WELCOME & INTRODUCTIONS

Treatment Updates: Multiple Myeloma

Welcome to LLS Community

We are a community of blood cancer patients, survivors, and caregivers. We're here to support you, give you trusted information and resources, and help you feel connected. No one should have to face a blood cancer diagnosis alone.

To join LLS Community, visit www.LLS.org/community.

Program will begin shortly

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2

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FREE TELEPHONE/WEB EDUCATION PROGRAM

TREATMENT UPDATES: MULTIPLE MYELOMA

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Senior Director, Education & Support
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Houston, TX

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FREE TELEPHONE/WEB EDUCATION PROGRAM

TREATMENT UPDATES: MULTIPLE MYELOMA

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DISCLOSURES

Treatment Updates: Multiple Myeloma

Advisory Board- GSK, Janssen

Speaker Bureau-GSK, Janssen

Research support- BMS, Blue Bird Bio

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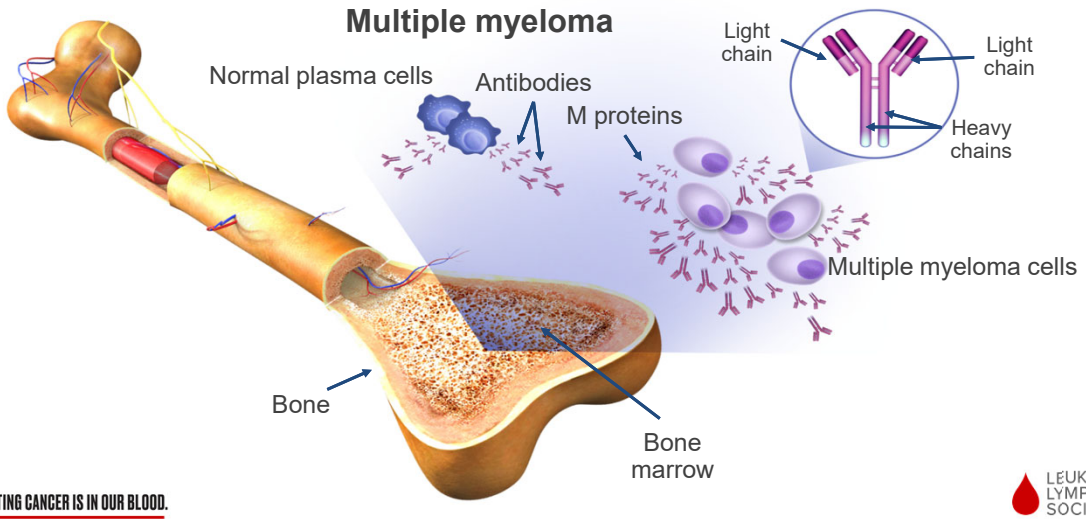
WHAT IS MULTIPLE MYELOMA?



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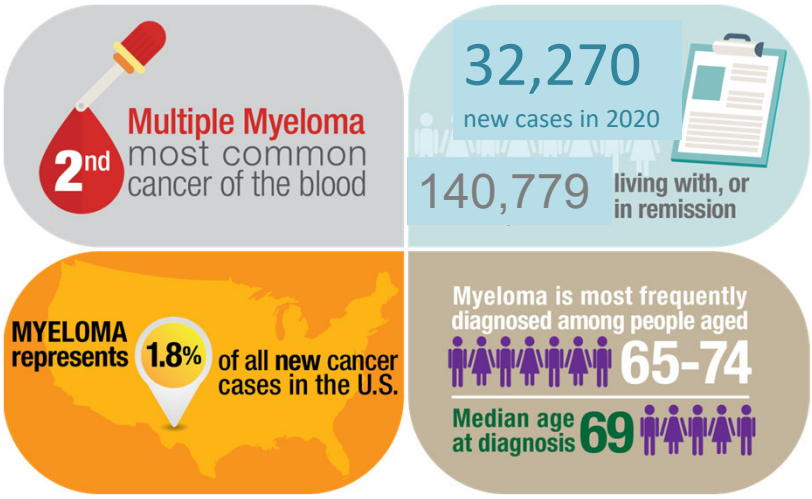
HOW COMMON IS MULTIPLE MYELOMA?



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SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD. http://seer.cancer.gov/statfacts/html/mulmy.html.

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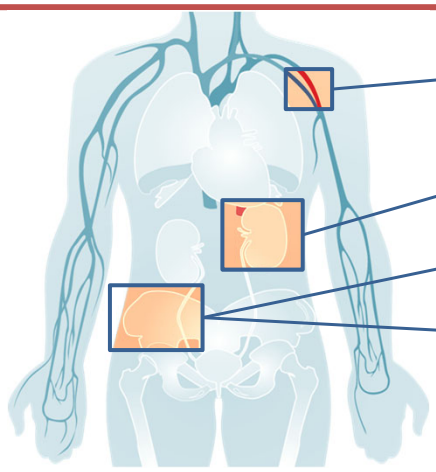
EFFECTS OF MYELOMA AND COMMON SYMPTOMS



Low blood counts	→ • Weakness • Fatigue • Infection
Decreased kidney function	→ Weakness
Bone damage	→ Bone pain
Bone turnover	→ • Loss of appetite • Weight loss

About 10% to 20% of patients with newly diagnosed myeloma do not have any symptoms.

MMRF. Multiple myeloma symptoms, side effects, and complications. https://themmrf.org/multiple-myeloma/symptoms-side-effects-and-complications/.
Campbell K. *Nurs Times.* 2014;110:12.
Kyle R et al. *Mayo Clin Proc.* 2003;78:21.

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MULTIPLE MYELOMA: TREATMENT PARADIGM

Goal is to achieve a deep response, obtain CR, optimize PFS and OS

Induction
RVD+/-Dara
CyBorD
DRd

→

Consolidation
Auto HCT
(if eligible)
or
Doublet/Triplet
regimens

→

Maintenance
IMiD
PI

→

Relapsed/ Refractory
Plethora

CyBorD: cytoxan, velcade , dexamethasone
RVD: revlimid, velcade, dexamethasone
IMiD: immunomodulating agent
PI: proteasome inhibitor

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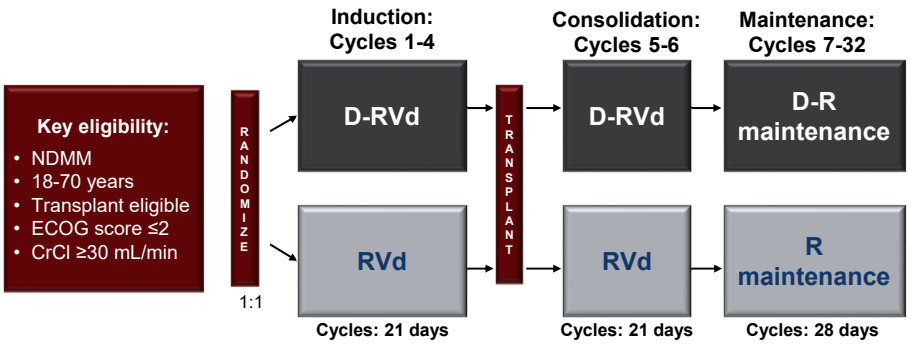
GRIFFIN: PHASE 2, RANDOMIZED, OPEN-LABEL STUDY OF D-RVD VS RVD IN ASCT-ELIGIBLE NDMM (N = 222)



Primary objective: sCR rate after consolidation

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Voorhees PM et al. *Blood*. 2020;136(8):936-945.

