Talquetamab-tgvs

An HCP Tool from AIM with Immunotherapy

Talquetamab-tgvs (Talvey) is a bispecific T-cell engaging antibody directed against GPRC5D and CD3. It is indicated for the treatment of adult patients with relapsed or refractory (R/R) multiple myeloma who have received at least 4 prior lines of therapy.

Clinical trial results for talquetamab-tgvs

In a Phase 2, single-arm, open-label, multicenter study called MonumenTAL-1 (NCT03399799, NCT04634552) the results suggested safety was clinically manageable and efficacy was observed.

- The data also showed that > 70% overall response rate (i.e. stringent complete response + complete response + very good partial response + partial response) in heavily pre-treated patients with relapsed/refractory multiple myeloma that were treated with talquetamab-tgvs.
- The complete response was approximately 32% of patients receiving talquetamab-tgvs, which included those with stringent complete response and complete response.
- Response rates were similar for patients receiving 0.4 mg/kg weekly (74% 106 or 143 patients) and patients receiving 0.8 mg/kg every other week (69% 107 of 154 patients) talquetamab-tgvs.
- Fifty-nine percent of patients continued to respond for at least 9 months following treatment.

Molecular biology and pharmacology for talquetamab-tgvs

Talquetamab-tgvs is a bispecific IgG4 antibody, sometimes referred to as a bispecific antibody. It is designed so that each Fab arm of the antibody binds to a different antigen. The bi-directed antibody property allows talquetamab-tgvs to promote T cell-mediated tumor cell killing.

One of the Fab antibody regions is directed against CD3, which is located on a T cell, and the other Fab region is directed against the G protein-coupled receptor, GPRC5D, located on the surface of malignant plasma cells. Talquetamab-tgvs binding to CD3 on the T cell and the GPRC5D on the cancer cell causes the T cell to be adjacent to the myeloma cell. In addition, when CD3 is engaged, it facilitates the release of cytokines. Pharmacodynamic studies measured an increase of IL-6, IL-10, and IL-2R with step-up doses during talquetamab-tgvs treatment. Ultimately, the increase of cytokines will increase the inflammatory response of the immune system.

Special notes

Talquetamab-tgvs is approved under the accelerated approval program by the FDA. Continued approval is contingent upon the accuracy of reporting and verification of the clinical benefit, durability of response and rate of response.

This document is intended to assist providers in optimizing the management of talquetamab-tgvs in eligible patients.

DRUG DOSAGE AND ADMINISTRATION

Talquetamab-tgvs is a subcutaneous injection that comes in different dosage strengths. It is provided as an injection of either a single-dose vial of 3 mg/1.5 mL (2 mg/mL) or 40 mg/mL and administered as a subcutaneous injection under the skin in the abdomen, thigh, or another area, avoiding bruises, tattoos, or scars. Patients should be hospitalized for 48 hours after all doses of the step-up dosing regimen, due to the risk of cytokine release syndrome and/or neurologic toxicity. The schedule for dosing is either weekly or bi-weekly as indicated below.

Pretreatment medications

The first time talquetamab-tgvs is administered, it is given 1 to 3 hours after pretreatment medications in the step-up dosing schedule to reduce the risk for cytokine release syndrome. Subsequently, pre-medications are administered to any patient that previously experienced cytokine release syndrome with their previous doses. The pretreatment medications include a corticosteroid, usually oral or intravenous dexamethasone (16 mg), an antihistamine, usually diphenhydramine 50 mg, and an antipyretic, like oral or intravenous acetaminophen at 650 mg to 1,000 mg.

