The Rise and Rise of Cellular Immunotherapy for Multiple Myeloma
ASH & ASCO Updates 2023

GRIFFIN 4 yr follow up

MAIA update

MASTER trial

DETERMINATION Trial

MajesTEC-1

KarMMA-3

CARTITUDE-4

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DISCLOSURE OF CONFLICTS OF INTEREST

Hamza Hashmi, MD has the following financial relationships to disclose:

Consultancy: BMS, Janssen, Sanofi

Honoraria: GSK, Karyopharm, Janssen

AND..

I AM A CELLULAR THERAPIST

AGENDA

1. What is the preferred Induction therapy for Newly Diagnosed Multiple Myeloma
2. Is Maintenance important and for how long? Doublets?
3. What is the role of Upfront Bone Marrow Transplant for Newly Diagnosed Multiple Myeloma?
4. How do I treat relapsed Myeloma?
5. How do I choose between CAR T and Bispecifics?

What is the ideal Induction therapy for Newly Diagnosed Multiple Myeloma

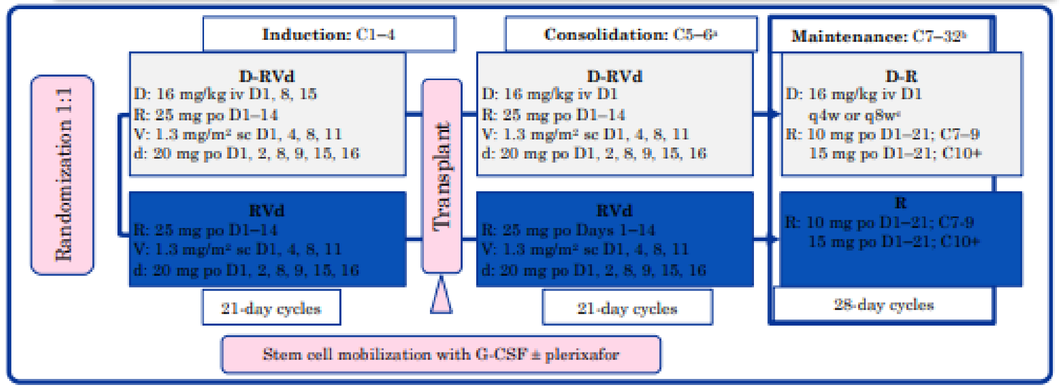
Standard Risk
High Risk
Transplant Eligible
Transplant Ineligible

GRIFFIN 4-Yr follow up Update: Dara + VRd With Dara-R Maintenance vs VRd With R Maintenance for ASCT-Eligible Patients With Newly Diagnosed MM

GRIFFIN: Phase 2 -Daratumumab Plus Lenalidomide, Bortezomib, and Dexamethasone in Transplant-Eligible NDMM – 24 Months of Maintenance

Study design

Key eligibility criteria: TE NDMM; 18–70 years; ECOG PS 0–2; CrCl ≥30 mL/min²



- **Primary endpoint:** sCR by end of consolidation
- **Secondary endpoints:** MRD negativity (NGS 10^{-5}), ORR, ≥VGPR, CR, PFS, OS

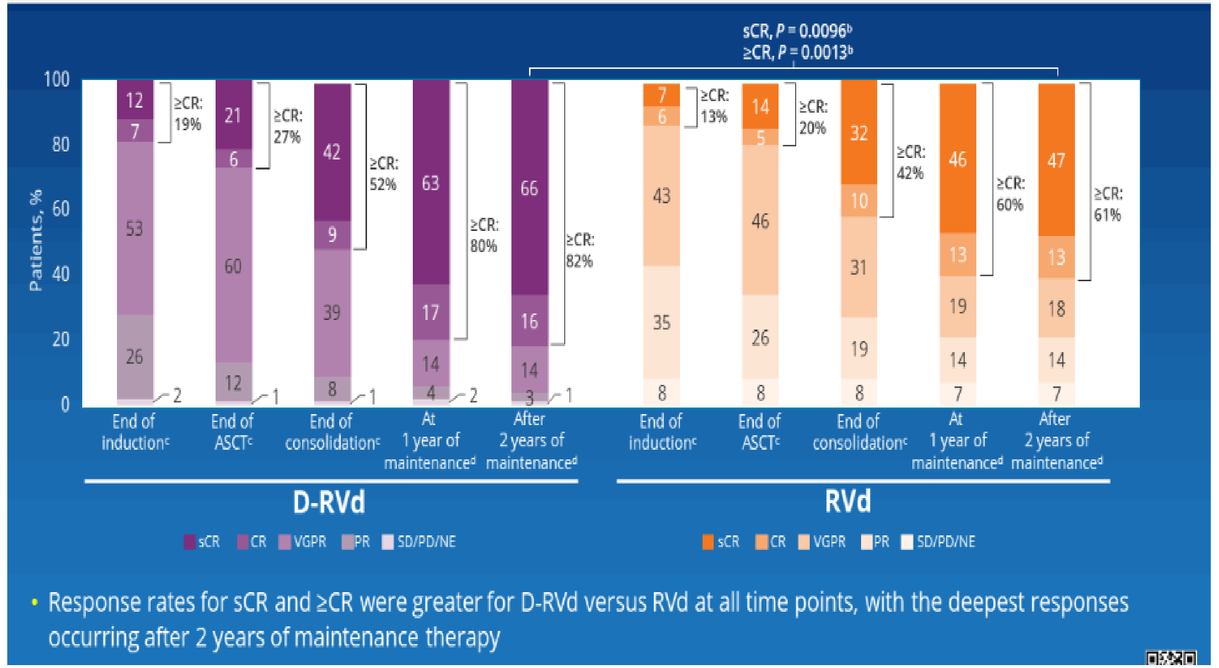
[a]Consolidation initiated 60–100 days post transplant; [b]Patients who complete maintenance cycles 7–32 may continue single-agent lenalidomide thereafter; [c]Protocol amendment allowed q4w dosing option. Phase 2 trial – patient enrollment between December 2016 and April 2018.

Patient disposition

n (%)	D-RVd (n=104)	RVd (n=103)
Treated with maintenance therapy	90 (87)	70 (68)
Completed maintenance therapy	67 (64)	44 (43)
Discontinued treatment during maintenance therapy	21 (20)	21 (20)
Adverse event	8 (8)	7 (7)
Progressive disease	3 (3)	7 (7)
Patient withdrawal	2 (2)	4 (4)
Lost to follow-up	2 (2)	0
Death	1 (1)	1 (1)
Other	5 (5)	2 (2)

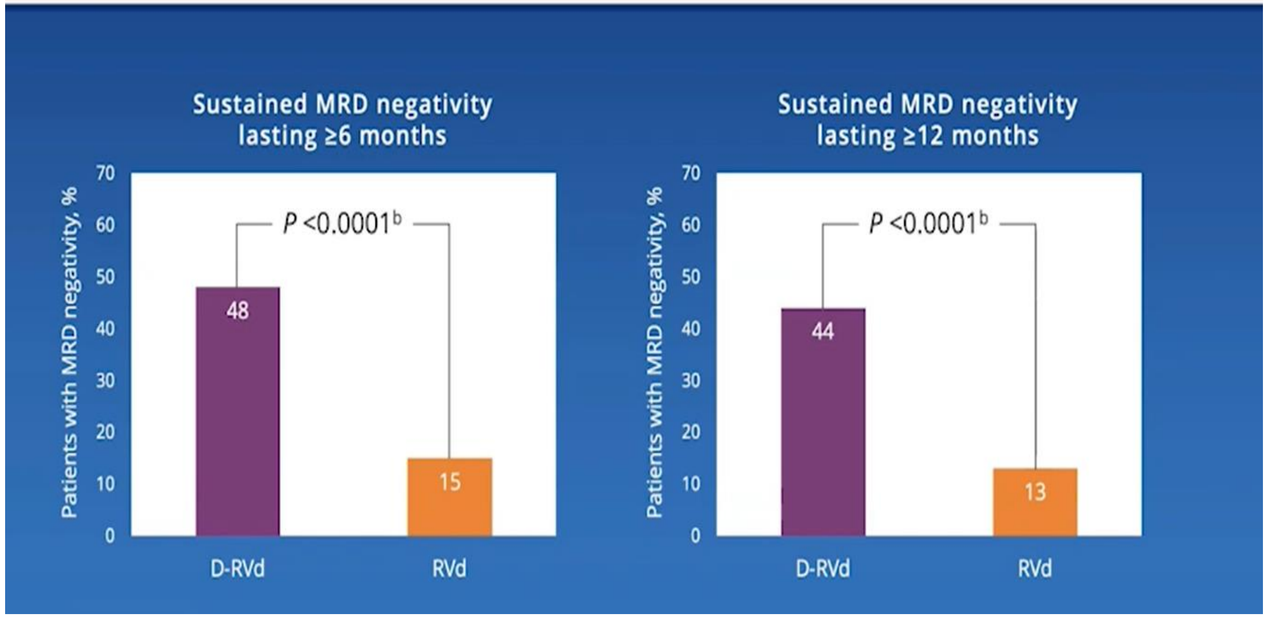
Laucbach JP, et al. ASH 2021

GRIFFIN: Responses Deepened Over Time[a]



- Response rates for sCR and ≥CR were greater for D-RVd versus RVd at all time points, with the deepest responses occurring after 2 years of maintenance therapy

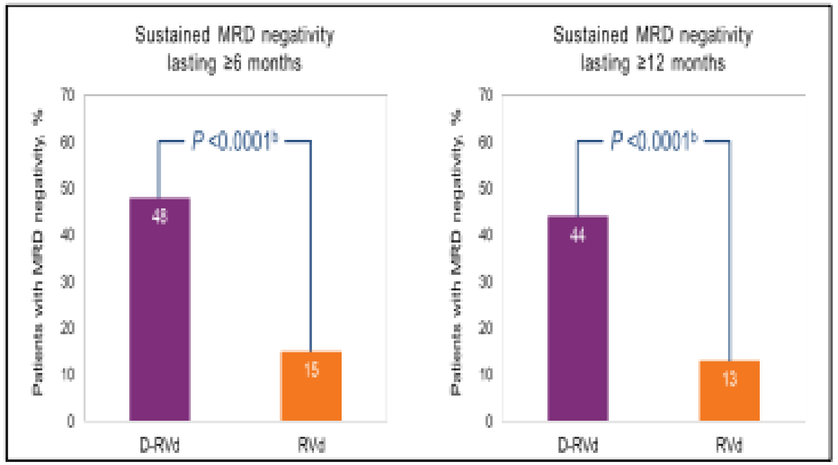
GRIFFIN: D-RVd Improved Rates of Durable MRD Negativity[a] (10^{-5}) Lasting ≥6 Months or ≥12 Months Versus RVd

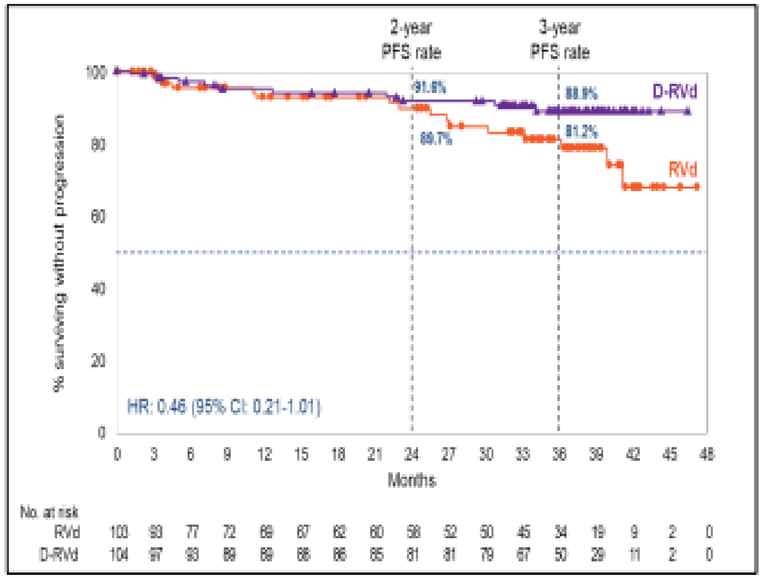


Laubach. ASH 2021

GRIFFIN Update: MRD and PFS Data

D-RVd Improved Rates of Durable MRD Negativity[a] (10^{-5}) Lasting ≥6 Months or ≥12 Months Versus RVd





[a]The threshold of MRD negativity was defined as 1 tumor cell per 10^5 white cells. MRD status was based on BM aspirates by NGS per IMWG. [b]P values calculated by Fisher's exact test.

After 2 years of maintenance: MRD negativity rate continued to favor daratumumab/RVd vs RVd (64% vs 30%, $P = <.0001$).

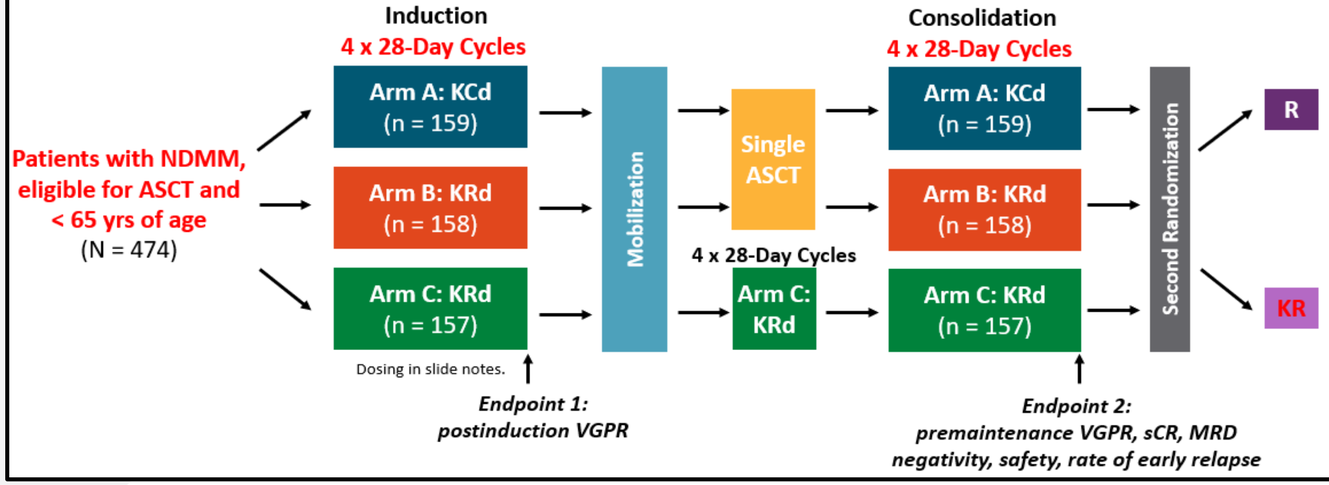
Median follow-up of 49.6 months: estimated 48-month PFS rate of 87.2%was observed in the daratumumab/RVd arm, compared to 70% in the RVd arm.

Median PFS was not reached in either treatment arm.

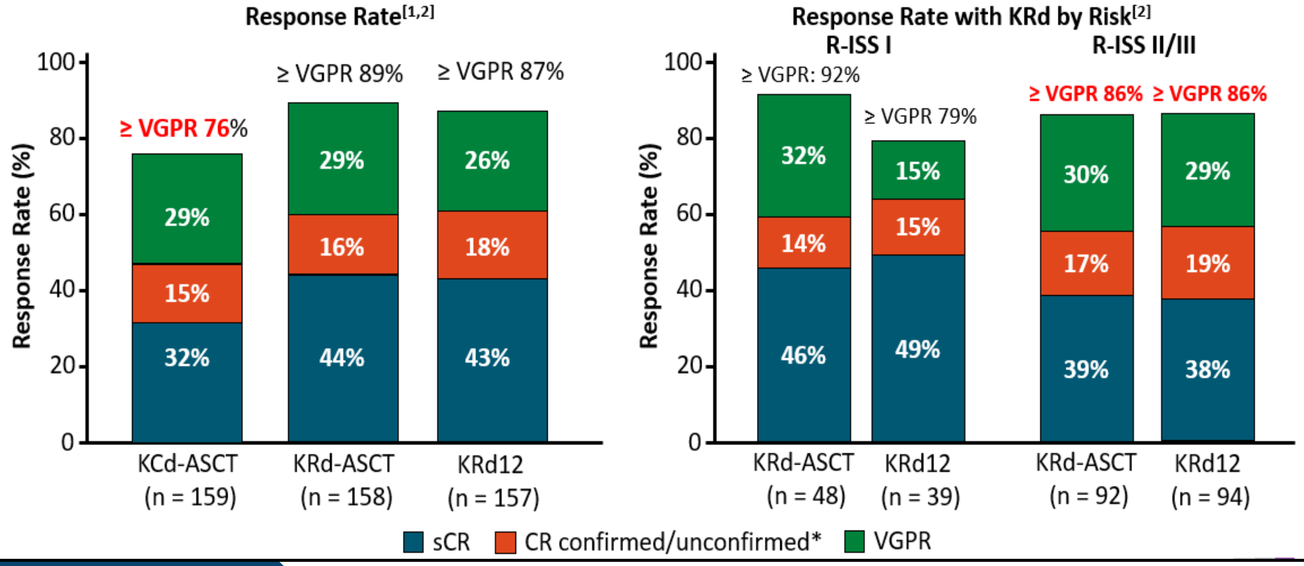
Sborv et al IMS 2022

FORTE: Carfilzomib + Cyclo/Dex vs Carfilzomib + Len/Dex, With or Without ASCT in NDMM

- Multicenter, randomized, open-label phase II study



FORTE: Premaintenance Response Rates



Slide credit: clinicaloptions.com

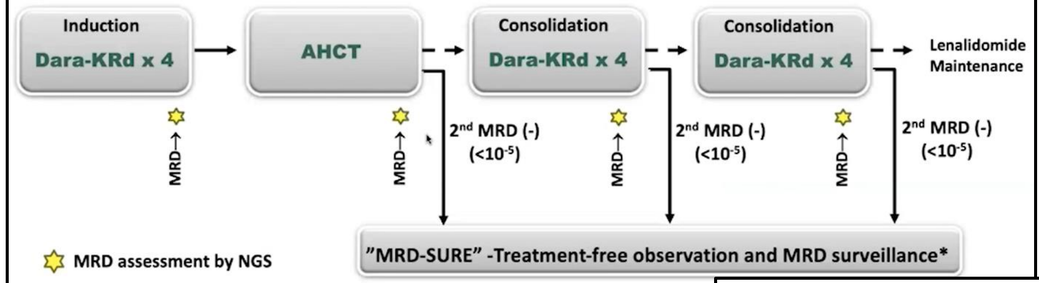
Daratumumab, Carfilzomib, Lenalidomide and Dexamethasone (Dara-KRd), Autologous Transplantation and MRD Response-Adapted Consolidation and Treatment Cessation-Final Primary Endpoint Analysis of the MASTER Trial

Treatment

Dara-KRd

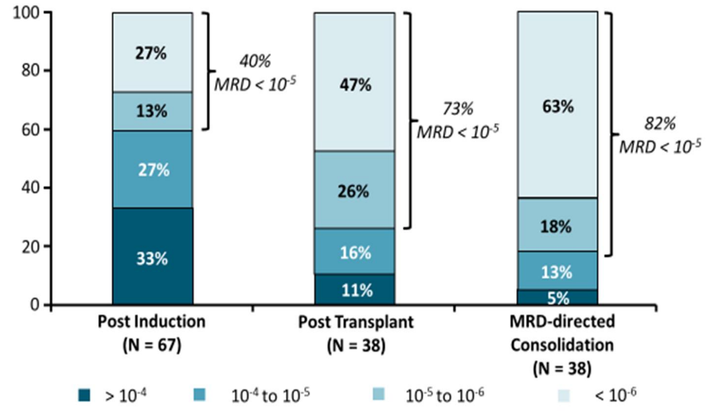
- Daratumumab 16 mg/m^2 days 1,8,15,22 (days 1,15 C 3-6; day 1 C >6)
- Carfilzomib (20) 56 mg/m^2 Days 1,8,15
- Lenalidomide 25 mg Days 1-21
- Dexamethasone 40mg PO Days 1,8,15,22

- 123 patients enrolled across 5 sites
- 118 (96%) with MRD trackable by ClonoSEQ®
- Median follow-up of 23.8 months

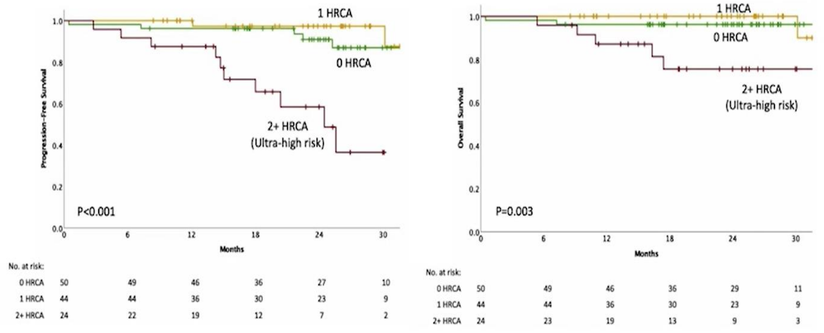


*24 and 72 weeks after completion of therapy

MASTER: MRD Response by Treatment Phase



Progression-Free and Overall Survival



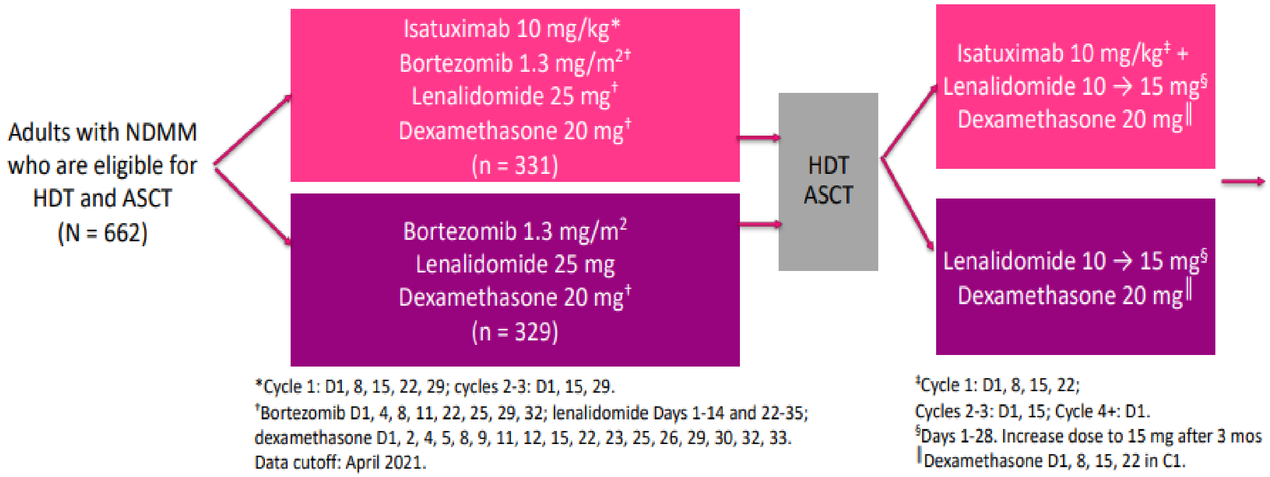
HRCA = gain/amp 1q, t(4;14), t(14;16), t(14;20) or del(17p)