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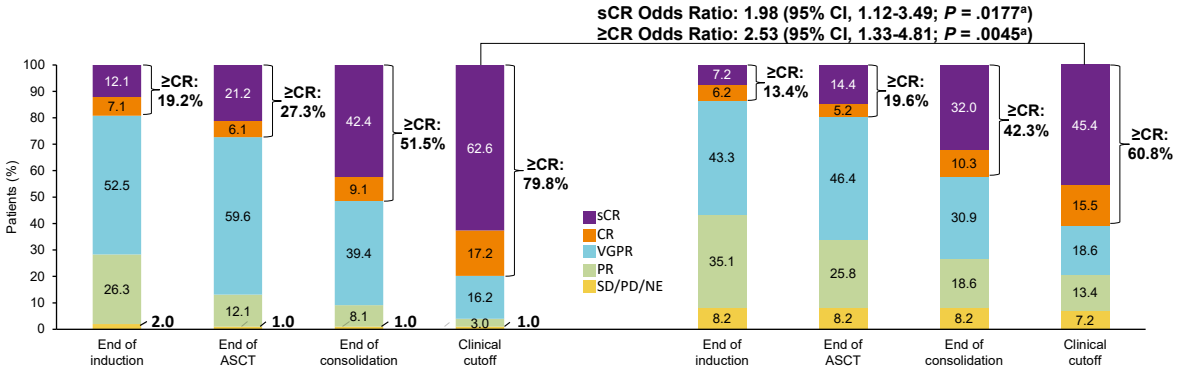
RESPONSES DEEPENED OVER TIME



- Median follow up at primary analysis (end of consolidation) was 13.5 months; median follow up at clinical cutoff was 22.1 months

Response rates and depths were greater for D-RVd at all time points

sCR D-Rvd vs RVd: OR 2.03 standard risk, OR 0.52 high risk (median FU 13.5 mo)

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Voorhees PM et al. *Blood*. 2020;136(8):936-945.

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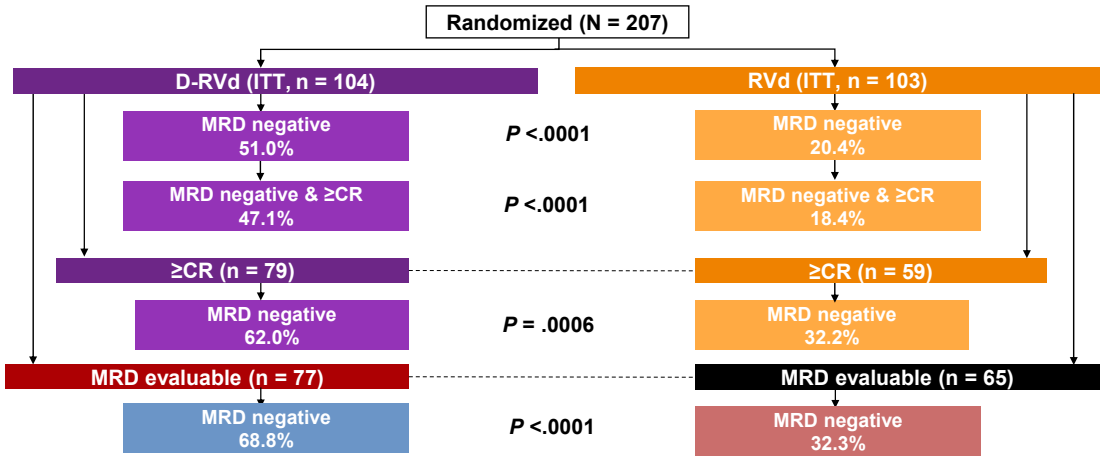
MRD (10^{-5}) NEGATIVITY AT CLINICAL CUTOFF



MRD- D-Rvd vs RVd : OR 4.72 (2.37-9.40) standard risk, OR 1.50 high risk (0.32-6.99) (median FU 22.1 mo)

Sustained MRD- ≥6 months 37.5% D-RVd vs 7.8% RVd, *P* <.0001
Sustained MRD- ≥12 months 28.8%D-RVd vs 2.9% RVd, *P* <.0001

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Voorhees PM et al. *Blood*. 2020;136(8):936-945. Kaufman JL et al. ASH. 2020; Abstract 549.

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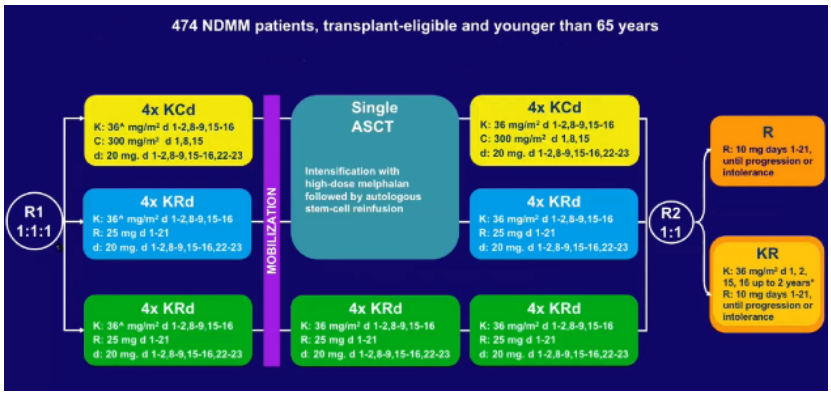
FORTE TRIAL: EFFICACY OF KRD WITH OR WITHOUT TRANSPLANT IN NEWLY-DIAGNOSED MM



Gay F et al. ASH 2020. Abstract 141
Gay et al. *JCO.* 2019;37.15: :8002

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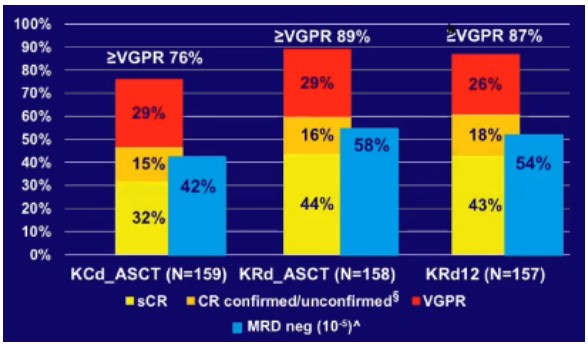
FORTE TRIAL: KRD-HCT AND KRD12 EQUALLY EFFECTIVE IN INDUCING HIGH-QUALITY RESPONSES

Pre-Maintenance RR, MRD



Gay F et al. ASH 2020. Abstract 141
Gay et al. *JCO.* 2019;37.15:8002

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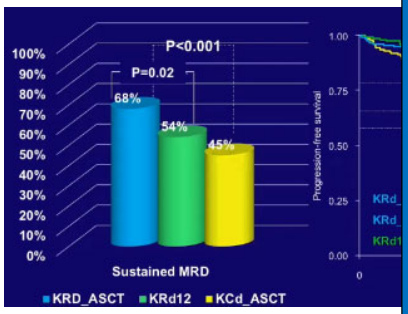
FORTE TRIAL: KRD + HCT SIGNIFICANTLY PROLONGED PFS AND SUSTAINED MRD

PFS: Median Follow

Rate of MRD: 10-5



Summary of Results

- ✓ KRD-HCT significantly prolonged PFS vs. KRD12 and KCd-HCT
- ✓ The benefit of KRD-HCT was observed in all groups of patients (ISS-1 and standard risk , 3 yr PFS 80-84%. ISS-2/3, high risk, 3 yr PFS 69-72%)
- ✓ KR maintenance also significantly prolonged PFS vs. R in all subgroups with a 30 month PFS of 81 vs. 68%, MRD neg 46 vs. 32%. No increase in maintenance discontinuation due to toxicity

BEATING CANCER IS IN OUR BLOOD. Gay F et al. ASH 2020. Abstract 141

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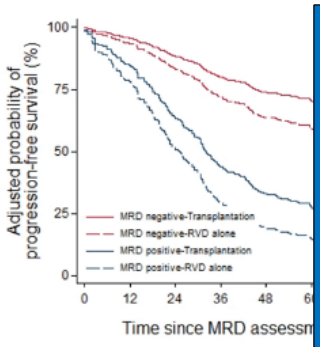
BENEFIT WITH AUTOLOGOUS HCT

Progression-Free Survival: MRD



Transplant Superior to R
Popu

Summary of Results

- ✓ HD Melphalan and auto HCT significantly reduced risk of progression or death by 30% vs. RVD
- ✓ Frontline transplant remains standard of care for NDMM
- ✓ More patients achieved MRD negativity with auto HCT
- ✓ Combining transplant with most efficient quadruplets seems to be the best strategy in order to cure as many patients as possible

BEATING CANCER IS IN OUR BLOOD. Perrot A et al. ASH 2020. Abstract 143

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OUTCOME INCORPORATING NOVEL THERAPIES INTO ASCT PARADIGM DURING INDUCTION, CONSOLIDATION, AND MAINTENANCE

