

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



Editor's Note: This is a transcript of a discussion on April 29, 2026. It has been edited and condensed for clarity. To obtain credit for participation [CLICK HERE](#).

Isabel Preeshagul, MD & Benjamin Levy, MD

Isabel Preeshagul: Welcome, everybody. I am Dr. Isabel Preeshagul from Memorial Sloan Kettering Cancer Center. I am a thoracic medical oncologist practicing there, and in this accredited webinar we are going to be discussing the exciting results from the TROPION-Lung02 trial: "Datopotamab deruxtecan (Dato-DXd) plus pembrolizumab with or without platinum-based chemotherapy for advanced metastatic non-small cell lung cancer (NSCLC)." This data was published in the March 21, 2026, issue of the *Journal of Thoracic Oncology* and I am thrilled to be joined by Dr. Benjamin Levy today from John Hopkins Sidney Kimmel Cancer Center, who is the lead author on this article. Dr. Levy, welcome. Thank you so much for joining us today. If you could just give a brief overview of this study and why you think it is relevant today.

Benjamin Levy: Thanks, Izzy. Pleasure to be here, and pleasure to be the lead author on this study, trying to reshape the narrative of antibody-drug conjugates (ADCs) and those compounds. The 3 components being the monoclonal antibody, the linker, and the payload. We're trying to understand why and where these fit in the continuum of non-small cell lung cancer, specifically advanced non-small cell lung cancer. Obviously, there are significant changes in the front line for patients without genomic alterations. We tend to use, for those patients, chemotherapy and immunotherapy, or immunotherapy alone, but there's still an opportunity to move the needle forward. And the introduction of the ADCs in the front line is really this effort to see whether these combination strategies work, and we'll talk about the role of ADCs in combination with immunotherapy, or in combination with immunotherapy and platinum in the front line. This is really important. This was a trial to try to evaluate these ADCs. We've learned about ADCs and their role in other particular spaces, specifically the genotypes, including EGFR and including HER2 alterations, but not really sure how to use them in the front line or in combination, and what the synergy is with platinum or with immunotherapy. That is what we did here. This was a trial looking at the safety and efficacy of dato DXD. This TROP2-ADC in combination with either pembrolizumab or in combination with platinum and immunotherapy pembrolizumab in patients with non-small cell lung cancer, and really focus on the first-line data. TROP2 ADCs are very exciting, and certainly this is an opportunity to look at this and see how we can leverage them in the front line.

Isabel Preeshagul: Thank you for that, and I definitely think this is a space where we can move the needle, and I am excited about seeing data about an ADC in the frontline setting. There was a small exploratory analysis, and I just want to touch upon this up front because there is a lot of data about various ADCs based off of immunohistochemistry

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



(IHC) expression. Can you talk to us about the utility of TROP2 as a biomarker, and how that was used in this study?

Benjamin Levy: Great point here. The biomarker search is still on for these compounds, and it is clinically intuitive and biologically intuitive to think that TROP2 expression would be what really drives the treatment effect for these TROP2 ADCs. For this study, all TROP2 expressions were allowed. It was not restricted by TROP2 IHC. We will talk about another biomarker, TROP2 normalized membrane ratio (NMR) by quantitative continuous scoring (QCS), and that is an interesting biomarker that we did look at here. For IHC, historically speaking, IHC has not really driven effect or been predictive of response for these TROP2 ADCs.

Isabel Preeshagul: I think that is helpful to know because it can be difficult to figure out when to use what ADC, and what ADC needs a specific biomarker expression to be offered and what does not. This is basically for all comers in the frontline setting without a targetable alteration.

Benjamin Levy: Absolutely, good point.

Isabel Preeshagul: Tell us just a little bit about the specific objectives of this study.

Benjamin Levy: At a very high level, the objectives are really no different than what we generally see from a phase 1b/2 trial. In any phase 1 effort, you are going to look at treatment-related adverse events, serious treatment-related adverse events, and adverse events of special interest, which I think are relevant here. These TROP2 ADCs have your traditional cytotoxic chemotherapy side effects, but they also have these adverse events (AEs) of special interest that we have to be mindful of ocular events, interstitial lung disease (ILD), and certainly stomatitis, and then the secondary endpoints that you see in any of these trials are the outcomes, response rates, progression-free survival (PFS), overall survival (OS), duration of response (DoR), and disease control rate (DCR). Those are the things that we were really looking at in this study.

