TALVEY®
(talquetamab-tgvs) Injection for subcutaneous use
2 mg/mL and 40 mg/mL

TALVEY® TREATMENT MANAGEMENT GUIDE

JUMP TO SECTION:

- Clinical results
- Dosing schedule and administration
- Safety and management

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TALVEY®. Initiate TALVEY® treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including immune effector cell-associated neurotoxicity

INDICATION AND USAGE

TALVEY® (talquetamab-tgvs) is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), and serious and life-threatening or fatal reactions, can occur with TALVEY®. Monitor patients for signs and symptoms of neurologic toxicity including ICANS during treatment and treat promptly. Withhold or permanently discontinue TALVEY® based on severity.

Because of the risk of CRS and neurologic toxicity, including ICANS, TALVEY® is available only through a restricted program called the TECVAYLI® and TALVEY® Risk Evaluation and Mitigation Strategy (REMS).

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CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS): TALVEY® can cause cytokine release syndrome, including life-threatening or fatal reactions. In the clinical trial, CRS occurred in 76% of patients who received TALVEY® at the recommended dosages, with Grade 1 CRS occurring in 57% of patients, Grade 2 in 17%, and Grade 3 in 1.5%. Recurrent CRS occurred in 30% of patients. Most events occurred following step-up dose 1 (29%) or step-up dose 2 (44%) at the recommended dosages. CRS occurred in 33% of patients with step-up dose 3 in the biweekly dosing schedule (N=153). CRS occurred in 30% of patients with the first 0.4 mg/kg treatment dose and in 12% of patients treated with the first 0.8 mg/kg treatment dose. The CRS rate for both dosing schedules combined was less than 3% for each of the remaining doses in Cycle 1 and less than 3% cumulatively from Cycle 2 onward. The median time to onset of CRS was 27 (range: 0.1 to 167) hours from the last dose, and the median duration was 17 (range: 0 to 622) hours. Clinical signs and symptoms of CRS include but are not limited to pyrexia, hypotension, chills, hypoxia, headache, and tachycardia. Potentially life-threatening complications of CRS may include cardiac dysfunction, acute respiratory distress syndrome, neurologic toxicity, renal and/or hepatic failure, and disseminated intravascular coagulation (DIC).

Initiate therapy with step-up dosing and administer pre-treatment medications (corticosteroids, antihistamine, and antipyretics) prior to each dose of TALVEY® in the step-up dosing schedule to reduce the risk of CRS. Monitor patients following administration accordingly. In patients who experience CRS, pre-treatment medications should be administered prior to the next TALVEY® dose.

Counsel patients to seek medical attention should signs or symptoms of CRS occur. At the first sign of CRS, immediately evaluate patient for hospitalization and institute treatment with supportive care based on severity, and consider further management per current practice guidelines. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

Neurologic Toxicity including ICANS: TALVEY® can cause serious, life-threatening neurologic toxicity or fatal neurologic toxicity, including ICANS.

In the clinical trial, neurologic toxicity, including ICANS, occurred in 55% of patients who received the recommended dosages, with Grade 3 or 4 neurologic toxicity occurring in 6% of patients. The most frequent neurologic toxicities were headache (20%), encephalopathy (15%), sensory neuropathy (14%), and motor dysfunction, including ataxia/cerebellar ataxia (10%). ICANS was reported in 9% of 265 patients where ICANS was collected and who received the recommended dosages. Recurrent ICANS occurred in 3% of patients. Most patients experienced ICANS following step-up dose 1 (3%), step-up dose 2 (3%), step-up dose 3 of the biweekly dosing schedule (1.8%), or the initial treatment dose of the weekly dosing schedule (2.6%) (N=156) or the biweekly dosing schedule (3.7%) (N=109). The median time to onset of ICANS was 2.5 (range: 1 to 16) days after the most recent dose with a median duration of 2 (range: 1 to 22) days. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. Clinical signs and symptoms of ICANS may include but are not limited to confusional state, depressed level of consciousness, disorientation, somnolence, lethargy, and bradyphrenia.

Monitor patients for signs and symptoms of neurologic toxicity during treatment and treat promptly. At the first sign of neurologic toxicity, including ICANS, immediately evaluate the patient and provide supportive care based on severity. Withhold or permanently discontinue TALVEY® based on severity and consider further management per current practice guidelines [see Dosage and Administration (2.5)].

Due to the potential for neurologic toxicity, patients receiving TALVEY® are at risk of depressed level of consciousness. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during the step-up dosing schedule and for 48 hours after completion of the step-up dosing schedule, and in the event of new onset of any neurological symptoms, until symptoms resolve.

TECVAYLI® and TALVEY® REMS: TALVEY® is available only through a restricted program under a REMS, called the TECVAYLI® and TALVEY® REMS because of the risks of CRS and neurologic toxicity, including ICANS.

Further information about the TECVAYLI® and TALVEY® REMS program is available at www.TEC-TALREMS.com or by telephone at 1-855-810-8064.

Oral Toxicity and Weight Loss: TALVEY® can cause oral toxicities, including dysgeusia, dry mouth, dysphagia, and stomatitis.

In the clinical trial, 80% of patients had oral toxicity, with Grade 3 occurring in 2.1% of patients who received the recommended dosages. The most frequent oral toxicities were dysgeusia (49%), dry mouth (34%), dysphagia (23%), and ageusia (18%). The median time to onset of oral toxicity was 15 (range: 1 to 634) days, and the median time to resolution to baseline was 43 (1 to 530) days. Oral toxicity did not resolve to baseline in 65% of patients.

TALVEY® can cause weight loss. In the clinical trial, 62% of patients experienced weight loss, regardless of having an oral toxicity, including 29% of patients with Grade 2 (10% or greater) weight loss and 2.7% of patients with Grade 3 (20% or greater) weight loss. The median time to onset of Grade 2 or higher weight loss was 67 (range: 6 to 407) days, and the median time to resolution was 50 (range: 1 to 403) days. Weight loss did not resolve in 57% of patients who reported weight loss.

Monitor patients for signs and symptoms of oral toxicity. Counsel patients to seek medical attention should signs or symptoms of oral toxicity occur and provide supportive care as per current clinical practice, including consultation with a nutritionist. Monitor weight regularly during therapy. Evaluate clinically significant weight loss further. Withhold TALVEY® or permanently discontinue based on severity.

Infections: TALVEY® can cause infections, including life-threatening or fatal infections.

In the clinical trial, serious infections occurred in 16% of patients, with fatal infections in 1.5% of patients. Grade 3 or 4 infections occurred in 17% of patients. The most common serious infections reported were bacterial infection (8%), which included sepsis, and COVID-19 (2.7%).

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Monitor patients for signs and symptoms of infection prior to and during treatment with TALVEY® and treat appropriately. Administer prophylactic antimicrobials according to local guidelines. Withhold or consider permanent discontinuation of TALVEY® as recommended based on severity.

Cytopenias: TALVEY® can cause cytopenias, including neutropenia and thrombocytopenia.

In the clinical trial, Grade 3 or 4 decreased neutrophils occurred in 35% of patients, and Grade 3 or 4 decreased platelets occurred in 22% of patients who received TALVEY®. The median time to onset for Grade 3 or 4 neutropenia was 22 (range: 1 to 312) days, and the median time to resolution to Grade 2 or lower was 8 (range: 1 to 79) days. The median time to onset for Grade 3 or 4 thrombocytopenia was 12 (range: 2 to 183) days, and the median time to resolution to Grade 2 or lower was 10 (range: 1 to 64) days. Monitor complete blood counts during treatment and withhold TALVEY® as recommended based on severity.

Skin Toxicity: TALVEY® can cause serious skin reactions, including rash, maculo-papular rash, erythema, and erythematous rash.

In the clinical trial, skin reactions occurred in 62% of patients, with Grade 3 skin reactions in 0.3%. The median time to onset was 25 (range: 1 to 630) days. The median time to improvement to Grade 1 or less was 33 days.

Monitor for skin toxicity, including rash progression. Consider early intervention and treatment to manage skin toxicity. Withhold TALVEY® as recommended based on severity.

Hepatotoxicity: TALVEY® can cause hepatotoxicity. Elevated ALT occurred in 33% of patients, with Grade 3 or 4 ALT elevation occurring in 2.7%; elevated AST occurred in 31% of patients, with Grade 3 or 4 AST elevation occurring in 3.3%. Grade 3 or 4 elevations of total bilirubin occurred in 0.3% of patients. Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TALVEY® or consider permanent discontinuation of TALVEY® based on severity [see Dosage and Administration (2.5)].

Embryo-Fetal Toxicity: Based on its mechanism of action, TALVEY® may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TALVEY® and for 3 months after the last dose.

Adverse Reactions: The most common adverse reactions (≥20%) are pyrexia, CRS, dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, weight decreased, dry mouth, xerosis, dysphagia, upper respiratory tract infection, diarrhea, hypotension, and headache.

The most common Grade 3 or 4 laboratory abnormalities (≥30%) are lymphocyte count decreased, neutrophil count decreased, white blood cell decreased, and hemoglobin decreased.

Please read full Prescribing Information, including Boxed WARNING, for TALVEY®.

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Glossary

AR, adverse reaction
ASTCT, American Society for Transplantation and Cellular Therapy
B, B-cell
BCMA, B-cell maturation antigen
c, Cycle
CAR-T, chimeric antigen receptor T-cell
CD, cluster of differentiation
CI, confidence interval
CNS, central nervous system
COVID, coronavirus disease
CR, complete response
CRS, cytokine release syndrome
CTCAE, Common Terminology Criteria for Adverse Events
d, Day
del(17p), deletion 17p
DIC, disseminated intravascular coagulation
DOR, duration of response
DP, disease progression
ECOG PS, Eastern Cooperative Oncology Group performance status
eCRF, electronic case report form
EMA, European Medicine Agency
EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30
EQ-5D-5L VAS, EuroQol 5-Dimension 5-Level Visual Analogue Scale
FDA, U.S. Food and Drug Administration
GPRC5D, G protein-coupled receptor class C group 5 member D
HRQOL, health-related quality of life
ICANS, immune effector cell-associated neurotoxicity syndrome
ICE, immune effector cell-associated encephalopathy
IgG, immunoglobulin G
IMWG, International Myeloma Working Group
IRC, Independent Review Committee
ISS, International Staging System
LTFU, long-term follow-up
mDOR, median duration of response
MedDRA, Medical Dictionary for Regulatory Activities
mFU, median follow-up
MM, multiple myeloma
MOA, mechanism of action
mRNA, messenger ribonucleic acid
mTTCR, median time to complete response or better
mTTR, median time to response
N/A, not applicable
NCI, National Cancer Institute
NE, not estimable
ORR, overall response rate
P, plasma cell
PFS, progression-free survival
PI, proteasome inhibitor

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del(17p), deletion 17p
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DP, disease progression
ECOG PS, Eastern Cooperative Oncology Group performance status
eCRF, electronic case report form
EMA, European Medicine Agency
EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30
EQ-5D-5L VAS, EuroQol 5-Dimension 5-Level Visual Analogue Scale
FDA, U.S. Food and Drug Administration
GPRC5D, G protein-coupled receptor class C group 5 member D
HRQOL, health-related quality of life
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mDOR, median duration of response
MedDRA, Medical Dictionary for Regulatory Activities
mFU, median follow-up
MM, multiple myeloma
MOA, mechanism of action
mRNA, messenger ribonucleic acid
mTTCR, median time to complete response or better
mTTR, median time to response
N/A, not applicable
NCI, National Cancer Institute
NE, not estimable
ORR, overall response rate
P, plasma cell
PFS, progression-free survival
PI, proteasome inhibitor
PR, partial response
PRO, patient-reported outcome
pts, patients
QW, once weekly
Q2W, every 2 weeks
REMS, Risk Evaluation and Mitigation Strategy
RRMM, relapsed or refractory multiple myeloma
SC, subcutaneous
sCR, stringent complete response
SE, standard error
SmPC, summary of product characteristics
SUD, step-up dose
t, translocation
TCR, T-cell redirection
TTR, time to response
VGPR, very good partial response

TALVEY® overview

TALVEY® is the first and only FDA-approved bispecific antibody developed to target GPRC5D[1,2]

- GPRC5D is expressed on the surface of multiple myeloma cells and nonmalignant plasma cells[1,3–7]
  - It is also expressed on healthy tissues such as epithelial cells in keratinized tissues of the skin and tongue
- GPRC5D expression is independent of other targets, including BCMA[8]

MonumenTAL-1 study design

The efficacy of TALVEY® as a single agent was evaluated in 219 patients with relapsed or refractory multiple myeloma in the single-arm, open label, multicenter, phase 1/2 MonumenTAL-1 trial.[1,9]

Patient characteristics[1]

- In patients naïve to T-cell redirection therapy*:
  - 22% had ISS stage III disease
  - 29% had high-risk cytogenetics†
  - 22% had extramedullary disease
  - 73% were triple-class refractory
- In patients exposed to T-cell redirection therapy*:
  - 81% had prior CAR-T therapy
  - 25% had prior bispecific antibody therapy

*T-cell redirection therapy refers to both CAR-T and bispecific antibody therapy.[1]
†Baseline cytogenetic data were not available in 11% of patients.[1]

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TALVEY®. Initiate TALVEY® treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including immune effector cell-associated neurotoxicity

INDICATION AND USAGE

TALVEY® (talquetamab-tgvs) is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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Clinical trial results

Primary data | Longer-term data | Patient-reported outcomes

In the MonumenTAL-1 primary analysis,

TALVEY® provided powerful efficacy[1]

Efficacy was based on ORR and DOR as assessed by an IRC using IMWG criteria.[1*]

Naïve to T-cell redirection therapy[†]: Q2W dosing[1]

ORR[‡]	**73.6%** (65/87) **(95% CI, 63.0%–82.4%)**
mTTR	**1.3 months** (range: 0.2–9.2 months)
mDOR	**NE**

Durable responses in patients exposed to T-cell redirection therapy[1†]

Exposed to T-cell redirection therapy: QW dosing[1†]

ORR[‡]	**72%** (23/32) **(95% CI, 53.0%–86.0%)**
≥9-month DOR	**59.0%**

*Efficacy results reflect patients who have received ≥4 prior lines of therapy.[1]
†T-cell redirection therapy refers to both CAR-T and bispecific antibody treatment.[1]
‡ORR: sCR+CR+VGPR+PR.