	Patient characteristics			Best Response Post induction			Best Response on Study			
Regimen/Trial	N	ISS-3	High-risk	≥ VGPR	MRD $<10^{-5}$	MRD $<10^{-6}$	≥ VGPR	≥ CR	MRD $<10^{-5}$	MRD $<10^{-6}$
IFM/DFCI 2009 RVD-AHCT-RVD (R 1yr)	350	17%	18%	47%			88%	59%		30% (NGS)
FORTE KRD-AHCT-KRD (R vs KR)	158	15%	33%	73%			89%	60%	58% (NGF)	
CASSIOPEIA DaraVTD-AHCT-DaraVTD	543	15%	15%	65%	35% (NGF)		85%	54%	64% (NGF)	39% (NGS)
GRIFFIN Dara RVD-AHCT-Dara RVD – (R-Dara)	104	14%	16%	72%			96%	80%	69 % (NGS)	
MASTER Dara-KRd-AHCT-Dara-KRd (R)	81	20%	28%	90%	40% (NGS)	27% (NGS)	100%	95%	82% (NGS)	63% (NGS)

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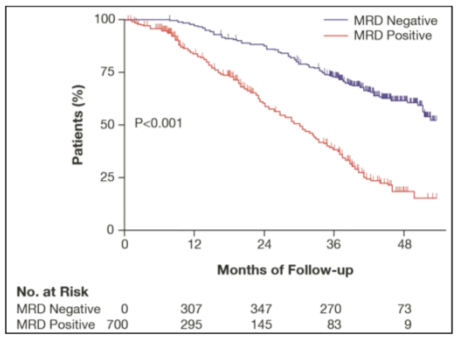
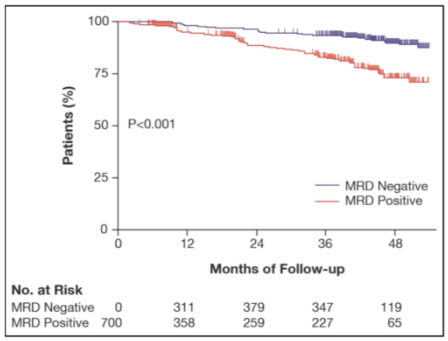
MRD PREDICTS SURVIVAL (7-COLOR FLOW)

MRD=minimal residual disease

PFS by MRD



OS by MRD



PFS: HR 0.3, 95% CI (0.23-0.37)

OS: HR 0.34, 95% CI (0.22-0.51)

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Attal M et al. *N Engl J Med*. 2017;376:1311-1320

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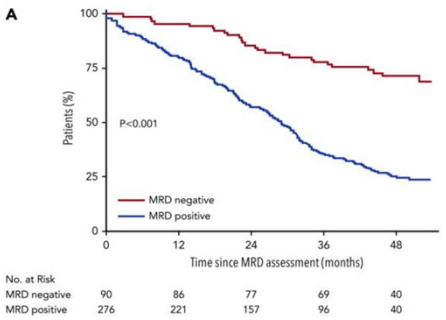
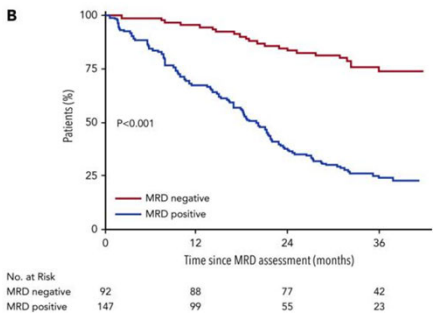
MRD: INDEPENDENT PROGNOSTIC FACTOR FOR PFS

PFS by MRD: Start of maintenance



PFS by MRD: After 12 months of maintenance



PFS: MRD + 29 mo vs. MRD+ NR

PFS: MRD + 20 mo vs. MRD- NR

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Perrot et al. *Blood.* 2018;132 (23):2456-2464

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FIRST-LINE THERAPY WHEN TRANSPLANT IS NOT A CONSIDERATION

Primary Therapy for Non-Transplant Candidates

Preferred Regimens
- Bortezomib/lenalidomide/dexamethasone (category 1)[j]
- Daratumumab[f]/lenalidomide/dexamethasone (category 1)
- Lenalidomide/low-dose dexamethasone (category 1)[k]
- Bortezomib/cyclophosphamide/dexamethasone[e]

Other Recommended Regimens
- Carfilzomib/lenalidomide/dexamethasone
- Ixazomib/lenalidomide/dexamethasone
- Daratumumab[f]/bortezomib/melphalan/prednisone (category 1)
- Daratumumab[f]/cyclophosphamide/bortezomib/dexamethasone

Useful In Certain Circumstances
- Bortezomib/dexamethasone
- Cyclophosphamide/lenalidomide/dexamethasone
- Carfilzomib/cyclophosphamide/dexamethasone[g]

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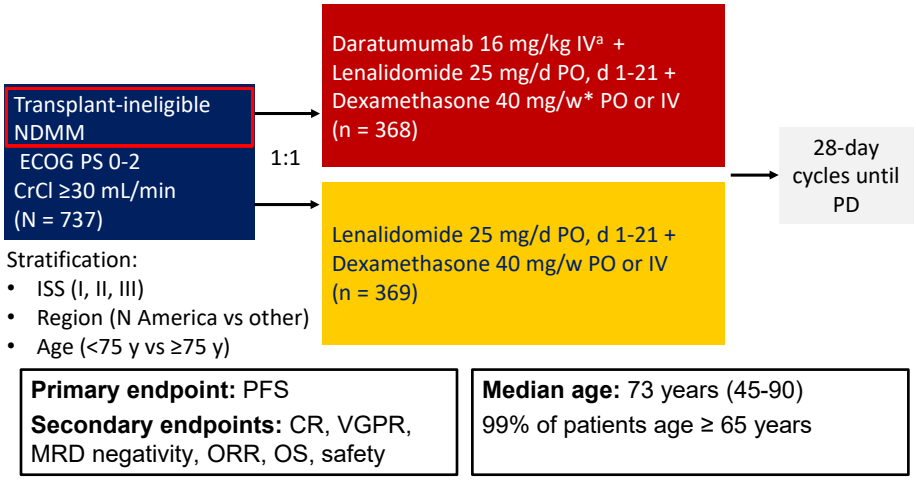
PHASE III MAIA STUDY DESIGN: ASCT-INELIGIBLE NEWLY-DIAGNOSED MYELOMA



Primary endpoint: PFS
Secondary endpoints: CR, VGPR, MRD negativity, ORR, OS, safety

Median age: 73 years (45-90)
99% of patients age ≥ 65 years

[a]QW cycles 1-2, Q2W cycles 3-6, Q4W cycle ≥7.

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PHASE III MAIA: EFFICACY

Outcome	Daratumumab + Rd (n = 368)	Rd (n = 369)	HR (95% CI)	P Value
Median PFS, mo 30 mo-PFS, %	NR 71	31.9 56	0.56 (0.43-0.73)	<.0001
Median OS, mo Events, n (%)	NR 62 (17)	NR 76 (21)	0.78 (0.56-1.1)	
ORR, % Stringent CR CR VGPR PR	93 30 17 32 14	81 12 12 28 28		<.0001
MRD negativity, %	24	7		< .0001

- Median follow-up: 28 months
- Daratumumab favored in most subgroups, including age, race, ISS stages, ECOG PS scores
- Reduced risk of progression or death with MRD negativity in both arms

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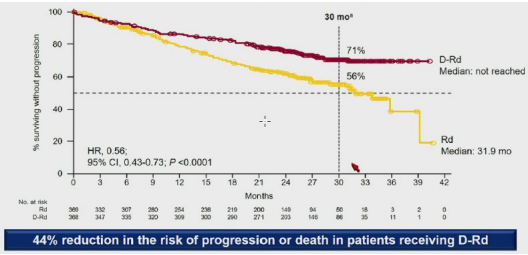
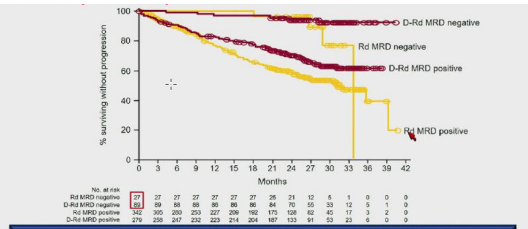
PHASE III MAIA: PRIMARY ENDPOINT—PFS



