WELCOME & INTRODUCTIONS

Multiple Myeloma: Understanding My Treatment Options

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.

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Program will begin shortly

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THE CHANGING LANDSCAPE OF MYELOMA TREATMENT

Amrita Y. Krishnan, MD
Professor, Department of Hematology & Hematopoietic Cell Transplantation
Director, Judy and Bernard Briskin Center for Multiple Myeloma Research
City of Hope Medical Center
Duarte, CA

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DISCLOSURES

Multiple Myeloma: Understanding My Treatment Options

Consultant:

- **Celgene, Janssen, Adaptive**

Speakers Bureau:

- **Celgene, Takeda**

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History of Myeloma

- 3300 BC - Pre-Columbian America
- 3200-500 BC - Egyptian mummies – Thebe
- 200-1300 AD - American Indian Skeletons
- 11th-15th Century AD - Iceland

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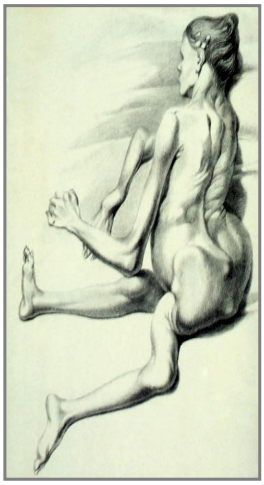
First descriptions…

Sarah Newbury, 39 F

- 1840: Severe back pain while stooping
- April 1842: Fractured femurs
- April 15, 1844: St. Thomas Hospital
- Rx: Orange peel infusion, rhubarb pills, arrow-root, mutton chop, wine, a pint of Porter and opiates
- April 20, 1844: Death



Solly S, Med Chir Trans Lond 27:435, 1844

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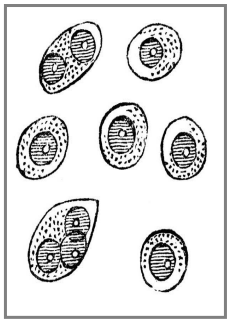
Sarah Newbury: Autopsy

- Multiple fractures
- Thorax reduced in size with compression of lungs
- Bone marrow: Modena red with round or oval cells with 1 or 2 nuclei

The disease began with a "morbid action of the blood vessels in which the earthy matter of the bone marrow is absorbed and thrown out by the kidneys in the urine"

Samuel Solly, 1844



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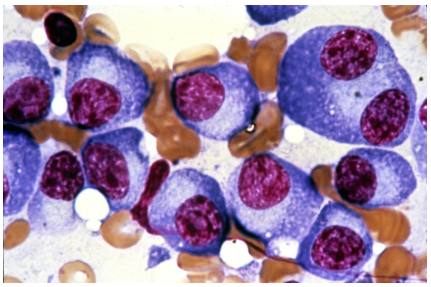
Myeloma

- MM is characterized by
  - Excessive numbers of abnormal plasma cells in the bone marrow
  - Overproduction of intact monoclonal immunoglobulins (IgG, IgA, IgD, or IgE) or Bence-Jones protein (free antibody light chains) and concomitant drop in other immunoglobulins



Kufe. *Cancer Medicine*. 6th ed. 2003:2219

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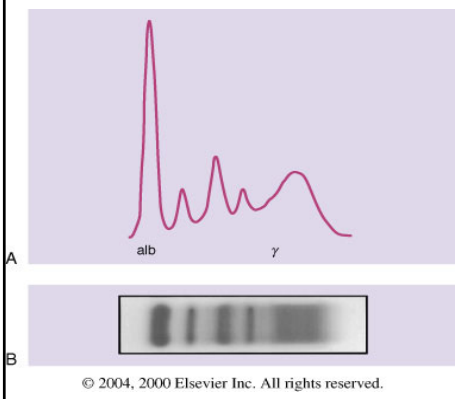
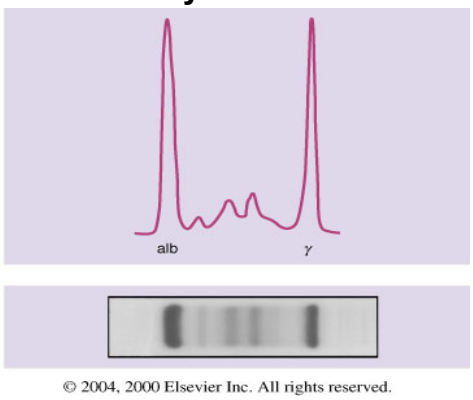
Serum Protein Electrophoresis

Normal



Monoclonal Protein in Myeloma



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Kyle RA and Rajkumar SV. Cecil Textbook of Medicine, 22nd Edition, 2004

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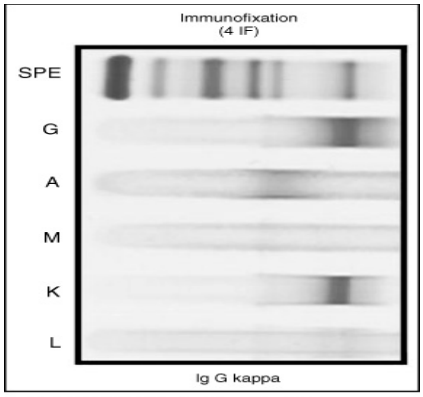
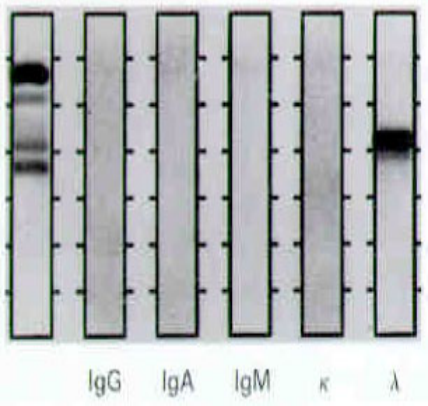
Immunofixation to Determine Type of Monoclonal Protein



IgG kappa M protein



Lambda Light Chains

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Kyle RA and Rajkumar SV. Cecil Textbook of Medicine, 22nd Edition, 2004

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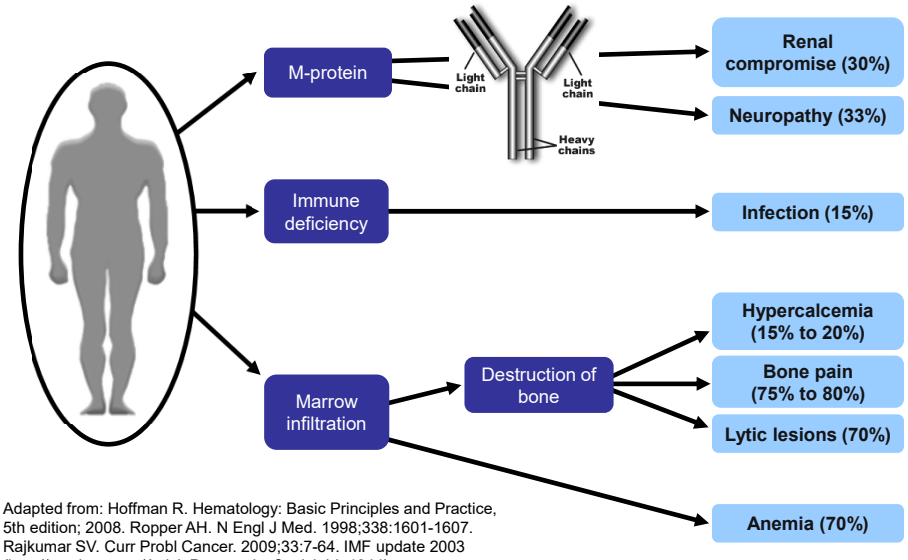
Clinical Manifestations of Symptomatic Multiple Myeloma



Adapted from: Hoffman R. Hematology: Basic Principles and Practice, 5th edition; 2008. Ropper AH. N Engl J Med. 1998;338:1601-1607. Rajkumar SV. Curr Probl Cancer. 2009;33:7-64. IMF update 2003 (http://myeloma.org/ArticlePage.action?articleId=1044).

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Initial Diagnostic Evaluation

Evaluation	
History and physical	
Blood workup	CBC with differential and platelet counts BUN, creatinine Electrolytes, calcium, albumin, LDH Serum quantitative immunoglobulins Serum protein electrophoresis and immunofixation β_2-M Serum free light chain assay
Urine	24-hr protein Protein electrophoresis (quantitative Bence-Jones protein) Immunofixation electrophoresis
Other	Skeletal survey Unilateral bone marrow aspirate and biopsy evaluation with immunohistochemistry or flow cytometry, cytogenetics, and FISH MRI and PET/CT as clinically indicated

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NCCN. Clinical practice guidelines in oncology: multiple myeloma. v.1.2013.

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Induction Therapy

- Combination therapy with 3 drugs is standard for fit patients, true also for patients with renal failure
- Ongoing trials are investigating 4-drug combinations
- Which three drugs?
- Goal of therapy; MRD?

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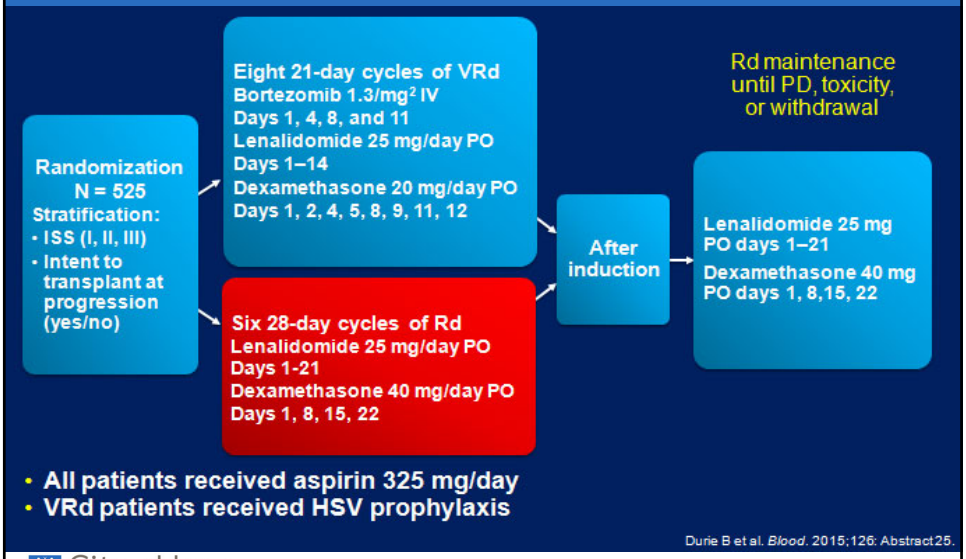
SWOG S0777: Study Design



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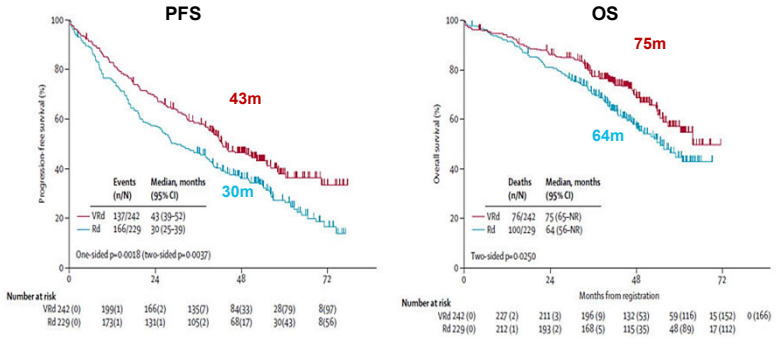
SWOG: VRd→Rd vs Continuous Rd
Bortezomib Twice a Week IV ×8 Cycles

ORR (CR) (%): 8 (16) vs. 71(8)

G3-4 AEs: PN (33%)



SWOG study was not specifically conducted in elderly patients with newly diagnosed MM

VRD lite: **Bz SQ/w & Rd ×9 c followed by 6 BzR consolidation resulted in ORR of 86% (66% ≥ VGPR).**
Median PFS: 35 m; median OS: not reached

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Durie B et al. Lancet .2017;389:519.
O' Donnell E et al. Br J Haematol. 2018;182:222.

