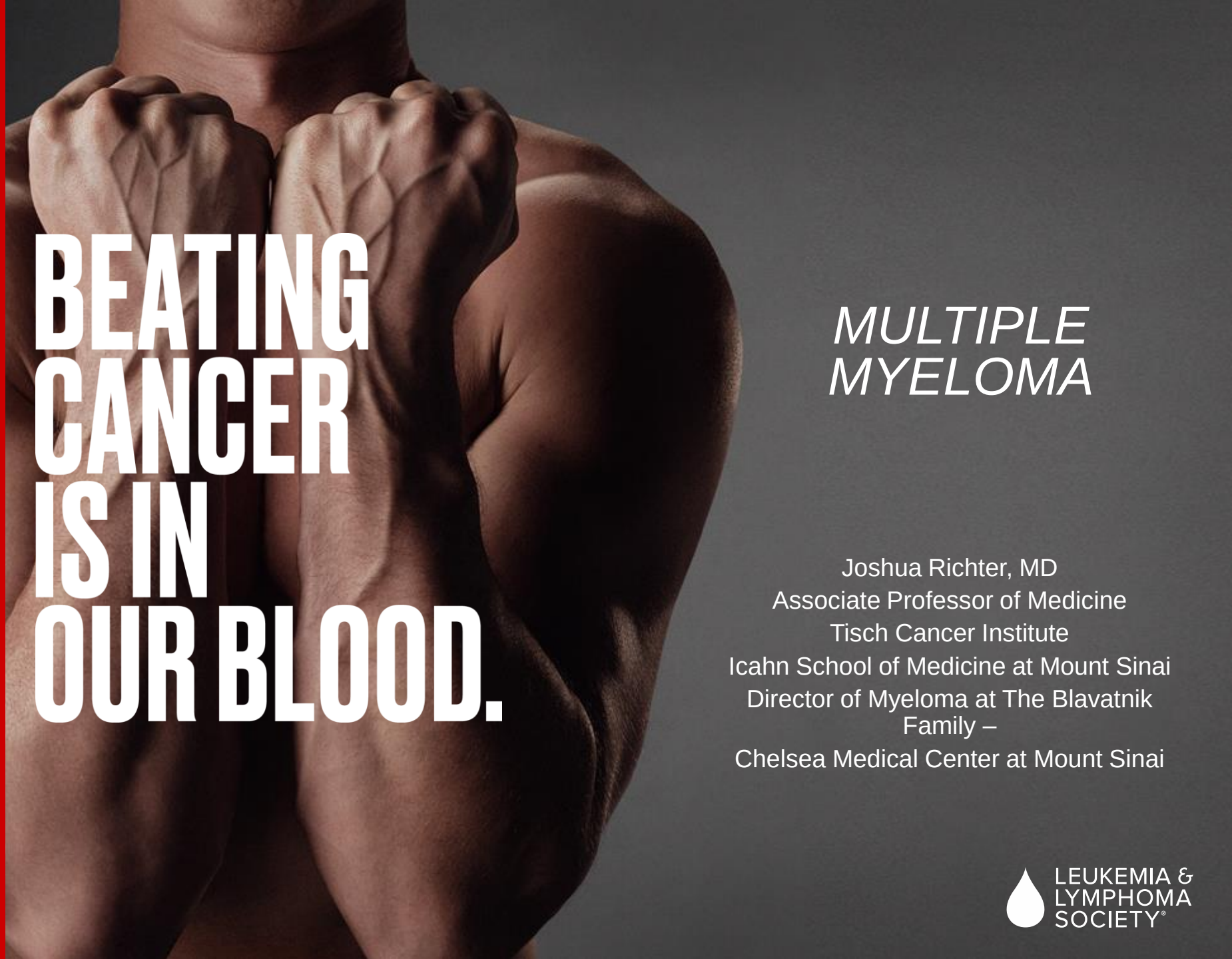



# *MULTIPLE MYELOMA*

Joshua Richter, MD
Associate Professor of Medicine
Tisch Cancer Institute
Icahn School of Medicine at Mount Sinai
Director of Myeloma at The Blavatnik Family –
Chelsea Medical Center at Mount Sinai

LEUKEMIA & LYMPHOMA SOCIETY®

# A LETTER FROM DR. WILLIAM MACINTYRE TO HENRY BENCE JONES REGARDING PATIENT THOMAS ALEXANDER MCBEAN

***Saturday, November 1, 1845:***

***Dear Dr Jones,***

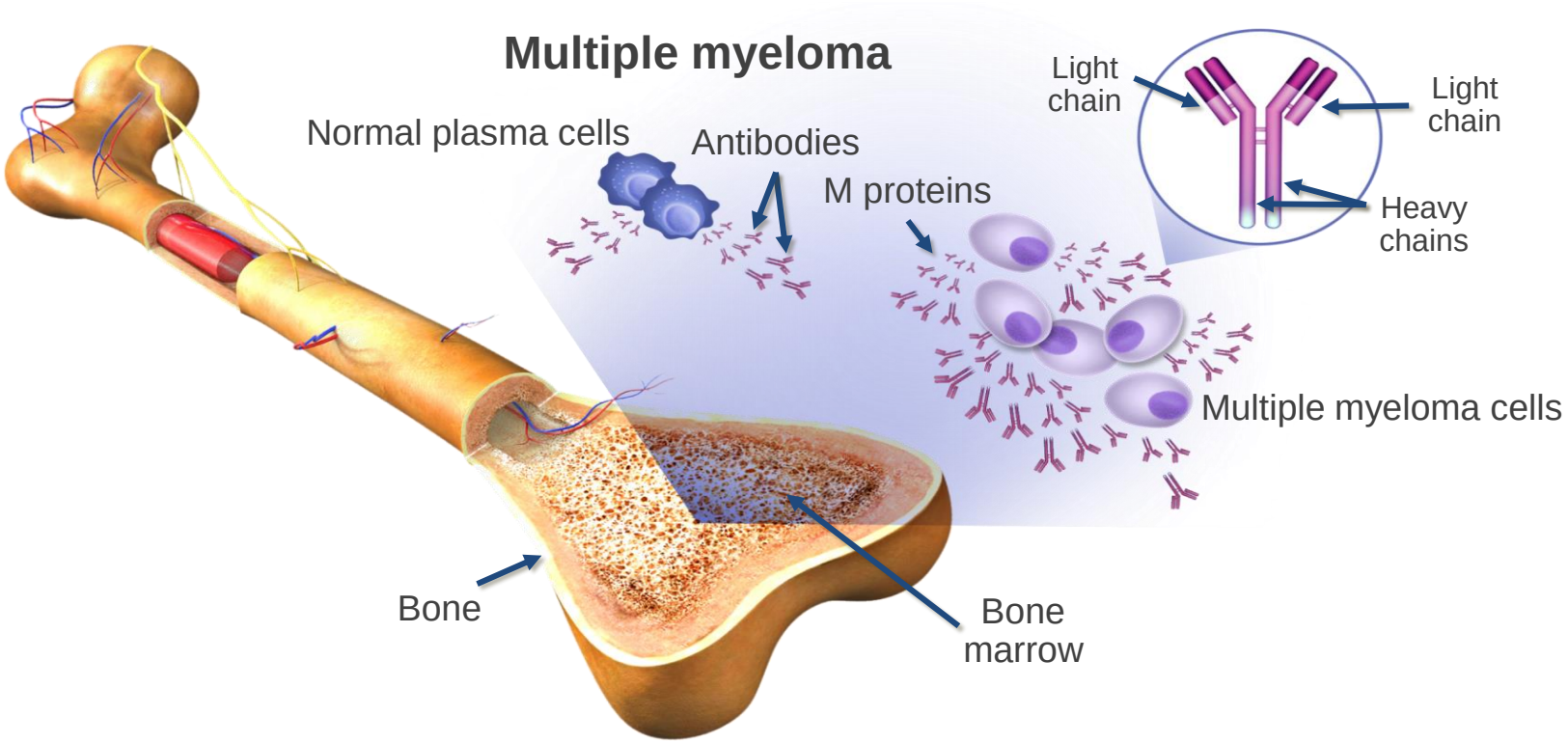
***The tube contains urine of very high specific gravity. When boiled it becomes slightly opaque. On the addition of nitric acid, it effervesces, assumes a reddish hue, and becomes quite clear; but as it cools, assumes the consistence and appearance which you see. Heat liquefies it. What is it?***



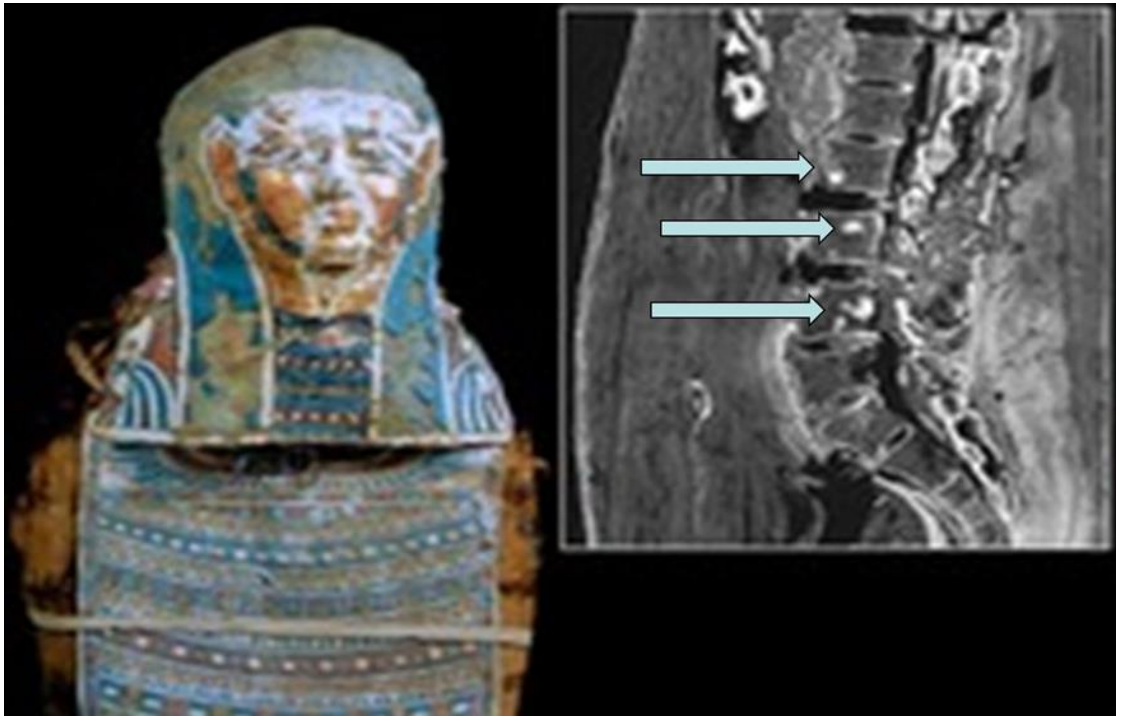
Multiple myeloma. Robert A. Kyle and S. Vincent Rajkumar Blood. 2008 111: 2962-2972

Bence Jones H. Chemical pathology. Lancet. 1847;2:88–92

# WHAT IS MULTIPLE MYELOMA?



# MYELOMA IN MUMMIES



Ancient affliction. A high-resolution CT scan of the lumbar spine region of a 2150-year-old Egyptian mummy revealed small, round lesions.

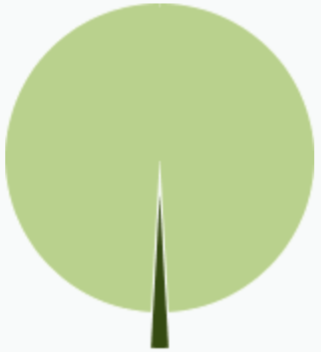
# SARAH NEWBURY:  FIRST REPORTED CASE OF MYELOMA


**Figure 2. Sarah Newbury, the first reported patient with multiple myeloma.** (A) Bone destruction in the sternum. (B) The patient with fractured femurs and right humerus. (C) Bone destruction involving the femur. Adapted from Solly[7] with permission.

Multiple myeloma. Robert A. Kyle and S. Vincent Rajkumar Blood. 2008 111: 2962-2972

| | Common Types of Cancer | Estimated New Cases 2022 | Estimated Deaths 2022 |
|---|---|---|---|
| 1. | Breast Cancer (Female) | 287,850 | 43,250 |
| 2. | Prostate Cancer | 268,490 | 34,500 |
| 3. | Lung and Bronchus Cancer | 236,740 | 130,180 |
| 4. | Colorectal Cancer | 151,030 | 52,580 |
| 5. | Melanoma of the Skin | 99,780 | 7,650 |
| 6. | Bladder Cancer | 81,180 | 17,100 |
| 7. | Non-Hodgkin Lymphoma | 80,470 | 20,250 |
| 8. | Kidney and Renal Pelvis Cancer | 79,000 | 13,920 |
| 9. | Uterine Cancer | 65,950 | 12,550 |
| 10. | Pancreatic Cancer | 62,210 | 49,830 |
| | - | - | - |
| 14. | Myeloma | 34,470 | 12,640 |

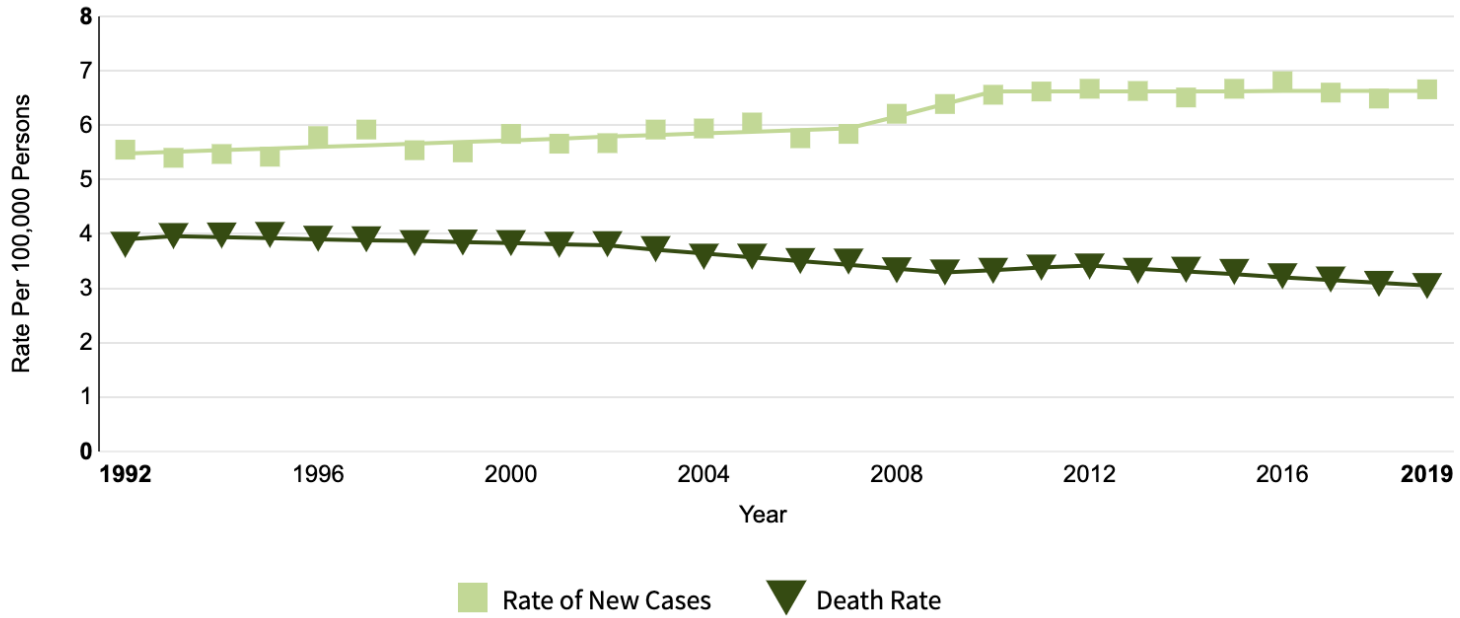
Myeloma represents 1.8% of all new cancer cases in the U.S.



| | |
|---|---|
| Estimated New Cases in 2022 | 34,470 |
| % of All New Cancer Cases | 1.8% |

| | |
|---|---|
| Estimated Deaths in 2022 | 12,640 |
| % of All Cancer Deaths | 2.1% |

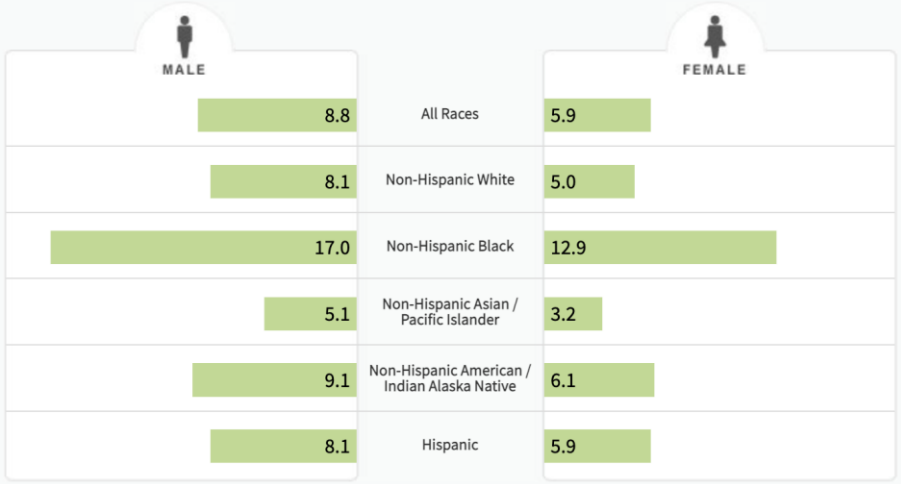
| 5-Year Relative Survival |
|---|
| **57.9%** |
| 2012–2018 |




BEATING CANCER IS IN OUR BLOOD.

