AIM WITH IMMUNOTHERAPY FOUNDATION | IMMUNO-ONCOLOGY ESSENTIALS

Intralesional Therapy for Melanoma

An HCP Tool From the Immuno-Oncology Essentials Initiative

Talimogene laherparepvec (Imlygic®; T-VEC) is a first-in-class oncolytic viral immunotherapy recently approved by the Food and Drug Administration (FDA) as intralesional treatment of unresectable cutaneous, subcutaneous, and/or nodal melanoma recurrent after initial surgery.

This document is part of an overall HCP tool to assist healthcare providers in optimizing the care of melanoma in patients receiving newer anti-melanoma therapies.

PREPARATION AND HANDLING

T-VEC is a live, attenuated virus. Consequently, there are exposure and transmission risks to healthcare personnel and family members/caregivers

- Healthcare providers who are immunocompromised or pregnant should not prepare or administer T-VEC and should avoid direct contact with the T-VEC injection site, dressings, or body fluids of treated patients
- Those preparing and/or administering T-VEC should wear protective clothing and avoid accidental exposure. If accidental exposure occurs, the exposed individuals should clean the affected area
- Clean all surfaces that may have come into contact with T-VEC and treat all T-VEC spills with a virucidal agent and blot using absorbent materials. Dispose contaminated materials as biohazardous waste
- Similarly, caregivers/family members should be instructed to wear protective gloves when assisting patients to apply or change occlusive dressings and should put used dressings, gloves, and cleaning materials in a sealed plastic bag and dispose of the bag in the regular trash

STORAGE AND DRUG-DOSING/ADMINISTRATION

- T-VEC can be kept in stock but must be stored in a freezer to maintain temperature at -90 °C to 70 °C. If an ultra-low freezer is not available, Amgen can provide access to one (1-866-IMLYGIC)
- For more immediate procurement, you can also use the IMLYGIC just-in-time delivery system. This allows you to keep T-VEC in the original shipping container for up to 96 hours after it is sealed for delivery
- Thawing of T-VEC vials requires about 30–45 minutes. Ideally, IMLYGIC should be thawed immediately prior to administration. The lower dose of T-VEC can be refrigerated for up to 12 hours; the higher dose can be refrigerated for up to 48 hours
- T-VEC is administered by intralesional injection into cutaneous, subcutaneous, and/or nodal lesions that are visible, palpable, or detectable by ultrasound
- T-VEC is available in single-use vials of 1 mL that contain either 106 (1 million) or 108 (100 million) PFU/mL

  ◊ The lower T-VEC concentration (106 PFU/mL) is used for the initial dose. The higher T-VEC concentration (108 PFU/mL) should be used for the second and all subsequent treatments. The second treatment occurs 3 weeks after initial treatment and all subsequent lesions occur 2 weeks after previous treatment

  ◊ Inject lesion(s) from largest to smallest until either all lesions are injected or a maximum injection volume of 4 mL is reached for the treatment session. The volume per lesion size is shown the table at right (you may not be able to inject every lesion at each treatment session)

  ◊ At the first treatment session, lesions are injected in size order from largest to smallest or until the maximum dose is reached. Thereafter, the HCP should treat any new lesions first, then inject in size order starting with the largest lesion

T-VEC Injection Volume Per Lesion Size

Lesion size (longest dimension)	Injection volume
> 5 cm	Up to 4 mL
> 2.5 cm to 5 cm	Up to 2 mL
> 1.5 cm to 2.5 cm	Up to 1 mL
> 0.5 cm to 1.5 cm	Up to 0.5 mL
≤ 0.5 cm	Up to 0.1 mL

Closely clustered lesions can be measured as a single lesion.

STORAGE AND DRUG-DOSING/ADMINISTRATION

Continued

- Using a single insertion point, the injection should be made on multiple radial tracks, rotating and pulling the needle back to achieve even and complete dispersion (see diagram).

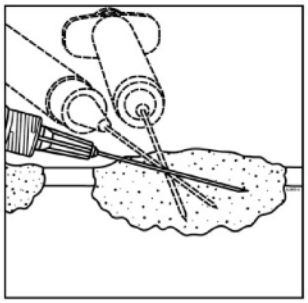

Figure 1: Injection administration for cutaneous lesions

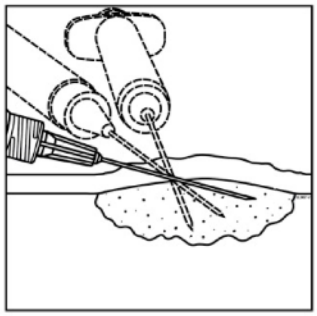

Figure 2: Injection administration for subcutaneous lesions

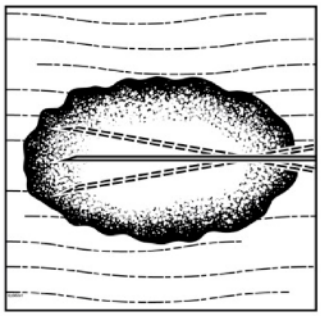

Figure 3: Injection administration for nodal lesions

- To reduce risk of over- or under-injecting, prepare individual syringes with the exact amount of T-VEC to be injected into each lesion.
- To prevent drug leakage, securely attach the needle to syringe prior to injection and slowly withdraw the needle after T-VEC is fully injected.
- Slow and steady pressure should be applied to the syringe. This helps if the lesion is difficult to inject or prone to drug leakage.

