MYELOMA matters

a podcast series from MMRF MULTIPLE MYELOMA Research Foundation

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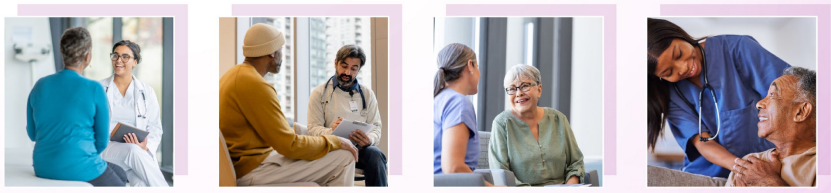

Bispecific Antibody Horizons: Dosing Strategies and Meeting Updates in Myeloma Care

2

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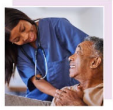

Highlights from ASCO and EHA 2024

Teclistamab

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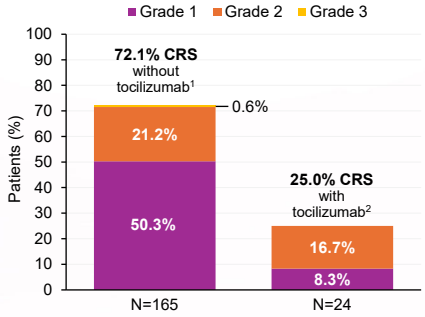
MajesTEC-1 Prophylactic Tocilizumab Cohort: CRS Incidence and Severity



Prophylactic tocilizumab cohort (N=24)[2]			
Characteristic	No CRS (n=18)	CRS Grade 1 (n=2)	CRS Grade 2 (n=4)
BMPCs, % median (range)	8.0 (0–80)	19 (8–30)	62.5 (30–80)
ISS stage, %			
I	72.2	50	50
II	22.2	50	50
III	5.6	0	0
No. of EMPs, median (range)	0 (0–4)	0 (0)	0 (0–2)

- **25% CRS with prophylactic tocilizumab**
  - Grade 1 (n=2), grade 2 (n=4); no grade 3 events
  - All initial events occurred during SUD; 3 recurrent events
  - Median time to onset: 2 days (range, 1–3)
  - Median duration: 2 days (range, 2–4)
  - All events resolved
- **No disease characteristic associated with CRS, consistent with pivotal cohort**
  - Small sample size precludes clinically meaningful conclusions

CRS, cytokine release syndrome; BMPC, bone marrow plasma cell; ISS, International Staging System; EMP, extramedullary plasmacytoma.
1. Martin TG, et al. *Cancer*. 2023;129(13):2035-2046; 2. van de Donk NWCJ et al. ASCO 2024. Abstract 7517.

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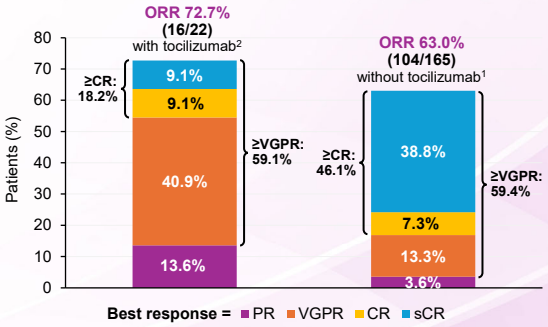
MajesTEC-1 Prophylactic Tocilizumab Cohort: CRS Incidence and Severity

Response to teclistamab (22 of 24 patients evaluable)

- Responses were similar to those seen in the MajesTEC-1 pivotal population[1]
  - The lower ≥CR rate in the prophylactic tocilizumab cohort is likely due to limited availability of bone marrow samples to confirm CR and duration of follow-up
  - At 8.1 months median follow-up, no impact on teclistamab efficacy was observed



1. Garfall AL et al. ASCO 2024. Abstract 7540; 2. van de Donk NWCJ et al. ASCO 2024. Abstract 7517.

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Real-World Less-Frequent Dosing of Teclistamab