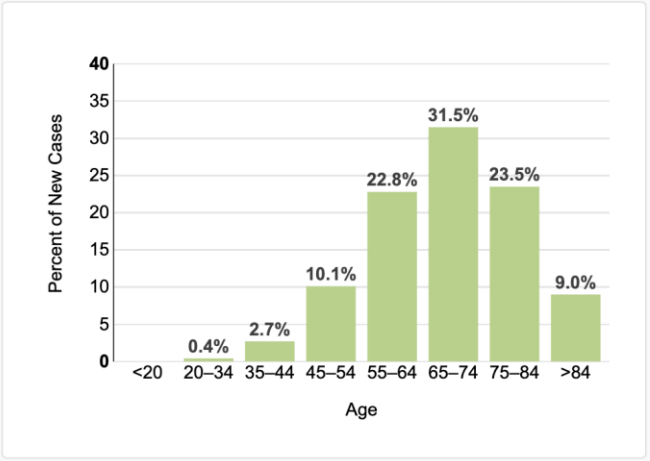
LEUKEMIA & LYMPHOMA SOCIETY®

## Rate of New Cases per 100,000 Persons by Race/Ethnicity & Sex: Myeloma




SEER 22 2015–2019, Age-Adjusted

## Percent of New Cases by Age Group: Myeloma

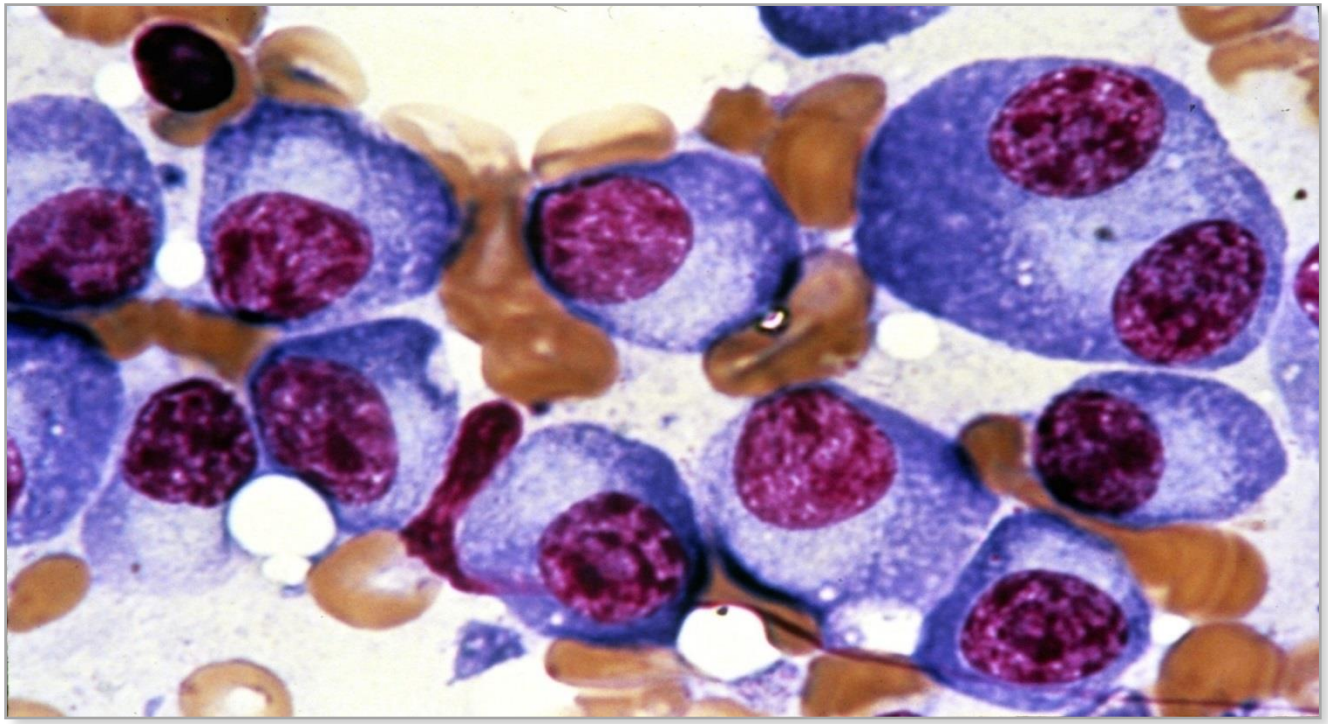



Myeloma is most frequently diagnosed among people aged 65–74.

| Median Age At Diagnosis |
| --- |
| 69 |

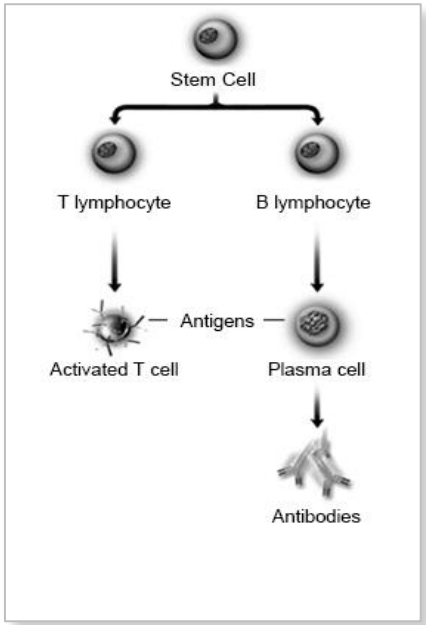
SEER 22 2015–2019, All Races, Both Sexes

# MYELOMA CELLS

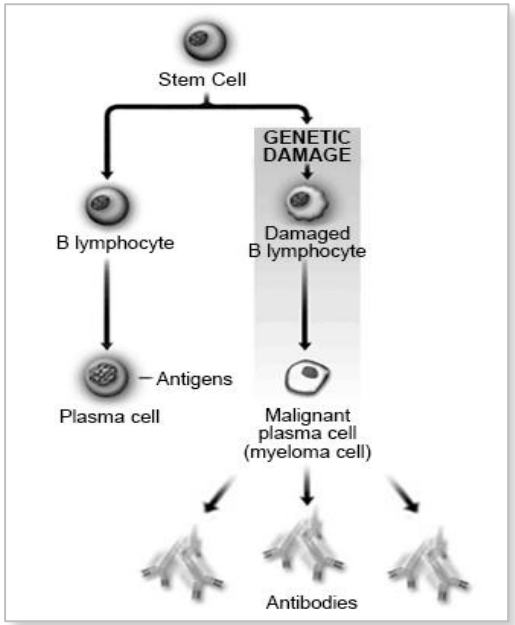


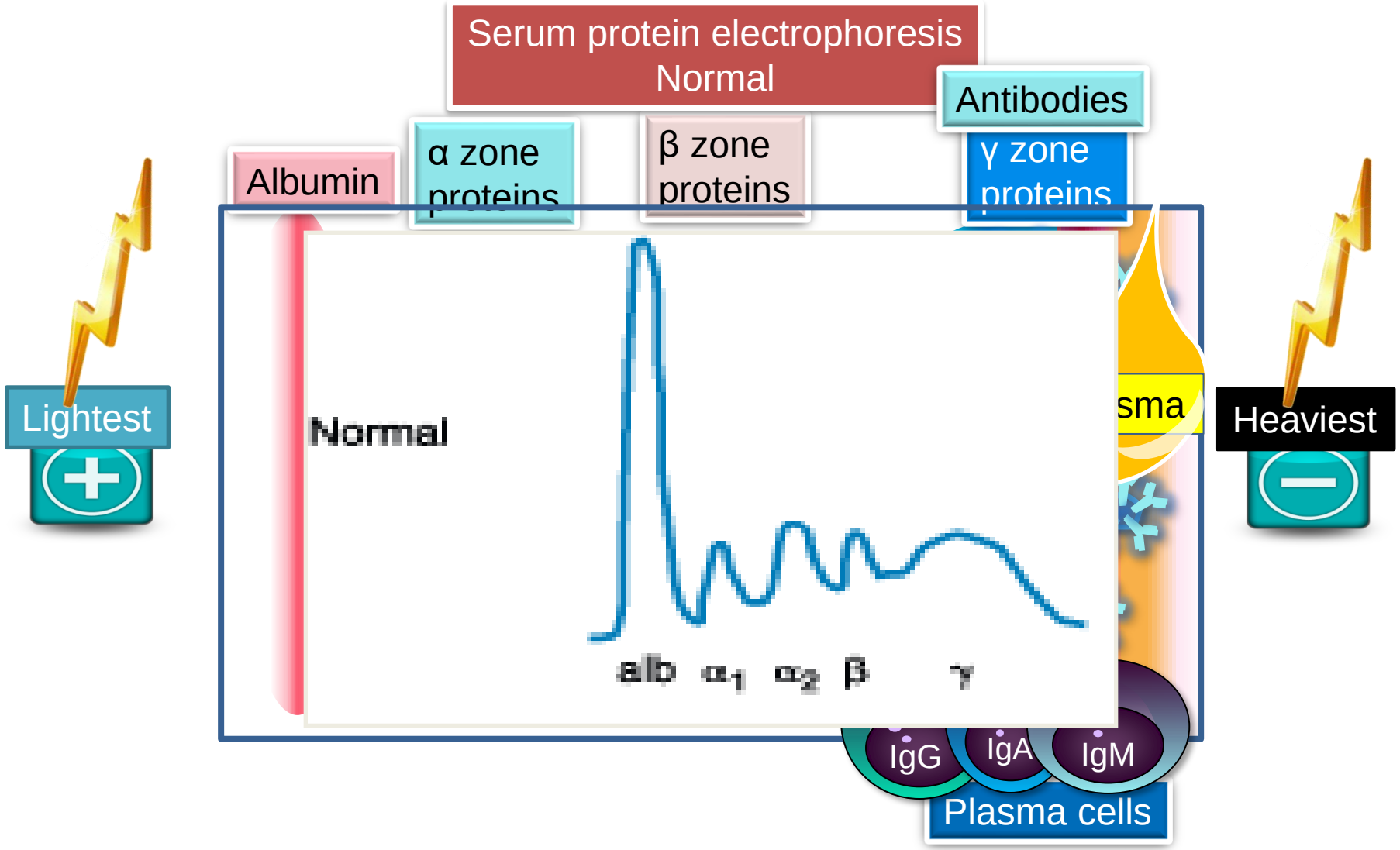
# NORMAL VS ABNORMAL PLASMA CELLS

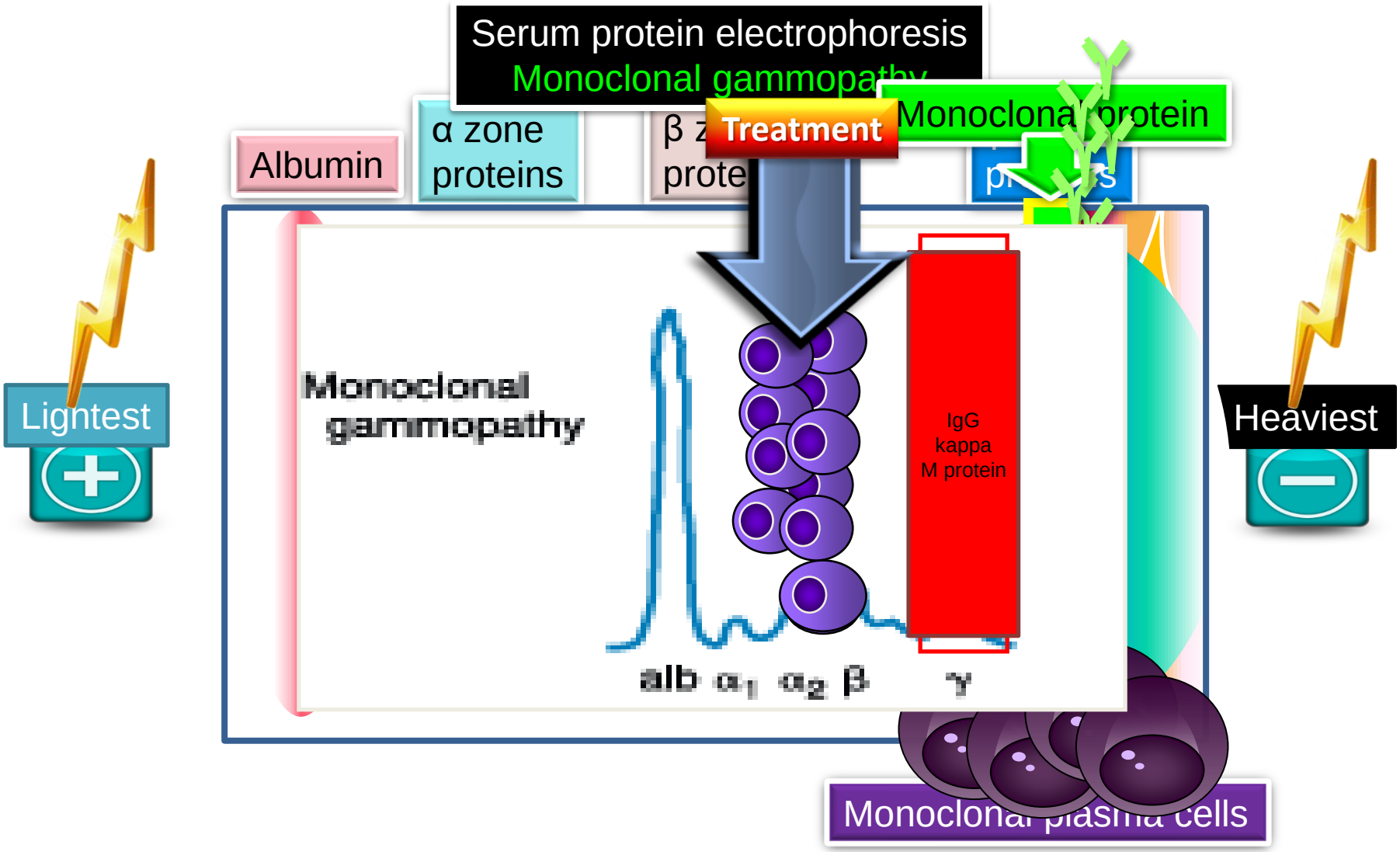
Normal



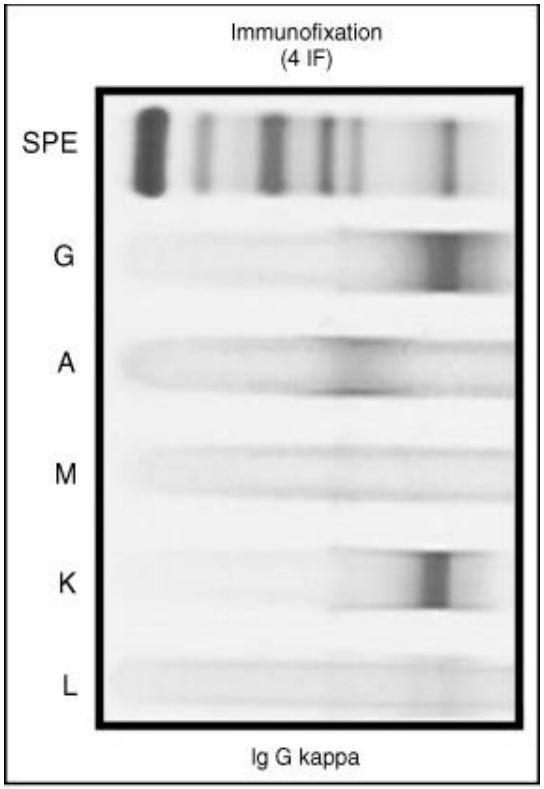

Abnormal




Serum protein electrophoresis
Normal
Albumin
α zone proteins
β zone proteins
γ zone proteins
Antibodies
Lightest
Heaviest
Normal
alb
α1
α2
β
γ
sma
IgG
IgA
IgM
Plasma cells