44% reduction in the risk of progression or death in patients receiving D-Rd



- >3-fold higher MRD negativity achieved with D-Rd
- Lower risk of progression or death with MRD negativity

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PHASE III MAIA: SAFETY

TEAE, %	Daratumumab + Rd (n = 364)		Rd (n = 365)	
	Any Grade	Grade ¾	Any Grade	Grade 3/4
Hematologic				
Neutropenia	57	50	42	35
Anemia	35	12	38	20
Thrombocytopenia	19	7	19	9
Lymphopenia	18	15	12	11
Nonhematologic				
Diarrhea	57	7	46	4
Constipation	41	2	36	<1
Fatigue	40	8	28	4
Peripheral edema	38	2	29	<1
Back pain	34	3	26	3
Asthenia	32	4	25	4
Nausea	32	1	23	<1
Pneumonia	23	14	13	8
DVT and/or pulmonary embolism	12	6	13	6
Infusion-related reaction	41	3	--	--
Invasive second primary malignancy	3		4	
TEAE resulting in death	7		6	

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NDMM WITHOUT SCT

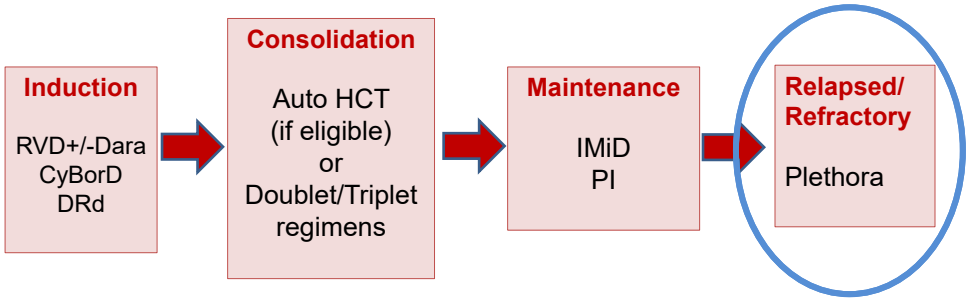
Study	SWOG 777 VRd vs Rd		RVd-lite	ALCYONE Dara VMP vs VMP		MAIA DaraRd vs Rd	
N	242	229	50	356	350	368	368
Median age	63		73	71		73	
Median F/u, mos	55		30	40		36	
ORR	82%	72%	86%	91%	74%	93%	81%
CR	16%	8.4%	44%	46%	25%	49%	25%
Median PFS, mos	43	30	35.1	36	19	NR	34
PFS HR (95% CI)	0.71 (0.56-0.91)		N/A	0.42 (0.34-0.51)		0.56 (0.44-0.71)	
OS or PFS2	75 mos	64 mos	NR	78% @ 3y	68% @ 3y	PFS2: NR	47
OS HR (95% CI)	OS 0.71 (0.52–0.96)		N/A	0.60 (0.46-0.80)		PFS2 HR 0.69 (0.53-0.91)	
	*V for 6 mos (biw q21 d * 8 cycles)		*V for 17 mos (qwk: 35d *9; q2wk: 28d *6)	*V for 12 mos (6 wk cycles, biw *1, qwk * 8)			

Durie BGM. *Lancet.* 2017;389:519. O'Donnell EK. *Br J Haematol.* 2018;182:222. Mateos MV. *N Engl J Med.* 2018;378:518-528. Mateos MV. *Lancet.* 2020;395:132-141.

25

MULTIPLE MYELOMA: TREATMENT PARADIGM

Goal is to achieve a deep response, obtain CR, optimize PFS and OS



CyBorD: cytoxan, velcade , dexamethasone
RVD: revlimid, velcade, dexamethasone
IMiD: immunomodulating agent
PI: proteasome inhibitor

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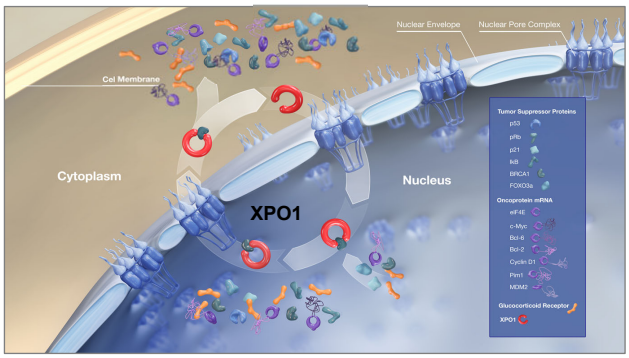
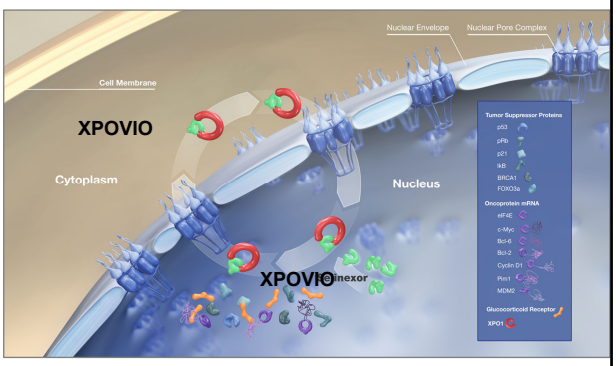
XPOVIO IS FROM A NEW CLASS OF DRUG, SELECTIVE INHIBITOR OF NUCLEAR EXPORT (SINE)

Without XPOVIO



With XPOVIO



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Tai YT et al. *Leukemia* 2014;28:155; Schmidt J et al. *Leukemia* 2013;27:2357.

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XPOVIO IS A NEW AGENT FOR MYELOMA PATIENTS WHO HAVE EXHAUSTED MANY OF THE EXISTING THERAPIES

Drug	Formulation		Approval
XPOVIO (selinexor)		80 mg taken twice a week or 100 mg taken once a week	• In combination with dexamethasone for **relapsed/refractory myeloma** patients who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody • In combination with Velcade and dexamethasone for **relapsed/refractory myeloma** patients who have received at least 1 prior therapy

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EFFICACY OF XPOVIO IN RELAPSED/REFRACTORY MYELOMA: XPOVIO + DEXAMETHASONE

	No. Patients with ≥PR (%)[1]
Total	32 (26)
Previous therapies to which the disease was refractory, n (%)	
Velcade, Kyprolis, Revlimid, Pomalyst, and Darzalex	21 (25)
Kyprolis, Revlimid, Pomalyst, and Darzalex	26 (26)
Velcade, Kyprolis, Pomalyst, and Darzalex	25 (27)
Kyprolis, Pomalyst, and Darzalex	31 (26)

Additional analyses showed clinical benefit with XPOVIO regardless of patient age and renal function.[2,3]

1. STORM Trial. Chari A et al. *N Engl J Med.* 2019;381:727; 2. Gavriatopoulou M et al. Presented at the 17th International Myeloma Workshop; September 12–15, 2019. Abstract FP-110; 3. Vogl DT et al. Presented at the 17th International Myeloma Workshop; September 12–15, 2019. Abstract FP-111.

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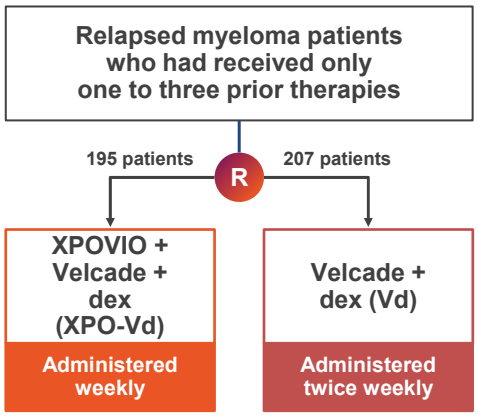
XPOVIO, VELCADE, AND DEXAMETHASONE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA



- More patients responded in the XPO-Vd group than in the Vd group (76.4% vs 62.3%).
- Longer time until disease progression in the XPO-Vd group than in the Vd group (median 20.3 vs 12.9 months).
- More patients experienced low platelet counts, fatigue, and nausea, and fewer patients experienced peripheral neuropathy in the XPO-Vd group than in the Vd group.