MASTER trial

Courtesy Luciano J Costa

Phase III GMMG-HD7

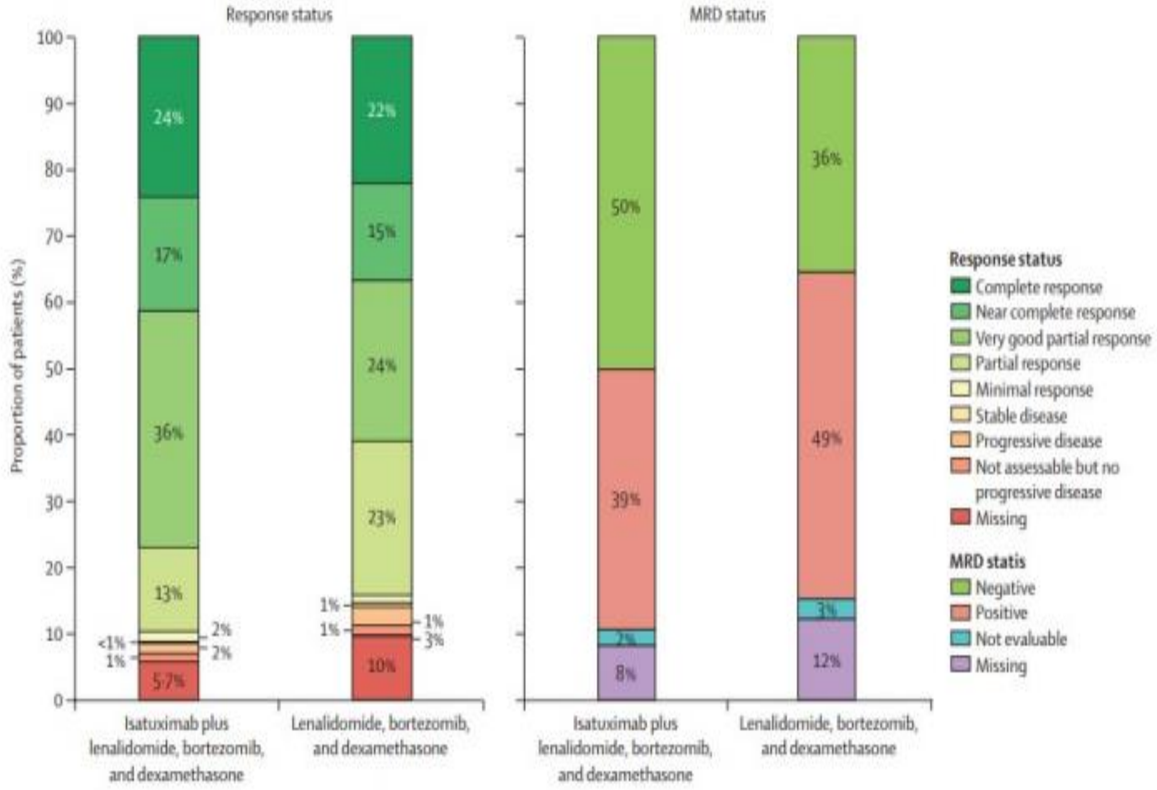
- Open-label, randomized, multicenter phase III trial



*Cycle 1: D1, 8, 15, 22, 29; cycles 2-3: D1, 15, 29.
†Bortezomib D1, 4, 8, 11, 22, 25, 29, 32; lenalidomide Days 1-14 and 22-35; dexamethasone D1, 2, 4, 5, 8, 9, 11, 12, 15, 22, 23, 25, 26, 29, 30, 32, 33.
Data cutoff: April 2021.

‡Cycle 1: D1, 8, 15, 22; Cycles 2-3: D1, 15; Cycle 4+: D1.
§Days 1-28. Increase dose to 15 mg after 3 mos
‖Dexamethasone D1, 8, 15, 22 in C1.

Primary endpoint: MRD negativity at end of induction (NGF, sensitivity 10^{-5}) stratified according to R-ISS
Secondary endpoints: CR after induction, safety
MRD negativity assessed after cycle 3, HDT, 12 mos, and 24 mos as well as at end of study

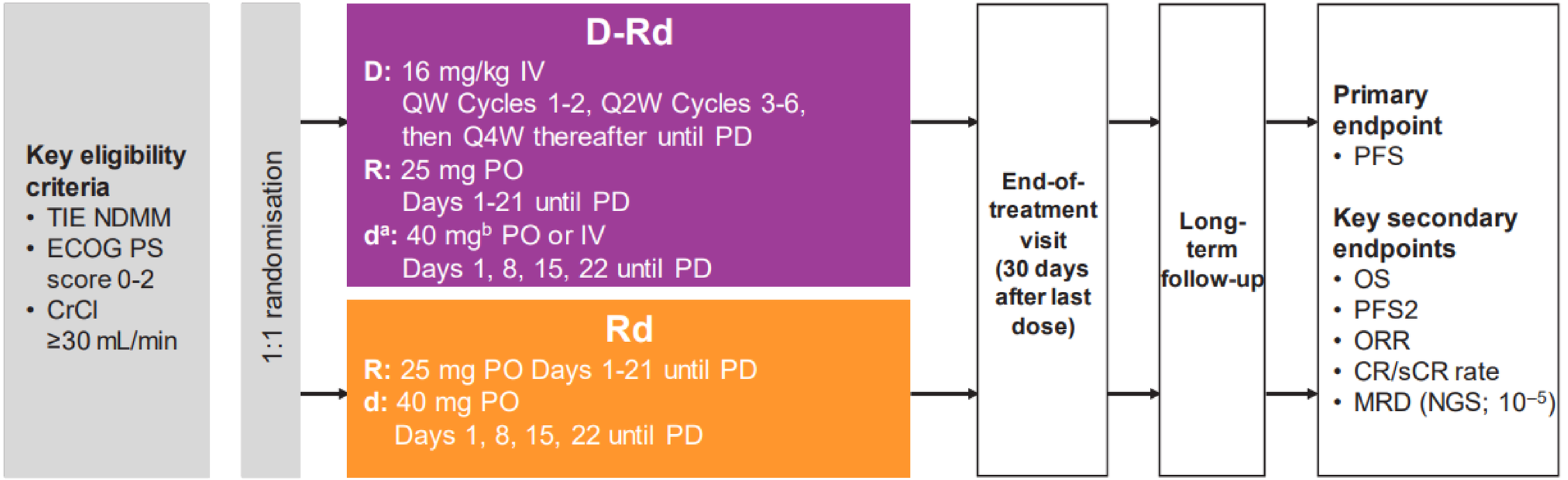


Goldschmidt et al. Lancet Haemat 2022

SOUTH CAROLINA ONCOLOGY SOCIETY

MAIA

– Patients were enrolled in MAIA from March 2015 through January 2017

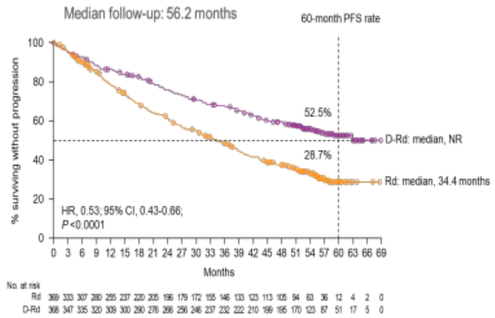


MAIA is a multicentre, randomised, open-label, active-controlled, phase 3 study of D-Rd versus Rd alone in patients with NDMM who are transplant ineligible

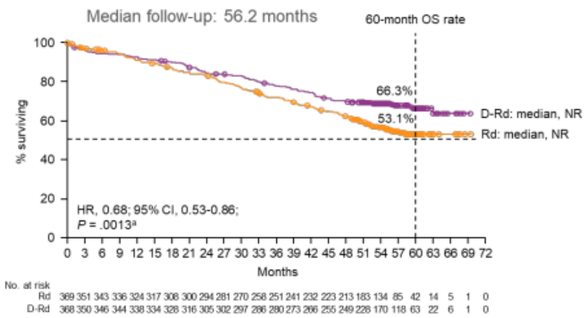
Kumar et al ASH 2022

MAIA updated PFS/OS

PFS



OS

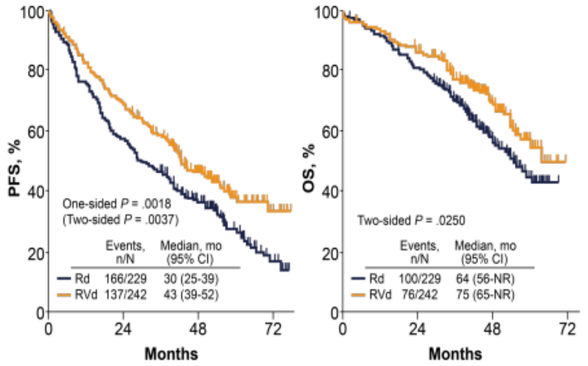


D-Rd demonstrated a significant benefit in OS, with a 32% reduction in the risk of death, in patients with NDMM who are transplant ineligible

Kumar et al ASH 2022

SWOG S0777: RVd Versus Rd Pts Without Immediate Intent for ASCT

Initial Therapy
RVd for eight 21-d cycles vs Rd for six 28-d cycles in patients not intending to proceed to upfront transplant, followed by Rd in both arms (N = 525)



	VRd	Rd	HR (95% CI); p value
mPFS	43 mo	30 mo	0.712 (0.56–0.91); p = 0.0018
mOS	75 mo	64 mo	0.71 (0.52-0.96); p = 0.025
ORR	81.5%	71.5%	
CR	15.7%	8.4%	

Grade III neurotoxicity worse in VRd group (33% vs 11%, p < 0.0001)

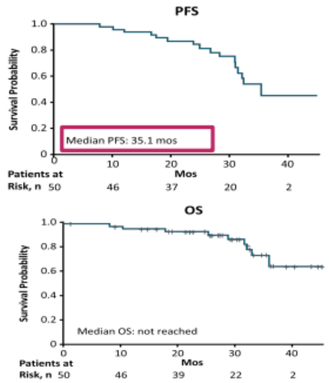
Durie B et al. Lancet. 2017

Elderly/Frail - Phase 2 RVd-Lite

Induction 35-day cycle x 9C
Len 15mg po D1-21
Bort 1.3mg/m2 SC D1, 8, 15, 22
Dex 20mg po
D1, 2, 8, 9, 15, 16, 22, 23 (<=75yo)
D1, 8, 15, 22 (>75yo)

Consolidation 35-day cycle x 6C
Len 15mg po D1-21
Bort 1.3mg/m2 SC D1, 15

- **Results**:
  - 86% ORR, 66% ≥VGPR
  - Median follow-up: 30 mo
  - Median PFS: 35.1 mo
  - Median OS: NR
  - Median age: 73 yo (65-91yo)
  - Peripheral neuropathy: 62%
  - Only 1 patient had grade 3 symptoms



O'Donnell et al. Br J Haematol 2018

DRVd 'Lite'?

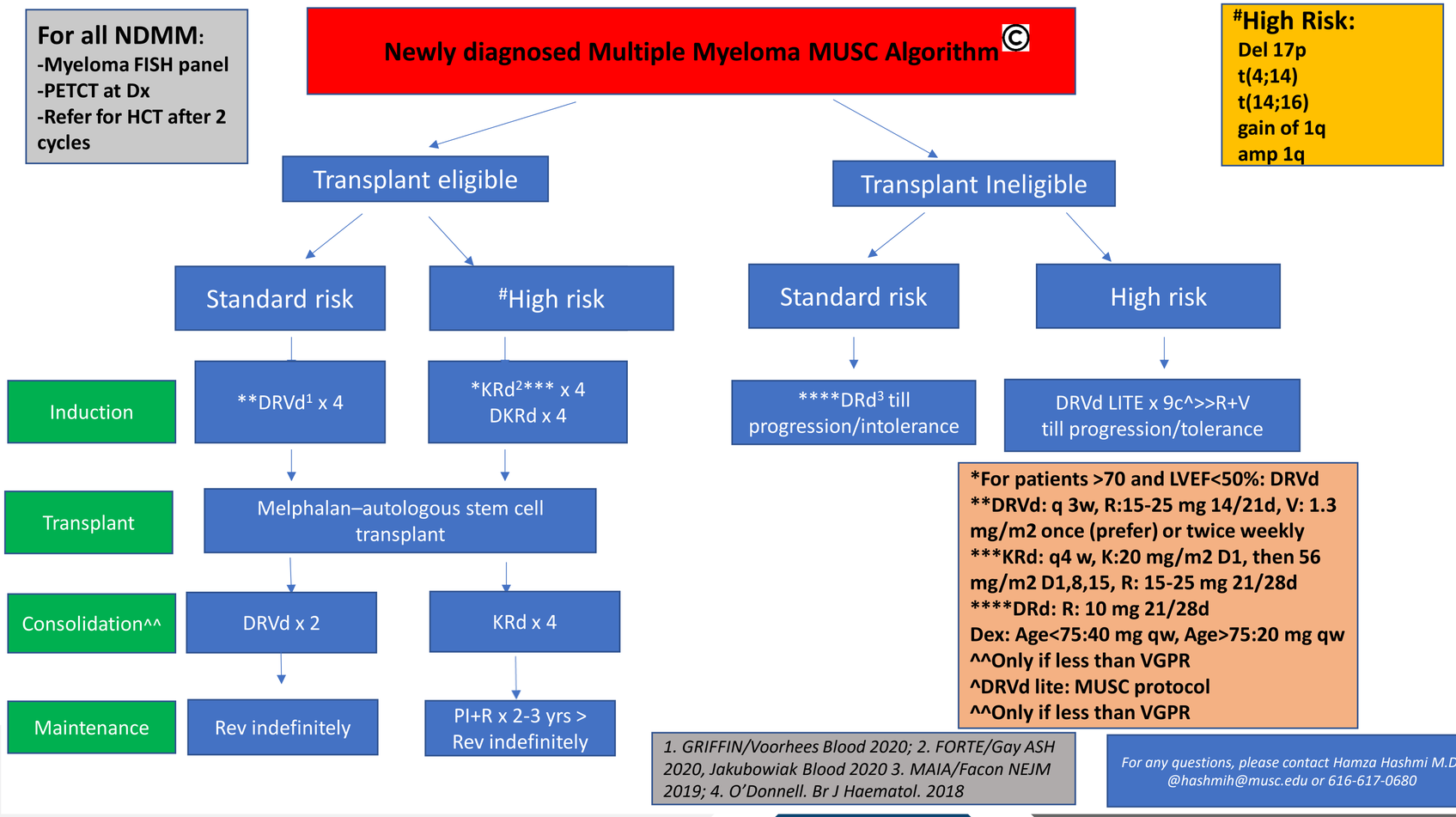
Dara qw x 8w>q2 wks x 16wks>q4wks
R 10-15 mg 21/28 days
Velcade D 1,8,15 every 28 days
Dex 20 mg weekly

TAKE HOME MESSAGE

-Dara RVd is the new SOC induction regimen for Newly Diagnosed Transplant Eligible Myeloma

-KRd may be preferred regimen for young and high-risk patients (FORTE)

-DRd is the crowned emperor for Newly Diagnosed Transplant Ineligible Myeloma, DRVd 'lite' is a protocol of choice for high-risk patients



1. GRIFFIN/Voorhees Blood 2020; 2. FORTE/Gay ASH 2020, Jakubowiak Blood 2020 3. MAIA/Facon NEJM 2019; 4. O'Donnell. Br J Haematol. 2018

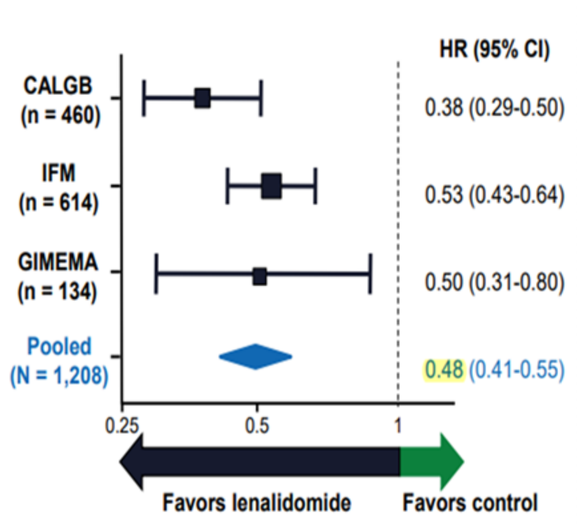
For any questions, please contact Hamza Hashmi M.D. @hashmih@musc.edu or 616-617-0680

What is the Ideal Maintenance Therapy?

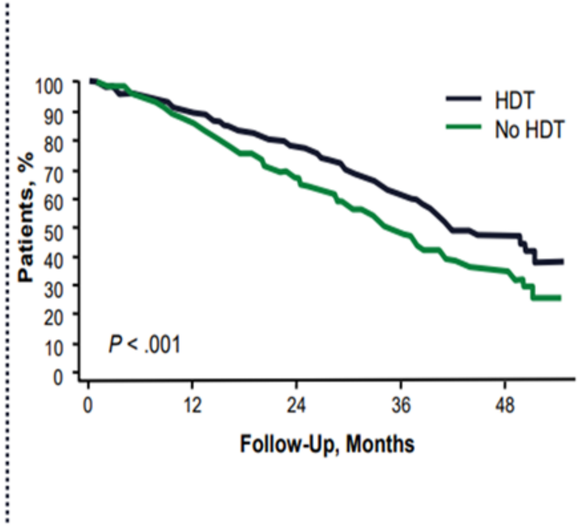
Single agent Lenalidomide
Lenalidomide + Proteasome inhibitors?
Daratumamab +Lenalidomide
Duration of Maintenance chemotherapy?

Summary of Lenalidomide Maintenance

Meta-Analysis of Lenalidomide Maintenance[1]



PFS With Early ASCT and Lenalidomide Maintenance[2]



McCarthy et al. JCO 017

	Continuous $n = 58$, (%)		Intermittent $n = 14$, (%)		Continuous to intermittent $n = 24$, (%)	
Dose modification*	31 (54)		4 (30)		2 (8)	
Reduction	27 (47)		1 (7)		2 (8)	
Interruption	4 (7)		3 (21)		0 (0)	
Discontinuation	0 (0)		0 (0)		0 (0)	
	*p value for any dose modification = 0.076				–	
Median time to dose modification (interquartile range: IQR), months	6 (3–16)		7 (5–12)		– (21–30)	
Median duration of exposure (IQR), months	25 (19–39)		15 (9–20)		33 (23–41)	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Hematologic	18 (31)	10 (17)	3 (22)	–	2 (8)	1 (4)
Neutropenia	11 (19)	9 (16)	1 (7)	1 (7)	0 (0)	0 (0)
Infections	2 (3)	–	2 (15)	–	0 (0)	0 (0)
Thrombocytopenia	3 (5)	1 (2)	0 (0)	0 (0)	2 (8)	1 (4)
Anemia	2 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Any grade		Any grade		Any grade	
Non-hematologic	18 (31)		1 (7)		0 (0)	
Thrombosis	0 (0)		0 (0)		0 (0)	
Rash	5 (9)		0 (0)		0 (0)	
Fatigue	6 (10)		0 (0)		0 (0)	
Diarrhea	3 (5)		0 (0)		0 (0)	

Journal of Oncology Pharmacy Practice
Volume 28, Issue 7, October 2022, Pages 1613-1616

https://doi.org/10.1177/10781552221112320

SAGE journals

Practice Issues

Safety and tolerability of lenalidomide maintenance dosing in patients with multiple myeloma post-autologous stem cell transplant

Abigail Shockley [1], James A Davis [1], Kelly J Gaffney [1], Deidra Smith [1], Erin Weeda [2], and Hamza Hashmi [3]

- The higher incidence of lenalidomide dose modifications in the continuous arm suggests that majority of patients are not able to tolerate continuous lenalidomide maintenance.
- A more tolerable option for maintenance may be an intermittent schedule, as reflected by the favorable safety outcomes in this group