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Clinical trial results

Primary data | **Longer-term data** | Patient-reported outcomes

You are now viewing a subsequent follow-up analysis of the MonumenTAL-1 trial. This information is not included in the current full Prescribing Information. These longer-term follow-up data reflects the patients naïve and exposed to TCR therapy* receiving TALVEY® Q2W and QW; any increase in n-value is due to this longer-term follow-up and additional patients.

MonumenTAL-1 longer-term follow-up analysis at a median follow-up of >30 months in patients naïve to T-cell redirection therapy[10]*

ORR† and DOR were assessed by an IRC using IMWG criteria.[1]‡

LONGER-TERM DATA

Naïve to T-cell redirection therapy*: Q2W dosing[10]

ORR†	**71.1%** (64/90) **(95% CI, 60.6%–80.2%)**
mTTR	**1.3 months** (range: 0.2–3.6 months)
mTTCR	**5.8 months** (range: 1.2–13.1 months)
mDOR	**17.9 months** (95% CI, 12.5–26.0 months)

MonumenTAL-1 longer-term follow-up analysis at a median follow-up of >28 months in patients exposed to T-cell redirection therapy[10]*

ORR† and DOR were assessed by an IRC using IMWG criteria.[1]‡

LONGER-TERM DATA

Exposed to T-cell redirection therapy: QW dosing[10]*

72.4%

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Clinical trial results

Primary data | **Longer-term data** | Patient-reported outcomes

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ORR† and DOR were assessed by an IRC using IMWG criteria.[1]‡

LONGER-TERM DATA **Naïve to T-cell redirection therapy*:** Q2W dosing[10]

ORR†	**71.1%** (64/90) **(95% CI, 60.6%–80.2%)**
mTTR	**1.3 months** (range: 0.2–3.6 months)
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MonumenTAL-1 longer-term follow-up analysis at a median follow-up of >28 months in patients exposed to T-cell redirection therapy[10]*

ORR† and DOR were assessed by an IRC using IMWG criteria.[1]‡

LONGER-TERM DATA **Exposed to T-cell redirection therapy:** QW dosing[10]*

ORR†	**72.4%** (42/58) **(95% CI, 59.1%–83.3%)**
mTTR	**1.2 months** (range: 0.2–7.5 months)
mTTCR	**2.6 months** (range: 1.0–12.9 months)
mDOR	**19.2 months** (95% CI, 6.7–NE months)

*T-cell redirection therapy refers to both CAR-T and bispecific antibody treatment.[1]
†ORR: sCR+CR+VGPR+PR.
‡Efficacy results reflect patients who have received ≥4 prior lines of therapy.[1]

Clinical trial results

Primary data | Longer-term data | **Patient-reported outcomes**

You are now viewing patient-reported symptoms and health-related quality of life outcomes from the MonumenTAL-1 study. This information is not included in the current full Prescribing Information and has not been evaluated by the FDA. No conclusions should be drawn. The information should be understood in context of the methodology.

PROs from MonumenTAL-1[11]

Study design

- MonumenTAL-1 is a single-arm, nonblinded study and included patients who received ≥3 prior systemic therapies
- 154 TCR-naïve patients received TALVEY® Q2W, and 118 patients had available PRO data, with a median follow-up of 23.4 months
- PROs were assessed at screening (referred to as "baseline" and assessed prior to step-up doses), Day 1 of Cycle 1 (first full dose), and Day 1 of every other cycle
- Patients in the TCR-naïve QW cohort and TCR-exposed cohort were not included in the PRO analysis
- For the phase 2 part of the study, change from baseline in patient-reported symptoms, functioning, and HRQOL was a secondary endpoint
- EORTC QLQ-C30 is a cancer-specific questionnaire with a 1-week recall period that includes several single items (fatigue, pain, dyspnea, sleep disturbance, appetite loss, constipation, diarrhea, and nausea and vomiting)

Analysis

- The PRO assessments used descriptive statistics: number and percentage were used to report categorical variables, with means, medians, and ranges used to report continuous variables. There was no imputation of missing data. No *P* values were presented and no adjustments for multiplicity were made
- Compliance rates for completion of PROs were quantified as the number of assessments received divided by the number of assessments expected (number of patients on treatment) at each time point. Compliance for completion was >95% of patients at baseline and >80% at most posttreatment visits
- Changes relative to baseline in the EORTC QLQ-C30 scales and EQ-5D-5L VAS were fitted to a mixed-effects repeated-measures model. This included patient as a random effect. Baseline PRO value and time were fixed effects. Results are presented as least-squares means with 95% CIs

Overall limitations

- The number of patients remaining on treatment declined over time, with no imputation performed. Therefore, sample sizes for later cycles were small, which limits the strength of the conclusions that can be drawn. A decline in the number of patients was noted from

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Neurologic toxicity, including immune effector cell-associated neurotoxicity

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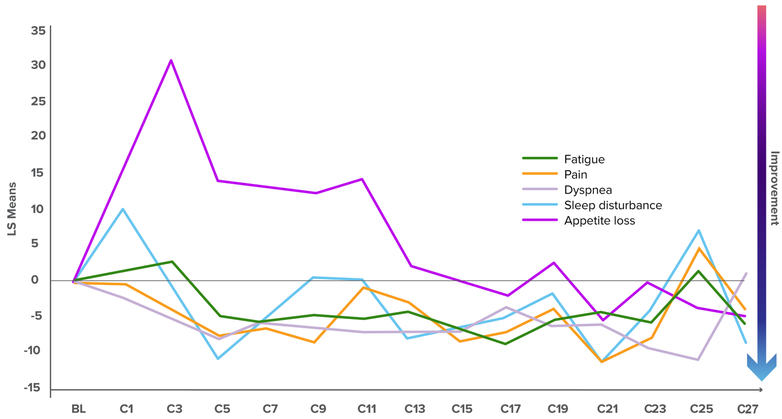
Overall limitations

- The number of patients remaining on treatment declined over time, with no imputation performed. Therefore, sample sizes for later cycles were small, which limits the strength of the conclusions that can be drawn. A decline in the number of patients was noted from baseline to Cycle 3; however, compliance rates for PRO assessments remained consistent throughout this period and thereafter
- There is a potential for responder bias. Given that MonumenTAL-1 is a phase 1/2 study and TALVEY® is relatively early in its development cycle, the PRO assessment tools used in the study assessed overall HRQOL and general cancer-related symptoms and impacts; therefore, GPRC5D-related AEs were not captured
- Finally, MonumenTAL-1 is a single-arm, nonblinded study; there was no comparator

Changes in patient-reported symptoms over time



	BL	C1	C3	C5	C7	C9	C11	C13	C15	C17	C19	C21	C23	C25	C27
Fatigue	104	94	78	70	63	62	47	39	36	35	29	34	21	12	8
Pain	104	95	78	70	63	62	47	36	36	33	28	33	20	12	8
Dyspnea	105	95	79	69	64	62	48	39	35	35	28	34	21	12	8
Sleep disturbance	103	93	77	68	61	61	46	36	36	32	28	33	19	12	7
Appetite loss	102	93	76	66	60	60	46	35	35	33	28	32	19	12	8

PRO assessments included EORTC QLQ-C30. Changes from baseline in EORTC QLQ-C30 symptom scores, adjusted for variability using least-squares means, are reported.

Dosing schedule and administration

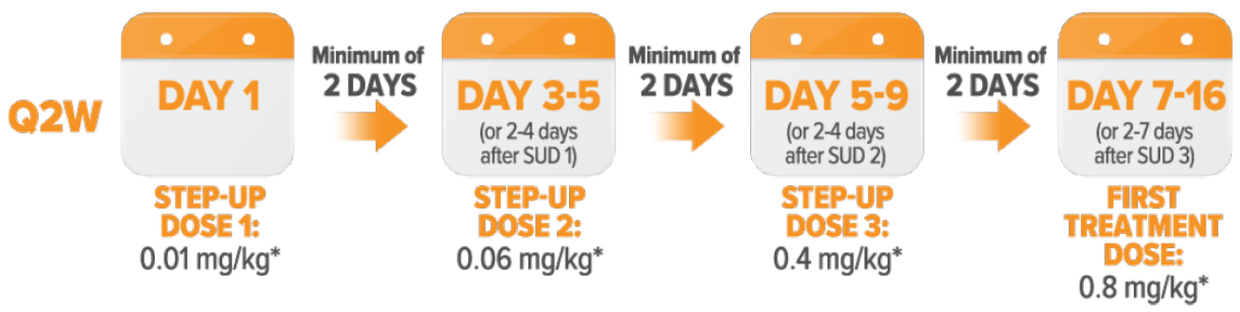
Dosing schedule | Pretreatment medication | Administration

Q2W and QW dosing available starting after first treatment dose[1]

Healthcare professionals should determine the appropriate level of monitoring and support for patients when receiving the step-up dosing of TALVEY® based upon their clinical and medical experience, judgment and operational considerations. TALVEY® should only be administered by a qualified healthcare professional with appropriate medical support to manage severe ARs such as CRS and ICANS.

- The 2 mg/mL (3 mg/1.5 mL) vial should be used for the 0.01 mg/kg and 0.06 mg/kg doses
- The 40 mg/mL vial should be used for the 0.4 mg/kg and 0.8 mg/kg doses
- For the step-up dosing schedule, you will need both vial sizes

TALVEY® is administered via subcutaneous injection by a healthcare provider Q2W following the step-up dosing schedule[1]



Step-up doses may be administered between 2 to 4 days after the previous dose and may be given up to 7 days after the previous dose to allow for resolution of ARs. The full step-up dosing schedule can be completed in 7 days for Q2W.

Following step-up dosing, ongoing biweekly dosing begins. Maintain a minimum of 12 days between Q2W doses.

TALVEY® is given until disease progression or unacceptable toxicity.

Restarting after dose delay +

TALVEY® is administered via subcutaneous injection by a healthcare provider QW following the step-up dosing schedule[1]

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Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TALVEY®. Initiate TALVEY® treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including immune effector cell-associated neurotoxicity

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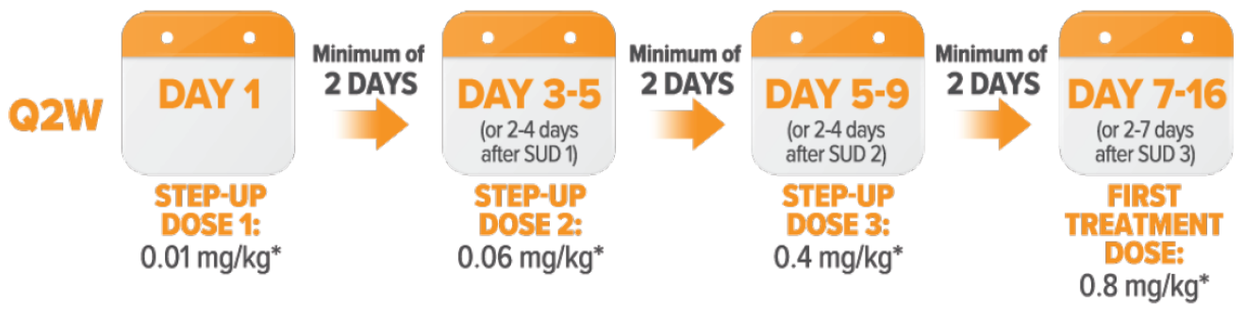


Step-up doses may be administered between 2 to 4 days after the previous dose and may be given up to 7 days after the previous dose to allow for resolution of ARs. The full step-up dosing schedule can be completed in 7 days for Q2W.

Q2W: 0.8 mg/kg*

Following step-up dosing, ongoing biweekly dosing begins. Maintain a minimum of 12 days between Q2W doses.

TALVEY® is given until disease progression or unacceptable toxicity.

Restarting after dose delay +

TALVEY® is administered via subcutaneous injection by a healthcare provider QW following the step-up dosing schedule[1]

Step-up doses may be administered between 2 to 4 days after the previous dose and may be given up to 7 days after the previous dose to allow for resolution of ARs. The full step-up dosing schedule can be completed in 5 days for QW.

QW: 0.4 mg/kg*

Following step-up dosing, ongoing weekly dosing begins. Maintain a minimum of 6 days between QW doses.

TALVEY® is given until disease progression or unacceptable toxicity.

Restarting after dose delay +

*Based on actual body weight.

Dosing schedule and administration

Dosing schedule | Pretreatment medication | Administration

Q2W and QW dosing available starting after first treatment dose[1]

Recommendations for restarting therapy with TALVEY® after dose delays[1]

Dose delays may be required to manage toxicities

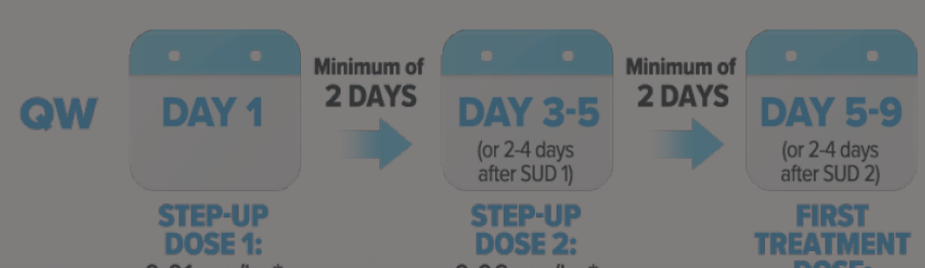
Administer pretreatment medications prior to restarting TALVEY® and monitor patients following administration.

If a dose of TALVEY® is delayed, restart therapy based on the recommendations in Table 3 and Table 4 in the full Prescribing Information.

Dosing schedule	Last dose administered	Time from last dose administered	TALVEY® recommendation*
Q2W dosing schedule	0.01 mg/kg	More than 7 days	Restart at **0.01 mg/kg**
	0.06 mg/kg	8 to 28 days	Repeat at **0.06 mg/kg**
		More than 28 days	Restart at **0.01 mg/kg**
	0.4 mg/kg	8 to 28 days	Repeat at **0.4 mg/kg**
		29 to 56 days	Restart at **0.06 mg/kg**
		More than 56 days	Consider permanent discontinuation. If restarting TALVEY®, begin at **0.01 mg/kg**
	0.8 mg/kg	15 to 28 days	Continue at **0.8 mg/kg**
		29 to 56 days	Restart at **0.4 mg/kg**
		More than 56 days	Consider permanent discontinuation. If restarting TALVEY®, begin at **0.01 mg/kg**

Restarting after dose delay +

TALVEY® is administered via subcutaneous injection by a healthcare provider QW following the step-up dosing schedule[1]



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Dosing schedule and administration

Dosing schedule | Pretreatment medication | Administration

Q2W and QW dosing available starting after first treatment dose[1]

Healthcare professionals should determine the appropriate level of monitoring and support for patients when receiving the step-up dosing of TALVEY® based upon their clinical and

Recommendations for restarting therapy with TALVEY® after dose delays[1]

Dose delays may be required to manage toxicities

Administer pretreatment medications prior to restarting TALVEY® and monitor patients following administration.

