CHAMPIONING MEDICALLY INTEGRATED ONCOLOGY:

Celebrating a Decade of Impact

2025 NCODA INTERNATIONAL FALL SUMMIT

Myeloma:
From Current to Cutting Edge

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Championing Medically Integrated Oncology: CELEBRATING A DECADE OF IMPACT

OBJECTIVES

1. Discuss the role of quadruplet therapy in transplant-eligible and transplant-ineligible multiple myeloma and identify appropriate use in the frontline setting

2. Review chimeric antigen receptor (CAR) T-cell therapies' use in relapsed/refractory multiple myeloma

3. Summarize the role of BCMA-targeting bispecific antibodies in the management of relapsed/refractory multiple myeloma

4. Determine an evidence-based treatment plan for relapsed/refractory multiple myeloma with available sequencing data

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DISCLOSURES

There are no relevant conflicts of interest to disclose for this presentation for the following speakers and planners:

- Jordan Snyder, PharmD, BCOP
- Tahsin Imam, PharmD
- Shawnny Eugene, PharmD

Multiple Myeloma

- Multiple myeloma is characterized by the abnormal proliferation of malignant plasma cells
- Accounts for 1% of all cancer diagnosis and 10% of all hematologic malignancies
- Median age at diagnosis is 65 years
- Occurs more commonly in men and African Americans
- Cause of nearly 13,000 deaths in the United States each year

Rajkumar S. *Am J Hematol*. 2024;99:1802-24.

Plasma Cell Disorder Spectrum

Monoclonal Gammopathy of Undetermined Significance (MGUS)	Smoldering Myeloma	Multiple Myeloma
• Asymptomatic • Increases risk of developing multiple myeloma at ~1% per year	• Asymptomatic • Increases risk of developing multiple myeloma at ~10% per year	• Rate of progression depends on cytogenetics and development of new mutations

Nieto MJ, et al. *J Clin Haematol.* 2023;4(1):35-42.

Quad Therapy in Newly Diagnosed Myeloma

Doublets to Triplets

Trial	Population	Intervention	Outcomes	Impact
VISTA (2010)	NDMM, transplant ineligible (N=682)	VMP vs MP	•35% reduced risk of death at 3 years (HR 0.653, P<0.001) •3-year OS: 68.5% vs 54%	Addition of bortezomib significantly prolongs survival
GIMEMA-MMY-3006 (2012)	NDMM, transplant eligible (N=474)	VTD vs TD	•Median PFS: 60 months vs 41 months •10-year survival estimate: 34% vs 17%	Addition of bortezomib into double HSCT improved PFS and OS
SWOG S0777 (2017)	NDMM, without immediate HSCT (N=525)	VRD vs RD	•Median PFS: 43 mo vs 30 mo (HR 0.712, 95% CI 0.56-0.906; P=0.0018) •Median OS: 75 mo vs 64 mo (HR 0.709; 95% CI 0.524-0.959; P=0.025)	Triplet therapy became standard of care in NDMM

V: bortezomib; M: melphalan; P: prednisone; T: thalidomide; D: dexamethasone; R: lenalidomide; IMID: immunomodulator; mo: months, HR: hazard ratio, CI: confidence interval, PFS: progression free survival, OS: overall survival

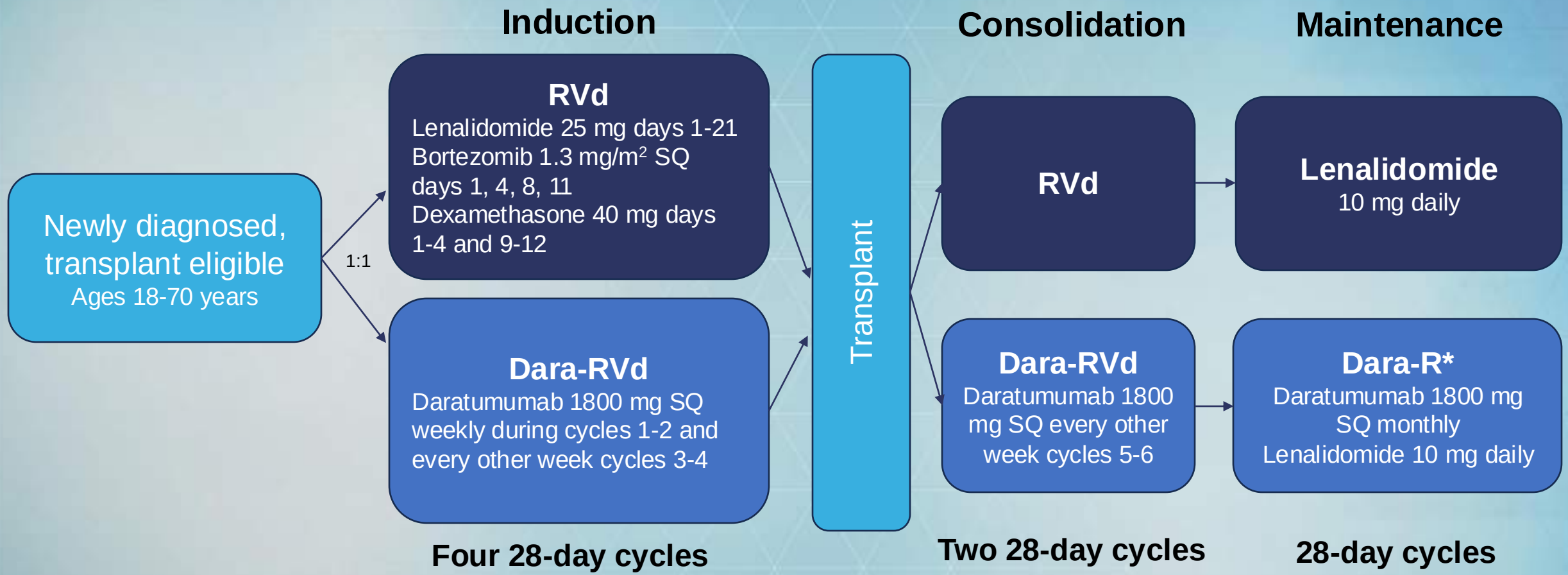
Mateos MV, et al. *J Clin Oncol*. 2010;28(13):2259-2266.; Tacchetti P, et al. *Lancet Haematol.* 2020;7(12):e861-e873. ; Durie BG, et al. *The Lancet*. 2017;389(10068):519-527.

Quad Therapies in Transplant Eligible

Trial	Population	Intervention	Outcomes	Impact
CASSIOPEIA (2019)	NDMM, transplant eligible (N=1085)	DaraVTD vs VTD with post HSCT consolidation and maintenance	•sCR at day 100: 29% vs 20% •Median PFS: NR in either group	Clinical benefits seen in induction, consolidation, and maintenance Less impact in US as RVD considered superior to VTD
GRIFFIN (2020)	NDMM, transplant eligible (N=207)	DaraRVD vs RVD with post HSCT consolidation and maintenance with DaraR or R	•ORR post-consolidation: 99% vs 91.8% (P=0.016) •4-year PFS: 87.2% vs 70% (HR 0.45; 95% CI 0.21-0.95; P=0.032) •Median OS: NR for both groups	Addition of dara to RVD resulted in higher response rates with deepening responses over time

Moreau P, et al. *Lancet*. 2019;394:29-38.; Moreau P, et al. *Lancet Oncol.* 2024;25(8):1003-1014.; Voorhees PM, et al. *Blood*. 2020;136(8):936-945.; Voorhees PM, et al. *Lancet Oncol*. 2023;10(10):E825-E837.

PERSEUS



*If MRD (-) at 24 months, daratumumab was discontinued

Sonneveld P, et al. *NEJM*. 2024;390:301-313.

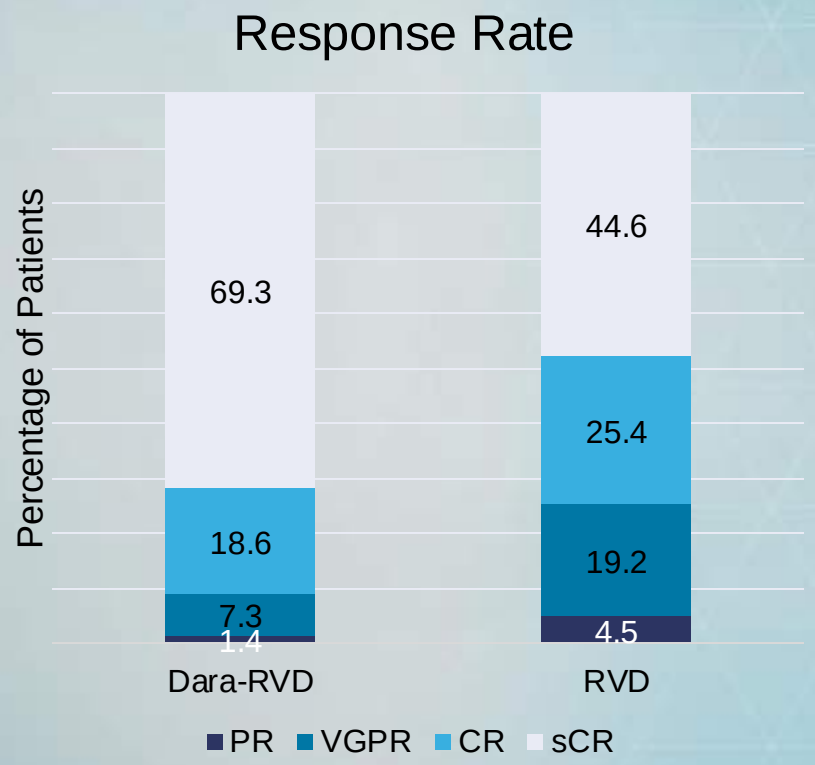
PERSEUS – Patient Demographics

Baseline Characteristics	DaraRVd (n=355)	RVd (n=354)
Median Age, years (range)	61 (32-70)	59 (31-70)
Male, n (%)	211 (59.4)	205 (57.9)
Race, n (%) • White • Black	 330 (93) 5 (1.4)	 323 (91.2) 4 (1.1)
ECOG PS, n (%) • 0-1	 335 (94.3)	 338 (95.4)
Cytogenetic Risk, n (%) • Standard • High	 264 (74.4) 76 (21.4)	 266 (75.1) 78 (22)
Median time since diagnosis, months	1.2	1.1

PS: performance status

Sonneveld P, et al. *NEJM*. 2024;390:301-313.