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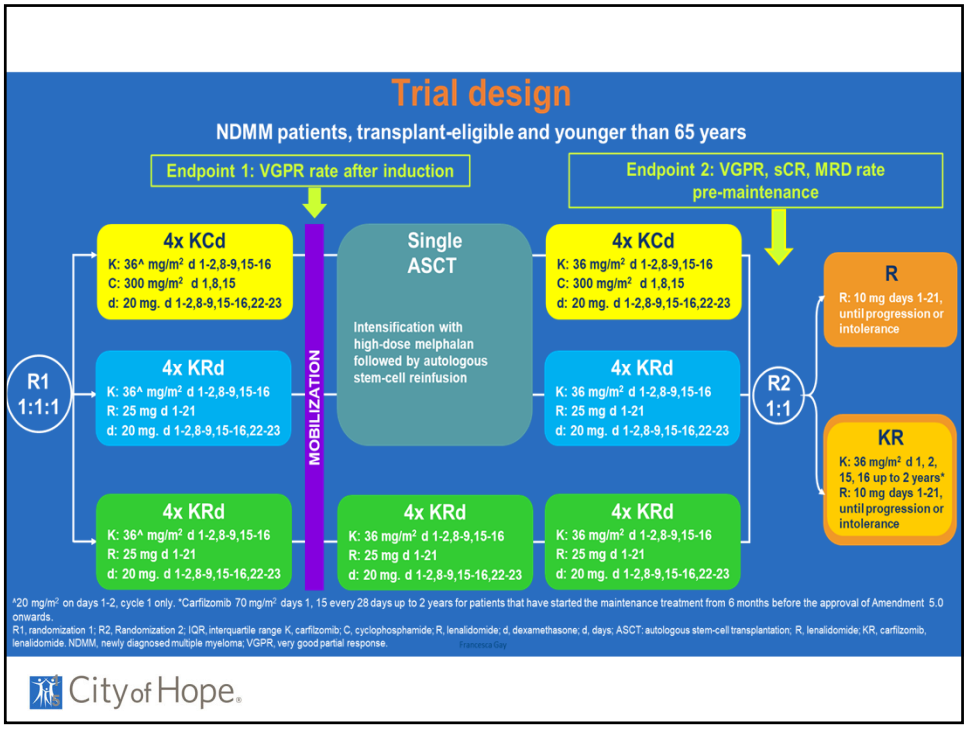
Trial design
NDMM patients, transplant-eligible and younger than 65 years
Endpoint 1: VGPR rate after induction
Endpoint 2: VGPR, sCR, MRD rate pre-maintenance
R1 1:1:1
4x KCd
K: 36^ mg/m² d 1-2,8-9,15-16
C: 300 mg/m² d 1,8,15
d: 20 mg. d 1-2,8-9,15-16,22-23
4x KRd
K: 36^ mg/m² d 1-2,8-9,15-16
R: 25 mg d 1-21
d: 20 mg. d 1-2,8-9,15-16,22-23
4x KRd
K: 36^ mg/m² d 1-2,8-9,15-16
R: 25 mg d 1-21
d: 20 mg. d 1-2,8-9,15-16,22-23
MOBILIZATION
Single ASCT
Intensification with high-dose melphalan followed by autologous stem-cell reinfusion
4x KRd
K: 36 mg/m² d 1-2,8-9,15-16
R: 25 mg d 1-21
d: 20 mg. d 1-2,8-9,15-16,22-23
4x KCd
K: 36 mg/m² d 1-2,8-9,15-16
C: 300 mg/m² d 1,8,15
d: 20 mg. d 1-2,8-9,15-16,22-23
4x KRd
K: 36 mg/m² d 1-2,8-9,15-16
R: 25 mg d 1-21
d: 20 mg. d 1-2,8-9,15-16,22-23
4x KRd
K: 36 mg/m² d 1-2,8-9,15-16
R: 25 mg d 1-21
d: 20 mg. d 1-2,8-9,15-16,22-23
R2 1:1
R
R: 10 mg days 1-21, until progression or intolerance
KR
K: 36 mg/m² d 1, 2, 15, 16 up to 2 years*
R: 10 mg days 1-21, until progression or intolerance
^20 mg/m² on days 1-2, cycle 1 only. *Carfilzomib 70 mg/m² days 1, 15 every 28 days up to 2 years for patients that have started the maintenance treatment from 6 months before the approval of Amendment 5.0 onwards.
R1, randomization 1; R2, Randomization 2; IQR, interquartile range K, carfilzomib; C, cyclophosphamide; R, lenalidomide; d, dexamethasone; d, days; ASCT: autologous stem-cell transplantation; R, lenalidomide; KR, carfilzomib, lenalidomide. NDMM, newly diagnosed multiple myeloma; VGPR, very good partial response.
Francesca Gay
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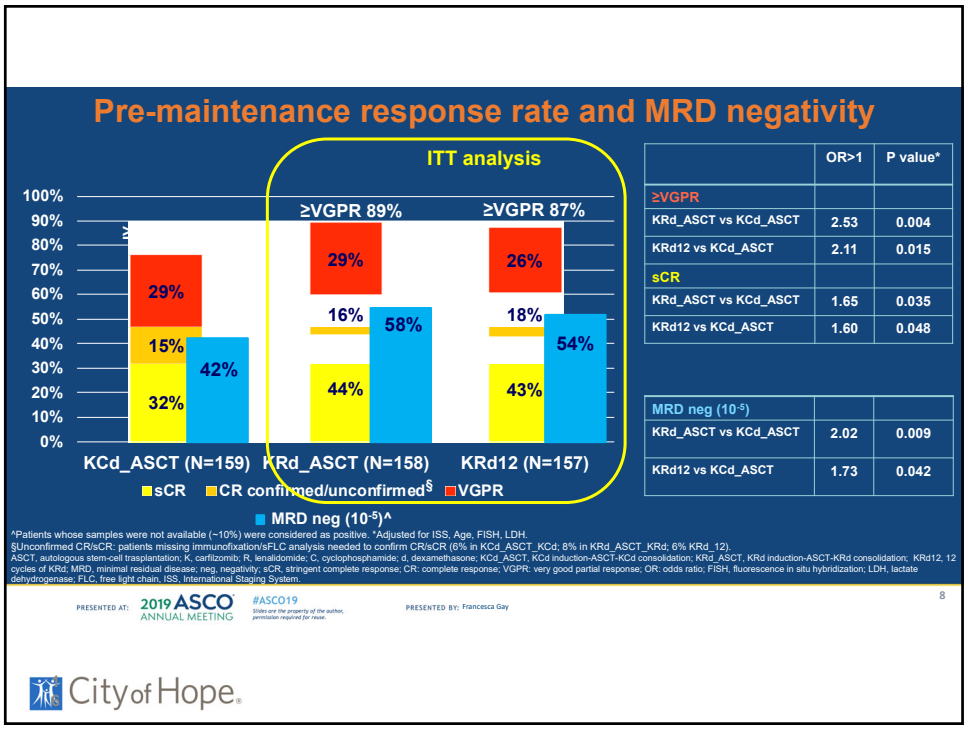
Pre-maintenance response rate and MRD negativity
ITT analysis
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
≥VGPR 89%
≥VGPR 87%
29%
15%
32%
42%
29%
16%
44%
58%
26%
18%
43%
54%
KCd_ASCT (N=159)
KRd_ASCT (N=158)
KRd12 (N=157)
sCR
CR confirmed/unconfirmed§
VGPR
MRD neg (10⁻⁵)^
OR>1
P value*
≥VGPR
KRd_ASCT vs KCd_ASCT 2.53 0.004
KRd12 vs KCd_ASCT 2.11 0.015
sCR
KRd_ASCT vs KCd_ASCT 1.65 0.035
KRd12 vs KCd_ASCT 1.60 0.048
MRD neg (10⁻⁵)
KRd_ASCT vs KCd_ASCT 2.02 0.009
KRd12 vs KCd_ASCT 1.73 0.042
^Patients whose samples were not available (~10%) were considered as positive. *Adjusted for ISS, Age, FISH, LDH.
§Unconfirmed CR/sCR: patients missing immunofixation/sFLC analysis needed to confirm CR/sCR (6% in KCd_ASCT_KCd; 8% in KRd_ASCT_KRd; 6% KRd_12).
ASCT, autologous stem-cell trasplantation; K, carfilzomib; R, lenalidomide; C, cyclophosphamide; d, dexamethasone; KCd_ASCT, KCd induction-ASCT-KCd consolidation; KRd_ASCT, KRd induction-ASCT-KRd consolidation; KRd12, 12 cycles of KRd; MRD, minimal residual disease; neg, negativity; sCR, stringent complete response; CR: complete response; VGPR: very good partial response; OR: odds ratio; FISH, fluorescence in situ hybridization; LDH, lactate dehydrogenase; FLC, free light chain, ISS, International Staging System.
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PRESENTED AT: 2019 ASCO ANNUAL MEETING #ASCO19
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PRESENTED BY: Francesca Gay
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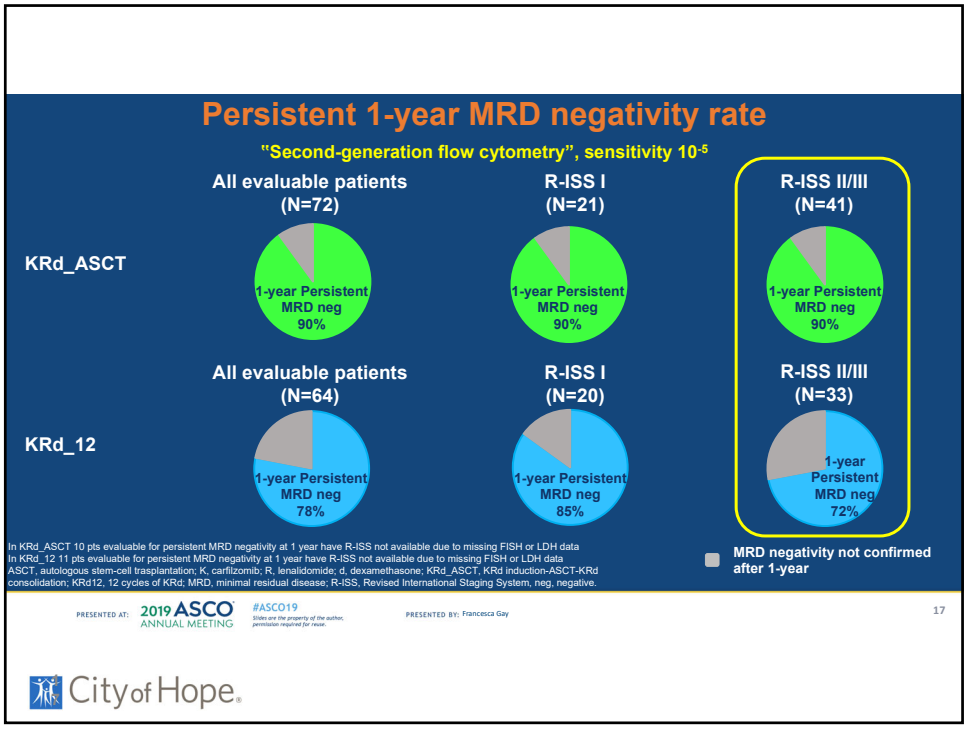

