

Intralesional Therapy

Consensus statements for best practices in administration from the Melanoma Nursing Initiative

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BACKGROUND: Talimogene laherparepvec (T-VEC) is the first intralesional therapy for melanoma approved by the U.S. Food and Drug Administration. This oncolytic viral immunotherapy has improved outcomes for patients with locoregional recurrent melanoma and is showing promise in combination with systemic therapies.

OBJECTIVES: This article aims to provide oncology nurses with expert guidance on best practices in incorporating intralesional therapy for patients diagnosed with melanoma in practice.

METHODS: Members of the Melanoma Nursing Initiative explored issues related to administration of T-VEC in melanoma. The current literature and clinical experiences were reviewed.

FINDINGS: The author offers a care step pathway (CSP) and commentary detailing best practices in infection control, drug storage, pharmacy interface, patient flow, space/staff allocation, patient education, and adverse event management with T-VEC. The CSP will help nurses improve patient outcomes and streamline the workflow with this novel therapeutic approach.

KEYWORDS

intralesional therapy; talimogene laherparepvec; T-VEC; implementation

DIGITAL OBJECT IDENTIFIER

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TALIMOGENE LAHERPAREPVEC (T-VEC) (IMLYGIC®) RECEIVED APPROVAL from the U.S. Food and Drug Administration (FDA) in 2015 for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma that recurs after initial surgery (Amgen, 2017b). This is the first intralesional treatment for melanoma and the first-in-class oncolytic viral immunotherapy approved by the FDA (Harrington et al., 2016).

Injecting an agent directly into the tumor is an attractive strategy for melanoma because cutaneous, subcutaneous, and nodal lesions are accessible for treatment (Agarwala, 2015). Interest in intralesional immunotherapy has been longstanding, but early attempts with intralesional Bacillus Calmette-Guérin (BCG) resulted in fatal cases of anaphylaxis and disseminated disease (de la Monte & Hutchins, 1986; Mastrangelo, Bellet, Berkelhammer, & Clark, 1975). Other intralesional approaches, such as plasmid interleukin-12 and PV-10 (rose bengal disodium 10%), have shown promise (Algazi et al., 2016; Foote et al., 2017; Thompson et al., 2015). Preliminary data suggest a synergistic effect of combining T-VEC with systemic immunotherapy in melanoma (Puzanov et al., 2016). T-VEC is also being studied for use with systemic therapy and in other cancer types, including nonmelanoma skin cancers, breast cancer, lymphoma, and sarcoma (see Table 1). Because the role of intralesional therapy in oncology is likely to expand, nurses can expect a greater demand for its clinical use.

Intralesional oncolytic viral immunotherapy is new to clinical practice and poses unique challenges for integration into the clinical workflow. To date, oncology nurses have played a central role in the setup and day-to-day administration of T-VEC. Members of the Melanoma Nursing Initiative (MNI) identified a lack of knowledge about intralesional therapy as one of several barriers to optimal melanoma care. The author developed the care step pathway (CSP) and the outline for this article based on a literature review, multiple online conferences with the MNI, and clinical experience at the first institution to offer T-VEC in Boston, Massachusetts. This article reviews the MNI consensus regarding best practices for addressing the nursing challenges in delivering intralesional therapy in melanoma.

Background

T-VEC is composed of a herpes simplex virus (HSV)-1 modified by the insertion of a gene encoding for the immunostimulatory cytokine human

granulocyte-macrophage colony-stimulating factor (GM-CSF) and removal of two nonessential genes to reduce neurovirulence and tumor suppression (Orloff, 2016). In simple terms, T-VEC has been modified to replicate specifically within tumor cells, resulting in cell destruction or lysis. Tumor cell lysis leads to release of tumor cell antigens, which stimulates the body's antitumor immune response. This resulting immune response can extend beyond the injected lesion (Agarwala, 2016; Amgen, 2017b; Orloff, 2016). Investigators have observed regression of uninjected and injected lesions with T-VEC treatment (Agarwala, 2016).

Efficacy and Safety

In a phase 3 trial, T-VEC provided significantly better response rates versus subcutaneously administered GM-CSF in patients with unresectable stage IIIB or IV melanoma (N = 436). Durable response rate (i.e., continuous complete or partial response for six months or longer as a primary outcome) was 16.3% for T-VEC (95% confidence interval [CI] [12.1, 20.5]) versus 2.1% (95% CI [0, 4.5], $p < 0.0001$) for GM-CSF. T-VEC also was associated with a significantly greater overall response rate (26.4%, 95% CI [21.4, 31.5]) versus GM-CSF (5.7%, 95% CI [1.9, 9.5]) (Andtbacka et al., 2015). In that study, the estimated probability of response lasting at least a year was 65% (95% CI [51, 76]) with T-VEC. Although Andtbacka et al. (2015) found that the median overall survival was longer with T-VEC versus GM-CSF (23.3 versus 18.9 months), this did not reach significance ($p = 0.051$). The median time to response was 4.1 months. Patients with earlier stages of disease (stages IIIB, IIIC, and IVM1a) with no bone, brain, lung, or other visceral disease derived greater benefit than the overall population in terms of durable and overall response and the risk of developing visceral or bone metastases (Andtbacka et al., 2015; Andtbacka, Ross, et al., 2016; Harrington et al., 2016). T-VEC was well tolerated (see Table 2), and no deaths were considered related to treatment (Andtbacka et al., 2015).

Findings and Steps for Incorporation Into Practice

Introducing a live, attenuated viral therapy, such as T-VEC, requires implementation of infection control procedures for staff members who handle the medication and for anyone exposed to surfaces in contact with the medication. The nurse or other healthcare provider responsible for office setup needs to address staff concerns about possible exposure to the herpes virus. Universal biohazard precautions are required for handling T-VEC (Amgen, 2017b) (see Figure 1). In addition, incorporation requires practice changes, and resources are available to support these infrastructure changes (see Figure 2).