PERSEUS – Results



	Dara-RVd (n=355)	RVd (n=354)
Overall Response, n (%)	343 (96.6)	332 (93.8)
MRD (-) Status, n (%) • 10^{-5} • 10^{-6}	 267 (75.2) 231 (65.1)	 168 (47.5) 114 (32.2)
Sustained MRD (-) for ≥ 12 months, n (%)	230 (64.8)	105 (29.7)
PFS at 48 months, % (95% CI)	84.3 (79.5-88.1)	67.7 (62.2-72.6)

PR: partial response, VGPR: very good partial response, CR: complete response; sCR: stringent complete response, MRD: minimal residual disease, PFS: progression free survival, CI: confidence interval

Slightly higher rates of adverse events in Dara-RVD arm vs. RVD arm including: cytopenias, infection, diarrhea, and infusion reactions

Sonneveld P, et al. *NEJM*. 2024;390:301-313.

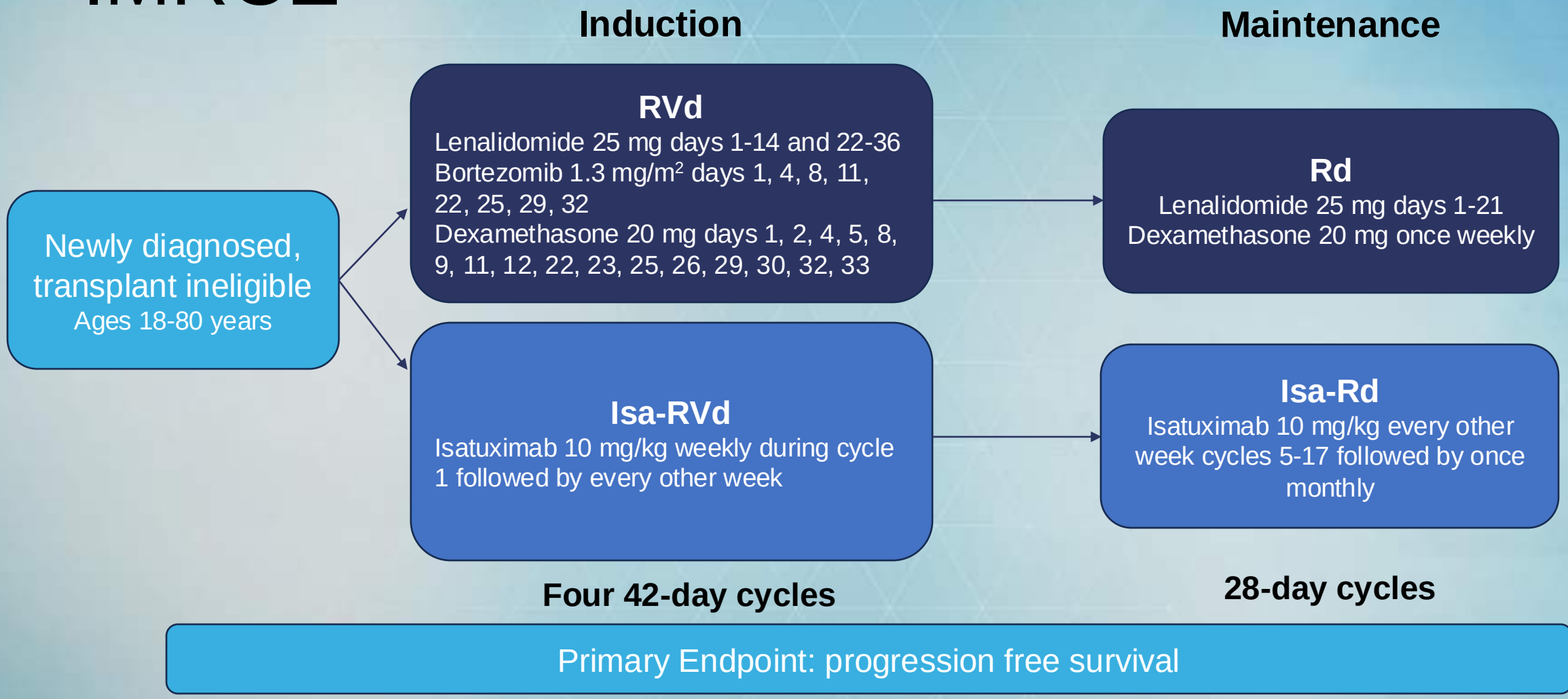
Quad Therapy in Transplant-Ineligible

Trial	Population	Intervention	Outcomes	Impact
ALCYONE (2018)	NDMM, transplant ineligible (N=706)	DaraVMP vs VMP	• 18-month PFS: 71.6% vs 50.2% (HR 0.5; 95% CI 0.38-0.65; p<0.001) • ORR: 90.9% vs 73.9% (p<0.001)	Consideration for quad therapy growing Less impact in US as VRD considered superior to VMP

NDMM: newly diagnosed multiple myeloma, V: bortezomib, M: melphalan, P: prednisone, PFS: progression free survival, CI: confidence interval, ORR: overall response rate, R: lenalidomide

Mateos MV, et al. *NEJM*. 2018;378:518-528

IMROZ



Facon T, et al. *NEJM*. 2024; DOI:10.1056/NEJMoa2400712

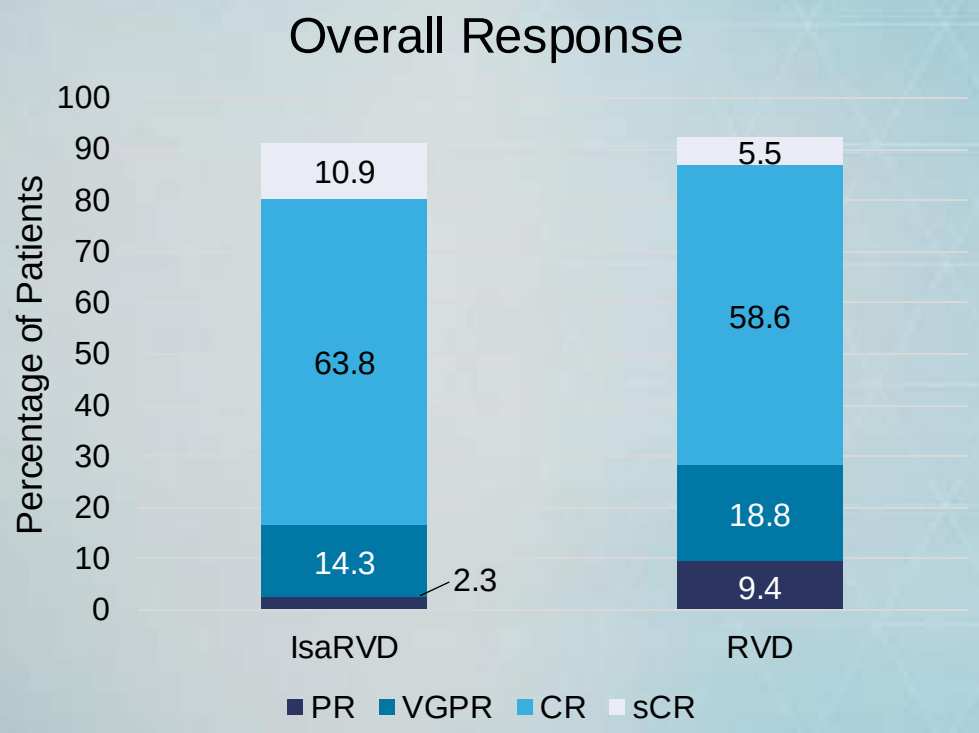
IMROZ – Patient Demographics

Baseline Characteristic	IsaRVd (n=265)	RVd (n=181)
Median Age, years (range)	72 (60-80)	72 (55-80)
Male, n (%)	143 (54)	94 (51.9)
Race • White • Black	 192 (72.5) 2 (0.8)	 131 (72.4) 2 (1.1)
ECOG PS • 0 - 1	 235 (88.7)	 162 (89.5)
Cytogenetic Risk • Standard • High	 207 (78.1) 40 (15.1)	 140 (77.3) 34 (18.8)
Median time since diagnosis, months	1.2	1.2