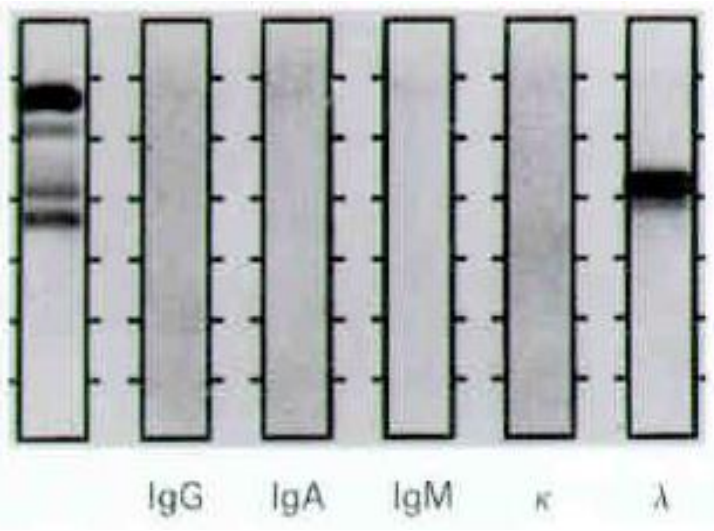

Serum protein electrophoresis
Monoclonal gammopathy
Treatment
Monoclonal protein
Albumin
α zone proteins
Lightest
Heaviest
Monoclonal gammopathy
IgG kappa M protein
alb α1 α2 β γ
Monoclonal plasma cells

# Immunofixation to Determine Type of Monoclonal Protein





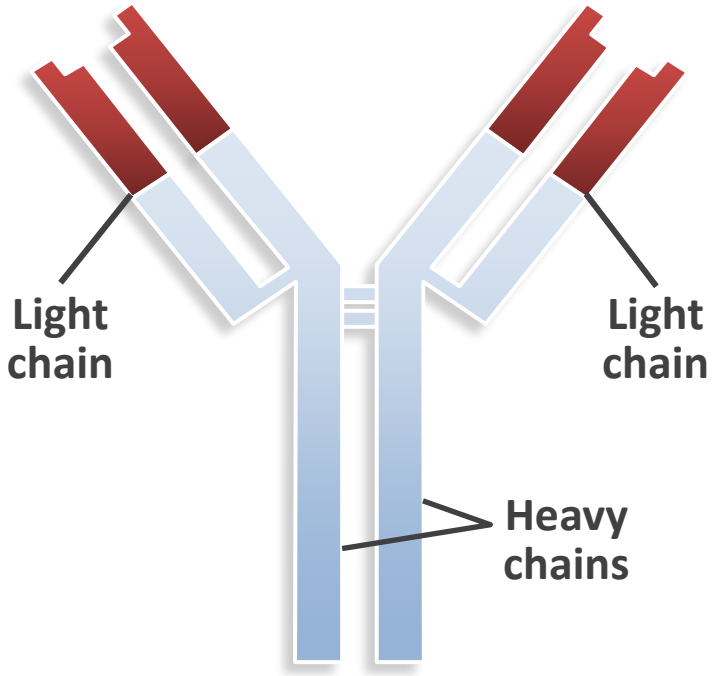

IgG kappa M protein




Lambda Light Chains

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

# IMMUNOGLOBULIN

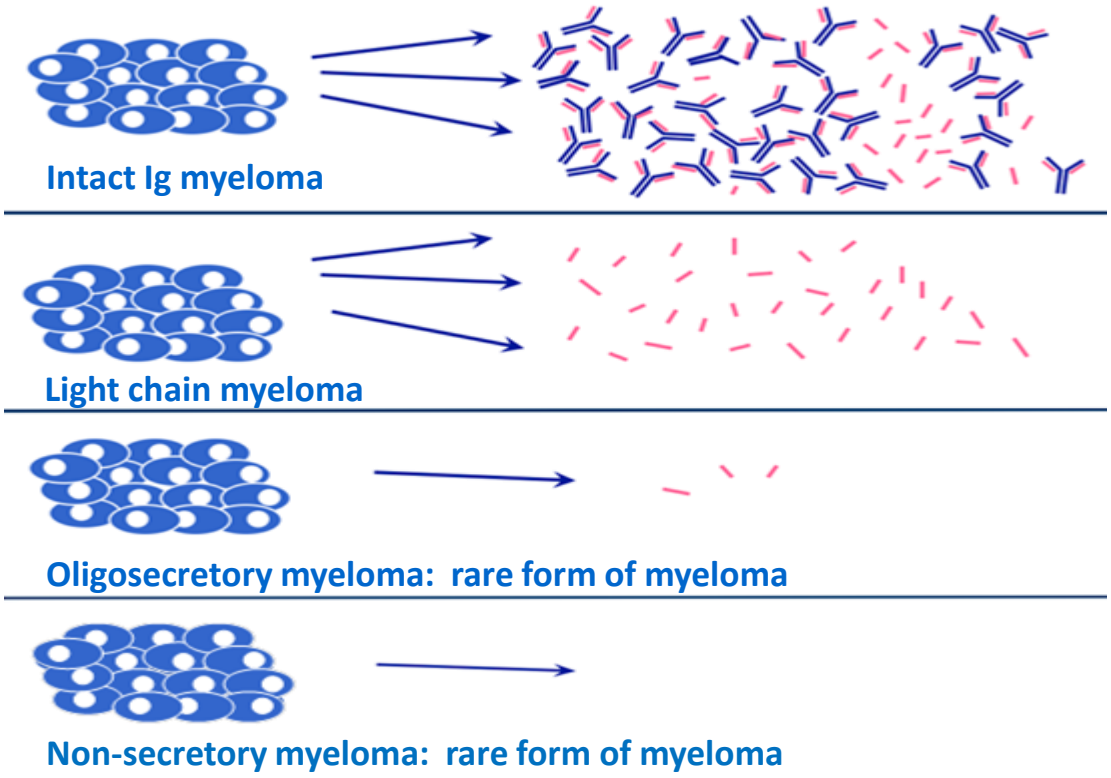



**Heavy chains: IgG, IgA, IgM, IgD, IgE**

**Light chains are known as kappa (κ) or lambda (λ)**

**Most common isotype is IgGκ followed by IgGλ then IgAκ and IgAλ; rare cases of IgD and IgE**

# MEASURING THE MYELOMA PROTEIN



# KEY ITEMS THAT DEFINE THE DIAGNOSIS

## MGUS

- M protein <3 g/dL
- Clonal plasma cells in BM <10%
- No myeloma-defining events

***1% risk of progression/year to multiple myeloma or related conditions***

## Smoldering Myeloma

- M protein ≥3 g/dL (serum) or ≥500 mg/ 24 hrs (urine)
- Clonal plasma cells in BM ≥10%–60%
- No myeloma-defining events

***10% risk of progression/year to active myeloma***

## Multiple Myeloma

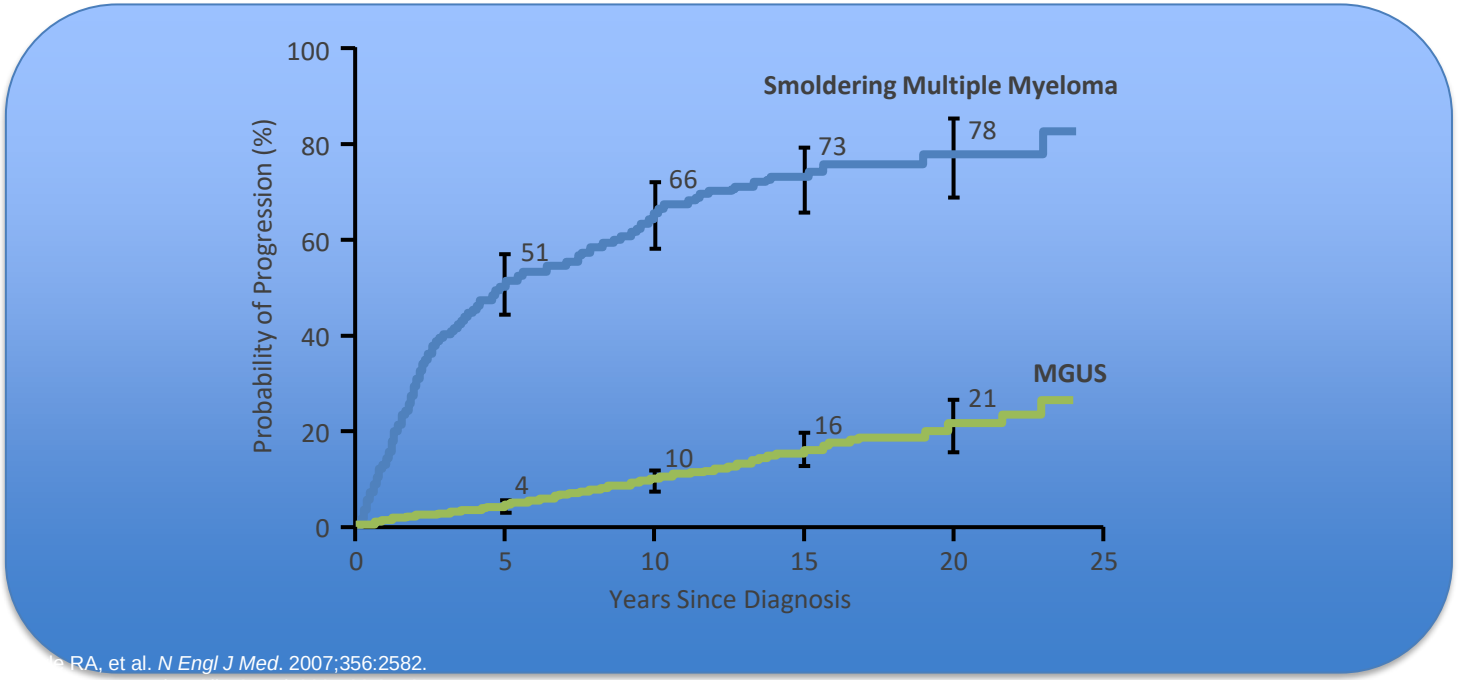
- Underlying plasma cell proliferative disorder
- AND ≥1 myeloma-defining events
- ≥1 CRAB* feature
- Clonal plasma cells in BM ≥60%
- Serum free light chain ratio ≥100
- >1 MRI focal lesion

***C: Calcium elevation (>11 mg/dL or >1 mg/dL higher than ULN)**
**R: Renal insufficiency (creatinine clearance <40 mL/min or serum creatinine >2 mg/dL)**
**A: Anemia (Hb <10 g/dL or 2 g/dL < normal)**
**B: Bone disease (≥1 lytic lesions on skeletal radiography, CT, or PET-CT)**

Rajkumar SV et al. *Lancet Oncol*. 2014;15:e538.

# Progression to Symptomatic Myeloma

**Risk factors: higher M spike, higher plasma cell burden, type of M protein, abnormal free light-chain ratio, circulating plasma cells**




RA, et al. *N Engl J Med*. 2007;356:2582.

# MYELOMA STAGING

National Comprehensive Cancer Network®

## NCCN Guidelines Version 3.2016
## Multiple Myeloma

NCCN Guidelines Index
Multiple Myeloma Table of Contents
Discussion

**STAGING SYSTEMS FOR MULTIPLE MYELOMA[1]**

| Stage | International Staging System (ISS) | Revised-ISS (R-ISS) |
|---|---|---|
| I | Serum beta-2 microglobulin <3.5 mg/L, Serum albumin ≥3.5 g/dL | ISS stage I and standard-risk chromosomal abnormalities by iFISH[2] and Serum LDH < the upper limit of normal |
| II | Not ISS stage I or III | Not R-ISS stage I or III |
| III | Serum beta-2 microglobulin ≥5.5 mg/L | ISS stage III and either high-risk chromosomal abnormalities by iFISH[2] or Serum LDH > the upper limit of normal |

Return to Clinical Presentation (MYEL-1)

[1]Palumbo A, Avet-Loiseau H, Oliva S, et al. Revised international staging system for multiple myeloma: A report from International Myeloma Working Group. J Clin Oncol 2015;33:2863-2869.
[2]Standard-risk: No high-risk chromosomal abnormality. High-risk: Presence of del(17p) and/or translocation t(4;14) and/or translocation t(14;16)

**Note: All recommendations are category 2A unless otherwise indicated.**
**Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.**



MYEL-A

**TABLE 4: THE DURIE AND SALMON STAGING SYSTEM**

| *STAGE* | *CRITERIA* | *MEASURED MYELOMA CELL MASS (myeloma cells in billions/m²)** |
|---|---|---|
| **STAGE I** (low cell mass) | *All of the following:*<br>• Hemoglobin value >10g/dL<br>• Serum calcium value normal or <10.5mg/dL<br>• Bone x-ray, normal bone structure (scale 0), or solitary bone plasmacytoma only<br>• Low M-component production rates IgG value <5g/dL; IgA value <3g/dL<br>• Urine light chain M-component on electrophoresis <4g/24h | 600 billion* |
| **STAGE II** (intermediate cell mass) | *Fitting neither Stage I nor Stage III* | 600 to 1,200 billion*<br>**myeloma cells in whole body* |
| **STAGE III** (high cell mass) | *One or more of the following:*<br>• Hemoglobin value <8.5g/dL<br>• Serum calcium value >12mg/dL<br>• Advanced lytic bone lesions (scale 3)<br>• High M-component production rates IgG value >7g/dL IgA value >5g/dL<br>• Bence Jones protein >12g/24h | >1,200 billion* |
| **SUBCLASS-IFICATION** (either A or B) | • A: relatively normal renal function (serum creatinine value) <2.0 mg/dL<br>• B: abnormal renal function (serum creatinine value) >2.0 mg/dL<br>*Examples: Stage IA (low cell mass with normal renal function) Stage IIIB (high cell mass with abnormal renal function)* | |

MAYO CLINIC

# mSMART 3.0: Classification of Active MM

## High-Risk

- High Risk genetic Abnormalities [a,b]
  - t(4;14)
  - t(14;16)
  - t(14;20)
  - Del 17p
  - p53 mutation
  - Gain 1q
- RISS Stage 3
- High Plasma Cell S-phase[c]
- GEP: High risk signature

- Double Hit Myeloma: Any 2 high risk genetic abnormalities
- Triple Hit Myeloma: 3 or more high risk genetic abnormalities

## Standard-Risk[a]

All others including:

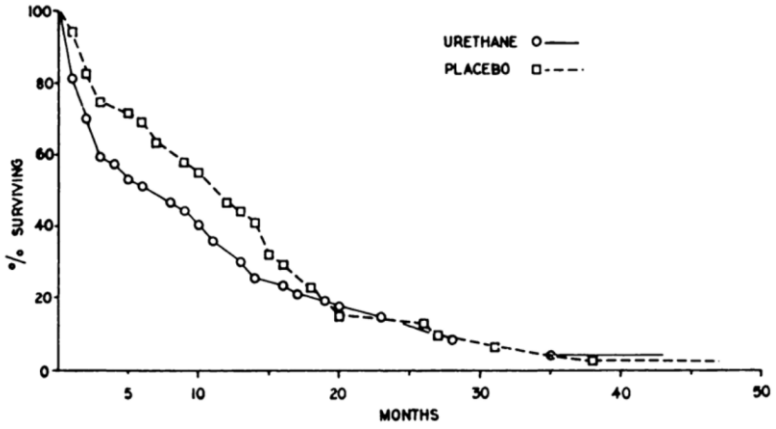
- Trisomies
- t(11;14)[d]
- t(6;14)

[a] Trisomies may ameliorate
[b] By FISH or equivalent method
[c] Cut-offs vary
[d] t(11;14) may be associated with plasma cell leukemia

Dispenzieri et al. Mayo Clin Proc 2007;82:323-341; Kumar et al. Mayo Clin Proc 2009 84:1095-1110; Mikhael et al. Mayo Clin Proc 2013;88:360-376. //last reviewed March 2022