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Selected 4-Drug Combinations Being Studied in Newly Diagnosed Myeloma

4-Drug Combo	4th Drug	Selected supportive trials, NCT#
VRd-Dara	daratumumab (CD38 MAb)	Janssen, NCT03652064, NCT03412565, NCT02874742; EMN, NCT03710603
VRd-Isa	isatuximab (CD38 MAb)	Heidelberg, NCT03617731; IMROZ, NCT03319667
VRd-Elo	elotuzumab (SLAMF7 MAb)	DFCI, NCT02375555; Heidelberg, NCT02495922
KRd-Dara	daratumumab (CD38 MAb)	MMY1001, NCT01998971; MSKCC, NCT03290950, Chicago, NCT03500445
KRd-Isa	isatuximab (CD38 MAb)	Tubingen, NCT03104842
KRd-Elo	elotuzumab (SLAMF7 MAb)	Chicago, NCT02969837
IRd-Dara	daratumumab (CD38 MAb)	Toulouse, NCT03669445; Mayo, NCT03012880

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VRd, bortezomib, lenalidomide, dexamethasone; KRd, carfilzomib, lenalidomide, dexamethasone; IRd, ixazomib, lenalidomide, dexamethasone

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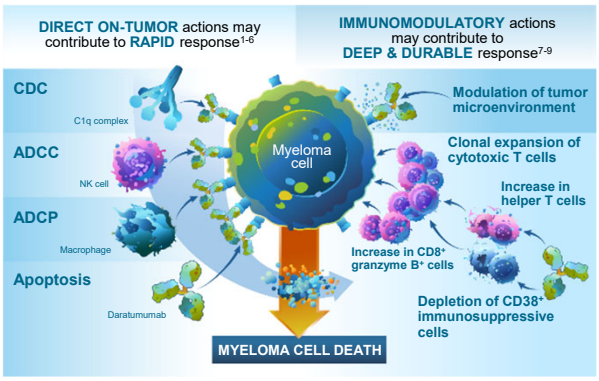
Daratumumab



Current/Ongoing Phase 3 Trials

- **RRMM**
  - D-Rd (POLLUX) & D-Vd (CASTOR)
  - D-Pd (APOLLO)* & D-Kd (CANDOR)*
- **NDMM non-transplant**
  - D-VMP (ALCYONE) & D-Rd (MAIA)
  - D-VRd (CEPHEUS)*
- **NDMM transplant**
  - D-VTd Part 1 (CASSIOPEIA)
  - D-VRd (PERSEUS)*
  - D-R maintenance (AURIGA)*

* Pending results.

CDC, complement-dependent cytotoxicity; ADCC, antibody-dependent cellular cytotoxicity; NK, natural killer; ADCP, antibody-dependent cellular phagocytosis; RRMM, relapsed/refractory multiple myeloma; D, daratumumab; R, lenalidomide; d, dexamethasone; V, bortezomib; P, pomalidomide; K, carfilzomib; NDMM, newly diagnosed multiple myeloma; MP, melphalan and prednisone; T, thalidomide.

1. DARZALEX® US PI; 2019. 2. Liszewski MK, et al. *Adv Immunol.* 1996;61:201-283. 3. Debets JM, et al. *J Immunol.* 1988;141(4):1197-1201. 4. Overdijk MB, et al. *mAbs.* 2015;7(2):311-321. 5. Lokhorst HM, et al. *N Engl J Med.* 2015;373(13):1207-1219. 6. Plesner T, et al. *Blood.* 2012;120:73. 7. Krejcik J, et al. *Blood.* 2016;128(3):384-394. 8. Adams III HC, et al. *Cytometry A.* 2019;95(3):279-289. 9. Chiu C, et al. Poster presented at: ASH 2016; San Diego, CA.

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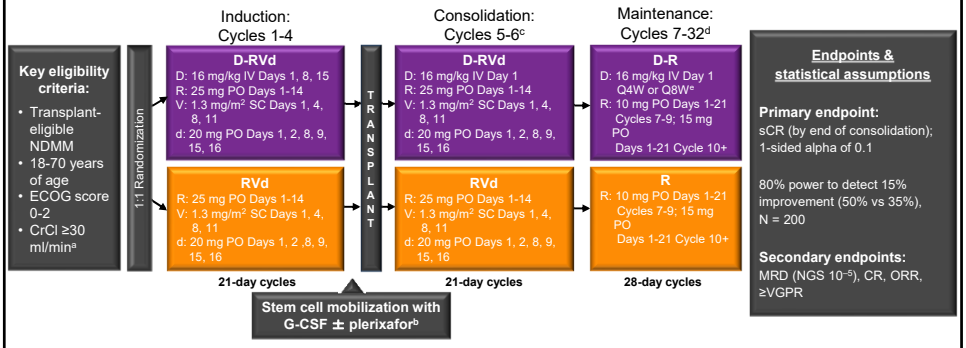
GRIFFIN (NCT02874742): Randomized Phase

- Phase 2 study of D-RVd vs RVd in transplant-eligible NDMM, 35 sites in US with enrollment from 12/2016 and 4/2018



D-RVd, daratumumab-lenalidomide/bortezomib/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; NDMM, newly diagnosed multiple myeloma; US, United States; ECOG, Eastern Cooperative Oncology Group; CrCl, creatinine clearance; IV, intravenously; PO, orally; SC, subcutaneously; G-CSF, granulocyte colony-stimulating factor; D-R, daratumumab-lenalidomide; Q4W, every 4 weeks; Q8W, every 8 weeks; sCR, stringent complete response; MRD, minimal residual disease; NGS, next-generation sequencing; CR, complete response; ORR, overall response rate; VGPR, very good partial response.

[a]Lenalidomide dose adjustments were made for patients with CrCl ≤50 mL/min. [b]Cyclophosphamide-based mobilization was permitted if unsuccessful. [c]Consolidation was initiated 60-100 days post transplant. [d]Patients who complete maintenance cycles 7-32 may continue single-agent lenalidomide thereafter. [e]Protocol Amendment 2 allowed for the option to dose daratumumab Q4W, based on pharmacokinetic results from study SMM2001 (NCT02316106).

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Most Common TEAEs[a]

	D-RVd (n = 99)		RVd (n = 102)	
	Any grade	Grade 3 or 4	Any grade	Grade 3 or 4
Hematologic, n (%)				
Neutropenia	48 (49)	32 (32)	32 (31)	15 (15)
Thrombocytopenia	43 (43)	16 (16)	31 (30)	8 (8)
Leukopenia	34 (34)	15 (15)	27 (27)	7 (7)
Anemia	32 (32)	8 (8)	32 (31)	6 (6)
Lymphopenia	30 (30)	23 (23)	29 (28)	23 (23)
Non-hematologic, n (%)				
Fatigue	61 (62)	5 (5)	56 (55)	4 (4)
Peripheral neuropathy[b]	58 (59)	7 (7)	74 (73)	7 (7)
Diarrhea	53 (54)	6 (6)	43 (42)	4 (4)
Constipation	46 (47)	2 (2)	41 (40)	1 (1)
Nausea	46 (47)	1 (1)	47 (46)	1 (1)
Upper respiratory tract infection	46 (47)	1 (1)	37 (36)	1 (1)
Pyrexia	39 (39)	2 (2)	25 (25)	3 (3)
Insomnia	39 (39)	2 (2)	30 (29)	1 (1)
Cough	38 (38)	0	25 (25)	0
Edema peripheral	32 (32)	2 (2)	35 (34)	3 (3)
Back pain	32 (32)	1 (1)	28 (28)	4 (4)
Infusion-related reactions	41 (41)	5 (5)	–	–

- Any-grade infections occurred in 81 (82%) patients in the D-RVd arm and 56 (55%) patients in the RVd arm; grade 3/4 infections were similar between groups (17 [17%] patients each)
  - Pneumonia occurred in 10 (10%) patients in the D-RVd arm and 9 (9%) patients in the RVd arm

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TEAE, treatment-emergent adverse event.
[a]Any-grade TEAEs are listed that occurred in ≥30% of patients in either group. The safety analysis population included all randomized patients who received ≥1 dose of study treatment; analysis was according to treatment received. [b]Includes patients with neuropathy peripheral and peripheral sensory neuropathy.

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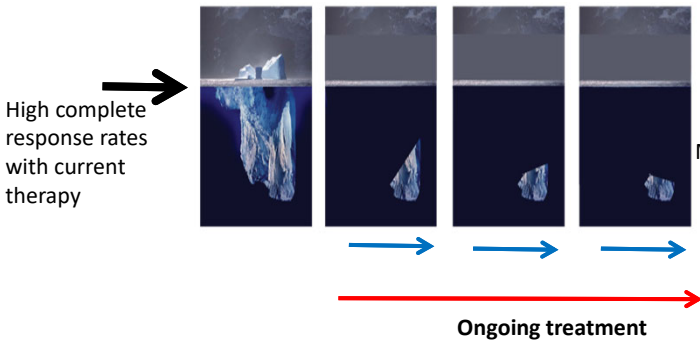
The impact of myeloma treatment



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Adapted from: "Iceberg" by Created by Uwe Kils (iceberg) and User:Wiska Bodo (sky). – (Work by Uwe Kils) http://www.ecoscope.com/iceberg/.

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Consequences of MRD

leads to relapse

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Determination Trial (IFM 2009): Newly Diagnosed Multiple Myeloma

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 6, 2017 VOL. 376 NO. 14

Lenalidomide, Bortezomib, and Dexamethasone with Transplantation for Myeloma

Michel Attal, M.D., Valerie Lauwers-Cances, M.D., Cyrille Hulin, M.D., Xavier Leleu, M.D., Denis Caillot, M.D., Martine Escoffre, M.D., Bertrand Arnulf, M.D., Margaret Macro, M.D., Karim Belhadj, M.D., Laurent Garderet, M.D., Murielle Roussel, M.D., Catherine Payen, M.D., Claire Mathiot, M.D., Jean P. Fermand, M.D., Nathalie Meuleman, M.D., Sandrine Rollet, M.S., Michelle E. Maglio, B.S., Andrea A. Zeytoonjian, B.S., Edie A. Weller, Ph.D., Nikhil Munshi, M.D., Kenneth C. Anderson, M.D., Paul G. Richardson, M.D., Thierry Facon, M.D., Hervé Avet-Loiseau, M.D., Jean-Luc Harousseau, M.D., and Philippe Moreau, M.D., for the IFM 2009 Study*

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

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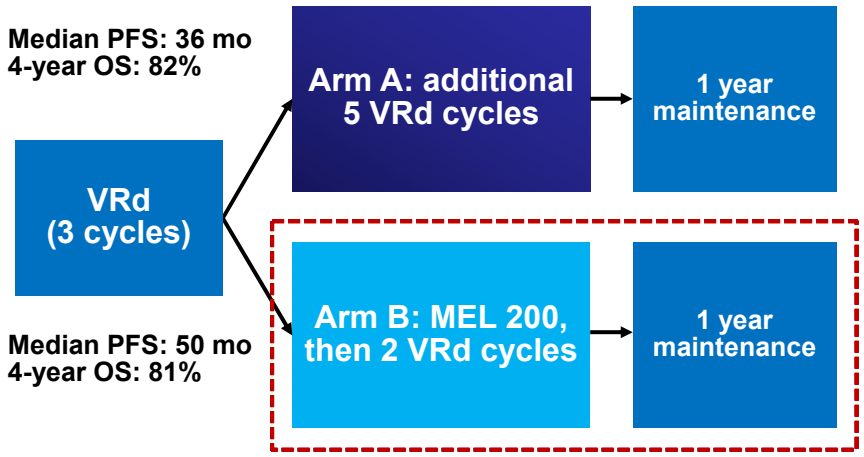
Determination Trial (IFM 2009): Newly Diagnosed Multiple Myeloma



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

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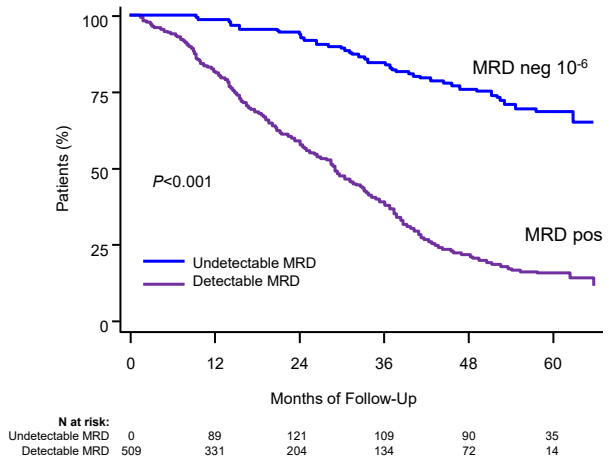
IFM 2009 Follow-Up Study: Focus on MRD



At median follow-up of 55 months, median PFS for MRD-negative patients not reached *vs* 29 months for MRD-positive patients

MRD neg obtained in 30% (73/245) with VRd + transplant and 20% (54/264) with VRd alone

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Perrot A et al. Blood. 2018;Sep 24 [Epub ahead of print].