- Retrospective observational study of RRMM patients who started treatment with teclistamab
- 86 RRMM patients who received ≥1 Tec dose were included in this analysis
- Median prior LOT was 6; 37% patients received a BCMA-directed therapy before Tec
- Results were reported for overall population and the three subgroups of interest:
  1. Early initiators: patients treated within the first 4 months since commercial Tec was first used
  2. Recent initiators: patients treated with Tec after March 31, 2023
  3. Patients with less-frequent dosing: patients who switched from QW to less-frequent dosing (eg, Q2W)
- In this real-world analysis, patients treated with Tec had multiple high-risk features; despite these disease characteristics, Tec demonstrated comparable ORR to MajesTEC-1
- 94% of patients who switched to less frequent dosing maintained their initial treatment response

Tan CR et al. EHA 2024. Abstract P902

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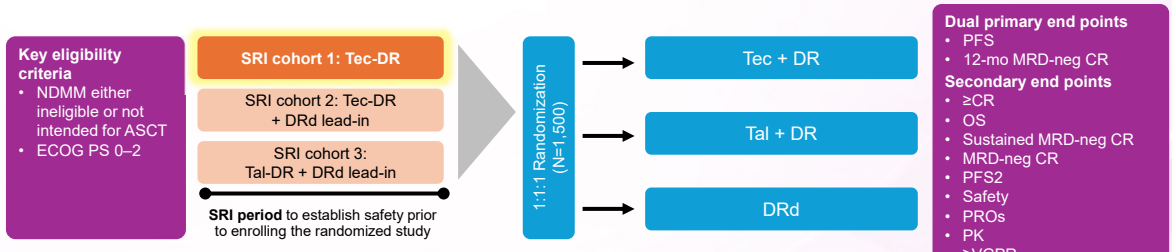
MajesTEC-7 Trial Design



SRI cohort 1: Tec-DR	mFU	Cycle 1	Cycle 2	Cycles 3–6	Cycle 7 + until PD
	13.8 mo (range, 2.0–15.4)	Tec step-up + D	Tec 1.5 mg/kg QW + DR	Tec 3 mg/kg Q2W + DR	Tec 3 mg/kg Q4W + DR

Touzeau C et al. ASCO 2024. Abstract 7506.

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MajesTEC-7 (Tec-DR) SRI Cohort 1: *Safety*

At median follow-up of 13.8 months

- 61.5% of patients had CRS, occurring mostly in cycle 1, and all cases resolved
  - Grade 1: 57.7%
  - Grade 2: 3.8%
- One case of ICANS (grade 1) in cycle 1 that resolved

26 patients received tec-DR with median of 15 cycles (range, 2–17); 23/26 (88.5%) remained on treatment

- Median relative dose intensity
  - Tec: 97.0%
  - Dara: 95.8%
  - Len: 58.6% (17 patients dose reduced)

TEAE, n (%)	SRI cohort 1 (N=26)	
	Any grade	Grade 3/4
Any TEAE	100.0	92.3
Hematologic AEs, n (%)	84.6	65.4
Neutropenia	57.7	57.7
Anemia	30.8	3.8
Thrombocytopenia	15.4	15.4
Febrile neutropenia	11.5	11.5
Eosinophilia	11.5	0
Nonhematologic AEs, n (%)		
Diarrhea	69.2	3.8
CRS	61.5	0
Cough	53.8	0
Dysgeusia	38.5	N/A
Constipation	34.6	0
Injection site erythema	34.6	0
Nausea	30.8	0
COVID-19	30.8	11.5
Muscle spasms	30.8	0
Bronchitis	26.9	0
URTI	26.9	3.8

Touzeau C et al. ASCO 2024. Abstract 7506.

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MajesTEC-7 (Tec-DR) SRI Cohort 1: *Infections*

TEAE, n (%)	SRI cohort 1 (N=26)	
	Any grade	Grade 3/4
Infections*	100	30.8
COVID-19	30.8	11.5
Bronchitis	26.9	0
URTI	26.9	3.8
Rhinitis	23.1	0
Pneumonia	11.5	3.8
Influenza pneumonia	3.8	3.8
Pneumonia pneumococcal	3.8	3.8
Pneumonia viral	3.8	3.8
Staphylococcal sepsis	3.8	3.8

*All-grade infections in ≥20% or grade 3/4 infections in ≥1 patient.
Touzeau C et al. ASCO 2024. Abstract 7506.