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Dosing schedule	Last dose administered	Time from last dose administered	TALVEY® recommendation*
QW dosing schedule	0.01 mg/kg	More than 7 days	Restart at **0.01 mg/kg**
	0.06 mg/kg	8 to 28 days	Repeat at **0.06 mg/kg**
		More than 28 days	Restart at **0.01 mg/kg**
	0.4 mg/kg	8 to 28 days	Continue at **0.4 mg/kg**
		29 to 56 days	Restart at **0.06 mg/kg**
		More than 56 days	Consider permanent discontinuation. If restarting TALVEY®, begin at **0.01 mg/kg**

Q2W: 0.8 mg/kg*

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Restarting after dose delay +

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Dosing schedule and administration

Dosing schedule | **Pretreatment medication** | Administration

Pretreatment medications[1]

1 to 3 hours before each step-up dose

Administer the following pretreatment medications before each dose in the step-up dosing schedule to reduce the risk of CRS:

- Corticosteroid (oral or intravenous dexamethasone 16 mg or equivalent)
- Antihistamine (oral or intravenous diphenhydramine 50 mg or equivalent)
- Antipyretics (oral or intravenous acetaminophen 650 mg to 1000 mg or equivalent)

Subsequent doses

Administration of pretreatment medications may be required for subsequent doses for patients who repeat doses within the step-up phase due to dose delays or for patients who experienced CRS.

Important dosing information[1]

Administer pretreatment medications prior to each dose of TALVEY® in the step-up dosing schedule as recommended [see *Dosage and Administration (2.2, 2.3) in the full Prescribing Information*].

TALVEY® should only be administered by a qualified healthcare professional with appropriate medical support to manage severe reactions such as CRS and neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS) [see *Warnings and Precautions (5.1, 5.2) in the full Prescribing Information*].

Due to the risk of CRS and neurologic toxicity, including ICANS, patients should be hospitalized for 48 hours after administration of all doses within the TALVEY® step-up dosing schedule [see *Dosage and Administration (2.5) and Warnings and Precautions (5.1, 5.2) in the full Prescribing Information*].

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Neurologic toxicity, including immune effector cell-associated neurotoxicity

INDICATION AND USAGE

TALVEY® (talquetamab-tgvs) is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Dosing schedule and administration

Dosing schedule | Pretreatment medication | **Administration**

Preparation and administration[1]

TALVEY® should be administered by a healthcare provider with adequate medical equipment and personnel to manage severe reactions such as CRS and neurologic toxicity, including ICANS.

Due to the risk of CRS and neurologic toxicity, including ICANS, patients should be hospitalized for 48 hours after administration of all doses within the TALVEY® step-up dosing schedule.

Key things to consider:

- TALVEY® is supplied as a ready-to-use solution for injection
- TALVEY® does not need dilution prior to administration
- Do not combine TALVEY® vials of different concentrations (eg, the 2 mg/mL vial and the 40 mg/mL vial) to achieve treatment dose
- Total dose, injection volume, and number of vials are based on the patient's actual body weight
- Use aseptic technique to prepare and administer TALVEY®

Dosage calculations +

Administration steps[1]

Before administration | During administration | Storage

- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit
- Check that the TALVEY® solution for injection is colorless to light yellow. Do not use if the solution is discolored, cloudy, or if foreign particles are present
- Remove the appropriate strength TALVEY® vial(s) from refrigerated storage (36°F to 46°F) and bring to room temperature (59°F to 86°F) for at least 15 minutes. Do not warm TALVEY® in any other way
- Once the vial is equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake
- Withdraw the required injection volume of TALVEY® from the vial(s) into an appropriately sized syringe using a transfer needle
  - Each injection volume should not exceed 2.0 mL. Divide doses requiring greater than 2.0 mL equally into multiple syringes

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TALVEY®. Initiate TALVEY® treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including immune effector cell-associated neurotoxicity

INDICATION AND USAGE

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- Once the vial is equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake
- Withdraw the required injection volume of TALVEY® from the vial(s) into an appropriately sized syringe using a transfer needle
  - Each injection volume should not exceed 2.0 mL. Divide doses requiring greater than 2.0 mL equally into multiple syringes
- TALVEY® is compatible with stainless steel injection needles and polypropylene or polycarbonate syringe material
- Replace the transfer needle with an appropriately sized needle for injection

Dosing schedule and administration

Dosing schedule | Pretreatment medication | **Administration**

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- Use aseptic technique to prepare and administer TALVEY®

Dosage calculations +

Administration steps[1]

Before administration | **During administration** | Storage

- Inject the required volume of TALVEY® into the subcutaneous tissue of the abdomen (preferred injection site)
  - TALVEY® may also be injected into the subcutaneous tissue of other sites (eg, thigh)
  - If multiple injections are required, TALVEY® injections should be at least 2 cm apart
- Do not inject into tattoos, scars, or areas where the skin is red, bruised, tender, hard or not intact
- Any unused medicinal product or waste material should be disposed of in accordance with local requirements

Dosing schedule and administration

Dosing schedule | Pretreatment medication | **Administration**

Preparation and administration[1]

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Dosage calculations +

Administration steps[1]

Before administration | During administration | **Storage**

- Prepared syringes should be administered immediately. If this is not possible, store the TALVEY® solution for up to 24 hours in a refrigerator at 36°F to 46°F, followed by up to 24 hours at room temperature of 59°F to 86°F
- Discard if stored for more than 24 hours in a refrigerator or for more than 24 hours at room temperature. If stored in the refrigerator, allow the solution to come to room temperature before administration

Dosing schedule and administration

Dosing schedule | Pretreatment medication | Administration

Preparation of TALVEY®[1]

Use the following tables to determine total dose, injection volume, and number of vials required based on patient's actual bodyweight.

0.01 mg/kg dose | 0.06 mg/kg dose | 0.4 mg/kg dose | 0.8 mg/kg dose

0.01 mg/kg dose: Injection volumes using TALVEY® 2 mg/mL vial

Body weight (kg)	Total dose (mg)	Volume of injection (mL)	Number of vials (1 vial = 1.5 mL)
35 to 39	0.38	0.19	1
40 to 45	0.42	0.21	1
46 to 55	0.5	0.25	1
56 to 65	0.6	0.3	1
66 to 75	0.7	0.35	1
76 to 85	0.8	0.4	1
86 to 95	0.9	0.45	1
96 to 105	1.0	0.5	1
106 to 115	1.1	0.55	1
116 to 125	1.2	0.6	1
126 to 135	1.3	0.65	1
136 to 145	1.4	0.7	1
146 to 155	1.5	0.75	1
156 to 160	1.6	0.8	1

to 46°F) and bring to room temperature (59°F to 86°F) for at least 15 minutes. Do not warm TALVEY® in any other way

- Once the vial is equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake
- Withdraw the required injection volume of TALVEY® from the vial(s) into an appropriately sized syringe using a transfer needle
  - Each injection volume should not exceed 2.0 mL. Divide doses requiring greater than 2.0 mL equally into multiple syringes

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Neurologic toxicity, including immune effector cell-associated neurotoxicity

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Dosing schedule and administration

Dosing schedule | Pretreatment medication | Administration

Preparation of TALVEY®[1]

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0.06 mg/kg dose: Injection volumes using TALVEY® 2 mg/mL vial

Body weight (kg)	Total dose (mg)	Volume of injection (mL)	Number of vials (1 vial = 1.5 mL)
35 to 39	2.2	1.1	1
40 to 45	2.6	1.3	1
46 to 55	3.0	1.5	1
56 to 65	3.6	1.8	2
66 to 75	4.2	2.1	2
76 to 85	4.8	2.4	2
86 to 95	5.4	2.7	2
96 to 105	6.0	3.0	2
106 to 115	6.6	3.3	3
116 to 125	7.2	3.6	3
126 to 135	7.8	3.9	3
136 to 145	8.4	4.2	3
146 to 155	9.0	4.5	3
156 to 160	9.6	4.8	4

to 46°F) and bring to room temperature (59°F to 86°F) for at least 15 minutes. Do not warm TALVEY® in any other way

- Once the vial is equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake
- Withdraw the required injection volume of TALVEY® from the vial(s) into an appropriately sized syringe using a transfer needle
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Dosing schedule and administration

Dosing schedule | Pretreatment medication | Administration

Preparation of TALVEY®[1]

Use the following tables to determine total dose, injection volume, and number of vials required based on patient's actual bodyweight.

0.01 mg/kg dose | 0.06 mg/kg dose | 0.4 mg/kg dose | 0.8 mg/kg dose

0.4 mg/kg dose: Injection volumes using TALVEY® 40 mg/mL vial

Body weight (kg)	Total dose (mg)	Volume of injection (mL)	Number of vials (1 vial = 1.0 mL)
35 to 39	14.8	0.37	1
40 to 45	16	0.4	1
46 to 55	20	0.5	1
56 to 65	24	0.6	1
66 to 75	28	0.7	1
76 to 85	32	0.8	1
86 to 95	36	0.9	1
96 to 105	40	1.0	1
106 to 115	44	1.1	2
116 to 125	48	1.2	2
126 to 135	52	1.3	2
136 to 145	56	1.4	2
146 to 155	60	1.5	2
156 to 160	64	1.6	2

to 46°F) and bring to room temperature (59°F to 86°F) for at least 15 minutes. Do not warm TALVEY® in any other way

- Once the vial is equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake
- Withdraw the required injection volume of TALVEY® from the vial(s) into an appropriately sized syringe using a transfer needle
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Dosing schedule and administration

Dosing schedule | Pretreatment medication | **Administration**

Preparation of TALVEY®[1]

Use the following tables to determine total dose, injection volume, and number of vials required based on patient's actual bodyweight.

0.01 mg/kg dose | 0.06 mg/kg dose | 0.4 mg/kg dose | **0.8 mg/kg dose**

0.8 mg/kg dose: Injection volumes using TALVEY® 40 mg/mL vial

Body weight (kg)	Total dose (mg)	Volume of injection (mL)	Number of vials (1 vial = 1.0 mL)
35 to 39	29.6	0.74	1
40 to 45	34	0.85	1
46 to 55	40	1.0	1
56 to 65	48	1.2	2
66 to 75	56	1.4	2
76 to 85	64	1.6	2
86 to 95	72	1.8	2
96 to 105	80	2.0	2
106 to 115	88	2.2	3
116 to 125	96	2.4	3
126 to 135	104	2.6	3
136 to 145	112	2.8	3
146 to 155	120	3.0	3
156 to 160	128	3.2	4

to 46°F) and bring to room temperature (59°F to 86°F) for at least 15 minutes. Do not warm TALVEY® in any other way

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TALVEY® (talquetamab-tgvs) Injection for subcutaneous use
2 mg/mL and 40 mg/mL

Safety

The 3 Es:

Expectations, Education, and Evaluation

To ensure patients understand the signs and symptoms of an AR related to TALVEY®, it may be helpful to structure conversations using the **"3 Es:"**

EXPECTATIONS | **EDUCATION** | **EVALUATION**

- Set clear **EXPECTATIONS** on what ARs are associated with TALVEY® and when patients can expect them
- Provide patients and care partners with **EDUCATION** on how to recognize, communicate with their HCPs, and manage ARs
- **EVALUATE** patients' ARs for the potential need of supportive measures and/or withhold or discontinue treatment

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Safety

Incidence and management of ARs: CRS[1]

Understanding CRS and its presentation[1,12]

CRS, including life-threatening or fatal reactions, can occur in patients receiving TALVEY®. CRS is caused by a large, rapid release of cytokines into the blood from immune cells affected by the immunotherapy. Cytokines are immune substances that have different actions in the body.

Signs and symptoms of CRS may include[1]:

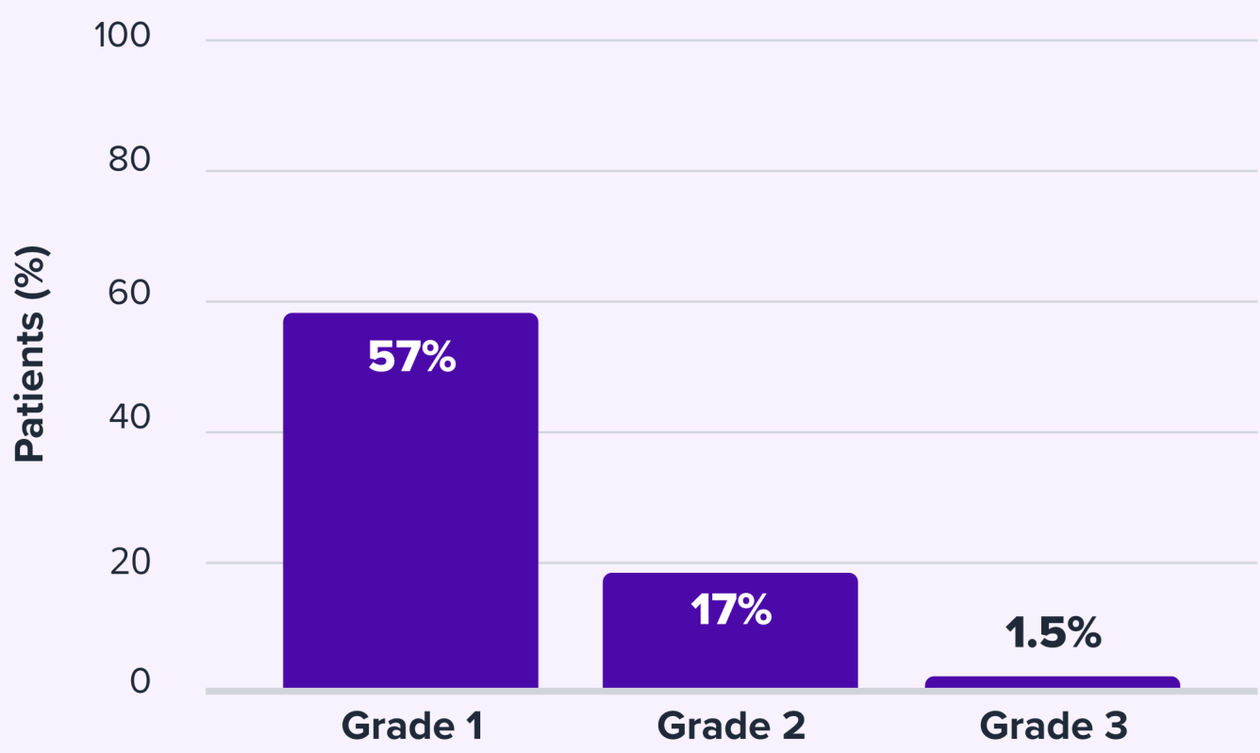
- fever (100.4°F or higher)
- difficulty breathing
- dizziness or lightheadedness
- headache
- chills
- fast heartbeat

In the clinical trial, CRS occurred in 76% of patients (N=339) who received TALVEY® at the recommended dosage.