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What is the definition and objectives of maintenance?

- Therapy administered for a prolonged period to maintain the response previously achieved
- Maintenance therapy must
  - Be convenient
  - Be safe and well tolerated long term
  - Not prevent the use, or reduce the efficacy, of other future treatments
- **Objective:** To eliminate MRD or maintain the absence of MRD, reduce the risk of relapse, and finally prolong PFS and OS

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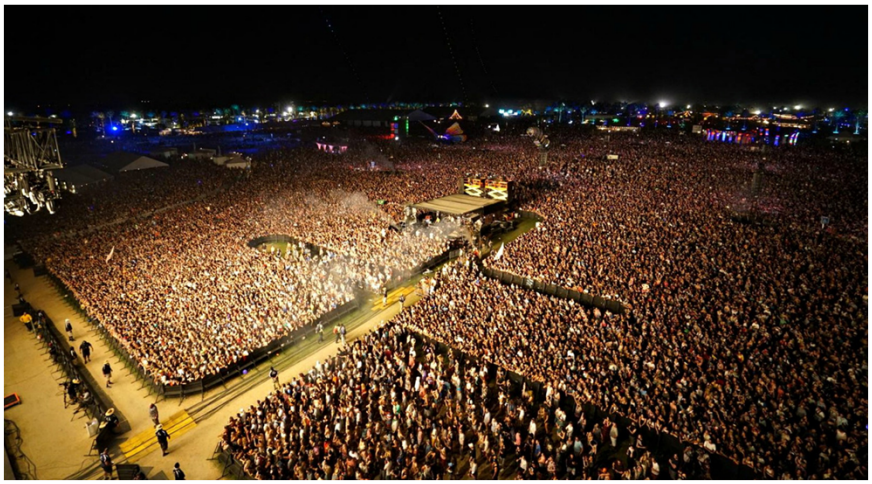
Maintenance for Everyone



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What are the options to maintain the response after ASCT?

- Thalidomide
- Bortezomib
- Lenalidomide
- Other agents

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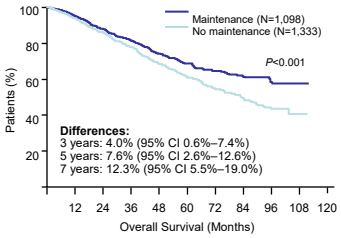
Maintenance With Thalidomide

- Benefit in OS in the long-term follow-up
- **Compromises important aspects of QoL**
  - Worsening of cognitive function, dyspnea, swollen legs, constipation, thirst, dry mouth, balance problems[1]
  - Improving appetite and sleep
- **High incidence of neuropathy**
  - 70% of patients treated for 12 months



The above clinical regimens are not approved by regulatory authorities. This information is just to discuss maintenance treatment research evolution.
Morgan GJ et al. *Blood.* 2012;119:5374.

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Maintenance With Bortezomib

Study Details	n	Treatment	Outcome	
			PFS	OS
HOVON 65 MM/ GMMG-HD4[1]	413	PAD × 3 → HDM → bortezomib every 2 weeks for 2 years	35 mo	90 mo
	414	VAD × 3 → HDM → thalidomide daily for 2 years	28 mo *P*= 0.001	83 mo RMS_{8y} (4.8 months) *P*=0.04
Median follow-up: 91 months				
PETHEMA/GEM[2]	89	VT (1 cycle bortezomib every 3 months, thalidomide daily) for 3 years	50.6 mo	OS not significantly different between arms
	87	Thalidomide (daily for 3 years)	40.3 mo	
Median follow-up: 58.6 months	90	Interferon-α2b (3 × per week for 3 years)	35.5 mo *P*<0.0 03	

HOVON 65/GMMG HD4[1]
- 5% PN grade 3–4 during maintenance
- 11% discontinuation due to bortezomib toxicity

PETHEMA[2]
- 48.8% (VT), 34.4% (T), and 1% (α2-IFN) PN grade 2–3
- 21.9% (VT), 39.7% (T) ,and 20% (α2-IFN) discontinuation due to toxicity

Bortezomib maintenance after double-ASCT is effective in patients with del(17p) and renal impairment

1. Sonneveld P et al. Blood. 2015;126: Abstract 27.
2. Rosinol L et al. Leukemia .2017;31:1922.

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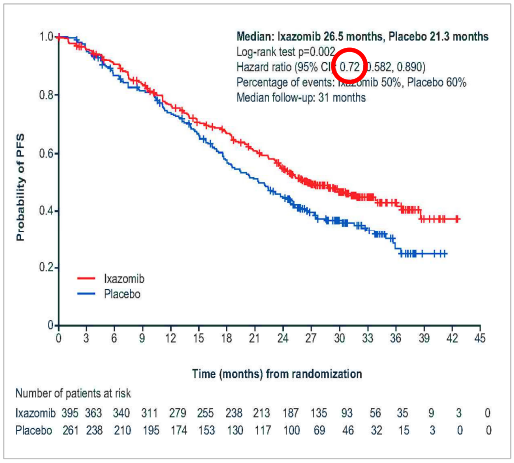
Tourmaline MM3 Trial: Ixazomib vs Placebo Following ASCT in NDMM Patients (2 years)



Ixazomib as maintenance

- 28% reduction in the risk of progression/death with ixazomib maintenance
- Upgraded the responses and increased conversions to MRD negativity over control
- Resulted in a favorable safety profile, including an absence of risk of second primary malignancies and low rates of peripheral neuropathy

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Dimopoulos MA et al. Blood. 2018;132: Abstract 301. Presentation Sunday, December 2 at 7:30 AM.

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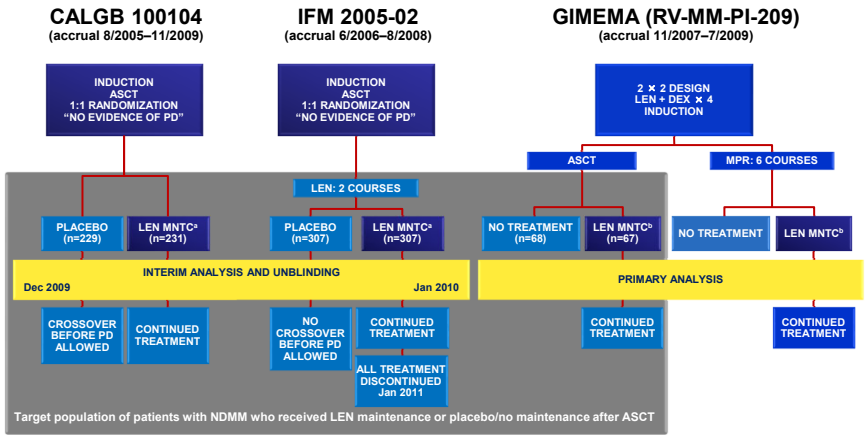
Meta-Analysis Evaluating the Role of Len as Maintenance After ASCT



[a] Starting dose of 10 mg/day on days 1–28/28 was increased to 15 mg/day if tolerated and continued until PD.
[b] Patients received maintenance 10 mg/day on days 1–21/28 until PD.

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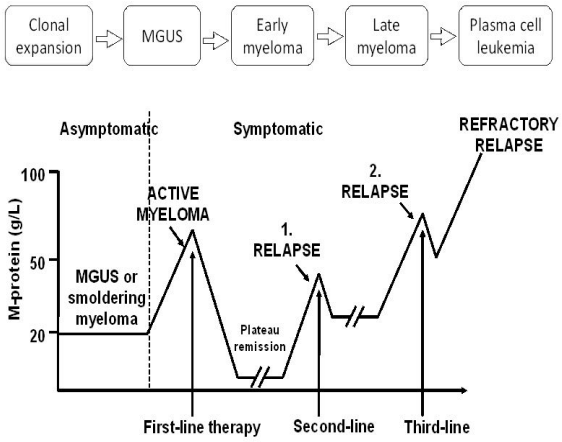
Attal M et al. J Clin Oncol. 2016;34: Abstract 8001.

32

Relapse is the hallmark of multiple myeloma



- Definitions
- Relapse from CR / Biochemical Progression / Clinical Relapse
- Biological Correlates
- Choosing when to treat
- Risk Stratification of Relapse

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Definitions – Relapse

- From CR
  - Mainly used for clinical trials
  - Reappearance of serum or urine M-protein by immunofixation or electrophoresis or abnormal FLC ratio
  - Development of ≥5% plasma cells in BM
  - Any other sign of progression (ie, new plasmacytoma, lytic bone lesion, or hypercalcemia)
- Clinical relapse
  - New CRAB findings
  - New plasmacytomas or bone lesions (fractures do not necessarily count)
  - Increasing size of existing plasmacytomas (≥50%)
  - Hyperviscosity related to paraprotein

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Kumar et al, Lancet Oncol, 2017

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Definitions – *Progression*

- Increase of 25% from lowest confirmed response value in one or more of:
  - Serum M-protein (absolute increase must be ≥0.5 g/dL)
  - Serum M-protein increase ≥1 g/dL, if the lowest M component was ≥5 g/dL
  - Urine M-protein (absolute increase must be ≥200 mg/24 h)
  - Light chain disease: the difference between involved and uninvolved FLC levels (absolute increase must be >10 mg/dL)
- Non-secretory: 25% increase in bone marrow plasma-cell percentage irrespective of baseline status (absolute increase must be ≥10%)
- Appearance of a new lesion(s), ≥50% increase from nadir
- ≥50% increase in circulating plasma cells (minimum of 200 cells per μL) if this is the only measure of disease

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Kumar et al, Lancet Oncol, 2017

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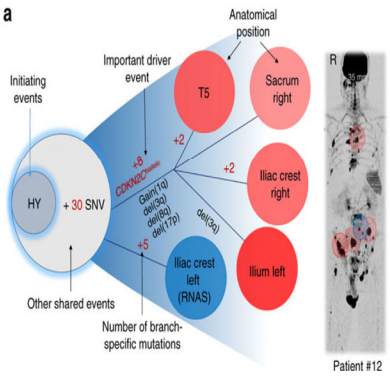
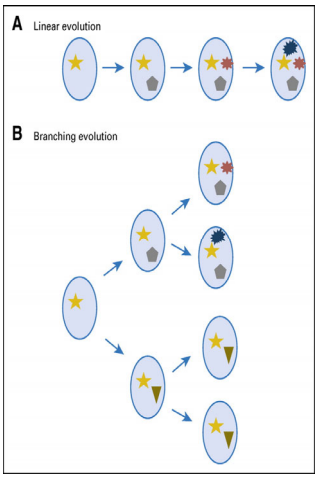
Multiclonal disease with spatial and temporal heterogeneity

