Evolving Paradigms in Immuno-Oncology: Optimizing Patient Care Through Innovative Delivery Approaches of Immune Checkpoint Inhibitors

CEC Podcast Transcript

Roxana Dronca, MD:

Hello, I'm Dr. Roxana Dronca. Welcome to today's program – Evolving Paradigms in Immuno-Oncology: Optimizing Patient Care Through Innovative Delivery Approaches of Immune Checkpoint Inhibitors. This CME activity is provided by Creative Educational Concepts and supported through an independent educational grant. Over the next half an hour, we'll explore how innovations in immune checkpoint inhibitor [ICI] delivery, particularly subcutaneous formulations, are changing the way we think about access, efficiency, and patient experience in cancer care. The content today may include the discussions of investigational or non-FDA-approved [U.S. Food and Drug Administration] uses of agents. I will disclose any such discussions as we go through the material.

I am a medical oncologist at the Mayo Clinic in Jacksonville, where I serve as the director of the Mayo Clinic Comprehensive Cancer Center in Florida and lead our Cancer Care Beyond Walls program. My work focuses on improving access to high-quality oncology care for patients where they live, whether that means integrating multidisciplinary models, expanding telehealth, or bringing treatment directly to patients' homes. Much of my research centers on immunotherapy for solid tumors and understanding how treatment delivery can influence both outcomes and quality of life. These experiences have reinforced how critical it is to match innovations in science with innovation in care delivery, which is exactly what we'll explore together today.

Before we get started, let's briefly review what we'll focus on today. We'll look at how advances in immune checkpoint inhibitor therapy, particularly subcutaneous formulations, are shaping the next phase of immune oncology, and I will share some key data on efficacy and safety from recent studies, and we'll discuss practical strategies for implementing subcutaneous administration in different care settings.

This slide outlines the rapid evolution of immunotherapy over the past decade. We began in 2011 with ipilimumab as the first approved checkpoint inhibitor agent in melanoma. By 2014, nivolumab and pembrolizumab expanded the field between 2015 and 2017. Approvals moved into non-small cell lung cancer, renal cell carcinoma, and Hodgkin's lymphoma, establishing ICIs as a core therapeutic class across major tumors. From 2018 to 2022, indications broadened further, including the first tumor-agnostic approvals, as well as the emergence of bispecific antibodies. Most recently in 2024 and 2025, we have seen the introduction of subcutaneous immune checkpoint inhibitor formulations with three subcutaneous agents now available across tumor types – reflecting not just scientific progress, but also the progress in how immunotherapy is delivered and accessed.

Immune checkpoint inhibitor agents are now used broadly, driving high patient volumes and significant infusion center demand. Many patients, though, struggle with logistical or geographical barriers to cancer therapy, including IV [intravenous] therapy. So subcutaneous administration may offer a way to potentially ease this pressure: reducing treatment burden, improving access, and supporting more efficient care delivery.

The slide compares IV and subcutaneous agents. IV infusions require more time, equipment, and chair use, while subcutaneous injections take only a few minutes and are far easier to schedule. Subcutaneous formulations have slightly lower bioavailability, but achieve comparable systemic exposure as we will see. And clinically, multiple trials have demonstrated noninferiority of subcutaneous formulations relative to their IV counterparts. Safety is similar, with fewer infusion-related reactions. While there are more injection site reactions, as we will

see with the subcutaneous formulations, these are usually mild and easy to manage. For patients, subcutaneous delivery offers a faster, less invasive experience, and for healthcare systems, it frees infusion capacity and may help with cost and staffing pressures while also opening the door to outpatient and potentially home-based treatments. So now that we have reviewed how subcutaneous administration compares with intravenous delivery, I would like to bring in the patient perspective, because these advances ultimately come down to what they mean for the people receiving treatment. I'm joined today by Mrs. DiGennaro, who has experienced immunotherapy delivered under the skin. Thank you so much for being here and for sharing our experience with us.

Louise DiGennaro:

Hi, Dr. Dronca. Thank you for having me.

Roxana Dronca, MD:

Of course. It is a pleasure to have you. I would like to ask you, what was it like receiving your immunotherapy as an injection under the skin?

Louise DiGennaro:

Well, the first time I went to have this done, it was just to me a miracle. It's improved the quality of my life in a way that I can hardly describe. I went into the infusion center actually on a number of occasions. I actually had the medication waiting for me, and the nurse described what it would be like, and basically it was an injection in my abdomen. It took five minutes, literally five minutes. There was no pain or discomfort at all with the needle going in or out, and at the end of the five minutes, they simply put a Band-Aid on me and off I went. And I had absolutely no adverse reactions, side effects, no discomfort at all. It just changed my life.