PS: performance status

Facon T, et al. *NEJM*. 2024; DOI:10.1056/NEJMoa2400712

IMROZ – Results



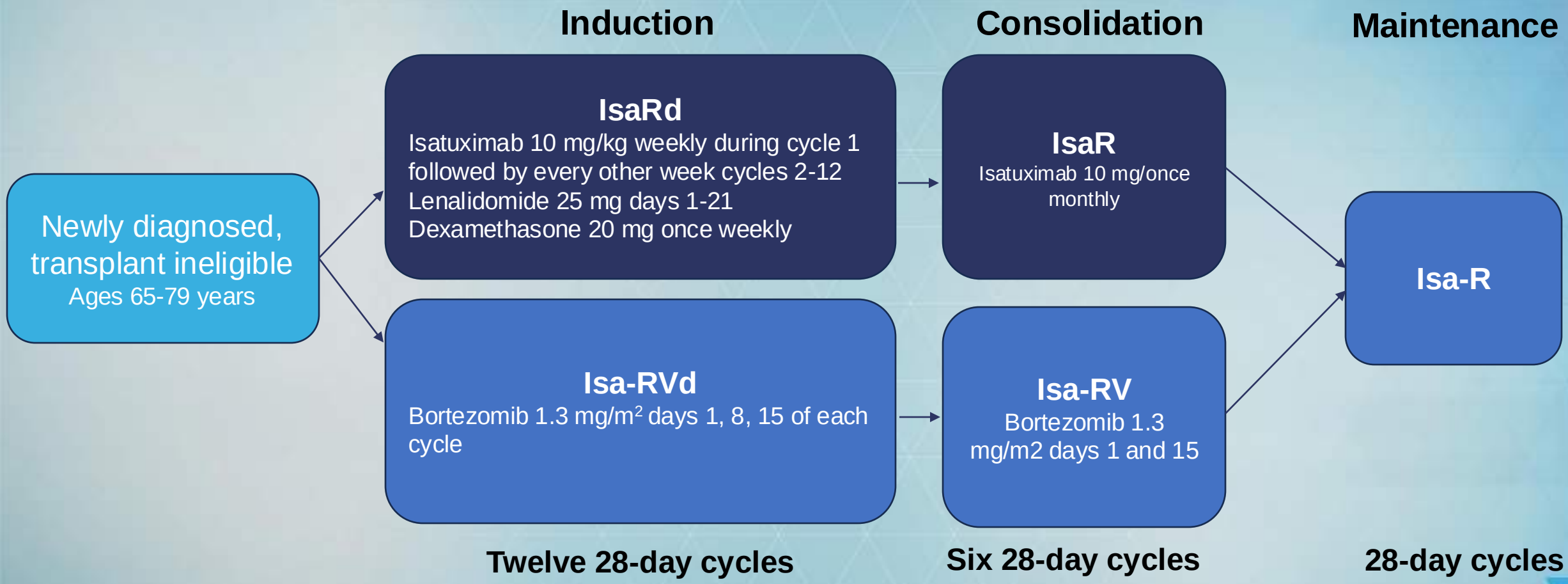
	IsaRVd (n=265)	RVd (n=181)
ORR, %	91.3	92.3
CR or better, %	74.7	64.1
60-month PFS, %	63.2	45.2
MRD- 10^{-5}, %	58.1	43.6
Estimated OS at 60 months, %	72.3	66.3

PR: partial response, VGPR: very good partial response, CR: complete response; sCR: stringent complete response, ORR: overall response rate, MRD: minimal residual disease, PFS: progression free survival, OS: overall survival

Slightly higher rates of adverse events with IsaRVd despite higher rates of discontinuation with RVd

Facon T, et al. *NEJM*. 2024; DOI:10.1056/NEJMoa2400712

BENEFIT



Leleu X, et al. *Nature Med*. 2024;30:2235-2241.

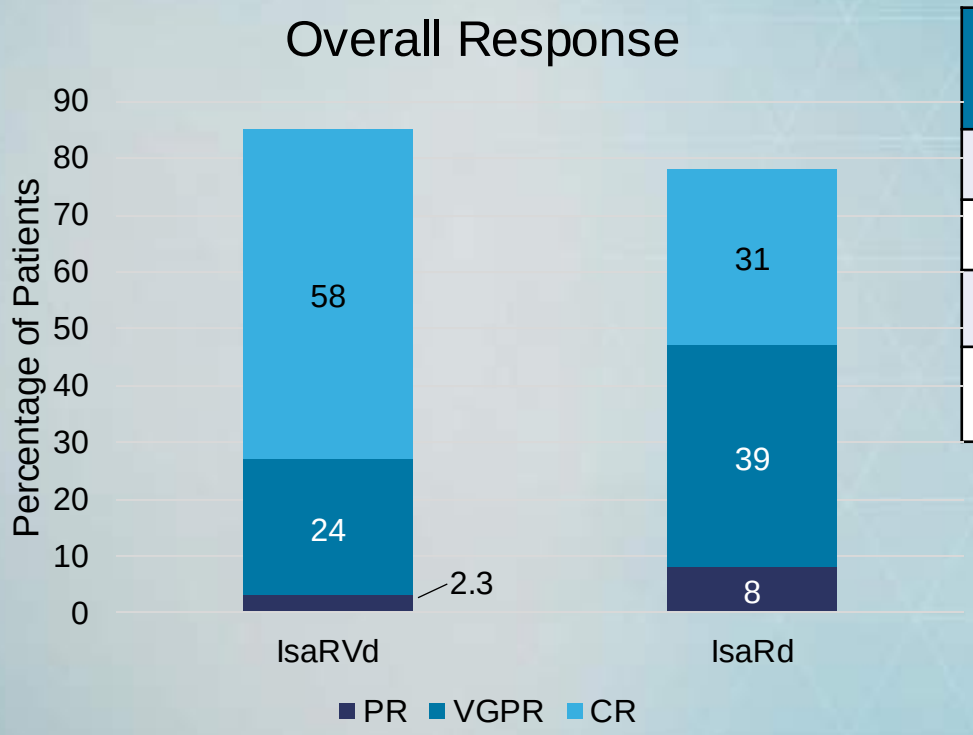
BENEFIT – Patient Demographics

Baseline Characteristic	IsaRVd (n=135)	IsaRd (n=135)
Median Age, years (IQR)	73.2 (71-76)	73.6 (71-76)
Male, n (%)	74 (55)	71 (53)
ECOG PS, n (%) • 0 or 1	 125 (93)	 119 (88)
Cytogenetic Risk, n (%) • Standard • High	 68 (53) 13 (10)	 75 (60) 10 (8)
Median time from diagnosis, months	1	0.9

PS: performance status

Leleu X, et al. *Nature Med*. 2024;30:2235-2241.

BENEFIT – Results



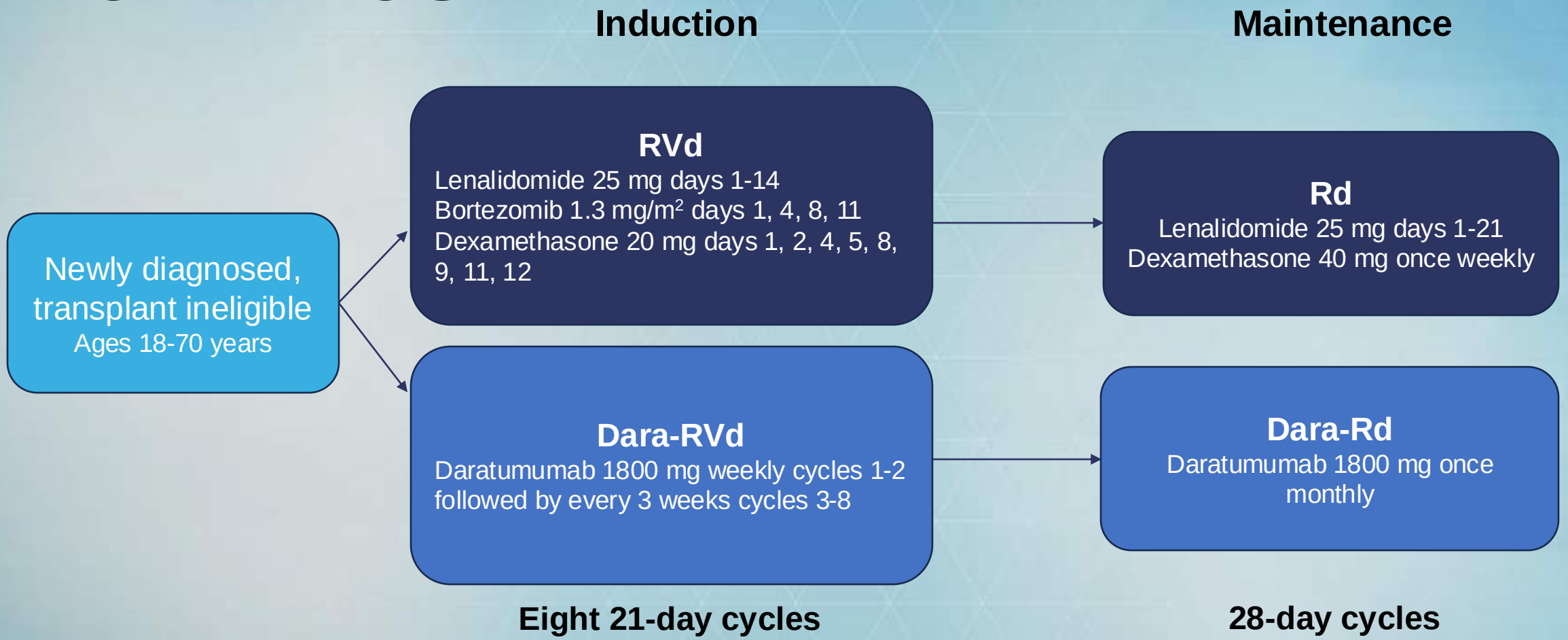
	IsaRVd (n=135)	IsaRd (n=135)
ORR, %	85	78
CR or better, %	58	31
24-month PFS, % (95% CI)	85.2 (79.2-91.7)	91.5 (86.5-96.8)
24-month OS, % (95% CI)	91.1 (86.1- 96.4)	80.0 (73.3- 87.4)