SIDE EFFECTS AND THEIR MANAGEMENT

Management strategies for preventing and managing T-VEC–related adverse events are outlined in the Care Step Pathway below. The most commonly reported adverse events include constitutional or administration site symptoms (fatigue, chills, pyrexia, influenza-like illness, and injection site pain) and gastrointestinal disorders (nausea and vomiting). Herpetic infections (cold sores and ocular herpetic infection) have also been reported in T-VEC–treated patients. The most commonly reported grade 3 adverse event is cellulitis, with an incidence of 2%.

- T-VEC is contraindicated in immunocompromised or pregnant patients.
- HCPs should contact patients 1–2 days after the first T-VEC injection to assess treatment tolerability and provide counsel about AE recognition and management. Follow-up phone calls and/or visits are important for continued monitoring and management of potential drug-related adverse events.
- If the patient reports pain with injection after topical anesthetic, ice packs may be applied to the site for 5 to 10 minutes. If the pain persists, injection of 1% lidocaine around the lesion periphery may be considered.
    - ◊ Local anesthetic should NOT be injected into the lesion itself, as this may affect T-VEC stability and efficacy.

Care Step Pathway – Adverse Events (AEs) After T-VEC

Prevention of AEs

- Review potential AEs with the patient
- Suggest premedication with ibuprofen/acetaminophen prior to injection and the evening of/next morning after injection (to reduce the impact of fever/chills)
- Stress importance of keeping infection site covered for 1 week and avoiding touching or scratching injection sites or dressing
- Ensure that the patient has dressing materials/gloves
- Advise patient to call the office regarding:
  - Any change in vision, even if small
  - Canker sores, cold sores, any tingling skin lesions
  - Persistent fever (>101.0°F; 38.3°C), chills, nausea/vomiting, aches, pains
  - Any red, swollen area that is expanding, especially if accompanied by fever
- Advise patient to plan rest periods and get some light exercise daily (like walking or yoga) to combat fatigue
- Assure 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/multiple blankets the night of treatment to reduce the impact of chills

Patient Evaluation/Nursing Assessment

Look:
- Does the patient appear unwell?
- Does the patient appear dehydrated?
- Currently febrile?
- If febrile, are rigors present?
- Is the patient achy?
- Is the injection site stinging or painful?
- Any blistering lesions in a herpetic pattern? Are they painful or tingling? Any changes in vision?
- 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, any nausea or vomiting
- Whether the patient has been taking enough fluids
- How the patient has been handling dressing changes
- Patient discomfort level
- If cellulitis is present, has the patient taken the full course of antibiotics?

Recognize:
- How the patient has been managing the injection site (dressing/avoidance of touching/scratching)
- Presence of herpetic lesions
- Signs of ocular herpes
- Signs of cellulitis (particularly refractory cellulitis)

Management of AEs

Nausea/Vomiting
- Oral antiemetics
- IV antiemetics for subsequent T-VEC cycles
- Fluids/bland food

Flu-like Symptoms, Fever/Chills
- Acetaminophen/non-steroidal anti-inflammatory drugs (NSAIDs)
- Warm packs, blankets

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

Injection-Site Pain/Swelling
- Elevation, ice
- Acetaminophen
- Avoid compression because it may be painful

Cellulitis
- Anticipate complete blood count (CBC) draw, blood cultures, and start of empiric antibiotics
- Consider hospitalization for intravenous antibiotics if oral antibiotics fail or the patient develops weakness in arms/legs

QUESTIONS & ANSWERS

Q. What should I tell a patient who is concerned about sharing a shower, toothbrush, dishes, or laundry facilities with other people? Is there a transmission risk?

A. Advise the patient that there is not a risk unless he/she has uncovered, draining lesions or leaves used dressing materials where others could come in contact with them. All lesions must be covered with an airtight and watertight dressing for 1 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.

Q. What should I tell a patient to do if the lesion is oozing? Is this a transmission risk?

A. There is little risk of transmission as long as the lesions 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.

Q. How do I advise a patient who is concerned when a lesion leaks on a counter surface or a bandage with drainage touches the bathroom vanity? How should the patient clean it up?

A. You can advise the patient to put on gloves and wipe down the surface with a 1:10 bleach solution. Instructions on how to make such a solution are available at https://www.verywell.com/make-your-own-disinfectant-solution-998274. Advise the patient to use disposable materials for wiping, place them in a sealed plastic bag, and throw them in the household trash.

Click here for downloadable action plans to customize for your patients

PATIENT RESOURCES

Financial Assistance

Amgenassistonline.com
or call 1-888-4ASSIST

Additional Information Resources

AIM at Melanoma Foundation (Nurse on Call, patient symposia, drug resources, etc)
http://www.AIMatMelanoma.org

ADDITIONAL RESOURCES

- Chesney J, Awasthi S, Curti B, et al. Phase IIIb safety results from an expanded-access protocol of talimogene laherparepvec for patients with unresected, stage IIIB-IVM1c melanoma. *Melanoma Res*. 2018;28:44-51.
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- Hoffner B, Iodice GM, Gasal E. Administration and handling of talimogene laherparepvec: an intralesional oncolytic immunotherapy for melanoma. *Oncol Nurs Forum*. 2016;43:219-226.
- Imlygic® [prescribing information]. Thousand Oaks, CA: Amgen Inc; 2017.
- Imlygic® Clinical Overview and Handling Guide. Available at: http://www.imlygic.com/-/media/project/imlygic/pdf/imlygic-clinical-overview.pdf. Accessed August 8, 2017.
- Seery V. Intralesional therapy: consensus statements for best practices in administration from the Melanoma Nursing Initiative. *Clin J Oncol Nurs*. 2017; 21(Suppl. 4):76-86.