Roxana Dronca, MD:

That is amazing to hear. And you described a bit about how long the visit took or takes with the subcutaneous approach. How do you feel that this approach fits into your usual schedule or daily routine? Is it better than with the intravenous therapy?

Louise DiGennaro:

Well, it's a lot better. With the intravenous therapy, you're sitting in a chair. I have very difficult veins to access. I've been told they're very small and now they're pretty scarred, so that, sometimes finding a vein would take time, and it would take – it seemed to take more time to get the medication to be available. And then it was about 30 minutes, 35 minutes for the infusion itself, and then again, removing the IV and so forth. And I had some experience with bruising and bleeding so that after the experience, I was kind of cautious because of the concerns for the bleeding that sometimes happened. Not always.

Roxana Dronca, MD:

I understand.

Louise DiGennaro:

So, I mean, subcutaneous had none of that.

Roxana Dronca, MD:

Would the availability of the subcutaneous formulation influence, for instance, your decision to continue treatment, or would you have elected to continue treatment regardless of the method? It's just that this is allowing you, as you mentioned, the comfort and the ease of administration.

Louise DiGennaro:

Certainly having subcutaneous available to me, I wouldn't think twice about continuing this for as long as it was affected. With the IV, it was very anxiety-provoking for me, just anticipating what was going to happen with finding veins and so forth. But it was very anxiety-provoking. I don't think I ever would've stopped IV therapy if it was helping me. So I would go through anything to receive the treatment that I needed.

Roxana Dronca, MD:

Understand. Thank you so much for providing this perspective, and I will return to you after we discuss a couple of the data regarding the subcutaneous administration.

Louise DiGennaro:

All righty, thank you.

Roxana Dronca, MD:

So thank you again for sharing that perspective. I think it really highlights how delivery method can shape the overall treatment experience and not just the logistics of care. I think the way we deliver care is just as important as the care that we deliver. So, let's shift back to the clinical data and look at how efficacy is evaluated when developing subcutaneous formulations of existing immune checkpoint inhibitors. The IMscin001 study evaluating subcutaneous atezolizumab was a phase III randomized open-label, multi-center noninferiority trial, which enrolled patients with histologically or cytologically documented locally advanced or metastatic non-small cell lung cancer who are naive to cancer immunotherapy. Patients were randomly assigned two to one to receive subcutaneous 1,875 milligrams of atezolizumab or 1,200 milligrams of the IV formulation once every three weeks. Trough concentrations and overall drug exposures were comparable between the subcutaneous and IV administration, as we see here, meeting predefined pharmacokinetic equivalence criteria. Clinically, median PFS [progression-free survival] was essentially identical, 2.8 months for the subcutaneous versus 2.9 months for the IV atezolizumab, and the overall response rate was similar at 12% versus 10%. Overall, subcutaneous atezolizumab demonstrated noninferior pharmacokinetics with similar efficacy and safety to the IV dosing.

CheckMate 67T evaluated subcutaneous nivolumab in patients with histologically confirmed advanced or metastatic clear cell renal cell carcinoma with or without sarcomatoid features and demonstrated pharmacokinetic equivalence to the IV dosing. Again, drug exposure and trough concentrations were within the required margins, confirming noninferiority. Clinically, outcomes were very similar. Median PFS was 6.34 months

with a subcu versus 5.65 months with the IV nivolumab, and the overall response rate was 24.2% with the subcutaneous versus 18.2% with the IV nivolumab. Safety profiles were consistent across arms.

In study 3475A-D77, patients with untreated stage four non-small cell lung cancer were randomly assigned again in a two to one ratio to receive either subcutaneous pembrolizumab at 790 milligrams every six weeks, plus platinum doublet chemotherapy or intravenous pembrolizumab at 400 milligrams every six weeks, plus chemotherapy. Subcutaneous pembrolizumab given with chemotherapy demonstrated pharmacokinetic noninferiority to the IV administration. Drug exposure and trough levels were slightly higher with the subcutaneous dosing, but remained within acceptable equivalence margins. Clinically, again, outcomes were comparable. Overall response rate was 45.5% with subcu versus 43.1% with IV. Pembrolizumab and median PFS was 8.1 versus 7.8 months. Safety profiles were again consistent between arms.