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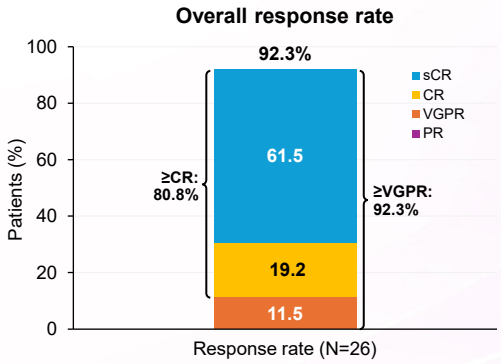
MajesTEC-7 (Tec-DR) SRI Cohort 1: *Efficacy*



- 92.3% ORR (80.8% ≥CR); all responses were ≥VGPR
- No disease progressions

CR, complete response; DR, daratumumab and lenalidomide; ORR, overall response rate; PR, partial response; sCR, stringent complete response; SRI, safety run-in; tec, teclistamab; VGRP, very good partial response.

Touzeau C et al. ASCO 2024. Abstract 7506.

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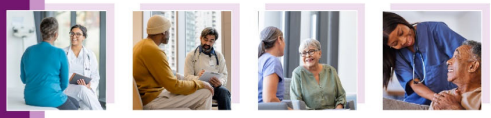

Highlights from ASCO and EHA 2024

Elranatamab

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Long-Term Survival After Elranatamab Monotherapy in RRMM Patients: MagnetisMM-3

- 123 BCMA-naïve RRMM patients were treated with elranatamab
  - 32% had extramedullary disease; 15% had high-risk disease
- Elranatamab continued to demonstrate deep and durable responses in heavily pretreated (median 5 prior LOTs; 96.7%, TCR), BCMA-naïve RRMM patients
  - MRD negativity rate was 90.3% in evaluable patients with ≥CR
  - Median PFS was 17.2 months
  - Median OS was 24.6 months
- No new safety signals were observed. Although longer follow-up is needed, few SPMs were seen (<5%; all squamous cell carcinomas)
  - No hematologic SPMs were reported

SPM, secondary primary malignancy; TCR, triple-class refractory.
Mohty M et al. EHA 2024. Abstract P932.

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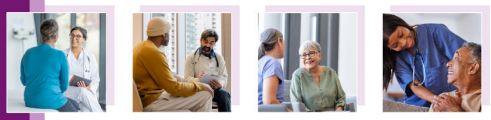

Highlights from ASCO and EHA 2024

Linvoseltamab and ABBV-383

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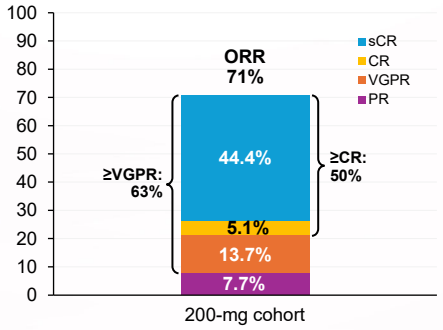
LINKER-MM1: Linvoseltamab Response Rates



- Median duration of follow-up for the 117 patients was 14.3 months*
- ORR was 71%, with 50% of patients achieving CR or better
  - Median DOR was 29.4 months; estimated DOR at 12 months: 81%
  - Median PFS was NR; estimated PFS at 12 months: 70%
  - Median OS was 31.4 months; estimated OS at 12 months: 75%

*phase 1: 12 patients; phase 2: 105 patients

CI, confidence interval; CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; NE, not evaluable; NR, not reached; ORR, overall response rate; PFS, progression-free survival; TEAE, treatment-emergent adverse event.

Lentzsch S et al. EHA 2024. Abstract S212.

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LINKER-MM1: Linvoseltamab Adverse Events

TEAEs, n (%)	Any grade	Grade 3–4
Number of patients with TEAE	100.0	73.5
Hematologic TEAEs		
Neutropenia*	42.7	41.9
Anemia*	38.5	30.8
Non-hematologic TEAEs		
CRS	46.2	0.9
Diarrhea	37.6	1.7
Cough	36.8	0
Fatigue	33.3	0
Arthralgia	29.9	0
Hypokalemia*	24.8	3.4
Headache*	23.1	0.9
Nausea	23.1	0
COVID-19*	22.2	9.4
Back pain	20.5	2.6
Dyspnea	20.5	0.9

*Composite terms.