Exposure and Transmission Risk

Reports of healthcare provider and caregiver exposure to or infection with T-VEC are limited. An accidental needlestick to the

TABLE 1.
T-VEC CLINICAL INTERVENTIONAL STUDIES
IN PROGRESS AS OF AUGUST 2017

TITLE	PHASE	TRIAL ID
Melanoma		
Ipilimumab with or without talimogene laherparepvec in unresected melanoma	1/2	NCT01740297
Pembrolizumab with or without talimogene laherparepvec or talimogene laherparepvec placebo in unresected melanoma (KEYNOTE-034)	1b/3	NCT02263508
Talimogene laherparepvec and pembrolizumab in treating patients with stage III–IV melanoma	2	NCT02965716
Efficacy and safety of talimogene laherparepvec neoadjuvant treatment plus surgery versus surgery alone for melanoma	2	NCT02211131
PV-10 versus chemotherapy or oncolytic viral therapy for treatment of locally advanced cutaneous melanoma	3	NCT02288897
Lymphoma, nonmelanoma skin cancers		
Talimogene laherparepvec and nivolumab in treating patients with refractory lymphomas or advanced or refractory non-melanoma skin cancers	2	NCT02978625
Breast cancer		
Talimogene laherparepvec in combination with neoadjuvant chemotherapy in triple negative breast cancer	1/2	NCT02779855
Talimogene laherparepvec (T-VEC) for breast cancer local recurrence	2	NCT02658812
Sarcoma		
Talimogene laherparepvec and radiation therapy in treating patients with newly diagnosed soft tissue sarcoma that can be removed by surgery	2	NCT02923778
TVEC and preop radiation for sarcoma	1/2	NCT02453191
Solid tumors		
A study of T-VEC (talimogene laherparepvec) with or without radiotherapy for melanoma, Merkel cell carcinoma, or other solid tumors	2	NCT02819843

T-VEC—talimogene laherparepvec

Note. List derived by searching Clinicaltrials.gov using keyword *talimogene laherparepvec*; limited to interventional studies and phase 2 and 3 studies, excluding terminated and published studies.

finger of a healthcare provider during the phase 3 trial led to a herpetic lesion at the injury site. A quantitative polymerase chain reaction test was positive for T-VEC. The case resolved with acyclovir therapy (FDA, 2015). Another accidental needlestick exposure in an animal handler and a splashback to the eye were asymptomatic. In addition, of 177 patients in a family and caregiver surveillance program, 15 reported living with others or having a caregiver or close contact who reported signs and symptoms possibly related to the patients' participation in a T-VEC clinical trial (Amgen, 2015).

An interim report of a phase 2 study evaluated the shedding of T-VEC on skin and body fluids and transmission of T-VEC from patients (n = 30) to others. Preliminary findings from the study of biodistribution of T-VEC are shown in Table 3 (Andtbacka, Amatruda, et al., 2016; Gangi & Zager, 2017). The authors noted that transient, low levels of T-VEC were present in blood and urine during treatment, with low risk of transmission to clinicians or close contacts. Harrington et al. (2016) found that, in the event of accidental infection or exposure, T-VEC is susceptible to antiviral agents, such as acyclovir and famciclovir, and the authors further reiterated the low likelihood of household transmission.

TABLE 2.
ADVERSE EVENTS IN A PHASE 3 T-VEC TRIAL

ADVERSE EVENT	T-VEC (N = 292)	GM-CSF (N = 127)
Fatigue	50.3%	36.2%
Chills	48.6%	8.7%
Fever	42.8%	8.7%
Nausea	35.6%	19.7%
Flu-like illness	30.5%	15%
Injection site pain	27.7%	6.3%
Vomiting	21.2%	9.4%
Diarrhea	18.8%	11%
Headache	18.8%	9.4%
Myalgia	17.5%	5.5%
Arthralgia	17.1%	8.7%
Pain in extremity	16.4%	9.4%
Pain	16.1%	10.2%

GM-CSF—granulocyte-macrophage colony-stimulating factor; T-VEC—talimogene laherparepvec
Note. Adverse events are any grade, occurring in 15% or greater of T-VEC group.
Note. Based on information from Andtbacka et al., 2015.

“Risk relates directly to contact with drainage from injected lesions and/or bodily fluids. General close contact would not be expected to create a risk.”

Screening the Clinician and Patient

Healthcare providers who are pregnant or immunocompromised (e.g., those taking corticosteroids or other immunosuppressive therapy, or with conditions such as HIV, leukemia, or lymphoma) should not prepare or administer T-VEC or touch patient injection sites, dressings, or body fluids (Amgen, 2017b). Clinical staff must be trained in infectious control precautions before administering T-VEC. Likewise, patients who are pregnant or immunocompromised should not receive T-VEC (Amgen, 2017b) and, therefore, should be screened for those conditions. In the author’s practice, patients may be on physiologic doses of corticosteroids (i.e., prednisone 10 mg per day or less) and receive T-VEC safely. Patients also should be asked about the health status of close contacts and caregivers (Amgen, 2017b). Clinical judgment can be used in evaluating risk for these individuals. Risk relates directly to contact with drainage from injected lesions and/or bodily fluids. General close contact would not be expected to create a risk. Because T-VEC may result in immune-mediated events, the clinician should consider the risk and benefits in patients with underlying autoimmune disease (Amgen, 2017b).

Initial Patient Evaluation and Education

Pretreatment evaluation includes assessment of lesions to be injected and the patient’s functional status for the ability to travel to treatments, change injection site dressings, and manage adverse events (AEs). Patients with lesions in hard-to-reach locations (e.g., the back) may need someone to change their dressings. Enlisting the help of home healthcare services to change dressings is an option, but those agencies may have concerns about infection control, and such services can be difficult to arrange, depending on the patient’s insurance. If neither family nor home healthcare services are available, then the nurse may have

the patient return to the clinic for dressing changes and wound assessments.

Prior to initiating T-VEC therapy, patients and their caregivers should be counseled about benefits and risks of T-VEC, universal precautions, and dressing change procedures. Nurses must be prepared to answer questions about herpes exposure and transmission risk and infection control precautions (see Table 4). They should inform the patient about the time commitment for the administration sessions for planning purposes (e.g., expect about two hours from start to finish; first session lasts the longest). The nurse should review the potential AEs and the possibility of premedicating with ibuprofen or acetaminophen per the doctor or nurse practitioner (if not contraindicated) on the day of treatment (see Figure 3). Patients should be provided with written instructions and other resources, and this education should be repeated on the first day of treatment.