Isabel Preeshagul: Thank you. When we are combining new agents that maybe folks that are listening here have not ever used before, and certainly not in combination, you touched upon AEs, and you touched upon some specific unique AEs, because I think a lot of folks listening are familiar with antibody drug conjugates in the breast space, but maybe using datopotamab deruxtecan in combination with chemo and immune-oncology therapy (I/O) or I/O alone is new. Could you tell us a little bit about some of those more

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



unique toxicities that you saw and how you mitigate those, like the stomatitis and the ocular toxicity?

Benjamin Levy: Front and center was the stomatitis that we really have to be mindful of. This occurred in more than 50% of patients, and it's something that we really need to keep our eye on if we're going to use this compound. When we talk about mitigation strategies for stomatitis, we're really looking at some of the ongoing efforts here. The first thing that I would say is that, potentially, steroid rinses preemptively may help these patients, and certainly we need to be mindful of these proactive strategies for stomatitis. Also, ice chips. We didn't use this in the trial, but they certainly can be used during infusions. Patients using or sucking on ice chips while they're getting the infusion may mitigate the toxicity of the stomatitis. The other 2 things that are important for AEs of special interest are ILD. ADCs are starting to have this narrative that they are linked to ILD, we saw this in our study. The ILD was pretty low. The incidence of ILD varied by grading and overall incidence and occurred in around 17% of patients receiving the doublet and a quarter of patients receiving triplet therapy. The rate of grade 3 ILD was 1% to 3% of these patients, but nevertheless still there, and we need to be mindful of it. There were some, you know, grade 1 and grade 2 ILD, but again, we just need to keep our eyes on this moving forward. Mitigating this is really important, to do with the fact that CT scans were done routinely. So we need to be mindful to educate patients of symptoms of ILD, including worsening shortness of breath and cough. And then, finally, the other AE of special interest is ocular toxicities. Now, these are fairly infrequent. I would say, with the ocular toxicities, it is important to consider steroid drops and artificial tears and then partnering with your optometrist or ophthalmologist here to make sure that they are aware of these toxicities. But clearly these exist.

We need to be mindful that these are separate from what we generally see with traditional chemotherapy. As these drugs begin to unfold in our clinic and our clinical trials, we are just going to have to be more proactive in mitigating these strategies with some of the things that I talked about.

Isabel Preeshagul: Great. It sounds like patient education and medical team education is really at heart here, and it is all about being proactive rather than reactive, which is really important. Let us dive a little bit into the results here, and what you saw with these cohorts, and what excited you.

Benjamin Levy: At a very high level, I just want to briefly describe the cohorts. There were 6 cohorts in this study, looking at Dato-DXd, our TROP2 ADC, at either 4 mg/kg or 6 mg/kg,

and that was either combined with pembrolizumab at 200 mg, and that was cohort 1 and cohort 2. Then cohort 3 through 6 was also Dato-DXd plus pembrolizumab, and again, the

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



Dato-DXd could have been either 4 mg/kg or 6 mg/kg and then either combined with carboplatin or cisplatin. The bottom line here is that there was both a dose escalation and dose expansion within each of these cohorts and really trying to look at the synergy of Dato-DXd with pembrolizumab or the synergy of Dato-DXd with pembrolizumab plus platinum chemotherapy at 2 different doses, 4 mg/kg or 6 mg/kg.

Importantly, there were 142 patients that were treated. What was really critical for us is to look at those 96 patients, of the 142 patients that were treated in the treatment naïve

setting, because this is what this study was all about. This is the largest group of patients reported on yet, looking at the combination strategies in the frontline with a TROP2 ADC.

When we start looking at the results of the study, looking at patients in the overall patient population, we separated out between those who received doublet and those who received triplet therapy. Doublet arm was Dato-DXd plus pembrolizumab, triplet arm was Dato-DXd plus pembrolizumab plus either cisplatin or carboplatin.

The overall population at a very high level, response rates of the doublet cohort, around 43%, response rates in the triplet cohort, around 50%. Durations of response in the doublet cohort, 20 months vs 14 months in the triplet. Looking at PFS in the doublet cohort around 10 months, quite competitive, and the triplet, around 7 months, and then OS, always important, but again, this is a phase 1b study. In the doublet cohort, the OS was around 25 months and in the triplet, it was 18 months.

What we really wanted to focus on is the treatment-naïve patient population. We need to remember that is really where we are trying to look. There were 42 patients in the doublet cohort and 54 in the triplet, so 96 patients were treatment naïve. Again, the largest group reported so far for frontline TROP2 ADC and again, very similar trends here. Competitive outcomes, response rates in the doublet and triplet cohort in the frontline, treatment naïve, around 55%, in both cohorts. Then PFS in the doublet cohort 11.2 months, in the triplet cohort around 7 months. The OS has not been reached in the doublet cohort in the first line at the time of the reporting of this study and published, and the triplet cohort, it was around 18 months.