So this next slide highlights investigational subcutaneous immune checkpoint inhibitors currently in development. Sasanlimab, I think it's important to note that was designed specifically for subcutaneous delivery rather than adapted from an IV formulation. This agent is currently being studied in high-risk non-muscle invasive bladder cancer in combination with BCG [Bacillus Calmette-Guérin], and has shown a significant improvement in event-free survival in the phase III CREST trial. Toripalimab is being evaluated with gemcitabine and cisplatin for nasopharyngeal carcinoma, with early phase I data indicating safety and efficacy comparable to the IV form. Together, these agents illustrate the next generation of immunotherapies where the subcutaneous administration is integrated in drug design from the outset.

The IMscin002 study looked at patient preference for subcutaneous versus IV atezolizumab. A strong majority of patients, as we see here, close to 71% preferred the subcutaneous administration compared with 21% of patients who prefer the IV. The main reasons were shorter time in clinic, greater comfort during administration, and reduced emotional distress. I think we've heard many of these reasons from our patient today. Switching between the subcutaneous and IV agent was well-tolerated with no new safety signals, and overall, patients clearly favor the subcutaneous route because it reduces treatment burden and improves the overall treatment experience.

We've just seen that in the IMscin002 studies, most patients preferred receiving their treatment subcutaneously. So to help bring these findings to life, I'd like to return to Mrs. DiGennaro to hear a bit more about her perspective on treatment preference and her overall experience. What stood out to you as the biggest difference compared with the IV treatment?

Louise DiGennaro:

Well, the biggest difference is the time, but also there was just no discomfort at all. On one occasion, I did note some redness and swelling around the site of injection, but had I not made it a point just to check, I'd never know that because there was no pain involved – it only lasted like 24 hours. It wasn't even significant enough for me to portal you. So it was fine, and the nurses took time to really explain what was going on, and I also felt it was three to five minutes they could inject you. And I have found that the slower they go and utilize the full five minutes, the easier it seemed to be.

Roxana Dronca, MD:

I understand. So taking a little bit more time to inject the drug made it a little bit more comfortable afterwards.

Louise DiGennaro:

Mm-hmm.

Roxana Dronca, MD:

And the redness that you mentioned and the swelling, was it that with the first treatment, or?

Louise DiGennaro:

That was with the second treatment.

Roxana Dronca, MD:

With the second treatment. And no discomfort or itching that you mentioned associated with it?

Louise DiGennaro:

No.

Roxana Dronca, MD:

Did you have to apply a compress or cold compress or do anything at all about it?

Louise DiGennaro:

Really nothing.

Roxana Dronca, MD:

Nothing. So it was pretty much self-limited within 24 hours.

Louise DiGennaro:

Mm-hmm.

Roxana Dronca, MD:

I think that is pretty consistent with what other patients who experience this type of injection site reactions note: that they are usually very mild and very little symptoms associated with it and pretty much self-limited.

Louise DiGennaro:

Just one other thing. When I started on subcutaneous, I don't know if it was psychological, but I actually felt better. I had more energy and I was just out more, doing more. And I don't know if it was just the relief of no longer having to deal with an IV, but it made a big difference in my overall feeling of wellness, actually, which was interesting, I thought.

Roxana Dronca, MD:

I remember actually you telling me after you switched that you did not even feel like a cancer patient that day when you had the injection, and you walked out after a few minutes, and there was no IV pole and –

Louise DiGennaro:

Really?

Roxana Dronca, MD:

...no IV line. So I'm glad to hear. I'm glad to hear that. I think it is extremely important that as I mentioned, that we deliver the care that brings comfort to our patients, and I think this allows a lot of patients to stay in the treatment longer-term. You mentioned that it would've continued anyway, but I think at some point potentially we could have had to consider a port or some other form to continue with the IV injection. So thank you for sharing that perspective. As I mentioned, I will come back to you in a little bit once we discuss the ways we deliver these type of therapies now and what are some innovations that we can bring to the field.

Louise DiGennaro:

Okay, thank you.

Roxana Dronca, MD:

So move on and look at our next slide. We see that across pivotal trials, the safety profile of subcutaneous immune checkpoint inhibitors has been fully consistent with their IV counterpart. No new immune-related toxicities or safety patterns emerge. As we've heard, injection site reactions were slightly more common with the subcutaneous dosing, but were almost always in the trials as well – grade one or two and self-limited. Immunogenicity remained low, with less than 1% ADA [anti-drug antibody] positivity and no neutralizing antibodies of clinical concern. So importantly, anti-drug antibodies did not affect efficacy or safety, and routine immune-related AE monitoring and management remain unchanged for the subcutaneous formulations.

