Administration of Talquetamab

Center for Medicare & Medicaid Services
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Unmet Need for Heavily Treated Multiple Myeloma Patients

- Despite recent advances in treatment, nearly all myeloma patients will relapse[1, 2]
- Many will receive multiple lines of therapy throughout their disease course, increasing the likelihood of retreatment with similar classes of therapies[1, 3]
- Subsequently, efficacy outcomes decrease with each line of therapy as ~79% of patients become refractory to the three main myeloma drug classes (Proteasome Inhibitors (PIs), Immunomodulatory Drugs (IMiDs), and anti-CD38 antibodies)[1]

1. Ghandi et al, 2019 2. Rajkumar, 2019. 3. Madduri et al, 2020.

Outcomes are Poor for Patients Refractory to the Three Main Classes of Myeloma Therapies

- Outcomes for triple-class refractory (1 PI, 1 IMiD, 1 anti-CD38) and penta-refractory (2 PIs, 2 IMiDs, 1 anti-CD38) patients are poor, with a median overall survival (OS) of 9.2 and 5.6 months, respectively[1]

- Current treatment options for patients with triple-class refractory disease are limited by toxicities and accessibility

1. Ghandi et al, 2019

Talquetamab Product Overview

- Talquetamab is a full-sized bispecific antibody that binds to CD3 on T-cells and GPRC5D on myeloma cells. Talquetamab recruits CD3-expressing T-cells to myeloma cells that express GPRC5D, resulting in activation of the T-cell receptor pathway and lysis of GPRC5D-expressing MM cells, this is mediated by secreted perforin and various granzymes stored in the secretory vesicles of cytotoxic T-cells. These activated T-cells also lead to the production of cytokines, chemical signals that activate other T-cells to create a microenvironment that leads to further immune activation, augmenting the anti-tumor response.

- Talquetamab is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody
  - On June 29, 2022, Talquetamab was granted Breakthrough Therapy Designation by the Food and Drug Administration (FDA).[1]
  - Johnson & Johnson Healthcare Systems Inc., on behalf of Janssen Pharmaceuticals, plans to submit a New Technology Add-on Payment Application for Federal Fiscal Year 2025.

- TALVEY™ (talquetamab) received FDA accelerated approval on August 9, 2023.

1. Janssen announces U.S. FDA Breakthrough Therapy Designation granted for Talquetamab for the treatment of relapsed or refractory multiple myeloma. June 29, 2022. https://www.jnj.com/janssen-announces-u-s-fda-breakthrough-therapy-designation-granted-for-talquetamab-for-the-treatment-of-relapsed-or-refractory-multiple-myeloma

Talquetamab: Overall Safety Profile from MonumenTAL-1 Trial - Hematologic Adverse Events (AEs)

AEs (≥20% of any RP2D cohort), n (%)	0.4 mg/kg SC QW* (n 143) mFU, 11 months†		0.8 mg/kg SC Q2W* (n 145) mFU, 5 months‡	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Anemia	64 (45)	45 (32)	57 (39)	36 (25)
Neutropenia	49 (34)	44 (31)	41 (28)	32 (22)
Lymphopenia	40 (28)	37 (26)	38 (26)	37 (26)
Thrombocytopenia	39 (27)	29 (20)	39 (27)	24 (17)

- **AEs were graded by CTCAE v4.03**
- **Most high-grade AEs were cytopenias**
- **Cytopenias were generally limited to the first few cycles**

Infections

- At **0.4 mg/kg QW** and **0.8 mg/kg Q2W**, respectively:
  - Infections occurred in **57%** and **50%** of patients
    - Grade 3/4 in **17%** and **12%** of patients
  - **4%** (5)§ and **3%** (4)‖ of patients had opportunistic infections
  - **9%** (13) and **11%** (16) of patients had COVID-19
    - Grade 3/4 in **1%** and **2%** of patients
    - 2 patients died from COVID-19
  - **13%** and **10%** of patients received intravenous immunoglobulin

Data cutoff date: May 16, 2022.

*With 2–3 step-up doses.

†Range: 1-26 months, with lower range denoting patients who died.

‡Range: 0-18 months, with lower range denoting patients who died.

§Includes 2 cases of esophageal candidiasis, and 1 case each of adenovirus infection, fungal sepsis, and retinitis viral.

‖Includes 1 case each of cytomegalovirus infection, cytomegalovirus viraemia, herpes ophthalmic, and esophageal candidiasis.

CTCAE=Common Terminology Criteria for Adverse Events; mFU=median follow-up; RP2D=recommended phase 2 dose.

Reference: Chari A, et al. Presented at 64th American Society of Hematology (ASH) Annual Meeting; December 10-13, 2022; New Orleans, LA.

