

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



Editor's Note: This is a transcript of a discussion on June 30, 2026. It has been edited and condensed for clarity. To obtain credit for participation [CLICK HERE](#).

Jamie Chaft: Welcome. I'm Dr. Jamie Chaft from Memorial Sloan Kettering Cancer Center. In this accredited webinar, we're going to discuss the trial first-line sunvozertinib in non-small cell lung cancer with EGFR exon 20 insertions. It was published online in the *New England Journal of Medicine* at the end of May, and presented at the American Society of Clinical Oncology Annual Meeting in Chicago. Today I am joined by Dr. Elaine Shum from the Perlmutter Cancer Center at NYU Langone Health, who was one of the main investigators on the WU-KONG28 study. Welcome. Thank you for joining us. And I am going to ask you to just start with a broad overview of the study and why it was conducted.

Elaine Shum: Great. Thank you so much, Jamie, for having me here with you today to share these results from the WU-KONG28 trial. Sunvozertinib is an EGFR tyrosine kinase inhibitor that is specifically designed to target *EGFR* exon 20 insertions, including a broad spectrum of exon 20 subtypes. It also has activity against sensitizing and uncommon *EGFR* mutations. It was FDA approved last year for patients with metastatic *EGFR* exon 20 insertions in the second line and beyond, although access in the US has been challenging.

The WU-KONG28 study is a phase 3 international randomized study that was conducted to investigate sunvozertinib vs platinum-based chemotherapy in the frontline setting. Patients with metastatic *EGFR* exon 20 insertions, first-line treatment has included a chemotherapy backbone. The PAPILLON trial has been the first-line standard with the combination of amivantamab and chemotherapy, but there have not been any oral chemotherapy-free regimens for patients in this front-line setting. For some patients, an oral regimen could be more convenient if there is an acceptable safety profile.

Jamie Chaft: Sure. What were the key objectives of this study?

Elaine Shum: Standard for a phase 3 trial, the primary endpoint was progression-free survival (PFS), and some key secondary endpoints included overall survival (OS), objective response rates (ORR), duration of response (DoR), and safety.

Jamie Chaft: This trial included patients with locally advanced and metastatic non-small cell lung cancer with *EGFR* exon 20 insertions. Were there any other key inclusion criteria of relevance?

Elaine Shum: The key inclusion criteria included patients who were 18 years of age or older. They had to have a diagnosis of advanced or metastatic nonsquamous, non-small

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cell lung cancer, and they could not have received any prior treatment for their advanced or metastatic disease. Of note, patients with brain metastases were allowed, but the metastases had to have been stable, following local therapy, before they could be enrolled.

Jamie Chaft: Who was excluded?

Elaine Shum: Key exclusion criteria along the lines of what was in the inclusion [criteria] are that patients that had received any prior systemic treatment for their locally advanced or metastatic non-small cell lung cancer were not able to be enrolled and they also could not have received any prior treatment with an *EGFR* exon 20 insertion targeted therapy. In addition, they could not have any significant cardiac history, including QTc prolongation, and atrial fibrillation that was not well controlled.

Jamie Chaft: Pretty standard. This was a large international phase 3 randomized study, 154 sites, 15 countries. What was the treatment paradigm? How were patients randomized?

Elaine Shum: In this phase 3 study, patients were randomized one-to-one to receive either sunvozertinib at 300 mg daily until disease progression, or chemotherapy with carboplatin and pemetrexed for 4 to 6 cycles, given every 3 weeks, followed by maintenance pemetrexed until disease progression. Of note, patients in the chemotherapy group were allowed to cross over to receive sunvozertinib after they had confirmed disease progression assessed by blinded independent central review.

Jamie Chaft: Right, so no immunotherapy in the control arm, just chemotherapy.

Elaine Shum: Correct. Just chemotherapy.

Jamie Chaft: All right. What were your patient demographics in this study?

Elaine Shum: As mentioned already, the study had 324 total patients, of which 163 were randomized to receive sunvozertinib and 161 received chemotherapy. Of this total, more than 50% were women, and the majority had no history of smoking. Noted about two-thirds were Asian, and there were about 31% of patients who were enrolled in North America or European countries. Between the 2 groups of sunvozertinib and chemotherapy, the 2 groups were generally well balanced, although there were more men that were randomized to receive sunvozertinib, and the sunvozertinib group also had a higher percentage of patients who actually had more than 3 organs involved at baseline.

Jamie Chaft: I actually think those demographics are pretty remarkable, because usually the studies we see enrolled in Asia are predominantly, if not almost all, men. More than half women [in the study] is pretty impressive. A key primary finding of this analysis was

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prolonged progression-free survival with sunvozertinib compared to chemotherapy. We are not surprised by this, but we are excited to see it. This was assessed by blinded independent central review. Would you describe the other efficacy endpoints?

Elaine Shum: There was a median follow-up of about 2 years or 24 months in the sunvozertinib group and 18 months in the chemotherapy group. The median PFS was 10.3 months for sunvozertinib and 7.5 months for chemotherapy. There was a hazard ratio of 0.65. The objective response, as assessed by blinded independent central review, was about 59% with sunvozertinib and 31% in the chemotherapy group. The median duration of response for sunvozertinib was 11.2 months and 7.1 months for chemotherapy. At the time of this primary analysis for PFS, the overall survival data is still immature at only 39%. At that time point, it comes out to about 29.8 months for sunvozertinib and 28.8 months for chemotherapy. Again, this data is still very immature.