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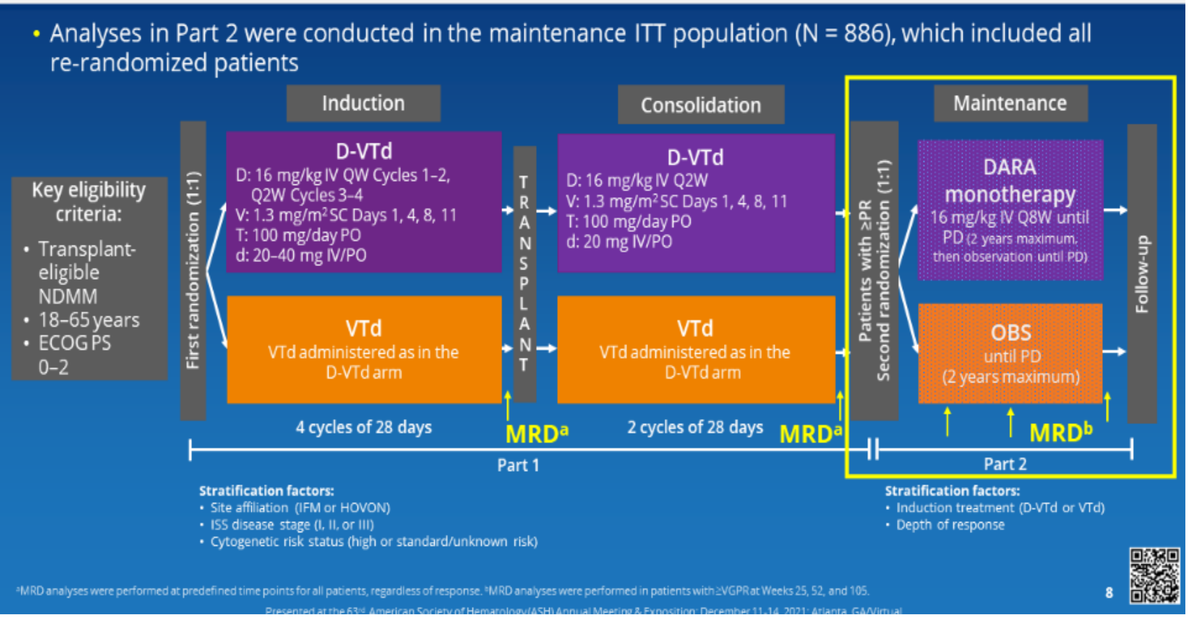
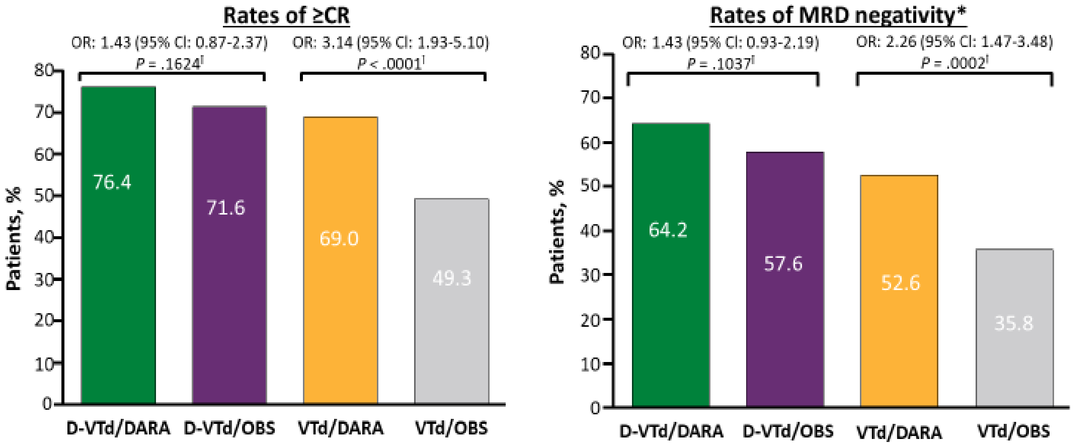
CASSIOPEIA: Maintenance



Moreau ASH 2021

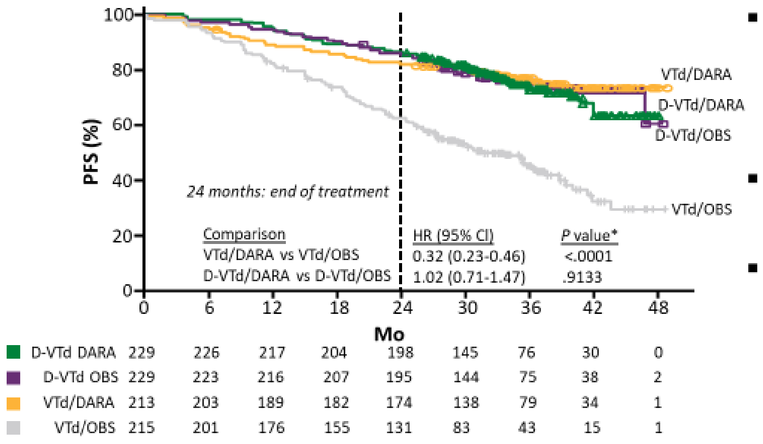
CASSIOPEIA Part 2: Response by Combination of Induction/Consolidation and Maintenance Therapy



*MRD negativity at 10^{-5} by next-generation sequencing. †Nominal *P* values.

Moreau. ASCO 2021. Abstr 8004. Reproduced with permission.

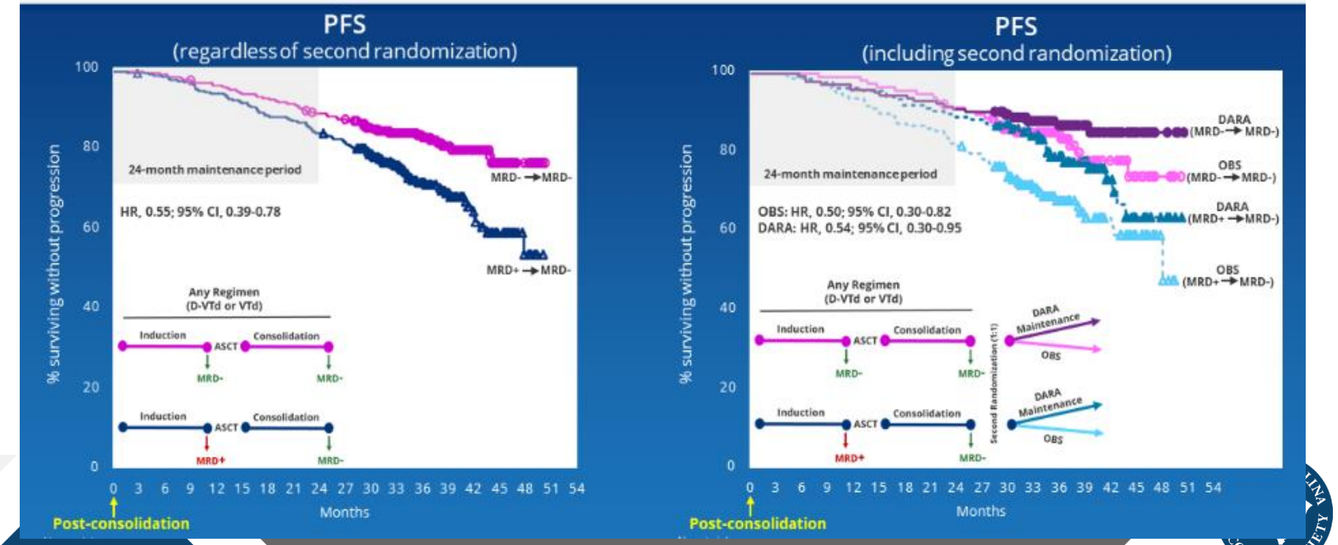
CASSIOPEIA Part 2: PFS by Combination of Induction/Consolidation and Maintenance Therapy



- Significant interaction between maintenance and consolidation in prespecified analysis
- PFS benefit for VTd/DARA vs VTd/OBS
- Comparable PFS for D-VTd/DARA vs D-VTd/OBS

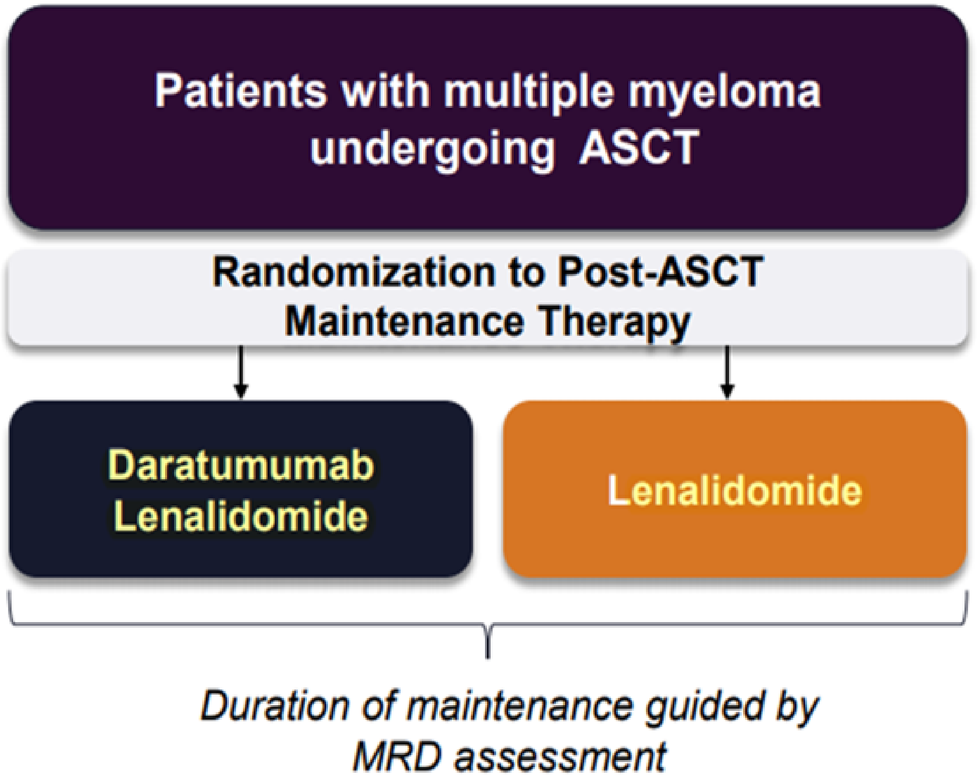
Moreau. ASCO 2021. Abstr 8004. Reproduced with permission.

CASSIOPEIA: PFS Based on MRD-negativity (MFC; 10^{-5}) Status Post-induction and Post–consolidation



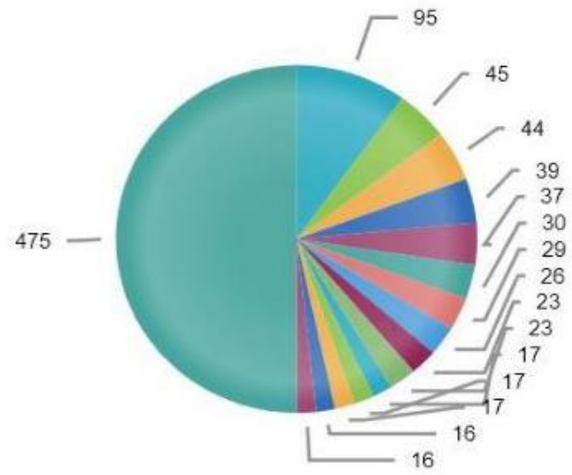
SWOG S1803: Daratumumab + Lenalidomide as Post-ASCT Maintenance[1]

- **Phase 3 Study**
- Daratumumab + lenalidomide or lenalidomide as post-ASCT maintenance
- MRD will be used to direct duration of treatment
  - At 2 years, patients randomized to discontinue or continue maintenance if MRD-negative
  - MRD-positive patients all continue maintenance



Courtesy BMT CTN

Patient Intervention Accrual by site



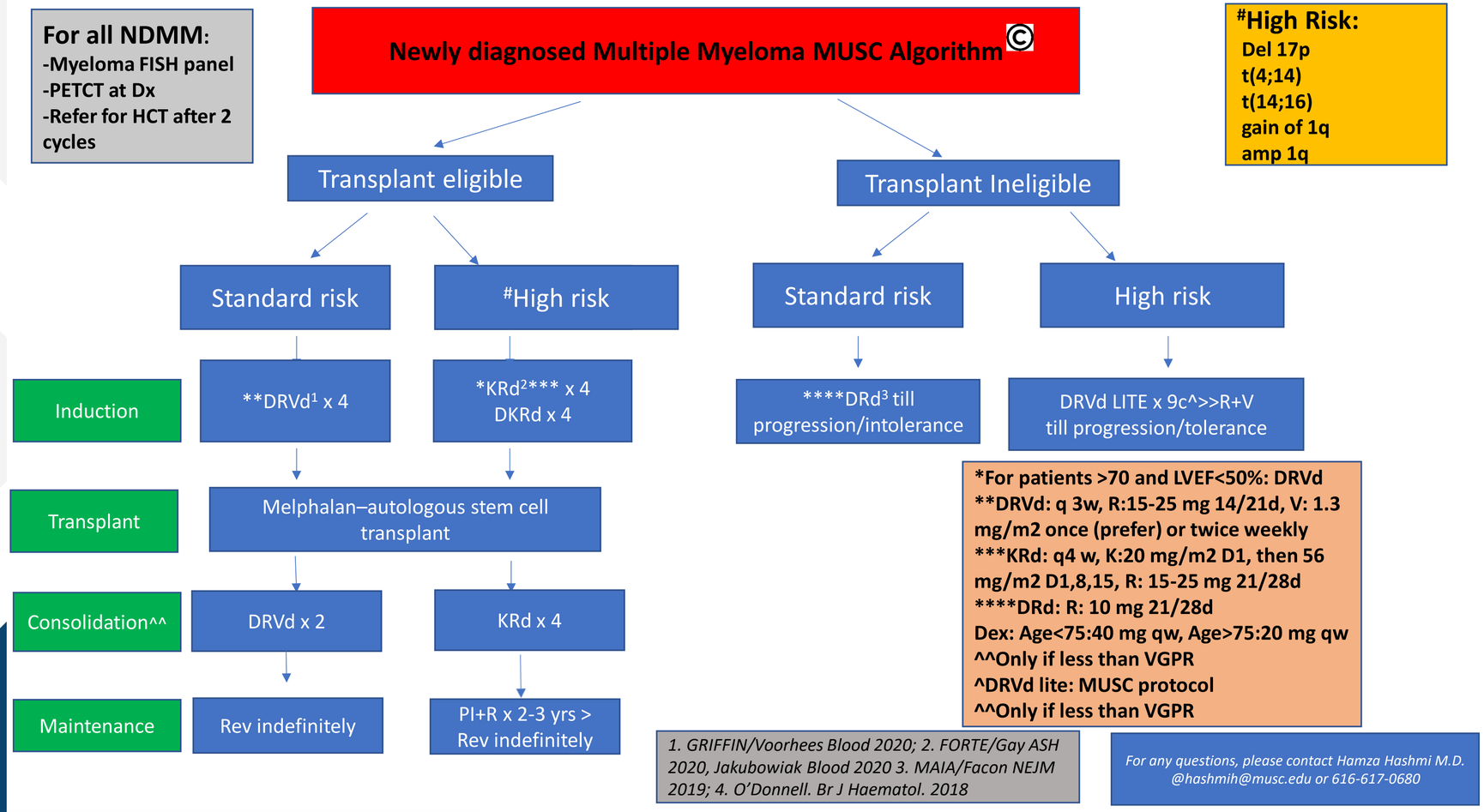
	Site	Accrual
1	City of Hope Comprehensive Cancer Center (CA)	95
2	Medical College of Wisconsin (WI)	48
3	Washington University School of Medicine (MO)	48
4	Moffitt Cancer Center (FL)	39
5	Medical University of South Carolina (SC)	37
6	University of Pennsylvania/Abramson Cancer Center (PA)	30
7	Ohio State University Comprehensive Cancer Center (OH)	29
8	University of Kansas Hospital-Westwood Cancer Center (KS)	26
9	Loyola University Medical Center (IL)	23
10	M D Anderson Cancer Center (TX)	23
11	Mayo Clinic Rochester (MN)	19
12	University of Wisconsin Carbone Cancer Center (WI)	18
13	Oregon Health Sciences University (OR)	17
14	Levine Cancer Institute (NC)	17
15	University of California Davis (CA)	16
XX	CANADIAN SITES activated (n=3)	3

TAKE HOME MESSAGE

-Whether patients who receive Dara in induction need Dara for maintenance remains unknown

-Observation alone for maintenance is a cardinal sin

-SWOG S1803 trial [D-R vs R for post HCT maintenance] will answer many important questions



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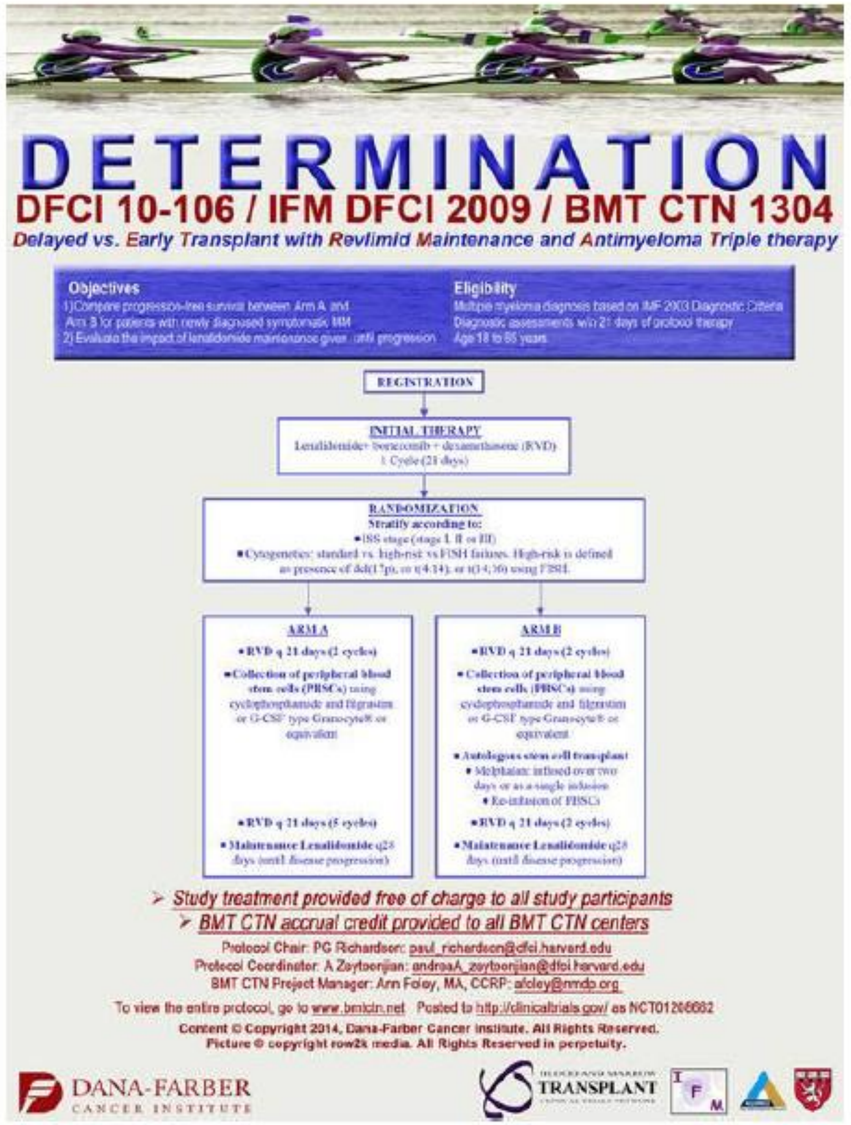
What is the role of Upfront Bone Marrow Transplant for Newly Diagnosed Multiple Myeloma?

OR

Why is Bone Marrow Transplant the ***TOM BRADY*** of Myeloma

2010



DETERMINATION

DFCI 10-106 / IFM DFCI 2009 / BMT CTN 1304

Delayed vs. Early Transplant with Revlimid Maintenance and Antimyeloma Triple therapy

Objectives

1)Compare progression-free survival between Arm A and Arm B for patients with newly diagnosed symptomatic MM

2) Evaluate the impact of lenalidomide maintenance given until progression

Eligibility

Multiple myeloma diagnosis based on IMF 2003 Diagnostic Criteria

Diagnostic assessments w/in 21 days of protocol therapy

Age 18 to 65 years

REGISTRATION

INITIAL THERAPY

Lenalidomide+ bortezomib + dexamethasone (RVD)

1 Cycle (21 days)

RANDOMIZATION

Stratify according to:

- ISS stage (stage I, II or III)
- Cytogenetics: standard vs. high-risk vs FISH failures. High-risk is defined as presence of del(17p), or t(4;14), or t(14;16) using FISH.