As observed in other immunotherapy studies (Wolchok et al., 2009), some patients receiving T-VEC display pseudoprogression before achieving response. More than half of those who responded to T-VEC first showed at least a 25% increase in lesion size or developed new lesions before improving. Patients should be educated about the phenomenon of pseudoprogression so that they do not become discouraged if it occurs. Nurses should reassure patients that pseudoprogression will not necessarily lead to treatment cessation (Andtbacka et al., 2015).

T-VEC patient education should include the need for contraception in women of childbearing potential to prevent

FIGURE 1. UNIVERSAL PRECAUTIONS FOR HANDLING T-VEC

- Nurses and other staff preparing, handling, or administering T-VEC should wear a protective gown, goggles/mask or face shield/mask, and gloves, and cover any open wounds with occlusive bandages. Clean gloves are sufficient for administering the injection; sterile gloves would be used for preparation by the pharmacy.
- If occupational exposure occurs (e.g., to eyes or mucous membranes), flush the area with clean water for at least 15 minutes.
- If exposure to broken skin or through a needlestick occurs, then clean the affected area thoroughly with soap and water and/or a disinfectant.
- Wipe any T-VEC spills with a virucidal agent (e.g., 1% sodium hypochlorite or 70% isopropyl alcohol), and blot with absorbent materials. Wear gloves, gown, and goggles/mask or face shield/mask while cleaning spills.
- Dispose of all materials that come in contact with T-VEC (e.g., vial, syringe, needle, cotton gauze, gloves, masks, dressings) in accordance with universal biohazard precautions. Wear gloves while handling these materials.

T-VEC—talimogene laherparepvec

Note. Based on information from Amgen, 2017b.

FIGURE 2. RESOURCES ABOUT INTRALESIONAL THERAPY FOR NURSES AND PATIENTS

FOR ADMINISTRATION

PRACTICE SETUP

Freezer for T-VEC storage

- Call 1-866-IMLYGIC

Operational planning checklist: Suggested procedures for storing, ordering, and safe handling of T-VEC

- www.imlygic.com/-/media/Project/Imlygic/PDF/operational-planning-checklist.ashx

List of treatment centers offering T-VEC

- Call 1-888-4ASSIST, Monday–Friday from 9 am–8 pm EST

FOR PATIENTS AND NURSES

DRUG ACCESS AND FINANCIAL RESOURCES

Cost assistance, benefits verification, state-specific payer information, sample letters of medical necessity and of medical appeal, coding and billing forms, third-party patient support options

- www.amgenassist360.com/hcp/imlygic-reimbursement-financial-assistance (for nurses)
- www.imlygic.com/patient/#assist (for patients)

Amgen First Step™ Program: Co-pay assistance for commercially insured patients

- www.amgenfirststep.com

CO-PAY ASSISTANCE, TRAVEL, LODGING, COUNSELING, AND SUPPORT

Amgen Assist 360™: Referral to independent charitable organizations for assistance with cost of co-pay, travel, lodging, counseling, and other support

- www.amgenassist360.com/patient/imlygic-cost-nurse-ambassador-assistance

PATIENT INFORMATION ABOUT T-VEC

- www.imlygic.com/imlygic-patient-brochure.pdf

PATIENT ADVOCACY AND NURSE SUPPORT

Toolkits for intralesional therapy, downloadable patient materials, and community nurse portal

- www.themelanomanurse.org

Speak with an oncology nurse on the phone or by email

- 1-877-246-2635

- www.aimatmelanoma.org/living-with-melanoma/nurse-on-call

Patient and caregiver resources

- www.aimatmelanoma.org/living-with-melanoma/patient-caregiver-resources

Patient symposiums

- www.aimatmelanoma.org/living-with-melanoma/patient-caregiver-symposiums

T-VEC—talimogene laherparepvec

pregnancy during treatment (Amgen, 2017b). If a pregnant woman is infected with wild-type HSV-1, there is a risk of viral shedding and transmission during birth or through placental transfer, which could lead to serious AEs if the fetus contracts the infection. Although no clinical data on T-VEC infections in pregnant women exist, there could be a risk to the fetus/neonate if T-VEC acted in a similar manner (Amgen, 2017b). The effect of T-VEC on fertility for women and men is not known, as this has not been studied (Amgen, 2017b). However, men are advised to use condoms during sexual activity to prevent inadvertent drug transfer (Amgen, 2017b). For all patients who are sexually active, the use of condoms is generally recommended to prevent potential T-VEC transfer via body fluids (Amgen, 2017b).

Setup

Ideally, two clinicians should be involved in the delivery of T-VEC: one to perform the injection and the other to assist with applying the occlusive dressing. This practice reduces the risk of contaminating the bandages with T-VEC. However, injections can be performed by one person if necessary. If possible, it is advantageous to perform all injections in a treatment room designated for that purpose.

The room should be cleaned between patients. Work surfaces and spills should be contained and treated with a virucidal agent (e.g., 1% sodium hypochlorite, 70% isopropyl alcohol) and absorbent materials. Common disinfectants have reduced T-VEC infectivity by more than 99.99% within one minute. In addition, infectivity was reduced on plastic surfaces that were not cleaned by about 99% following exposure to room temperature for four hours (Amgen, 2015, 2016, 2017b). At the author’s facility, the bed sheets are changed and all surfaces wiped down with an antibacterial solu-

tion between T-VEC patients. After all T-VEC treatments for the day are completed, the room is terminally cleaned (i.e., detachable objects are removed, surfaces are cleaned with disinfectant down to the floor, and detachable items are returned after sanitization).