# A Controlled Trial of Urethane Treatment in Multiple Myeloma

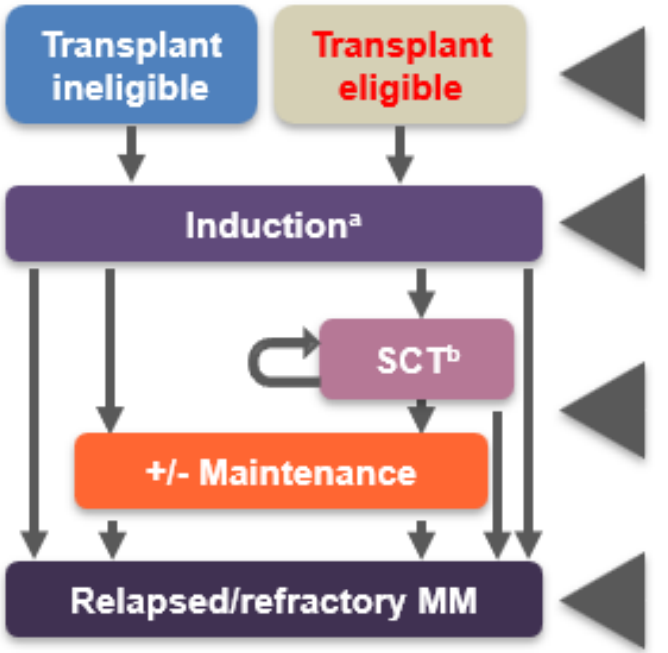
*By* James F. Holland, Henry Hosley, Carol Scharlau, Paul P. Carbone, Emil Frei, III, Clyde O. Brindley, Thomas C. Hall, Bruce I. Shnider, G. Lennard Gold, Louis Lasagna, Albert H. Owens, Jr. and Sherwood P. Miller





Blood 1966; 27: 328-342

# ALGORITHM FOR TREATMENT OF MM PER NCCN GUIDELINES AND PALUMBO ET AL.




Eligibility determined by age, performance status, and comorbidities; exact criteria may vary by institution[1]

Assess for response

Patients with response or stable disease after induction ± SCT may receive maintenance therapy until progression or intolerance[2]

Consider **disease**- and **patient**-related factors[3]

- Quality and duration of previous responses
- Aggressiveness of disease

- Age
- Preexisting toxicities
- Performance status
- Bone marrow reserve
- Renal function

[a] Consolidation therapy after induction is widely accepted, although no specific guidelines are available.[1]
[b] Planned tandem or second SCT in response to progression. SCT, stem cell transplant.[2]

1. Palumbo A and Anderson K. *N Engl J Med*. 2011;364:1046-1060.
2. NCCN guidelines.

# CHOOSING THERAPIES FOR MYELOMA

| IMiDs | Proteasome Inhibitors | Anthracyclines | Alkylators | Steroids | Antibodies | SINE | ADC | CAR-T | *Bispecific Ab* |
|---|---|---|---|---|---|---|---|---|---|
| **Thalidomide** | **Bortezomib** | **Doxil** | **Melphalan** | **Dexamethasone** | **Elotuzumab** | **Selinexor** | **Belantamab** | **Ide-cel** | ***Teclistamab*** |
| **Lenalidomide** | **Carfilzomib** | **Doxorubicin** | **Cytoxan** | **Prednisone** | **Daratumumab** | | | **Cilta-cel** | |
| **Pomalidomide** | **Ixazomib** | | **Bendamustine** | **Solumedrol** | **Isatuximab** | | | | |

# FACTORS IN SELECTING MM THERAPY

## PATIENT

- Age/frailty
- Performance status
- Lifestyle/pt preferences
- Drug metabolism
- Compliance/adherence
- Caregiver support
- Renal insufficiency
- Comorbidities
  - Neuropathy
  - Cardiac
  - Diabetes
  - Low blood counts

## DISEASE

**Burden**

- ISS/LDH
- Rate of rise
- Marrow burden
- CRAB symptoms
- Extramedullary – PCL, CNS

**Biology**

- Molecular
  - del[17p], t(4;14), t(14;16), ch 1 abnormalities
  - GEP

## TREATMENT

**Trial Availability**

**If Previously Treated**

- Depth/duration
- Relapse > 60d vs Refractory

**Toxicity**

- Myelosuppresion
- Neuropathy
- VTE
- Secondary cancers

**Administration route**

**Single or combination**

**Cost and copays**

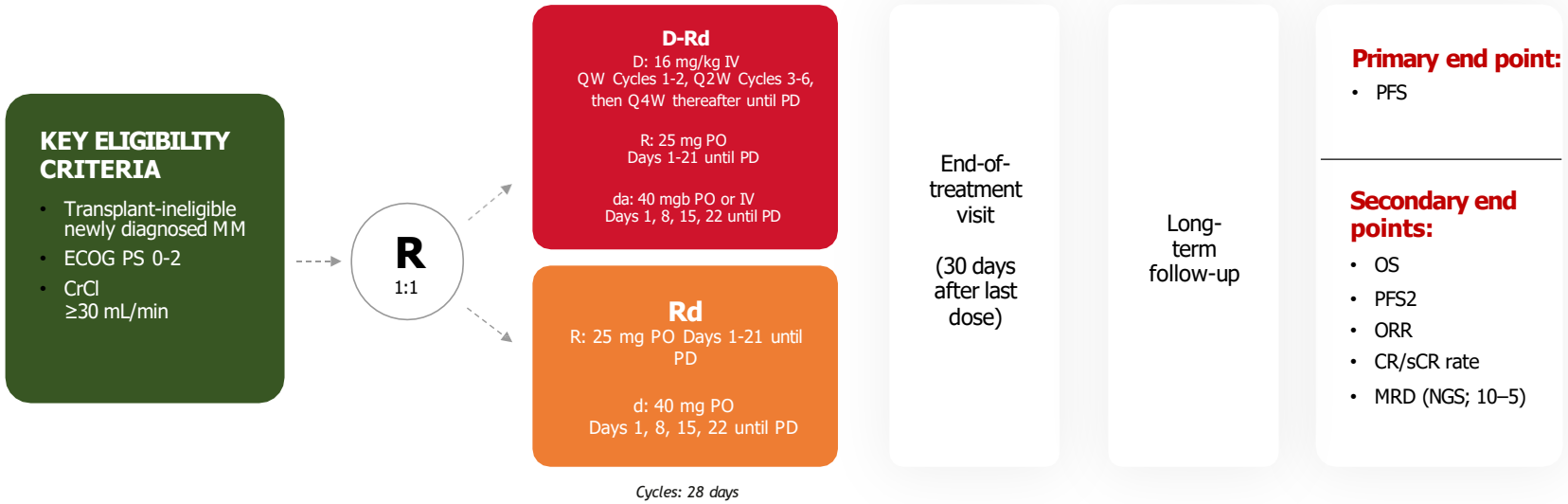
**Access**

Rajkumar SV, Kumar S. *Blood Cancer J*. 2020;10(9):94.

# MAIA: STUDY DESIGN

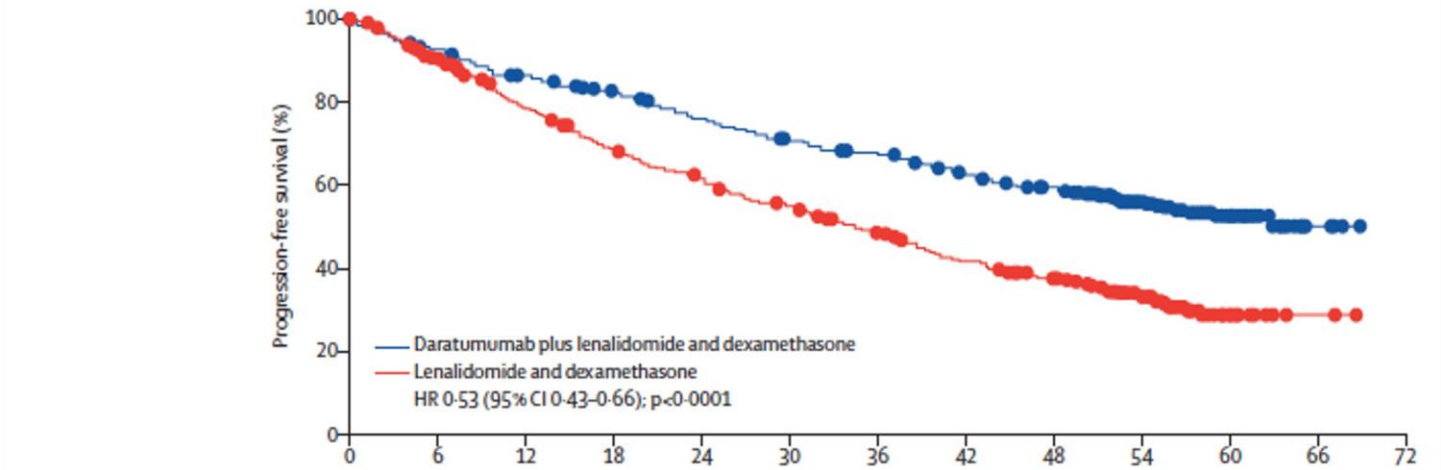
PATIENTS WERE ENROLLED FROM MARCH 2015 THROUGH JANUARY 2017






**MAIA is a multicentre, randomised, open-label, active-controlled, phase 3 study**

# MAIA: UPDATED 5-YEAR PFS DATA

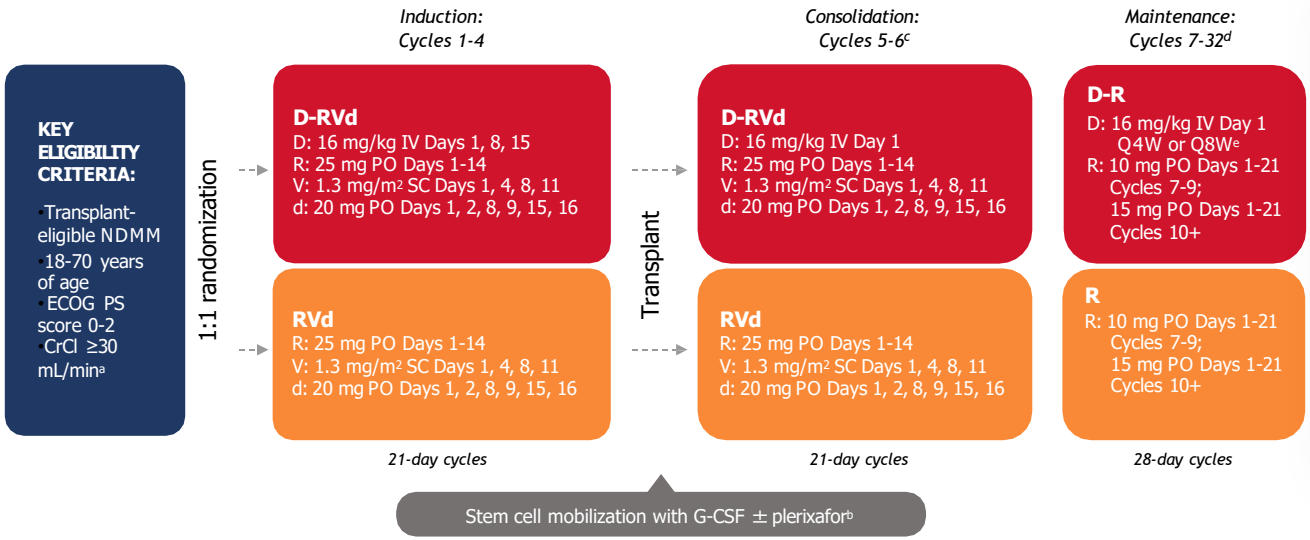



| Number at risk (number censored) | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lenalidomide and dexamethasone | 369 (0) | 307 (29) | 255 (41) | 220 (44) | 196 (46) | 172 (49) | 146 (55) | 123 (58) | 105 (64) | 63 (95) | 12 (140) | 2 (150) | 0 (152) |
| Daratumumab plus lenalidomide and dexamethasone | 368 (0) | 335 (6) | 309 (9) | 290 (14) | 266 (16) | 246 (18) | 232 (20) | 210 (25) | 195 (30) | 123 (92) | 51 (158) | 5 (203) | 0 (208) |

*Moreau, P et al. Lancet Oncol. 22: 1378, 2021.*

# GRIFFIN: RANDOMIZED PHASE I






**ENDPOINTS AND STATISTICAL ASSUMPTIONS**

Primary endpoint: sCR rate (by end of consolidation); 1-sided alpha of 0.1

80% power to detect 15% improvement (50% vs 35%), N = 200

Secondary endpoints: Rates of MRD negativity (NGS $10^{-5}$), ORR, ≥VGPR, CR

*Presented By Jonathan Kaufman at ASH 2020*

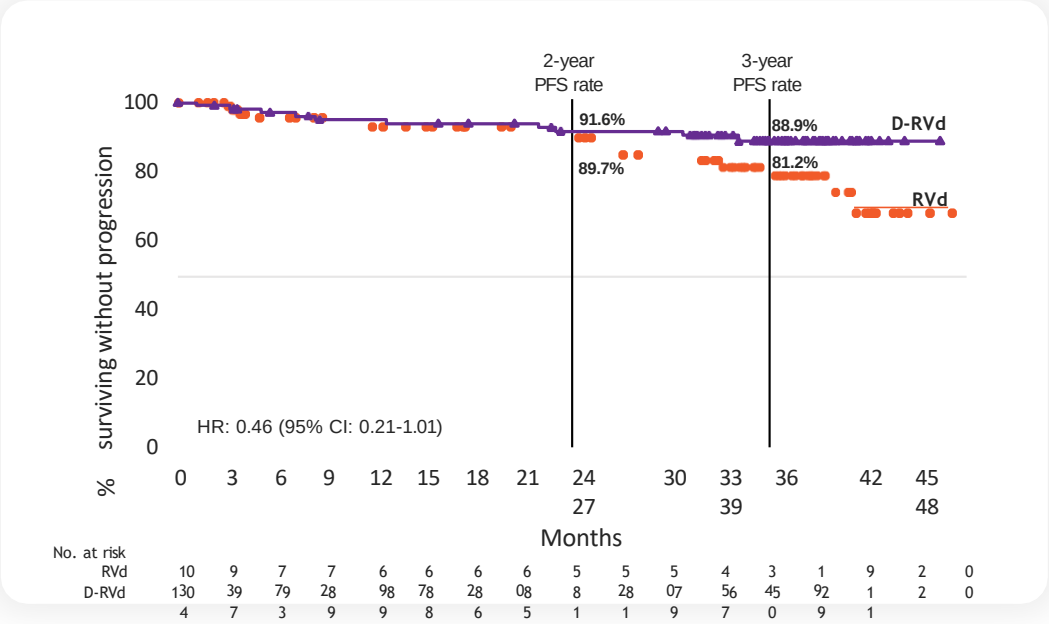
# GRIFFIN: PROGRESSION FREE SURVIVAL

Median follow-up:
**38.6 months**

Median PFS was **not reached in either group**

There is a positive trend toward **improved PFS for D-RVd/DR versus RVd/R**

The separation of the PFS curves begins beyond 1 year of maintenance and suggests a **benefit of prolonged DR therapy**