ARM A

- RVD q 21 days (2 cycles)
- Collection of peripheral blood stem cells (PBSCs) using cyclophosphamide and filgrastim or G-CSF type Granocyte® or equivalent
- RVD q 21 days (5 cycles)
- Maintenance Lenalidomide q28 days (until disease progression)

ARM B

- RVD q 21 days (2 cycles)
- Collection of peripheral blood stem cells (PBSCs) using cyclophosphamide and filgrastim or G-CSF type Granocyte® or equivalent
- Autologous stem cell transplant
  - Melphalan: infused over two days or as a single infusion
  - Re-infusion of PBSCs
- RVD q 21 days (2 cycles)
- Maintenance Lenalidomide q28 days (until disease progression)

➢ *Study treatment provided free of charge to all study participants*

➢ *BMT CTN accrual credit provided to all BMT CTN centers*

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Protocol Coordinator: A Zeytoonjian: andreaA_zeytoonjian@dfci.harvard.edu

BMT CTN Project Manager: Ann Foley, MA, CCRP: afoley@nmdp.org

To view the entire protocol, go to www.bmtctn.net Posted to http://clinicaltrials.gov/ as NCT01208662

DANA-FARBER CANCER INSTITUTE

TRANSPLANT

2022

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Triplet Therapy, Transplantation, and Maintenance to Progression in Myeloma

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DOI: 10.1056/NEJMoa2204925

Courtesy Paul Richardson

Courtesy Paul Richardson

DETERMINATION investigators and sites (n=56)

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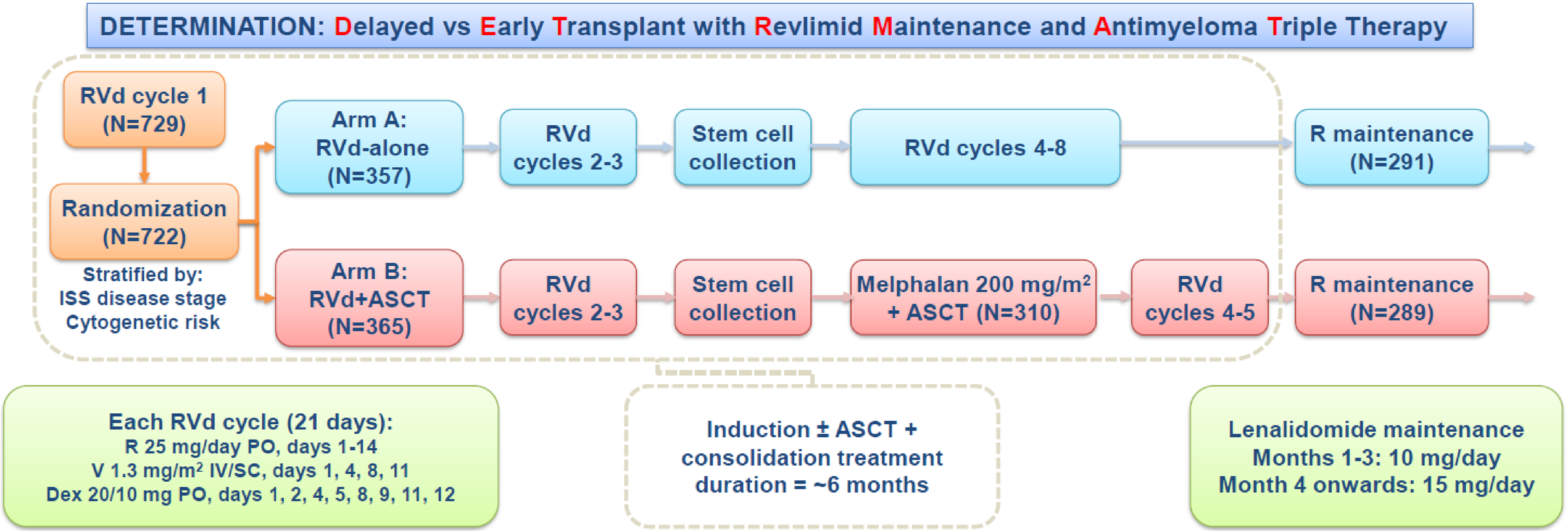
DETERMINATION: study design and patient disposition



d/Dex, dexamethasone; DOR, duration of response; ISS, International Staging System; IV, intravenous; PO, orally; R, lenalidomide; SC, subcutaneous; TTP, time to progression; V, bortezomib

Primary endpoint: PFS

Secondary endpoints: response rates; DOR; TTP; OS; QoL; safety

Courtesy Paul Richardson

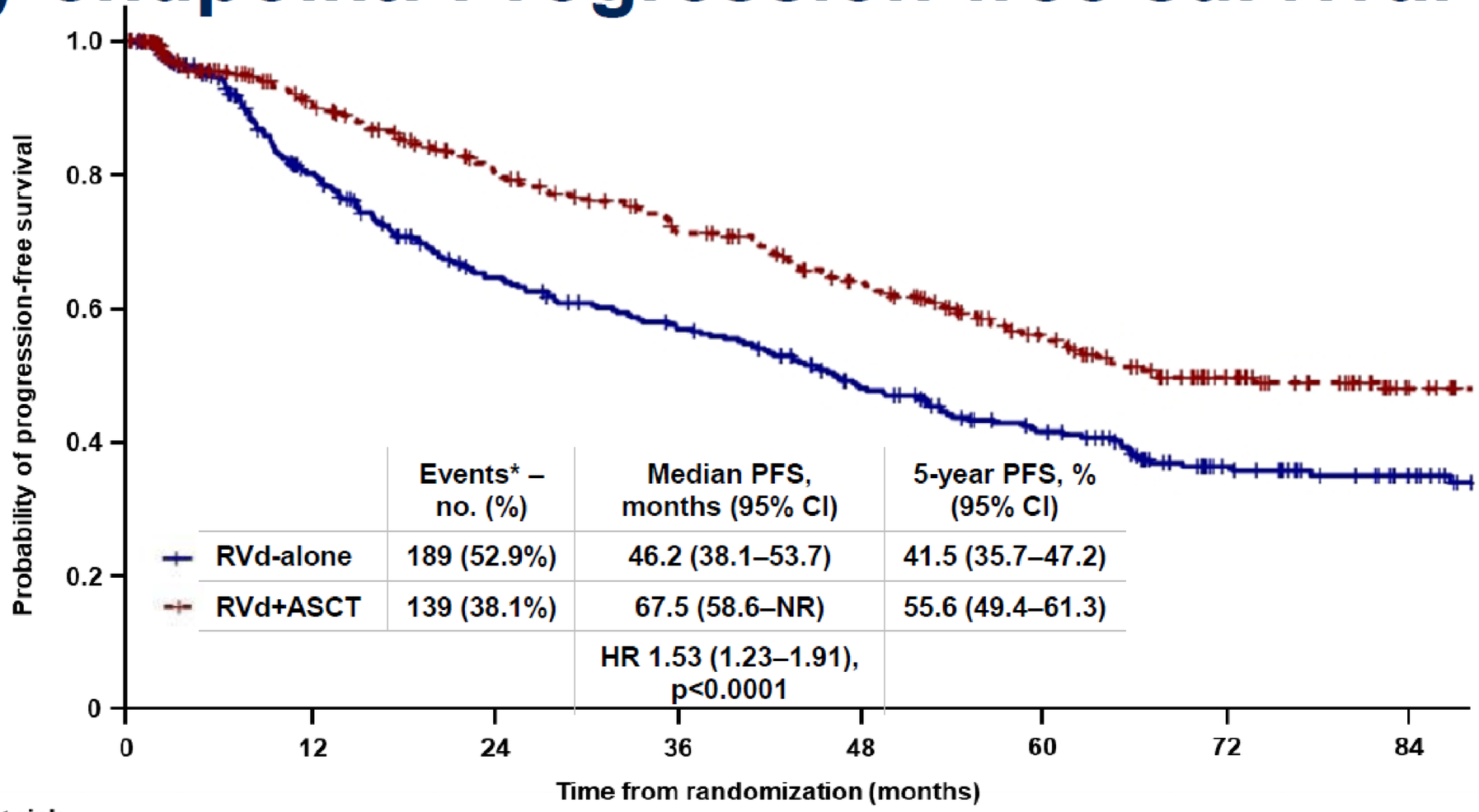
Patient demographics and disease characteristics

Characteristic	RVd-alone (N=357)	RVd+ASCT (N=365)
Median age (interquartile range) – years	57 (25–66)	55 (30–65)
Male/female, %	56.6 / 43.4	58.9 / 41.1
Race: White, Caucasian / Black, African-American / Other, %	76.4 / 18.8 / 4.8	75.8 / 18.4 / 5.8
ECOG performance status: 0 / 1 / 2, %	42.9 / 49.6 / 7.6	45.1 / 44.2 / 10.7
BMI: <25 / 25 to <30 / ≥30, %	22.4 / 39.5 / 38.1	22.2 / 34.8 / 43.0
MM disease type: IgG / IgA / Light chain only / Other, %	66.7 / 21.8 / 10.3 / 1.2	59.3 / 28.2 / 12.2 / 0.3
ISS disease stage: I / II / III, %	49.9 / 36.4 / 13.7	50.4 / 36.7 / 12.9
Elevated lactate dehydrogenase (≥225 U/L), %	27.0	25.4
Cytogenetics: high-risk* / standard-risk, %	19.8 / 80.2	19.4 / 80.6
Cytogenetics: t(4;14) / t(14;16) / del 17p,† %	9.6 / 3.0 / 11.4	8.2 / 4.4 / 10.0
Revised-ISS disease stage:‡ I / II / III, %	30.9 / 60.7 / 8.4	31.2 / 62.6 / 6.2

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group. *High-risk includes t(4;14), t(14;16), and deletion 17p. †Cutoff threshold for positivity per institutional standards. ‡Classified using ≥225 U/L cutoff for elevated lactate dehydrogenase level. Patients registered between October 1, 2010, and January 30, 2018.

Courtesy Paul Richardson

Primary endpoint: Progression-free survival (PFS)



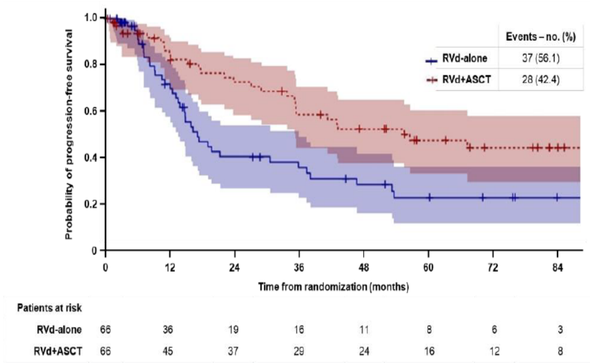
	Events* – no. (%)	Median PFS, months (95% CI)	5-year PFS, % (95% CI)
RVd-alone	189 (52.9%)	46.2 (38.1–53.7)	41.5 (35.7–47.2)
RVd+ASCT	139 (38.1%)	67.5 (58.6–NR)	55.6 (49.4–61.3)
		HR 1.53 (1.23–1.91), p<0.0001	

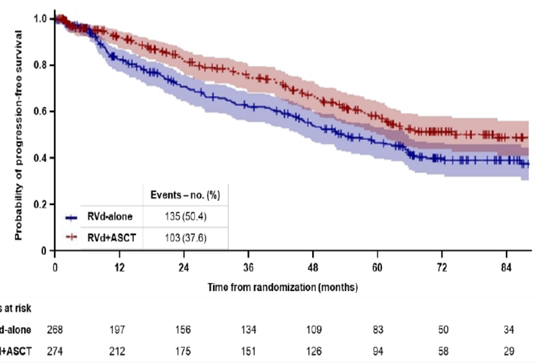
Patients at risk								
RVd-alone	357	250	187	160	126	96	60	40
RVd+ASCT	365	276	226	191	160	118	77	42

CI, confidence interval; HR, hazard ratio; Data cutoff: 12/10/21. *PFS events: disease progression or death.

Courtesy Paul Richardson

PFS by stratification factor – cytogenetic risk





Shaded areas indicate 95% CIs

Median PFS, months	RVd-alone	RVd+ASCT
High-risk	17.1	55.5
	HR 1.99 (95% CI 1.21–3.26)	

Median PFS, months	RVd-alone	RVd+ASCT
Standard-risk	53.2	82.3
	HR 1.38 (95% CI 1.07–1.79)	

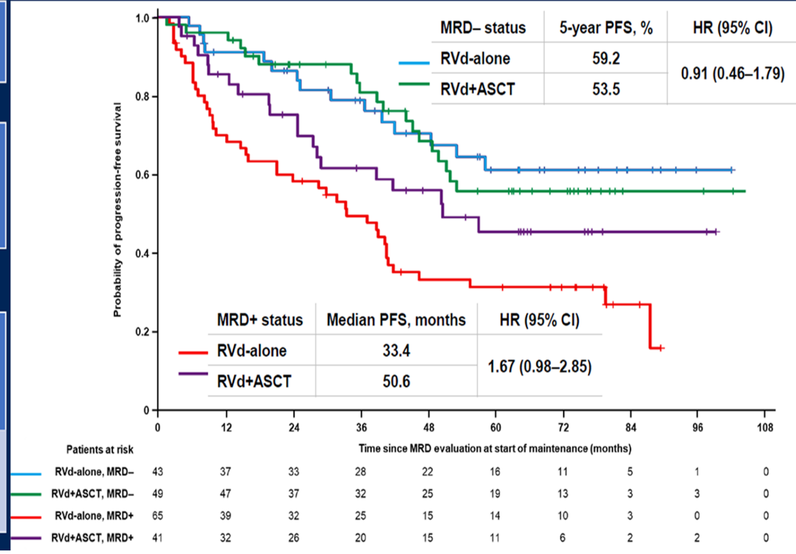
MRD / PFS by MRD status

Preliminary analysis

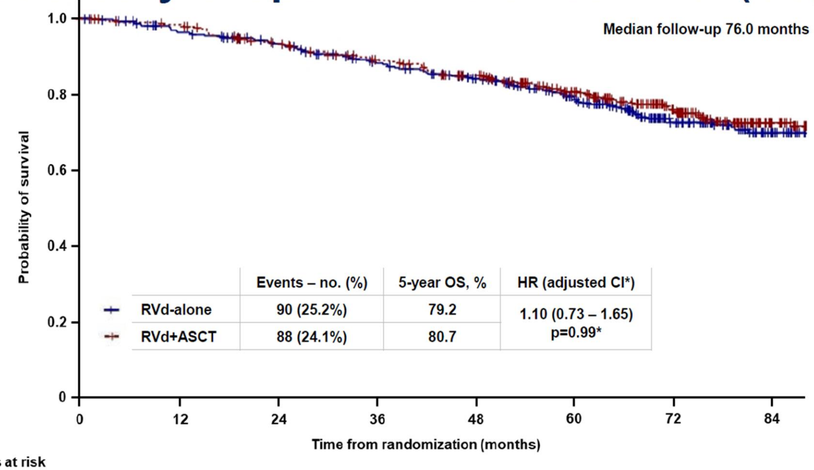
108 RVd-alone, 90 RVd+ASCT patients with samples from start of maintenance

Rate of MRD-negative status (NGS, 10^{-5}):
39.8% vs 54.4%

Odds ratio 0.55 (unadjusted 95% CI 0.30–1.01)



Key secondary endpoint: Overall survival (OS)

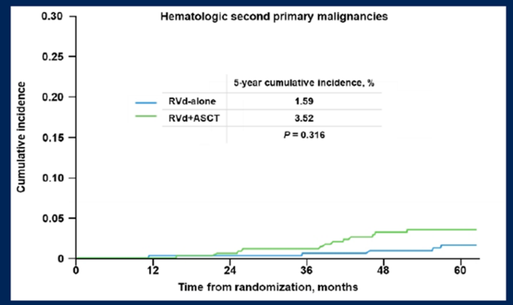


Data cutoff:12/10/21

*CIs and p-value adjusted using Bonferroni's correction to control overall family-wise error rate for secondary outcomes. Therefore, CIs use an α level of 0.05/7.

Second primary malignancies

- 5-year cumulative incidence of SPMs (RVd-alone vs RVd+ASCT):
  - All : 9.7% vs 10.8%
  - Invasive: 4.9% vs 6.5%
  - Hematologic: 1.59% vs 3.52%



SPMs, %	RVd-alone (N=357)	RVd+ASCT (N=365)
Any	10.4	10.7
Any invasive SPM	5.3	6.8
Any hematologic SPM	2.5	3.6
ALL, n	7	3
AML/MDS, n	0*	10*
CLL/CML, n	2	0
Any solid tumor SPM	3.4	3.3
Any non-invasive solid tumor SPM	0	0.5
Any non-melanoma skin cancer	5.9	4.1

* p=0.002

Courtesy Paul Richardson

TAKE HOME MESSAGE

Editorial

‘A Stitch in Time Saves Nine’: Early stem cell transplant continues to improve outcomes in patients with newly diagnosed multiple myeloma

Hamza Hashmi, James A. Davis & Al-Ola Abdallah

Received 04 May 2023, Accepted 16 Jun 2023, Accepted author version posted online: 19 Jun 2023

Download citation https://doi.org/10.1080/17474086.2023.2227789 Check for updates

-Upfront ASCT remains the *TOM BRADY of Myeloma*

-All HIGH-RISK patients should be offered upfront ASCT

-OS benefit may emerge over longer follow up, remember median follow up has not been reached!!

-Trial not applicable to older patients who may grow frail(er) over time

-Stem cell storage and collection is not a luxury all patients have

-A young fit patient with a STANDARD risk Myeloma and a cooperative insurance may be of offered ‘delayed’ ASCT

How Do I treat Relapsed Refractory Multiple Myeloma?

CD38 antibody + Pomalyst + Dex
vs
CD38 antibody + Carfilzomib + Dex

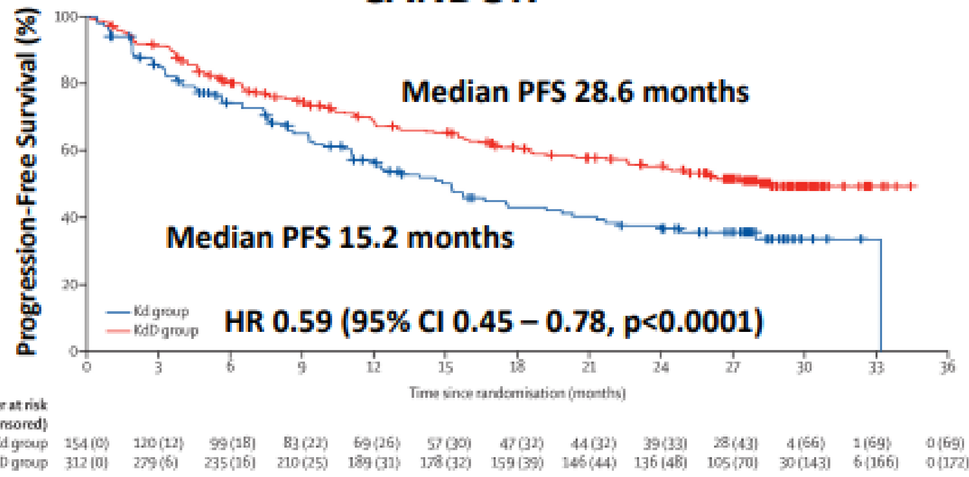
When do I use Venetoclax based therapy

Role of Selinexor based combinations

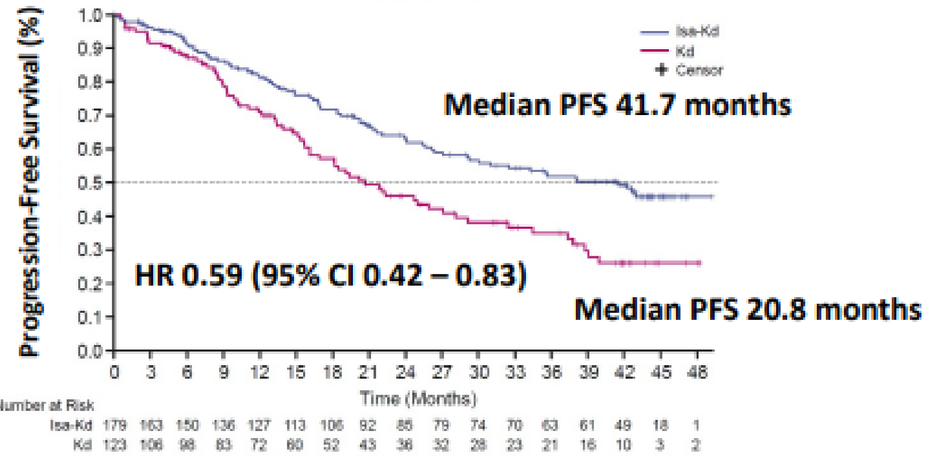
CD38 mAbs + Carfilzomib and Dexamethasone in Early Relapsed Myeloma

- **CANDOR: Phase III study of carfilzomib and dexamethasone ± daratumumab**
- **IKEMA: Phase III study of carfilzomib and dexamethasone ± isatuximab**
- **1 – 3 prior lines of therapy, treatment until disease progression**
- **Median prior lines of therapy (experimental / control): CANDOR 2 / 2; IKEMA: 2 / 2**
- **Lenalidomide refractory (experimental / control): CANDOR 32% / 36%; IKEMA: 32% / 34%**

CANDOR



IKEMA



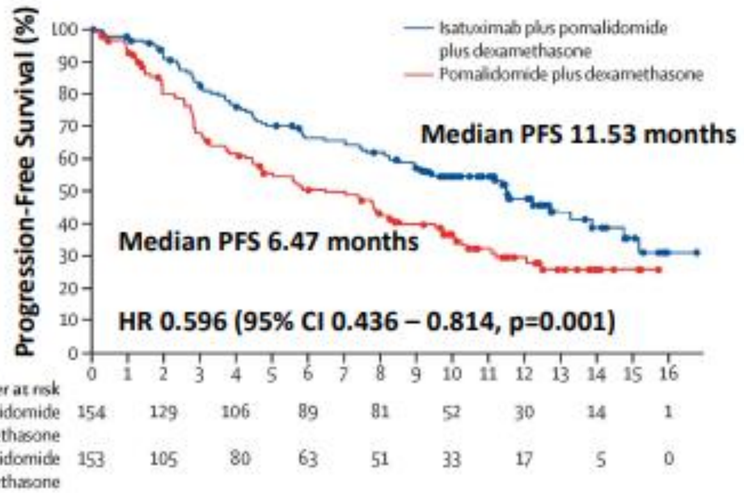
	CANDOR		IKEMA	
Regimen	**DKd**	**Kd**	**Isa-Kd**	**Kd**
MRD-	**18%**	**4%**	**33.5%**	**15.4%**

Dimoupolos, M, et al. Lancet 2020;396:186-97.
Usmani, SZ, et al. Lancet Oncol 2022;23:65-76.
Moreau, P, et al. Lancet 2021;397:2361-71.
Martin, T, et al. Blood Adv 2022;6:4506-15.
Moreau, P, et al. ESMO 2022.