TABLE 4.
PATIENT EDUCATION: POTENTIAL QUESTIONS AND ANSWERS

QUESTION	ANSWER
I share a shower/toothbrush/dishes/laundry facilities with other people. Does that pose a transmission risk?	Not unless you have uncovered, draining lesions or leave used dressing materials where others could come into contact with them. All lesions must be covered with an airtight and watertight dressing for one week after injection. Draining lesions must remain covered with an airtight and watertight dressing until they are no longer draining. Dressing should be changed once a week.
My spouse will be changing my dressings. What precautions must he or she take to prevent transmission?	Caregivers should wear protective gloves when assisting patients in applying or changing dressings. Pregnant women and people with weakened immune systems should not serve as caregivers or have contact with wounds or dressings. Caregivers should be instructed to place used dressing materials, gloves, and anything in contact with the wound into a sealed plastic bag. That bag can be disposed of in household waste.
My pregnant daughter may be changing my dressings. Is that a problem?	Pregnant women and people with weakened immune systems should not change dressings and must avoid contact with the injection site, anything that touches the injection site, and body fluids of patients treated with T-VEC.
Is it a problem if my lesions are oozing?	Not as long as they remain covered and no one who is pregnant or has a weakened immune system comes into contact with the lesions. Draining lesions must remain covered with an airtight and watertight dressing until they are no longer draining. Dressing should be changed once a week.
What if my lesions leak onto a counter surface, or a bandage with drainage touches the bathroom vanity? How do I clean it up?	Put on gloves, and wipe down the surface with a 1:10 bleach and water solution. Use disposable materials for wiping, place in a sealed plastic bag, and throw them in the household trash.
What precautions should I and my family members or other close contacts take to avoid getting herpes?	Household members, caregivers, sex partners, or people sharing the same bed, pregnant women, and newborns should avoid contact with injected lesions, dressings, injection site leakage, and body fluids of anyone treated with T-VEC.
How should I dispose of used dressings, gloves, and cleaning materials?	Place used dressings and cleaning materials into a sealed plastic bag and dispose of in household waste.

T-VEC—talimogene laherparepvec
Note. Based on information from Amgen, 2017b.

TABLE 3.
BIODISTRIBUTION OF T-VEC DNA AFTER T-VEC ADMINISTRATION

BODY SYSTEM	T-VEC DNA DETECTION
Blood	57% of patients after cycle 1 96% of patients after cycle 2 9% of patients after cycle 3
Urine	7% of patients after cycle 1 19% of patients after cycle 2 5% of patients after cycle 3 Highest levels: day after treatment in cycle 2
Injection site skin	90% of patients; 13% had infectious virus (within first week).
Occlusive dressings	17% (72/430 swabs); 69% of patients; one infectious
Orolabial region	1 patient (but noninfectious) on swabs

T-VEC—talimogene laherparepvec
Note. Based on information from Andtbacka, Amatruda, et al., 2016.

FIGURE 3.
CARE STEP PATHWAY TO MANAGE ADVERSE EVENTS AFTER T-VEC

PREVENTION OF ADVERSE EVENTS

- Review potential adverse events.
- Suggest premedication with ibuprofen or acetaminophen prior to injection, the evening after, and the next morning to reduce fever and chills.
- Stress the importance of keeping the injection site covered for one week and avoiding touching or scratching injection sites or dressing.
- Ensure that the patient has dressing materials and gloves.
- Advise patient to call the office regarding the following:
 - Any change in vision, even if it is small
 - Canker sores, cold sores, or any tingling skin lesions
 - Persistent fever (greater than 101°F [38.3°C]), chills, nausea and vomiting, aches, or pains
 - Any red, swollen area that is expanding, particularly if accompanied by fever
- Advise patient to plan rest periods and get some light exercise daily (like walking or yoga) to combat fatigue.
- Ensure access to an oral antiemetic to take the night of treatment if necessary, the following morning, and on an as-needed basis.
- Suggest use of a heating blanket or multiple blankets the night of treatment to reduce the effect of chills.

PATIENT EVALUATION AND NURSING ASSESSMENT

Look

- Does the patient appear unwell?
- Does the patient appear dehydrated?
- Is the patient currently febrile?
 - If febrile, are rigors present?
- Are there any blistering lesions in a herpetic pattern? Are they painful or tingling?
- Is the dressing dry?
- Is the injection site red, warm, or edematous?
- Is there excessive swelling?

Listen

- Onset and duration of fevers, chills, malaise, or joint pain
- Medications taken for fevers (acetaminophen, ibuprofen, other) and how often
- Eating habits and any nausea or vomiting
- Whether the patient has had enough fluids
- How the patient has been handling dressing changes
- Patient discomfort level
- If cellulitis is present, whether the patient has taken the full course of antibiotics
- Whether there are changes in vision
- Whether the patient is achy
- Whether the injection site is stinging or painful

Recognize

- How the patient has been managing the injection site (e.g., dressing, avoidance of touching or scratching)
- Presence of herpetic lesions
- Signs of ocular herpes
- Signs of cellulitis (particularly refractory cellulitis)

MANAGEMENT OF ADVERSE EVENTS

Nausea and vomiting

- Oral antiemetics
- IV antiemetics for subsequent T-VEC cycles
- Fluids and bland food

Flu-like symptoms or fever and chills

- Acetaminophen or nonsteroidal anti-inflammatory drugs
- Warm packs, blankets

Herpetic lesions

- Refer patients with vision changes to an ophthalmologist.
- Consider testing herpetic lesions to determine if they are related to T-VEC.
- Weigh the benefits and risk of antivirals, such as acyclovir.

Injection-site pain or swelling

- Elevation, ice
- Acetaminophen
- Avoid compression because it may be painful.

Cellulitis

- Anticipate complete blood count draw, blood cultures, and start of empiric antibiotics.
- Consider hospitalization for IV antibiotics if oral antibiotics fail or if the patient develops weakness in arms or legs.

RED FLAGS

- Signs of ocular herpes
- Signs of cellulitis (particularly refractory cellulitis)

T-VEC—talimogene laherparepvec

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The practice may consider scheduling all T-VEC injections on the same day each week to facilitate workflow.