Median time to onset: 27 hours (range: 0.1 to 167) from the last dose

Median duration: 17 hours (range: 0 to 622)

Incidence of CRS[1]



Managing CRS +

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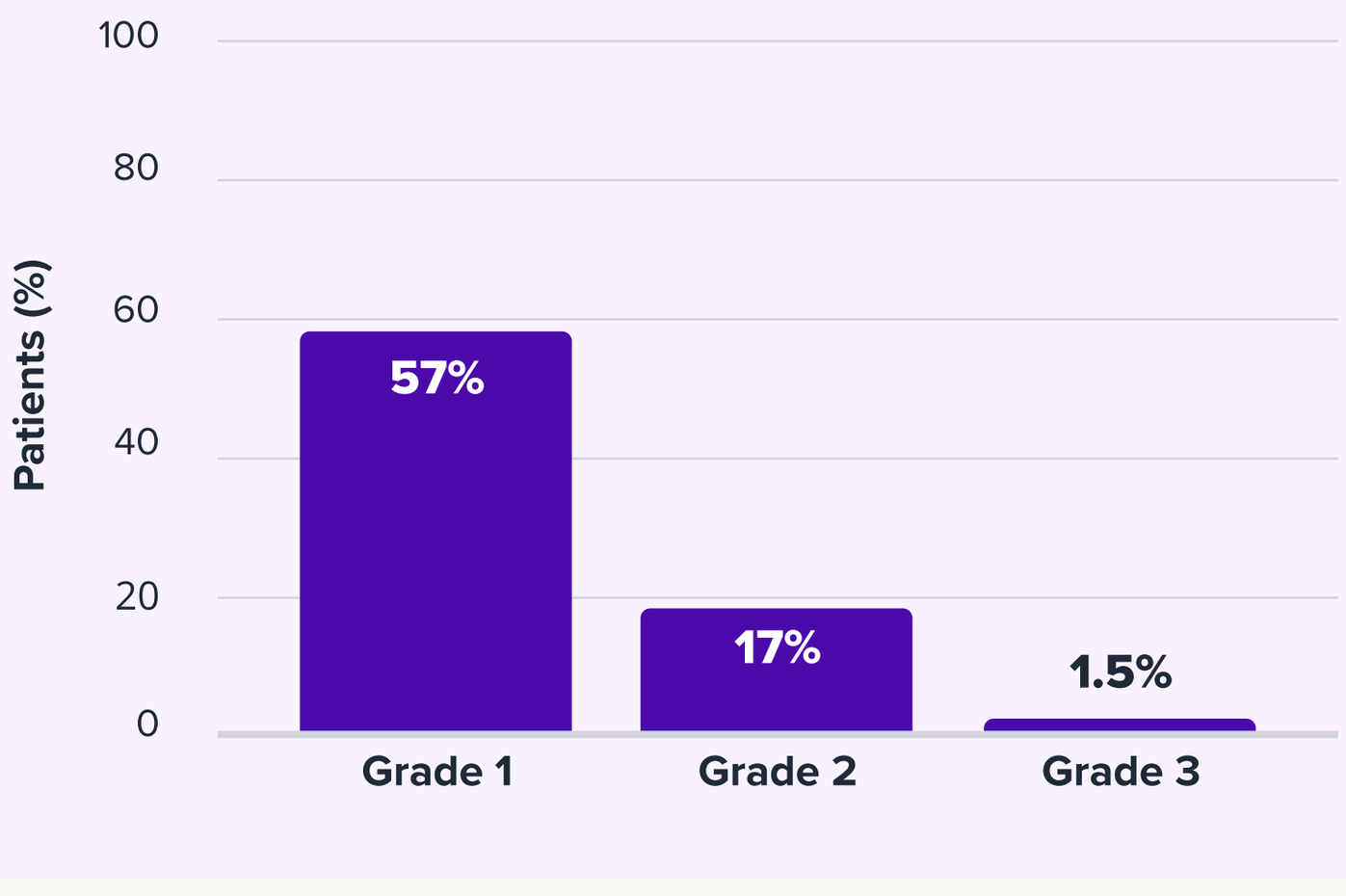
Incidence of CRS | CRS after each dose

Incidence of CRS[1]



Managing CRS +

Safety

Incidence and management of ARs: CRS[1]

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Median duration: 17 hours (range: 0 to 622)

Incidence of CRS | **CRS after each dose**

CRS experienced after each dose of TALVEY (N=339)[1]

Q2W	QW
Step-up dosing schedule	
Step-up dose 1 **29%**	
Step-up dose 2 **44%**	
Step-up dose 3 (n=153) **33%**	First treatment dose **30%**
First treatment dose **12%**	N/A
Dosing after step-up schedule	
Each remaining dose in Cycle 1 **<3%**	
Cumulatively from Cycle 2 onwards **<3%**	

Managing CRS +

Incidence and management of ARs: CRS[1]

Managing CRS[1]

If CRS is suspected, withhold TALVEY® until CRS resolves or permanently discontinue based on severity, and manage according to the recommendations in the table below.

- Identify CRS based on clinical presentation
- Evaluate and treat other causes of fever, hypoxia, and hypotension
- Administer supportive care, which may include intensive care for severe or life-threatening CRS
- Consider laboratory testing to monitor for DIC and hematology parameters, as well as pulmonary, cardiac, renal, and hepatic function

Recommendations for management of CRS

CRS Grade*	Presenting symptoms	Actions
Grade 1	Temperature ≥100.4°F (38°C)†	• Withhold TALVEY® until CRS resolves‡ • Administer pretreatment medication prior to next dose
Grade 2	Temperature ≥100.4°F (38°C)† with either: • Hypotension responsive to fluids and not requiring vasopressors, or • Oxygen requirement of low-flow nasal cannula§ or blow-by	• Withhold TALVEY® until CRS resolves • Administer pretreatment medications prior to next dose • Patients should be hospitalized for 48 hours following the next dose‡
Grade 3	Temperature ≥100.4°F (38°C)† with either: • Hypotension requiring 1 vasopressor, with or without vasopressin, or • Oxygen requirement of high-flow nasal cannula,§ facemask, nonrebreather mask, or Venturi mask	<u>Duration less than 48 hours</u> • Withhold TALVEY® until CRS resolves • Provide supportive therapy, which may include intensive care • Administer pretreatment medications prior to the next dose • Patients should be hospitalized for 48 hours following the next dose‡ <u>Recurrent or duration greater than or equal to 48 hours</u> • Permanently discontinue TALVEY® • Provide supportive therapy, which may include intensive care
Grade 4	Temperature ≥100.4°F (38°C)† with either: • Hypotension requiring multiple vasopressors (excluding vasopressin) • Or, oxygen requirement of positive pressure (eg, continuous positive airway pressure [CPAP], bilevel positive airway pressure [BIPAP], intubation, and mechanical ventilation)	• Permanently discontinue TALVEY® • Provide supportive therapy, which may include intensive care.

*Based on ASTCT grading for CRS (Lee et al. 2019).
†Attributed to CRS. Fever may not always be present concurrently with hypotension or hypoxia as it may be masked by interventions such as antipyretics or anticytokine therapy (eg, corticosteroids).
‡See Table 3 and Table 4 in the full Prescribing Information for recommendations on restarting TALVEY® after dose delays for ARs.
§Low-flow nasal cannula is ≤6 L/min, and high-flow nasal cannula is >6 L/min.

Managing CRS +

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Safety

Introduction | CRS | Neurotoxicity | ARs | Infections

Incidence and management of ARs: CRS[1]

Understanding CRS and its presentation[1,12]

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- chills
- fast heartbeat

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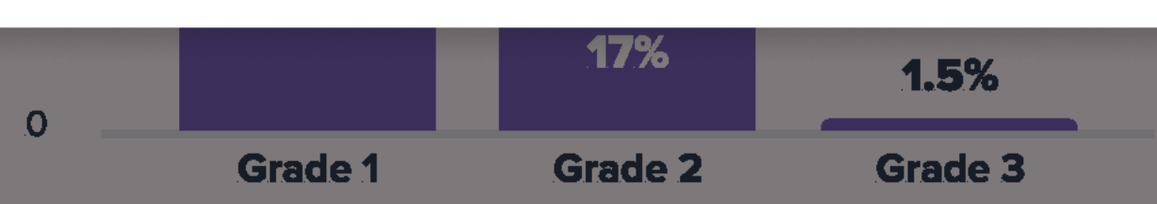
Median time to onset: 27 hours (range: 0.1 to 167) from the last dose

Median duration: 17 hours (range: 0 to 622)

Patient counseling information for CRS[1]

- Speak with your patients about the signs and symptoms associated with CRS. These include:
  - fever (100.4°F or higher)
  - difficulty breathing
  - feeling anxious
  - low blood pressure
  - headache
  - chills
  - fast heartbeat
- Encourage your patients to seek medical attention if they experience any signs or symptoms of CRS
- Advise patients that they should be hospitalized for 48 hours after administration of all doses within the TALVEY® step-up dosing schedule



Managing CRS +

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TALVEY®. Initiate TALVEY® treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including immune effector cell-associated neurotoxicity

INDICATION AND USAGE

TALVEY® (talquetamab-tgvs) is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Safety

Incidence and management of ARs: Neurologic toxicity, including ICANS[1]

Understanding neurologic toxicity, including ICANS, and its presentation

Neurologic toxicity, including ICANS, and serious and life-threatening or fatal reactions, can occur with TALVEY®.

Clinical signs and symptoms of ICANS may include but are not limited to:

- confusional state
- depressed level of consciousness
- disorientation
- somnolence
- lethargy
- bradyphrenia

Neurologic toxicity, including ICANS, occurred in 55% of patients at the recommended dosages.

ICANS was reported in 9% of 265 patients where ICANS data were collected and who received TALVEY® at the recommended dosages.

The most frequent neurologic toxicities were headache (20%), encephalopathy (15%), sensory neuropathy (14%), and motor dysfunction, including ataxia/cerebellar ataxia (10%).

Median time to onset: 2.5 days (range: 1 to 16) from the last dose

Median duration: 2 days (range: 1 to 22)

ICANS can occur concurrently with CRS, following resolution of CRS, or in the absence of CRS.

ICANS experienced after each dose of TALVEY® (N=265)	
Q2W	**QW**
Step-up dosing schedule	
Step-up dose 1 **3%**	
Step-up dose 2 **3%**	
Step-up dose 3	First treatment dose (n=156)

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

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Neurologic toxicity, including immune effector cell-associated neurotoxicity

INDICATION AND USAGE

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Median duration: 2 days (range: 1 to 22)

ICANS can occur concurrently with CRS, following resolution of CRS, or in the absence of CRS.

ICANS experienced after each dose of TALVEY® (N=265)	
Q2W	**QW**
Step-up dosing schedule	
Step-up dose 1 **3%**	
Step-up dose 2 **3%**	
Step-up dose 3 **1.8%**	First treatment dose (n=156) **2.6%**
First treatment dose (N=109) **3.7%**	N/A

At the first sign of neurologic toxicity, including ICANS, withhold TALVEY® and consider neurology evaluation. Rule out other causes of neurologic symptoms.