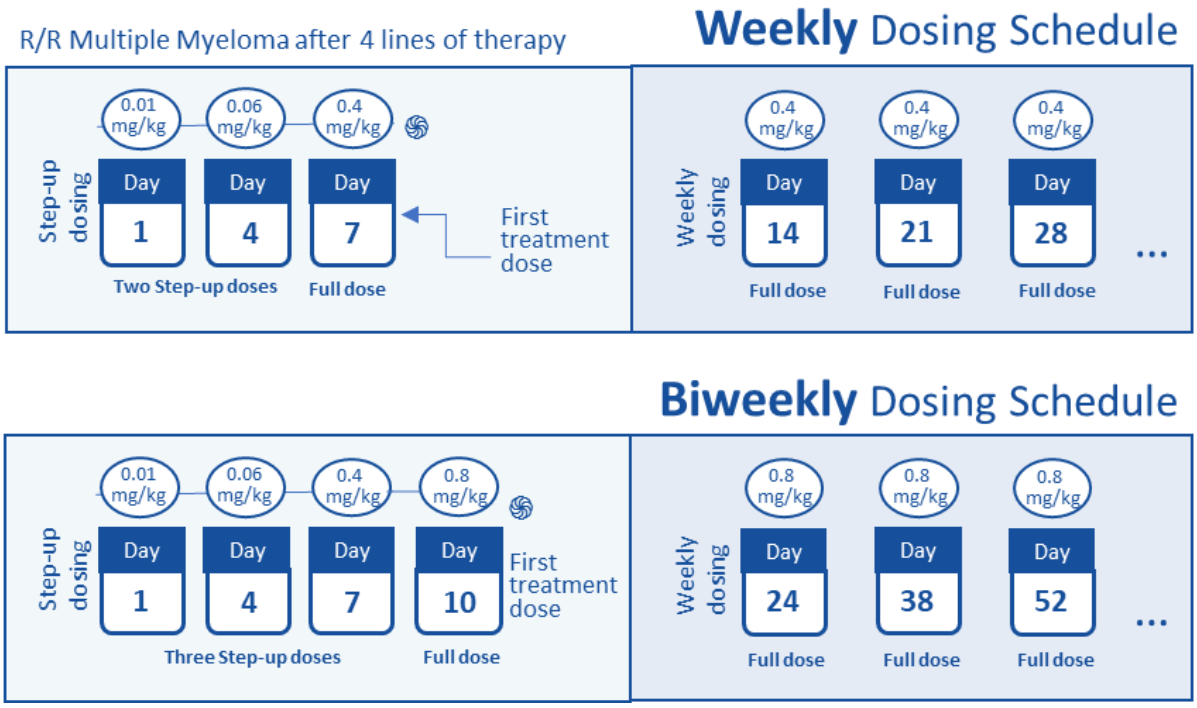
Dosing Schedules – Weekly and Bi-weekly:

Talquetamab-tgvs is given using a step-up dosing regimen that starts at 0.01 mg/kg, based on actual body weight. The second dose (0.06 mg/kg) can be given between 2-4 days after the first dose (0.01 mg/kg). In addition, the second dose can be administered up to 7 days following the first dose to allow for resolution of adverse reactions.

Depending on whether the patient will receive weekly or bi-weekly dosing, the next dose may be the final, for weekly, or the third step-up, for bi-weekly. For weekly, the full dose / treatment dose is 0.4 mg/kg once per week. A minimum of 6 days should occur between the weekly doses.

For bi-weekly dosing, the first treatment dose of 0.8 mg/kg occurs on day 10, but may be administered between 2 to 7 days after the third step of dose of 0.4 mg/kg. The final dose in the bi-weekly schedule is 0.8 mg/kg. This is given every two weeks, starting two weeks after the first treatment dose and every two weeks thereafter.

Step-up dosing illustration for talquetamab-tgvs:



Notes on the talquetamab-tgvs Risk Evaluation and Mitigation Strategy (REMS)

- In order to prescribe this medication, the prescriber has to be certified with the drug safety program, Risk Evaluation and Mitigation Strategy (REMS). This requires enrollment into the program, along with completing the training associated with REMS.
- Prescribers are required to counsel patients receiving talquetamab-tgvs about the black boxed warnings (e.g. cytokine release syndrome and neurologic toxicity) and provide patients with the Patient Wallet Card.
- Patients need to carry their Wallet Card with them at all times and show it to any health care provider they see.
- In addition, the pharmacy dispensing the medication must be certified, along with the health care center that administers it to the patient.