Talquetamab: Overall Safety Profile from MonumenTAL-1 Trial - Non-Hematologic Adverse Events (AEs)

AEs (≥20% of any RP2D cohort), n (%)	0.4 mg/kg SC QW[a] (n 143) mFU, 11.0 months[b]		0.8 mg/kg SC Q2W[a] (n 145) mFU, 5.1 months[c]	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
CRS	113 (79.0)	3 (2.1)	105 (72.4)	1 (0.7)
Skin-related AEs[d]	80 (55.9)	0	98 (67.6)	1 (0.7)
Nail-related AEs[e]	74 (51.7)	0	63 (43.4)	0
Dysgeusia[f]	69 (48.3)	NA	67 (46.2)	NA
Rash-related AEs[g]	56 (39.2)	2 (1.4)	39 (26.9)	8 (5.5)
Weight decreased	57 (39.9)	3 (2.1)	47 (32.4)	2 (1.4)
Pyrexia	53 (37.1)	4 (2.8)	35 (24.1)	1 (0.7)
Asthenia	37 (25.9)	3 (2.1)	13 (9.0)	2 (1.4)
Dry mouth	36 (25.2)	0	53 (36.6)	0
Diarrhea	34 (23.8)	3 (2.1)	32 (22.1)	0
Dysphagia	34 (23.8)	0	33 (22.8)	3 (2.1)
Fatigue	32 (22.4)	5 (3.5)	29 (20.0)	1 (0.7)
Decreased appetite	25 (17.5)	2 (1.4)	29 (20.0)	2 (1.4)

- **Low rates of grade 3/4 nonhematologic AEs** were observed
- **Low rates of discontinuation due to AEs** were observed with QW (4.9%) and Q2W (6.2%) schedules
- **Most common AEs were CRS, skin-related events, and dysgeusia**
  - Rates of high-grade skin, nail, and rash-related events were low
  - Dysgeusia was managed with supportive care, and at times with dose reduction
- At 0.4 mg/kg QW and at 0.8 mg/kg Q2W,
  - 8.4% and 13.8% had dose delays due to AEs
  - 14.7% and 6.2% had dose reductions due to AEs
- At time of cut-off, no patients in these cohorts died due to drug-related AEs

Data cut-off date: May 16, 2022.
AEs were graded by CTCAE v4.03 with CRS events graded per Lee et al 2014 criteria.
[a]With 2-3 step-up doses. [b]Range 0.5-26.1, with lower range denoting patients who died. [c] Range, 0.2-17.9, with lower range denoting patients who died. [d] Includes skin exfoliation, dry skin, pruritus, palmar-plantar erythrodysesthesia syndrome. [e] Includes nail discoloration, nail disorder, onycholysis, onychomadesis, onychoclasis, nail dystrophy, nail toxicity, and nail ridging. [f] Per CTCAE, the maximum grade of dysgeusia is 2. [g] Includes rash, maculopapular rash, erythematous rash, erythema. AE adverse event; CRS, Cytokine release syndrome; CTCAE, Common Terminology Criteria for AEs; mFU, median follow-up; NA, not applicable; RP2D recommended phase 2 dose; Q2W every other week; QW, weekly; SC, subcutaneous.

Talquetamab: Overall Safety Profile from MonumenTAL-1 Trial - Cytokine Release Syndrome

Parameter	0.4 mg/kg (n 143)	0.8 mg/kg SC Q2W* (n 145)
Patients with CRS, n (%)	113 (79)	105 (72)
Median days to onset, (range)†	2 (1–8)	2 (1–8)
Median duration in days, (range)	2 (1–13)	2 (1–29)
Patients with CRS up to 1st full dose, n (%)		
1st step-up dose	48 (34)	38 (26)
2nd step-up dose	70 (49)	58 (40)‡
1st full dose	38 (27)	19 (13)
Patients with CRS after 1st full dose,§ n (%)	19 (13)	13 (9)
Patients who received supportive measures,‖ n (%)	106 (74)	100 (69)
Tocilizumab¶	50 (35)	53 (37)
Steroids	5 (4)	4 (3)
Oxygen	8 (6)	10 (7)
Vasopressor	2 (1)	1 (1)
Patients with >1 CRS event, n (%)	46 (32)	46 (32)

Maximum CRS Grade#, n (%)	0.4 mg/kg SC QW* (n 143)	0.8 mg/kg SC Q2W* (n 145)
Grade 1	89 (62)	79 (55)
Grade 2	21 (15)	25 (17)
Grade 3	3 (2)	1 (1)

Data cutoff date: May 16, 2022

*With 2–3 step-up doses.

†Relative to the most recent dose.

‡Patients received third step-up dose and occurrence of CRS was 35% (n=50).

§Cumulative at any point after first full dose.

‖Patients could receive >1 supportive therapy.

¶Tocilizumab was allowed for all CRS events and was allowed at Grade 1 CRS; the protocol did not recommend prophylactic tocilizumab use.

#Graded per ASTCT criteria.

ASTCT American Society for Transplantation and Cellular Therapy.

Reference: Chari A, et al. Presented at 64th American Society of Hematology (ASH) Annual Meeting; December 10 13, 2022; New Orleans, LA.