- Administer supportive care, which may include intensive care for severe or life-threatening neurologic toxicity, including ICANS

Managing neurologic toxicity, including ICANS +

Clinical signs and symptoms of ICANS may include but are not limited to:

- confusional state
- somnolence

Managing neurologic toxicity, including ICANS[1]

Recommendations for management of ICANS

Grade*	Presenting symptoms†	Actions
Grade 1	ICE score 7–9,‡ or depressed level of consciousness§: awakens spontaneously	• Withhold TALVEY® until ICANS resolves‖ • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management • Consider nonsedating antiseizure medicines (eg, levetiracetam) for seizure prophylaxis
Grade 2	ICE score 3–6,‡ or depressed level of consciousness§: awakens to voice	• Withhold TALVEY® until ICANS resolves • Administer dexamethasone¶ 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management • Consider nonsedating antiseizure medicines (eg, levetiracetam) for seizure prophylaxis • Patients should be hospitalized for 48 hours following the next dose of TALVEY®‖
Grade 3	ICE score 0–2,‡ if ICE score is 0, but the patient is arousable (eg, awake with global aphasia) and able to perform assessment, or depressed level of consciousness§: awakens only to tactile stimulus, or seizures,§ either: • any clinical seizure, focal or generalized, that resolves rapidly, or • nonconvulsive seizures on electroencephalogram (EEG) that resolve with intervention, or raised intracranial pressure: focal/local edema on neuroimaging§	<u>First occurrence of Grade 3 ICANS:</u> • Withhold TALVEY® until ICANS resolves • Administer dexamethasone¶ 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management • Consider nonsedating antiseizure medicines (eg, levetiracetam) for seizure prophylaxis • Provide supportive therapy, which may include intensive care • Patients should be hospitalized for 48 hours following the next dose of TALVEY®‖ <u>Recurrent Grade 3 ICANS:</u> • Permanently discontinue TALVEY® • Administer dexamethasone¶ 10 mg intravenously and repeat dose every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management • Consider nonsedating antiseizure medicines (eg, levetiracetam) for seizure prophylaxis • Provide supportive therapy, which may include intensive

Managing neurologic toxicity, including ICANS +

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

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Neurologic toxicity, including immune effector cell-associated neurotoxicity

INDICATION AND USAGE

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Managing neurologic toxicity, including ICANS[1]

Recommendations for management of ICANS

Grade*	Presenting symptoms†	Actions
Grade 1	ICE score 7–9,‡ or depressed level of consciousness§: awakens spontaneously	• Withhold TALVEY® until ICANS resolves‖ • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management • Consider nonsedating antiseizure medicines (eg, levetiracetam) for seizure prophylaxis
Grade 2	ICE score 3–6,‡ or depressed level of consciousness§: awakens to voice	• Withhold TALVEY® until ICANS resolves • Administer dexamethasone¶ 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management • Consider nonsedating antiseizure medicines (eg, levetiracetam) for seizure prophylaxis • Patients should be hospitalized for 48 hours following the next dose of TALVEY®‖
Grade 3	ICE score 0–2,‡ if ICE score is 0, but the patient is arousable (eg, awake with global aphasia) and able to perform assessment, or depressed level of consciousness§: awakens only to tactile stimulus, or seizures,§ either: • any clinical seizure, focal or generalized, that resolves rapidly, or • nonconvulsive seizures on electroencephalogram (EEG) that resolve with intervention, or raised intracranial pressure: focal/local edema on neuroimaging§	<u>First occurrence of Grade 3 ICANS:</u> • Withhold TALVEY® until ICANS resolves • Administer dexamethasone¶ 10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management • Consider nonsedating antiseizure medicines (eg, levetiracetam) for seizure prophylaxis • Provide supportive therapy, which may include intensive care • Patients should be hospitalized for 48 hours following the next dose of TALVEY®‖ <u>Recurrent Grade 3 ICANS:</u> • Permanently discontinue TALVEY® • Administer dexamethasone¶ 10 mg intravenously and repeat dose every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management • Consider nonsedating antiseizure medicines (eg, levetiracetam) for seizure prophylaxis • Provide supportive therapy, which may include intensive care
Grade 4	ICE score 0‡ (patient is unarousable and unable to perform ICE assessment) or depressed level of consciousness,§ either: • patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or • stupor or coma, or seizures,§ either: • life-threatening prolonged seizure (>5 minutes), or • repetitive clinical or electrical seizures without return to baseline in between, or motor findings§: • deep focal motor weakness such as hemiparesis or paraparesis, or raised intracranial pressure/cerebral edema,§ with signs/symptoms such as: • diffuse cerebral edema on neuroimaging, or • decerebrate or decorticate posturing, or • cranial nerve VI palsy, or • papilledema, or • Cushing's triad	• Permanently discontinue TALVEY® • Administer dexamethasone¶ 10 mg intravenously and repeat dose every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper • Alternatively, consider administration of methylprednisolone 1000 mg per day intravenously and continue methylprednisolone 1000 mg per day intravenously for 2 or more days • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management • Consider nonsedating antiseizure medicines (eg, levetiracetam) for seizure prophylaxis • Provide supportive therapy, which may include intensive care

*Based on ASTCT 2019 grading for ICANS.
†Management is determined by the most severe event, not attributable to any other cause.
‡If patient is arousable and able to perform ICE Assessment, assess: **Orientation** (oriented to year, month, city, hospital = 4 points); **Naming** (name 3 objects, eg, point to clock, pen, button = 3 points); **Following Commands** (eg, "show me 2 fingers" or "close your eyes and stick out your tongue" = 1 point); **Writing** (ability to write a standard sentence = 1 point; and **Attention** (count backwards from 100 by ten = 1 point). If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points.
§Attributable to no other cause.
‖See Table 3 and Table 4 in the full Prescribing Information for recommendations on restarting TALVEY® after dose delays for ARs.
¶All references to dexamethasone administration are dexamethasone or equivalent.

Recommendations for management of neurologic toxicity (excluding ICANS)[1]

Adverse Reaction	Severity*	Actions
Neurologic Toxicity* (excluding ICANS)	Grade 1	• Withhold TALVEY® until neurologic toxicity symptoms resolve or stabilize.†‡
	Grade 2 Grade 3 (First occurrence)	• Withhold TALVEY® until neurologic toxicity symptoms improve to Grade 1 or less.†‡ • Provide supportive therapy.
	Grade 3 (Recurrent) Grade 4	• Permanently discontinue TALVEY®. • Provide supportive therapy, which may include intensive care.

*Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03.
†See Table 3 and Table 4 in the full Prescribing Information for recommendations on restarting TALVEY® after dose delays for ARs.
‡For ataxia/balance disorder, perform benefit-risk assessment prior to resuming treatment with TALVEY®.

Patient counseling information about neurologic toxicity[1]

- Speak with your patients about the signs and symptoms associated with neurologic toxicity, including ICANS. These include:
  - headache
  - feeling confused
  - being less alert or aware
  - feeling disoriented
  - trouble speaking or writing
  - shaking (tremors)
  - numbness and tingling (feeling like “pins and needles”)
  - problems with walking, or loss of balance or coordination
  - feeling sleepy
  - feeling very sleepy with low energy
  - slow or difficulty thinking
  - seizures
  - muscle weakness
  - memory loss
  - burning, throbbing, or stabbing pain
  - fast eye movements that you cannot control
- Encourage your patients to seek medical attention if they experience any signs or symptoms of ICANS
- Advise patients not to drive or operate heavy or potentially dangerous machinery during and for 48 hours after completion of the step-up dosing schedule, and in the event of new onset of any neurologic toxicity symptoms until they resolve

The ICE Assessment Tool, a 5-part questionnaire, may be used to help determine whether or not your patients are experiencing ICANS. It includes the following questions and directions[1]:

- **Orientation**
  - What month and year is it and which city and hospital are you in?
- **Naming**
  - Identify 3 objects that your healthcare provider points to
- **Following commands**
  - Follow simple directions (eg, “Touch your nose”)
- **Writing**
  - Ask your patient to write down a sentence that you tell them
- **Attention**
  - Count backwards from 100 by 10s

If patient is arousable and able to perform ICE Assessment, assess: **Orientation** (oriented to year, month, city, hospital = 4 points); **Naming** (name 3 objects, eg, point to clock, pen, button = 3 points); **Following Commands** (eg, “show me 2

Step-up dose 1
3%

Step-up dose 2
3%

Step-up dose 3 | First treatment dose (N=156)

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Neurologic toxicity, including immune effector cell-associated neurotoxicity

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  - Ask your patient to write down a sentence that you tell them
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  - Count backwards from 100 by 10s

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Safety

Safety profile of TALVEY®

Primary analysis safety | Longer-term safety data

ARs (≥10%) in patients with relapsed or refractory multiple myeloma who received TALVEY® in MonumenTAL-1[1]

System organ class Adverse reaction	TALVEY® (N=339)	
	Any Grade (%)	Grade 3 or 4 (%)
General disorders and administration site conditions		
Pyrexia*	83	4.7†
Fatique*	37	3.5†
Chills	19	0
Pain*	18	1.8†
Edema*	14	0
Injection site reaction*	13	0
Immune system disorders		
Cytokine release syndrome	76	1.5†
Gastroinestinal disorders		
Dysgeusia‡,§	70	0
Dry mouth§	34	0
Dysphagia	23	0.9†
Diarrhea	21	0.9†
Stomatitis‖	18	1.2†
Nausea	18	0
Constipation	16	0
Oral disorder¶	12	0
Skin and subcutaneous tissue disorders		
Nail disorder#	50	0†
Skin disorder**	41	0.3†
Rash††	38	3.5†
Xerosis‡‡	30	0
Pruritus	19	0.3†
Musculoskeletal and connective tissue disorder		
Musculoskeletal pain*	43	3.2†
Investigations		
Weight decreased	35	1.5†
Infections and infestations		
Upper respiratory tract infection*	22	2.7†
Bacterial infection including sepsis§§‖‖	19	9
COVID-19*‖‖	11	2.7
Fungal infection‖‖¶¶	10	0.6
Vascular disorders		
Hypotension*	21	2.9
Nervous system disorders		
Headache*	21	0.6†
Encephalopathy##	15	1.8†
Sensory neuropathy***	14	0
Motor dysfunction†††	10	0.6†
Metabolism and nutrition disorders		
Decreased appetite	19	1.2†
Respiratory, thoracic, and mediastinal disorders		
Cough*	17	0
Dyspnea*‖‖	11	1.8
Hypoxia*	10	1.5†
Cardiac disorders		

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Neurologic toxicity, including immune effector cell-associated neurotoxicity

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Safety profile of TALVEY®

Primary analysis safety | Longer-term safety data

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Dry mouth§	34	0
Dysphagia	23	0.9†
Diarrhea	21	0.9†
Stomatitis‖	18	1.2†
Nausea	18	0
Constipation	16	0
Oral disorder¶	12	0
Skin and subcutaneous tissue disorders		
Nail disorder#	50	0†
Skin disorder**	41	0.3†
Rash††	38	3.5†
Xerosis‡‡	30	0
Pruritus	19	0.3†
Musculoskeletal and connective tissue disorder		
Musculoskeletal pain*	43	3.2†
Investigations		
Weight decreased	35	1.5†
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Fungal infection‖‖¶¶	10	0.6
Vascular disorders		
Hypotension*	21	2.9
Nervous system disorders		
Headache*	21	0.6†
Encephalopathy##	15	1.8†
Sensory neuropathy***	14	0
Motor dysfunction†††	10	0.6†
Metabolism and nutrition disorders		
Decreased appetite	19	1.2†
Respiratory, thoracic, and mediastinal disorders		
Cough*	17	0
Dyspnea*‖‖	11	1.8
Hypoxia*	10	1.5†
Cardiac disorders		
Tachycardia*	11	0.6†

ARs were graded based on CTCAE, version 4.03, with the exception of CRS, which was graded per ASTCT 2019 criteria.

*Includes other related terms.

†Only Grade 3 reactions occurred.

‡Dysgeusia: ageusia, dysgeusia, and taste disorder.

§Per CTCAE version 4.03, maximum toxicity grade for dysgeusia is 2 and maximum toxicity grade for dry mouth is 3.

‖Stomatitis: cheilitis, glossitis, glossodynia, mouth ulceration, oral discomfort, oral mucosal erythema, oral pain, stomatitis, swollen tongue, tongue discomfort, tongue erythema, tongue edema, and tongue ulceration.

¶Oral disorder: oral disorder, oral dysethesia, oral mucosal exfoliation, oral toxicity, and oropharyngeal pain.

#Nail disorder: koilonychia, nail bed disorder, nail cuticle fissure, nail discoloration, nail disorder, nail dystrophy, nail hypertrophy, nail pitting, nail ridging, nail toxicity, onychoclasis, onycholysis, and onychomadesis.

**Skin disorder: palmar-plantar erythrodysesthesia syndrome, palmoplantar keratoderma, skin discoloration, skin exfoliation, and skin fissures.

††Rash: dermatitis, dermatitis acneiform, dermatitis contact, dermatitis exfoliative, dermatitis exfoliative generalized, erythema, exfoliative rash, rash, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pruritic, rash pustular, rash vesicular, and stasis dermatitis.

‡‡Xerosis: dry eye, dry skin and xerosis.

§§Bacterial infection including sepsis: campylobacter infection, carbuncle, cellulitis, citrobacter infection, clostridium difficile colitis, clostridium difficile infection, cystitis escherichia, cystitis klebsiella, diverticulitis, escherichia pyelonephritis, folliculitis, gastroenteritis escherichia coli, helicobacter gastritis, human ehrlichiosis, impetigo, klebsiella sepsis, moraxella infection, otitis media acute, pitted keratolysis, pseudomonal bacteremia, pyuria, relapsing fever, renal abscess, skin infection, staphylococcal infection, tooth abscess, tooth infection, urinary tract infection enterococcal, and urinary tract infection pseudomonal.

‖‖Contains fatal outcome(s).

¶¶Fungal infection: body tinea, candida infection, fungal foot infection, fungal infection, fungal skin infection, genital candidiasis, esophageal candidiasis, onychomycosis, oral candidiasis, oral fungal infection, oropharyngeal candidiasis, tinea pedis, vulvovaginal candidiasis and vulvovaginal mycotic infection.

##Encephalopathy: agitation, altered state of consciousness, amnesia, aphasia, bradyphrenia, confusional state, delirium, depressed level of consciousness, disorientation, encephalopathy, hallucination, lethargy, memory impairment, mood altered, restlessness, sleep disorder, and somnolence.

***Sensory neuropathy: dysesthesia, hyperesthesia, hypoesthesia, hypoesthesia oral, immune-mediated neuropathy, neuralgia, neuropathy peripheral, paresthesia, peripheral sensory neuropathy, polyneuropathy, sciatica, and vestibular neuronitis.

†††Motor dysfunction: dysarthria, dysgraphia, dysmetria, dysphonia, gait disturbance, muscle atrophy, muscle spasms, muscular weakness, and tremor.

Safety

Safety profile of TALVEY®

Primary analysis safety | **Longer-term safety data**

You are now viewing a subsequent follow-up analysis of the MonumenTAL-1 trial. This information is not included in the current full Prescribing Information.

ARs (≥20%) in patients with relapsed or refractory multiple myeloma who received TALVEY® in the MonumenTAL-1 longer-term follow-up analysis[10]*

LONGER-TERM DATA: System organ class / Adverse reaction	TALVEY® (N=375)	
	Any Grade (%)	Grade 3 or 4 (%)
General disorders and administration site conditions		
Pyrexia*	83.2	4.5†
Fatigue*	43.7	3.5†
Pain*	24.3	2.4†
Chills	20.3	0.3†
Immune system disorders		
Cytokine release syndrome	76.3	1.3†
Gastrointestinal disorders		
Dry mouth	35.2	0
Diarrhea	26.1	1.3†
Dysphagia	23.7	0.8†
Nausea	20.5	0
Stomatitis‡	20.8	1.1†
Constipation	20	0
Skin and subcutaneous tissue disorders		
Nail disorder§	57.3	0
Skin disorder‖	43.7	0
Rash¶	39.5	3.2†
Xerosis#	35.5	0
Pruritus	24.3	0.3†
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain*	52.8	3.5§
Investigations		
Weight decreased	40.5	3.5†
Infections and infestations		
Upper respiratory tract infection*	35.7	2.1†
COVID-19*,**	20.8	3.7
Vascular disorders		
Hypotension††	22.4	3.2
Nervous system disorders		
Dysgeusia‡‡	72.8	0
Headache*	21.9	0.5†
Metabolism and nutrition disorders		
Decreased appetite	24.8	1.3†
Respiratory, thoracic, and mediastinal disorders		
Cough*	24.5	0

Note: CRS was originally graded by Lee criteria (Lee et al 2014) in Phase 1 and by ASTCT consensus grading system (Lee et al 2019) in Phase 2, with conversion of grade in Phase 1 to ASTCT based on data in eCRF. Toxicity grade by ASTCT is presented in this table, for both Phase 1 and Phase 2.