So now that we have seen how subcutaneous delivery has evolved in other biologics, let's turn to what that means operationally when integrating subcutaneous immune checkpoint inhibitors into routine oncology care. To integrate these agents into practice, I think sites need to determine where injections will occur, whether in the infusion clinic or potentially in the outpatient area or exam rooms in injection clinics, with future potential for home administration as we will see. Staff should be trained in the subcutaneous technique, injection site management – as we've heard from our patient – as well as patient education so they know what to expect supported by pharmacist coordination. Monitoring is minimal. Brief observation, documentation of site reaction and patient comfort, and use of patient feedback to refine scheduling should be considered.

As subcutaneous immunotherapies are adopted across different practice settings, maybe academic centers could potentially implement it more rapidly due to existing infrastructure and staffing and act as training and workflow hubs. Community practices, on the other hand, benefit from reduced logistics and could use shared protocols from academic partners as well as use telehealth support. In rural and underserved areas, though, I think it's important where distance to infusion centers is a major barrier, subcutaneous delivery combined with visiting nurses, mobile unit, and telehealth can significantly expand access and support equitable cancer care.

This slide outlines a possible framework for transitioning patients from IV to subcutaneous immunotherapy. One can begin with IV induction, for instance, for one to three cycles to confirm tolerance and early efficacy. And once disease is stable and an FDA-approved subcutaneous version exists, patients can transition: receiving dose equivalence, obtaining consent, and giving the first subcutaneous dose under brief observation. During subcutaneous maintenance, patients remain on the standard schedule with continued monitoring of adherence, patient-reported outcomes, ongoing response, and of course tolerability.

So as we move on towards this more subcutaneous administration, I think some of the key practical questions that we will have to answer are determining which patients are best suited for subcutaneous immunotherapy? What drives or limits adoption across different practice settings, as we've reviewed? How can multidisciplinary teams support safe and efficient implementation, especially in community clinic? And looking ahead, could subcutaneous delivery extend to new drug classes or even home-based cancer care?

To that end, the Mayo Clinic's Cancer Care Beyond Walls program was established in 2023 in an effort to bring quality cancer care to patients in their homes or closer to their communities and expand access to care, especially for rural and underserved populations. Our first randomized clinical trial compares home-based versus in-clinic cancer therapy for a variety of chemotherapy and immunotherapy agents. Early results presented at ASCO [American Society of Clinical Oncology] in 2025 are very encouraging. Patients report extremely high satisfaction, with 73% of patients expressing strong preference for receiving care at home. Safety has been excellent, with no greater or higher adverse events related to treatment location. The model has been tested across common cancers, including breast, colorectal, prostate, multiple myeloma, melanoma, and others, with participants leaving a median of 20 miles from the cancer center in the cohort of the first 50 patients, which is now expanded to a range of 75 to 100 miles for the rest.

This work is being extended through a novel clinical trial funded by the Florida Department of Health, which is evaluating home-based cancer care for patients in the rural Florida panhandle using the Cancer Care Beyond Walls framework: leveraging remote laboratory testing, telehealth visits, and shipment of medications for administration by local home health providers. So overall, these data show that home-based cancer care is not only feasible and safe, but also highly valued by patients.

So as we've seen, the future of cancer care delivery is evolving quickly, with new approaches like subcutaneous immunotherapy and even home-based treatment models helping to bring care closer to patients. So to close our discussion, I'd like to return to our dear patient, Mrs. DiGennaro, and hear her perspective on how these innovations could shape patient experience moving forward. So, Mrs. DiGennaro, if you had the choice to receive future treatments closer to home or in a different setting, what would make that appealing for you or what would you want to make sure stays the same about your cancer care experience?

Louise DiGennaro:

Well, I personally enjoy interacting with my clinicians as much as possible, because I do like coming into the clinic and interacting with others and get their input. However, I think the home-based program, I mean, if the day were to come that I couldn't make it into the clinic, that I didn't have the support available to get me there, I would certainly welcome something like that and I can see how valuable that would be. And also, sometimes people might not want to come into the clinic. They would prefer the privacy of their own home. So my preference is to interact with as many professionals as possible, but I think that really home care is the way of the future if it can continue. I think it's beautiful for certain people that need it.