SIDE EFFECTS AND MANAGEMENT

The **most common adverse reactions** (≥20%) associated with talquetamab-tgvs include cytokine release syndrome, diarrhea, dry mouth, dysgeusia, dysphagia, fatigue, headache, hypotension, musculoskeletal pain, nail disorder, pyrexia, rash, skin disorder, upper respiratory tract infection, weight decreased, and xerosis.

Among the **adverse reactions possible** from talquetamab-tgvs, the most common (≥30%) Grade 3 or 4 lab abnormalities include hemoglobin decreased, lymphocyte count decreased, neutrophil count decreased, and white blood cell decreased.

Black Boxed Warnings

There are **2 warnings associated with talquetamab-tgvs**. Clinical trials have suggested that these are significant, yet short-term issues with talquetamab-tgvs that usually resolved within the first few weeks of treatment. These warnings consist of cytokine release syndrome (CRS) and neurologic toxicities, which includes the immune effector cell-associated neurotoxicity syndrome (ICANS). With the first signs of either boxed warnings, immediate clinical evaluation, management of side effects, withholding of or permanent discontinuation of the drug is warranted.

Warnings and Precautions

There are **6 warnings associated with talquetamab-tgvs**. These include cytopenia, embryo-fetal toxicity, hepatotoxicity, infections, oral toxicity with weight loss, and skin toxicity. These can be long-term adverse effects and have a negative impact on the quality of life.

Cytokine Release Syndrome

Cytokine Relsease Syndrome (CRS), including life-threatening or fatal reactions are possible after administration with talquetamab-tgvs. Data from the MonumenTAL-I trial suggested that 79.0% of the patients receiving 0.4 mg/kg talquetamab-tgvs experienced CRS along with 74.5% of the patients receiving 0.8 mg/kg. Most of these occurred following the step-up doses.

Clinical symptoms of CRS are chills, headache, hypotension, hypoxia, pyrexia, and tachycardia. Complications that can be life-threatening include acute respiratory distress syndrome, cardiac dysfunction, disseminated intravascular coagulation, neurologic toxicity, renal and/or hepatic failure. Patients need to be hospitalized for 48 hours after drug administration for all of the step-up doses to monitor for CRS.

Neurologic Toxicities

Neurologic toxicities, including immune-effector cell-associated neurotoxicity (ICANS), and serious and life-threatening or fatal reactions, are associated with administration of talquetamab-tgvs. Neurologic toxicity occurred in 55% of patients in the clinical trial who received talquetamab-tgvs, with 6% of those at Grade 3 or Grade 4. Most frequently, these toxicities manifested as encephalopathy (15%), headache (20%), motor dysfunction (10%), and sensory neuropathy (14%). ICANS was reported in 9% of patients who received talquetamab-tgvs.

Cytopenias

Neutropenia and thrombocytopenia are possible adverse reactions. During clinical trials, approximately 35% of patients experienced a Grade 3 or 4 decrease in neutrophils. The median time to onset for Grade 3 or 4 neutropenia was 22 days, but ranged between 1 to 312 days.

For platelets, approximately 22% of patients experienced a Grade 3 or 4 drop. The median time to onset for Grade 3 or 4 thrombocytopenia was 12 days, but ranged between 2 to 183 days.

Hepatotoxicity

During clinical trials, elevated ALT occurred in 33.0% of patients. Approximately 2.7% were Grade 3 or 4. Similarly, elevated AST occurred in 31.0% of patients. Approximately 3.3% were Grade 3 or 4 AST elevations. Patients experiencing liver toxicity may report abdominal discomfort, anorexia, fatigue, jaundice, or dark urine. Patients need to have their liver enzymes and bilirubin monitored at baseline and then against during treatment.

