Evidence and value summary: TALVEY®

Triple-class exposed relapsed/refractory multiple myeloma (RRMM) current challenges & gaps in care

Low response rates[1,2]

~30%

ORR in patients with TCE RRMM[a,b]

Poor survival rates[1]

3.4 months mPFS
9.3 mOS[a]

Shorter remission[3]

Time to progression decreases by 9 months between 1st-2nd vs 4th-5th LOT[c]

Recycling of therapies[4]

Suboptimal responses from retreatment with same therapies[d]

TALVEY®: first-in-class, GPRC5D-targeting, T-cell redirecting bispecific antibody[5,6]

Indication[5]

TALVEY® (talquetamab) is a bispecific **GPRC5D-directed CD3 T-cell engager** indicated for treatment of adult patients with **RRMM after four or more prior LOTs**, 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[5]

TALVEY is administered via SC injection (weight-based dosing) by a healthcare provider QW or Q2W following the step-up dosing schedule (*Please refer to the dosing tables in the USPI to determine the total volume, dose, and number of vials*)

Pretreatment[e]
Administered 1-3 hours prior to each step-up dose

Step-up dosing*
May be administered 2-4 days after previous dose (up to 7 days if adverse reaction)

Treatment dosing
Two options:
- ***0.4** mg/kg **QW***
- ***0.8** mg/kg **Q2W***

*Patients should be hospitalized for 48 hours after each step-up dose due to risk of CRS and neurologic toxicity, including ICANS

TALVEY®: clinical evidence[5-7]

MonumenTAL-1: A phase 1/2, open-label, single-arm, multicenter study of talquetamab in adult patients with RRMM, who previously received at least 3 prior LOT including a PI, an immunomodulatory agent, and an anti-CD38 mAb

With a median of 6-14 months follow-up, talquetamab demonstrated an ORR of >70% in patients naïve and exposed to TCR[5]

	TCR naïve[f]		TCR exposed[f]			
Dosing	**0.4 mg/kg SC QW**		**0.8 mg/kg SC Q2W**		**0.4 mg/kg SC QW**	**0.4 mg/kg SC QW OR 0.8 mg/kg Q2W**
Reference source	*USPI*[5]	*ASCO 2023*[6,g]	*USPI*[5]	*ASCO 2023*[6,g]	*USPI*[5]	*ASH 2023*[7,h]
Population (n)	100[i] (efficacy analysis population)	143	87[i] (efficacy analysis population)	145	32[j]	70
Median follow-up, mo	13.8	18.8	5.9	12.7	10.4	18.4
Select efficacy						
ORR, %	73	74.1	73.6	71.7	72	67.1
sCR/CR/VGPR, %	26/9/22	23.8/9.8/25.9	20/13/25	29.7/9/22.1	--	32.9/8.6/14.3
Median DOR, mo (95% CI)	9.5 (6.5-NE)	9.5 (6.7-13.3)	NE	NR (13.0-NE)	--	--
12-mo PFS rate, %	--	34.9	--	54.4	--	44.1 (32.1–55.4)
12-mo OS rate, %	--	76.4	--	77.4	--	--

Selected safety profile (N=339)[5]
Please refer to the full Prescribing Information for a complete listing of all adverse events, including serious adverse events.

Boxed Warning: CRS and neurologic toxicities, including ICANS

Any grade CRS: 76%
- *Grade ≥3*: 1.5%
- *Median time to onset:* 27 hours (range, 0.1–167) from the last dose
- *Median duration:* 17 hours (range, 0–622)

Any grade neurologic toxicity, including ICANS: 55%[k]
- *Grade ≥3:* 6%
- *Any grade ICANS*: 9%[l]
- *Median time to ICANS onset:* 2.5 days (range, 1–16) after the most recent dose
- *Median duration of ICANS:* 2 days (range, 1–22)

Other adverse events
- *Oral toxicity:* 80%; Grade 3: 2.1%
- *Weight loss:* 62% (regardless of having an oral toxicity); Grade 2: 29%; Grade 3: 2.7%
- *Serious infections:* 16%; Fatal infections: 1.5%
- *Skin reactions:* 62%; Grade 3: 0.3%

TALVEY®: economic considerations[8]

- Introducing TALVEY® as a treatment option for the indicated population is **associated with a modest budget impact**
- **Usual care is associated with twice the cost per responder** as compared with TALVEY®