PR: partial response, VGPR: very good partial response, CR: complete response, ORR: overall response rate, PFS: progression free survival, CI: confidence interval, OS: overall survival

Slightly higher rates of adverse events with IsaRVd versus IsaRd including high rates of peripheral neuropathy

Leleu X, et al. *Nature Med*. 2024;30:2235-2241.

CEPHEUS



Primary Endpoint: Overall MRD (-)

Usmani S, et al. *Nature Med*. 2025;31:1195-1202.

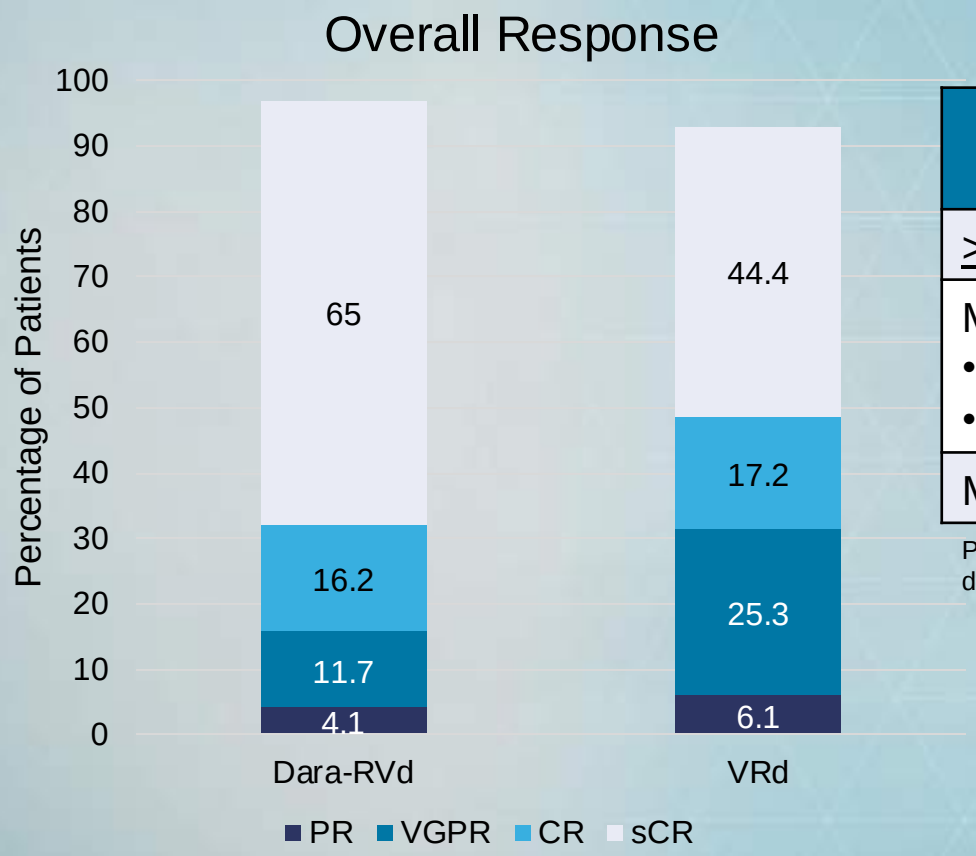
CEPHEUS – Patient Demographics

Baseline Characteristic	DaraRVd (N=197)	RVd (N=198)
Median Age, years (range)	70 (42-79)	70 (31-80)
Male, n (%)	87 (44)	111 (56.1)
Race, n (%) • White • Black	 162 (82.2) 10 (5.1)	 156 (78.8) 9 (4.5)
ECOG PS, n (%) • 0 -1	 174 (88.3)	 184 (92.9)
Cytogenetic Risk, n (%) • Standard • High	 149 (75.6) 25 (12.7)	 149 (75.3) 27 (13.6)
Median time since diagnosis, months	1.2	1.3

PS: performance status

Usmani S, et al. *Nature Med*. 2025;31:1195-1202.

CEPHEUS – Results



	DaraRVd (n=135)	RVd (n=135)
≥ CR, %	81.2	61.6
MRD (-) rate, % • 10^{-5} • 10^{-6}	 60.9 46.2	 39.4 27.3
Median PFS, months	NR	52.6

PR: partial response, VGPR: very good partial response, CR: complete response, MRD: minimal residual disease, PFS: progression free survival

Slightly higher rates of adverse events with DaraRVd compared to RVd including: cytopenias, infection, pneumonia, injection site reactions

Usmani S, et al. *Nature Med*. 2025;31:1195-1202.

Quad Therapy in Newly Diagnosed Myeloma

- Quad therapy has changed the landscape of newly diagnosed multiple myeloma
- Quad therapy showed higher rates of MRD-negativity and response rates in transplant-eligible and –ineligible myeloma
- Higher rates of adverse events were seen in patients receiving quad therapy, but did not impact outcomes

Sonneveld P, et al. *NEJM*. 2024;390:301-313.; Facon T, et al. *NEJM*. 2024; DOI:10.1056/NEJMoa2400712; Leleu X, et al. *Nature Med*. 2024;30:2235-2241.;Usmani S, et al. *Nature Med*. 2025;31:1195-1202.

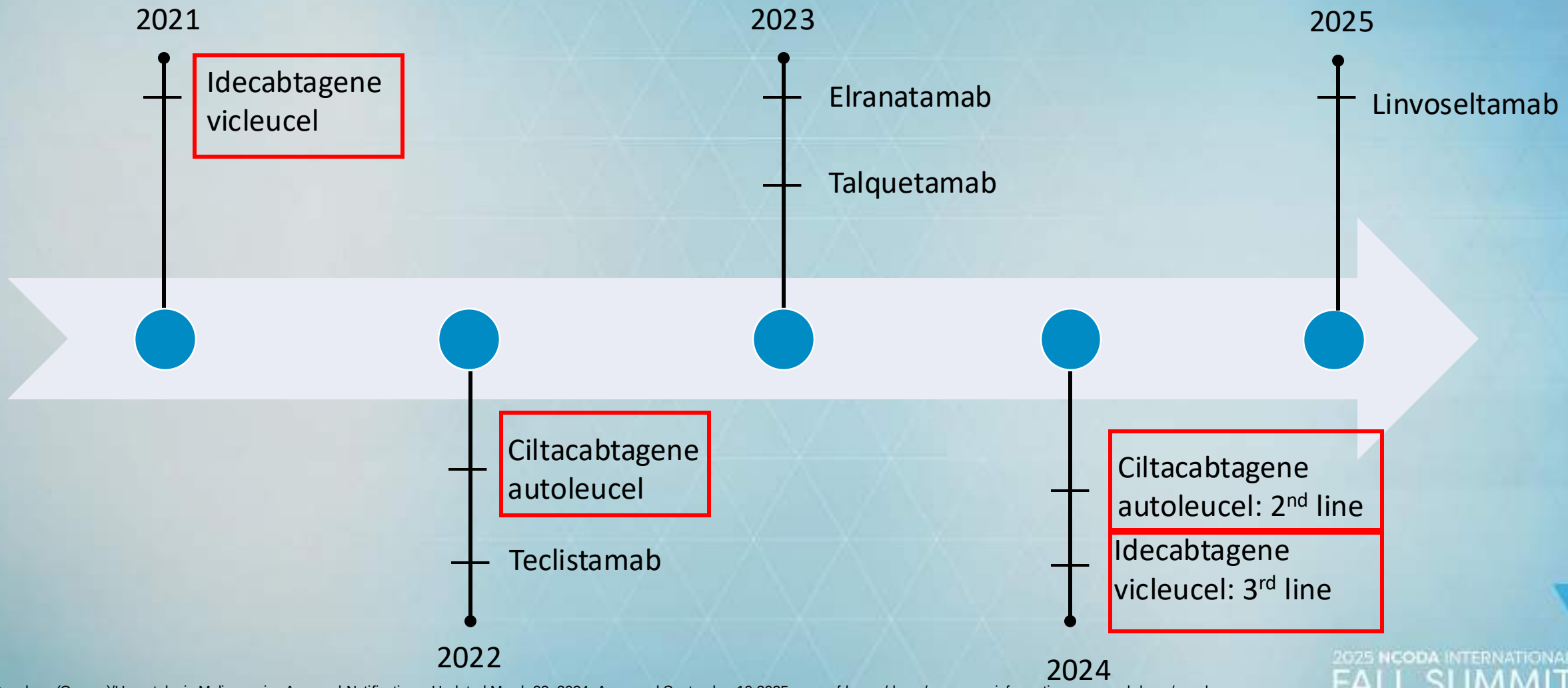
QUESTION 1

PL is a 52-year-old male with a past medical history of hypertension and GERD. He presents in clinic with newly diagnosed multiple myeloma. ECOG PS is 0 and labs are unremarkable. He is deemed a transplant candidate. What is an appropriate 1st line regimen for PL?