Patients with draining lesions are considered potentially infectious (Amgen, 2017b); their time in the waiting area should be minimized to avoid contact with immunosuppressed individuals. This risk should be low if the draining lesion is covered with an occlusive bandage. Open or ulcerated lesions that are not draining also should be covered with an occlusive bandage, and time in the waiting room should be minimized. Most patients do not have draining lesions and can follow the same intake procedures as other patients. The healthcare provider should inform waiting room staff about which patients should be sent to the clinical area immediately upon arrival rather than be asked to wait in the reception room.

PREINJECTION DRUG PREPARATION

To evaluate the amount of drug required for injections, it is helpful to review the manufacturer’s recommended dosing. T-VEC is dosed at a lower concentration for the first visit (i.e., 10⁶ [1 million] plaque-forming units [PFU] per milliliter) with the intention of seroconverting patients not previously exposed to HSV (i.e., HSV-negative patients). The second, more concentrated therapeutic dose (i.e., 10⁸ [100 million] PFU/ml) is given three weeks later. Subsequent treatments at the 10⁸ PFU/ml dose occur every two weeks, pending treatment response, tolerability, and patient condition (Amgen, 2017b; Rehman, Silk, Kane, & Kaufman, 2016).

The dose per lesion depends on lesion size, measured as the longest dimension of each lesion (see Table 5). Patients can receive a maximum of 4 ml per treatment session, but that may be an insufficient amount to inject every lesion (Amgen, 2017b). At the first treatment session, lesions are injected in size order from largest to smallest or until the maximum dose is reached. Thereafter, the healthcare provider should treat any new lesions first, then inject in size order, starting with the largest lesion.

TABLE 5.
T-VEC INJECTION VOLUME PER LESION SIZE

LESION SIZE (LONGEST DIMENSION)	MAXIMUM INJECTION VOLUME
Greater than 5 cm	Up to 4 ml
Greater than 2.5 cm–5 cm	Up to 2 ml
Greater than 1.5 cm–2.5 cm	Up to 1 ml
Greater than 0.5 cm–1.5 cm	Up to 0.5 ml
0.5 cm or less	Up to 0.1 ml

T-VEC—talimogene laherparepvec

Note. Closely clustered lesions can be measured as a single lesion.

Note. Based on information from Amgen, 2017b.

IMPLICATIONS FOR PRACTICE

- Anticipate the infection control, procedural, and educational challenges of incorporating the first intralesional oncolytic viral immunotherapy in clinical practice.
- Develop a workflow and staffing plan to safely and effectively deliver intralesional oncolytic viral immunotherapy.
- Educate patients about self-management techniques and communication strategies to ensure safe use of intralesional oncolytic viral immunotherapy.

Marking the location and size of each lesion on a lesion tracking sheet provided by the manufacturer is helpful (see Figure 4). A record should be kept for every patient and updated at each treatment session, noting lesion size, change in size, and which lesions were injected. Ideally, all lesions should be measured, even if they will not be injected at a given session, to track any changes in size. Alternatively, photos of the lesions could also be used for tracking. If multiple lesions are present, the clinician should avoid injecting painful lesions. Lesions that recur after response can be reinjected, with at least two weeks between treatments. Treatment should continue for at least six months or until all lesions have resolved or other therapy is needed (Amgen, 2017b).

T-VEC is stored at –90°C to –70°C (–130°F to –94°F) in a freezer, which the manufacturer will provide upon request. Once thawed, it must be administered immediately or refrigerated for a limited time period: 12 hours or less for the lower dose (10⁶ PFU/ml) and 48 hours or less for the higher dose (10⁸ PFU/ml). T-VEC cannot be refrozen after it has thawed (Amgen, 2017b). Therefore, accurate dose measurement is important to avoid wasting medication. Syringes should be drawn up immediately before administration (Amgen, 2017b). If T-VEC is intended for use within 96 hours, a just-in-time delivery ordering system is also available, which requires coordination of scheduling of the patient visit with T-VEC administration (Amgen, 2017a).

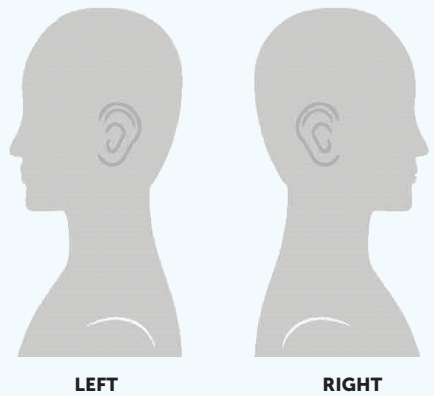
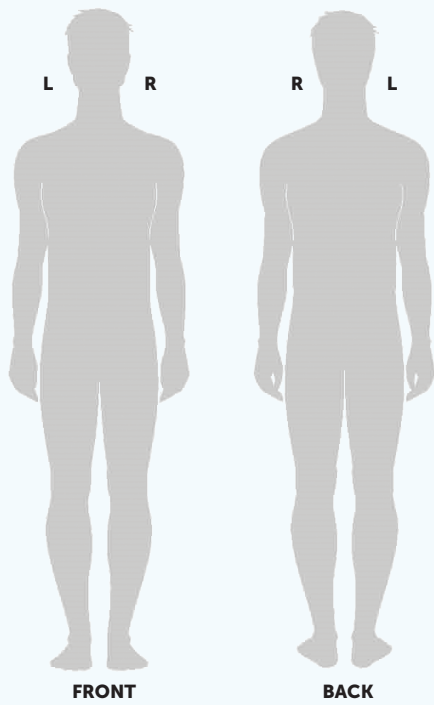
The drug order should be verified per each institution’s policy for chemotherapy or biotherapy prior to sending it to the pharmacy. A pharmacy staff member should take the requested quantity of drug from the freezer upon receipt of the order. Both concentrations come in 1-ml vials. Thawing requires about 30–45 minutes, which should be taken into consideration when scheduling the patient’s appointment. This waiting period offers an opportunity to assess the patient further, invite any questions, and apply topical anesthetic (e.g., lidocaine) to areas for planned injection. Patients who have not taken ibuprofen or acetaminophen to reduce risk and severity of fever and chills should be offered such medication per doctor or nurse practitioner order, if not contraindicated.

