were 20 progression events [and 16 patients on the placebo arm did cross over]. The majority remained on that crossover selpercatinib at the time of the study analysis at the cutoff, but 3 of them had died, despite having the opportunity to get selpercatinib for at least a year for those patients. Starting selpercatinib in that postsurgery setting, you might get more benefit than you do when you wait for recurrence. Certainly, you delay recurrence, but that may be to the point of hopefully achieving really long-term disease control in the adjuvant setting use.

Jamie Chaff: Let us focus on your results. Tell us a little bit about the patients who were enrolled in the study.

Journal Club Spotlights: Current Advancements in Non-Small Cell Lung Cancer



Jonathan Goldman: One hundred and fifty-one patients [enrolled]. About 60% were Asian, 70% were nonsmokers, and a little over half, 60%, were female. I think in some ways maybe represented where the patients were enrolled. A lot were enrolled from Asian sites. We do not necessarily think there is an ethnicity difference with this mutation, for example, in contrast to *EGFR*. Just over 20 [patients] in each arm were stage IB, the other [patients] were stage II and III. The majority had surgery, the majority had chemotherapy, with just a handful getting radiation. Some patients got both surgery and radiation.

Jamie Chافت: Tell me about the primary endpoint, EFS.

Jonathan Goldman: The hazard ratio was 0.17, so about an 83% reduction in events. We can talk some more about the details, but a lot of the benefit was seen in the stage III patients. Also when you include the overall population, the whole population stage IB, II, and IIIA, still quite a meaningful hazard ratio benefit, perhaps even greater than the primary endpoint of stage II and III. [In] the stage IB patients, the event rate was quite small. So, hard to be too statistically focused on that group of patients. But the overall was really meaningful.

Jamie Chافت: What about safety? I think given the rarity of this mutation, some of our doctors may not have used this drug before. Tell us a little bit about managing [patients on selipercatinib].

Jonathan Goldman: I think it is such an important point, because many of us think of it as a quite well tolerated oral agent, but there are clearly toxicities, and there were a lot of dose modifications, dose holds, dose reductions, and some patients discontinued. Some of the toxicities: there is this unusual hypersensitivity reaction which happened in 7.6% of patients in the early days of treatment. You can have a rash, fever and liver function test (LFT) elevations. Interestingly, that [LFT elevation] often responds really well to a dose hold, sometimes steroids, and you can usually restart with good tolerability, but a couple of patients discontinued treatment who had that event. LFT elevations are also pretty common, about 60% of patients. That was the most common reason for treatment discontinuation. In review, retrospectively, a lot of those were grade 1 and 2 events, so it could have been considered to hold treatment, wait until resolution, and restart at a lower dose. In the metastatic setting, that is what we often do. I certainly understand that tolerance for toxicity is different in the adjuvant setting, but certainly for a higher stage patient, that is what I would do now, certainly, that we have the results of this trial. Hypertension is also a class effect and requires attention, sometimes needing initiation of antihypertensives, but should not be too challenging a toxicity.

Journal Club Spotlights: Current Advancements in Non-Small Cell Lung Cancer



Jamie Chaft: We checked the thyroid on this drug, which is not so unique to us anymore now that we all use immunotherapy. All right, so what are your conclusions from the study? Is this going to change the standard of care?

Jonathan Goldman: Absolutely. To me, I think it is a clear practice-changing trial. I think there are a couple of ways that are really important, but at the simplest, I do think that a stage IB, II, or III patient with a *RET* fusion non-small cell lung cancer, after definitive therapy, with or without chemotherapy, should get selpercatinib for 3 years. I think it was overall tolerated with the points that we talked about and definitely fits in the same paradigm as osimertinib or alectinib in a meaningful way to improve recurrence-free survival. I also think that now that we have 3 targets in this adjuvant setting, I think it clearly drives us and everyone to use NGS testing. Up until now you could do tumor mutation specific tests for *EGFR* and *ALK*, but I think these types of trials and this concept is just going to become more important. As you said, also finding these mutations may significantly change your thinking about the use of immunotherapy or your overall approach to the early-stage patient. I think, really, on that first diagnostic biopsy, we should be getting NGS on all of our patients.

Jamie Chaft: Totally agree. Well, thank you. Thank you, Jonathan, for joining us and for bringing precision medicine further into the early stage. This was a great discussion.

Jonathan Goldman: Thanks so much, Jamie. It was a great discussion. I appreciate your questions and the opportunity to talk about this.