

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



Editor's Note: This is a transcript of a discussion on April 23, 2026. It has been edited and condensed for clarity. To obtain credit for participation [CLICK HERE.](#)

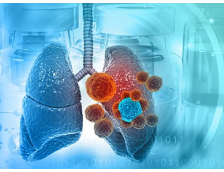
Jamie Chaft: Welcome, everyone. I am Dr. Jamie Chaft from Memorial Sloan Kettering Cancer Center. In this accredited webinar, we are going to discuss updates to the PAPILLON study. Specifically, the recent article presented regarding patient-reported outcomes (PRO) and time to symptomatic progression (TTSP) from the PAPILLON study of amivantamab plus chemotherapy compared to chemotherapy as first-line treatment of EGFR exon 20 insertion positive advanced lung cancer. This article was published in March of 2026 in *Lung Cancer*. I'm pleased to be joined by Dr. Aaron Mansfield from the Mayo Clinic who was one of the main authors of this study. Aaron, thank you for joining me, welcome. I would ask you to start with just a broad overview of the study and focus in on what your recent article has updated us on.

Aaron Mansfield: Thanks for having me, I appreciate it. So, just as a really brief background, amivantamab had an accelerated approval for patients with EGFR mutations with exon 20 insertions. And following that accelerated approval, the PAPILLON study was designed to try to determine whether amivantamab had activity in the front line. The study was constructed where we had to look at what the standard of care was for this patient population, which was a little different than the classic exon19 and L858R mutations that we see in EGFR. This study added amivantamab to chemotherapy and compared it to chemotherapy alone, with the primary endpoint of progression-free survival (PFS). Those data have been presented, and this more recent publication, however, is really focused on the time to symptomatic progression and patient-reported outcomes to really see how well patients were doing on this study. And just to reference the original report, the PAPILLON study was positive. It demonstrated that the combination of amivantamab with chemotherapy resulted in a significant improvement in progression-free survival. It had a hazard ratio of around 0.4, and it improved the median progression-free survival over 11 months compared to around 6 for the chemotherapy arm.

Jamie Chaft: Great, and this specific publication is focusing largely on the patient-reported outcomes and time to symptomatic progression, so what were the secondary endpoints of your study?

Aaron Mansfield: We want our drugs to not only help our patients live longer, but better, and these were key secondary endpoints. Patients who went on the clinical trial completed these Patient-Reported Outcomes Measurement Information System (PROMIS) and

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European Organization for Research and Treatment of Cancer (EORTC) instruments while they were participating in the study.

Jamie Chافت: Great, and I think this is particularly relevant, the primary endpoint of this study was an improvement in progression-free survival. Yet, we have struggled a little with this novel agent in our disease, with a drastically different safety profile than the agents we are used to. I think understanding how patients felt when they progressed and what their quality of life (QOL) was is really important. Could you give us a little overview of the methods of this study? We know it was a phase 3 study comparing amivantamab with chemo to chemo alone, what were the key inclusion criteria?

Aaron Mansfield: This was a randomized phase 3 study. It was unblinded just by the nature of amivantamab, just to point that part out. It was felt it would be hard to randomize with that component and how it was administered differently from the chemotherapy component. The study included adults 18 years or older with nonsquamous, non-small cell lung cancer (NSCLC) with 1 exception, they were not to have been treated previously, but it did allow patients who had received a tyrosine kinase inhibitor (TKI) that was not thought to have been effective. And that is a whole other conversation, but we essentially have not had an effective TKI in this setting, and this study allowed for someone to go onto the study with limited prior use of a TKI and because of the population we are looking at, patients must have had documented an EGFR exon 20 insertion mutation.

Jamie Chافت: And were there any key exclusion criteria? Anything clinically relevant?

Aaron Mansfield: Nothing much different than other clinical trials, but patients with untreated symptomatic brain metastases or central nervous system (CNS) disease were excluded, or other major concurrent illnesses.

Jamie Chافت: This study was global, conducted in over 200 sites, in 26 countries. How were the patients treated in the intervention arm?