- Median exposure to treatment (200 mg) was 53.0 weeks (range 1.0–167.0)
- The most common TEAEs were CRS, neutropenia, and anemia
- ICANS occurred in 9 patients (7.7%; 2.6% for each grade 1, 2, and 3); all events were concurrent with CRS or IRRs
- TEAEs that led to death within 30 days of the last treatment dose were reported in 6 patients (5.1%), 5 due to infection, and 1 due to renal failure

TEAE, treatment-emergent adverse event.

Lentzsch S et al. EHA 2024. Abstract S212.

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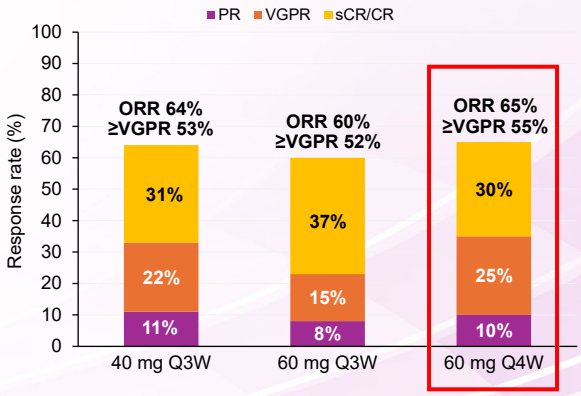
ABBV-383 Adverse Events and Response Rates

n (%)	Q4W 60 mg n=21	
	Any grade	Grade 3/4
Any TEAE	100	86
Hematologic		
Neutropenia	57	29
Anemia	62	29
Thrombocytopenia	43	19
Lymphopenia	52	43
Nonhematologic		
CRS	43	0
Fatigue	38	0
Diarrhea	33	0
Nausea	19	0
Cough	38	0
Vomiting	5	0
Pyrexia	14	0



CRS, cytokine release syndrome; Q3W, every 3 weeks; Q4W, every 4 weeks; TEAE, treatment-emergent adverse event.
Weisel K et al. EHA 2024. Abstract S211.

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Key Points

- Prophylactic tocilizumab may help mitigate frequency of CRS with teclistamab and elranatamab
- Real-world data from less-frequent dosing of teclistamab showed similar ORRs to clinical trials
- Combination of bispecific with standard myeloma treatment looks promising
- Early-phase trials of investigational BCMA-directed antibodies show promising results
- Phase 3 trials of emerging bispecifics are ongoing or planned

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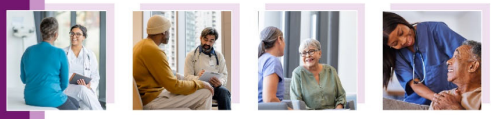

GPRC5D-Directed Bispecific Antibody Therapy: Highlights From ASCO and EHA 2024

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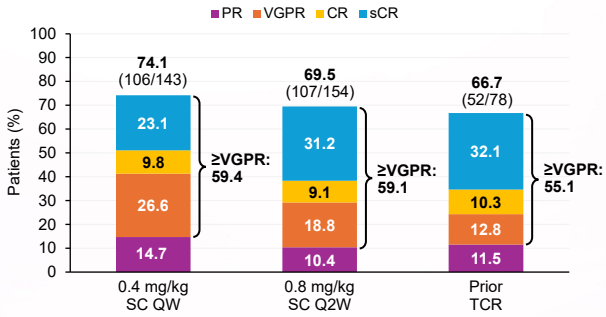
Talquetamab Response Rates and Adverse Events



	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
mPFS, mo	7.5	11.2	7.7

Any grade adverse events, %	0.4 mg/kg SC QW (n=143)	0.8 mg/kg SC Q2W (n=154)	Prior TCR (n=78)
Taste related*	72	71	76
Skin related*	57	73	64
Nail related	55	53	59
Rash related	40	30	32

*Composite terms.

Rasche L et al. EHA 2024. Abstract P915.