Taking 10 steps back here, what we are seeing is pretty interesting responses in the front line, both with doublet and triplet, durable responses. We just have to wait until the OS comes out here, but I think the focus of this publication and this effort and this study is really looking at these outcomes in the first line.

Isabel Preeshagul: Thank you for breaking that down. I was most interested in the treatment naïve population because we are trying to figure out where this cocktail could

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



possibly live in our treatment algorithm. Could you talk to us just a little bit about that TROP2 biomarker that you did mention, the NMR by QCS?

Benjamin Levy: I think this is really important. I think if you are out there as an everyday clinician, you are looking at what is coming down the pike in biomarkers, at a very high level, we need to remember, this is the first artificial intelligence (AI)-assisted biomarker in solid tumor malignancy. We are just scratching the surface. We are at the beta version of this, and it has got its imperfections, but I think this will create a foundation for future efforts. TROP2 QCS NMR is really a way where you take a slide, you digitize it, you create a digital image of that slide, and then you use computational pathology to measure TROP2

expression, both on the cell surface and within the cell. This can accurately do this way better and more consistently than the naked eye. By doing this, you are able to accurately and reliably and consistently locate that TROP2 biomarker, that protein level on the cell surface and inside the cell, and come up with a ratio. The bottom line is that ratio that they come up with, using computational pathology, using artificial intelligence, they are able to come up with a reliable ratio of how much TROP2 expression there is inside the cell vs on the cell membrane. That is better able to predict the efficacy of this compound than just TROP2 IHC. It turns out the more TROP2 protein you have internally, the more likely you are to respond to this drug, which is counterintuitive. The more TROP2 you have internally vs what is expressed on the cell surface, the more likely you are to derive a benefit, at least based on this dataset and based on retrospective analysis from TROPION-Lung01.

Isabel Preeshagul: I think that is really cool, and I am glad that this paper included something novel like that and is making everyone think a little bit more. Thank you for sharing that tidbit. Could you just give me your take-home message, your elevator pitch on this study and what you want everyone listening here to take back to clinic tomorrow.

Benjamin Levy: This is a great way to round third, head home, and finish up here. What we know, right now, about TROP2 ADCs is that, at least in the second line, they have not outperformed docetaxel. Important to note that they did not really outperform docetaxel. I think the next logical step is to look at this compound up front to see if there is any synergy with platinum chemotherapy and pembrolizumab. At a very high level, we saw that in this trial. We saw meaningful activity and durable responses in combination with pembrolizumab and in combination with pembrolizumab and platinum chemotherapy, specifically in treatment-naïve patients and in an all-comer approach and in all histologies, independent of TROP2 expression. There is meaningful activity in the frontline.

The second thing I will say is we need to be mindful of toxicity. The AEs of special interest that we talked about earlier, the stomatitis, the ocular events, and the ILD. Those are

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



things that we have to be very mindful as we use these drugs, or if we are going to use these drugs in the frontline. I always say, “Is the juice worth the squeeze here?” I think we will learn more once we have these phase 3 studies comparing the regimen that we exploited here vs the control arm of KEYNOTE-189 or single-agent pembrolizumab.

The third thing I will say is the thing that we just talked about, which is that this artificial intelligence-assisted computational pathology biomarker seems complicated. It is very complicated to think about, but this is where we are going to be in the next 10, 15, 20 years in cancer care is really digging down deep, using AI to help decide what are those right biomarkers, clinical features, pathological features that predict who is going to respond and who does not. This is one of those first efforts, I think. The trial showed meaningful activity in the front line, be mindful of toxicity, and look out for the TROP2 NMR by QCS biomarker for more studies and finally, the phase 3 efforts that are coming out will either confirm or negate our study. You got the TROPION-Lung07 and TROPION-Lung08 each looking at Dato-DXd, this TROP2 ADC in the frontline where, compared to a control arm that is a reference regimen, that is the standard. This seems poised to be a part of non-small cell lung cancer treatment for patients in the future. I am very much looking forward to and very happy to be a part of the story and telling chapter 1 of a story that I hope will have many chapters and will be a novel.

Isabel Preeshagul: Thank you for that. I have learned so much today, and thanks for the recap. I am excited about what is to come in this space, and Ben, I appreciate you taking time to chat with me today.

Benjamin Levy: Thanks, Izzy. It has been a wonderful opportunity. I appreciate the time.