Aaron Mansfield: For the intervention arm, patients received amivantamab with carboplatin and pemetrexed. Amivantamab was started with a weekly dosing, and the first dose was split because of the background of infusion-related reactions. We gave a lower dose on day one and a higher dose on day 2, and then we had to give it weekly for 4 doses until it aligned with the subsequent cycles.

Jamie Chافت: Okay, so we will circle back to that towards the end of our discussion and talk about how the new subcutaneous (SUBQ) formulation might alter these patient-reported

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outcomes in an even more favorable way, but let us dive into the data. Can you provide an overview, very broad, of who enrolled in this study?

Aaron Mansfield: There were over 300 patients who enrolled. Their demographics were what you would expect for an EGFR exon 20 insertion population. The median age was in the low 60s. Based on the sites that were open, much of the accrual did come from Asia. It had primarily never-smokers. Just under a quarter of patients in each arm had a history of brain metastases that were asymptomatic and treated. Overall, they had really good performance status.

Jamie Chافت: Right, and because we have been giving this regimen for quite some time now, the key finding of the original trial was efficacy, that adding amivantamab to chemo improved progression-free survival compared to chemo alone, which was our standard. Can you update us on what your publication added in terms of time to symptomatic progression?

Aaron Mansfield: The key finding here was the time to symptomatic progression, and what we saw here when you look at the median period of follow-up, there were fewer patients on the experimental arm of amivantamab in chemotherapy who had symptomatic progression compared to the chemotherapy alone arm. Those numbers [the proportion of patients without symptomatic progression] were 71% [amivantamab + chemotherapy arm] compared to 59% [chemotherapy arm] at that median, but then when you look at different landmarks that was retained at different landmarks, and in fact, the effect was more pronounced later on in the study.

Jamie Chافت: Great. And what about the key patient-reported outcomes?

Aaron Mansfield: So, the key patient-reported outcomes were based on these 2 questionnaires from PROMIS and EORTC. These 2 questionnaires really look at their overall functional status and quality of life. One is an 8-question questionnaire and the other has 30 questions. And what we saw, most importantly, at the beginning of the study, their reports were pretty similar between the 2 arms. Because clinical trials require patients to have a good performance status coming in, I do not think there were many surprises there. And when you look at physical function across the 2 arms, there was not a whole lot of change in physical function based on what arm the patients were assigned to. But the quality-of-life status is where we really start to see changes, even as early as 6 months. What we saw was that it was much better for the amivantamab arm than the chemotherapy alone arm at 6 months, and then even later at 12 months. And again, that effect just gets more pronounced with time. I think partially this was tied to chemotherapy, which had

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higher rates of discontinuation earlier on in the study, and patients, despite what you mentioned about the challenges of amivantamab, patients stayed on amivantamab with chemotherapy for longer than chemotherapy alone.

Jamie Chaft: That's great. What are your takeaways? What are your conclusions?

Aaron Mansfield: It was actually—given some of these challenges with amivantamab—at first, surprising to me to see how well function was preserved and how quality of life was superior to the chemotherapy alone arm, and I essentially interpreted that some of what we were measuring is really tied to efficacy of the regimen, and that with improved disease control, we are seeing sustained function in our patients and better quality. Now, we also have to ask what the questionnaire is and is not measuring. The primary report did measure the adverse events, but some of that is not in these questionnaires, which really focuses on function and some of the quality, which I thought the adverse event data would have played into more.

Jamie Chaft: I absolutely have to agree with you. I was surprised by the quality-of-life data, understanding that the adverse event profile is substantially more challenging with the addition of amivantamab to chemotherapy. I do not often hold much water in that cup of QOLs, but I think this study is particularly impactful. Just to reiterate, did the trial achieve its primary endpoint of improving PFS?

Aaron Mansfield: Yes, absolutely. I do not think there is any question about that. This had a hazard ratio of 0.4. I think the PFS improvement is incontrovertible. Adding amivantamab to chemotherapy resulted in a PFS benefit for this patient population.