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GPRC5D-Associated Adverse Events

Affected area	Symptoms and effects	Management
Oral	• Taste changes • Difficulty swallowing • Dry mouth	• Can lead to weight loss • Most successfully managed with dose modification • Supportive measures may be used (eg, NaCl mouth rinse, artificial saliva spray, diet modification)
Skin	• Rash • Skin peeling	Relatively benign, not painful, self-limiting, and manageable with emollients
Nails	• Nail thinning and loss	Mostly aesthetic but takes time to resolve

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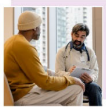

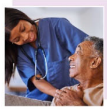

Highlights from ASCO and EHA 2024

Infectious Complications with Bispecific Antibodies

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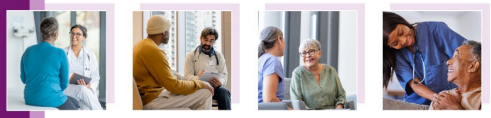
Infectious Complications With BCMA- and GPRC5D-Directed Bispecifics or CAR T-cell Therapy

- In this retrospective analysis, Mersi and colleagues evaluated infectious complications of any grade in 137 patients treated with either BCMA-, GPRC5D-directed bsAbs or CAR T-cell therapy
- Of these
  - 58 patients received CAR T
  - 47 received BCMA-targeted bsAbs
  - 32 received GPRC5D-targeted bsAbs
- Most patients experienced infectious complications while being treated with these novel immunotherapies
  - The rates were 76% for CAR-T therapy, 85% for BCMA- and 59% for GPRC5D-targeting bsAbs
  - Across all groups, viral infections of the respiratory tract were predominant
  - With BCMA bsAbs, on average, infectious complications occurred every 5th day
  - With GPRC5D bsAbs, on average, infectious complications occurred every 11th day

Mersi J et al. EHA 2024. Abstract P948.

23



Highlights from ASCO and EHA 2024

Cevostamab

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Cevostamab Adverse Event Summary

Key inclusion criteria

- RRMM
- Triple-class refractory
- Prior BCMA-targeted ADC or CAR T-cell therapy
- Prior BCMA-targeted bispecific antibodies not permitted
- ECOG PS 0–1

%, unless stated	Prior ADC (n=10)	Prior CAR-T (n=11)	All (N=21)
Grade 3–4 hematological AEs			
Anemia	40	18	29
Neutropenia	30	55	43
Thrombocytopenia	20	18	19
Any CRS	90	55	71
Gr 1	40	9	24
Gr 2	50	46	48
Any ICANS	20	9	14
Gr 1	10	9	10
Gr 4	10	0	5

Infections:
- Any AE: 12 patients (57%)
- Grade 3: 5 patients (24%)
- No Grade 4+
- Mainly respiratory tract infections

No rare pathogens or OIs
- Viral: 31%, including 4 COVID cases
- Bacterial: 35%
- Unknown pathogen: 35%

Kumar S et al. EHA 2024. Abstract S210.

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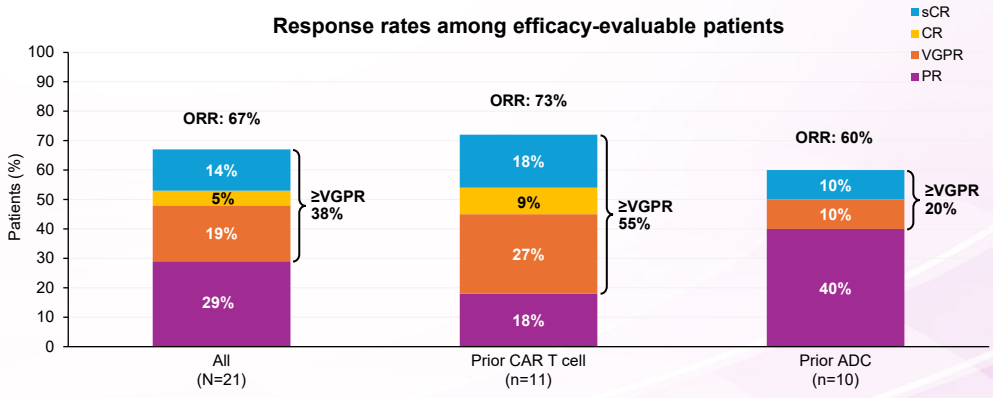
Cevostamab Response Rates



At data cutoff, with a median follow-up of 11 (range: 2–16) months, 6/14 responders were still in response.

CI, confidence interval; CR, complete response; PR, partial response; sCR, stringent complete response; VGPR, very good partial response
Kumar S et al. EHA 2024. Abstract S210.