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TALVEY®. Initiate TALVEY® treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

INDICATION AND USAGE

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Safety

Safety profile of TALVEY®

Primary analysis safety | **Longer-term safety data**

You are now viewing a subsequent follow-up analysis of the MonumenTAL-1 trial. This information is not included in the current full Prescribing Information.

ARs (≥20%) in patients with relapsed or refractory multiple myeloma who received TALVEY® in the MonumenTAL-1 longer-term follow-up analysis[10]*

LONGER-TERM DATA: System organ class / Adverse reaction	TALVEY® (N=375)	
	Any Grade (%)	Grade 3 or 4 (%)
General disorders and administration site conditions		
Pyrexia*	83.2	4.5†
Fatigue*	43.7	3.5†
Pain*	24.3	2.4†
Chills	20.3	0.3†
Immune system disorders		
Cytokine release syndrome	76.3	1.3†
Gastrointestinal disorders		
Dry mouth	35.2	0
Diarrhea	26.1	1.3†
Dysphagia	23.7	0.8†
Nausea	20.5	0
Stomatitis‡	20.8	1.1†
Constipation	20	0
Skin and subcutaneous tissue disorders		
Nail disorder§	57.3	0
Skin disorder‖	43.7	0
Rash¶	39.5	3.2†
Xerosis#	35.5	0
Pruritus	24.3	0.3†
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain*	52.8	3.5§
Investigations		
Weight decreased	40.5	3.5†
Infections and infestations		
Upper respiratory tract infection*	35.7	2.1†
COVID-19*,**	20.8	3.7
Vascular disorders		
Hypotension††	22.4	3.2
Nervous system disorders		
Dysgeusia‡‡	72.8	0
Headache*	21.9	0.5†
Metabolism and nutrition disorders		
Decreased appetite	24.8	1.3†
Respiratory, thoracic, and mediastinal disorders		
Cough*	24.5	0

Note: CRS was originally graded by Lee criteria (Lee et al 2014) in Phase 1 and by ASTCT consensus grading system (Lee et al 2019) in Phase 2, with conversion of grade in Phase 1 to ASTCT based on data in eCRF. Toxicity grade by ASTCT is presented in this table, for both Phase 1 and Phase 2.
Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of talquetamab or until the start of subsequent anticancer therapy, if earlier. Note: The output includes the diagnosis of CRS; the symptoms of CRS are included. Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 24.1.

*Includes other related terms.
†Only Grade 3 reactions occurred.
‡Stomatitis: cheilitis, glossitis, glossodynia, mouth ulceration, oral discomfort, oral mucosal erythema, oral pain, stomatitis, swollen tongue, tongue discomfort, tongue erythema, tongue edema, and tongue ulceration.
§Nail disorder: koilonychia, nail bed disorder, nail cuticle fissure, nail discoloration, nail disorder, nail dystrophy, nail hypertrophy, nail pitting, nail ridging, nail toxicity, onychoclasis, onycholysis, and onychomadesis.
‖Skin disorder: palmar-plantar erythrodysesthesia syndrome, palmoplantar keratoderma, skin discoloration, skin exfoliation, and skin fissures.
¶Rash: dermatitis, dermatitis acneiform, dermatitis contact, dermatitis exfoliative, dermatitis exfoliative generalized, erythema, exfoliative rash, rash, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pruritic, rash pustular, rash vesicular, and stasis dermatitis.
#Xerosis: dry eye, dry skin, and xerosis.
**Contains fatal outcome(s).
††Hypotension: hypotension and orthostatic hypotension.
‡‡Dysgeusia: ageusia, dysgeusia, and taste disorder.

Safety

Incidence and management of ARs: Infections[1,10]

Understanding infections associated with TALVEY®[1]

TALVEY® can cause serious infections, including life-threatening or fatal infections

- In the primary analysis, serious infections occurred in 16% of patients, with fatal infections in 1.5% of patients
- 17% of patients reported Grade 3/4 infection
- The most common serious infections reported were bacterial infection (8%), which included sepsis, and COVID-19 (2.7%)

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Low rate of Grade 3/4 infections (8.3%) and death due to infections (1.3%)[10]*

Occurrence and death due to infection in patients receiving TALVEY®

LONGER-TERM DATA — Infection type	Patients in the MonumenTAL-1 Trial longer-term follow-up population (n=375)	
	Any Grade (%)	Grade 3 or 4 (%)
Infections and infestations	**55.7**	**8.3**
Upper respiratory tract infection†	35.7	2.1‡
COVID-19†§	20.8	3.7
Bacterial infection‖	12.5	3.2
Fungal infection¶	10.7	0.3‡

Death due to infection

1.3%

Ongoing Grade 3/4 infections +

IgG levels over time +

*Median follow-up for MonumenTAL-1 cohorts: TCR-naïve Q2W was >30 months; TCR-exposed was >28 months; TCR-naïve QW was >37 months.[10]

‡Includes other related terms

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COVID-19[†§]	20.8	3.7
Bacterial infection[‖]	12.5	3.2
Fungal infection[¶]	10.7	0.3[‡]

Death due to infection

Ongoing Grade 3/4 infections +

IgG levels over time +

*Median follow-up for MonumenTAL-1 cohorts: TCR-naïve Q2W was >30 months; TCR-exposed was >28 months; TCR-naïve QW was >37 months.[10]

[†]Includes other related outcomes.

[‡]Only Grade 3 ARs occurred.

[§]Contains fatal outcome(s).

[‖]Bacterial infection includes: campylobacter infection, carbuncle, cellulitis, citrobacter infection, clostridium difficile colitis, clostridium difficile infection, cystitis escherichia, cystitis klebsiella, diverticulitis, escherichia pyelonephritis, folliculitis, gastroenteritis escherichia coli, helicobacter gastritis, human ehrlichiosis, impetigo, klebsiella sepsis, Moraxella infection, otitis media acute, pitted keratolysis, pseudomonal bacteremia, pyuria, relapsing fever, renal abscess, skin infection, staphylococcal infection, tooth abscess, tooth infection, urinary tract infection enterococcal and urinary tract infection pseudomonal.

[¶]Fungal infection includes: body tinea, candida infection, fungal foot infection, fungal infection, fungal skin infection, genital candidiasis, esophageal candidiasis, onychomycosis, oral candidiasis, oral fungal infection, oropharyngeal candidiasis, tinea pedis, vulvovaginal candidiasis and vulvovaginal mycotic infection.

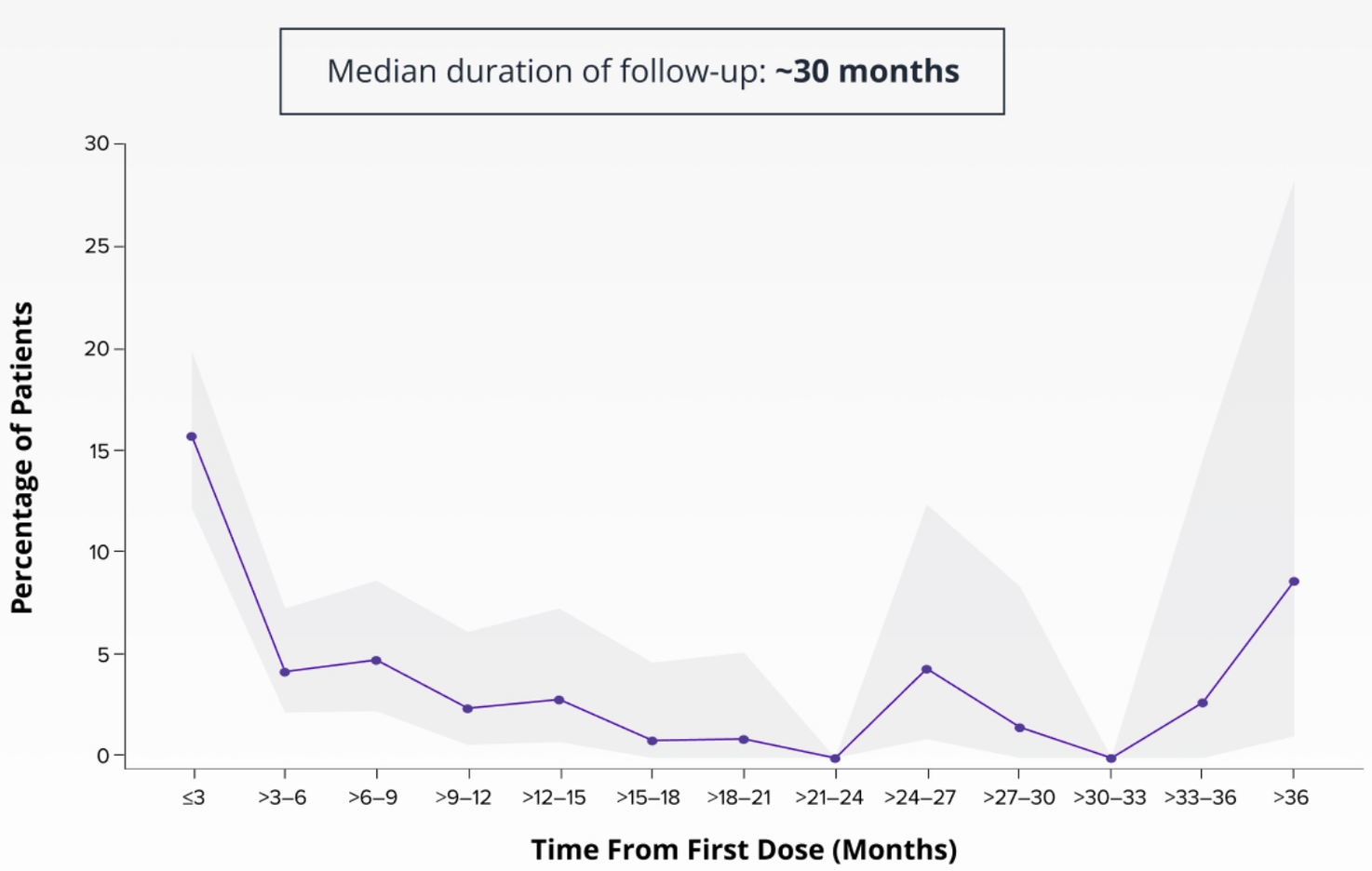
Safety

Introduction | CRS | Neurotoxicity | ARs | Infections

Incidence and management of ARs: Infections[1,10]

Incidence of Grade 3/4 infections over time[10]*

LONGER-TERM DATA | **Percentage of patients on TALVEY® with ongoing Grade 3+ infections[14]**



Number of subjects	375	285	209	163	137	117	106	89	68	64	52	36	23
Treated with AR(s)	59	12	10	4	4	1	1	0	3	1	0	1	2

*Median follow-up for MonumenTAL-1 cohorts: TCR-naïve Q2W was >30 months; TCR-exposed was >28 months; TCR-naïve QW was >37 months.[10]

Fungal infection[11]	10.7	0.3[§]

Death due to infection

1.3%

Ongoing 3+ infection +

IgG levels over time +

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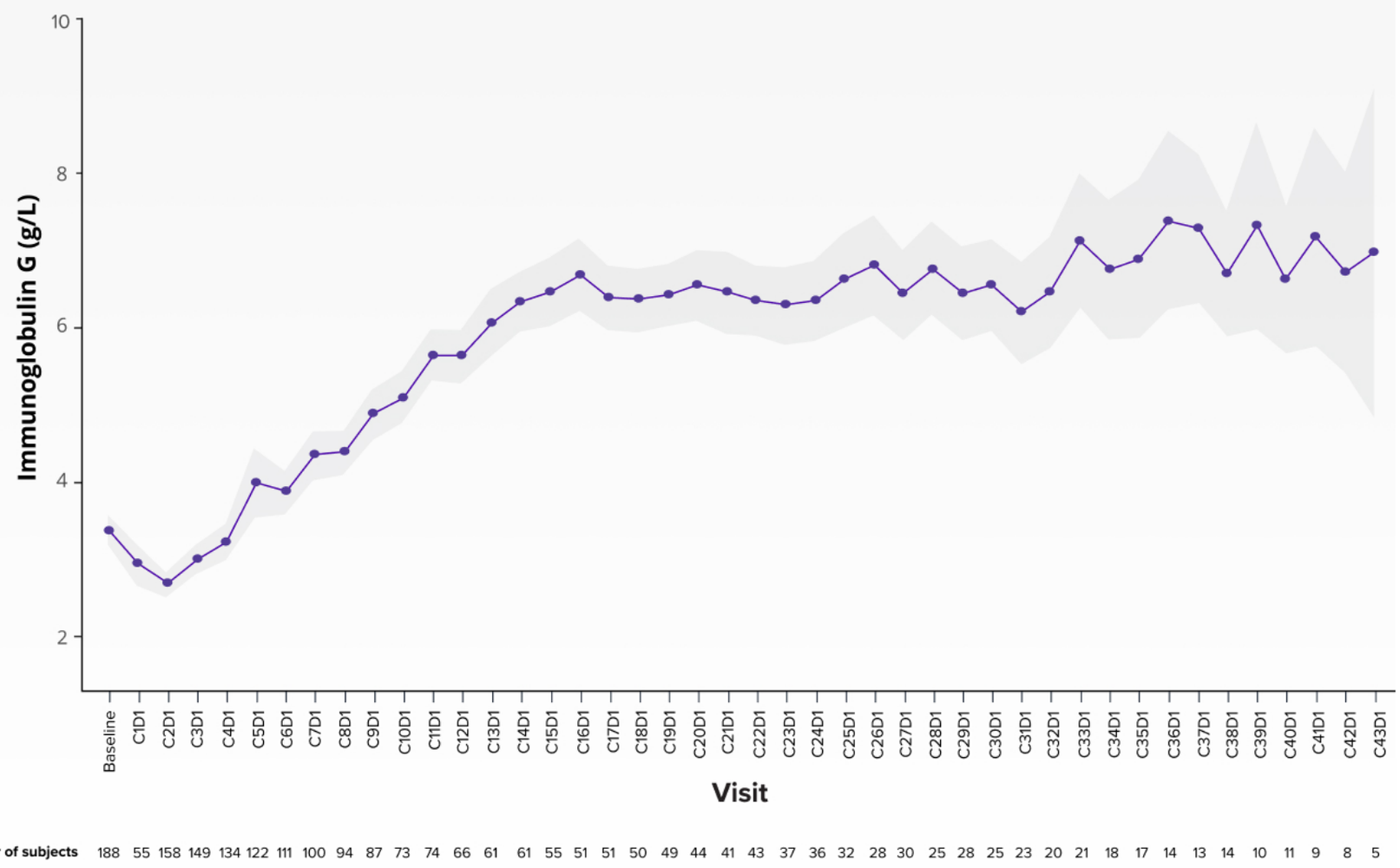
Incidence and management of ARs: Infections[1,10]