a. IsaRVd
b. DaraRVd
c. RVd
d. DRd

CAR-T in Early Relapse

T-Cell Approvals in Multiple Myeloma



FDA. Oncology (Cancer)/Hematologic Malignancies Approval Notifications. Updated March 22, 2024. Accessed September 19 2025.. www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notification

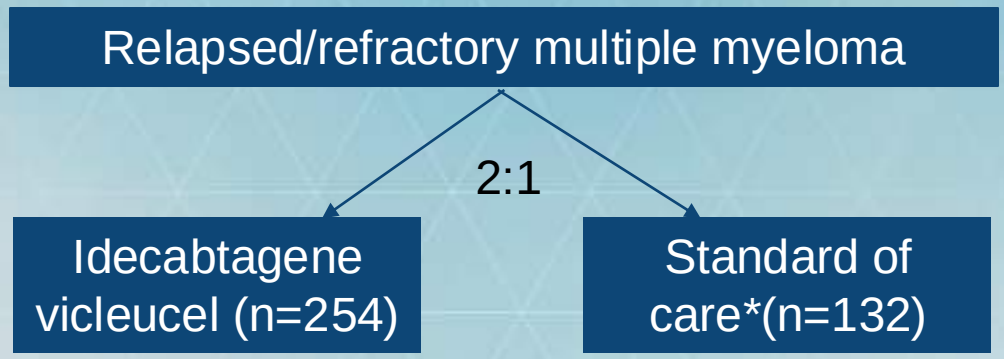
CAR-T in Late Relapse

Trial	Population	Intervention	Outcomes	Conclusions
KarMMa	Relapsed myeloma • Following ≥ 3 lines of therapy	Idecabtagene vicleucel	• ORR: 73% (95% CI: 66-81) • ≥ CR: 33% • mPFS: 8.8 months (95% CI: 5.6-11.6)	Ide-cel induced responses in heavily pre-treated patients with multiple myeloma
CARTITUDE-1	Relapsed myeloma • Following ≥ 3 lines of therapy	Ciltacabtagene autoleucel	• ORR: 97% (95 CI: 91.2-99.4) • sCR: 67% • 5-year PFS: 33% • mOS: 60.7 months (95% CI: 41.9-NE)	Early, deep, and durable responses were achieved in heavily pre-treated patients with cilta-cel

mPFS: median progression free survival; Ide-cel: idecabtagene vicleucel; CR: complete response; CI: confidence interval, mPFS: median progression free survival, mOS: median overall survival, NR: not reached; Cilta-cel: ciltacabtagene autoleucel, sCR: stringent complete response

Munshi NC, et al. *N Engl J Med* 2021;384:705-16; Berdeja JG, et al. *Lancet*. 2021;398(10307): 314-24. Jagannath S, et al. *J Clin Oncol*. 2025;43:2766-71.

KarMMa-3

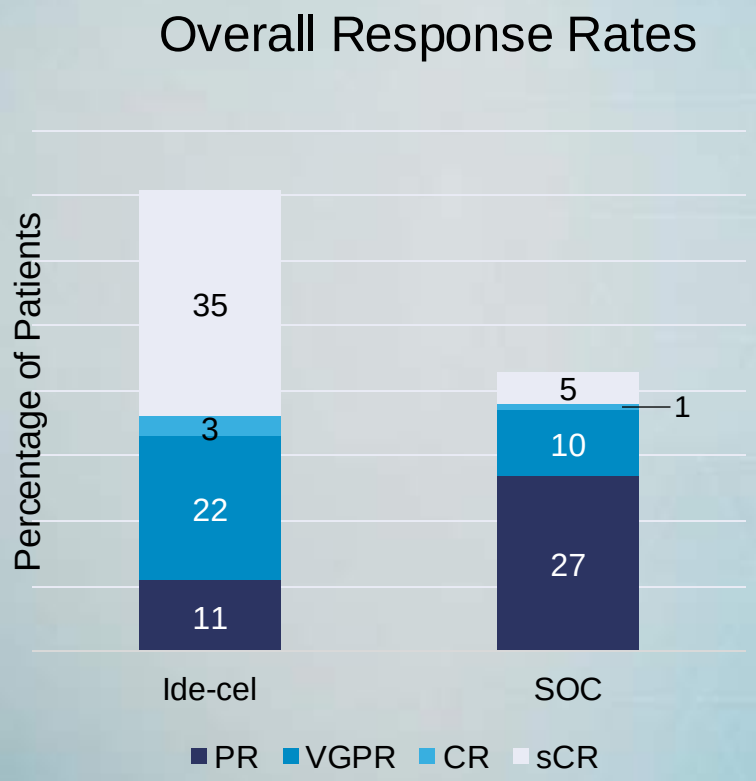


	Ide-cel (n=254)	SOC (n=132)
Median age (range), years	63 (30-81)	63 (42-83)
Extramedullary disease, n (%)	61 (24)	32 (24)
High tumor burden, n (%)	71 (28)	34 (26)
High risk cytogenetics, n (%)	107 (42)	61 (46)
Median prior lines (range)	3 (2-4)	3 (2-4)
Previous autologous HSCT, n (%)	214 (84)	114 (86)
Triple-class refractory, n (%)	164 (65)	89 (67)

*Standard of care (SOC) regimens include: daratumumab, pomalidomide, dexamethasone; daratumumab, bortezomib, dexamethasone; ixazomib, lenalidomide, dexamethasone; carfilzomib, dexamethasone; elotuzumab, pomalidomide, dexamethasone

Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388:1002-14.

KarMMa-3: Results



	Ide-cel (n=254)	SOC (n=132)
Median PFS, mo (95% CI)*	13.3 (11.8-16.1)	4.4 (3.4-5.9)
6-month PFS, %	73	30
Median time to response, mo (range)	2.9 (0.5-13)	2.1 (0.9-9.4)
Median duration of response, mo (95% CI)	14.8 (12-18.6)	9.7 (5.4-16.3)

*p < 0.001; VGPR: very good partial response; sCR: stringent complete response; mo: months

Progression-free survival benefit with Ide-cel was seen across subgroups, including presence or absence of high-risk cytogenetics, high tumor burden, or triple-class refractory status

Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388:1002-14.

KarMMa-3: Toxicity

	Ide-cel (n=250)	SOC (n=126)
CRS, n (%)	197 (88)	0 (0)
Neutropenia, n (%)	195 (78)	55 (44)
Anemia, n (%)	165 (66)	45 (36)
Infection, n (%)	146 (58)	68 (54)
Thrombocytopenia, n (%)	136 (54)	36 (29)
Nausea, n (%)	112 (45)	34 (27)
Diarrhea, n (%)	85 (34)	30 (24)
Neurotoxic event, n (%)	34 (15)	0 (0)

CRS: cytokine release syndrome

Median time to onset of CRS: 1 day (1-14 days)

Median duration of CRS: 3.5 days (1-51 days)

72% of patients receiving Ide-cel required tocilizumab for CRS

28% of patients receiving Ide-cel required corticosteroids for CRS

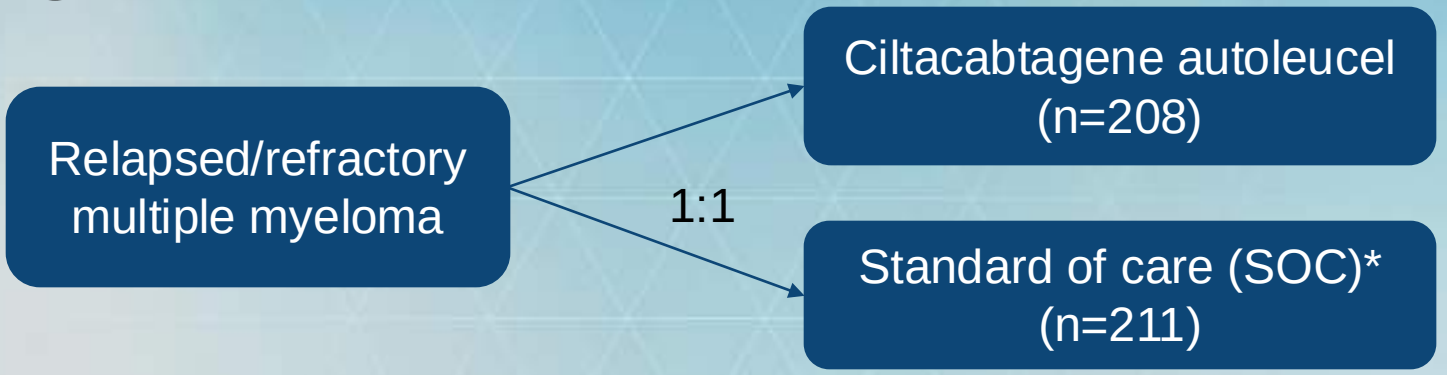
Median time to onset of neurotoxic event: 3 days (1-317 days)

Median duration of neurotoxic event: 2 days (1-37 days)

Ide-cel resulted in significantly longer PFS versus SOC regimens. These results were observed across subgroups and may benefit difficult to treat patients

Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388:1002-14.