Spatial genomic heterogeneity in multiple myeloma revealed by multi-region sequencing



Acquired genomic events with progression



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Rasche L et al Nature Communications 8, Article number: 268(2017)

36

Indications for treatment

- Clinical relapse (CRAB or plasmacytomas)
- Significant biochemical progression without clinical relapse
  - Doubling of the M-component in two consecutive measurements separated by 2 months with the reference value of 5 g/L, (=0.5 g/dL) or
  - In two consecutive measurements any of the following increases:
    - the absolute levels of serum M protein by ≥10 g/L (=1.0g/dL), or
    - an increase of urine M protein by ≥500 mg per 24 hours, or
    - an increase of involved FLC level by ≥20 mg/dL (= 200 mg/L) (plus an abnormal FLC ratio) or 25% increase (whichever is greater)

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Ludwig et al, The Oncologist, 2014

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Selecting Treatment for Relapsed/Refractory Myeloma: General Principles

- Duration of initial response defines biology
- Triplet (2 active classes + dexamethasone) preferred over doublet
  - With ≥ 1 agent from a new or nonrefractory class
- Consider disease risk, PS, age, and comorbidities when selecting therapy and optimal doses
  - Consider BM biopsy at each relapse to assess risk
- Take into account prior and residual toxicities
- Treat to maximum response and maintain on ≥ 1 agent until progression or tolerability

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Slide credit: clinicaloptions.

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Phase III Lenalidomide-Based Therapy for R/R Myeloma

Trial	ORR, %	≥ CR, %	≥ VGPR, %	Median PFS, Mos	Median OS, Mos	Median F/u (OS), Mos
ASPIRE: KRd vs Rd[1]	87 vs 67	32 vs 9	70 vs 40	26.3 vs 16.6 HR: 0.69	48.3 vs 40.4 HR: 0.79	67.0
TOURMALINE-MM1: IxaRd vs Rd[2]	78 vs 72	14 vs 7	48 vs 39	20.6 vs 14.7 HR: 0.74	NR	23.0
POLLUX: DRd vs Rd[3-5]	93 vs 76	57 vs 23	80 vs 49	44.5 vs 17.5 HR: 0.44	NR vs NR HR: 0.63	36.0
ELOQUENT-2: ERd vs Rd[6,7]	79 vs 66	5 vs 9	36 vs 30	19.4 vs 14.9 HR: 0.73	48.3 vs 39.6 HR: 0.78	60.5

1. Stewart. ASH 2017. Abstr 743. 2. Moreau. NEJM. 2016;374:1621. 3. Dimopoulos. NEJM. 2016;375:1319.
4. Dimopoulos. ASH 2017. Abstr 739. 5. Bahlis. ASH 2018. Abstr 1996. 6. Dimopoulos. EHA 2017. Abstr S456.
7. Lonial. ASCO 2018. Abstr 8040.

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Slide credit: clinicaloptions.com

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Phase III PI-Based Therapy for R/R Myeloma

Trial	ORR, %	≥ CR, %	≥ VGPR, %	Median PFS, Mos	Median OS, Mos	Median F/u (OS), Mos
ENDEAVOR: Kd vs Vd[1]	77 vs 63	13 vs 6	54 vs 29	18.7 vs 9.4 HR: 0.53	NR vs 24.3 HR: 0.79	12.5
CASTOR: DVd vs Vd[2,3]	84 vs 63	29 vs 10	62 vs 29	16.7 vs 7.1 HR: 0.31	NR HR 0.63	19.4
PANORAMA-1: PanoVd vs Vd[4,5]	61 vs 55	11 vs 6	28 vs 16	12.0 vs 8.1 HR: 0.63	40 vs 36 HR: 0.94	--
Elotuzumab (phase II) EVd vs Vd[6]	66 vs 63	4 vs 4	36 vs 27	9.7 vs 6.9 HR: 0.72	NR HR: 0.61	16.0
MMY1001 (phase I): DKd vs Kd[7]	84	27	71	NR (1-yr PFS: 71%)	NR (1-yr OS: 82%)	12.0

1. Dimopoulos. Lancet Oncol. 2016;17:27. 2. Palumbo. NEJM. 2016;375:754. 3. Lentzsch. ASCO 2017. Abstr 8036. 4. San-Miguel. Lancet Oncol. 2014;15:1195. 5. San-Miguel. ASH 2015. Abstr 3026. 6. Jakubowiak. Blood. 2016;127:2833. 7. Chari. ASCO 2018. Abstr 8002.

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Slide credit: clinicaloptions.com

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Pomalidomide-Based Salvage Therapy for R/R Myeloma

Trial	Patient Population	Primary Endpoint	ORR, %	≥ VGPR, %	Median PFS, Mos	Median OS, Mos
Pom/Dex (N = 302)[1] Phase III trial vs HD Dex	R/R; ≥ 2 lines of tx including len and btz	PFS	31 vs 10	6 vs < 1	4.0 vs 1.9	12.7 vs 8.1
Bortezomib + Pom/Dex (N = 559)[2] Phase III trial vs Vd	1-3 lines of tx with len exposure; prior PI ok	PFS	82 vs 50	53 vs 18	11 vs 7	NR
Carfilzomib + Pom/Dex (N = 57)[3]	R/R to most recent tx; 1-3 lines of tx; len refractory	MTD, PR rate	62	23	10.3	NR (1 yr: 67%)
Daratumumab + Pom/Dex (N = 103)[4]	R/R; ≥ 2 lines of tx, including len and btz	MTD	60	42	8.8	17.5
Ixazomib + Pom/Dex (N = 32)[5]	1-5 lines of tx, including len and PI; len refractory	MTD activity	48; high risk: 58	20	--	--
Elotuzumab + Pom/Dex (N = 60)[6] Phase II trial vs Pom/Dex	≥ 2 lines of tx including IMiD and PI; refractory to last tx	PFS	53 vs 26	20	10.3 vs 4.8	--

1. San Miguel. Lancet Oncol. 2013;14:1055. 2. Richardson. ASCO 2018. Abstr 8001. 3. Bringhen. Leukemia. 2018;32:1803.
4. Chari. Blood. 2017;130:974. 5. Krishnan. Leukemia. 2017;[Epub]. 6. Dimopoulos. EHA 2018. Abstr LBA2606.

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Slide credit: clinicaloptions.com

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Myeloma therapy

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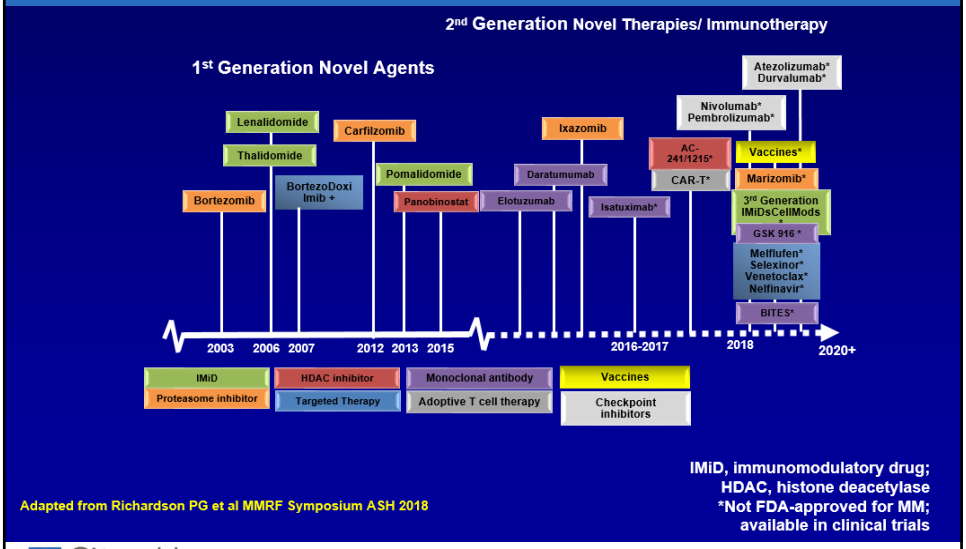
Continuing Evolution of Multiple Myeloma Treatment: Selected New Classes and Targets 2018–2020



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Mechanisms of Relapse

- Increased frequency of T reg
- Increased CD38 expression on T regs
- A proliferating ligand (APRIL) promotes T regs viability
- APRIL upregulates genes involved in immunosuppression
- Cell adhesion mediated immunoresistance

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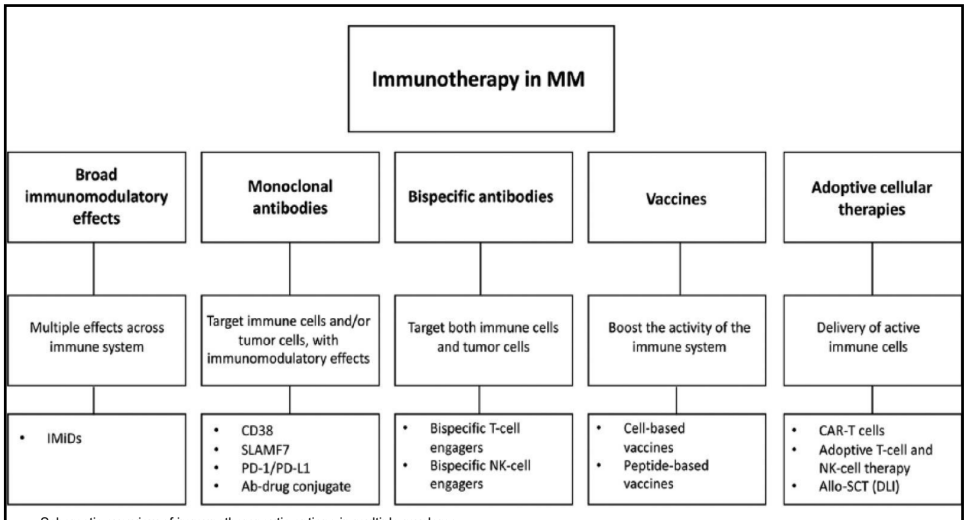

Schematic overview of immunotherapeutic options in multiple myeloma.
Ab: antibody; allo-SCT: allogeneic stem cell transplantation; CAR T-cells: chimeric antigen receptor T-cells; DLI: donor lymphocyte infusion; IMiDs: immunomodulatory drugs; NK: natural killer; PD-1: programmed death receptor 1; PD-L1: programmed death ligand 1; SLAMF7: signaling lymphocytic activation molecule family 7.

Franssen LE et al. Ther Adv Hematol. 2019 Jan 18;10:2040620718822660. doi: 10.1177/2040620718822660. eCollection 2019.