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Key Points

- Long-term efficacy and safety of talquetamab confirmed
- Infectious complications with bispecific antibodies are frequent but typically low grade
  - Infections more common with BCMA-directed bispecific antibody therapy
- Early-phase trial of cevostamab, an investigational FcRH5-directed bispecific antibody, shows promising results

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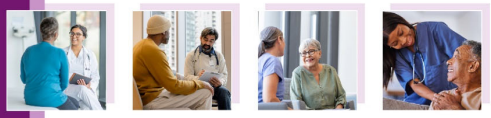

Optimizing the Use of BCMA-Directed Bispecific Antibody Therapy

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- 72-yr-old woman with high-risk MM; PS of 2 at most recent progression
  - 1q21 amplification (2 extra copies), del(17q)
- Treatment history
  - D-Rd, no ASCT; R maintenance: best response was VGPR with DOR of 1.5 year
  - XVd DOR 1 yr
  - D-Pd: best response was PR with DOR of 9 months
  - KCd: best response was PR with DOR of 3 months and aggressive relapse (CAR T has not been planned)
- Consider BCMA-directed bispecific

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Elranatamab Dosing Schedule

Dosing schedule	Day	Dose	
Step-up dosing schedule* (48-hour hospitalization after first step-up dose; 24-hour after second step-up dose)	1	Step-up dose 1	12 mg
	4	Step-up dose 2	32 mg
	8	First treatment dose	76 mg
Weekly dosing schedule	1 week after first treatment dose and weekly thereafter through week 24	Subsequent treatment doses	76 mg
Biweekly dosing schedule	Week 25 and every 2 weeks thereafter	Subsequent treatment doses	76 mg

*A minimum of 2 days should be maintained between step-up doses.

ELREXFIO (elranatamab) prescribing information. Pfizer. Revised 8/2023.

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Teclistamab Dosing Schedule

Dosing schedule	Day	Dose	
Step-up dosing schedule (48-hour hospitalization after each step-up dose)	1	Step-up dose 1	0.06 mg/kg
	4	Step-up dose 2	0.3 mg/kg
	7	First treatment dose	1.5 mg/kg
Weekly dosing schedule	1 week after first treatment dose and weekly thereafter	Subsequent treatment doses	1.5 mg/kg once weekly
Biweekly dosing schedule	**For patients with RRMM who have achieved and maintained ≥CR for a minimum of 6 months:** Reduce dosing to 1.5 mg/kg every 2 weeks		

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 any adverse reactions.

TECVAYLI (teclistamab) prescribing information. Janssen Biotech. Revised 5/2024.

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Safety Experience with Approved BCMA Bispecifics

Elranatamab AEs of Interest[1,2]	Teclistamab AEs of Interest[3]
Infections All grade: 70% Grade 3/4: 47%	**Infections** All grade: 78% Grade 3/4: 52%
CRS All grade: 70% No grade 3/4 CRS 90.6% of CRS events occurred with the step-up doses	**CRS** All grade: 72% Only 0.6% of CRS was Grade 3 No grade 4/5 CRS
ICANS 4.9%	**ICANS** 3%

1. Lesokhin A et al. Nat Med. 2023;29:2259-2267; 2. Tomasson M et al. ASH 2023. Abstract 3385; 3. van de Donk N et al. ASCO 2023. Abstract.8011.

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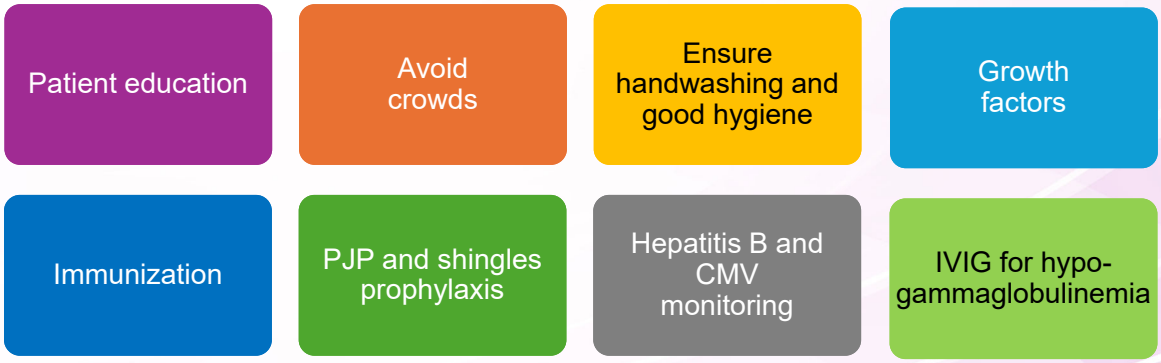
Infection Prevention and Management