TALVEY® future considerations: ongoing clinical trials

MonumenTAL-3[9] (confirmatory trial)
- RRMM
- Tal+Dara SC + dex ± pom vs DPd
- Phase 3 | Recruiting

TRIMM-2[10]
- RRMM
- Dara SC + Tec/Tal ± pom
- Phase 1b | Active not recruiting

RedirecTT-1[11]
- RRMM
- Tal + Tec ± Dara
- Phase 1b/2 | Recruiting

TALVEY®: summary

- Unique MOA (GPRC5D-targeting) addressing unmet needs[5]
- ORR of >70% in patients naïve and exposed to TCR (median follow-up: 6-14 months)[5]
- Flexible dosing[5] (QW or Q2W option after SUD schedule)
- Modest budget impact[8]
- Currently being studied in ongoing clinical trials as potential combination therapy for RRMM[9-11]

For additional information, please see TALVEY® Prescribing Information here.

[a]Retrospective study examining natural history and outcomes of 275 patients with MM refractory to CD38 mAb at 14 US academic institutions (MAMMOTH trial). [b]Prospective, international study detailing the use of real-life standard of care in treatment of TCE patients with RRMM (N=248; LocoMMotion trial). [c]Over a 7-year period. Analysis does not include therapies or indications approved after 2018. [d]Retrospective analysis of data from 34 consecutive patients with RRMM treated with DARA-POM-D at single institute from January 2015 through July 2016. Three cohorts of patients included in the analysis: cohort 1=DARA and POM naïve (n=12); cohort 2=DARA and/or POM refractory (n=22); cohort 3=DARA and POM refractory (sub-cohort of cohort 2: n=12). [e]Pretreatment consists of corticosteroid, antihistamines, and antipyretics. [f]T-cell redirection therapy refers to both CAR-T and bispecific antibody treatment. [g]Data cut-off for ASCO 2023 presentation was January 17, 2023. [h]Data cut off for ASH 2023 presentation: October 11, 2023. [i]Efficacy analysis population of the USPI includes patients who received≥4 prior lines of therapy. [j]Prior TCR population in the USPI only includes patients who had received ≥4 prior LOT at the 0.4 mg/kg weekly dose. [k]Due to potential neurologic toxicity, patients receiving TALVEY® are at risk of depressed level of consciousness and are advised to refrain from driving or operating heavy or potentially dangerous machinery. See USPI for more details. [l]ICANS was reported in 9% of 265 patients where ICANS was collected and who received TALVEY® at the recommended dosages

ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T-cell; CD, cluster of differentiation; CR, complete response; CRS, cytokine release syndrome; Dara, daratumumab; Dex, dexamethasone; DOR, duration of response; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group Performance Status; GPRC5D, G-protein-coupled receptor class C group 5 member D; ICANS, immune effector cell–associated neurotoxicity syndrome; LOT, line of therapy; mAb, monoclonal antibody; mo, month; MOA, mechanism of action; mOS, median overall survival; mPFS, median progression-free survival; NCT, National Clinical Trial; NE, not estimable; NR, not reported; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; Pom, pomalidomide; PR, partial response; Q2W, every 2 weeks; QW, every week; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous; sCR, stringent complete response; SUD, step-up dosing; Tal, talquetamab; Tec, teclistamab; TCE, triple-class exposed; TCR, T-cell redirection therapy; USPI, United States Prescribing Information; VGPR, very good partial response.

1. Gandhi UH, et al. *Leukemia.* 2019;33(9):2266-2275. 2. Mateos MV, et al. *Leukemia.* 2022;36:1371–1376. 3. Bruno AS, et al. *Expert Rev Hematol.* 2020;13(9):1017-1025. 4. Nooka AK, et al. *Cancer.* 2019;125:2991-3000. 5. TALVEY® (talquetamab) [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. 6. Schinke C, et al. Presented at ASCO 2023 annual meeting; June 2-6, 2023. Poster Presentation 8036. 7. Jakubowiak AJ, et al. Presented at ASH annual meeting; December 9–12, 2023. Poster presentation 3377. 8. Talquetamab economic modelling. 9. MonumenTAL-3 NCT05455320. www.clinicaltrials.gov. Accessed March 7, 2024. 10. TRIMM-2 NCT04108195. www.clinicaltrials.gov. Accessed March 7, 2024. 11. RedirecTT-1 NCT04586426. www.clinicaltrials.gov. Accessed March 7, 2024.

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