IgG levels over time[10]*

LONGER-TERM DATA

Average IgG for patients on TALVEY® over time[14]



*Median follow-up for MonumenTAL-1 cohorts: TCR-naïve Q2W was >30 months; TCR-exposed was >28 months; TCR-naïve QW was >37 months.[10]

Fungal infection[a]	10.7	0.3[3]

Death due to infection

1.3%

Ongoing 3+ infection +

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Low rate of Grade 3/4 infections (8.3%) and death due to infections (1.3%)[9*]

Occurrence, discontinuation, and death due to infection in patients receiving TALVEY®

Patient counseling information about serious infections[1]

- Advise your patients that serious infections, including life-threatening or fatal infections, have been reported in patients receiving TALVEY®
- Let your patients know that they will be monitored for signs and symptoms of infection prior to and during treatment with TALVEY® and treated appropriately
- If local guidelines recommend, tell your patients that they will be given prophylactic antimicrobials
- Advise patients to read the infection section in the Medication Guide

1.3%

Ongoing 3+ infection +

IgG levels over time +

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Select ARs

Discontinuations and dose reductions due to select ARs observed in the MonumenTAL-1 longer-term follow-up analysis[10]*

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ORAL/TASTE ARs (N=375)[10]

Dysgeusia†:

- Incidence: 72.8%
- Grade 3/4: N/A
- Discontinuation: 0.8%
- Dose reduction: 5.6%

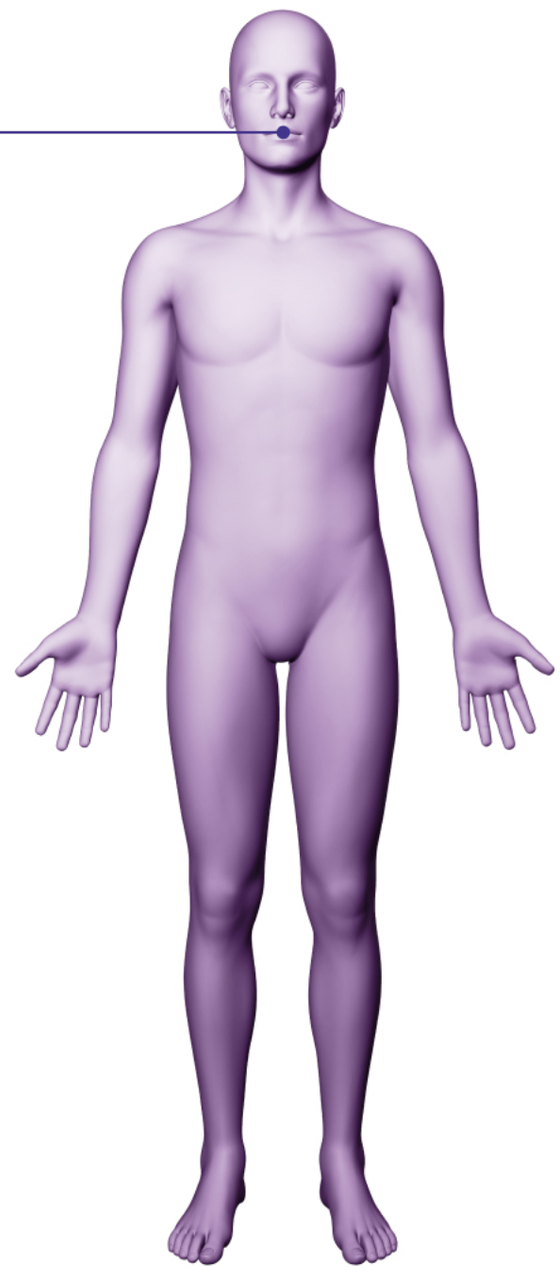
Dry mouth:

- Incidence: 35.2%
- Grade 3: 0%
- Discontinuation: 0%
- Dose reduction: 1.6%

Dysphagia:

- Incidence: 23.7%
- Grade 3/4‡: 0.8%
- Discontinuation: 0%
- Dose reduction: 0.8%

Management recommendations +



WEIGHT LOSS (N=375)[10]

Weight loss:

- Incidence: 40.5%
- Grade 3/4‡: 3.5%
- Discontinuation: 1.1%
- Dose reduction: 3.5%

Weight loss over time +

Management recommendations +

Additional consensus AR recommendations +

SKIN-RELATED ARs (N=375)[10]

Rash§:

- Incidence: 39.5%

Xerosis‖:

- Incidence: 35.5%

IMPORTANT SAFETY INFORMATION

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- Incidence: 23.7%
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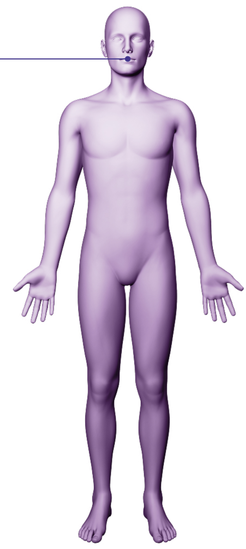
Management recommendations +



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Weight loss over time +

Management recommendations +

Additional consensus AR recommendations +

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- Incidence: 39.5%
- Grade 3/4‡: 3.2%
- Discontinuation: 0.5%
- Dose reduction: 0.5%

Xerosis‖:

- Incidence: 35.5%
- Grade 3/4: 0%
- Discontinuation: 0.3%
- Dose reduction: 0.3%

Skin disorder¶:

- Incidence: 43.7%
- Grade 3/4: 0%
- Discontinuation: 0.5%
- Dose reduction: 1.3%

Pruritus:

- Incidence: 24.3%
- Grade 3/4‡: 0.3%
- Discontinuation: 0%
- Dose reduction: 0.5%

Management recommendations +

NAIL DISORDER (N=375)[10]

Nail disorder:**

- Incidence: 57.3%
- Grade 3/4: 0%
- Discontinuation: 0%
- Dose reduction: 0.8%

Management recommendations +

Discontinuation due to an AR in the primary analysis[††]

9%

ARs which resulted in permanent discontinuation of TALVEY® in >1% of patients included ICANS (N=339).

Discontinuation due to ARs in the long-term follow-up[10]

7.5%

Updated discontinuation rate reflects longer-term follow-up* data of MonumenTAL-1 cohorts with a total N value of 375.

*Median follow-up for MonumenTAL-1 cohorts: TCR-naïve Q2W was >30 months; TCR-exposed was >28 months; TCR-naïve QW was >37 months.[10]

†Dysgeusia includes: ageusia, dysgeusia, hypogeusia, and taste disorder.[10]

‡Only Grade 3 ARs occurred.[10]

§Rash includes: dermatitis, dermatitis acneiform, dermatitis contact, dermatitis exfoliative, dermatitis generalised, exfoliative rash, rash, rash erythematous, rash macular, rash maculopapular, rash papular, rash pruritic, rash pustular, rash vesicular, and stasis dermatitis.[10]

‖Xerosis includes: dry eye and dry skin.[10]

¶Skin disorder includes: palmar-plantar syndrome, palmoplantar keratoderma, skin discoloration, skin exfoliation, and skin fissures.[10]

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Oral and taste ARs

Management recommendations and dose modifications from the TALVEY® full Prescribing Information[1]

Management recommendations

- Monitor for oral toxicity and weight loss
- Advise patients to seek medical attention should signs or symptoms of oral toxicity occur and provide supportive care as per current clinical practice, including consultation with a nutritionist

Dose modifications

- **Grade 1/2:** Provide supportive care and consider withholding TALVEY® if they're unresponsive to supportive care*
- **Grade 3:** Withhold TALVEY® until resolution to Grade 1 or better and provide supportive care*
- **Grade 4:** Permanently discontinue TALVEY®

Additional clinical management recommendations[13]

You are now viewing additional considerations related to the management of TALVEY® ARs, including supportive measures based on the experiences from the clinical sites that participated in the MonumenTAL-1 study, from the article "Clinical management of patients with RRMM treated with talquetamab." The considerations are purely descriptive and there is no clinical correlation or clinical analysis demonstrating that these steps mitigate oral, skin, and nail ARs. This information is not included in the current full Prescribing Information and has not been evaluated by the FDA. No conclusions should be drawn. The information should be understood in context of the methodology.

Methodology[13]

- All patients were enrolled in the MonumenTAL-1 trial
- The MonumenTAL-1 trial included 339 patients that received subcutaneous TALVEY® at the 2 recommended phase 2 doses: 0.4 mg/kg QW (n=143) and 0.8 mg/kg Q2W (n=145)
  - The trial included 51 patients who received prior T-cell redirection therapy
- The paper includes management of each AR per MonumenTAL-1 trial experience, investigator advice, including patient counseling and specialist input, and the US Prescribing Information and EMA SmPC
- The study was not powered to assess the efficacy of investigator-recommended AR management strategies or standardized guidelines for management of ARs

Dysgeusia management

Rash[§]:

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Xerosis[‖]:

- Incidence: 35.5%

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Oral and taste ARs

Management recommendations and dose modifications from the TALVEY® full Prescribing Information[1]

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Dysgeusia management

- Local oral steroids and antifungals
- Mineral and vitamin support with zinc and biotin
- Salivary stimulants and maintenance of adequate hydration
- Food enhancement with spicy, sour, or other aromatic flavor additives
- Dose modifications,† including reductions, delays, or skips

Dry mouth management

- Dental health agents
- Saliva substitutes to aid lubrication of foods
- Antibacterial agents
- Increased hydration (sipping water throughout the day) and intraoral topical agents (topical saliva sprays or sugar-free chewing gum)‡
- Sodium lauryl sulphate-free toothpastes and corticosteroid mouthwashes
- Dose reductions, delays, or skips were potentially effective management strategies
- Patients should be advised to maintain routine dental visits, including regular cleanings

Dysphagia management

- Antifungal agents
- Analgesics
- Corticosteroids for inflammation
- Mouthwashes
- Encourage frequent intake of liquids, particularly while consuming food, or use of artificial saliva
- Encourage smaller bites of food and encourage experimentation with foods with different textures, such as sauces/broths, being mindful of fat and sodium intake
- Dose reductions, delays or skips were the most effective management strategy
- Patients should be referred to gastroenterology consult

*See Table 3 and Table 4 in the full Prescribing Information for recommendations on restarting TALVEY® after dose delays for ARs.
†Further characterization of the resolution or improvement in taste changes upon dose reduction is under assessment.
‡Measures for dry mouth are consistent with the role of saliva in oral health, providing lubrication and antimicrobial properties.

Weight loss

Management recommendations and dose modifications from the TALVEY® full Prescribing Information[1]

Management recommendations

- Monitor for oral toxicity and weight loss
- Evaluate clinically significant weight loss further

Dose modifications

- **Grade 1/2:** Provide supportive care and consider withholding TALVEY® if the patient is unresponsive to supportive care*
- **Grade 3:** Withhold TALVEY® until resolution to Grade 1 or better and provide supportive care*
- **Grade 4:** Permanently discontinue TALVEY®

Additional clinical management recommendations[13]

You are now viewing additional considerations related to the management of TALVEY® ARs, including supportive measures based on the experiences from the clinical sites that participated in the MonumenTAL-1 study, from the article "Clinical management of patients with RRMM treated with talquetamab." The considerations are purely descriptive and there is no clinical correlation or clinical analysis demonstrating that these steps mitigate oral, skin, and nail ARs. This information is not included in the current full Prescribing Information and has not been evaluated by the FDA. No conclusions should be drawn. The information should be understood in context of the methodology.

Methodology[13]

- All patients were enrolled in the MonumenTAL-1 trial
- The MonumenTAL-1 trial included 339 patients that received subcutaneous TALVEY® at the 2 recommended phase 2 doses: 0.4 mg/kg QW (n=143) and 0.8 mg/kg Q2W (n=145)
  - The trial included 51 patients who received prior T-cell redirection therapy
- The paper includes management of each AR per MonumenTAL-1 trial experience, investigator advice, including patient counseling and specialist input, and the US Prescribing Information and EMA SmPC
- The study was not powered to assess the efficacy of investigator-recommended AR management strategies or standardized guidelines for management of ARs

Interventions to manage weight decrease

Rash[§]:

- Incidence: 39.5%

Xerosis[‖]:

- Incidence: 35.5%

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TALVEY®. Initiate TALVEY® treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY® until CRS resolves or permanently discontinue based on severity.

Neurologic toxicity, including immune effector cell-associated neurotoxicity

INDICATION AND USAGE

TALVEY® (talquetamab-tgvs) is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Weight loss

Management recommendations and dose modifications from the TALVEY® full Prescribing Information[1]

Management recommendations

- Monitor for oral toxicity and weight loss
- Evaluate clinically significant weight loss further

Dose modifications

- **Grade 1/2:** Provide supportive care and consider withholding TALVEY® if the patient is unresponsive to supportive care*
- **Grade 3:** Withhold TALVEY® until resolution to Grade 1 or better and provide supportive care*
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Additional clinical management recommendations[13]

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Interventions to manage weight decrease

- Patients should be referred to a dietician or nutritionist at the onset of therapy to maintain a balanced diet and weight, irrespective of the presence of oral events
- Nutritional support (eg, vitamins, minerals, high-caloric shakes) may help maintain weight

*See Table 3 and Table 4 in the full Prescribing Information for recommendations on restarting TALVEY® after dose delays for ARs.