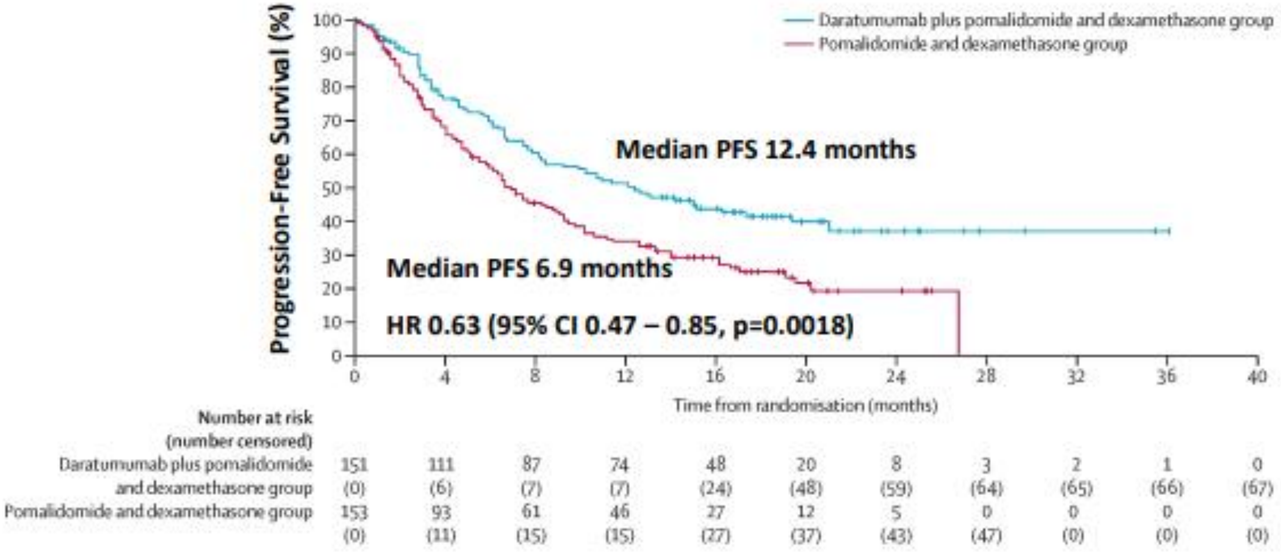
CD38 mAbs + Pomalidomide and Dexamethasone in Early Relapsed Myeloma

- **APOLLO: Phase III study of pomalidomide and dexamethasone ± daratumumab**
- **ICARIA: Phase III study of pomalidomide and dexamethasone ± isatuximab**
- **APOLLO: 1 – 3 prior lines of therapy, ICARIA ≥2 prior lines of therapy; treatment until disease progression**
- **Median prior lines of therapy (experimental / control): ICARIA 3 / 3; APOLLO: 2 / 2**
- **Lenalidomide refractory (experimental / control): ICARIA 94% / 92%; APOLLO 79% / 80%**
- **Lenalidomide and PI refractory (experimental / control): ICARIA 72% / 70%; APOLLO 42% / 42%**

ICARIA



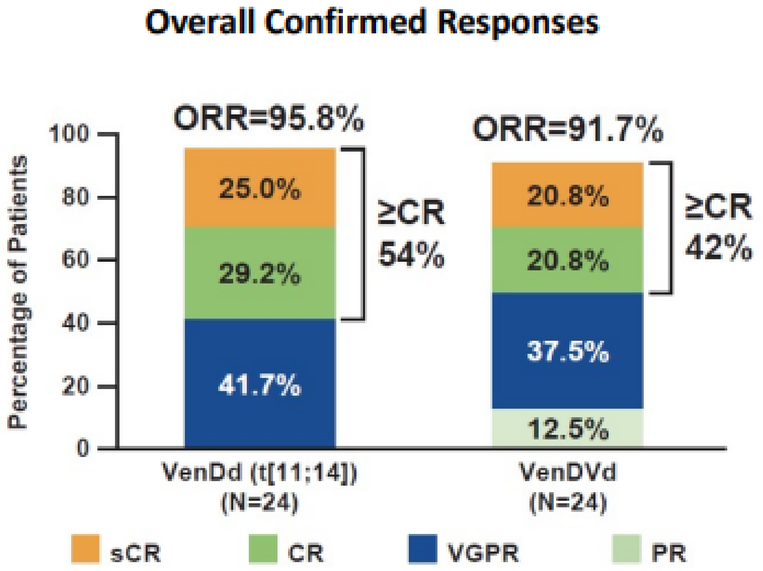
APOLLO

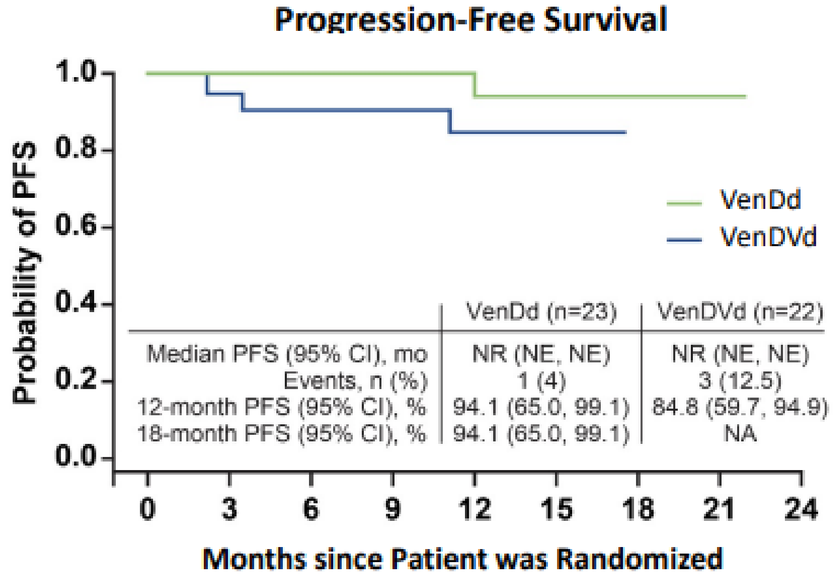


Attal, M, et al. Lancet 2019;394:2096 - 2107

Dimopoulos, M, et al. Lancet Oncol 2021;22:801-812

Daratumumab, Venetoclax and Dexamethasone in Relapsed, t(11;14)+ Myeloma





Patients at Risk

VenDd	24	23	22	22	15	8	3	1
VenDVd	24	20	19	18	8	3		

Kaufman, J et al. ASH 2020.

Selinexor-Based Triplets

	SVd (N = 40)		SKd (N = 24)	SPd (N = 32)	Dara-Sd (N = 30)
Study Phase	I		I	I	I
Pt Population	50% PI refractory, 3 median prior lines of therapy		Carfilzomib naïve, 50% bort refractory, 3 median prior regimens	Len Refractory, Pom Naïve, 3 median prior regimens	Dara Naïve, 85%/76% PI/IMiD Refractory, 3 median prior regimens
ORR	PI Sens / Naïve	PI Refractory	70.8%	56%	73%
	84%	43%			
≥CR	11%	5%	16.7%	3%	0%
VGPR	26%	19%	33.3%	15.2%	37%
PR	47%	19%	20.8%	39.4%	37%
Median PFS, mos	17.8	6.1	Not reported	12.2	12.5

Bahlis NJ et al. Blood 2019;132:2546-54.
Gasparetto C et al. ASCO 2020 (SKd and Dara-Sd)
Chen C et al. ASH 2020

How do I treat TRIPLE / PENTA CLASS REFRACTORY MULTIPLE MYELOMA

CAR T vs Bispecific: A Sophie's Choice

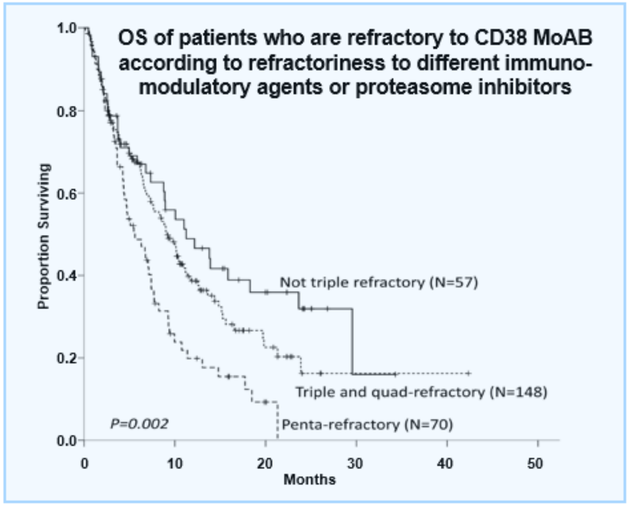
Patients With MM Refractory to CD38-Targeting Monoclonal Antibodies Have a Poor Prognosis

The MAMMOTH study

- Retrospective study of 275 patients from 14 academic centers in the US who had MM refractory to CD38 monoclonal antibodies (MoAB)
- Median number of prior therapies = 4 (range 1-16)
- Prior autologous stem cell transplantation = 72%

Efficacy

- mOS from T_0 for the entire cohort: 8.6 months (95% CI 7.5-9.9)
- At least 1 subsequent treatment regimen was given post T_0 in 249 (90%) patients
  - ORR to first regimen after T_0 = 31%
  - mPFS = 3.4 months
  - mOS = 9.3 months



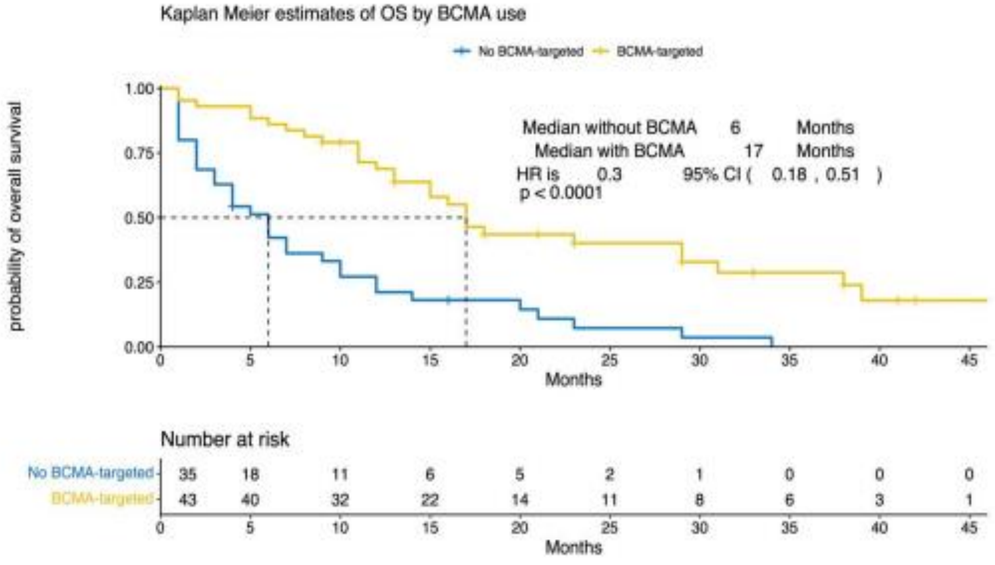
cancers

MDPI

Article

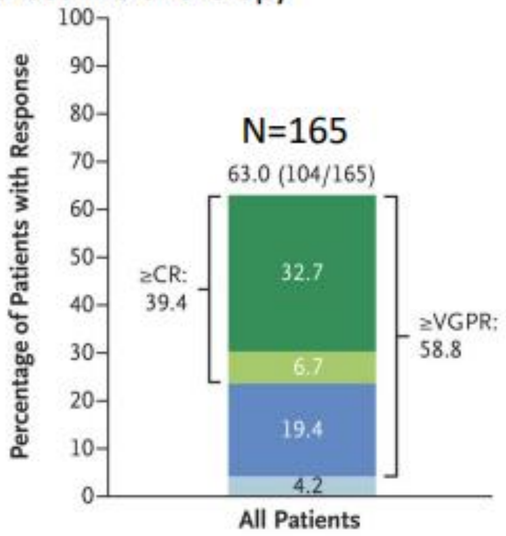
Outcomes of Penta-Refractory Multiple Myeloma Patients Treated with or without BCMA-Directed Therapy

Shebli Atrash [1,2,*], Aytaj Mammadzadeh [3], Fulei Peng [4], Omar Alkharabsheh [2,5], Aimaz Afrough [2,6], Wei Cui [2,7], Zahra Mahmoudjafari [2,8], Al-Ola Abdallah [2,9] and Hamza Hashmi [2,10]

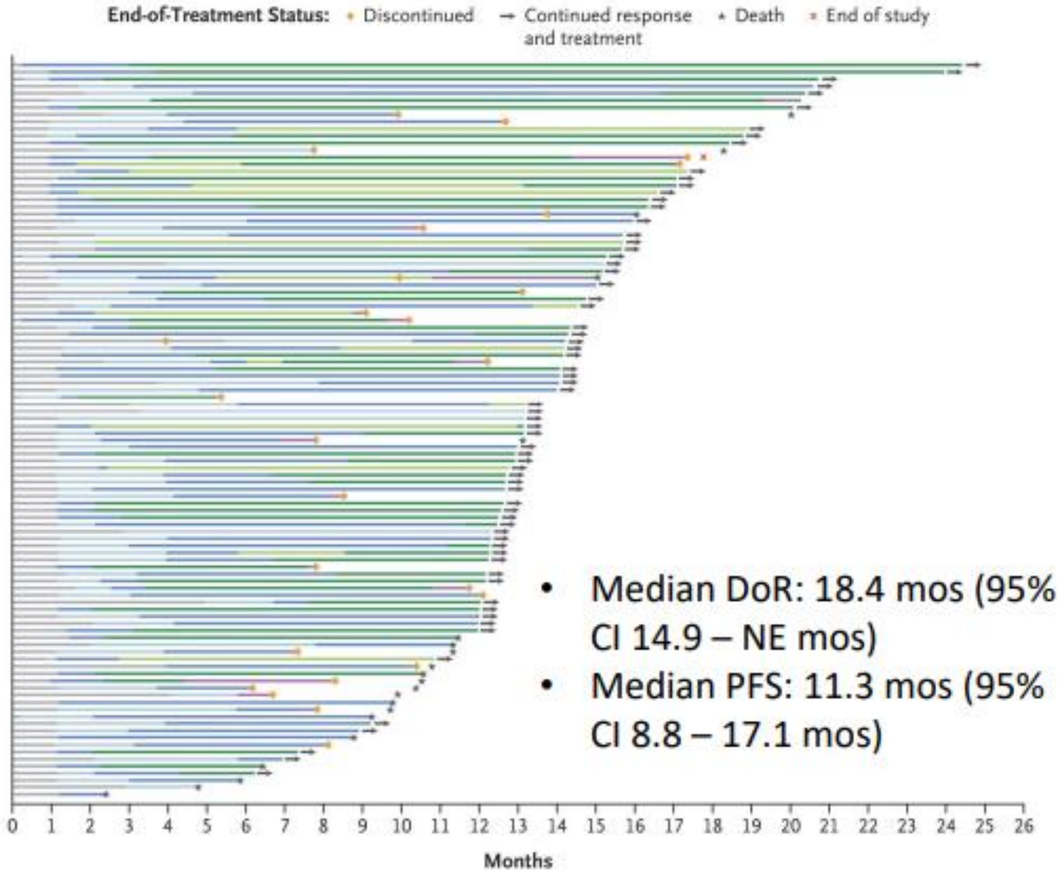


MajesTEC-1: Phase I/II Study of Teclistamab in RRMM

- 17% with EMM, 25.7% with HRCGs
- Median Prior Lines of Therapy: 5 (2 – 14)
- 77.6% triple class refractory, 89.7% refractory to last line of therapy



- Neutropenia 70.9% (64.2% ≥grade 3), hypogammaglobulinemia 74.5%
- Infections 76.4% (44.8% ≥grade 3)
- 12 COVID-19 deaths

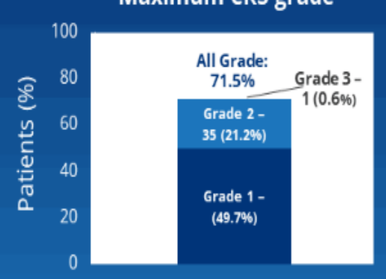


- Median DoR: 18.4 mos (95% CI 14.9 – NE mos)
- Median PFS: 11.3 mos (95% CI 8.8 – 17.1 mos)

Moreau P, et al NEJM 2022

MajesTEC-1: Cytokine Release Syndrome

Parameter	Safety Analysis Set N=165
Patients with CRS, n (%)	118 (71.5)
Patients with ≥2 CRS events	54 (32.7)
Time to onset (days), median (range)	2 (1–6)
Duration (days), median (range)	2 (1–9)
Patients who received supportive measures[a], n (%)	109 (66.1)
Tocilizumab	60 (36.4)
Low-flow oxygen by nasal cannula[b]	21 (12.7)
Steroids	13 (7.9)
Single vasopressor	1 (0.6)



- All CRS events were grade 1/2, except for 1 transient-grade 3 CRS event that fully resolved, and 97% of events were confined to step-up and cycle 1
- All CRS events resolved, with no treatment discontinuations due to CRS
- Over the course of their treatment, 2.4% of patients received >1 dose of tocilizumab for a single CRS event

MajesTEC-1: Neurotoxicity

Parameter	Safety Analysis Set N=165
Patients with neurotoxicity, n (%)	21 (12.7)
Headache	14 (8.5)
ICANS[a]	5 (3.0)
Encephalopathy	2 (1.2)
Tremor	2 (1.2)
Patients with grade ≥3 events	0
Time to onset, median (range) days	2.5 (1–7)
Duration, median (range) days	3.0 (1–37)
Patients requiring supportive measures for neurotoxicity, n (%)	12 (7.3)
Tocilizumab	3 (1.8)
Dexamethasone	3 (1.8)
Levetiracetam	1 (0.6)

- The overall incidence of neurotoxicity was low
- The most commonly reported neurotoxicity event was headache (14 patients [8.5%])
- All events were grade 1/2
- There were no treatment discontinuations or dose reductions due to neurotoxicity[b]
- 12 patients (7.3%) required supportive measures for neurotoxicity
- There were 5 patients with ICANS events at the RP2D
  - All were grade 1/2
  - Most (7/9) ICANS events were concurrent with CRS; all resolved

MajesTEC-1: Overall Safety Profile

Safety Analysis Set N=165		
AEs ≥20%, n (%)	Any Grade	Grade 3/4
Hematologic		
Neutropenia	108 (65.5)	94 (57.0)
Anemia	82 (49.7)	57 (34.5)
Thrombocytopenia	63 (38.2)	35 (21.2)
Lymphopenia	56 (33.9)	53 (32.1)
Nonhematologic		
CRS	118 (71.5)	1 (0.6)
Injection site erythema	42 (25.5)	0 (0)
Fatigue	41 (24.8)	3 (1.8)
Nausea	40 (24.2)	1 (0.6)
Headache	36 (21.8)	1 (0.6)
Diarrhea	34 (20.6)	4 (2.4)

Teclistamab was well tolerated; no patients required dose reduction

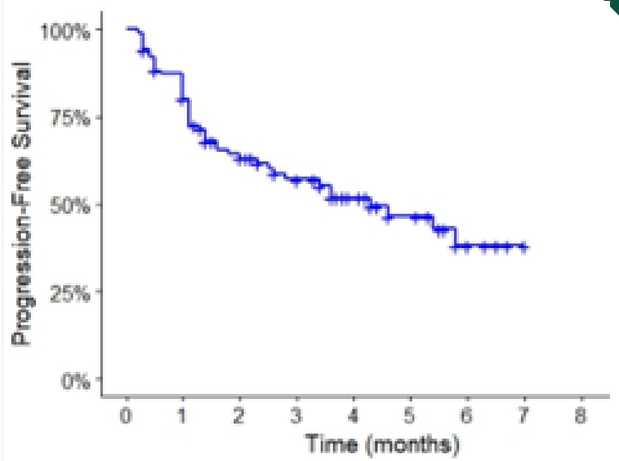
- Only 1 patient discontinued due to an AE (adenoviral pneumonia)
- Serious AEs occurred in 88 patients (53.3%)
  - Teclistamab-related serious AEs[a] occurred in 33 patients
- Injection-site reactions occurred in 58 patients (35.2%; all grade 1/2)
- Infections occurred in 104 (63%) patients (grade 3/4: 35.2%)
  - 9 (5.5%) patients had opportunistic infections[b]
- 119 patients (72.1%) had evidence of hypogammaglobulinemia[c]
  - 41 of these patients received IVIG at any time during the study (at physician discretion)
- There were 9 deaths due to AEs; none were related to teclistamab
  - COVID-19 (n=7)
  - Pneumonia (n=1)
  - Hemoperitoneum (n=1)

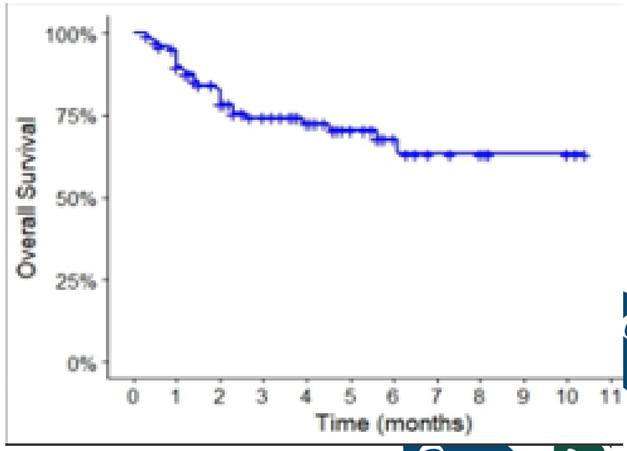
Courtesy Saad Z Usmani

REAL WORLD EXPERIENCE with TECLISTAMAB for RRMM

Characteristic	N (%)
Female: Male ratio	1.17
Age, years, median (range)	66.5 (35–87)
IgG subtype	54 (53%)
R-ISS III	25 (25)
High risk cytogenetics	55 (54)
EMD	45 (44)
Prior LOT (median, range)	6 (–17)
Refractory to PI	102 (100)
Refractory to IMiDs	102 (100)
Refractory to anti-CD38 MoAb	102 (100)
Prior ASCT	60 (59)
Double refractory	94 (92)
Triple Refractory	94 (92)
Penta refractory	67%
BDT refractory	56 (55%)

Characteristic	Best ORR n (%)
Full cohort (n=102)	65 (64)
PR	18 (18)
VGPR	18 (18)
CR/sCR	29 (28)
Age>70 (n=33)	23 (70)
Non-Hispanic Black (n=25)	17 (68)
Ineligible for MajesTEC-1 trial (n=83)	49 (59)
RISS III (n=25)	13 (52)
High-risk cytogenetics (n=55)	34 (62)
EMD (n=44)	20 (45)
CrCl < 40 mL/min (n=13)	7 (54)
Refractory status	
Four or less prior LOT (n=23)	18 (78)
>4 lines of prior therapy (n=79)	47 (59)
Double refractory (n=94)	58 (62)
Triple Refractory (n=94)	58 (62)
Penta refractory (n=68)	45 (66)
BCMA refractory	38 (64%)
Prior belantamab mafodotin (n=17)	12 (71)
Prior BCMA directed CAR T (n=33)	20 (61)
≥ 2 prior BCMA directed therapies (n=9)	6 (67)





ORR 65%, VGPR or better 45%
60% Ineligible for MajesTEC-1
6 mo PFS 40%, 6 mo OS 65%

Hashmi et al ASH 2023

BCMA x CD3 Targeted Antibodies

Bispecific Antibody	Teclistamab (JNJ-64007957)	Elranatamab (PF-06863135)	Linvoseltamab (REGN5458)	ABBV-383	Alnuctamab BMS-93269	HPN217
Structure/Function	Humanized antibody	Humanized antibody	*Veloci-Bi*® platform fully human antibody	Low CD3 affinity fully human antibody	Humanize antibody 2 BCMA + 1 CD3	Trispecific 50kDa (albumin)
Treatment	Weekly SC	Weekly SC	Weekly IV	IV q3w	Qwk -> Q4wk SQ	Q2wk IV
Patients	n= 165	n= 123	n= 252	n= 174	n= 68	n= 62
Median prior lines	5	5	5	5	4	6
Triple-class refractory	78%	97%	81%	80%	63%	76%
ORR at RP2d	63%	61%	64%	58-61%	65%	73%
RP2D (n)	1.5 mg/kg SC **(n=165)**	76 mg SQ **(n=123)**	200 mg IV (n=58)	40 to 60 mg IV (n=52 n=59)	30 mg SQ (n=26)	?12 or 24 mg (n=13)
PFS	11.3 mos (8.8-17.1)	NE @ 12 mos	NR	13.7 or 11.2 mos	NR	NR
DOR	18.4 mos (14.9-NE)	NE @12 mos	89% @ 6 mos	NE	NE	NR
Median f/u	14.1 mos	10.4 mos	3.2 mos	6.8	4.6 mos	
AEs, (All/(Gr 3+);						
CRS	72% (0.6%)	58% (0%)	44% (1%)	60% (1%)	53% (0%)	27 (0%)
Infections	76% (45%)	67% (35%)	54% (29%)	(22%)	34% (9%)	45% (16%)
Neutropenia	71% (64%)	48% (48%)	25% (23%)	34% (26%)	37%(32%)	16% (13%)
Anemia	52% (37%)	48% (37%)	36% (31%)	37% (16%)	38%(25%)	44% (34%)
Thrombocytopenia	40% (21%)	26% (24%)	18% (6%)	29% (11%)	24%(9%)	NR
Neuro	Neurotoxicity 15% (0.1)	NR/ PN?	ICANS 2% (1%)	5% (0.1%)	ICANS 3 (0%)	16% (0%)
# Deaths	68/(41 due to PD)	21 (/11 due to PD)	NR	46	1	NR
Hypogamma/IVIg	75%//39%	75%/40%	NR	NR		

Moreau et al. *N Engl J Med.* Jun 5 2022. Bahlis et al ASH 2022 Bumma et al ASH 2022; Voorhees et al ASH 2022 Wong et al ASH 2022;; Abdallah et al ASH 2022.