XPO-Vd data was approved by the FDA for use as second-line treatment in RRMM.

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RRMM, relapsed/refractory multiple myeloma
BOSTON Study. Dimopoulos MA et al. *J Clin Oncol.* 2020;38: Abstract 8501.

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SUPPORTIVE CARE STRATEGIES FOR XPOVIO

Gastrointestinal

Consult with your doctor if nausea, vomiting, or diarrhea occur or persist. Begin prophylactic anti-nausea medications.

Low sodium (hyponatremia)

Maintain fluid intake.

Fatigue

Stay hydrated and active.

Low blood counts (cytopenias)

Report signs of bleeding right away.
Report signs of fatigue or shortness of breath.

BEATING CANCER IS IN OUR BLOOD.

Chari A et al. Manuscript under preparation.

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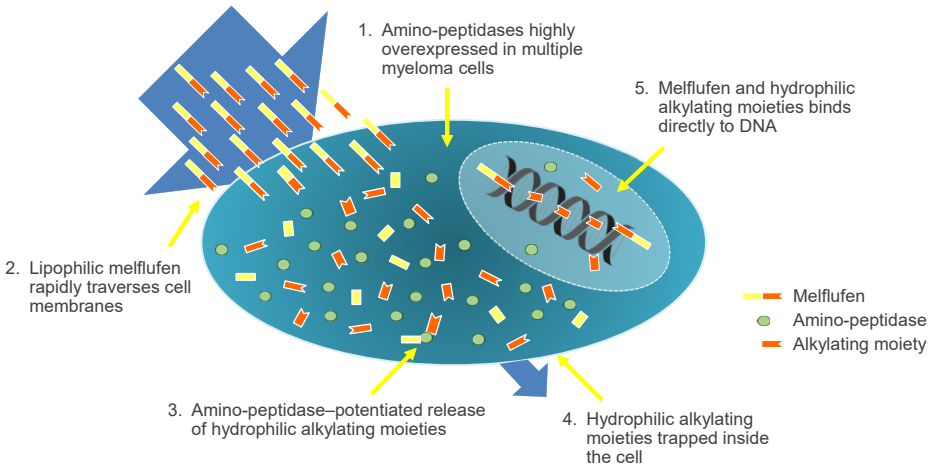
MELFLUFEN IS A PEPTIDE DRUG CONJUGATE
FDA APPROVED 2.27.21



BEATING CANCER IS IN OUR BLOOD.

1. Chauhan D et al. *Clin Cancer Res*. 2013;19:3019; 2. Wickström M et al. *Invest New Drugs*. 2008;26:195; 3. Ray A et al. *Br J Haematol*. 2016;174:397; 4. Strese S et al. *Biochem Pharmacol*. 2013;86:888; 5. Wickström M et al. *Oncotarget*. 2017;8:66641.

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PHASE 2, PIVOTAL, SINGLE-ARM, MULTICENTER STUDY OF MELFLUFEN IN RRMM

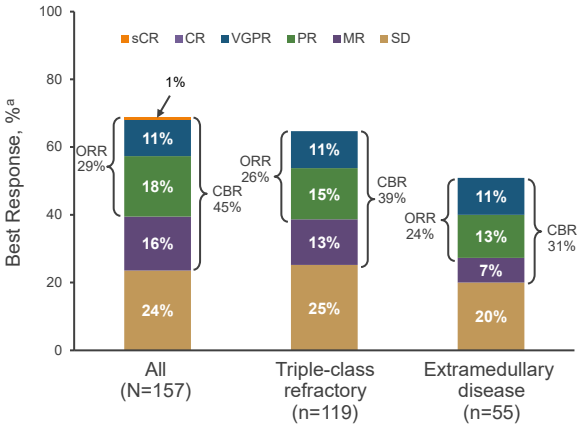
Adult patients with
- Relapsed/refractory MM refractory to Pomalyst or anti-CD38 monoclonal antibody or both
- ≥2 prior lines of therapy, including an immunomodulatory drug and a proteasome inhibitor
- ECOG PS ≤2

↓

Melflufen (IV) on day 1 + dex (oral) on days 1, 8, 15, and 22 of a 28-day cycle
(until disease progression or unacceptable toxicity)

Any-grade and grade 3/4 adverse events occurred in 100% and 94% of patients, respectively

The most common grade 3/4 adverse events were low blood counts



BEATING CANCER IS IN OUR BLOOD.

Horizon Study. Richardson PG et al. *J Clin Oncol*. December 9, 2020 [Epub ahead of print].

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PHASE 1B/2A OPEN-LABEL STUDY IBERDOMIDE + DEXAMETHASONE IN RRMM

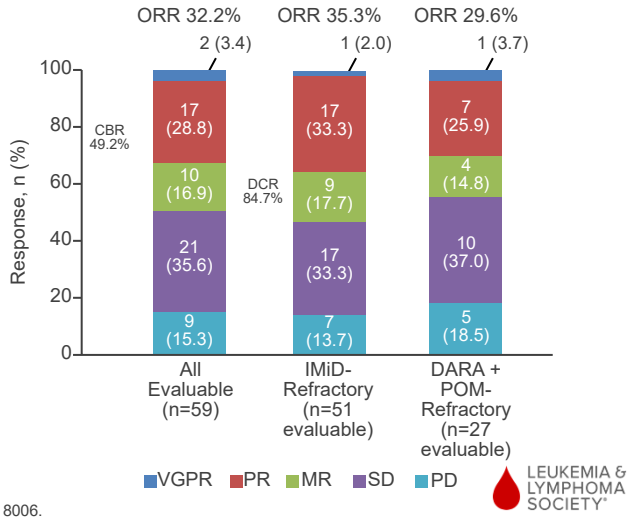
- Relapsed/refractory MM
- Prior Revlimid or Pomalyst
- Prior proteasome inhibitor
- Documented progressive disease during or within 60 days of last antimyeloma therapy

Iberdomide
(D1–21)
Dose escalation: 0.3 to 1.3 mg

+

Dexamethasone
(D1,8,15, 22)
- 40 mg (for age ≤75 yrs) or
- 20 mg (for age >75 yrs)

28-day cycles



BEATING CANCER IS IN OUR BLOOD.

Lonial S et al. *J Clin Oncol*. 2019;37: Abstract 8006.

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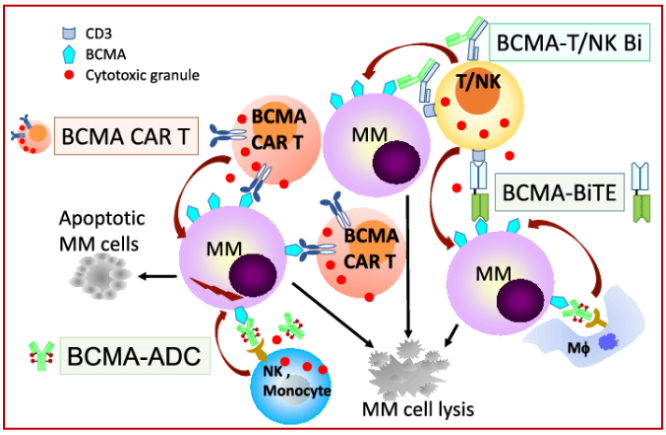
B-CELL MATURATION ANTIGEN (BCMA): A NEAR-PERFECT TARGET IN MULTIPLE MYELOMA



BEATING CANCER IS IN OUR BLOOD.