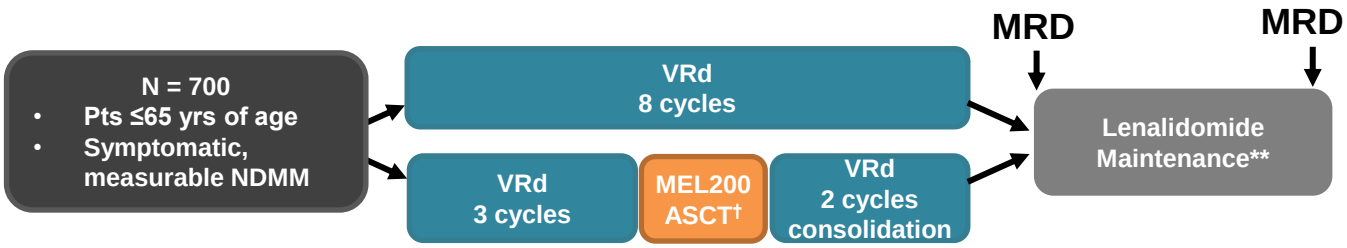


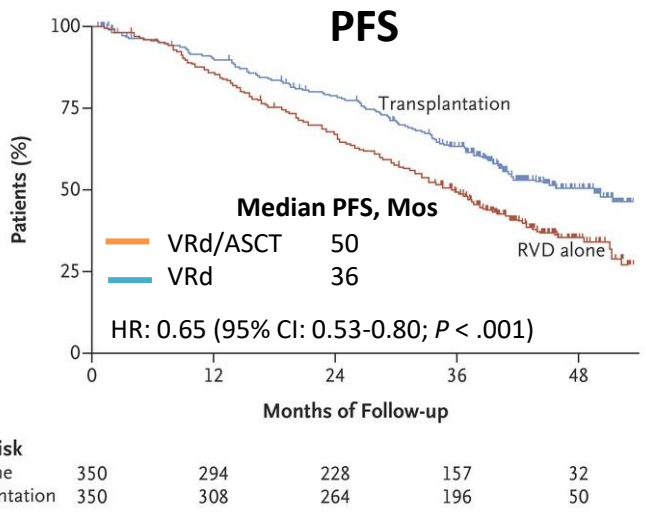

*Laubach J, et al. ASH 2021*
*HR, hazard ratio.*

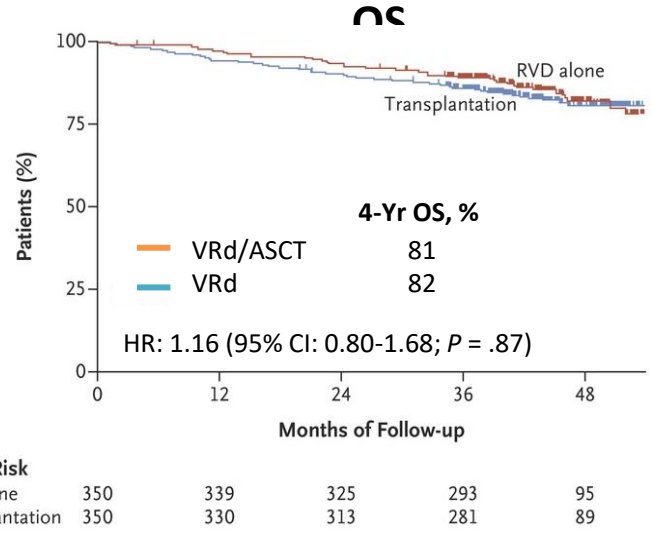
# VRD ± ASCT IN NDMM

# *PHASE III DETERMINATION TRIAL (IFM/DFCI 2009)*



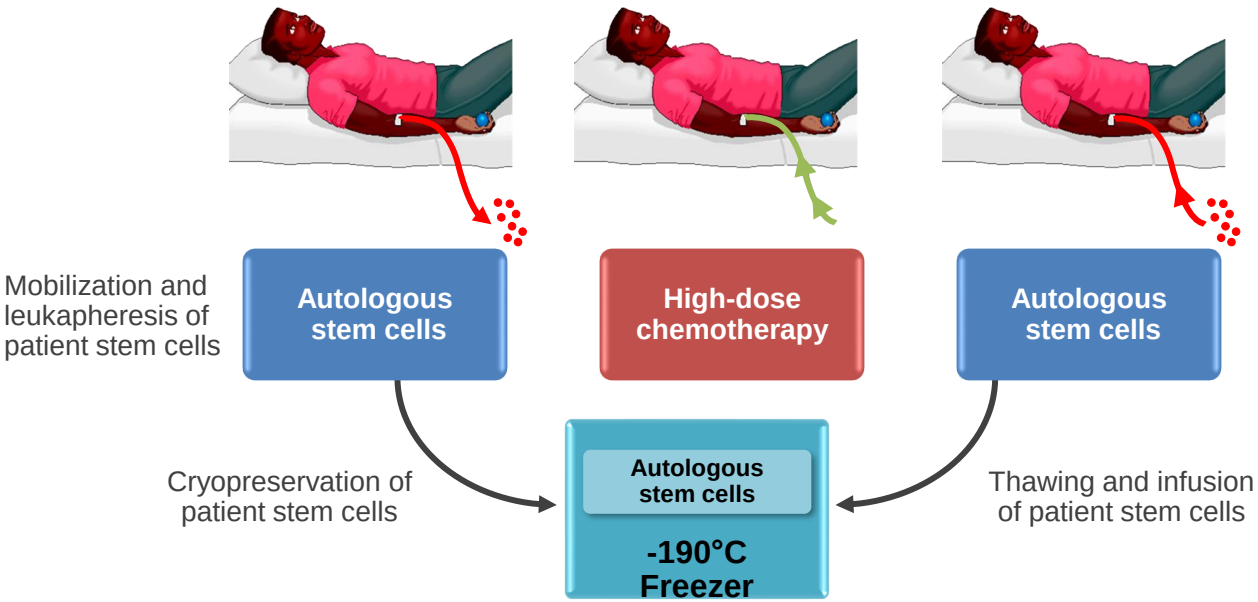


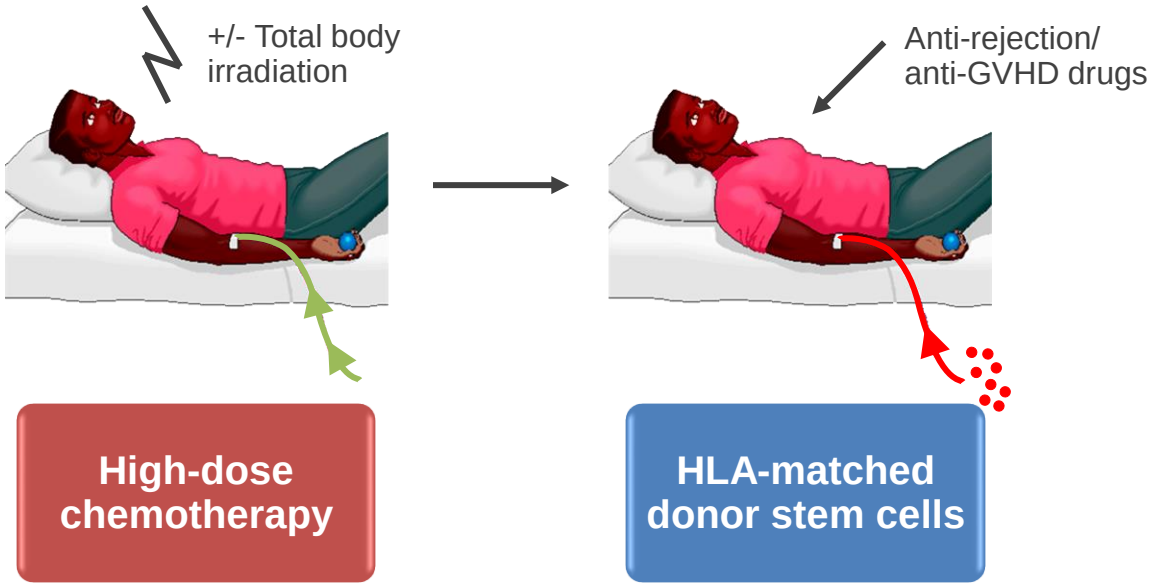




. Attal M, et al. *N Engl J Med* 2017; 376:1311-1320. DOI: 10.1056/NEJMoa1611750

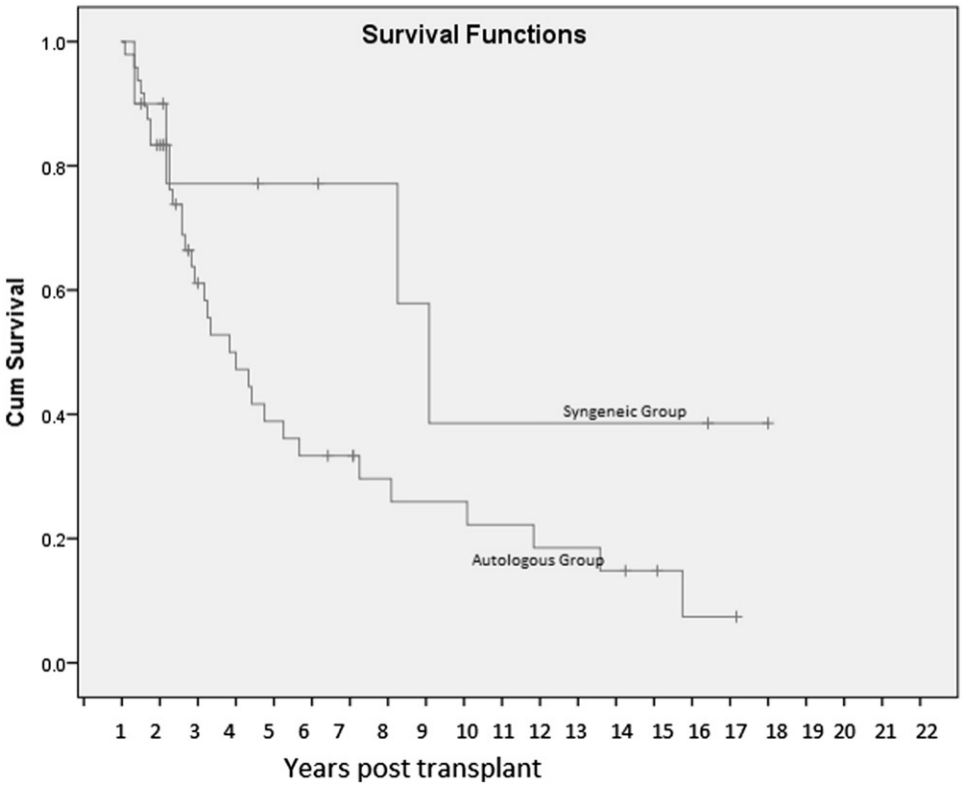
# AUTOLOGOUS STEM CELL TRANSPLANT

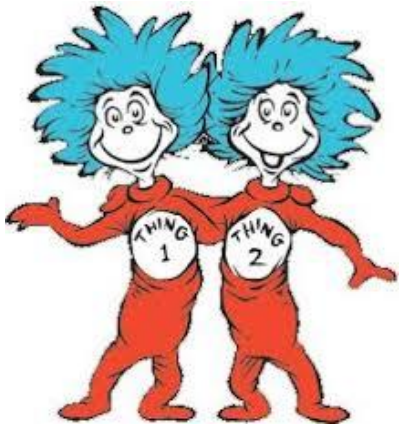


# ALLOGENEIC STEM CELL TRANSPLANT



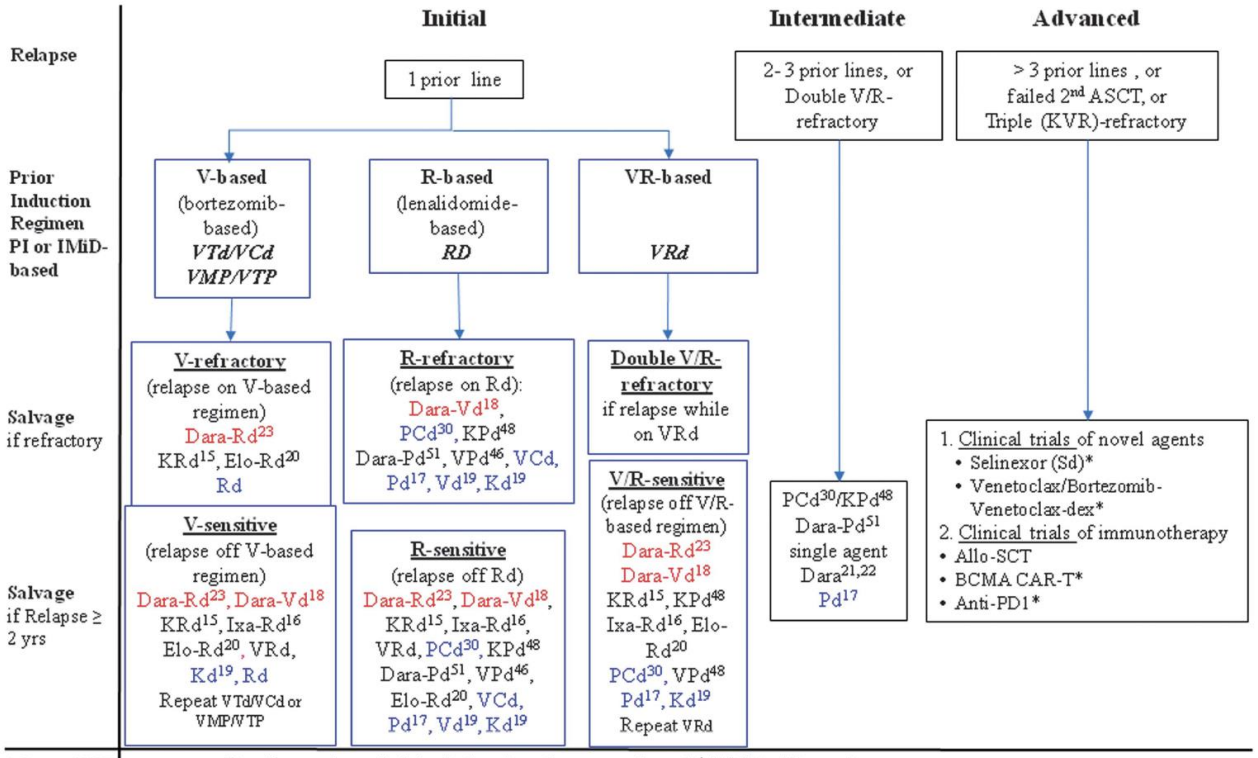
# SYNGENEIC TRANSPLANTATION




Mohyuddin, et al. Leuk Lymphoma. . 2018 Feb;59(2):515-518

# SEQUENCING STRATEGIES




Abbreviations: Regimen in "red" font: most potent, 1st choice; "blue" font: less expensive regimens; PI: proteasome inhibitor, IMiD: immunolomodulatory agent; V: bortezomib; R: lenalidomide; VTd: bortezomib-thalidomide-dexamethasone, VCd: bortezomib-cyclophosphamide-dexamethasone, VMP: bortezomib-melphalan-prednisolone, VTP: bortezomib-thalidomide-prednisolone, VRd: bortezomib-lenalidomide-dexamethasone, Rd: lenalidomide-dexamethasone, Kd: carfilzomib-dexamethasone, KRd: carfilzomib-lenalidomide-dexamethasone, Ixa-Rd: ixazomib-lenalidomide-dexamethasone, Dara-Rd: daratumumab-lenalidomide-dexamethasone, Elo-Rd: Elotumumab-lenalidomide-dexamethasone, Pd: pomalidomide-dexamethasone; PCd: pomalidomide-cyclophosphamide-dexamethasone, KPd: carfilzomib-pomalidomide-dexamethasone, Dara-Pd: daratumumab-pomalidmide-dexamethasone, SCT: stem cell transplantation, CAR-T: chimeric antigen receptor T cell, *: ongloing clinical trials, number in superscript: reference in the manuscript