Skin-related ARs

Management recommendations and dose modifications from the TALVEY® full Prescribing Information[1]

Management recommendations:

- Monitor for skin toxicity, including rash progression
- Consider early intervention and treatment to manage skin toxicity

Dose modifications:

- **Grade 3/4:** Withhold TALVEY® until AR improves to Grade 1 or baseline*

Additional clinical management recommendations[13]

You are now viewing additional considerations related to the management of TALVEY® ARs, including supportive measures based on the experiences from the clinical sites that participated in the MonumenTAL-1 study, from the article "Clinical management of patients with RRMM treated with talquetamab." The considerations are purely descriptive and there is no clinical correlation or clinical analysis demonstrating that these steps mitigate oral, skin, and nail ARs. This information is not included in the current full Prescribing Information and has not been evaluated by the FDA. No conclusions should be drawn. The information should be understood in context of the methodology.

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Rash and other skin management

Based on the experiences from the MonumenTAL-1 trial, prophylaxis is not needed; however, management of skin toxicities should begin with early intervention.

Prophylactic treatment

Rash[§]:

- Incidence: 39.5%

Xerosis[‖]:

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IMPORTANT SAFETY INFORMATION

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Neurologic toxicity, including immune effector cell-associated neurotoxicity

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Rash and other skin management

Based on the experiences from the MonumenTAL-1 trial, prophylaxis is not needed; however, management of skin toxicities should begin with early intervention.

Prophylactic treatment

- Liberal use of emollients (especially after bathing) and adequate hydration

Interventions to manage skin ARs

- Emollients and corticosteroids
- Topical corticosteroids, with potency selected based on the site and severity
- Short pulses of oral corticosteroids for generalized rashes not controlled by topical corticosteroids and/or for rashes occurring over large surface areas
- Referral to dermatology in cases in which patients experience persistent or Grade 3/4 skin toxicities or to rule out other rare etiologies of rashes

*See Table 3 and Table 4 in the full Prescribing Information for recommendations on restarting TALVEY® after dose delays for ARs.

Nail-related ARs

Additional clinical management recommendations[13]

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Interventions to manage nail-related ARs

- Emollients and moisturizers
- Nail soaks
- Topical moisturizers, including emollients
- Topical corticosteroids
- Occlusion to concentrate the effect of topical corticosteroids and/or moisturizers on nails
- Vitamin E oil and biotin
- Systemic hydration
- Dose modifications including reductions, delays, or skips may be effective; thus, nail health should be monitored with each physical examination

Rash[§]:

- Incidence: 39.5%

Xerosis[‖]:

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Nail-related ARs

Additional clinical management recommendations[13]

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IMWG Immunotherapy Committee Consensus Recommendations for the Management of On-Target, Off-Tumor Toxicities[14]

These recommendations were developed by a panel of 37 experts with broad experiences in the management of patients with RRMM. In order to define optimal management strategies, the experts reviewed articles with at least 50 patients enrolled, as well as 2 consensus papers, and held several virtual meetings from 2022 to 2023. Statements with a high agreement (>50%) were incorporated as recommendations.

GPRC5D-Targeted Therapy-Related Oral Symptom Management: Guidance and Recommendation

- **Patient education** prior to starting therapy about potential on-target, off-tumor adverse events
- **Supportive management** for oral symptoms
  - Dose interruptions or reductions reserved for severe or recurrent cases
- **Xerostomia/dysphagia**
  - Increased hydration (saliva substitutes)
  - Sugar-free chewing gum to stimulate saliva flow
  - Sodium lauryl sulphate-free toothpaste might be better tolerated
  - Dietary modifications may be needed to prevent weight loss
- **Nutritional supplements and early nutritional review** to optimize oral intake and limit weight loss, especially in patients with a low baseline weight
- **Treatment of oral comorbidities** (eg, candida, thrush, or nutritional deficiencies leading to glossitis) is encouraged
- **Regular dental review** to minimize the risk of periodontal disease and caries

GPRC5D-Targeted Therapy-Related Cutaneous AR Management: Guidance and Recommendation

- **Patient education** prior to starting therapy about potential on-target, off-tumor adverse events
- Early or prophylactic use of emollients and sunscreen
- Grade 1/2 skin rashes: Low-potency topical corticosteroids (eg, hydrocortisone and triamcinolone), with escalation to medium-potency corticosteroids
- For more extensive (eg, grade ≥3) rashes or rashes refractory to topical therapies
  - Short courses of oral steroids (eg, prednisone or prednisolone)
    - Longer-term corticosteroids should be avoided where possible due to the risk of infection

Rash[§]:

- Incidence: 39.5%

Xerosis[‖]:

- Incidence: 35.5%

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INDICATION AND USAGE

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- For more extensive (eg, grade ≥3) rashes or rashes refractory to topical therapies
  - Short courses of oral steroids (eg, prednisone or prednisolone)
    - Longer-term corticosteroids should be avoided where possible due to the risk of infection
- Dermatology consultation for rashes occurring beyond cycle 2 or refractory to emollients or low-potency steroids

Select ARs

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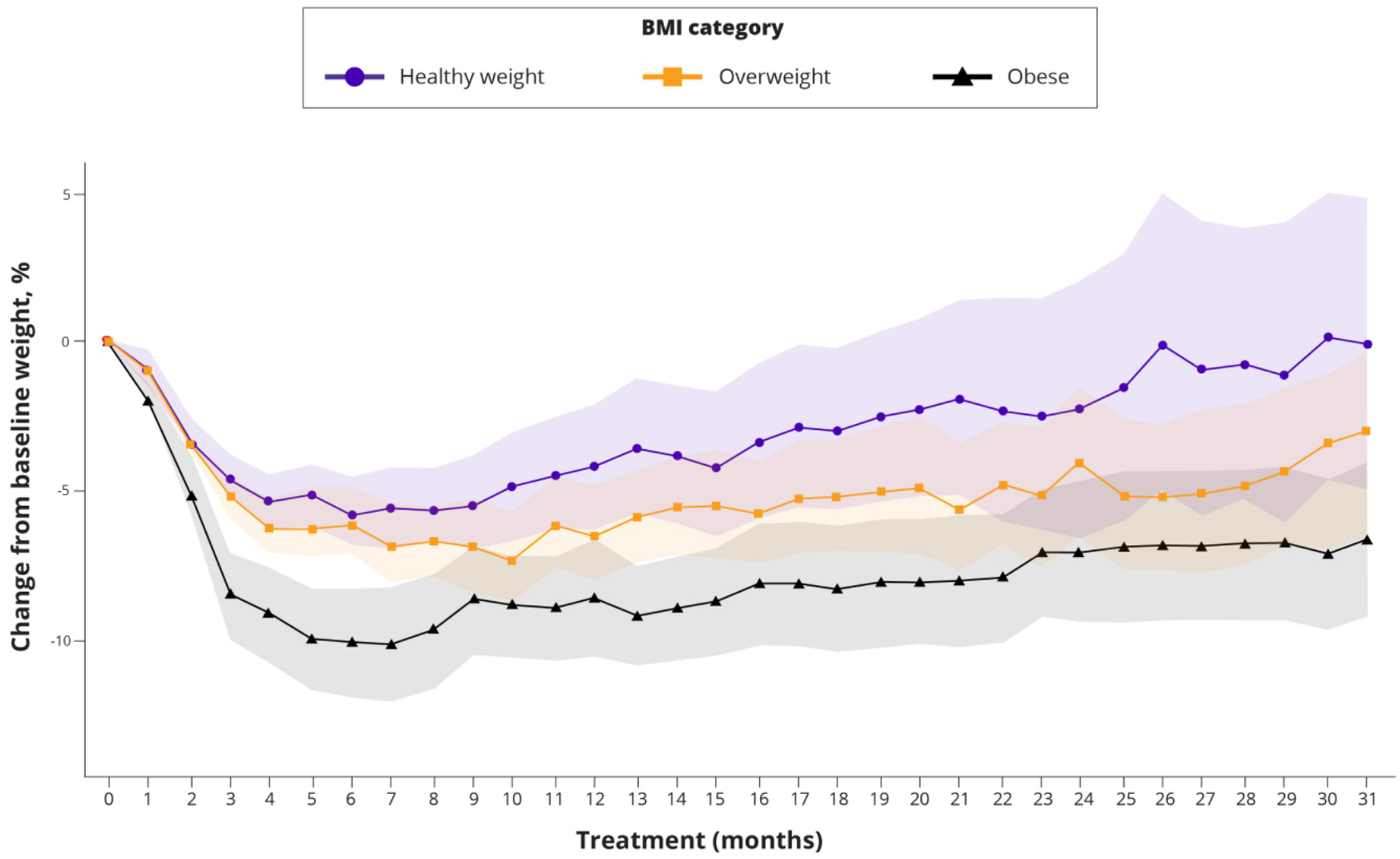
LONGER-TERM DATA

Weight loss over time in patients* from the MonumenTAL-1 trial[†‡§15]



Number of subjects																														
Healthy weight	138	137	121	109	92	81	73	68	60	55	54	52	48	46	43	41	40	36	36	35	33	31	28	25	22	21	20	19	19	17	16	16
Overweight	142	142	129	122	108	97	89	80	69	67	65	62	60	53	49	45	43	41	39	38	35	31	31	28	25	23	23	22	21	21	20	17
Obese	85	85	76	66	59	58	51	48	44	39	36	35	35	34	34	33	29	29	29	28	29	29	27	26	24	22	21	21	21	21	18	17

*Included patients in the TCR-naïve Q2W and QW cohorts and the TCR-exposed cohort.
†Efficacy and ongoing safety from MonumenTAL-1 were reported at a median follow-up of 30–38 months.
‡Data were plotted as mean percent change from baseline weight. BMI categories were defined as follows: healthy weight (18.5 to <25), overweight (25 to <30), obese (≥30). BMI was calculated as patient body weight (in kg) divided by patient height squared (in meters).
§Shaded areas represent the 95% CI.

SKIN-RELATED ARs (N=375)[10]

Rash[§]:

- Incidence: 39.5%

Xerosis[‖]:

- Incidence: 35.5%

IMPORTANT SAFETY INFORMATION

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INDICATION AND USAGE

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Patient counseling information

Coping tips for patients | Additional counseling info

Coping tips for patients

The recommendations below from The Leukemia & Lymphoma Society and the American Cancer Society may help people living with side effects. This information is not included in the current Prescribing Information and has not been evaluated by the FDA. For more tips, please see lls.org and cancer.org.

Tips for managing mouth problems[16,17]

- Maintain good dental hygiene
- Avoid smoking
- Keep mouth moist with hard candy, drinking water, or salivary substitutes

Tips for managing weight loss[18,19]

- Maintain a food journal
- Maintain a nutritious diet
- Engage in physical activity
- The healthcare provider will weigh you during treatment and may consult a nutritionist

Tips for managing skin problems[16]

- Take warm (not hot) baths or showers
- Pat skin dry
- Use unscented lotion or moisturizing cream
- Wash skin with mild soap and cleansers
- Avoid direct sunlight and apply sunscreen

Tips for managing nail changes[16]

- Wear gloves when cleaning or gardening
- Avoid biting and picking on nails and cuticles
- Wear comfortable shoes with extra room around the toes
- Keep fingernails and toenails neatly trimmed
- Ask your healthcare provider before you have a manicure

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Patient counseling information

Coping tips for patients | **Additional counseling info**

Additional counseling information

Advise patients to read the Medication Guide section of the full Prescribing Information.

TECVAYLI® and TALVEY® REMS[1,20]

A Risk Evaluation and Mitigation Strategy (REMS) is a program to manage known or potential serious risks associated with a drug product. Because of the risk of CRS and neurologic toxicity, including ICANS, TALVEY® is available only through a restricted program called the TECVAYLI® and TALVEY® Risk Evaluation and Mitigation Strategy (REMS).

- Let your patients know that they will be given a TALVEY® Patient Wallet Card that they should carry with them at all times and show to all their healthcare providers
- The card describes the signs and symptoms of CRS and neurologic toxicity, including ICANS, which, if experienced, should prompt the patient to seek immediate medical attention

Cytopenias[1,21]

- Advise your patients that treatment-emergent Grade 3 or 4 neutropenia has been reported
- Also advise them of similar reports about thrombocytopenia. This may result in easy bruising, excessive bleeding from wounds, or bleeding in mucous membranes and other tissue

Embryo-fetal toxicity[1]

- Let patients know that because of the way TALVEY® works, it may cause harm to a fetus when given to a pregnant woman
- Advise pregnant women of the potential risk to the fetus
- Recommend that women of reproductive potential use effective contraception during treatment with TALVEY® and for 3 months after their last dose

Lactation[1]

- It is not known whether TALVEY® is excreted in human milk, affects breastfed infants, or if it affects milk production. Because of this, advise patients not to breastfeed during treatment with TALVEY® and for at least 3 months after the last dose

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Appendix

Primary data | Longer-term data

In MonumenTAL-1 primary analysis,

TALVEY® provided powerful efficacy[1]

Efficacy was based on ORR and DOR as assessed by an IRC using IMWG criteria.[1]*

Naïve to T-cell redirection therapy†: QW dosing[1]

ORR‡	**73%** (73/100) **(95% CI, 63.2%–81.4%)**
mTTR	**1.2 months** (range: 0.2–10.9 months)
mDOR	**9.5 months** (95% CI, 6.5–NE months)

*Efficacy results reflect patients who have received ≥4 prior lines of therapy.[1]
†T-cell redirection therapy refers to both CAR-T and bispecific antibody treatment.[1]
‡ORR: sCR+CR+VGPR+PR.

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Appendix

Primary data | **Longer-term data**

You are now viewing a subsequent follow-up analysis of the MonumenTAL-1 trial. This information is not included in the current full Prescribing Information. These longer-term follow-up data reflect the patients naive to TCR therapy* receiving TALVEY® QW; any increase in n-value is due to this longer-term follow-up and additional patients.

MonumenTAL-1 longer-term follow-up analysis at a median follow-up of >37 months in patients naïve to T-cell redirection therapy[10]

ORR and DOR as assessed by an IRC using IMWG criteria.[1†]

LONGER-TERM DATA

Naïve to T-cell redirection therapy*: QW dosing[10]

ORR‡	**73%** (73/100) **(95% CI, 63.2%–81.4%)**
mTTR	**1.2 months** (range: 0.2–10.9 months)
mTTCR	**2.1 months** (range: 1.1–12.2 months)
mDOR	**10.2 months** (95% CI, 6.6–15.7 months)

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