Cho SF et al. Front Immunol 2018

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ANTIBODY-DRUG CONJUGATES (ADCS) IN MM

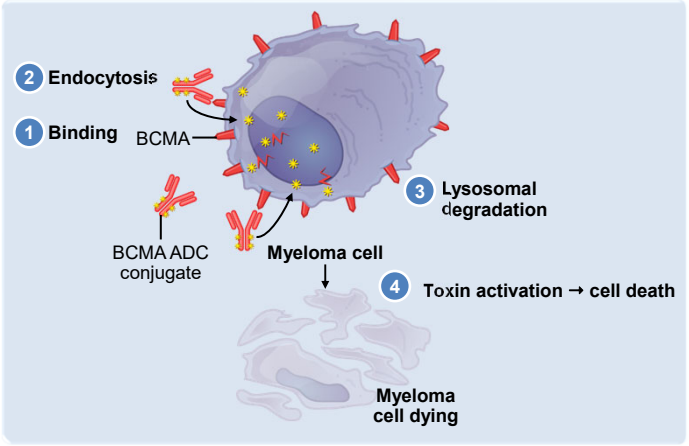
ADCs can selectively target and deliver drugs to myeloma cells

Components

Antibody

Stable linker

Toxin



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FIRST ADC APPROVED IN MM

Drug	Formulation		Approval
Blenrep (belantamab mafodotin)*		2.5 mg/kg IV over approximately 30 minutes once every 3 weeks	• For **relapsed/refractory** myeloma

*Black box warning: changes in the corneal epithelium resulting in changes in vision; belantamab mafodotin is available only through a restricted distribution program

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BLENREP IN RRMM

	Blenrep (2.5 mg/kg)	Blenrep (3.4 mg/kg)
N	97	99
Median no. lines of therapy, n (range)	7 (3–21)	6 (3–21)
Overall response rate (%)	31	34
Median PFS (mos)	2.9	4.9
Median OS (mos)	Not reached	Not reached

	Blenrep (2.5 mg/kg)	Blenrep (3.4 mg/kg)
N	95	99
Common adverse events, n (%)		
Grade 1–2		
Keratopathy	41 (43)	26 (27)
Grade 3–4		
Keratopathy	26 (27)	21 (21)
Thrombocytopenia	19 (20)	33 (33)
Anemia	19 (20)	25 (25)
Serious adverse events, n (%)	38 (40)	47 (47)

2 deaths: 1 sepsis (2.5 mg/kg) and 1 hemophagocytic lymphohistiocytosis (3.4 mg/kg)

PFS, progression-free survival; OS, overall survival

DREAMM-2 Study. Lonial S et al. *Lancet Oncol*. 2020;21:207.

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CURRENTLY AVAILABLE ADC *SIDE EFFECTS*

Blenrep

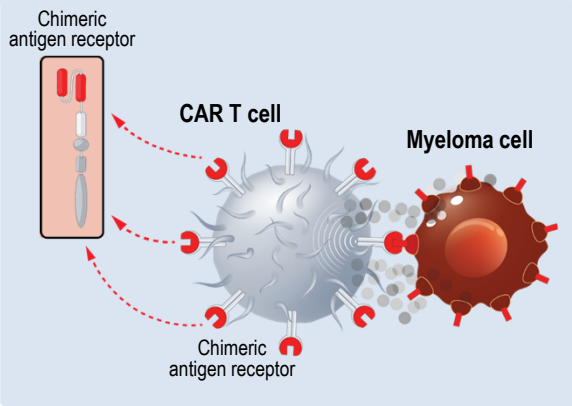
- Thrombocytopenia
- Keratopathy
- Decrease visual acuity
- Nausea
- Blurred vision
- Fever
- Infusion-related reactions
- Fatigue

Management

- Available only through a Risk Evaluation and Mitigation Strategies (REMS) due to the risk of ocular toxicity
- Patients receive ophthalmic examinations at baseline (within 3 weeks prior to the first dose), prior to each dose, and promptly for worsening symptoms
- Patients are advised to use preservative-free lubricant eye drops at least 4 times a day starting with the first infusion and continuing until end of treatment
- Patients should also avoid use of contact lenses unless directed by an ophthalmologist

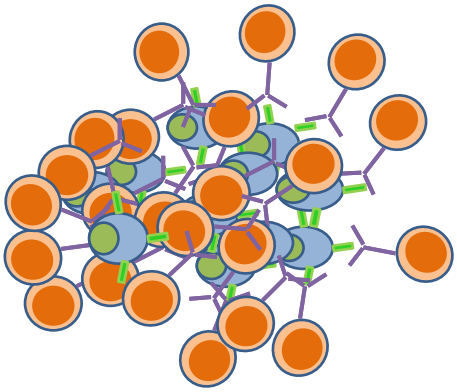
CAR T-CELL THERAPY

- Genetically modified T cells designed to recognize specific proteins on MM cells
- CAR T cells are activated once in contact with the MM cell and can destroy the MM cell
- CAR T cells can persist for long periods of time in the body
- CAR T cells are created from a patient's own blood cells, but the technology is evolving to develop "off-the-shelf" varieties



CAR, chimeric antigen receptor; MM, multiple myeloma
CAR T-cell therapy is not yet FDA-approved for patients with MM.

CHIMERIC ANTIGEN RECEPTOR T CELL



BCMA CAR-T cells vs Myeloma Cells

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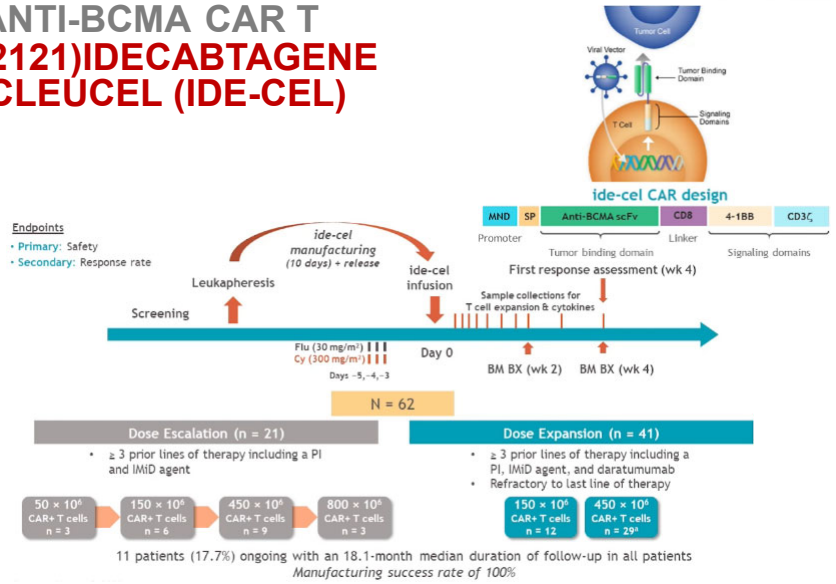
ANTI-BCMA CAR T (BB2121)IDECABTAGENE VICLEUCEL (IDE-CEL)



Raje, N et al. NEJM 2019; 380:1726-37
Lin Y, et al. ASH 2020. Abstract 131

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PHASE 1 CRB-401: BB2121 IN RR MULTIPLE MYELOMA

- Median age: 61 yrs (37-75)
- Inclusion: ≥ 3 lines of
- therapy (IMiD, PI, CD38)
- Median # of MM therapies: 6 (3-18)
- Cytogenetics: HR 27%
- Bridging therapy: 52%
- Prior ASCT: 91.9%
- IMiD/PI E/R: 100/80.6%
- IMiD/PI/CD38 E/R: 93.5/69.4%

Safety

AEs of special interest, n (%)	Any grade N = 62	Grade 3/4 N = 62
Any AE	62 (100)	61 (98.4)
Neutropenia	57 (91.9)	55 (88.7)
Febrile neutropenia	10 (16.1)	8 (12.9)
Anemia	47 (75.8)	35 (56.5)
Infection[a]	47 (75.8)	14 (22.6)
CRS[b]	47 (75.8)	4 (6.5)
Thrombocytopenia	46 (74.2)	35 (56.5)
Leukopenia	40 (64.5)	38 (61.3)
Lymphopenia	23 (37.1)	22 (35.5)
Neurologic toxicity[c]	22 (35.5)	1 (1.6)

- Median time to Recovery of G3/4 Cytopenias: 1.9 and 2.2 months
- 1 death within 8 weeks, Gr2 CRS, cytopenias, MR on D+31, hospice
- 7 deaths within 6 months (11.3%), 1 cardiac arrest, and 6 due to myeloma