Bispecific Antibody	Talquetamab (JNJ-64407564) Phase 1/2 MonumenTAL-1 Study GPRC x CD3			Forimtamig (RG6234) Phase 1 GPRC X CD3 (2:1)	Cevostamab (GO39775) Phase 1 FcRH5 X CD3
Treatment	0.4 mg/kg SQ QW	0.8 mg/kg SC Q2W	Either dose	SQ q 2wk *12 mos	IV q3w * 12 mos
Patients	n=143	n=145	n=51	n=57	n=161
Median prior lines	5	5	6	5	6
Triple-class refractory	74%	69%		63%	85%
ORR @RP2D	**74%**	**73%**	**63%** (prior CART/bisp 72%/44%)	**64%** (at 30-7200 ug)	**132-198 mg: (56.7%)**
PFS	**7.5 mos**	**11.9 mos**	**NR**		
DOR	**9.3 mos**	**13 mos**	**12.7+ mos**	**12.5 mos**	
AEs, (All/(Gr 3+)					prophylactic toci
CRS	79% (2%)	72% (0.7%)		79% (2%)	(+/-)
Infections	57% (17%)	50% (12%)		46% (26%)	80% (2%) -> **36% (2.3%) /90%(3.6%)**
Neutropenia	34% (31%)	28% (22%)		18% (16%)	43% (19%)
Anemia	45% (32%)	39% (25%)		49% (39%)	18% (16%) -> **Gr3+ 64% vs 39%**
Thrombocytopenia	27% (20%)	27% (17%)		26% (19%)	32% (22%)
ICANS	11% (1.6%)	10% (1.8%)		12% (4%)	% not reported
# Deaths	0 due to AEs	0 due to AEs		2 (1 due to AEs)	6 (3.7%)
Hypogamma/IVIg	NR/13%	NR/10%		NR	Diarrhea 26% (1%)
Other	Dysgeusia 48% (N/A) Skin 56% (0%) Nail 52% (0%)	Dysgeusia 46% (N/A) Skin 67% (0.7%) Nail 43% (0%)		Mucosal 77% (5%) Skin 86% (23%) Hair/nail 28% (0%)	

Courtesy Dr Carol Hoffman

First Results From the RedirecTT-1 Study With Teclistamab + Talquetamab Simultaneously Targeting BCMA and GPRC5D in Patients With Relapsed/Refractory Multiple Myeloma

Yael C Cohen[1], Daniel Morillo[2], Moshe Gatt[3], Michael Sebag[4], Kihyun Kim[5], Chang-Ki Min[6], Albert Oriol[7], Enrique M Ocio[8], Sung-Soo Yoon[9], María-Victoria Mateos[10], Michael P Chu[11], Paula Rodríguez-Otero[12], Irit Avivi[13], Yue Guo[14], Maria Krevvata[14], Michelle R Peterson[14], Melissa Beelen[14], Jill Vanak[14], Arnob Banerjee[14], Hila Magen[15]

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Courtesy Dr Y Cohen

Talquetamab + Daratumumab in Patients With Relapsed/Refractory Multiple Myeloma: Updated TRIMM-2 Results

Bhagirathbhai Dholaria[1], Katja Weisel[2], María-Victoria Mateos[3], Hartmut Goldschmidt[4], Thomas G Martin[5], Daniel Morillo[6], Donna Reece[7], Paula Rodríguez-Otero[8], Manisha Bhutani[9], Anita D'Souza[10], Albert Oriol[11], Laura Rosiñol[12], Nizar Bahlis[13], Kalpana Bakshi[14], Lijuan Kang[14], Lien Vandenberk[15], M Damiette Smit[16], Ralph Wäsch[17], Niels WCJ van de Donk[18], Ajai Chari[19]

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Courtesy Dr Dholaria

Presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting; June 2–6, 2023; Chicago, IL, USA & Virtual

TAKE HOME MESSAGE

-Teclistamab is off the shelf readily available

-Can be given day 1, 3, 5 inpatient settings and then outpatient (? Q2-4 weeks)

-CRS is common but manageable

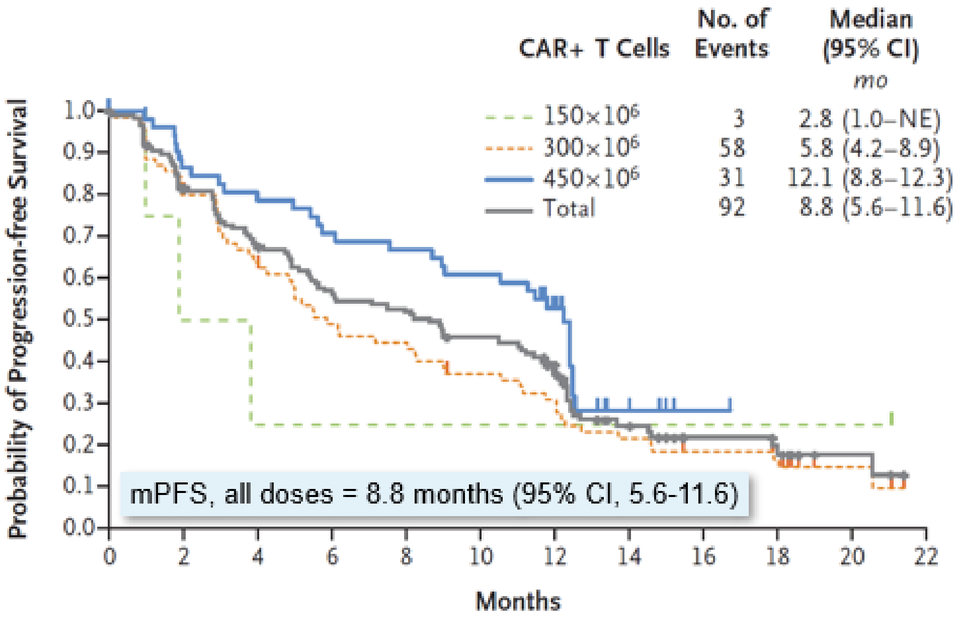
-Infections remain a major and need mitigation with antimicrobials & IVIG

-Efficacy is very similar to CAR T cell therapy (?EMD, high risk Disease)

-Teclistamab vs CAR T choice depends on how soon the patients need therapy

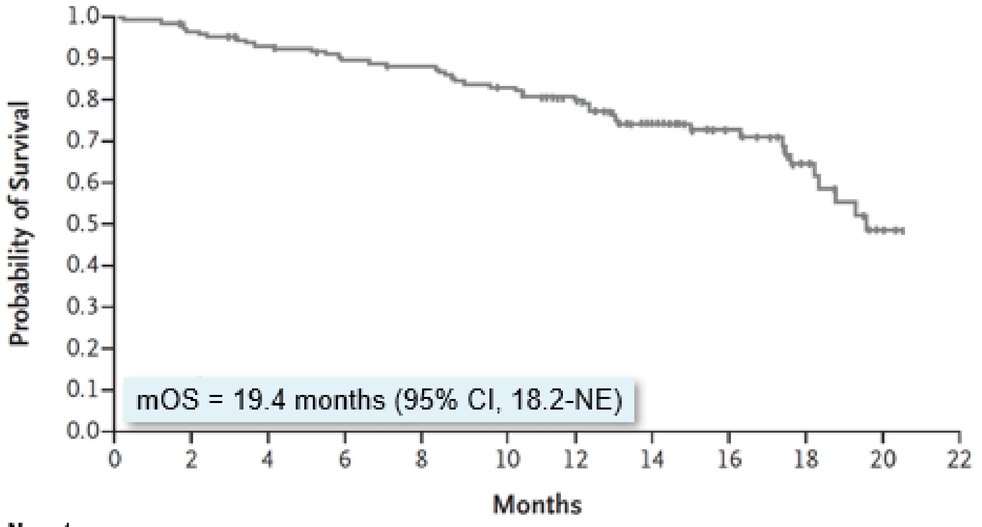
KarMMa Trial: Efficacy in the Treated Population (n = 128)

IRC-Assessed PFS



No. at Risk												
150×10⁶	4	2	1	1	1	1	1	1	1	1	1	0
300×10⁶	70	56	42	33	29	24	17	14	11	7	3	0
450×10⁶	54	44	40	36	34	31	17	4	1	0	0	
Total	128	102	83	70	64	56	35	19	13	8	4	0

IRC-Assessed OS



No. at Risk												
	128	122	114	108	104	97	82	55	38	27	12	0

ORR = 73% **sCR = 33%**

Munshi et al, NEJM 2021

2022 ASCO ANNUAL MEETING

Idecabtagene Vicleucel for Relapsed/Refractory Multiple Myeloma: Real-World Experience from the Myeloma CAR T Consortium

Doris K. Hansen MD*, Surbhi Sidana MD, *Lauren C. Peres PhD, Christelle Colin Leitzinger PhD, Leyla Shune MD, Alexandria Shrewsbury MS, CCRC, Rebecca Gonzalez PharmD, BCOP, Douglas W. Sborov MD, MS, Charlotte Wagner PharmD, Hamza Hashmi MD, Mehmet H. Kocoglu MD, Shebli Atrash MD, MS, Gary Simmons DO, Nilesh Kalariya MSN, APRN, Christopher Ferreri MD, Aimaz Afrough MD, Ankit Kansagra MD, Peter Voorhees MD, Rachid Baz MD, Jack Khouri MD, Melissa Alsina MD, **Joseph McGuirk DO**, Frederick L. Locke MD**, Krina K. Patel MD, MS****

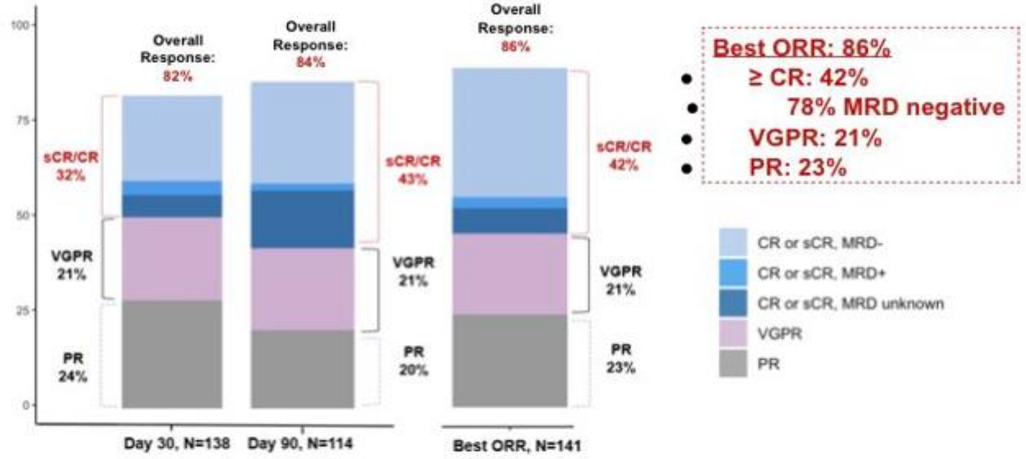
**DKH and SS are co-first authors. **JM, FLL, and KKP are co-senior authors*

Baseline Characteristics: 77% KarMMa Ineligible

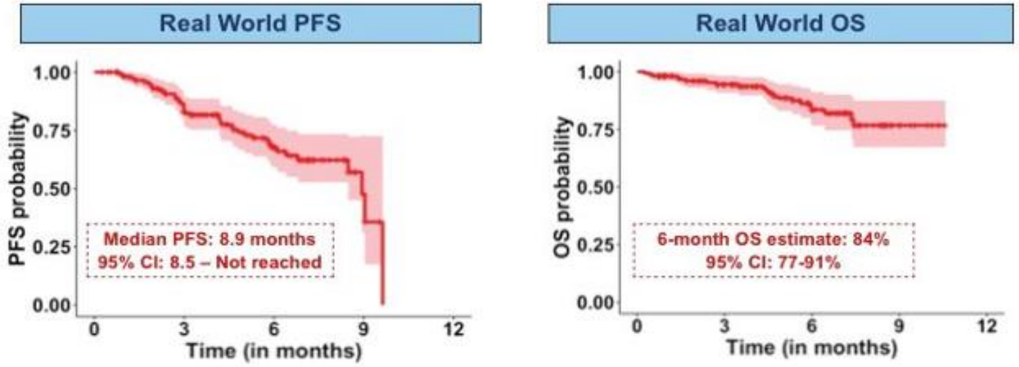
Characteristic	SOC Ide-cel (N=196)	KarMMa (N=128)
Age, median (range)	64 (36,83)	61 (33,78)
Male Sex, n (%)	113 (53)	76 (59)
Extramedullary disease, n (%)	92 (47)	50 (39)
ECOG PS, n (%)		
0-1	132 (80)	125 (98)
2-4	33 (20)	3 (2)
R-ISS, n (%)		
I	25 (18)	14 (11)
II	73 (54)	90 (70)
III	38 (28)	21 (16)
Unknown	60	3
High-risk cytogenetics, n (%)		
Any high-risk cytogenetics	64 (38)	45 (35)
del (17p)	43 (25)	23 (18)
t(4;14)	25 (15)	23 (18)
t(14;16)	9 (5)	6 (5)
Bridging therapy, n (%)	150 (77)	112 (88)
Prior BCMA therapy, n (%)	43 (22)	0
Prior lines of therapy, median (range)	7 (4,19)	6 (3,16)

*Patients with unknown ECOG PS and cytogenetics are not included in the table

Day 30, Day 90, and Best Overall Tumor Responses



Real World PFS and OS: Median F/U 5.3 months

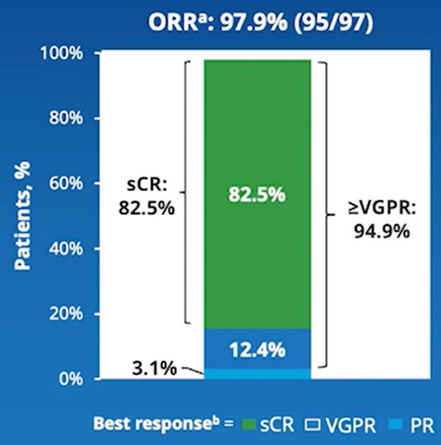


Courtesy Doris Hansen

CAROLINA ONCOLOGY SOCIETY

CARTITUDE-1: Efficacy Response

- Med prior lines =6
- No new safety signals; MNT incidence has decreased to 0.5% in CARTITUDE program



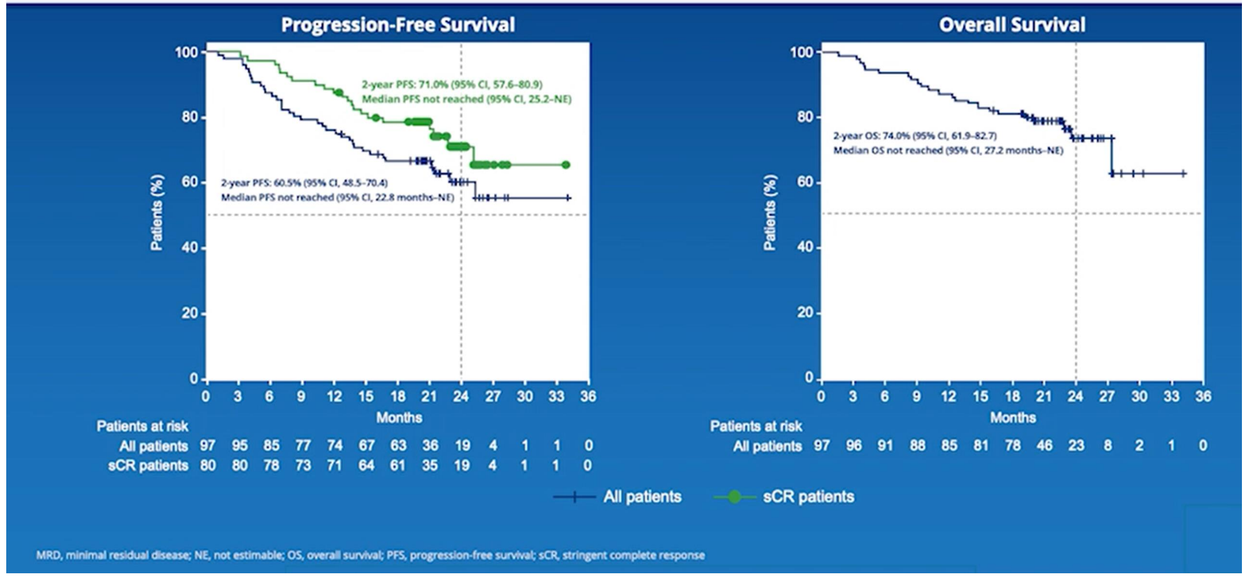
Responses deepened over time from the 1-year follow-up

Best response at any time	Median–1 year follow-up	Median–2 years follow-up
sCR, %	67	83

- Median time to first response was 1 month (range, 0.9–10.7)
- Median time to best response was 2.6 months (range, 0.9–17.8)
- Median time to CR or better was 2.9 months (range, 0.9–17.8)
- Median duration of response was not estimable (21.8 months–NE)

[a]ORR assessed by independent review committee; [b]No patient had CR or stable disease as best response.
CR, complete response; NE, not estimable; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

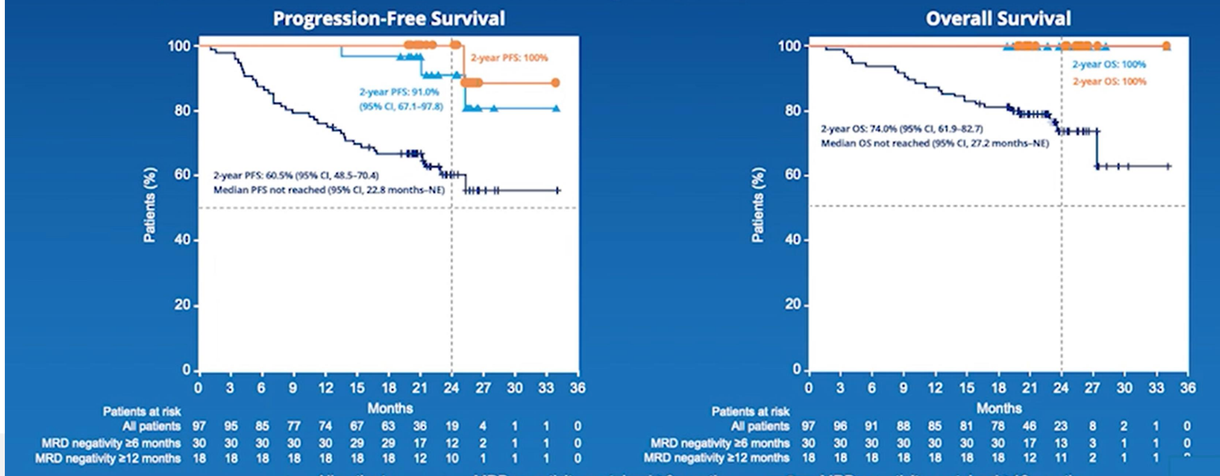
CARTITUDE-1: Progression-Free Survival and Overall Survival



MRD, minimal residual disease; NE, not estimable; OS, overall survival; PFS, progression-free survival; sCR, stringent complete response

CARTITUDE-1: Progression-Free Survival and Overall Survival by MRD Negativity (10^{-5}) sustained for ≥ 6 and 12 months

- Of the 61 patients evaluable for MRD, 92% were MRD-negative (at 10^{-5})



MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival

Courtesy Saad Usmani

If Ide-Cel is Yahoo, Cilta-Cel is Google

Comparable baseline features and toxicity, except timing of CRS and delayed neurotoxicity with cilta-cel

Baseline Features	Cilta-cel[1]	Ide-cel[3]
N	97	128
Target CAR-T Dose	0.75 million/kg	300-450 million
Median age	61 years	61 years
Median prior lines	6	6
Triple Class Refractory	88%	84%
Penta Refractory	42%	26%

Toxicity	Cilta-cel[1,2]	Ide-cel[3]
CRS (all; grade 3 or 4)	95% (5%)	84% (5%)
Median onset of CRS	7 days	1 day
ICANS (all; grade 3 or 4)	17% (2%)	18% (3%)
Infections (all; grade 3 or 4)	58% (20%)	69% (22%)
Grade 3 or 4 neutropenia > 1 month*	10%	41%
Grade 3 or 4 thrombocytopenia > 1 month*	25%	48%
Delayed neurotoxicity (all; grade 3 or 4)	12% (9%)	None**

Efficacy	Cilta-cel[1]	Ide-cel[3]
ORR; CR rate	98%;80%	73%;33%
MRD negativity rate (10^{-5})	58%	26%
PFS	Median NR, 18 m PFS: 66%	Median: 8.8 months
OS	Median NR, 18 m OS: 81%	Median: 19 months

. Madduri et al ASH 2020 abstract 177; 2. Usmani et al ASCO 2021abstract 8005; 3. Munshi et al. NEJM 2021;384(8):705-716;
Long term cytopenias: Cilta-cel: > 1 month from onset of cytopenias, Ide-cel: > 1 month post-CAR-T ; ** In package insert: grade 3 parkinsonism and grade 3 myelitis in another ide-cel trial

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Editorial

Idecabtagene vicleucel versus ciltacabtagene autoleucel: a Sophie's choice for patients with relapsed refractory multiple myeloma

James Davis, Mary McGann, Abigail Shockley & Hamza Hashmi

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SOUTH CAROLINA ONCOLOGY SOCIETY

Factors associated with refractoriness or early progression after Idecabtagene Vicleucel (Ide-cel) in Patients with Relapsed/Refractory Multiple Myeloma (RRMM): U.S. Myeloma CAR T consortium Real World Experience

Hamza Hashmi[1*], Doris Hansen[2*], Lauren Peres[2*], Omar Castaneda[3], Ciara Freeman[2], Gabriel De Avila[2], Surbhi Sidana[3], Leyla Shune MD[4], Douglas W Sborov[5], James Davis[1], Charlotte Wagner[5], Mehmet H. Kocoglu[6], Shebli Atrash[7], Peter Voorhees[7], Gary Simmons[8], Christopher Ferrer[8], Nilesh Kalariya[9], Aishwarya Sannareddy[10], Aimaz Afrough[10], Danai Dima MD[11], Jack Khouri[11], Joseph McGuirk[4], Fred Locke[2], Rachid Baz[2], Krina K. Patel, MD[2*], Melissa Alsina[2*]

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Poster No 2027

Poster cast link

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INTRODUCTION

- Ide-cel, a B-cell maturation antigen (BCMA) directed CAR T-cell therapy, has been approved for the treatment of RRMM after 4 prior lines of therapy.
- While response rates and survival outcomes have been very promising, there is a significant number of patients who do not respond or relapse early after ide-cel.
- Understanding the characteristics of these patients is important to help guide patient selection and development of novel strategies to improve outcomes.
- We evaluated factors associated with refractoriness or early progression (≤3 months after CAR T infusion) for patients treated with standard of care ide-cel.