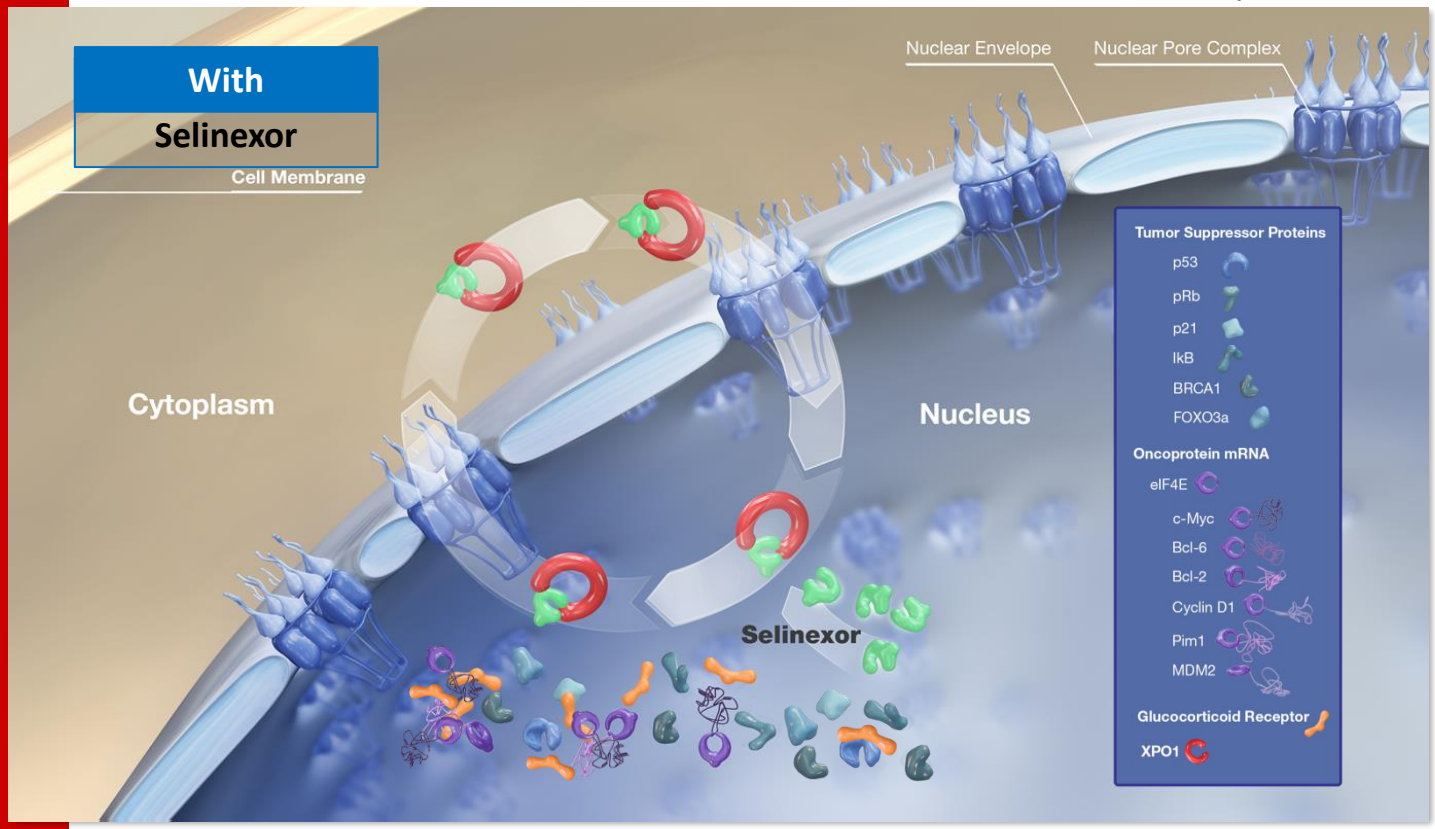


Chim, et al. Leukemia (2018) 32, 252–262

# SELINEXOR MECHANISM OF ACTION



First in Class, Oral Selective Inhibitor of Nuclear Export (SINE)




**FDA Approved 7/3/19**

**XPO1 in MM**

- Transports >200 proteins from the nucleus to cytoplasm
- Expression increased in MM vs normal PC/MGUS/SMM
- Correlates with shorter survival and increased bone disease

**Selinexor**

- Inhibits XPO1 through reversible covalent modification

- Currently FDA approved in combination with dexamethasone based on the **STORM** study
- Selinexor in combinations with bortezomib and dexamethasone was recently filed with FDA based on the **BOSTON** study
- Ongoing **STOMP** study looking into combinations of Selinexor with other anti-myeloma agents

Tai et al *Leukemia* 2014.
Schmidt et al *Leukemia* 2013.

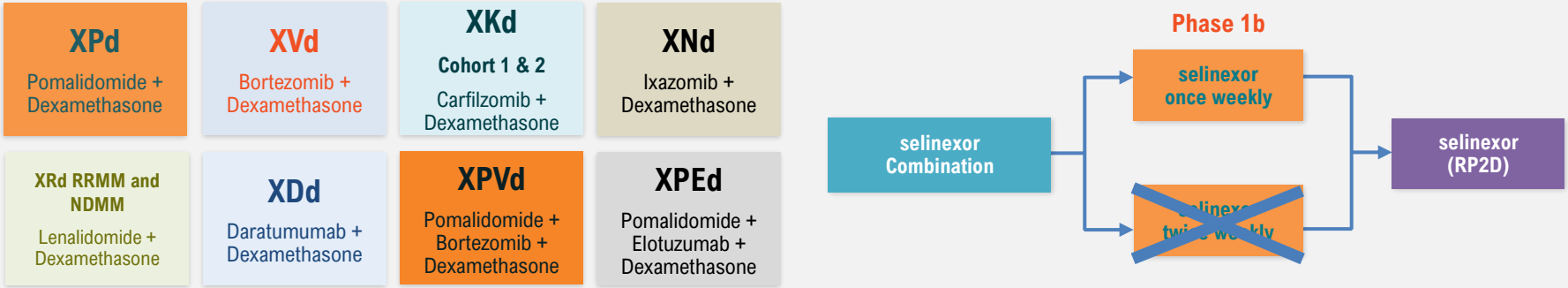
## STOMP: STUDY OVERVIEW & OBJECTIVES

SELINEXOR AND BACKBONE TREATMENTS OF MULTIPLE MYELOMA PATIENTS (STOMP): MULTI-CENTER, OPEN-LABEL, RANDOMIZED DOSE ESCALATION (PHASE 1) AND EXPANSION (PHASE 2) STUDY TO ASSESS THE MTD, EFFICACY, AND SAFETY OF SELINEXOR IN PATIENTS WITH RRMM

### Phase 1 (Dose Escalation) Objectives

**Primary:** to determine the MTD for selinexor QW or BIW when combined with SOC MM therapies

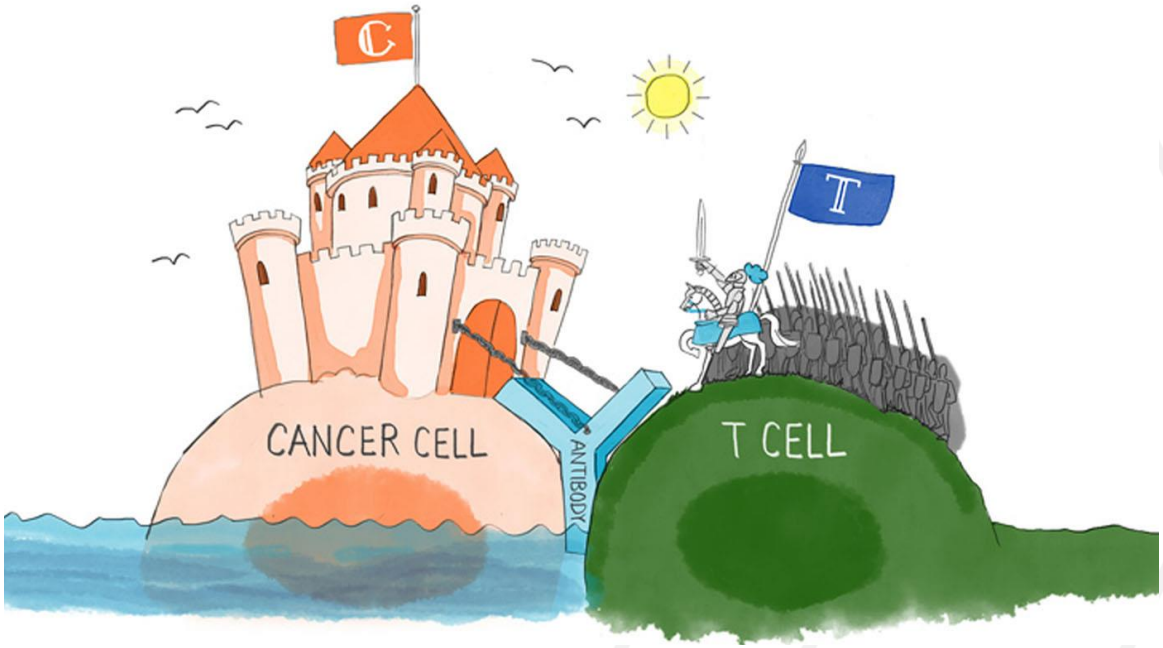
**Secondary:** to determine the RP2D schedule for each arm independently




BIW, twice weekly; MTD, maximum tolerated dose; QW, once weekly; RP2D, recommended phase 2 dose; RRMM, relapsed/refractory multiple myeloma; SOC, standard of care.

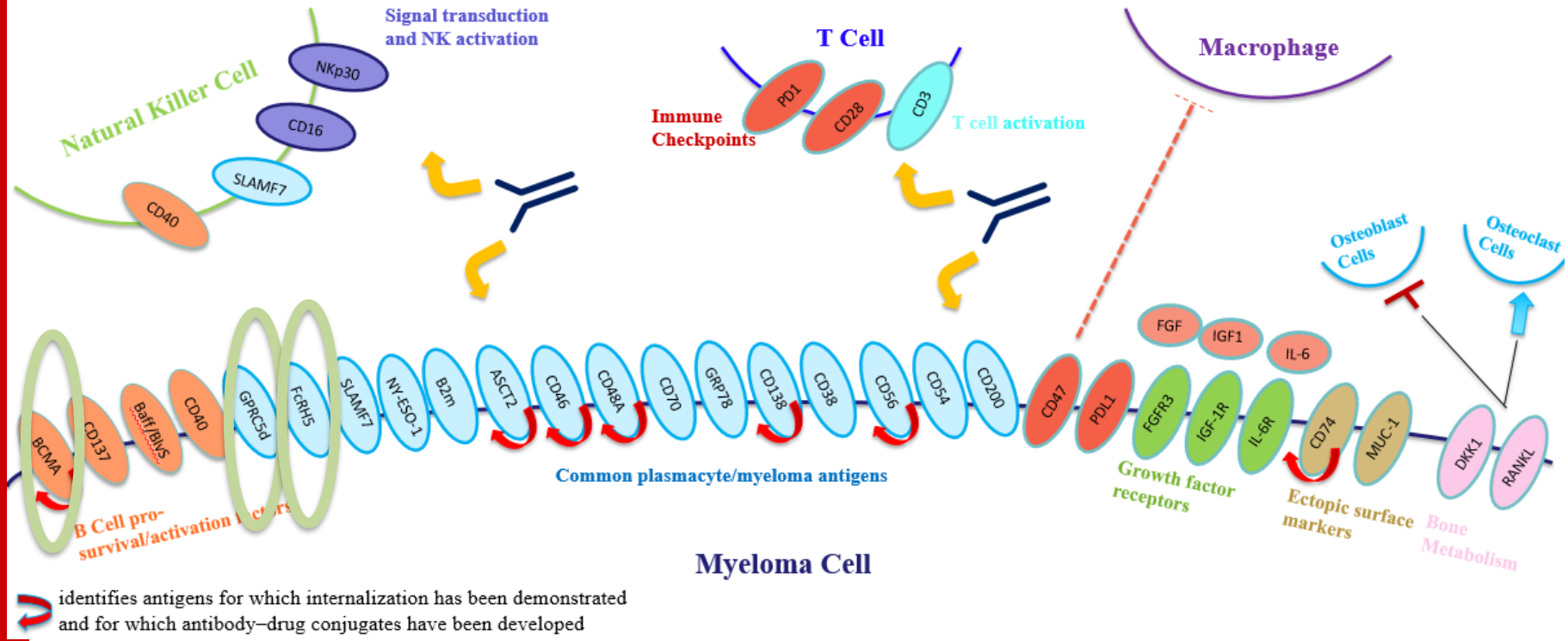
1. Bahlis N, et al. Blood Dec 2018 132(24):2546-2554. 2. Gasparetto C, et al. XDd Presented at EHA annual meeting, 2019. 3. Chen C, et al. XPd Presented EHA annual meeting, 2019 4. Gasparetto C, et al. XKd Presented at EHA annual meeting, 2019 5. White D, et al. XRd Presented at ASH Annual Meeting, December 2017 6. Data on file. Karyopharm Therapeutics, Inc.

# STARTING UP A BRAND NEW DAY --- STING




*https://www.bms.com/life-and-science/science/redirecting-immune-cells-fight-myeloma.html

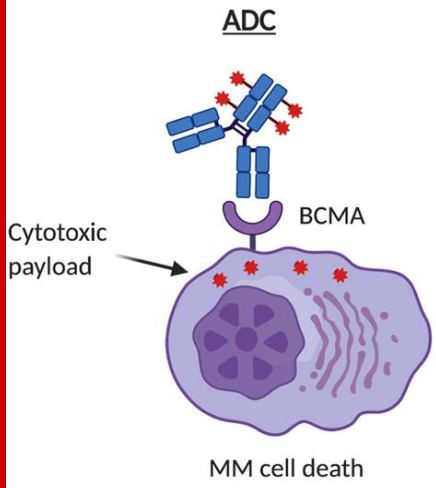
# IMMUNOTHERAPEUTIC TARGETS IN MULTIPLE MYELOMA

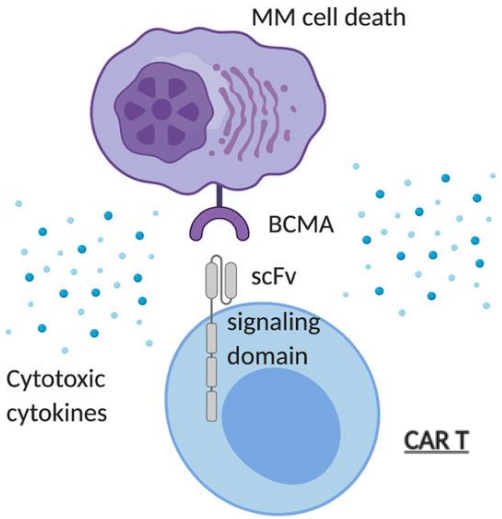


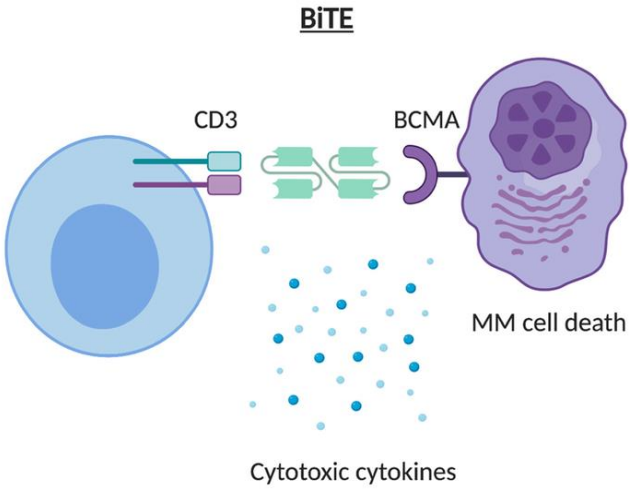

Lancman G et al. *Hematology Am Soc Hematol Educ Program.* 2020;1:264-271.