Jamie Chaff: With crossover, which was great. It is amazing, no matter how many times I see those control arm data, you always are so surprised at how poor chemotherapy is as our standard of care.

Elaine Shum: Definitely.

Jamie Chaff: Elaine, do you mind sharing with us some of the safety data from the study?

Elaine Shum: The most common grade 3 or higher adverse events in the sunvozertinib group was increased creatinine kinase level in about 21% of patients. This was mostly asymptomatic, which was a blood value that was detected on their routine blood testing. There was diarrhea that was about 14% [grade 3 or higher] of patients in the sunvozertinib arm, and anemia was about 9.2% [grade 3 or higher] of patients [for sunvozertinib]. In the chemotherapy group, again, not very surprising, but there were some additional cytopenias that were noted, such as decreased neutrophil count and platelet count. Otherwise, again, pretty much what we would have expected in a chemotherapy group. Other things that are often asked is what were the drug interruptions, dose reductions, and drug discontinuations from an adverse event. In the sunvozertinib group, about 58.3% did require a drug interruption, about 42% required a dose reduction, and about 12% had a drug discontinuation. For those dose reductions, diarrhea was the reason in about 8.6% of patients in the sunvozertinib group, and rash at only about 2.5% of patients in that sunvozertinib group.

Jamie Chaff: We often worry about interstitial lung disease in this patient population with other tyrosine kinase inhibitors. What did you see with sunvozertinib?

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Elaine Shum: It was relatively low in the study. Treatment discontinuation because of interstitial lung disease occurred in about 1.8% of patients, with sunvozertinib and pneumonitis classified in about 1.2% of patients.

Jamie Chaft: That is pretty low. I always find, in this patient population, it is a little difficult to differentiate what is disease and what is pneumonitis based on the pattern of spread.

Elaine Shum: Definitely.

Jamie Chaft: You were one of the lead authors of this study with experts from around the world. What is your conclusion? What is your takeaway?

Elaine Shum: From the study, we certainly saw a significantly improved progression-free survival compared to platinum-based chemotherapy alone for patients with advanced or metastatic *EGFR* exon 20 insertions in this frontline setting. Having an oral regimen for patients as chemotherapy-free is something that can be attractive for patients. We will look to see how this changes the landscape here.

Jamie Chaft: I think we are seeing this consistent trend whenever we find a biomarker-matched therapy, our outcomes are better than chemotherapy, which is great. How do you place this result into practice today, and can you?

Elaine Shum: As we mentioned already, the frontline standard has been amivantamab and platinum-based chemotherapy in the frontline setting. This trial did not have amivantamab and chemotherapy as its control arm here due to limited access of amivantamab around the world. There is going to be cross-trial comparisons about this. It is a very patient-centered discussion that you will have to have with patients about the toxicity profiles of sunvozertinib alone vs amivantamab and chemotherapy. We will talk a little bit also about just access of sunvozertinib in the US, of course, [since it] also adds an added wrinkle to that discussion. It is always great to have more options about sequencing of these regimens of sunvozertinib and amivantamab in *EGFR* exon 20 patients [and this] is something that definitely needs to be explored further as well.

Jamie Chaft: Sure. You already addressed the practice-changing element of this and those discussions in the clinic, but based on your experience of treating these patients, how do you manage the side effects? Let us pretend sunvozertinib is available in the clinic next week. What do you tell people about managing the rash and diarrhea?

Elaine Shum: We take a very aggressive approach. In many ways, from our experience with other *EGFR* targeted therapies, including amivantamab, many oncologists are very well

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versed in prophylactic guidelines for patients for diarrhea and rash. Being very liberal with antidiarrheal medications, for example, and also, various lotions and creams for rash. Usually, our upfront discussions are just being very proactive about getting ahead of those side effects before they even really start to rear their ugly heads.

Jamie Chaft: You are right. We are getting more familiar with these toxicities. This class, in particular, targeting exon 20, we have been plagued with diarrhea in the past. I am hoping we have become skilled at treating it. I will wrap up with asking you what questions remain unanswered. What about this trial was not in the article that you can share with us?

Elaine Shum: Definitely we need longer follow-up for that overall survival data to see where it ends up. As you mentioned, the crossover here is definitely a benefit for patients in the trial, but of course we would love to see where the numbers end up. There is always a question about patients with brain metastases. Again, patients with brain metastases were allowed, but they had to have treated metastases that were stable before enrollment and it was not required for patients actually to have serial MRIs of the brain to monitor for CNS disease, actually, throughout the trial. I think definitely some more studies really investigating CNS disease in this space I think also will help us to inform what treatment regimens patients should be getting and how we might sequence it. The last thing is, again, about two-thirds of patients were enrolled in Asia. The majority of patients in the study were Asian. After that, Caucasian patients were the other group that were represented. Certainly we need to expand our clinical trials to expand beyond Asian and Caucasian groups for this subtype. You strive to enroll a more diverse population.

Jamie Chaft: Definitely. Well, thank you, Dr. Shum, for discussing this important trial. Congratulations on your publication, and we look forward to having sunvozertinib in the clinic.

Elaine Shum: Thanks so much, Jamie.