CARTITUDE-4

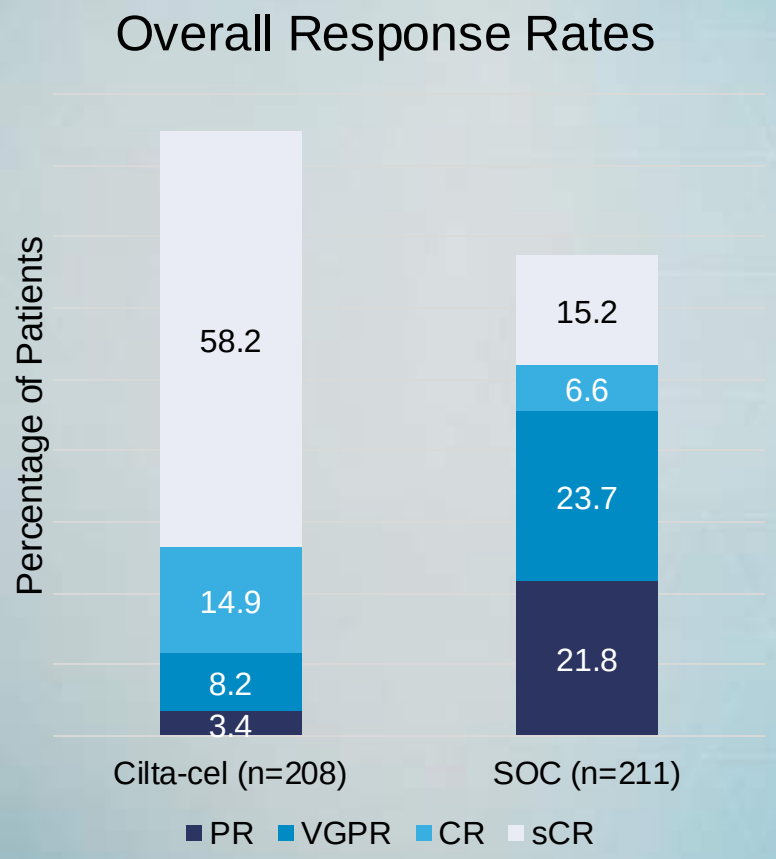


	Cilta-cel (n=208)	SOC (n=211)
Median age (range), years	61.5 (27-78)	61 (35-80)
Soft tissue plasmacytomas, n (%)	44 (21.2)	35 (16.6)
Bone marrow plasma cells > 60%, n (%)	42 (20.4)	43 (20.7)
High-risk cytogenetics, n (%)	123 (59.4)	132 (51)
Previous lines of therapy, n (%) 1 2 3	 68 (32.7) 83 (39.9) 57 (27.4)	 68 (32.2) 87 (41.2) 56 (26.2)
Triple-class refractory, n (%)	30 (14.4)	33 (15.6)

*SOC regimens include: pomalidomide, bortezomib, dexamethasone; daratumumab, pomalidomide, dexamethasone

San-Miguel J, et al. *N Engl J Med*. 2023;389:335-47.

CARTITUDE-4: Results



	Cilta-cel (n=208)	SOC (n=211)
Median time to response, mo (range)	2.1 (0.9-11.1)	1.2 (0.6-10.7)
Median time to best response, mo (range)	6.4 (1.1-18.6)	3.1 (0.8-20.6)
Minimal residual disease negative, n (%)	126 (60.6)	33 (15.6)
30-month PFS, %*	59.4	25.7
30-month OS, %	76.4	63.8

*p < 0.0001; VGPR: very good partial response; sCR: stringent complete response; mo: months; NR: not reached

PFS benefit with cilta-cel was seen across subgroups, including presence of high-risk cytogenetics and prior lines of therapy

Mateos MV, et al. Presented at 21st International Myeloma Society (IMS) Annual Meeting; September 25-28, 2024; San-Miguel J, et al. *N Engl J Med*. 2023;389:335-47.8

CARTITUDE-4: Toxicity

	Cilta-cel (n=208)	SOC (n=126)
Neutropenia, n (%)	187 (89.9)	177 (85.1)
CRS, n (%)	134 (76.1)	0 (0)
Infection, n (%)	129 (62)	148 (71.2)
Anemia, n (%)	113 (54.3)	54 (26)
Thrombocytopenia, n (%)	113 (54.3)	65 (31.2)
Nausea, n (%)	101 (48.6)	38 (18.3)
Hypogammaglobulinemia, n (%)	88 (42.3)	13 (6.2)

CRS: cytokine release syndrome

Median time to CRS onset: 8 days (1-23 days)

Median duration of CRS: 3 days (1-17 days)

Cilta-cel had a favorable risk-benefit profile compared to standard of care. Due to the progression free survival benefit, cilta-cel is an option for patients on first relapse

San-Miguel J, et al. *N Engl J Med*. 2023;389:335-47.

CAR-T in Earlier Lines

	KarMMa-3	CARTITUDE-4
Median age, years (range)	63 (30-81)	61.5 (27-78)
High risk cytogenetics, n (%)	107 (42)	123 (59.4)
ORR, n (%)	181 (71)	176 (84.6)
PFS, months, (95% CI)	13.3 (11.8-16.1) (18.6-month follow-up)	NR (15.9-month follow-up)
Any grade adverse events, n (%) • Cytokine release syndrome • Neutropenia • Thrombocytopenia • Infection • Neurotoxic events	 197 (88) 146 (58) 136 (54) 146 (58) 34 (15)	 134 (76.1) 187 (89.9) 113 (54.3) 129 (62) 36 (20.5)

ORR: overall response rate, NR: not reached

Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388:1002-14.; San-Miguel J, et al. *N Engl J Med*. 2023;389:335-47.

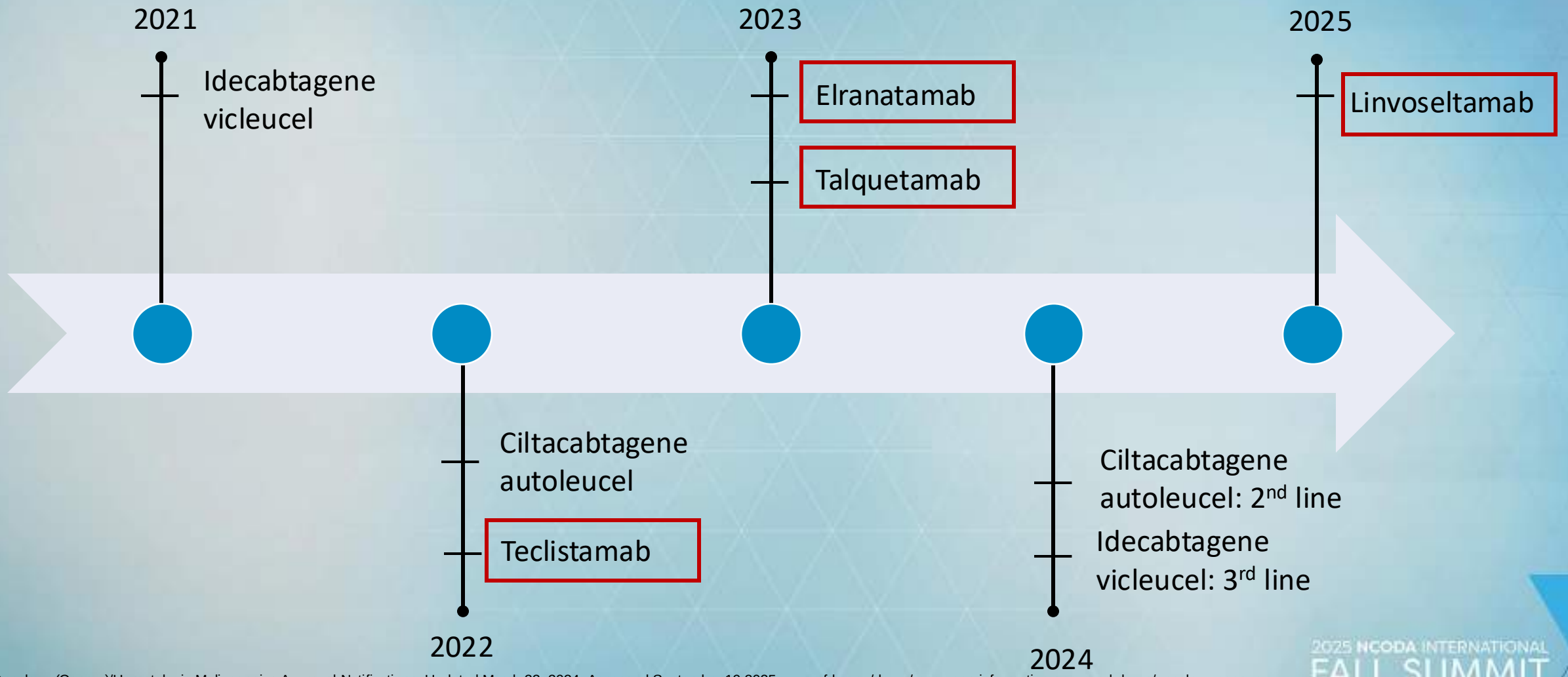
CAR-T in Relapsed/Refractory Myeloma

- CAR-T in earlier lines of therapy provides deep and durable remissions compared to standard of care chemotherapy
- May be an appropriate option in certain patients depending on performance and disease status
- No new safety signals identified when used in early relapse

Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388:1002-14.; San-Miguel J, et al. *N Engl J Med*. 2023;389:335-47.