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Key Points

- Bispecific antibodies as monotherapy are efficacious in RRMM
  - Early, deep, and durable responses for an off-the-shelf therapy
- Overall management strategy may help mitigate CRS and ICANS
  - Events are mostly low grade
- Vigilant monitoring, prophylaxis, and treatment can help mitigate risk of infections
  - Prophylactic antibiotics and antivirals are a must during the entire time of treatment
  - IVIG replacement is strongly encouraged for all patients

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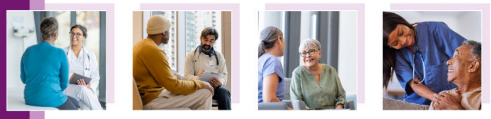

Optimizing the Use of GPRC5D-Directed Bispecific Antibody Therapy

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- 74-yr-old man with MM; PS of 1 at most recent progression
- Treatment history:
  - VRd, ASCT; R maintenance: best response was VGPR with DOR of 3.5 years
  - D-Pd: best response was VGPR with DOR of 18 months
  - KCd: best response was PR with DOR of 12 months
  - Xd: best response was PR with DOR of 4 months
  - BCMA-directed CAR-T: progression after 1 year
- Consider GPCR5D-directed bispecific antibody therapy

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GPRC5D-Associated Adverse Events

AEs of interest[1,2]	Overall (all- grade)	Comments
Skin-related events	~70%	Monitor for skin toxicity, including rash progression, for early intervention and treat appropriately
Nail-related events	~30-60%	Monitor for nail-bed disorder, discoloration, disorders, dystrophy, hypertrophy, ridging, onycholysis, and onychomadesis
Dysgeusia	~60%	Monitor for oral toxicity and weight loss; withhold or discontinue based on severity
CRS	~80%	One CRS event grade ≥3 in MonumenTAL-1
Infections	~30-50%	No CMV reactivation in MonumenTAL-1
Other considerations[2] • Monitor CBC • Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated		

1. Chari A et al. *N Engl J Med*. 2022;387:2232.; 2. TALVEY (talquetamab) prescribing information. Janssen Biotech. Revised 8/2023.

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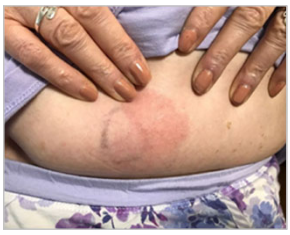
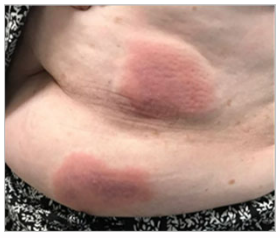
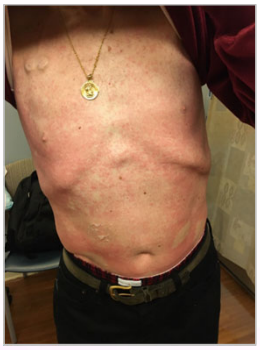
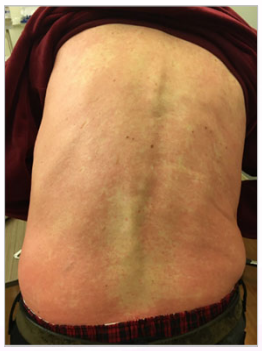
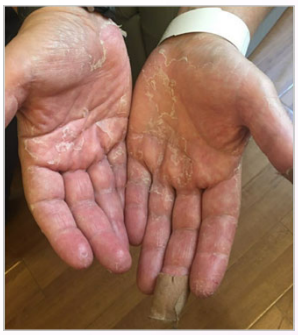
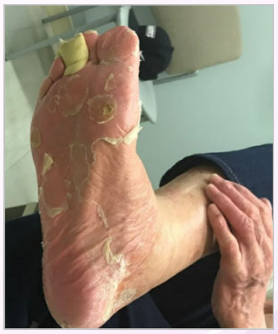

Products applied twice daily
- Ammonium lactate 12% cream
- Triamcinolone 0.1% cream
- Emollients
- Oral antihistamines as needed

Images courtesy of Dr. Ajai Chari.