Each institution typically devises its own medication preparation protocol based on manufacturer guidelines. At the author’s institution, a pharmacist or other pharmacy staff member draws up a separate syringe for each lesion with the requested dosage for that lesion (Rehman et al., 2016). Preparing a syringe with exactly the appropriate amount for each lesion reduces the risk of

FIGURE 4.
LESION TRACKING SHEET

DATE: _____ **DATE OF BIRTH:** _____
PATIENT NAME: _____ **MEDICAL RECORD NUMBER:** _____
MEDICATION NAME: _____ **CYCLE:** _____

Label lesion(s) on body diagram to match with corresponding number in chart.



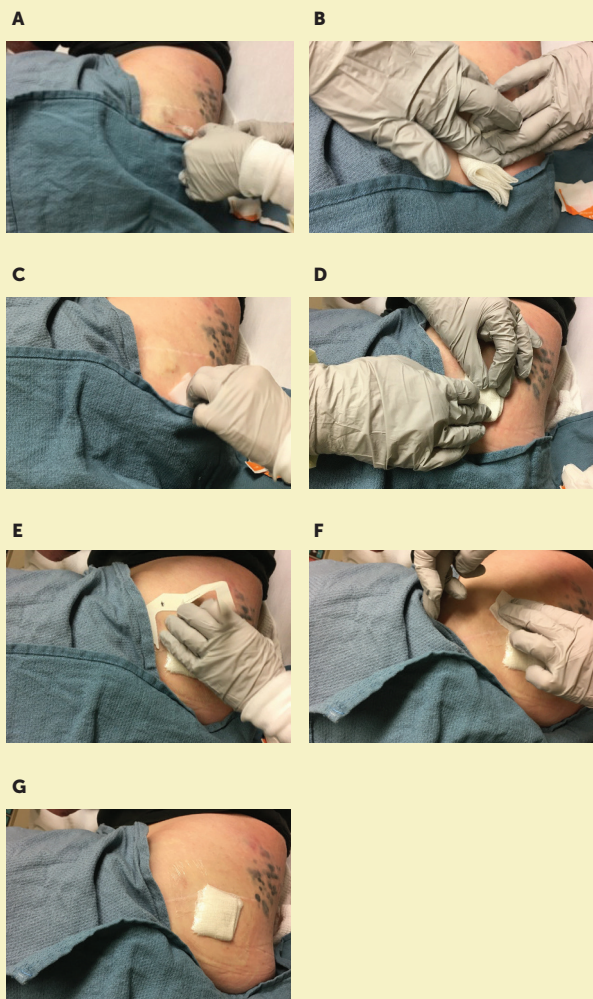
	SUBCUTANEOUS, CUTANEOUS, OR NODAL			SIZE (CM)	DOSE	CHANGES FROM PREVIOUS VISIT
1	S	C	N			
2	S	C	N			
3	S	C	N			
4	S	C	N			
5	S	C	N			
6	S	C	N			
7	S	C	N			
8	S	C	N			
9	S	C	N			
10	S	C	N			

TOTAL DOSE: _____

ADDITIONAL NOTES: _____

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FIGURE 5.
INJECTION AND DRESSING OF T-VEC



A—injection of T-VEC into the lesion; needle is moved along different tracks within the lesion without withdrawing it; B—holding gauze over the insertion site after the needle is withdrawn (injection nurse on right and assisting nurse on left); C—assisting nurse cleans injection site and surrounding area with alcohol; D—application of new sterile gauze; E—application of occlusive dressing over the injection site and surrounding area; F—assisting nurse wiping surface of the occlusive dressing with alcohol; G—injection site completely dressed with margins of occlusive dressing over the gauze; T-VEC—talimogene laherparepvec

Note. Images courtesy of Virginia Seery. Used with permission.

While wearing gown, gloves, goggles, and mask (or eye shield with mask), the nurse should attach a sterile 22- to 26-gauge needle to each syringe prior to injection (Amgen, 2017b). The needle must be attached securely to prevent drug leakage. Prior to palpating the lesion, the nurse should clean the fingertip of the glove and the injection site with alcohol, allow the areas to dry, then palpate the lesion prior to injecting. Lesions detectable by ultrasound guidance also can be injected (Amgen, 2017b).

Administration Technique

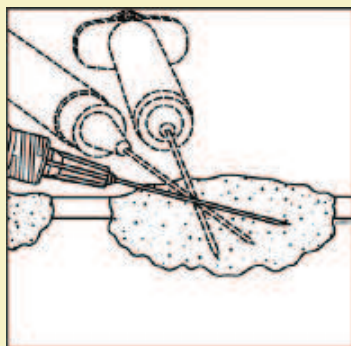
Figure 5 depicts the administration technique from start to finish. A single insertion point is used for each lesion (Amgen, 2017b). The injection should be made on multiple tracks, pulling the needle back after injecting a portion of the drug without withdrawing it from the lesion, then rotating it radially on another track (see Figure 6). This should be repeated until the entire lesion is treated. T-VEC should be injected evenly throughout the lesion. If patients report pain with injection after topical anesthetic, the nurse can add ice packs for 5–10 minutes (Rehman et al., 2016). If pain persists, the healthcare provider should consider injecting 1% lidocaine around the lesion periphery. Local anesthetic should not be injected into the lesion itself, because it may alter the pH and affect T-VEC stability (Hoffner, Iodice, & Gasal, 2016; Rehman et al., 2016). Care should be taken when injecting lesions near major airways, because obstructive airway disorder has been reported following T-VEC treatment (Amgen, 2017b).

Two injections can be performed in the same lesion if the radial reach of needle does not cover the entire lesion, but this should be avoided if possible. Multiple insertion points in the same lesion offer portals for possible drug leakage, reducing the amount of drug delivered to the patient and increasing exposure risk (Sloot, Rashid, Sarnaik, & Zager, 2016). If it is necessary to inject one lesion at multiple insertion points, then a new needle and syringe should be used for each separate injection (Amgen, 2017b). A temporary dressing should be placed over the first insertion point and taped in place prior to initiating the next injection into the same lesion. It is advisable to avoid having fingers near the lesion being injected to prevent needlesticks.