Raje, N. NEJM 2019; 380:1726-37
Lin Y, et al. ASH 2020. Abstract 131

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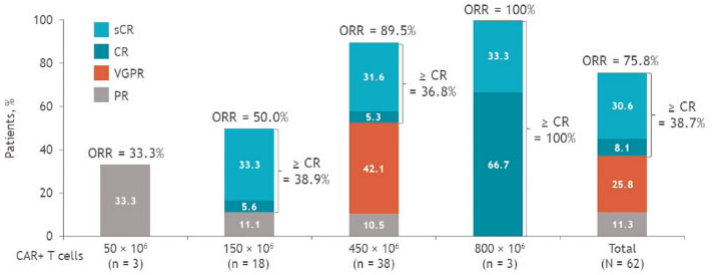
BB2121: ORR 75.8%, MEDIAN DOR 10.3 MONTHS

ORR



- All patients with a CR were MRD negative by NGS
- Median duration of response: 10.3 months (95% CI 7.7 -13.7 months)
- Half of 8 ongoing responders have DOR > 2 yrs. Dose-related increase in DOR
- No decrease in DOR for older patients, higher ISS scores, extramedullary plasmacytomas or bridging therapy

Lin Y, et al. ASH 2020. Abstract 131

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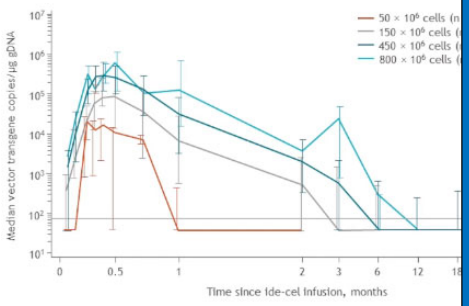
BB2121: CAR-T CELL EXPANSION, PERSISTENCE

Robust Ide-Cel Expansion with Long-Term Persistence



Summary of Results

- ✓ Favorable and durable responses at dose ≥ 150 x 106 with median OS of 34.2 months, ½ of ongoing responders with a DOR > 2 yrs
- ✓ In pivotal phase 2 KarMMa trial: ORR was 73% (including CR rate 33%), median DOR 10.7 months, median PFS 8.8 months and OS 19.4 months
- ✓ Ide-Cel is also being explored in ongoing clinical trials:

1. **KarMMa-2:** Phase 2 PD within 18 mos of 1L or inadequate response to HCT
2. **KarMMa-3:** Phase 3 Ide-Cel vs. standard regimens with 2-4 prior lines of therapy
3. **KarMMa-4:** Phase 1 study with high risk NDMM (R-ISS-3 per IMWG criteria)

Lin Y, et al. ASH 2020. Abstract 131; Delforge M, et al. ASH 2020. Abstract 2323; Munshi NC, et al. J Clin Oncol 2020; 38. Abstract 8503

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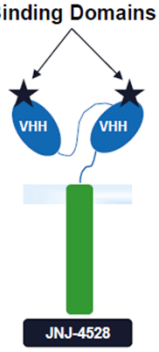
CARTITUDE-1: A PHASE 1B/2 OF CILTACABTAGENE AUTOLEUCEL (CILTA-CEL) IN RRMM

Characteristics and Design

- N=97 for Phase 1b + Phase 2 (Phase 2 N = 68)
- Median age: 61 years
- Inclusion: RRMM ≥ 3 lines of therapy or double refractory, prior IMiD, PI, anti-CD38
- M administered dose: 0.71 x 106 (0.51 – 0.95 x 106) CAR-T cells/kg
- M # of MM therapies: 6 (3-18)
- High-risk disease: 23%
- Triple refractory: 85%
- Penta refractory: 41%

Binding Domains



JNJ-4528: investigational CAR T-cell therapy comprised of 2 BCMA- targeting domains designed to confer avidity plus a 4-1BB costimulatory domain

Phase 1b portion, N = 29

Deep, durable responses and manageable safety in RRMM

BEATING CANCER IS IN OUR BLOOD. Madduri, D. ASH 2020. Abstract 177

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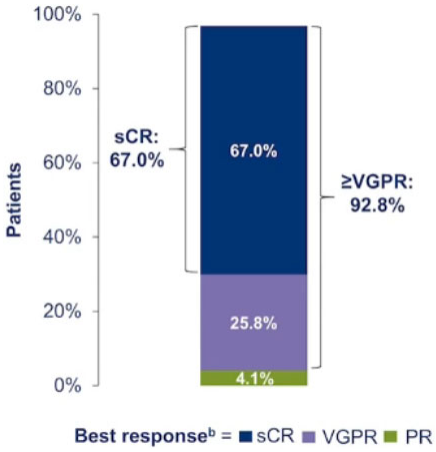
CARTITUDE-1: ORR = 96.9% (94/97)



Efficacy Data

- Median time to response: 1 month (0.9-8.5 months)
- Median time to MRD negativity: 1 month (0.8-7.7 months)
- Of evaluable patients, 93% achieved MRD negativity
- MRD – and sCR: 57.9%
- MRD – and ≥ VGPR: 86%

b: No patient had stable disease or progressive disease as best response

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Madduri, D. ASH 2019. Abstract 177

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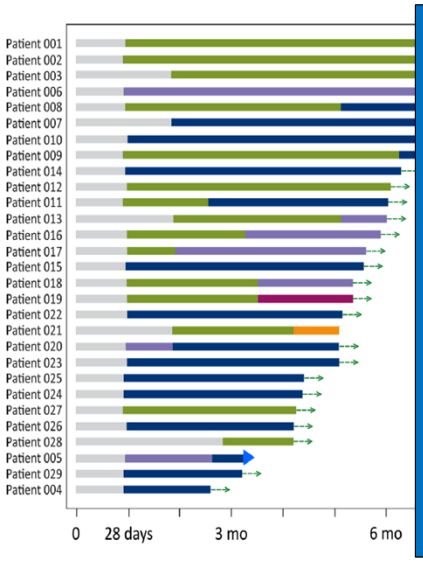
CARTITUDE-1: DURATION OF RESPONSE



Summary of Results

- ✓ Cilta-Cel has a manageable safety profile at recommended phase 2 dose
- ✓ CRS was mostly grades ½, median time to onset of CRS was 7 days
- ✓ CAR-T related neurotoxicities occurred in 20.6% with 10.3% having Grade ≥ 3
- ✓ ORR 96.9% with sCR 67%
- ✓ Median PFS not reached, 12 month PFS rate 76.6%, OS rate 88.5%
- ✓ Cilta-Cel under further investigation in other populations of MM patients in earlier line settings (Cartitude-2 and 4)

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Madduri, D. ASH 2019. Abstract 177

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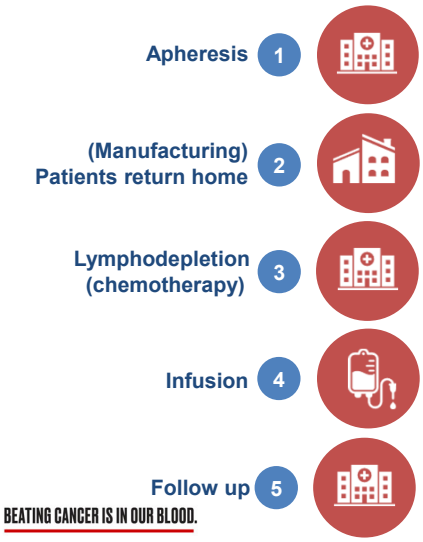
CAR T-CELL THERAPY PATIENT JOURNEY



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ADDITIONAL BCMA-DIRECTED CAR T CELLS IN MM

Study	Phase 1 study	LUMMICAR-2	CRB-402	PRIME	UNIVERSAL*
Agent	CT053	CT053	bb21217	P-BCMA-101	ALLO-715
No. patients	24	20	69	55	31
Median no. prior therapies	5 (2–11)	5 (3–11)	6 (3–17)	8 (2–18)	5 (3–11)
Overall response rate (%)	87.5	94	68	67	60
Complete response or better (%)	79.2	28	29	Not reported	Not reported
CRS, all grades (G3/4), %	62.5 (0)	79 (0)	70 (4†)	17 (0)	45 (0)
Neurotoxicity, all grades (G3/4), %	4 (4)	16 (5)	22 (7)	4 (4)	0
Duration of response (mos)	21.8	Not reported	17	Not reported	Not reported
Median progression-free survival (mos)	18.8	Not reported	Not reported	Not reported	Not reported

*No graft-versus-host disease; †Two deaths

BEATING CANCER IS IN OUR BLOOD. BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; G, grade