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- Starts ~C2, lasts for months
- Avoid frequent/long durations of water immersion
- Frequent application of emollients (Vaseline, Aquaphor)
- Vitamin E oil
- File to smooth the edges and corners of the nail plates
- Clear nail polish or nail hardeners
- Biotin supplements may be helpful

Images courtesy of Dr. Ajai Chari.

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Management of Dysgeusia and Xerostomia

Dysgeusia management

- Dose modifications, including reductions, delays, or skips were the most effective management strategy for dysgeusia
- Nutritional monitoring, such as for iron deficiencies, should be undertaken with appropriate supplementation
- High-caloric shakes should be considered to ensure adequate nutritional intake and to prevent weight loss due to dysgeusia or other oral events

Xerostomia management

- Dry mouth can be managed with increased hydration (sipping water throughout the day) and intraoral topical agents, such as topical saliva sprays or sugar-free chewing gum, to stimulate saliva flow
- Sodium lauryl sulfate–free toothpastes may be better tolerated than other toothpastes

Early referral to a dietician or nutritionist at the onset of therapy should be encouraged to provide guidance on maintaining a balanced diet and weight, irrespective of the presence of oral events.

Chari A et al. *Clin Lymph Myeloma Leuk*. 2024. Epub ahead of print.

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Talquetamab Dosing Schedule

Weekly			
Dosing schedule	**Day**	**Dose[a]**	
Step-up dosing schedule	1	Step-up dose 1	0.01 mg/kg
	4[b]	Step-up dose 2	0.06 mg/kg
	7[b]	First treatment dose	0.4 mg/kg
Weekly dosing schedule	1 week after first treatment dose and weekly thereafter[c]	Subsequent treatment doses	0.4 mg/kg once weekly
Biweekly (every 2 weeks)			
Dosing schedule	**Day**	**Dose[a]**	
Step-up dosing schedule	1	Step-up dose 1	0.01 mg/kg
	4[b]	Step-up dose 2	0.06 mg/kg
	7[b]	Step-up dose 3	0.4 mg/kg
	10[d]	First treatment dose	0.8 mg/kg
Biweekly dosing schedule	Biweekly after first treatment dose and thereafter[e]	Subsequent treatment doses	0.8 mg/kg biweekly

Additional Dosing Principles

[a]Based on actual body weight.

[b]Dose may be administered between 2-4 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.

[d]Dose may be administered between 2-7 days after step-up dose 3.

[e]Maintain a minimum of 12 days between biweekly doses.

TALVEY (talquetamab) prescribing information. Janssen Biotech. Revised 8/2023

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Key Take-Home Points

- Important to educate patients to be their own advocates and know what to look for and how to best reach the health care team
- Prepare patients for possibility of off-tumor, on-target effects of talquetamab
  - Patients who know these are common are usually able to cope much better

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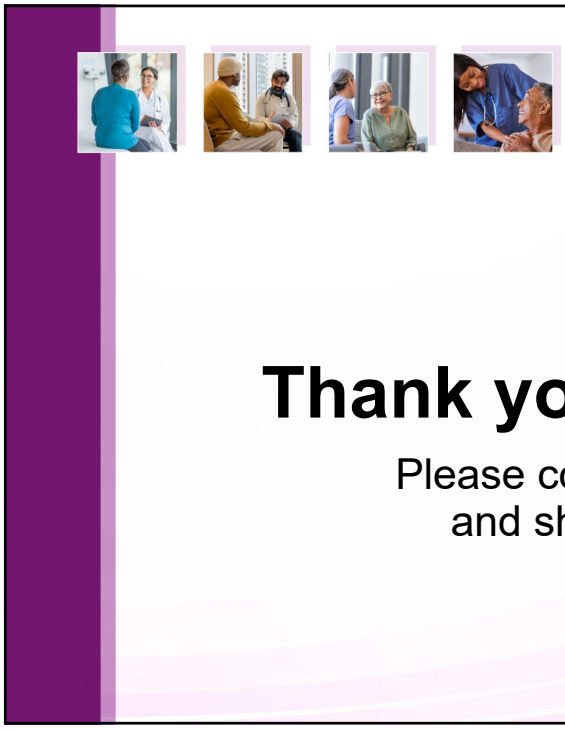
Thank you for joining us!
Please complete the evaluation
and share your feedback.

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