Talquetamab: Overall Safety Profile from MonumenTAL-1 Trial - Immune effector cell-associated neurotoxicity syndrome (ICANS)

Parameter	0.4 mg/kg SC QW* (n 122†)	0.8 mg/kg SC Q2W* (n 109†)
Patients with ICANS, n (%)	13 (11)	11 (10)
Median days to onset, (range)‡	2 (1–9)	3 (2–16)
Median duration in days, (range)	2 (1–22)	1 (1–15)
Outcome of ICANS, n (%)		
Number of ICANS events, n§	21	14
Recovered/resolved	18 (86)	11 (79)
Not recovered/not resolved	2 (10)	2 (14)
Fatal	0	0
Concurrent CRS‖		
Yes	14 (67)	8 (57)
No	7 (33)	6 (43)

Maximum ICANS Grade, n (%)	0.4 mg/kg SC QW* (n 122†)	0.8 mg/kg SC Q2W* (n 109†)
Grade 1	4 (3)	3 (3)
Grade 2	7 (6)	6 (6)
Grade 3	2 (2)	2 (2)

- ICANS occurred in **10%** to **11%** of patients across RP2D groups
- Most ICANS events were Grade 1 or 2
- **7%** to **8%** of patients received supportive measures for ICANS across RP2D groups, including tocilizumab and corticosteroids

Data cutoff date: May 16, 2022

*With 2–3 step-up doses.

†ICANS was only measured in phase 2.

‡Relative to the most recent dose.

§One ICANS event outcome was recovering or resolving in the 0.4 mg/kg SC QW group, and one ICANS event had an unknown outcome in the 0.8 mg/kg SC Q2W group.

‖Concurrent CRS considers ICANS events that occurred during or within 7 days of the end date of CRS.

Reference: Chari A, et al. Presented at 64th American Society of Hematology (ASH) Annual Meeting; December 10-13, 2022; New Orleans, LA.

Preparation and Administration

- Talquetamab should be administered via subcutaneous injection only. Use aseptic technique to prepare and administer.
- Talquetamab should be administered by a healthcare provider with adequate medical equipment and personnel to manage severe reactions, including cytokine release syndrome.
- Talquetamab 2 mg/mL vial and talquetamab 40 mg/mL vial are supplied as ready-to-use solution for injection that do not need dilution prior to administration.
- Remove the appropriate strength talquetamab vial(s) from refrigerated storage [2°C to 8°C (36°F to 46°F)] and equilibrate to ambient temperature [15°C to 30°C (59°F to 86°F)] for at least 15 minutes. Do not warm in any other way.
- Once equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake.
- Withdraw the required injection volume of talquetamab 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.
- Talquetamab is compatible with stainless steel injection needles and polypropylene or polycarbonate syringe material.
- Replace the transfer needle with an appropriately sized needle for injection.

Preparation and Administration cont.

- Patients receiving Talquetamab will follow either a weekly or biweekly (every two weeks) treatment schedule.
- Under both the weekly and biweekly dosing schedule, patients will be admitted to the hospital for the priming doses. It is expected that subsequent treatment doses will be administered in an ambulatory care setting.

Recommended Dose of Talquetamab			
Dosing Schedule	Phase	Day	Talquetamab Dose[a]
Weekly Dosing Schedule	Step-up Phase	Day 1	0.01 mg/kg
		Day 3[b]	0.06 mg/kg
		Day 5[b]	0.4 mg/kg
	Treatment Phase	Once a week thereafter[c]	0.4 mg/kg
Biweekly (Every 2 Weeks) Dosing Schedule	Step-up Phase	Day 1	0.01 mg/kg
		Day 3[b]	0.06 mg/kg
		Day 5[b]	0.4 mg/kg
		Day 7[b]	0.8 mg/kg
	Treatment Phase	Once every 2 weeks thereafter[c]	0.8 mg/kg

[a] Based on actual body weight.

[b] Dose 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 adverse reactions.

[c] Maintain a minimum of 6 days between weekly doses and a minimum of 12 days between biweekly (every 2 weeks) doses.

Documentation of Administration

- Talquetamab administration should be documented consistent with the documentation associated with other subcutaneous injections.
- Documentation of administration within the medical record would most commonly be found in the Medication Administration Record (MAR), physician orders, and progress notes.

Summary

- Outcomes are poor for patients who progress after treatment with the three main myeloma drug classes (PIs, IMiDs, and CD38 monoclonal antibodies).
- Existing therapies have limitations including efficacy, safety, and/or access.
- Despite new approved therapies, no standard of care exists for patients with triple, quad or penta-class refractory multiple myeloma.
- Talquetamab received breakthrough therapy designation by the FDA in the review of the product in the treatment of adult patients with relapsed or refractory multiple myeloma and who have received >4 lines of therapy.
- Talquetamab has a unique mechanism of action and is among the first FDA-approved bispecific antibody therapies for multiple myeloma that redirects T-cells via CD3 to GPRC5D-expressing multiple myeloma cells.

1. Janssen announces U.S. FDA Breakthrough Therapy Designation granted for Talquetamab for the treatment of relapsed or refractory multiple myeloma. June 29, 2022 https://www.jnj.com/janssen announces u s fda breakthrough therapy designation granted for talquetamab for the treatment of relapsed or refractory multiple myeloma