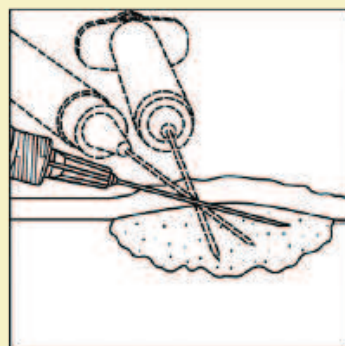
Some lesions accept the drug more easily than others, and leakage may occur if the lesion is resistant to drug injection. In such cases, the nurse should apply slow, steady pressure, moving the needle slightly if necessary. Once the drug is fully injected, the needle should be withdrawn slowly to reduce the risk of T-VEC leakage. Once the needle is withdrawn, the area should be immediately covered with sterile gauze for at least 30 seconds. Then, the injection site and surrounding area should be cleaned with an alcohol pad. Next, a new sterile gauze and occlusive dressing are applied. After this dressing is applied, the assisting clinician should wipe the occlusive dressing completely with alcohol as a final step. This occlusive dressing should remain in place for seven days. During the procedure, the nurse should talk with the

over- or underinjecting. Small-unit syringes allow for better injection control (Amgen, 2017b). Syringes are filled under a hood at the pharmacy to capture any aerosolized material, with the hood and work space cleaned prior to any other use. The syringes are capped and placed in a chemotherapy bag for transportation to the treatment room.

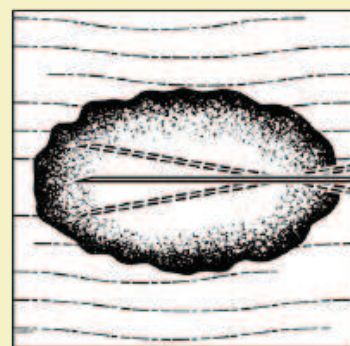
FIGURE 6.
T-VEC ADMINISTRATION FOR DIFFERENT TYPES OF LESIONS



Injection administration for cutaneous lesions



Injection administration for subcutaneous lesions



Injection administration for nodal lesions

T-VEC—talimogene laherparepvec

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patient during administration, offering support and inquiring about pain, discomfort, or other AEs.

Postinjection Treatment and Patient Counseling

As part of the postinjection nursing assessment, the patient should again be asked about discomfort, pain, or other symptoms. The patient should be given instructions on postprocedure care. The nurse should advise the patient that if the dressing comes off within the first week or is draining a large amount, then it should be replaced. The occlusive dressing may be covered to allow a patient to shower. Any draining injection sites must remain covered until the drainage stops. Gloves must be worn for all dressing changes. Patients should be advised to avoid touching or scratching the injection sites, even if covered, to prevent inadvertent transfer of T-VEC (Amgen, 2017b). Patients should be provided with gloves, alcohol pads, gauze, and occlusive dressing for home use and instructed about when to call the office if issues arise. The nurse should assess the patient's and family's understanding of these instructions and answer any questions.

Follow-Up

The nurse should call the patient one to two days after the first treatment to assess treatment tolerability and offer counsel about managing any AEs that may have occurred. Ideally, patients should be contacted the day before the second treatment with a reminder to take premedication prescribed for them (e.g., ibuprofen or acetaminophen for fever or chills, as well as antiemetic medication). In follow-up telephone calls/visits the nurse should perform a look, listen, and recognize assessment of potential AEs, including nausea and vomiting, flu-like symptoms, herpetic lesions, injection-site pain or swelling, and cellulitis. Of note, the

flu-like symptoms typically resolve within 24–72 hours (Amgen, 2017b). As mentioned previously, because immune-related events have been reported in patients treated with T-VEC, the benefits and risks of T-VEC should be discussed in patients who experience such events (Amgen, 2017b).

Another important consideration is distinguishing expected injection site pain or swelling from cellulitis (which occurs rarely, in about 2% of cases). Swelling and drainage from the injection site may occur in some patients, but persistent fever (longer than 48 hours), swelling, erythema, or warmth that expands rapidly should be evaluated for cellulitis. Herpetic cellulitis usually lasts no more than 24–48 hours (Rehman et al., 2016). Because T-VEC-related inflammation usually clears quickly, persistent or worsening symptoms of erythema, fever (up to 102°F or 38.9 °C, longer than 48 hours), or leukocytosis may signal bacterial cellulitis (Rehman et al., 2016).

Amgen offers testing of any suspected herpetic lesions that develop during T-VEC therapy for patients and caregivers. The herpes virus in T-VEC remains susceptible to acyclovir therapy, but acyclovir therapy can interfere with the effect of T-VEC on melanoma lesions (Amgen, 2017b). Therefore, the healthcare team needs to carefully balance the risk and benefit of acyclovir therapy in patients receiving T-VEC if a herpetic lesion develops.

Conclusion

T-VEC, the first-in-class intralesional oncolytic viral immunotherapy approved for melanoma, offers patients with local or regional metastatic disease the possibility of improved response rates with a favorable toxicity profile. Its viral composition may raise concerns about exposure and transmission among healthcare staff, patients, and family members. Storage and handling

requirements necessitate close coordination with the pharmacy. Nurses familiar with infection control recommendations, drug-handling requirements, and patient education topics detailed in this article are well equipped to contribute to their practice's adoption of intralesional therapy and overall patient outcomes and satisfaction.

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REFERENCES

Agarwala, S.S. (2015). Intralesional therapy for advanced melanoma: Promise and limitation. *Current Opinion in Oncology*, 27, 151–156. doi:10.1097/cco.0000000000000158

Agarwala, S.S. (2016). The role of intralesional therapies in melanoma. *Oncology (Williston Park)*, 30, 436–441.