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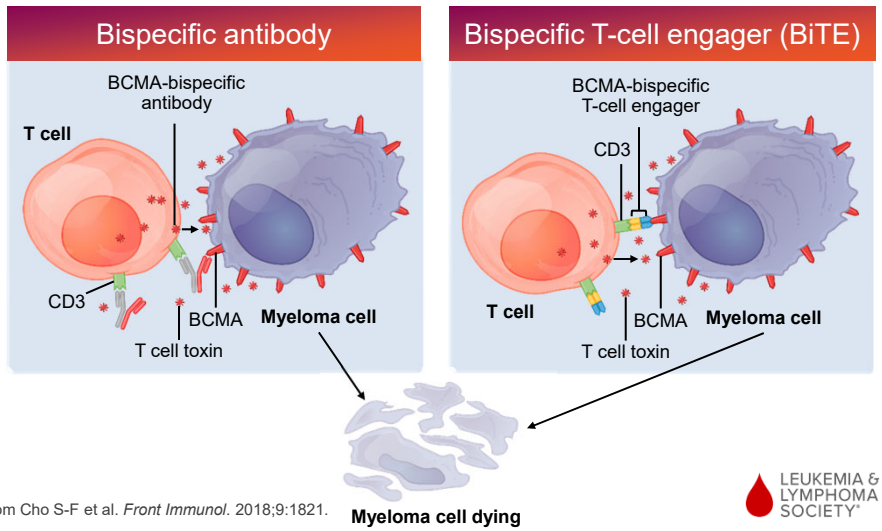
BISPECIFIC ANTIBODIES AND BISPECIFIC T-CELL ENGAGERS (BITES)

Bispecific antibodies can target two cell surface proteins at the same time



BEATING CANCER IS IN OUR BLOOD. Adapted from Cho S-F et al. *Front Immunol*. 2018;9:1821.

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BISPECIFIC ANTIBODIES AND BITES IN MM

Agent	Teclistamab	REGN54582	AMG-701
Bispecific or BiTE	**Bispecific**	**Bispecific**	**BiTE**
Target on myeloma cell	BCMA	BCMA	BCMA
No. patients	84 (IV), 65 (subq)	49	82
Median no. prior therapies (range)	6 (2–14)	5 (2–17)	6 (1–25)
Overall response rate (%)	69 (in 4 active IV/subq doses)	62.5 (at highest dose level)	26
CRS, all grades (G3/4), %	55 (0)	39 (0)	57 (10)
Neurotoxicity, all grades (G3/4), %	5 (3*)	12 (0)	8 (not reported)
Next steps	Planned phase 2 monotherapy dose is 1500 mcg/kg subq	Phase 1 dose escalation ongoing; phase 2 study recruiting	Further evaluation continuing

*Only IV formulation

BiTE, bispecific T-cell engager; IV, intravenous; subq, subcutaneous; CRS, cytokine release syndrome; G, grade

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BISPECIFIC ANTIBODIES AND BITES IN MM

Agent	Talquetamab	Cevostamab (formerly BFCR4350A)
Bispecific or BiTE	Bispecific	Bispecific
Target on myeloma cell	GPRC5D	FcRH5
No. patients	102 (IV), 55 (subq)	53
Median no. prior therapies (range)	6 (2–20)	6 (2–15)
Overall response rate (%)	69 (at recommended phase 2 dose of 405 mcg/kg subq)	53 (≥3.6/20 mg doses)
CRS, all grades (G3/4), %	54 (3*)	76 (2)
Neurotoxicity, all grades (G3/4), %	6 (2*)	Not reported

*Only IV formulation

BiTE, bispecific T-cell engager; IV, intravenous; subq, subcutaneous; CRS, cytokine release syndrome; G, grade

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KEY POINTS

- **XPOVIO (selinexor) can help when all else has been tried (supportive care required). Could be used earlier in treatment in combination with Velcade.**
- **The BCMA-targeting antibody–drug conjugate Blenrep (belantamab mafodotin [belamaf]) was recently approved for the treatment of relapsed or refractory myeloma and is active as monotherapy and in combination. Blenrep is available only through REMS due to the risk of ocular toxicity.**
- **Iberdomide and melflufen have shown promising efficacy and tolerability.**
- **CAR T and T-cell engaging antibodies (TCE) represent a new wave of myeloma treatments that are highly active even in heavily pre-treated patients.**
- **Toxicities of CAR T and TCE mainly consist of cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and low blood counts, all of which are treatable.**

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QUESTION & ANSWER

Treatment Updates: Multiple Myeloma

- **Ask a question by phone:**
  - Press star (*) then the number 1 on your keypad.
- **Ask a question by web:**
  - Type your question
  - Click enter

Due to time constraints, we can only take one question per person.
Once you've asked your question, the operator will transfer you back into the audience line.

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LLS EDUCATION & SUPPORT RESOURCES

HOW TO CONTACT US:

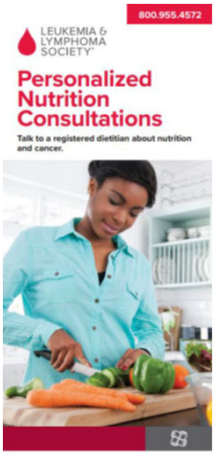
To contact an **Information Specialist** about disease, treatment and support information, resources and clinical trials:

Call: (800) 955-4572
Monday to Friday, 9 a.m. to 9 p.m. ET

Chat live online: www.LLS.org/InformationSpecialists
Monday to Friday, 10 a.m. to 7 p.m. ET

Email: infocenter@LLS.org
All email messages are answered within one business day.

CLINICAL TRIAL SUPPORT CENTER
Work one-on-one with an LLS Clinical Trial Nurse Navigator who will help you find clinical trials and personally assist you throughout the entire clinical-trial process.
www.LLS.org/Navigation



NUTRITION CONSULTATIONS
Our registered dietitian has expertise in oncology nutrition and provides free one-on-one consultations by phone or email.
www.LLS.org/Consult.

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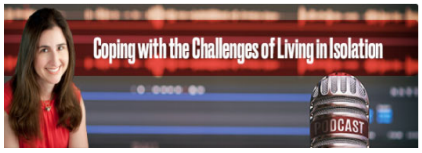
LLS EDUCATION & SUPPORT RESOURCES

Online Chats
Online Chats are free, live sessions, **moderated by oncology social workers**.

Banding Together Fridays Online Chat is specifically addressing questions and concerns about living with a blood cancer during COVID-19. Register now at **www.LLS.org/Chat**

Education Videos
View our free education videos on disease, treatment, and survivorship. To view all patient videos, please visit **www.LLS.org/EducationVideos**.



Patient Podcast
The Bloodline with LLS is here to remind you that after a diagnosis comes hope. To listen to an episode, please visit **www.TheBloodline.org**.

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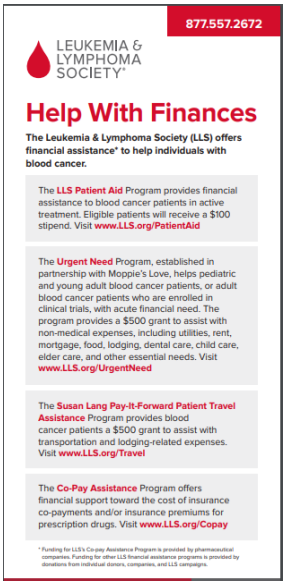
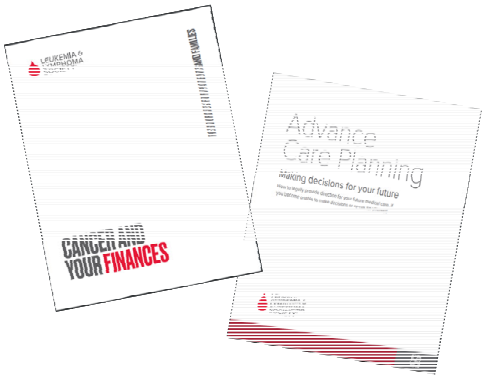
LLS EDUCATION & SUPPORT RESOURCES



The Leukemia & Lymphoma Society (LLS) offers the following financial assistance programs to help individuals with blood cancer: **www.LLS.org/Finances**



To order free materials: **www.LLS.org/Booklets**

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58


THANK YOU
We have one goal: A world without blood cancers
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