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Immunomodulatory Agents

- Bind cereblon leading to degardadation of Ikaros and Aiolos downregulation of IRF-4 and C-Myc
- Ikaros and Aiolos repress IL-2 transcription
- Activation of T cells and NK cells
- 1990 Thalidomide
- 2006 Lenalidomide approved
- 2013 Pomalidomide (2 prior lines of therapy)
- 2020 CC-220

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CC-220

- Iberdomide (CC-220; IBER) is a novel cereblon (CRBN) E3 ligase modulator (CELMoD) that:
  - Has a 20-fold higher binding affinity to CRBN than lenalidomide (LEN) or pomalidomide (POM)[6]
  - Induces more efficient degradation of target proteins, including Ikaros and Aiolos, than LEN or POM[6]
  - Has in vitro antimyeloma and immune co-stimulatory activity on T and natural killer (NK) cells[7]
  - Synergizes with other SoC agents in myeloma, including increasing apoptosis in MM cell lines treated with bortezomib (BORT) and enhancing the antibody-dependent cellular cytotoxicity (ADCC) activity of daratumumab (DARA)[8,9]

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Antibodies

- Potential targets
- CD38
- CD138
- Slam F7

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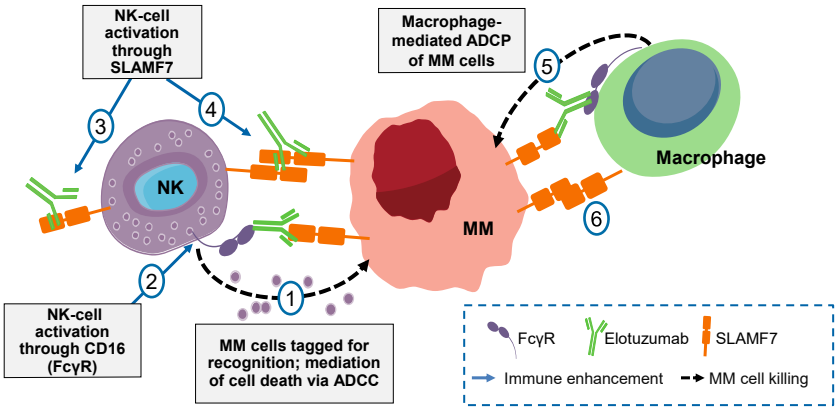
Elotuzumab: Immunostimulatory Mechanisms of Action



The immunomodulatory drug pomalidomide may synergize with elotuzumab through multiple mechanisms to increase the killing of MM cells

ADCC, antibody-dependent cell cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; FcγR, Fc gamma receptor; NK, natural killer; SLAMF7, signaling lymphocytic activation molecule F7

1. Hsi ED et al, *Clin Cancer Res* 2008 and Tai YT et al, *Blood* 2008. **2.** Balasa B et al, *Cancer Immunol Ther* 2015. **3.** Collins SM et al, *Cancer Immunol Ther* 2013 and Pazina T et al, *Oncoimmunology* 2017. **4.** Pazina T et al, EHA 2018 [PS1277]. **5.** Kurdi AT et al, *Mol Cancer Ther* 2018. **6.** Chen J et al, *Nature* 2017

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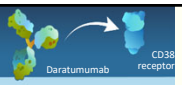
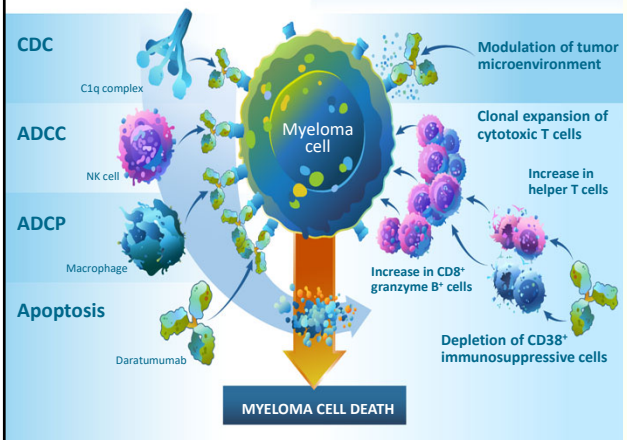
CD38 targeting



DIRECT ON-TUMOR actions may contribute to **RAPID** response[1-6]

IMMUNOMODULATORY actions may contribute to **DEEP & DURABLE** response[7-9]



- Daratumumab FIRST ONE
  - Human IgGκ monoclonal antibody targeting CD38 with a direct on-tumor and immunomodulatory mechanism of action
- Approved[10]
  - As **monotherapy** in many countries for heavily pretreated RRMM
  - In **combination** with standard of care regimens in RRMM after ≥1 prior therapy in many countries
- Efficacy
  - Daratumumab induces rapid, deep, and durable responses in combination with a PI (bortezomib)[11] or an IMiD (lenalidomide)[12] in RRMM

RRMM, relapsed or refractory multiple myeloma; CDC, complement-dependent cytotoxicity; ADCC, antibody-dependent cellular cytotoxicity; NK, natural killer; ADCP, antibody-dependent cellular phagocytosis; PI, proteasome inhibitor; IMiD, immunomodulatory drug.

1. DARZALEX US PI; 2017. 2. Liszewski MK, et al. *Adv Immunol*. 1996;61:201-283. 3. Debets JM, et al. *J Immunol*. 1988;141(4):1197-1201. 4. Overdijk MB, et al. *mAbs*. 2015;7(2):311-321. 5. Lokhorst HM, et al. *N Engl J Med*. 2015;373(13):1207-1219. 6. Plesner T, et al. *Blood*. 2012;120:73. 7. Krejcik J, et al. *Blood*. 2016;128(3):384-394. 8. Adams H, et al. Poster presented at: ASH; December 3-6, 2016; San Diego, CA. 9. Chiu C, et al. Poster presented at: ASH; December 3-6, 2016; San Diego, CA. 10. Blair H. *Drugs*. 2017;77(18):2013-2024. 11. Palumbo A, et al. *N Engl J Med*. 2016;375(8):754-766. 12. Dimopoulos MA, et al. *N Engl J Med*. 2016;375(14):1319-1331.

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RRMM: Daratumumab: 1-3 prior lines

POLLUX and CASTOR Study Designs[1,2]

Open-label, multicenter, randomized (1:1), active-controlled, phase 3 studies in RRMM patients with ≥1 prior line of therapy

POLLUX

RANDOMIZE

DRd (n = 286)
D 16 mg/kg IV
Every week: Cycles 1-2
Every 2 weeks: Cycles 3-6
Every 4 weeks until PD
R 25 mg PO (similar to Rd alone)
d 40 mg (similar to Rd alone)

Rd (n = 283)
R 25 mg PO
Days 1-21 of each cycle until PD
d 40 mg weekly until PD

Patient characteristics
- Median (range) prior lines: 1 (1-11)
- Prior V: 84%
- Prior R: 18%

CASTOR

RANDOMIZE

DVd (n = 251)
D 16 mg/kg IV
Every week: Cycles 1-3
Every 3 weeks: Cycles 4-8
V 1.3 mg/m^2 SC (similar to Vd alone)
d 20 mg (similar to Vd alone)

D only
Every 4 weeks: Cycles 9+

Vd (n = 247)
V 1.3 mg/m^2 SC on Days 1, 4, 8, 11 for 8 cycles
d 20 mg on Days 1, 2, 4, 5, 8, 9, 11, 12 for 8 cycles

Obs only

Patient characteristics
- Median (range) prior lines: 2 (1-10)
- Prior V: 66%
- Prior R: 42%

RRMM, relapsed or refractory multiple myeloma; DRd, daratumumab, lenalidomide, and dexamethasone; D, daratumumab; IV, intravenous; PD, progressive disease; R, lenalidomide; PO, orally; Rd, lenalidomide and dexamethasone; d, dexamethasone; DVd, daratumumab, bortezomib, and dexamethasone; V, bortezomib; SC, subcutaneous; Vd, bortezomib and dexamethasone; Obs, observation.

1. Dimopoulos MA, et al. *N Engl J Med*. 2016;375(14):1319-1331. 2. Palumbo A, et al. *N Engl J Med*. 2016;375(8):754-766.

PRESENTED AT: ASCO ANNUAL MEETING '17 | #ASCO17 Presented by: Katja Weisel

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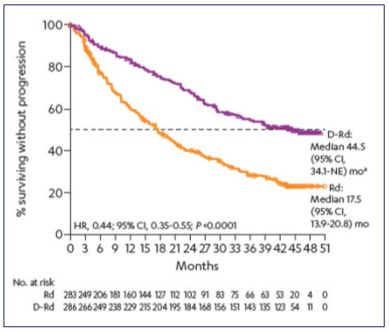
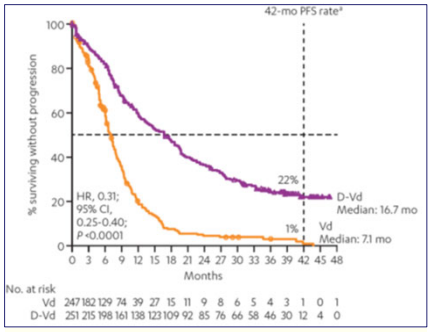
POLLUX and CASTOR: PFS





	n	Median PFS, mo
DRd group	286	44.5
Rd group	283	17.5

Median PFS, mo	DVd Group (n = 251)	Vd Group (n = 247)
All patients	16.7	7.1
1 prior therapy	27.0	7.9

Efficacy and safety in elderly patients was similar to that of the overall population in both trials[3]

1. Dimopoulos MA et al. *N Engl J Med*. 2016;375:1319-1331. 2. Lentzsch S et al. ASCO 2017. Abstract 8036. 3. Mateos MV et al. ASCO 2017. Abstract 8033., 4. Mateos MV et al. ASH 2018. Abstract 1996

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New Kids on the Block

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Global phase 3 pivotal study of isatuximab with Pd in RRMM - Study design

icaria mm

RRMM

≥2 prior lines with Len and PI

No prior therapy with pomalidomide

R

1:1
N=300

Isa-Pd

Isa: 10mg/kg on day 1, 8, 15, 22 in cycle 1 subsequently on day 1, 15
P: 4mg on days 1-21 of 28-day cycle
d: 40mg (20mg for ≥75yr) on day 1, 8, 15, 22

Pd

P: 4mg on days 1-21 of 28-day cycle
d: 40mg (20mg for ≥75yr) on day 1, 8, 15, 22

Treatment until PD or unacceptable AEs

Primary Endpoint:
PFS (IRC)

Key secondary endpoints:
ORR, OS

Sample size calculation:
~300 patients required to detect an HR of 0.6 with 90% power and 1-sided type 1 error of 2.5%

ICARIA-MM is the 1st randomized phase 3 trial adding a CD38 antibody to the Pd backbone

ICARIA-MM study: EFC14335; NCT02990338
AE, adverse event; d, dexamethasone; HR, hazard ratio; IRC, independent review committee; Isa, isatuximab; ORR, overall response rate; OS, overall survival; P, pomalidomide; PD, progressive disease; PFS , progression-free survival; R, randomization

Richardson PG, et al. Future Oncol 2018;14:1035-47

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Preliminary Results From a Phase 1b Study of TAK-079, an Investigational Anti-CD38 Monoclonal Antibody (mAb) in Patients With Relapsed/ Refractory Multiple Myeloma (RRMM)

Amrita Y. Krishnan, MD[1], Krina K Patel, MD, MSc[2], Parameswaran Hari, MBBS, MD[3], Sundar Jagannath, MD[4], Ruben Niesvizky, MD[5], Rebecca W Silbermann, MD[6], Deborah Berg, RN, MSN[7], Jianchang Lin, PhD[7], Eric R Fedyk, PhD[7], Antonio Palumbo, MD[7], and Keith E Stockerl-Goldstein, MD[8]

[1]City of Hope, Duarte, CA; [2]Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX; [3]Medical College of Wisconsin, Milwaukee, WI; [4]Tisch Cancer Institute / Multiple Myeloma Program, Mount Sinai School of Medicine, New York, NY; [5]Division of Hematology & Medical Oncology, Weill Cornell Medical College, New York, NY; [6]Knight Cancer Institute, Oregon Health & Science University, Portland, OR; [7]Takeda Pharmaceutical Company, Cambridge, MA; [8]Washington University School of Medicine, St. Louis, MO

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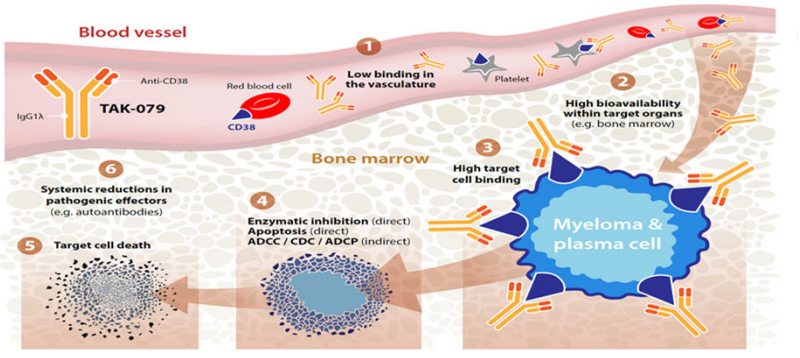
Therapeutic Hypothesis: Target Cell Selectivity Enhances Depletion

TAK-079 binds minimally to RBCs and platelets, focusing activity on high density CD38+ targets, leading to enhanced target cell depletion[1]. This profile could translate into differentiated efficacy and safety.