Algazi, A., Tsai, K.K., Takamura, K.T., Chen, L., Twitty, C., Dwyer, M., . . . Daud, A. (2016). Intratumoral electroporation of plasmid IL-12 can prime response to anti-PD1/PD-L1 blockade in patients with stage III/IV-M1a melanoma [Abstract CT134]. *Cancer Research*, 76(Suppl. 14), CT134. doi:10.1158/1538-7445.am2016-ct134

Amgen. (2015). *Background information for joint meeting of the Cellular, Tissue, and Gene Therapy, and Oncologic Drugs Advisory Committees*. Thousand Oaks, CA: Author. Retrieved from <https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/CellularTissueandGeneTherapiesAdvisoryCommittee/UCM444199.pdf>

Amgen. (2016). *Imlygic™ safety data sheet*. Retrieved from <http://msds.amgen.com/imlygic-safety-datasheet>

Amgen. (2017a). *Imlygic® (talimogene laherparepvec)*. Retrieved from <http://www.imlygic.com>

Amgen. (2017b). *Imlygic® (talimogene laherparepvec) [Package insert]*. Retrieved from http://pi.amgen.com/~media/amgen/repositorysites/pi-amgen-com/imlygic/imlygic_pi.ashx

Andtbacka, R.H., Amatruda, T., Mehnert, J., Walker, J., Zager, J.S., Nemunaitis, J., . . . Shilkrut, M. (2016, October). *Interim analysis of phase 2 trial to evaluate biodistribution and shedding of talimogene laherparepvec in unresected stage IIIB-IV melanoma patients*. Poster presented at the International Meeting on Replicating Virus Therapeutics, Vancouver, BC.

Andtbacka, R.H., Kaufman, H.L., Collichio, F., Amatruda, T., Senzer, N., Chesney, J., . . .

Coffin, R.S. (2015). Talimogene laherparepvec improves durable response rate in patients with advanced melanoma. *Journal of Clinical Oncology*, 33, 2780–2788. doi:10.1200/jco.2014.58.3377

Andtbacka, R.H., Ross, M., Puzanov, I., Milhem, M., Collichio, F., Delman, K.A., . . . Kaufman, H.L. (2016). Patterns of clinical response with talimogene laherparepvec (T-VEC) in patients with melanoma treated in the OPTiM phase III clinical trial. *Annals of Surgical Oncology*, 23, 4169–4177. doi:10.1245/s10434-016-5286-0

de la Monte, S.M., & Hutchins, G.M. (1986). Fatal disseminated bacillus Calmette-Guerin infection and arrested growth of cutaneous malignant melanoma following intralesional immunotherapy. *American Journal of Dermatopathology*, 8, 331–335.

Foote, M., Read, T., Thomas, J., Wagels, M., Burmeister, B., & Smithers, B.M. (2017). Results of a phase II, open-label, non-comparative study of intralesional PV-10 followed by radiotherapy for the treatment of in-transit or metastatic melanoma. *Journal of Surgical Oncology*. Advance online publication. doi:10.1002/jso.24580

Gangi, A., & Zager, J.S. (2017). The safety of talimogene laherparepvec for the treatment of advanced melanoma. *Expert Opinion on Drug Safety*, 16, 265–269. doi:10.1080/14740338.2017.1274729

Harrington, K.J., Andtbacka, R.H., Collichio, F., Downey, G., Chen, L., Szabo, Z., & Kaufman, H.L. (2016). Efficacy and safety of talimogene laherparepvec versus granulocyte-macrophage colony-stimulating factor in patients with stage IIIB/C and IVM1a melanoma: Subanalysis of the phase III OPTiM trial. *OncoTargets and Therapy*, 9, 7081–7093. doi:10.2147/ott.s115245

Hoffner, B., Iodice, G.M., & Gasal, E. (2016). Administration and handling of talimogene laherparepvec: An intralesional oncolytic immunotherapy for melanoma. *Oncology Nursing Forum*, 43, 219–226. doi:10.1188/16.ONF.219-226

Mastrangelo, M.J., Bellet, R.E., Berkelhammer, J., & Clark, W.H., Jr. (1975). Regression of pulmonary metastatic disease associated with intralesional BCG therapy of intracutaneous melanoma metastases. *Cancer*, 36, 1305–1308.

Orloff, M. (2016). Spotlight on talimogene laherparepvec for the treatment of melanoma lesions in the skin and lymph nodes. *Oncolytic Virotherapy*, 5, 91–98. doi:10.2147/ov.s99532

Puzanov, I., Milhem, M.M., Minor, D., Hamid, O., Li, A., Chen, L., . . . Andtbacka, R.H. (2016). Talimogene laherparepvec in combination with ipilimumab in previously untreated, unresectable stage IIIB-IV melanoma. *Journal of Clinical Oncology*, 34, 2619–2626. doi:10.1200/jco.2016.67.1529

Rehman, H., Silk, A.W., Kane, M.P., & Kaufman, H.L. (2016). Into the clinic: Talimogene laherparepvec (T-VEC), a first-in-class intratumoral oncolytic viral therapy. *Journal for Immunotherapy of Cancer*, 4, 53. doi:10.1186/s40425-016-0158-5

Sloot, S., Rashid, O.M., Sarnaik, A.A., & Zager, J.S. (2016). Developments in intralesional therapy for metastatic melanoma. *Cancer Control*, 23, 12–20.

Thompson, J.F., Agarwala, S.S., Smithers, B.M., Ross, M.I., Scoggins, C.R., Coventry, B.J., . . . Wachter, E.A. (2015). Phase 2 study of intralesional PV-10 in refractory metastatic melanoma. *Annals of Surgical Oncology*, 22, 2135–2142. doi:10.1245/s10434-014-4169-5

U.S. Food and Drug Administration. (2015). *Cellular, Tissue, and Gene Therapies Advisory Committee and Oncologic Drugs Advisory Committee meeting. BLA 125518 talimogene laherparepvec (Amgen)*. Retrieved from <https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/CellularTissueandGeneTherapiesAdvisoryCommittee/UCM444715.pdf>

Wolchok, J.D., Hoos, A., O'Day, S., Weber, J.S., Hamid, O., Lebbé, C., . . . Hodi, F.S. (2009). Guidelines for the evaluation of immune therapy activity in solid tumors: Immune-related response criteria. *Clinical Cancer Research*, 15, 7412–7420. doi:10.1158/1078-0432.ccr-09-1624

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