Infections

Life-threatening infections are associated with talquetamab-tgvs. In clinical trials, serious infections occurred in 16.0% of patients, with 1.5% experiencing a fatal infection. Grade 3 or 4 infections occurred in 17.0% of patients. The most common type of infection was bacterial and Covid-19. Prophylactic antimicrobials can be administered to patients following guidelines of the health center or clinical facility.

Oral Toxicity

In clinical trials, approximately 80.0% of patients experienced Grade 1 or 2 oral toxicities, with Grade 3 occurring in 2.1% of patients. These toxicities manifested as loss of taste or ageusia (18.0%), dry mouth (34.0%), metallic, bitter or other taste–dysgeusia (49.0%), and difficulty swallowing or dysphagia (23.0%). The median onset for oral toxicity was 15 days with a range between 1 to 634 days.

Although the receptor target for talquetamab-tgvs, GPRC5D, is expressed on the surface of multiple myeloma cells, it is also found on healthy tissues such as epithelial cells in the tongue. Therefore, talquetamab-tgvs can cause the release of proinflammatory cytokines in this area and the lysis of cells expressing GPRC5D. This coincides with the drug exposure as higher exposure increases the incidence of oral toxicity.

Skin Toxicity

Serious skin reactions, like erythema, erythematous rash, maculo-papular rash, or rash may occur. In clinical trials, 62% of patients experienced a skin toxicity, with <0.5% of those Grade 3 or above. The median time to onset was 25 days, with a range between 1 and 630 days.

The receptor target for talquetamab-tgvs, GPRC5D, is also found on the surface of some healthy tissues, such as epithelial cells in keratinized tissues of the skin. Therefore, talquetamab-tgvs can cause the release of proinflammatory cytokines in this area and the lysis of skin cells expressing GPRC5D. Higher drug exposure will increase the incidence of nail and skin toxicities. Preemptive treatment for skin toxicity may be warranted, depending on the clinician, patient, and health care setting.

Weight Loss

In the clinical trial, talquetamab-tgvs resulted in 62.0 % of patients experiencing weight loss, which was not associated with oral toxicity. Only 2.7% of these patients were Grade 3, which included a weight loss of 20% or more.

OTHER TAKEAWAYS ABOUT ADMINISTRATION

- Embryo-fetal toxicity is possible. No carcinogenicity or genotoxicity studies have been conducted. The mechanism of action suggests females of reproductive potential should use effective contraception during treatment and 3 months after the last dose.
- Pretreatment medication is necessary before administering talquetamab-tgvs.
- This drug is available only through the restricted Risk Evaluation and Mitigation Strategy (REMS). Dose delays may be necessary to manage toxicities.
- Educate patients and caregivers about side effects and the importance of reporting symptoms as soon as possible. In particular, counsel them to seek medical attention at the first sign of CRS.
- Talquetamab-tgvs is available only under a REMS program.

QUESTIONS & ANSWERS

Q. **How frequent are dose interruptions of talquetamab-tgvs due to an adverse reaction?**

A. In clinical trials, dosage interruptions due to an adverse reaction occurred in 56% of patients who were treated with talquetamab-tgvs. Many of these were due to a bacterial infection (7%), CRS (12%), COVID-19 (9%), neutropenia (6%), pyrexia (15%), rash (6%), and an upper respiratory tract infection (9%). The most common interruptions for Grade 3 or 4 laboratory abnormalities were a decrease in hemoglobin, lymphocyte count, neutrophil count, or white blood cell count.

Q. **What happens if a patient misses their next dose of talquetamab-tgvs?**

A. If the next dose of talquetamab-tgvs is missed or delayed for any reason, it may be necessary to repeat the "step-up" dosing schedule. This includes the pretreatment medications and the 48 hours post-injection monitoring of the patient for signs of CRS, neurologic problems, or other drug reactions described.