Bispecific T-Cell Engagers in Relapsed Myeloma

T-Cell Approvals in Multiple Myeloma



FDA. Oncology (Cancer)/Hematologic Malignancies Approval Notifications. Updated March 22, 2024. Accessed September 19 2025.. www.fda.gov/drugs/resources-information-approved-drugs/oncology-cancer-hematologic-malignancies-approval-notification

Bispecific T-Cell Engagers - Targets

BCMA
- Teclistamab
- Elranatamab
- Linvoseltamab

GPRC5D
- Talquetamab
- Forimtamig*

FcRH5
- Cevostamab*

*Available via investigational trial

Costa L, et al. *Leukemia*. 2025;39:543-54.

BCMA Bispecific T-Cell Engagers

Bispecific T-Cell Engager	Indication	Route	Maintenance Dosing	Hospitalization?	REMS
Teclistamab	Relapsed MM after 4 or more lines of therapy	SQ	• 1.5 mg/kg SQ once weekly x 6 months* • 1.5 mg/kg every 2 weeks	Yes – 48 hours after each step-up dose and first treatment dose	Yes
Elranatamab		SQ	• 76 mg SQ once weekly x 6 months • 76 mg SQ every 2 weeks x 6 months* • 76 mg SQ once monthly*	Yes – 48 hours after step-up dose 1 and 24 hours after step-up dose 2	Yes
Linvoseltamab		IV	• 200 mg IV once weekly weeks 4-13 • 200 mg IV every 2 weeks week 14-24 • 200 mg IV once monthly*	Yes – 24 hours after step-up dose 1 and 2	Yes

*In responders only; MM: multiple myeloma, SQ: subcutaneous, IV: intravenous

Tecvayli [Package Insert]. Horsham PA. Janssen Biotech. Updated: 8/2025. Elrexfio [Package Insert] New York, NY. Pfizer. Updated 7/2025. Lynozyfic [Package Insert] Tarrytown, NY. Regeneron. Updated: 7/2025.

MAJESTEC-1

Relapsed Multiple Myeloma

- ≥ 18 years
- 3 prior lines of therapy
- No prior BCMA exposure

→

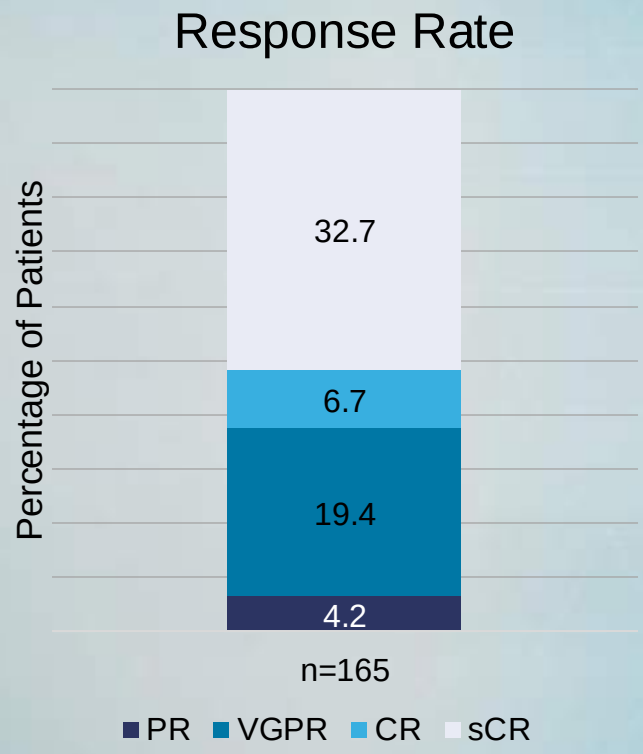
Teclistamab

- Target dose: 1.5 mg/kg SQ once weekly

Patient Characteristics	n=165
Median age (range), years	64 (33-84)
Soft tissue plasmacytomas, n (%)	28 (17)
High-risk cytogenetics, n / total n (%)	38/148 (15.5)
Median number of prior lines, n (range)	5 (2-14)
Refractory Status, n (%) • Triple-class • Penta-drug	128 (77.6) 50 (30.3)

Moreau P, et al. *N Engl J Med*. 2022; 387:495-505.

MAJESTEC-1 - Results



	n=165
VGPR or better, n (%)	97 (58.8)
Median PFS, months (95% CI)	11.3 (8.8-17.1)
Median OS, months (95% CI)	18.3 (15.1-NE)
Adverse Events	
Any Adverse Event, n (%)	165 (100)
Cytokine Release Syndrome, n (%)	119 (72.1)
Neutropenia, n (%)	117 (70.9)
Thrombocytopenia, n (%)	66 (40)
Pneumonia, n (%)	30 (18.2)
Neurotoxic Events, n (%)	24 (14.5)

Teclistamab provided deep and durable responses in a heavily pre-treated patient population

Moreau P, et al. *N Engl J Med*. 2022; 387:495-505.

MagnetisMM-3

Relapsed Multiple Myeloma

- ≥ 18 years
- 3 prior lines of therapy
- No prior BCMA exposure

→

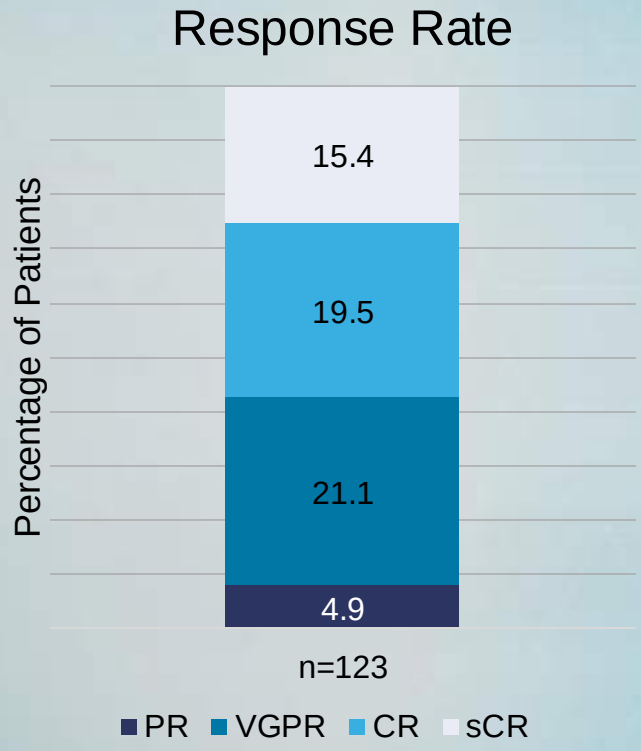
Elranatamab

- Target dose: 76 mg SQ once weekly x6 cycles followed by 76 mg SQ every 2 weeks

Patient Characteristics	n=123
Median age (range), years	68 (36-89)
Soft tissue plasmacytomas, n (%)	28 (17)
High-risk cytogenetics, n (%)	31 (25.2)
Median number of prior lines, n (range)	5 (2-22)
Refractory Status, n (%) • Triple-class • Penta-drug	 119 (96.7) 52 (42.3)

Lesokhim AM, et al. *Nature Med*.2023;29:2259-67.

MagnetisMM-3



	n=123
ORR, % (95% CI)	61 (51.8-69.6)
VGPR or better, n (%)	69 (56.1)
Median PFS, months (95% CI)	NE (9.9-NE)
Median OS, months (95% CI)	NE (13.9-NE)
Adverse Events	
Any Adverse Event, n (%)	123 (100)
Cytokine Release Syndrome, n (%)	71 (57.7)
Neutropenia, n (%)	60 (48.8)
Thrombocytopenia, n (%)	38 (30.9)
Infection, n (%)	86 (69.9)
ICANS, n (%)	4 (3.4)

Elranatamab demonstrated durable responses that continued to deepen after the transition to biweekly dosing

Lesokhim AM, et al. *Nature Med*.2023;29:2259-67.