# BCMA-TARGETED THERAPIES FOR MULTIPLE MYELOMA






***Antibody–Drug Conjugates (ADCs)***
*Belantamab mafodotin*
*CC-99712*

***CAR T-Cell Therapies***
*Idecabtagene vicleucel*
*Ciltacabtagene autoleucel*
*Orvacabtagene autoleucel*
*P-BCMA-101*
*bb21217*
*ALLO-715*

***Bispecific T-Cell Engagers***
*CC-93269*
*REGN5458*
*JNJ-64007957*
*PF-06863135*

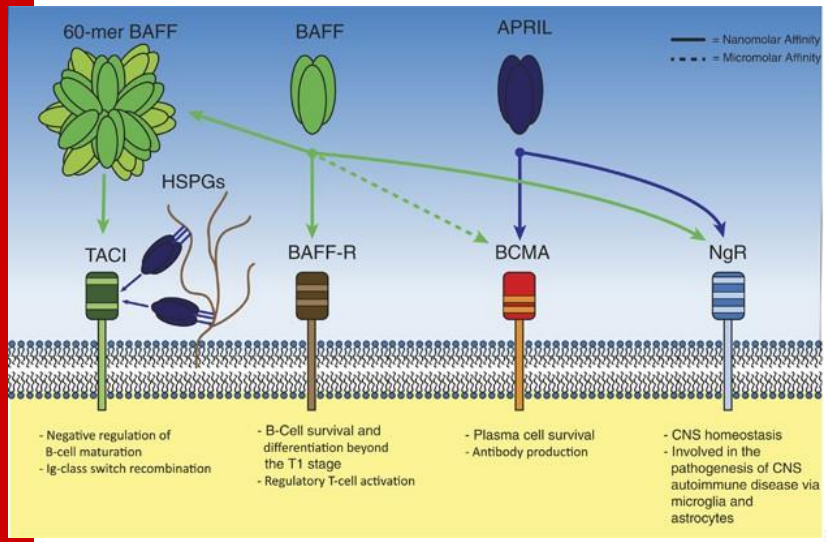
**Figure from: Yu, B., Jiang, T. & Liu, D. *J Hematol Oncol*. 2020;13:125**

# COMPARISON OF NEW MODALITIES

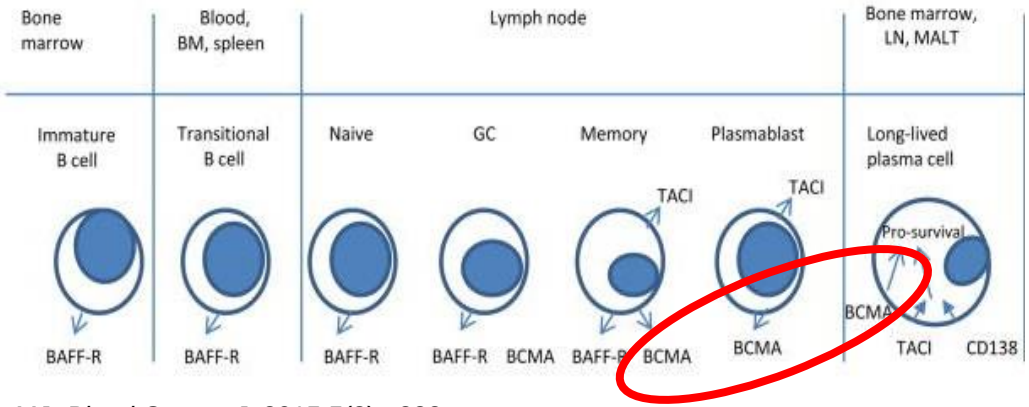
| | Chimeric antigen receptor T cells (CAR-T) | Bispecific antibodies | Antibody-drug conjugates |
|---|---|---|---|
| Pros | Unprecedented response rates including minimal residual disease (MRD) negativity in heavily pre-treated patients<br><br>One time intervention ; long chemo holiday resulting in median PFS ~1 year | Off the shelf<br><br>Deep responses<br><br>Limited severe cytokine release syndrome - ? elderly<br><br>Can be given in community settings | Off the shelf<br><br>Encouraging response rates<br><br>1 hour infusion every 3 weeks<br><br>No cytokine release syndrome<br><br>Can be given in community settings |
| Cons | Manufacturing time makes impractical for patients with aggressive/rapidly progressing disease<br><br>Requires complex infrastructure – stem cell lab, nursing, ICU/ER training – thus restricted to accredited centers<br><br>Cytokine release syndrome- ? role in elderly/frail<br><br>Impact of bridging chemo on remission duration<br><br>Cost given relapses are occurring even in MRD negative patients<br><br>Low white cells and platelets post CAR-T requiring ongoing/frequent monitoring and treatment<br><br>Management of CAR-T relapses challenging especially if soon after fludarabine /cyclophoshamide given impact on T cells | ? Need for admissions with initial doses until cytokine release syndrome risk low<br><br>Dosing/schedule to be determined<br><br>Need for continuous treatment until progression<br><br>Toxicities require further study – neuropathy, infections | Ocular toxicity – will require close collaboration with ophthalmology and may negatively impact quality of life<br><br>Thrombocytopenia<br><br>Need for continuous treatment until progression<br><br>Modest ORR and PFS in triple class/penta refractory |

Lancman, et al. ASH 2020.

# BCMA (B-CELL MATURATION ANTIGEN)




- Receptor for BAFF and APRIL
- Expressed on mature B cell subsets, PC's, and plasmacytoid DC's
- Maintains plasma cell homeostasis
  - BCMA-/- mice have normal B cell #s, impaired PC survival



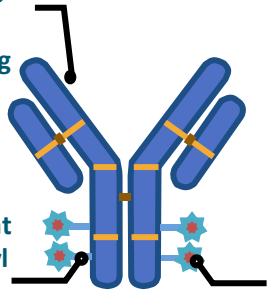

Hengeveld PJ, Kersten MJ. *Blood Cancer J.* 2015;5(2):e282.
Maus MV, June CH. *Clin Cancer Res*. 2013;19(8):1917-1919.

# BELANTAMAB MAFODOTIN: OVERVIEW



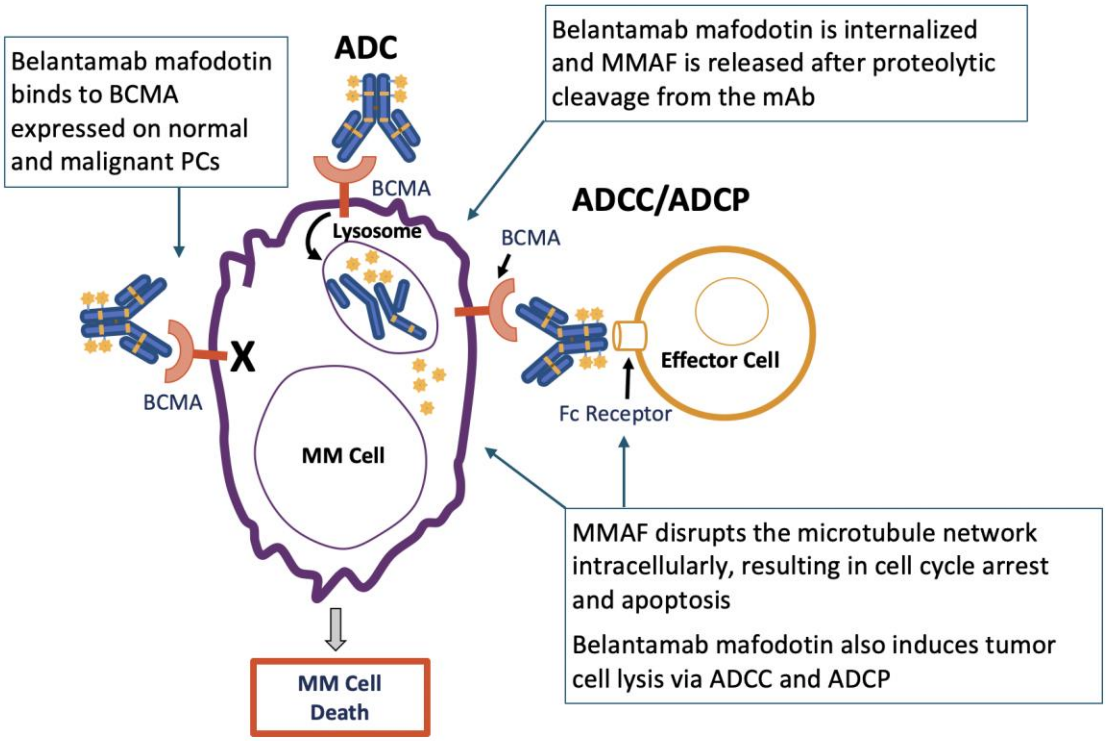
## Belantamab mafodotin: a BCMA-directed antibody and microtubule inhibitor conjugate comprising 3 components

1 Humanized anti-BCMA IgG1 mAb that binds to BCMA-expressing MM cells

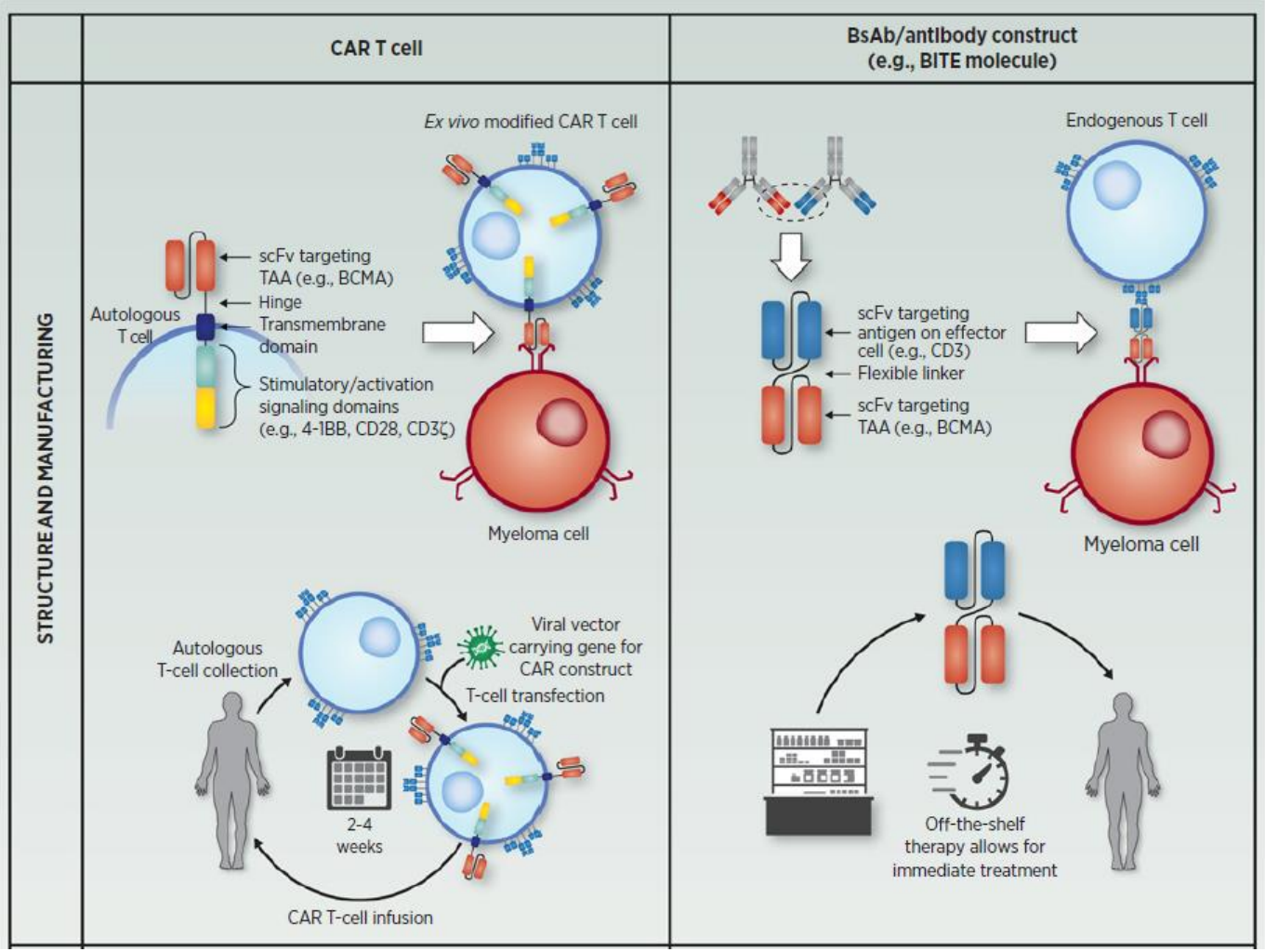


2 MMAF: microtubule-disrupting cytotoxic agent that leads to apoptosis of BCMA-expressing MM cells

3 Protease-resistant maleimidocaproyl linker that joins MMAF to mAb and releases payload only in target cell




Tai. Blood. 2014;123:3128. Farooq. Ophthalmol Ther. 2020;9:889.



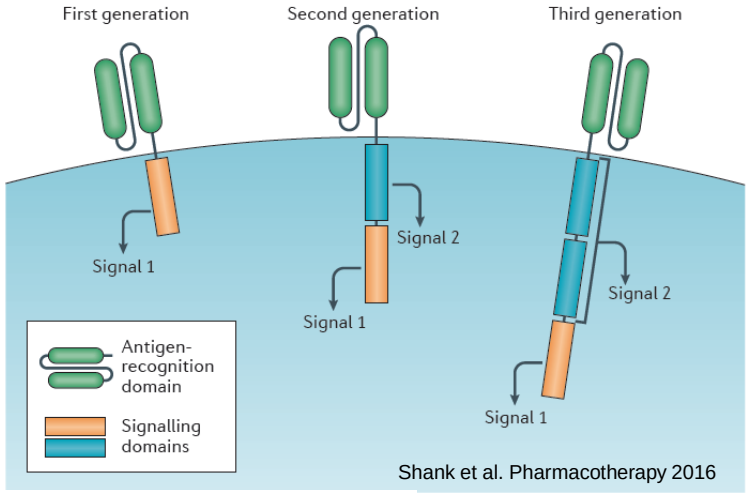

Cohen et al. Clin Cancer Res; 26(7) April 1, 2020.

# *Chimeric Antigen Receptor (CAR) T-cells are Genetically Engineered to Target Antigens on Cancer Cells*

CARs: Chimeric Antigen Receptor engineered to be expressed on the surface of T-cells

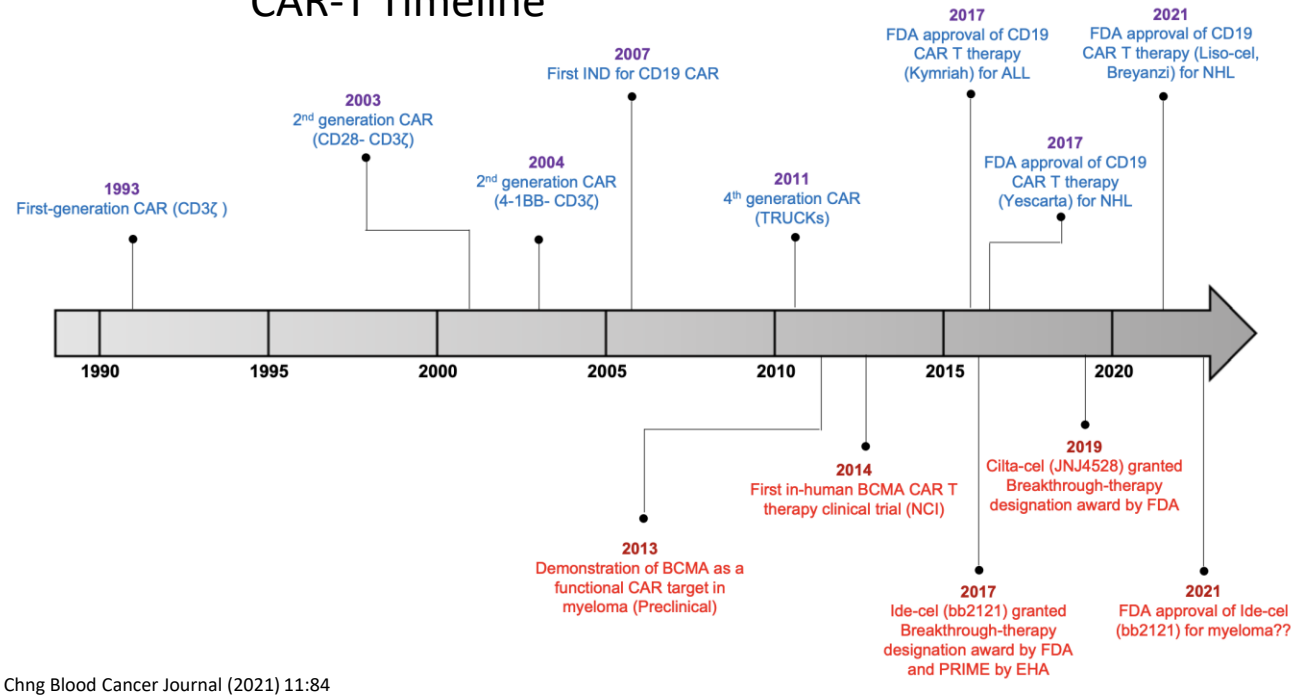
Chimeric: an antibody single chain variable fragment (scFv) linked to T-cell signaling domain – CD3ζ

CARs permit recognition of specific antigen by the T cell independent of MHC and the signaling domain stimulate T-cell proliferation, cytolysis and cytokine secretion to eliminate the tumor cells.