Q. **How do you modify doses in a patient experiences an adverse event?**

A. For patients who experience Grade 1 CRS, ICANS, infections (in the step-up phase), or neurologic toxicities, talquetamab-tgvs is withheld until the symptoms resolve. For Grade 2 CRS, the drug is withheld, pretreatments required and hospitalization before the next dose. For Grade 3 CRS, supportive therapy is also required, in addition to all of the previous actions. If the duration is greater than 48 hours, talquetamab-tgvs is permanently discontinued and supportive therapy may mean intensive care monitoring.

For patients who experience Grade 1 oral toxicity or weight loss, supportive care should be provided and a consideration of withholding talquetamab-tgvs if the patient is not responsive to the supportive care.

The management of ICANS is complicated and guidance is needed from experts at the treatment center.

Q. **What else should I tell my patients who will receive talquetamab-tgvs?**

A. The most impactful side effects are dysgeusia, xerostomia and loss of appetite. Some tips to help patients with taste changes and saliva production include:

- For saliva production and taste changes: biotene spray, hard candy, sour candy, sugarless gum, or lemon juice before eating meal. Other options include dexamethasone rinses, salt, and soda.
- Avoid spicy food, vinegar, pickled food.
- Eat small portions on a small plate.
- Suck on frozen fruit pops, ice chips, or sorbets.

Q. **What are possible signs and symptoms CRS in patients treated with talquetamab-tgvs?**

A. CRS or cytokine release syndrome is a serious and sometimes life-threatening occurrence. Patients should be hospitalized for 48 hours after the administration of talquetamab-tgvs to monitor for CRS and other adverse reactions. Patients might experience a fever of 100.4 F or higher, anxiety, chills, difficulty breathing, dizziness, a fast heartbeat, or a headache.

In addition, neurologic toxicity is also a black boxed warning. Symptoms of neurologic problems might include being less alert, confusion, disorientation, headache, low energy, memory loss, muscle weakness, numbness, pain (burning, stabbing or throbbing), seizures, shaking, sleepiness, slow thinking, tingling, trouble speaking or writing,

PATIENT RESOURCES

ADDITIONAL INFORMATION RESOURCES

American Cancer Society
Patient programs, services, 24/7 hotline, etc
https://www.cancer.org/

National Cancer Institute
Information about cancer types, treatment, side effects, find a clinical trial, etc
https://www.cancer.gov/

FINANCIAL ASSISTANCE

Cancer Financial Aid Coalition
Facilitates communication, educates and advocates for patients.
www.cancerfac.org

Centers for Medicare and Medicaid Services (CMS)
Apply to determine if you are eligible for government assistance.
www.cms.gov or www.medicare.gov
800-633-4227

Lazarex Foundation
Provides assistance with travel costs for clinical trial participation. Ask your social work counselor for a referral if you have been consented to a clinical trial for melanoma.
www.lazarex.org

Needymeds
Database to search for free or low-cost medications, help with medical transportation and other resources.
www.needymeds.org

Patient Advocate Foundation
Provides assistance with mediation, financial stability, and other assistance. Funds subject to availability. Patient must meet their eligibility for financial assistance.
www.patientadvocate.org
800-532-5274

The Sam Fund for Young Adult Survivors of Cancer
Assists cancer survivors ages 21-39 with their transition into post-treatment life. This program distributes grants and scholarships in an effort to enable survivors to pursue goals.
www.thesamfund.org
info@thesamfund.org

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PRESCRIPTION ASSISTANCE

CancerCare Co-Payment Assistance Foundation
Helps with the cost of medication. Availability of funds for patients with specific cancers is subject to availability.
www.cancercarecopay.org
1-866-552-6729

Medicine Assistance Tool
Database to search for patient assistance resources offered by pharmaceutical companies.
www.medicineassistancetool.org/

Patient Advocate Foundation Co-Pay Relief
Provides direct financial support to patients who medically qualify. Funds subject to availability.
https://copays.org
1-866-512-3861

Good Days
Provides assistance with insurance co-pays, and prescription medications. Funds subject to availability.
www.mygooddays.org