1. Fedyk et al. ASH 2019 abstract/poster 3136
RBCs, red blood cells

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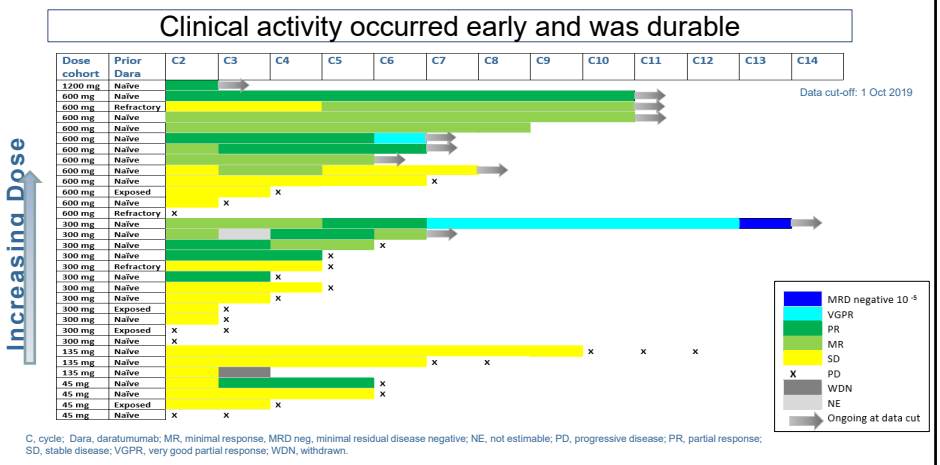
Time on Study by Dose and Best Response



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BCMA Targeting

- Antibody drug conjugates
- CAR T
- Bispecific T-cell Engagers

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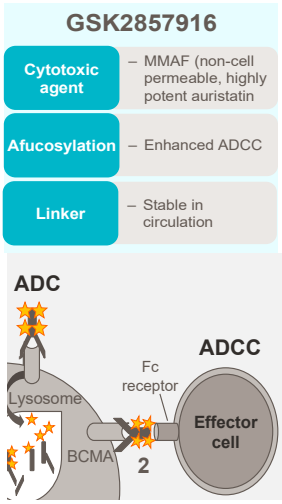
GSK-ADC Belantamab: DREAMM1 Phase 2 Part 2

- Study BMA117159: DRiving Excellence in Approaches to Multiple Myeloma (DREAMM)-1
- **Primary objectives: safety and tolerability, MTD, recommended Phase 2/Part 2 dose**
- Secondary objectives: ORR, PK, ADA (anti-drug antibodies)

Population:
- Relapsed, refractory MM
- Undergone stem cell transplant (if eligible)
- Prior treatment with ≥3 classes of alkylators, proteasome inhibitors and immunomodulators (if eligible)
- Progression on, or within 60 days of completion of the last therapy and measurable disease with at least one of the following:
  - Serum M-protein ≥0.5 g/dL
  - Urine M-protein ≥200 mg/24 h
  - Serum FLC assay: involved FLC level ≥5 mg/dL and an abnormal serum FLC ratio (<0.26 or >1.65)
  - Biopsy proven plasmacytoma (measured within 28 days of screening)

Premedication:
- **Prophylactic steroid eye drops before each dose**
- Premedication for infusion reactions not permitted with first dose and not mandated at subsequent doses

ADA, anti-drug antibodies; FLC, free light chain; FTIH, first-time-in-human; MM, multiple myeloma; MTD, maximum tolerated dose; ORR, overall response rate; PK, pharmacokinetics



Trudel et al. Ash 2017

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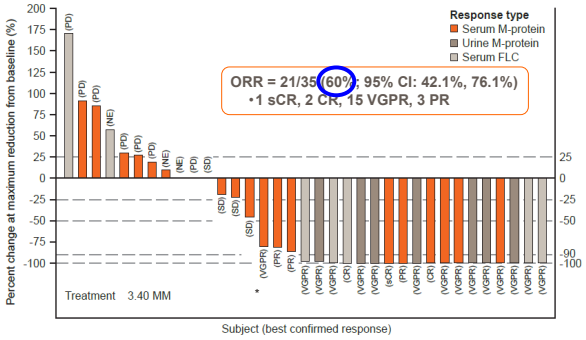
GSK-ADC: DREAMM1 Phase 2 Part 2:

- Results at 3.4 mg/kg IV Q3 Wk



89% Double refractory;
34% double + Dara refractory
29% Cyto High-risk

Updated Results

- ORR 60%
- 2 sCR
- 3 CR
- 14 VGPR
- 2 PR

- PFS: 12 months
- DOR: 14.3 months

- D/PI/IMiD refractory
  - PFS 6.2 m

Trudel et al. Ash 2017

Blood Cancer J 2019 Mar 20;9(4):37

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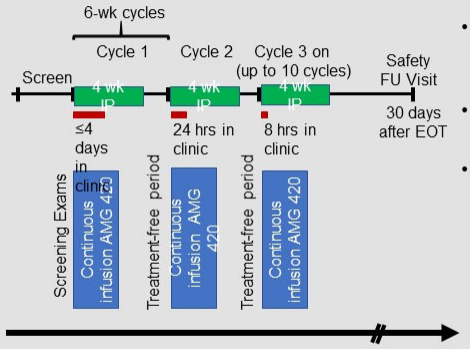
AMG-420 – Phase I Study Bispecific

Study Schematic / Objectives



- First-in-human (FIH) phase 1 dose escalation study* of AMG 420 for up to 10 cycles, depending on response.
- Single-patient cohorts [0.2-1.6 µg/day (d)] were followed by cohorts of 3-6 patients (3.2-800 µg/d).
- Objectives of this phase 1 study of AMG 420 in patients with relapsed and/or refractory (R/R) MM included:
  - Assessing safety and tolerability per CTCAE 4.03
  - Determining the maximum tolerated dose (MTD)
  - Assessing anti-tumor activity

* NCT02514239. EOT, end of treatment; FU, follow-up; IP, investigational product.

Median 4 PLT : ~25% Dara
~31% Double Refractory

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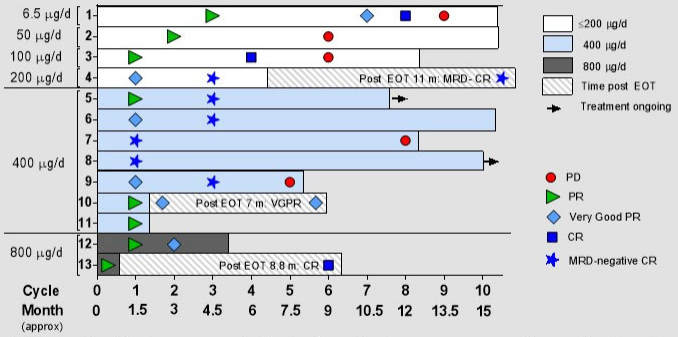
AMG-420 – Phase I Study

Responding Patients



Unless PD was the last response indicated, patients were responding at last evaluation.

As of Apr 8, 2019. CR, complete response; EOT, end of treatment; PD, progressive disease; PR, partial response.

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CC-93269-MM-001 PHASE 1 TRIAL (NCT03486067): STUDY DESIGN

Key Eligibility Criteria

- RRMM after ≥ 3 prior regimens
- Progressive disease within 60 days of last regimen
- No prior BCMA-directed therapy

Dose Schedule

Cycle (all 28-day cycles)

Screening | C1 | C2 | C3 | C4 | C5 | C6 | C7 | C8

Dose received

- *C1–3: Days 1, 8, 15, and 22*
- *C4–6: Days 1 and 15*
- *C7 onward: Day 1*
- *Treatment for up to 2 years*

All doses administered via IV over 2 hours

Part A: Dose Escalation

- Stage 1: Fixed doses
- Stage 2: Step-up in dose on C1D8

Part B: Cohort Expansion

Endpoints

Primary: Safety including DLTs, AEs, NTD, and MTD
Secondary: Preliminary efficacy including MRD, PK, ADA, and PD endpoints

ADA, anti-drug antibody; AE, adverse event; C, Cycle; D, Day; DLT, dose-limiting toxicity; IV, intravenous; MRD, minimal residual disease; MTD, maximum tolerated dose; NTD, non-tolerated dose; PD, pharmacodynamics; RRMM relapsed/refractory multiple myeloma.

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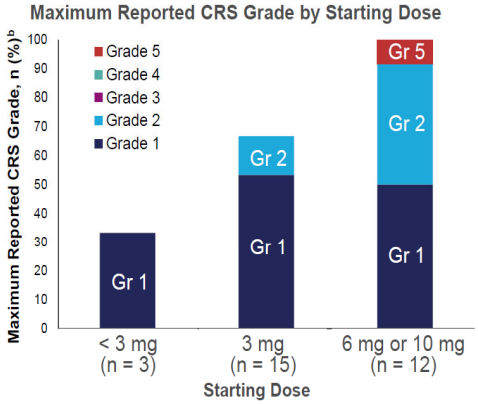
CYTOKINE RELEASE SYNDROME

Parameter	All Patients (N = 30)
Patients with a CRS event, n (%)	**23 (76.7)**
After first dose	23 (76.7)
After second dose	7 (23.3)
After third dose	2 (7.4)[a]
Maximum CRS grade, n (%)	
1	15 (50.0)
2	7 (23.3)
≥ 3	1 (3.3)
Time to onset, median (range), d	1 (1–9)
Duration, median (range), d	2 (1–6)
Tocilizumab use, n (%)	13 (43.3)
Corticosteroid use, n (%)	22 (73.3)



- Dexamethasone prophylaxis was administered to patients receiving ≥ 6 mg (Cohorts 5–9)
- In Cohort 7 (6→10 mg), 1 patient experienced grade 3 (6 mg) followed by grade 5 CRS (10 mg); contributing factors included myeloma progression with extensive extramedullary disease, and concomitant infection

Data as of October 28, 2019.
[a] 27 patients received a third dose; [b] Graded using the Lee criteria[1]
CRS, cytokine release syndrome; Gr, grade.