LINKER MM-1

Relapsed Multiple Myeloma

- ≥ 18 years
- 3 prior lines of therapy
- No prior BCMA immunotherapies

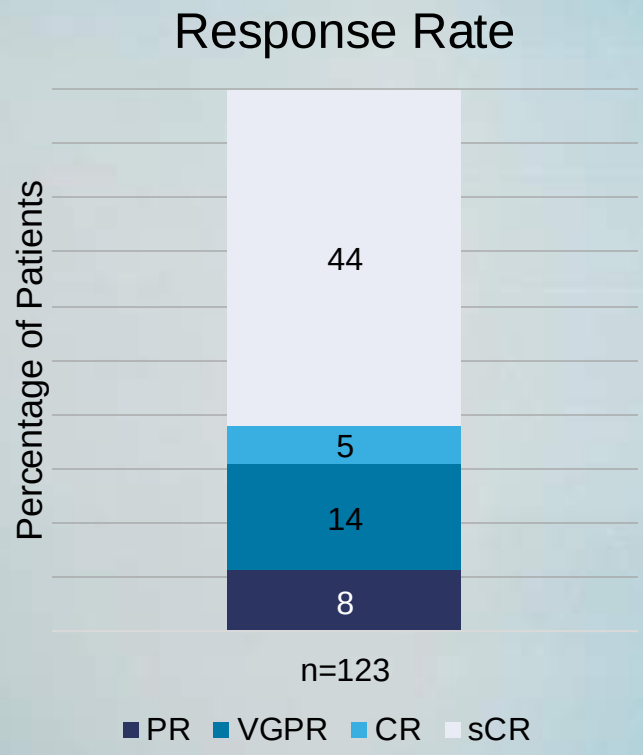
Linvoseltamab

- Target dose: 50 mg or 200 mg IV once weekly x 12 weeks followed by 200 mg IV every other week x 12 weeks followed by 200 mg IV once monthly

Patient Characteristics	200 mg (n=117)
Median age (range), years	70 (37-91)
Soft tissue plasmacytomas, n (%)	19 (16.2)
High-risk cytogenetics, n (%)	46 (39.3)
Median number of prior lines, n (range)	5 (2-16)
Refractory Status, n (%) • Triple-class • Penta-drug	 96 (82.1) 33 (28.2)

Bumma N, et al. *J Clin Oncol.* 2024;42:2702-12.

LINKER MM-1



	n=117
ORR, %	70.9
VGPR or better, n (%)	74 (63.2)
Median PFS, months (95% CI)	NR (17.3-NE)
Median OS, months (95% CI)	NR (31.4-NE)
Adverse Events	
Any Adverse Event, n (%)	117 (100)
Cytokine Release Syndrome, n (%)	54 (46.2)
Anemia, n (%)	45 (38.5)
Thrombocytopenia, n (%)	38 (30.9)
Infection, n (%)	87 (74.4)
ICANS, n (%)	9 (7.7)

Linvoseltamab offers clinical benefit in a high risk, heavily pre-treated population and increases patient convenience with less frequent dosing

Bumma N, et al. *J Clin Oncol*. 2024;42:2702-12.

BCMA Bispecific T-Cell Engagers

Bispecific T-cell Engager	ORR	≥ VGPR	PFS	CRS Rate		ICANS Rate	
				All Grades	≥ Grade 3	All Grades	≥ Grade 3
Teclistamab	63%	58.8%	11.3 mo (14.1 mo follow up)	72.1%	0.6%	14.5%	0.6%
Elranatamab	61%	56.1%	NR (14.7 mo follow up)	71%	0	3.4%	0
Linvoseltamab	70.9%	63.2%	NR (14.3 mo follow up)	46.2%	0.9%	7.7%	2.6%

Moreau P, et al. *N Engl J Med*. 2022; 387:495-505; Lesokhim AM, et al. *Nature Med*.2023;29:2259-67.; Bumma N, et al. *J Clin Oncol*. 2024;42:2702-12.

QUESTION 2

PL completed induction with Dara-RVd and completed as autologous stem cell transplant. He is currently on daratumumab + lenalidomide maintenance. During his 1-year work up, his bone marrow biopsy showed 30% monoclonal plasma cells.

What is an appropriate 2nd line therapy?

a. Teclistamab
b. Ide-cel
c. Cilta-cel
d. DRd

Sequencing BCMA Agents

- BCMA-targeting agents have changed the management of relapsed/refractory multiple myeloma
- Several BCMA-targeting agents available including: cilta-cel, ide-cel, teclistamab, elranatamab, linvoseltamab, belantamab (via clinical trial or compassionate use)
- Concerns with T-cell exhaustion and development of resistance are growing concerns with repeated BCMA-targeting agents
- With access to several agents, optimal sequencing while important, is still yet to be determined

Dimopoulos M, et al. ASCO Daily News. Sequencing Anti-BCMA Therapies in Multiple Myeloma: What Is Their Optimal Use with Other Available Treatment Options? 12/2024. Accessed 9/18/2025. https://dailynews.ascopubs.org/do/sequencing-anti-bcma-therapies-multiple-myeloma-their-optimal-use-other-available.; Quach H. *Blood.* 2024;144(23): 2365-67.

CARTITUDE-2 Cohort C

Evaluation of cilta-cel in BCMA-exposed relapsed/refractory myeloma

	All (n=20)	Prior ADC (n=13)	Prior BsAb (n=7)
Median age (range), years	62.5 (44-81)	66 (44-81)	60 (49-71)
High-risk cytogenetics, n (%)	3 (15)	2 (15.4)	1 (14.3)
Median prior lines, n (range)	8 (4-13)	8 (4-13)	8 (6-12)
Penta drug refractory, n (%)	11 (55)	7 (53.8)	4 (57.1)
Anti-BCMA refractory, n (%)	16 (80)	11 (84.6)	5 (71.4)

Time from last anti-BCMA to cilta-cel infusion: 62-944 days

Duration of prior anti-BCMA: 1-527 days

Cohen AD, et al. *Blood.* 2023;141(3):219-230.

CARTITUDE-2 Cohort C - Results

	All (n=20)	Prior ADC (n=13)	Prior BsAb (n=7)
ORR, % (95% CI)	60 (36.1-80.9)	61.5 (431.6-86.1)	57.1 (18.4-90.1)
MRD (-) 10-5, %	35	39	28
Median DOR, months (95% CI)	11.5 (7.9-NE)	11.5 (7.9-NE)	8.2 (4.4-NE)
Median PFS, months (95% CI)	9.1 (1.5-NE)	9.5 (0.99-NE)	5.3 (0.6-NE)

Patients more likely to respond if:

- Shorter duration of prior BCMA agent
- Longer time between cilta-cel and prior BCMA agent

Results suggest response after prior BCMA studies, larger prospective trials are needed for a better understanding of sequencing

No additional safety concerns identified

Cohen AD, et al. *Blood.* 2023;141(3):219-230.

Response with Bispecific T-cell Engagers After Prior BCMA Agents

MajesTEC-1 Teclistamab	MagnetisMM Elranatamab	Linker MM-1 Linvoseltamab

• 40 patients with prior BCMA
• ORR 52.5%
  • ADC: 55.2%
  • CAR-T: 53.3%
• 30% with CR or better
	• 86 patients with prior BCMA
	• ORR = 45.3%
	  • ADC: 41.4%
	  • CAR-T: 52.8%
	• 17.4% achieved CR or better
		• 10 patients with prior BCMA ADC
		• ORR 70%

Touzeau C, et al. Blood. 2024;144(23): 2375-88. Quach H. *Blood.* 2024;144(23): 2365-67.; Nooka A, et al. *J Clin Oncol.* 2023;41(suppl 16): abstract 8008. 2023 ASCO Annual Meeting.; Bumma N, et al. *J Clin Oncol.* 2024;42:2702-12.

Guidance for Sequencing

- Growing area of research, but available studies have small cohorts of patients
- Although a response may occur, overall response rates are lower than seen in BCMA-naïve patients
- A longer time between BCMA targeting agents may increase the chance of response
- Sequencing in the real-world may be depending on patient factors and availability of treatments

Dimopoulos M, et al. ASCO Daily News. Sequencing Anti-BCMA Therapies in Multiple Myeloma: What Is Their Optimal Use with Other Available Treatment Options? 12/2024. Accessed 9/18/2025. https://dailynews.ascopubs.org/do/sequencing-anti-bcma-therapies-multiple-myeloma-their-optimal-use-other-available.

Future Directions

- Optimization of CAR-T therapies – dual targeting, allogeneic CAR-T products, new targets
- Combination therapies with bispecific T-cell engagers and use in earlier lines of therapy
- Emergence of MRD (-) guided treatment decisions
- Trispecific antibodies currently under investigation
- Increasing access to novel therapies in the community

Biltibo E, et al. ASCO Ed Book. 2025;45(3):e473316

QUESTION 3

RT is a 71-year-old female with relapsed/refractory multiple myeloma. She has a past medical history of treatment-related peripheral neuropathy, hypothyroidism, and hypertension. She has previously received Dara-RVd, HSCT, Daratumumab/lenalidomide maintenance, KPd, DPd, and most recently cilta-cel (currently day +180). She is now progressing.

What would be an appropriate next line of therapy?

a. Elranatamab
b. Talquetamab
c. CyBorD
d. Belantamab
e. a or b

SUMMARY

- Landscape of multiple myeloma treatment is rapidly evolving
- Quad therapies have become the main stay in treatment of transplant-eligible and –ineligible newly diagnosed multiple myeloma
- The use of t-cell redirecting therapies are highly active in multiple myeloma and are continuing to be investigation in combination and in earlier lines of therapy
- BCMA-targeting agents are effective in a heavily pre-treated patient population, but optimal sequencing is still under investigation

Myeloma: From Current to Cutting Edge

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