Health Well Foundation
For patients who cannot afford insurance premiums, co-payments, co-insurance, or other out-of-pocket health care costs. Funds for patients subject to availability. Patient must also meet eligibility for financial assistance.
www.healthwellfoundation.org or grants@healthwellfoundation.org
1-800-675-8416

The Assistance Fund, Inc
Provides prescription copay and financial assistance, including health insurance premiums. Funds subject to availability.
www.theassistancefund.org
https://tafcares.org
1-855-845-3663

PAN Foundation
Provides financial assistance to cover out-of-pocket treatment costs. Funds subject to availability.
www.panfoundation.org
1-866-316-PANF (7263)

Patient Assistance Program
Comprehensive database of patient assistance programs offering free medications.
www.rxassist.org
info@rxassist.org

HOUSING

American Cancer Society – Hope Lodge
Provides free housing during treatment appointments. Requires a referral from your social worker.
www.cancer.org/
1-800-227-6333.

American Cancer Society – Extended Stay America
Partnership to offer discounted rooms for patients who have to be away from home for cancer treatment.
https://www.cancer.org/about-us/our-partners/extended-stay-america.html
1-800-227-2345

Healthcare Hospitality Network
Connects patients and their caregivers looking for lodging near their healthcare provider
https://members.hhnetwork.org/locate-a-house
1-800-318-8861

Joe's House
Helping patients with cancer find lodging throughout the U.S.
https://www.joeshouse.org/lodging?state=0
1-877-563-7468

National Council of State Housing Agencies
Emergency rental assistance programs available by state. Federal grants still available in some areas.
https://www.ncsha.org/emergency-housing-assistance/

TRANSPORTATION (AIR AND GROUND)

Air Charity Network
Provides access for people in need who are seeking free air transportation to specialized health care facilities
http://aircharitynetwork.org/
1-877-621-7177

Corporate Angel Network
Nonprofit organization that helps cancer patients by arranging free travel on corporate aircraft
https://www.corpangelnetwork.org/
info@corpangelnetwork.org
1-914-328-1313

Medicaid
Ground transportation only. Sets up rides and provides mileage reimbursement for Medicaid patients only.
1-877-633-8747

Mercy Medical Angels
Provides free medical transportation (flights, gas cards, bus and train tickets) for patients with financial needs who need to travel more than 50 miles. Patients must meet their eligibility for financial assistance.
www.mercymedical.org/

Pilots for Patients
Provides free flights to people in need of medical treatment. Patient must be medically stable to fly and be ambulatory. Ask your social worker about a referral.
www.pilotsforpatients.org
318-322-5112

ADDITIONAL RESOURCES

Chari AC, Minnema MC, Berdeja JG et al. Talquetamab, a T-Cell–Redirecting GPRC5D Bispecific Antibody for Multiple Myeloma. *N Engl J Med.* 2022; 387:2232-2244. DOI: 10.1056/NEJMoa220459

Chari A, Touzeau C, Schinke C et al. Safety and activity of talquetamab in patients with relapsed or refractory multiple myeloma (MonumenTAL-1): a multicentre, open-label, phase 1–2 study. *Lancet Haematol.* 2025;12(4):E269-281.

Miller KC, Hamadeh I, Tan CR. Perspectives on Talquetamab and its Utility in the Treatment of Multiple Myeloma: Safety, Efficacy and Place in Therapy. *Cancer Manag Res*. 2025:17:743-756. doi: 10.2147/CMAR.S441550.

Schinke CD, Minnema MC, van de Donk NWCJ et al. Pivotal phase 2 MonumenTAL-1 results of talquetamab (tal), a GPRC5DxCD3 bispecific antibody (BsAb), for relapsed/refractory multiple myeloma (RRMM). *J Clinic Oncol.* 2023;41(16). https://doi.org/10.1200/JCO.2023.41.16_suppl.8036

TALVEY™ (talquetamab-tgvs) injection [prescribing information]. Horsham, PA 19044, USA: Janssen Biotech, Inc. Available at: https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/TALVEY-pi.pdf. Accessed April 18, 2025. Revised August 2023.