1. Lee DW, et al. Blood. 2014;124:188-195.

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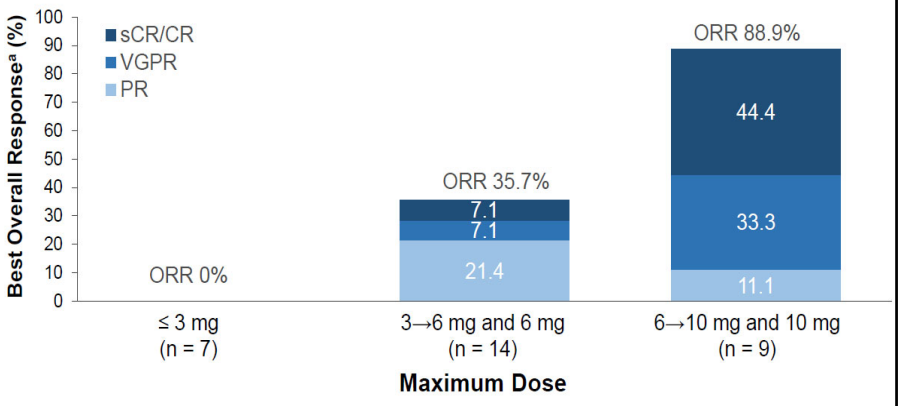
CC-93269 PRELIMINARY EFFICACY



- In all patients (N = 30), the ORR was 43.3% with a sCR/CR of 16.7%
- Among patients receiving 10 mg (n = 9), the ORR was 88.9% with a sCR/CR of 44.4%

Data as of October 28, 2019.
[a] Response as assessed by the investigator.
CR, complete response; ORR, overall response rate (PR or better); PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

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Bispecific T-cell engagers/antibodies under study for MM

City of Hope	
NCT03145181	Dose Escalation Study of JNJ-64007957, a Humanized BCMA CD3 DuoBody Antibody, in Participants with Relapsed or Refractory Multiple Myeloma
NCT03399799	Dose Escalation Study of JNJ-64407564 in Participants with Relapsed or Refractory Multiple Myeloma
NCT03275103	Dose Escalation Study of BFCR4350A in Participants with Relapsed or Refractory Multiple Myeloma
non-City of Hope	
NCT02514239	Phase I Dose Escalation of i.v. BI 836909 Monotherapy in Last Line Multiple Myeloma Patients
NCT03836053	Assessment of AMG 420 in Subjects with Relapsed and/or Refractory Multiple Myeloma
NCT03173430	Pilot Study of Blinatumomab in Combination with Salvage Autologous Stem Cell Transplantation for Patients with Refractory Multiple Myeloma

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Bispecific T-cell engagers/antibodies under study for MM

non-City of Hope	
NCT03269136	Phase 1 Study of PF-06863135, a BCMA-CD3 Bispecific Ab, in Relapsed/Refractory Multiple Myeloma
NCT03933735	A Study of TNB-383B in Subjects with Relapsed or Refractory Multiple Myeloma
NCT03275103	Study of ISB 1342, a CD38/CD3 Bispecific Antibody, in Subjects with Previously Treated Multiple Myeloma
NCT04108195	A Study of Subcutaneous Daratumumab Regimens in Combination with Bispecific T Cell Redirection Antibodies for the Treatment of Participants with Multiple Myeloma
NCT03761108	First in Human (FIH) Study of REGN5458 in Patients with Relapsed or Refractory Multiple Myeloma
NCT04083534	First in Human (FIH) Study of REGN5459 in Patients with Relapsed or Refractory Multiple Myeloma (MM)

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CAR T Cells

- BCMA targeting
- Slam F7 targeting
- BCMA CD38

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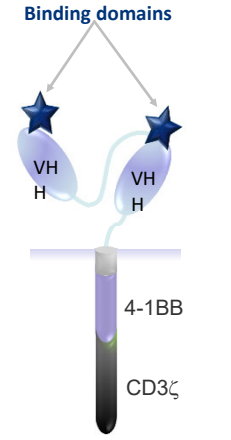
JNJ-4528: BCMA-targeted CAR T-Cell Therapy

- **JNJ-68284528 (JNJ-4528) is a structurally differentiated chimeric antigen receptor T (CAR-T) cell therapy**
  - Contains a CD3ζ signaling domain and 4-1BB costimulatory domain
  - 2 BCMA-targeting single domain antibodies designed to confer avidity
  - Identical to the CAR construct used in the LEGEND-2 study
- **LEGEND-2 (N = 74): Phase 1 investigator-initiated study conducted in China**
  - High, deep, and durable overall response and manageable safety in R/R MM[a,b]



JNJ-4528 CAR

[a]Zhao et al. *JHO* 2018;11(1):141; [b]Xu et al. *PNAS* 2019;116(19):9543; BCMA=B-cell maturation antigen; MM=multiple myeloma; R/R=relapsed/refractory; VHH=single variable domain on a heavy chain

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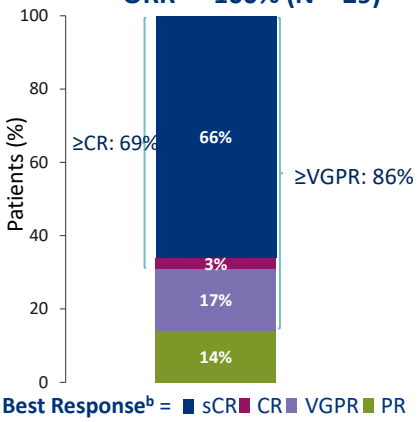
CARTITUDE-1: Overall Response Rate

Tumor Burden Reduction in All Patients

ORR[a] = 100% (N = 29)



- ORR and depth of response were independent of BCMA expression on MM cells at baseline
- Median time to first response = 1 mo (1 – 3)
- Median time to ≥CR = 1 mo (1 – 9)

[a]PR or better; Independent Review Committee-assessed, [b]No patient had stable disease or progressive disease as best response. CR=complete response; ORR=overall response rate; PR=partial response; sCR=stringent complete response; VGPR=very good partial response

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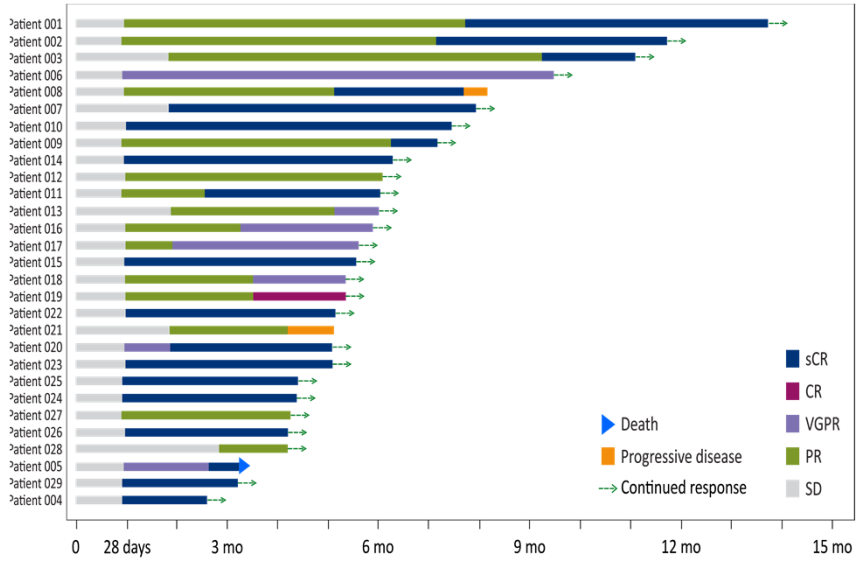
CARTITUDE-1: Duration of Response



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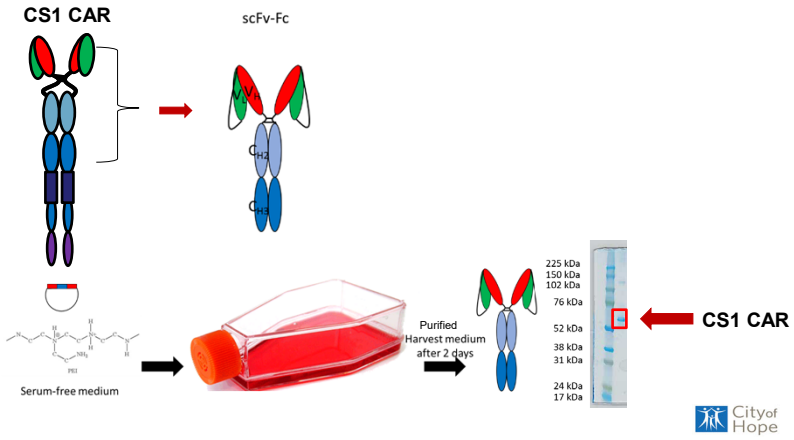
Building the CS1 CAR T Cell at City of Hope



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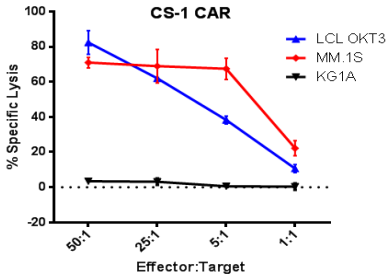
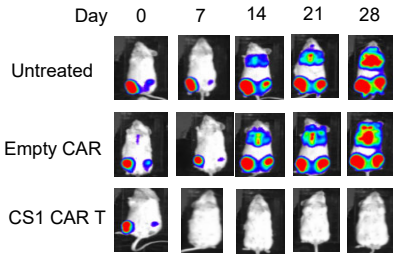
CS1 CAR T Cells Efficiently Kill Multiple Myeloma





Wang et al. Clin Cancer Res. 2018

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Conclusions
Myeloma 2020; immune directed

- Immune environment contributes to relapse
- New drugs immune targeting
- Sequencing?
- Cost?

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Q&A SESSION

Multiple Myeloma: Understanding My Treatment Options

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

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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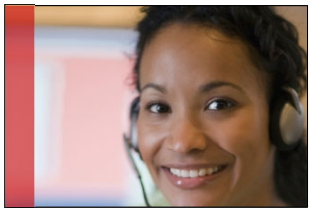
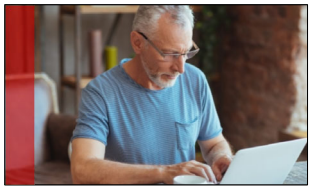
LLS EDUCATION & SUPPORT RESOURCES

- **Information Specialists**

  Master’s level oncology professionals, available to help cancer survivors navigate the best route from diagnosis through treatment, clinical trials and survivorship.
  - **EMAIL:** infocenter@LLS.org
  - **TOLL-FREE PHONE:** 1-800-955-4572
- **Caregiver Support:** www.LLS.org/caregiver
- **Free Education Booklets:** www.LLS.org/booklets
- **Free Telephone/Web Programs:** www.LLS.org/programs
- **Live, weekly Online Chats:** www.LLS.org/chat
- **LLS Community:** www.LLS.org/community





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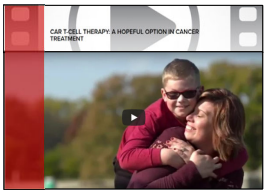
LLS EDUCATION & SUPPORT RESOURCES



- **LLS Podcast, *The Bloodline with LLS***

  Listen in as experts and patients guide listeners in understanding diagnosis, treatment, and resources available to blood cancer patients: **www.thebloodline.org**

- **Education Videos**

  Free education videos about survivorship, treatment, disease updates and other topics: **www.LLS.org/educationvideos**

- **Patti Robinson Kaufmann First Connection Program**

  Peer-to-peer program that matches newly diagnosed patients and their families: **www.LLS.org/firstconnection**

- **Free Nutrition Consults**

  Telephone and email consultations with a Registered Dietitian: **www.LLS.org/nutrition**

- **What to Ask**

  Questions to ask the treatment team: **www.LLS.org/whattoask**

- **Other Support Resources**

  LLS Community, discussion boards, blogs, support groups, financial assistance and more: **www.LLS.org/support**

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