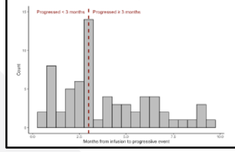
METHODS

Eleven U.S. centers contributed data. At the time of data cut off (5/2022) with median follow up of 6.4 months, 240 patients were leukapheresed, 215 patients were infused, 154 patients had at least 3 months follow up available and were the focus of this analysis. Of those, 67 patients had progressed with a progressive event defined as progression or death due to myeloma.

We investigated differences in patient, disease, and CAR-T related characteristics by time to progression (≤3 months, >3 months; did not progress) using chi-square or Kruskal-Wallis tests (Table A)

For factors identified as associated with progression, a multivariable Cox proportional hazard regression analysis was performed to examine the association between these factors and OS and PFS (Table B and C)

Association of number of early progression risk factors (0, 1, 2, or 3 factors) with OS and PFS was examined using Kaplan-Meier survival curves and log-rank tests (Figure A and B)

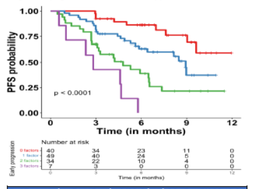


RESULTS

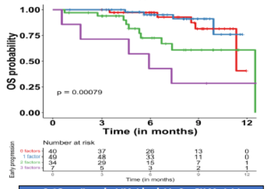
Table A. Baseline patient, disease, and CAR T related characteristics by time to progression (≤3 months, >3 months, did not progress)

Characteristics	Progressed <3m N=32	Progressed >3m N=35	Non Progressors N=87	P value
Age<= 65 years	19 (59%)	23 (66%)	40 (46%)	0.1
Male Sex	21 (66%)	18 (51%)	52 (60%)	0.5
IgG Kappa subtype	12 (38%)	7 (20%)	34 (39%)	0.12
Extramedullary disease, n (%)	20 (62%)	19 (54%)	35 (40%)	0.069
Marrow Burden>= 50%, n (%)	8 (31%)	10 (29%)	22 (27%)	>0.9
ECOG 0-1 at LD, n (%)	25 (81%)	25 (74%)	74 (87%)	0.2
R-ISS III at infusion, n (%)	9 (35%)	11 (37%)	15 (23%)	0.6
High-risk cytogenetics, n (%)	13 (48%)	13 (42%)	19 (26%)	0.079
Prior LOT, median (range)	7.0 (4.0, 18.0)	5.0 (4.0, 15.0)	7.0 (4.0, 17.0)	0.068
t(4;14) at infusion, n (%)	8 (30%)	5 (16%)	5 (6.9%)	0.015
Bridging Therapy	30 (94%)	30 (86%)	61 (71%)	0.014
Prior BCMA	15 (47%)	8 (23%)	14 (16%)	0.002
Belantamab Mafodotin, n (%)	10 (34%)	9 (26%)	10 (12%)	0.016
Ferritin>ULN at LD, n (%)	17 (53%)	21 (60%)	28 (32%)	0.008

A. Progression-free survival by no. of early progression risk factors i.e. High Risk Cytogenetics, Prior BCMA Therapy, Elevated Ferritin at LD



B. Overall survival by no. of early progression risk factors i.e. High Risk Cytogenetics, Prior BCMA Therapy, Elevated Ferritin at LD



B. *Progression Free Survival (Multivariable Cox PH Models)

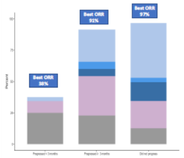
Characteristic	N	Event N	HR	95% CI	p-value
High-risk cytogenetics	45	27	1.71	0.99, 2.94	0.053
Prior BCMA	35	23	3.42	1.81, 6.49	<0.001
Baseline Ferritin ULN at LD	58	39	2.77	1.57, 4.88	<0.001

C. *Overall survival (Multivariable Cox PH Models)

Characteristic	N	Event N	HR	95% CI	p-value
High-risk cytogenetics	45	12	1.41	0.57, 3.46	0.5
Prior BCMA	35	11	4.45	1.72, 11.6	0.002
Baseline Ferritin> ULN at LD	58	16	2.26	0.92, 5.56	0.077

*For the multivariable analyses, we additionally adjusted for age, extramedullary disease, bridging therapy, and number of prior lines of therapy in all models

EFFICACY IN EARLY PROGRESSION



SAFETY	Progressed <3m N=32	Progressed >3m N=35	Non Progressors N=87	P value
Max CRS, n (%)				<0.001
No CRS	13 (41%)	4 (11%)	11 (13%)	
1-2	17 (53%)	31 (89%)	75 (86%)	
3+	2 (6.2%)	0 (0%)	1 (1%)	
Max ICANS, n (%)				0.7
No ICANS	25 (81%)	26 (84%)	65 (78%)	
1-2	3 (9.7%)	4 (13%)	14 (17%)	
3+	3 (9.7%)	1 (3.2%)	4 (4.8%)	
Tocilizumab, n (%)	11 (35%)	23 (66%)	65 (79%)	<0.001
Steroids, n (%)	6 (19%)	6 (17%)	25 (29%)	0.3
Anakinra, n (%)	3 (9.4%)	2 (5.7%)	2 (2.3%)	0.2

DISCUSSION

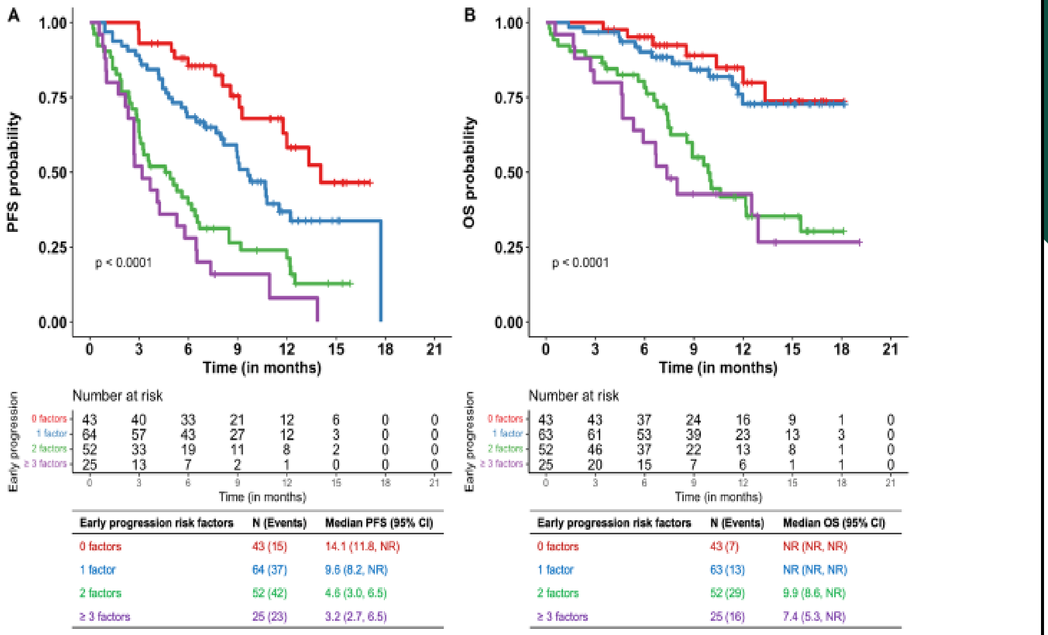
- Patients with **prior BCMA therapy, high-risk cytogenetics, elevated ferritin at LD** were more likely to have progressed early (≤3m).
- Of the variables associated with progression in univariate analysis, multivariable analyses showed that patients with **younger age** (HR=0.96), **prior BCMA therapy** (HR=3.42), **elevated ferritin at LD** (HR=2.77), and **high-risk cytogenetics** (HR=1.71) were associated with worse PFS (Panel A). For OS, only patients with **prior BCMA therapy** had significantly inferior OS (HR 4.45).
- Considering high-risk cytogenetics, prior BCMA therapy, and elevated ferritin at LD as modifiable factors associated with early progression, **patients with 2 or 3 of these risk factors had inferior PFS** (1 vs 2 vs 3: 8.9 vs 4.8 vs 2.8 m, respectively) and **OS** (1 vs 2 vs 3:NR vs 12.5 vs 5.9 m, respectively) vs patients with no early progression risk factors (PFS=NR, OS=11.3 m)

CONCLUSIONS

- Per this multicenter retrospective study, potential predictors of early progression after CAR T-cell therapy for RRMM included:
  - **Prior BCMA directed therapy**
  - **High-risk cytogenetics**
  - **Elevated ferritin at lymphodepletion**
- Presence of two of three of these factors negatively impact PFS and OS.

REFERENCES

Munshi NC, Anderson LD, Jr., Shah N, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. N Engl J Med. 2021;384(8):705-716.
Anderson LD et al. Poster presentation: 2021 ASCO Annual Meeting: June 4-8, 2021. Abstract 8016.



Early progression risk factors	N (Events)	Median PFS (95% CI)
0 factors	43 (15)	14.1 (11.8, NR)
1 factor	64 (37)	9.6 (8.2, NR)
2 factors	52 (42)	4.6 (3.0, 6.5)
≥ 3 factors	25 (23)	3.2 (2.7, 6.5)

Early progression risk factors	N (Events)	Median OS (95% CI)
0 factors	43 (7)	NR (NR, NR)
1 factor	63 (13)	NR (NR, NR)
2 factors	52 (29)	9.9 (8.6, NR)
≥ 3 factors	25 (16)	7.4 (5.3, NR)

Are these risk factors Modifiable , Actionable, Avoidable??

- **History of Extramedullary Disease**
- **Elevated Ferritin at lymphodepletion**
- **Prior BCMA directed therapy**
- **Plasma Cell Leukemia**
- **Fusion (4;14)**
- **Hispanic Ethnicity**
- **Use of Bridging Therapy**

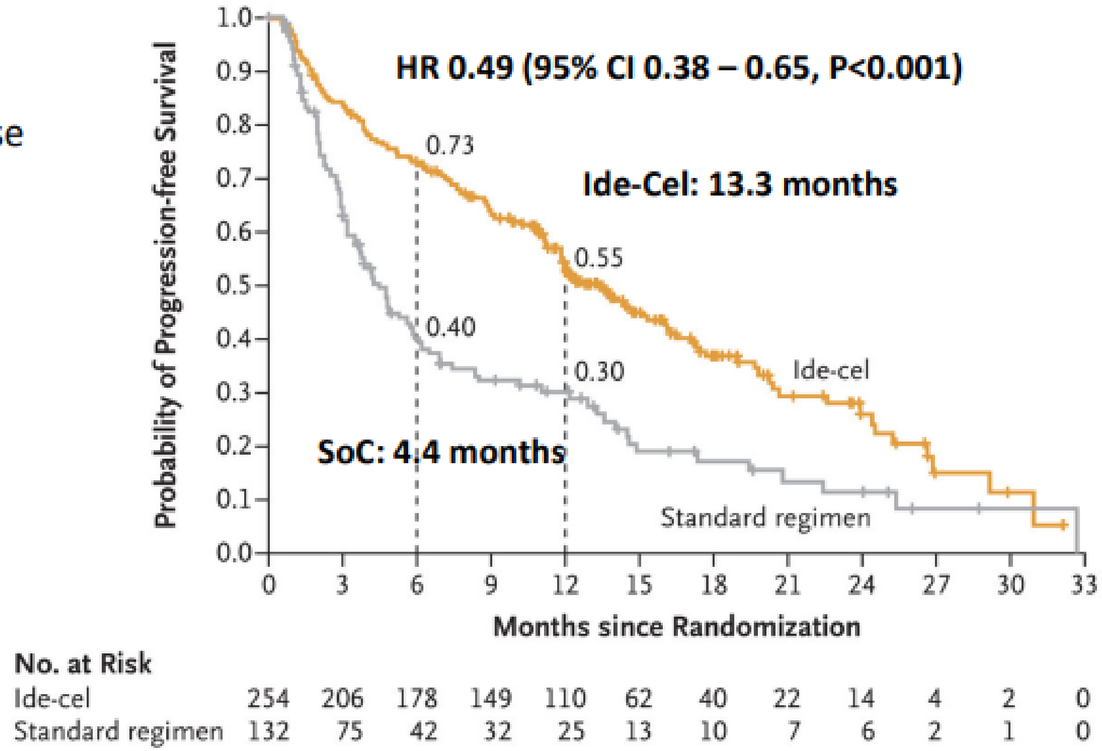
- Avoid use of BCMA therapy prior
- Close surveillance
- Initiation of Salvage at earliest signs of relapse
- Maintenance chemotherapy?
- Earlier lines of Therapy

KarMMA-3: Phase III Study of Idecabtagene Vicleucel vs Investigators Choice for RRMM

- **2:1 randomization**
- **2 – 4 prior lines of therapy, dara/IMiD/PI exposed, PD within 60 days of last regimen**
- **SoC regimens: Dara-Pom-Dex (43), Elo-Pom-Dex (30), Dara-Bortezomib-Dex (7), Ixa-Len-Dex (22), Car-Dex (30)**

- Median prior lines of therapy: 3 (range 2 – 4)
- 90% IMiD refractory, 95% dara refractory, 74% PI refractory, 65% - 67% triple class refractory disease
- 42% - 46% HRCGs

	Ide-Cel	SoC
ORR	**71%**	**42%**
sCR	**35%**	**5%**
CR	**3%**	**1%**
VGPR	**22%**	**10%**
PR	**11%**	**27%**



Rodriguez-Otero et al. NEJM 2023

Phase 3 Results From CARTITUDE-4: Cilta-cel Versus Standard of Care (PVd or DPd) in Lenalidomide-Refractory Multiple Myeloma

Binod Dhakal[1], Kwee Yong[2], Simon Harrison[3], María-Victoria Mateos[4], Philippe Moreau[5], Niels WCJ van de Donk[6], Surbhi Sidana[7], Rakesh Popat[8], Nikoletta Lendvai[9], Carolina Lonardi[10], Ana Slaughter[11], Jordan M Schecter[9], Katherine Li[12], Enrique Zudaire[12], Diana Chen[13], Jane Gilbert[14], Lida Pacaud[15], Nitin Patel[15], Jesús San-Miguel[16], Hermann Einsele[17]

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CARTITUDE-4 : Baseline Demographics and Disease Characteristics

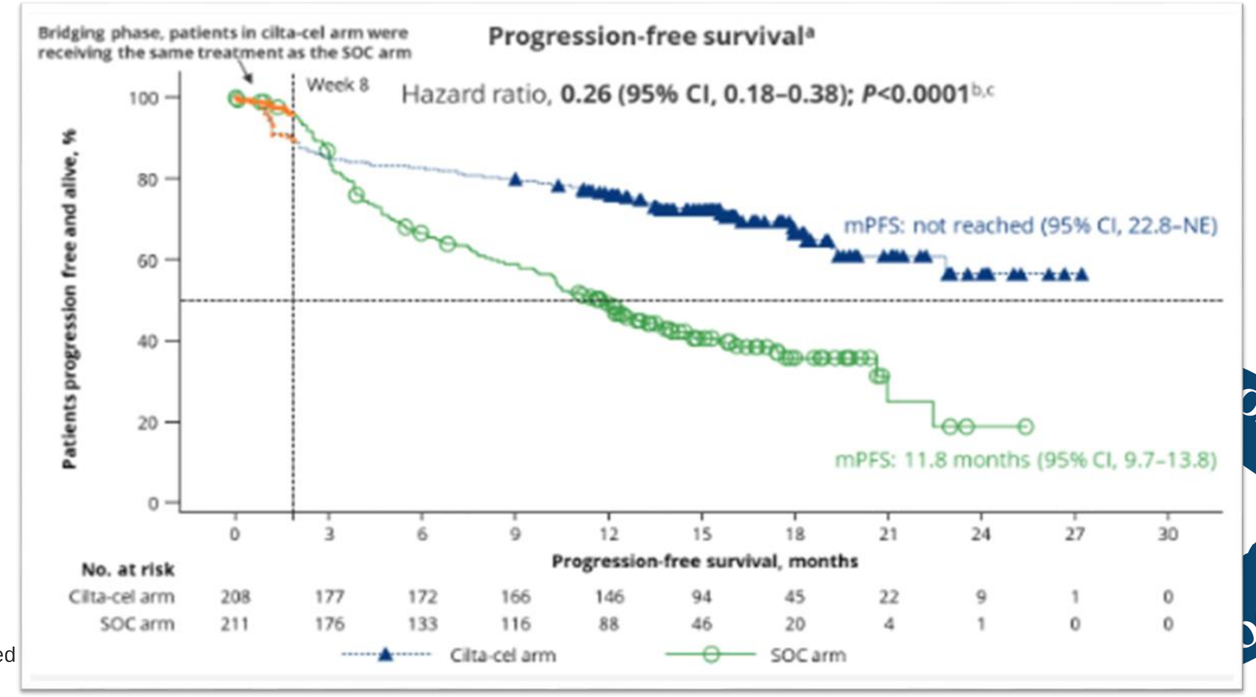
Baseline characteristic	ITT population	
	Cilta-cel (n=208)	SOC (n=211)
Age, median (range), years	61.5 (27–78)	61.0 (35–80)
Male, n (%)	116 (55.8)	124 (58.8)
White, n (%)	157 (75.5)	157 (74.4)
ECOG PS ≤1, n (%) [a,b]	207 (99.5)	210 (99.5)
ISS stage, n (%)		
I	136 (65.4)	132 (62.6)
II	60 (28.8)	65 (30.8)
III	12 (5.8)	14 (6.6)
Bone marrow plasma cells ≥60%,[c] n (%)	42 (20.4)	43 (20.7)
Presence of soft tissue plasmacytomas,[d] n (%)	44 (21.2)	35 (16.6)
Years since diagnosis, median (range)	3 (0.3–18.1)	3.4 (0.4–22.1)
Prior LOT, median (range)	2 (1–3)	2 (1–3)
1 prior LOT, n (%)	68 (32.7)	68 (32.2)
2 or 3 prior LOT, n (%)	140 (67.3)	143 (67.8)

Baseline characteristic	ITT population	
	Cilta-cel (n=208)	SOC (n=211)
Cytogenetic high risk, n (%)[e]	123 (59.4)	132 (62.9)
del(17p)	49 (23.7)	43 (20.5)
t(14;16)	3 (1.4)	7 (3.3)
t(4;14)	30 (14.5)	30 (14.3)
gain/amp(1q)	89 (43.0)	107 (51.0)
2 or more high-risk cytogenetic features	43 (20.8)	49 (23.3)
del(17p), t(14;16), or t(4;14)	73 (35.3)	69 (32.9)
Triple-class[f] exposed, n (%)	53 (25.5)	55 (26.1)
Penta-drug[g] exposed, n (%)	14 (6.7)	10 (4.7)
Refractory status, n (%)		
Triple-class refractory[f,h]	30 (14.4)	33 (15.6)
Bortezomib	55 (26.4)	48 (22.7)
Pomalidomide	8 (3.8)	9 (4.3)
Daratumumab	48 (23.1)	45 (21.3)
Any PI	103 (49.5)	96 (45.5)

[a]1 patient in each arm had ECOG PS of 2. [b]Latest nonmissing ECOG PS score on or prior to apheresis/cycle 1 day 1 is used. [c]In 206 (cilta-cel arm) and 208 (SOC arm) patients, maximum value from bone marrow biopsy and bone marrow aspirate is selected if both results are available. [d]Including extramedullary and bone-based plasmacytomas with measurable soft tissue component. [e]In 207 (cilta-cel arm) and 210 (SOC arm) patients. [f]Including 1 PI, 1 IMiD, and 1 anti-CD38 monoclonal antibody. [g]Including ≥2 PI, ≥2 IMiDs, and 1 anti-CD38 monoclonal antibody. [h]2 patients (cilta-cel arm) and 1 patient (SOC arm) were penta-drug refractory, including ≥2 PI, ≥2 IMiDs, and 1 anti-CD38 monoclonal antibody.
cilta-cel, ciltacabtagene autoleucel; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; ITT, intent-to-treat; LOT, line of therapy; PI, proteasome inhibitor; SOC, standard of care.