Roxana Dronca, MD:

I think you have just captured the whole Cancer Care Beyond Walls program in those sentences, because you are absolutely right. The patients who prefer the care in the clinic so far and their reasons to do so are related exactly to what you mentioned: the social interaction. So they value the interaction with the providers. They don't have any barriers in terms of travel. They feel well enough to be able to come to the clinic, and they like that social connection. On the other hand, the patients who prefer the care in the home are doing so because of the convenience and the comfort in the home, because of the barriers to come to the clinic every few weeks or every month. And I think this captures exactly what you said, the value for a lot of patients, especially if they don't feel well or they don't have somebody to drive them to the clinic. Do you even imagine a day where potentially you could self-administer the medication if you had a nurse on the other line on the video or that a caregiver could do that? Do you think that you could push that that far?

Louise DiGennaro:

I think I would feel more comfortable with myself doing it than my caregiver, but no, I think I could do that. I watched them do it, and so far it's just been my abdomen, but I know there are other sites they might be able to use. But it seems like something that I could learn how to do quite easily, yeah.

Roxana Dronca, MD:

That is very interesting to hear. And I think that is something actually that we are actively exploring, especially for patients who live in areas where maybe home health nurses are not available or mobile units are not available. So just, I know we've talked about the benefits and what you've experienced with the subcutaneous versus intravenous immunotherapy, but is there anything else that you would want other patients to know about your experience, or what advice would you give to someone who's just starting immunotherapy today?

Louise DiGennaro:

Well, I guess my advice would be it might be good to give IV a try and then go on to subcutaneous, because personally I did not want, and to this day, do not want a port. I feel that having a device implanted in me would be a constant reminder of what I'm going through. And for cancer patients, I think that's difficult, and that's why even walking away with a bruise was difficult for me. And I just feel as though subcutaneous is the way to go. I mean, it makes you feel normal: that you're not a cancer patient.

Roxana Dronca, MD:

Thank you very much. I think this is very powerful. The first time you said that to me was very, very powerful. So I really appreciate your time and your insight today. Thank you.

Louise DiGennaro:

Thank you for all you have done for me. Thank you, Dr. Dronca.

Roxana Dronca, MD:

Of course. So, I think hearing directly from patients reminds us that the most meaningful progress happens when every member of the care team works together towards a shared goal. You've heard how the nurse is providing the education, how everybody coming together really improves both outcomes and experiences for our patients. So to make innovations like subcutaneous immunotherapy successful, it's essential that we strengthen the collaboration across all disciplines involved in oncology care. And that begins with establishing clear communication panels: making sure that information flows seamlessly between physicians, nurses, pharmacists, and support staff. It also requires a shared commitment to evidence-based practice so that every decision is grounding in data while remaining patient-centered. Just as important is respect for each professional's unique expertise, recognizing how each perspective contributes to safety, efficiency, and overall patient experience. We should also take time to assess our own collaboration skills, our ability to give and receive feedback, and our willingness to adapt based on input from colleagues. And throughout all, patient and caregiver values and preferences must stay at the center of every conversation. At Mayo Clinic, we say the needs of the patients come first, and that's how we should always practice. Using the structured communication framework helps make that team more consistent and reliable, ensuring that every patient benefits from a unified coordinated approach to cancer care.

And as we wrap up, let's look at a few specific actionable goals that can help translate today's discussion into everyday practice. First, we can evaluate which patients are best suited for subcutaneous immunotherapy, considering factors like tumor type, treatment goals, patient comorbidities, logistical needs. We should also incorporate subcutaneous options into our patient conversations, making sure that treatment decisions reflect not only clinical data, but also individual preferences and access considerations. And collaboration, as we discussed, is key. Coordinating very closely with nursing, pharmacy, and the broader care team ensures that these therapies are implemented safely and efficiently. It is equally important to apply consistent monitoring and immune-related adverse event management strategies across both intravenous and subcutaneous routes. And finally, we can look for opportunities, as we've seen, to expand access through innovative delivery models from outpatient settings to home-based care so patients benefit from the full potential of these advances. Together, these goals represent practical next steps for integrating new delivery approaches while maintaining the highest standards for safety, collaboration, and patient-centered care.

For those of you who would like to explore this topic further or access additional certified educational programs, an option is the website listed on the slide. To receive CME or CE credit for today's activity, simply complete the post-test and evaluation online. Thank you again for joining me for this discussion on evolving paradigms in immuno-oncology. And thank you to Creative Educational Concepts for providing this activity. I hope today's session provides practical insights you can apply to enhance collaboration and optimize patient care through innovative delivery approaches of immune checkpoint inhibitors.