Jamie Chaft: Let's talk about how we are going to bring this into the clinic. We know that the side effects of amivantamab, particularly in the infusional formulation, are very challenging, both in terms of chair time, steroid use, and that hypersensitivity risk up front, followed by the other side effects, the dermatologic and swelling side effects over the long term, but we now have quality-of-life data that say, even with this formulation, despite all of those risks we talk about with our patients, that quality of life is better, and as you say, it does not measure everything, but we are in the clinic and we have subcutaneous amivantamab. How do you think this is going to change the discussion and the quality of life of our patients?

Aaron Mansfield: First, it has changed our nurse manager's life. We have converted our regimens so investigators can choose, our clinicians can choose between subcutaneous and intravenous (amivantamab formulation). And I think you could imagine we are going to

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primarily be using subcutaneous moving forward, just given the reduction of the infusion-related reactions and the chair time. I think it is a significant time commitment, not just for our patients, but for our nurses and staff and our resources to be able to give the intravenous formulation. We welcome the subcutaneous formulation with open arms. I think it is a huge step forward for our patients and for our resources.

Jamie Chaft: And for our audience who perhaps does not encounter this population as commonly as you or I may, how do you otherwise support these patients when they start therapy? Can you comment briefly on the supportive regimens to prevent the dermatologic toxicities?

Aaron Mansfield: I do want to credit the sponsor. I think they have been very responsive to what we have been sharing with them and the data they have been getting from the beginning of this in the phase 1 study days with the infusion-related reactions and then adjusting the dosing to try to accommodate that with the dermatologic toxicity. This led to the SKIPPirr trial, the COCOON trial, the PALOMA studies altering the formulation to SUBQ, learning about prophylactic dermatologic management to try to reduce the symptoms that our patients are having, and then as we started to give it with chemotherapy we learned that giving steroids might reduce some of these reactions we were seeing, so they took that feedback and did not just wash it away, they designed trials to prove and demonstrate whether those interventions were helpful or not. And we have adopted them pretty broadly, not word for word, *per se*, but sometimes there are issues with availability of some of the dermatologic prophylactic regimens, but we are giving doxycycline ahead of time, we are using the ointments, the hair shampoo, we are trying to counsel patients that these side effects can be severe and this will help prevent them or reduce them.

Jamie Chaft: So, for our clinicians listening, when they have a newly diagnosed patient with stage 4 EGFR exon 20 positive non-small cell lung cancer, can you envision a scenario where they are not giving amivantamab with chemo?

Aaron Mansfield: In clinical trial settings, there are other drugs in development, zipalertinib and sunvozertinib, but not widely available. We are going to have to interpret those data to see what emerges as a preferred agent. But, right now, in terms of accessibility, and in terms of guidelines, this is a preferred agent for the exon 20 insertion mutation space. These other drugs are either based on what trials are opening or closing, they are not widely available right now, especially in the United States.

Jamie Chaft: I totally agree with you, and I think particularly with the subcutaneous formulation, I cannot envision any patient in our practice, outside of a trial, of course, who

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would not be offered amivantamab and chemotherapy. So, what questions do we have left? What remains unanswered? The SUBQ formulation we talked about, but what more can we do?

Aaron Mansfield: I think one big thing about EGFR exon 20 insertion mutations, I just wanted to add, I think it sometimes gets misinterpreted. Sometimes people see there is an EGFR mutation, they start osimertinib or chemo plus osimertinib and then they are referred to me, and it is one where we do not expect there to be significant activity with osimertinib. There are unfortunately instances of that, and I think it is really important to know nowadays with EGFR, not all EGFR mutations are one and the same, and at least now we have different options based on whether it is a classic mutation or an exon 20 insertion mutation. I think the prophylaxis around amivantamab is critical to implement. We are not talking about its use with the TKI (lazertinib) here, but just with the chemotherapy in particular. Knowing there are regimens available to help minimize or reduce the dermatologic toxicity is critical, and as the subcutaneous amivantamab has been approved and is now widely available, it is the preferred mechanism of administration moving forward.

Jamie Chaft: Right, absolutely, fewer hypersensitivity reactions and less chair time. It's really a win-win.

Aaron Mansfield: Yes.

Jamie Chaft: Well, I would like to really thank you for your great work in this space, and for joining us to discuss this important study today. Thanks.

Aaron Mansfield: Thank you for having me.