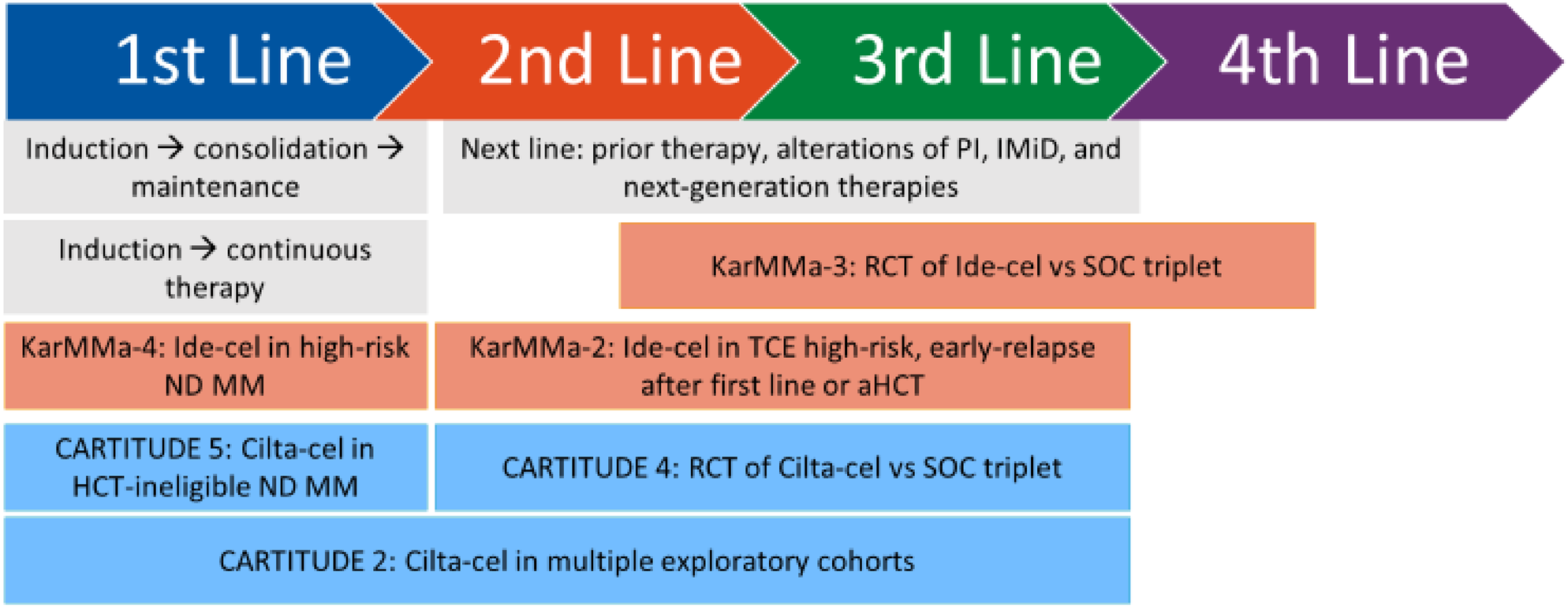
	Cilta-cel (n=208)	SOC (n=211)	HR[a]	Odds ratio
Median PFS, mo (95% CI)	NE (23–NE)	12 (10–14)	0.26 (0.18–0.38) (*P*<0.0001)	
12-mo PFS, % (95% CI)	76 (69–81)	49 (42–55)		
ORR, n (%)[b]	176 (85)	142 (67)		3 (*P*<0.0001)
≥CR[b]	152 (73)	46 (22)		10 (*P*<0.0001)
10^{-5} MRD negative,[c] n (%)	126 (61)	33 (16)		9 (*P*<0.0001)

[a]Per computerized algorithm by constant piecewise weighted log-rank test. [b]In 176 pts who received cilta-cel as study tx: ORR, 175 (99%); ≥CR, 152 (86%). [c]For MRD-evaluable pts: cilta-cel, 88% (126/144); SOC, 33% (33/101).



San-Miguel, et al. N Engl J Med

Emerging CART Therapies: Moving Closer to the Starting Line



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TAKE HOME MESSAGE

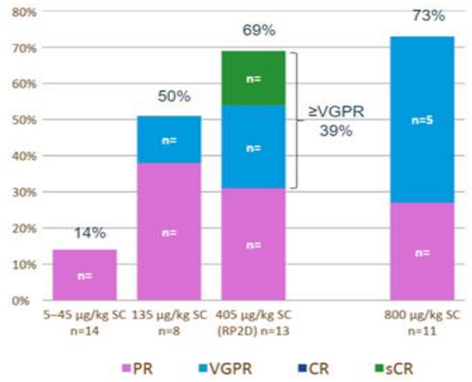
- CAR T is going to move in earlier lines of therapy
- Access to leukapheresis will be critical
- Refer early for CAR T (at the time of second relapse)
- CAR T may replace ASCT for high-risk Myeloma

HONORABLE MENTIONS

Source CCO, ASH 2021

Phase I, First-in-Human Study of Talquetamab, a G Protein-Coupled Receptor Family C Group 5 Member D (GPRC5D) x CD3 Bispecific Antibody, in Patients with RRMM
GPRC5D: Talquetamab: Overall Response Rate

ORRa for SC Doses



- **At the RP2D of 405 µg/kg SC**
  - 69% ORR (9/13)
  - Median 3.7-month (1.7–6.5) follow-up for responders
  - Median time to first confirmed response was 1 month (1–2)
  - 67% (6/9) of triple-class refractory patients responded
  - 100% (2/2) of penta-drug refractory patients responded
- **At most active doses of 20–180 µg/kg IV and 135–800 µg/kg SC**
  - 66% ORR (33/50)
  - ≥VGPR was 42%
  - 67% ORR (12/18) in IV cohorts and 66% ORR[a] (21/32) in SC cohorts

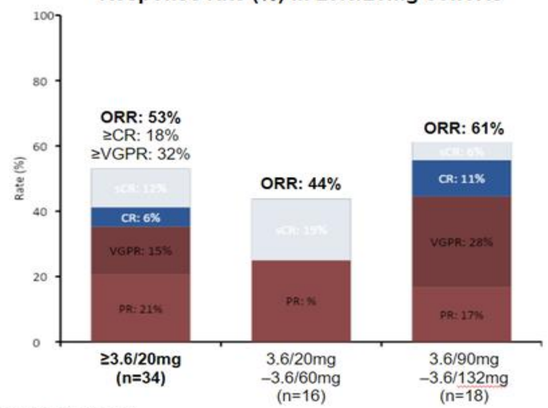
[a]Among response-evaluable patients who had at least 1 study treatment and 1 postbaseline disease evaluation; includes unconfirmed responses. CR, complete response; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

Chari et al. 62nd ASH Meeting 2020. Abstract #290
Phase 1 Study of Talquetamab in RRMM

Initial Clinical Activity and Safety of BFCR4350A, a FcRH5/CD3 T-Cell-Engaging Bispecific Antibody, in RRMM
Response rate: FCRH5

- 51/53 pts efficacy evaluable; no response in ≤3.6/10.8mg cohorts
- ORR* in ≥3.6mg/20mg cohorts
  - 53% (18/34) in all pts
  - 41% (7/17) in penta-drug refractory pts
  - 63% (5/8) in pts with prior anti-BCMA
- Median time to first response/best response: 29.5 days (range: 21–105)/57.5 days (range: 21–272)
- Response irrespective of target expression level in patients assessed to date
- MRD negativity by NGS ($<10^{-5}$) detected in 6/7 evaluable pts with ≥VGPR

Response rate (%) in ≥3.6/20mg cohorts



*best response of PR, VGPR, CR or sCR by IMWG uniform response criteria 2016; FcRH5, Fc receptor-homolog 5; BCMA, B-cell maturation antigen; MRD, minimal residual disease; NGS, next generation sequencing; ORR, overall response rate; sCR, stringent CR

MagnetisMM-1: Elranatamab in R/R MM

- Phase I trial of elranatamab, a BCMA-targeted CD3-engaging bispecific molecule

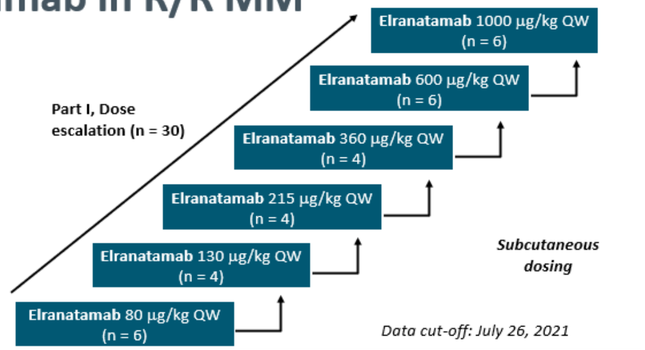
Prior Treatment	Elranatamab (N = 55)
Median no. of prior tx (range)	6 (2-15)
Triple-class exposed, n (%)	54 (98.2)
Triple-class refractory, n (%)	50 (90.9)
Prior BCMA-targeted tx, n (%)	12 (21.8)
▪ Anti-BCMA ADC	7 (12.7)
▪ CAR T-cell	9 (16.4)

*Refractory to ≥1 PI, 1 IMiD, and 1 anti-CD38 mAb

Efficacy Summary

- Elranatamab 1000 µg/kg Q2W achieved exposure associated with anti-myeloma efficacy
- Confirmed ORR: 69% (9/13) at recommended dose (1000 µg/kg Q1W)
- 70% (7/10) of patients with prior BCMA-targeted tx achieved response

Sebag. ASH 2021. Abstr 895.



- Heavily pretreated population
- Good efficacy rates
- Small study population

†acetaminophen, diphenhydramine, dexamethasone

Therapies for Triple Class Refractory MM

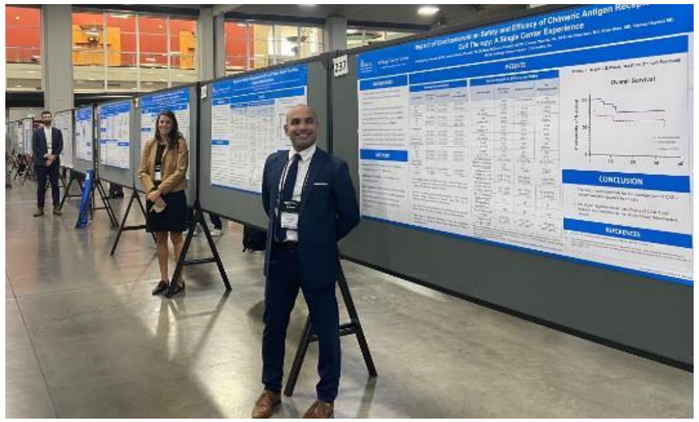
Regimen	Iberdomide		Mezigdomide	Modakafusp Alpha
N	107	41	101	30
Lines of Tx	6	7	6	7
% Penta Exposed % BCMA Exp	≤ 68%	NA 100% BCMA	NA; 30% BCMA	~73% 50% BCMA
% Dbl or triple class refractory	97% TCR	83%	100% TCR	93% TCR
ORR/ORR post BCMA	**26%**	34%	**40.6%**/50%	**43%**/27%
PFS months	**3**	**2.3**	**4.4**	**5.7 mo**
OS months	10.7	NR	NR	NR

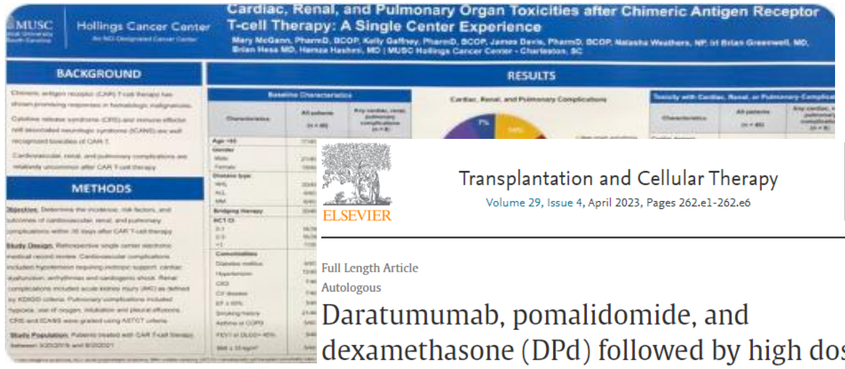
NA, not available; NR, not reached.

- In 2019, median OS of penta-refractory MM < 6 months
- Historically, ORR for accelerated approval (in US) and widespread clinical use: > 20%

SUMMARY

- Four-Drug induction should be the new SOC for all NDMM
- Control is the goal, Cure remains an illusion [not yet ready to stop maintenance early]
- BiTE versus CAR-T: Uber versus Lyft?
- Sequencing is more of an ART than SCIENCE
- Stem cell Transplant is here to stay!!





Transplantation and Cellular Therapy
Volume 29, Issue 4, April 2023, Pages 262.e1-262.e6

Full Length Article
Autologous

Daratumumab, pomalidomide, and dexamethasone (DPd) followed by high dose chemotherapy-Autologous Stem Cell Transplantation leads to superior outcomes when compared to DPd-alone for patients with Relapsed Refractory Multiple Myeloma

Hamza Hashmi [1 7], Shebli Atrash [2 7], Jayanshu Jain [3], Ghena Khasawneh [4], Meera Mohan [5 7], Zahra Mahmoudjafari [6 7], Wei Cui [3 7], Joseph McGuirk [6], Leyla Shune [6 7], Nausheen Ahmed [6 7], Al-Ola Abdallah [6 7]

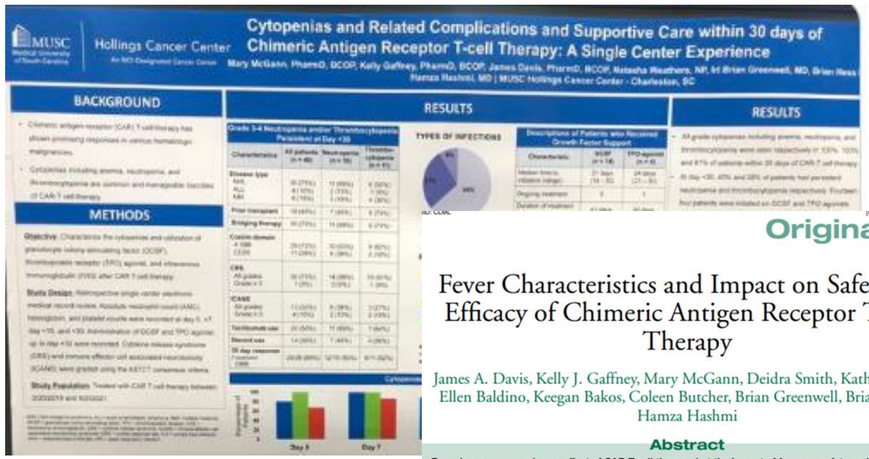
Transplantation and Cellular Therapy
journal homepage: www.tctjournal.org
ASTCT
American Society for Transplantation and Cellular Therapy

to the Editor

World Experience and Optimization of Outpatient Chimeric en Receptor T Cell Therapy

IcGann*, James A. Davis, Kelly J. Gaffney, Deidra Smith, Kathy Edwards, Brian T. Hess, Hashmi

Transplantation and Cellular Therapy
Available online 22 May 2023
In Press, Corrected Proof



Original Study

Fever Characteristics and Impact on Safety and Efficacy of Chimeric Antigen Receptor T-Cell Therapy

James A. Davis, Kelly J. Gaffney, Mary McGann, Deidra Smith, Kathy Edwards, Ellen Baldino, Keegan Bakos, Coleen Butcher, Brian Greenwell, Brian T. Hess, Hamza Hashmi

Abstract

Fever is a common adverse effect of CAR T-cell therapy, but the impact of fever on safety and efficacy are not well understood. The study sought to the impact of fever and its characteristics on safety and efficacy post CAR T-cell therapy. A total of 40 patients were included. While early-onset and higher magnitude fever do not appear to affect safety or efficacy of CAR T, absence of fever may reduce efficacy.

Background: Fever is a hallmark symptom of cytokine release syndrome (CRS) after chimeric antigen receptor (CAR) T-cell therapy. Fever characteristics and the impact of fever on safety and efficacy post CAR T are not well understood. We sought to explore the impact of fever and its characteristics on safety and efficacy post CAR T-cell therapy. **Patients and Methods:** We reviewed 40 patients with various hematologic malignancies (non-Hodgkin lymphoma, acute lymphoblastic leukemia, multiple myeloma) treated with CAR T-cell therapy between March 2019 and March 2022. We evaluated all patients who developed fever after CAR T infusion and analyzed the association of fever with toxicity (CRS and neurotoxicity) and efficacy (overall response (ORR) and complete response (CR) at day +90 post CAR T infusion). Fever was defined as per Lee criteria (equal to or greater than 38°C). CRS and immune-effector cell associated neurotoxicity syndrome (ICANS) were graded using American Society for Transplantation and Cellular Therapy grading system. **Results:** Fever occurred in 75% (30/40) of patients. Rates of all grade and grade 3+ CRS and ICANS were 75%, 2%, 33% and 10%, respectively. Fever occurred within 24 and 72 hours after CAR T infusion in 40% and 53% of patients, respectively. Fifty percent of patients received tocilizumab (toci) for CRS. After the first dose of toci, fever recurred in 38% of the patients, of which 67% had recurrence within 24 hours. Day +90 CR rates were 43% and 10% in patients with and without fever, respectively (Table 3). **Conclusion:** While fever is common after CAR T-cell therapy, early-onset and higher magnitude do not appear to affect safety or efficacy of CAR T. Absence of fever may affect response to CAR T.

Clinical Lymphoma, Myeloma and Leukemia, Vol. 000, No.xxx, 1–5
Keywords: CAR T, CRS, ICANS, Tocilizumab

Triplet Therapy, Transplantation, nd Maintenance to Progression in Myeloma

P.G. Richardson, S.J. Jacobus, E.A. Weller, H. Hassoun, S. Lonial, N.S. aje, E. Medvedova, P.L. McCarthy, E.N. Libby, P.M. Voorhees, R.Z. Orlowski, . Anderson, Jr., J.A. Zonder, C.P. Milner, C. Gasparetto, M.E. Agha, A.M. Khan, D.D. Hurd, K. Gowin, R.T. Kamble, S. Jagannath, N. Nathwani, M. Alsina, R.F. Cornell, H. Hashmi, E.L. Campagnaro, A.C. Andreescu, T. Gentile, Liedtke, K.N. Gouby, A.D. Cohen, T.H. Openshaw, M.C. Pasquini, S.A. Giralt, J.L. Kaufman, A.J. Yee, E. Scott, P. Torka, A. Foley, M. Fulciniti, K M.K. Samur, K. Masone, M.E. Maglio, A.A. Zeytoonjian, O. Na R.L. Schlossman, J.P. Laubach, C. Paba-Prada, I.M. Ghobrial, A. P. Moreau, H. Avet-Loiseau, M. Attal, K.C. Anderson, and N.C. for the DETERMINATION Investigators*

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Cellular Therapy

Efficacy and Safety of CD34+ Stem Cell Boost for Delayed Hematopoietic Recovery After BCMA Directed CAR T-cell Therapy

James A. Davis [1], Douglas W. Sborov [2], William Wesson [3], Kelley Julian [4], Al-Ola Abdallah [3], Joseph P. McGuirk [3], Nausheen Ahmed [3], Hamza Hashmi [5]

'Fast but after subcu is both a safe and cost-effective strategy

James A. Davis, Heather Youngberg, Kelly Gaffney, Marissa Duco, Hamza Hashmi

Subcutaneous daratumumab has less infusion related reactions (IRR) than the intravenous formulation, but requires post-injection observation. The study sought to demonstrate safety and costs benefits associated with differing observation periods of subcutaneous daratumumab. A total of 66 patients were included. Short post-injection observation was safe and resulted in reduced infusion chair time as well as administration related cost and resources.

Background: Daratumumab, an anti-CD38 monoclonal antibody, is a key component in the treatment paradigms of multiple myeloma and AL amyloidosis in both the newly diagnosed and relapsed and/or refractory setting. Intravenous (IV) daratumumab administration requires extended infusion times and is associated with higher rates of infusion related reactions (IRRs) when compared to the subcutaneous (SC) formulation. We report real world safety outcomes and infusion chair time savings associated with SC administration in daratumumab naïve patients. **Methods:** We retrospectively analyzed medical records at our institution for the incidence and severity of IRRs following differing observation periods post SC daratumumab administration. Infusion chair time was calculated to quantify chair time savings with SC administration. **Results:** Sixty-six daratumumab naïve patients were included. Nine percent of patients developed IRRs with SC daratumumab with all reactions occurring within six hours of the first dose. All reactions were grade ≤ 2 in severity and were reversible with supportive care. Over the 18 month study period, a total of 904 SC doses were administered, amounting to a potential 1785 hours of infusion chair time savings when compared to IV administration. **Conclusion:** SC daratumumab may be given safely with a short initial observation period and without observation for subsequent doses, resulting in reduced infusion chair time as well as administration related cost and resources.

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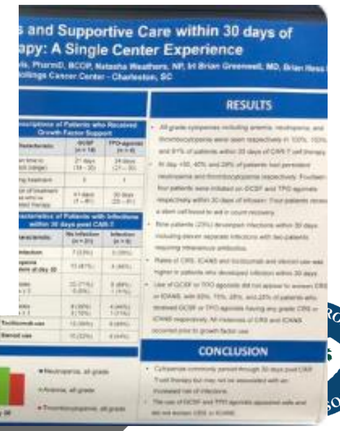
Keywords: Injection related reactions, Observation time, Darzalex, Pre-medication, Cost-saving



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Early cytopenias and ir relapsed or refractory multiple myeloma

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Editorial

Idecabtagene vicleucel versus Sophie's choice for patients wit multiple myeloma

James Davis, Mary McGann, Abigail Shockley & Hamza Hashmi

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THANK YOU!

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