Shank et al. Pharmacotherapy 2016

## CAR-T Timeline

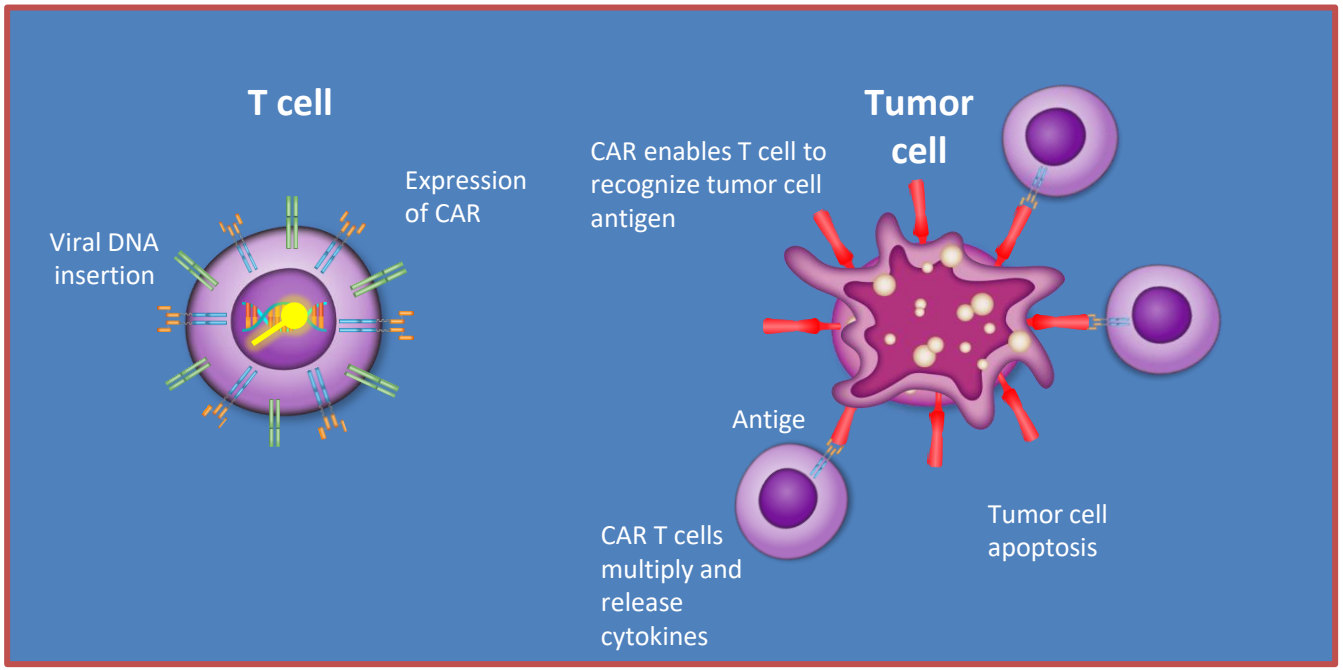



Teoh and Chng Blood Cancer Journal (2021) 11:84

LEUKEMIA & LYMPHOMA SOCIETY®

# HOW CAR T-CELL THERAPY WORKS

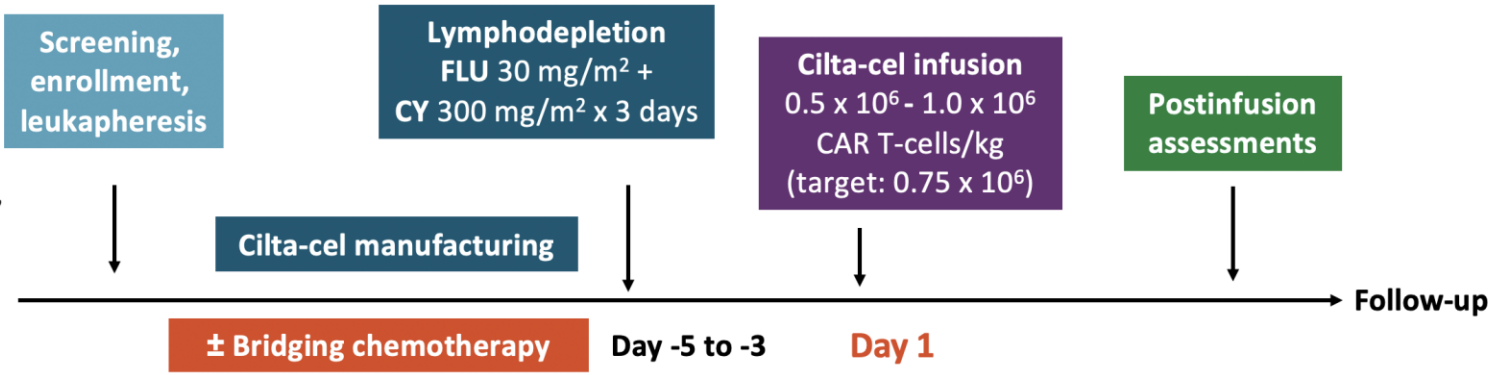




# CARTITUDE-1: Study Design

- Phase Ib/II trial conducted in the United States

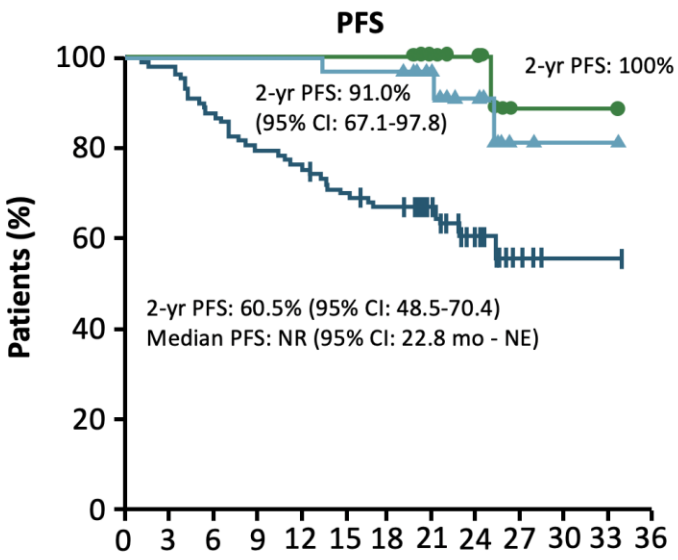
Patients with R/R MM with measurable disease, ECOG PS 0-1; ≥3 prior therapies including PI, IMiD, and anti-CD38 therapy, or double refractory to PI and IMiD (N = 113)



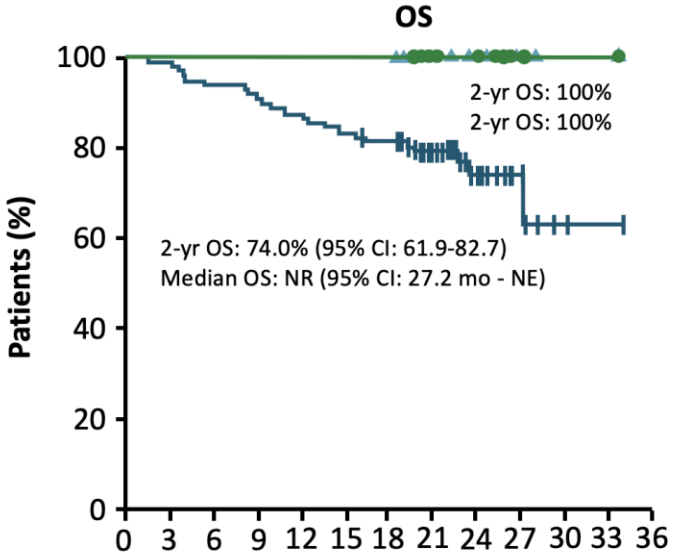

- Of 113 patients enrolled, 97 received cilta-cel; median administered dose: 0.71 x $10^6$ (0.51-0.95 x $10^6$) CAR+ viable T-cells/kg
- **Primary endpoint:** safety and RP2D (phase Ib), efficacy (phase II)

Martin. ASH 2021. Abstr 549.

# CARTITUDE-1: PFS and OS by MRD Status




| Patients at Risk, n | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| All patients | 97 | 95 | 85 | 77 | 74 | 67 | 63 | 36 | 19 | 4 | 1 | 1 | 0 |
| MRD negativity ≥6 mo | 30 | 30 | 30 | 30 | 30 | 29 | 29 | 17 | 12 | 2 | 1 | 1 | 0 |
| MRD negativity ≥12 mo | 18 | 18 | 18 | 18 | 18 | 18 | 18 | 12 | 10 | 2 | 1 | 1 | 0 |




| Patients at Risk, n | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| All patients | 97 | 96 | 91 | 88 | 85 | 81 | 78 | 46 | 23 | 8 | 2 | 1 | 0 |
| MRD negativity ≥6 mo | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 17 | 13 | 3 | 1 | 1 | 0 |
| MRD negativity ≥12 mo | 18 | 18 | 18 | 18 | 18 | 18 | 18 | 12 | 11 | 2 | 1 | 1 | 0 |

All patients — MRD negativity sustained ≥6 mo — MRD negativity sustained ≥12 mo

- 92% of 61 patients evaluable for MRD, were MRD negative ($10^{-5}$)

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# LIST OF CURRENTLY ONGOING REGISTERED CAR-T CELL CLINICAL TRIALS

| Developer | Name (NCT) | Target antigen | Tools, technology, vectorization, or other notes | Status | Country |
|---|---|---|---|---|---|
| **Single-target CAR-T cells** | | | | | |
| Janssen | CARTITUDE-1 (NCT03548207) | BCMA | JNJ-68284528 (former LCAR-B38M) | Phase 1b/2, active and not recruiting | USA, Japan |
| Janssen | CARTITUDE-4 (NCT04181827) | BCMA | Compare efficacy of JNJ-68284528 (former LCAR-B38M) with either pomalidomide, bortezomib and dexamethasone or daratumumab, pomalidomide and dexamethasone | Phase 3, not yet recruiting | USA, Australia, UK, EU |
| Juno (Celgene) | JCARH125 (NCT03430011) | BCMA | LVV, 4-1BB, human | Phase 1/2, recruiting | USA |
| Juno (MSKCC) | MSKCC huBCMA-CAR (NCT03070327) | BCMA | RVV, human, BCMA + > 1%, EGFRt/ BCMA-41BB, with or without lenalidomide | Phase 1, recruiting | USA |
| Juno (NCI, FHCRC) | JSMD194 (NCT03502577) | BCMA + gamma-secretase inhibition | LVV, 4-1BB, human | Phase 1, recruiting | USA |
| Juno (NCI, FHCRC) | FCARH143 (NCT03338972) | BCMA | LVV, 4-1BB, human | Phase 1, recruiting | USA |
| NCI | NCT03602612 | BCMA | Human | Phase 1, recruiting | USA |
| Bluebird (Celgene) | CRB-401 (NCT02658929) | BCMA | LVV, 4-1BB, murine (bb2121) | Phase 1, active and not recruiting | USA |
| Bluebird (Celgene) | CRB-402 (NCT03274219) | BCMA | LVV, 4-1BB, murine, bb21217 (uses the same design as bb2121, but adds the phosphoinositide 3-kinase inhibitor bb007 during ex vivo culture to enrich the drug product for memory-like T cells) | Phase 1, recruiting | USA |
| Celgene | KarMMa (NCT03361748) | BCMA | LVV, 4-1BB, murine (bb2121) | Phase 2, active and not recruiting | USA, Canada, EU, Japan |
| Celgene | KarMMa-2 (NCT03601078) | BCMA | In patients with RRMM (cohort 1), progressed <18 months of initial treatment including ASCT (Cohort 2a), and without ASCT (Cohort 2b) or, in subjects with inadequate response post ASCT | Phase 2, recruiting | USA, EU, UK |
| Celgene | KarMMa-3 (NCT03651128) | BCMA | Compared with daratumumab, pomalidomide and low-dose dexamethasone, or daratumumab, bortezomib and low-dose dexamethasone, or ixazomib, lenalidomide and low-dose dexamethasone | Phase 3, recruiting | USA, Canada, EU, Japan |
| Novartis (UPenn) | CART-BCMA | BCMA | LVV, 4-1BB, human | Active, closed | USA |
| Poseida | P-BCMA-101 (NCT03288493) | BCMA | PiggyBac, 4-1BB, human | Phase 1/2, recruiting | USA |
| KITE (Gilead) | KITE-585 (NCT03318861) | BCMA | NR | Phase 1, active and not recruiting | USA |
| Cartesian | Descartes-11 (NCT03994705, NCT03448978) | BCMA | Autologous CD8 + T-cells | Phase 1/2, recruiting | USA |
| Arcellx | ARM 1 (NCT04155749) | BCMA | non-scFv binding domain | Phase 1, recruiting | USA |
| Nanjing Legend Biotech (Janssen) | CARTIFAN-1 (NCT03758417) | BCMA | LCAR-B38M, LVV, 4-1BB, non-scFv | Phase 2 | China |
| Allife Medical Science and Technology | NCT03559764 | BCMA | NR | Phase 1, not yet recruiting | China |
| The Pregene Biotechnology (Henan Cancer Hospital) | NCT03664661 | BCMA | LVV, 4-1BB, and CD3ζ | Phase 1, recruiting | China |
| The Pregene Biotechnology (Henan Cancer Hospital) | NCT03661554 | BCMA | Humanized alpaca-derived single-domain antibody, 4-1BB and CD3ζ | Phase 1, recruiting | China |
| PersonGen BioTherapeutics | NCT04186052 | BCMA | NR | Early phase 1, recruiting | China |
| The Pregene Biotechnology (Henan Cancer Hospital) | NCT03322735 | BCMA | NR | Unknown | China |
| Hrain Biotechnology | NCT03943472 | BCMA | NR | Early phase 1, recruiting | China |
| Hrain Biotechnology | NCT03093168 | BCMA | RVV-mediated transduction of activated T cells to express a second-generation CAR with the 4-1BB costimulatory domain along with a EGFRt as a safety switch | Phase 1, recruiting | China |
| Hebei Yanda Ludaopei Hospital | C-CAR088 (NCT03751293) | BCMA | NR | Phase 1, recruiting | China |
| Shanghai Bioray Laboratory | NCT03492268 | BCMA | NR | Phase 1, recruiting | China |
| Carsgen Therapeutics | CT053 (NCT03716856, NCT03302403, NCT03815890039, NCT03975907, NCT03302403) | BCMA | fully human single chain fragment variant, a 4-1BB co-stimulatory domain and a CD3ζ signaling domain | Phase 1, Fast Track and Breakthrough (FDA), PRIME (EMA), recruiting | China |
| Beijing Immunochina Medical Science & Technology | IM21 (NCT03711864) | BCMA | Inclusion criteria: e.g., focal lesions of >1 found by functional imaging examination including PET/CT and/or whole-body MRI | Phase 1, recruiting | China |
| Nanjing Legend Biotech | NCT03672253 | BCMA | After CAR T relapse | Phase 1, active and not recruiting | China |

| Developer | Name (NCT) | Target antigen | Tools, technology, vectorization, or other notes | Status | Country |
|---|---|---|---|---|---|
| Southwest Hospital | NCT02954445 | BCMA | For CD19- B cell malignancies including MM | Phase 1, recruiting | China |
| Sorrento Therapeutics | CAR2 Anti-CD38 A2 (NCT03464916) | CD38 | NR | IND filing, Phase 1, recruiting | USA |
| UNC Lineberger Comprehensive Cancer Center | CAR138 (NCT03672318) | CD138 | NR | Phase 1, recruiting | USA |
| Chinese PLA General Hospital | CART-138 (NCT01886976) | CD138 | NR | Phase 1, unknown | China |
| EU (University Hospital Würzburg) | CARAMBA | SLAMF7 or CS1 | Humanized targeting domain, CARs equipped with an EGFRt safety switch triggered with anti-EGFR antibodies, "Sleeping Beauty" transposition | Phase 1, recruiting | EU |
| NCI | NCT03958656 | SLAMF7 or CS1 | Suicide gene incorporated | Preclinical | USA |
| City of Hope Medical Center (NCI) | CS1-CAR (NCT03710421) | SLAMF7 or CS1 | LVV, hinge-optimized, 4-1BB costimulatory CAR and a truncated EGFR | Phase 1, recruiting | USA |
| Celyad | CYAD-01 (NCT03018405) | NKG2-D | full-length native human NKG2D gene fused with CD3ζ. NKG2D associates with DAP10 for membrane stabilization and function | Dose escalation phase I, recruiting | USA/EU |
| Asclepius Technology | CAR-NK 92 (NCT03940833) | BCMA | CAR NK cell therapy | Dose escalation phase I, recruiting | China |
| **Allogeneic CAR-T cells** | | | | | |
| Allogene Therapeutics | ALLO-715 (NCT04093596) | BCMA | TRAC and CD52 KO, TALEN mRNA | Single-arm, open-label, phase 1, recruiting | USA |
| CRISPR Therapeutics | CTX-120 (NCT04244656) | BCMA | TRAC and PD1 KO, CRISPR/Cas9 | IND enabling, phase 1, recruiting | USA |
| Cellectis | UCART-CS1 (NCT04142619) | SLAMF7 or CS1 | TRAC and CS1 KO, TALEN mRNA | FDA approved IND application to initiate MELANI-01, phase 1 | MDACC, USA |
| Celyad | CYAD-211 | BCMA | Expression of a TRAC- inhibitory molecule peptide consisting of a truncated form of CD3ζ, RVV (co-expression of TRAC-inhibitory molecule with CAR) | IND submission | USA/EU |
| Precision BioSciences | PBCAR269A (NCT04171843) | BCMA | ARCUS genome editing | IND cleared, phase 1/2a, not yet recruiting | No sites documented yet |
| Shanghai Bioray Laboratory | UCART (NCT03752541) | BCMA | NR | NA, recruiting | China |
| **Multi-target CAR-T cells** | | | | | |
| Autolus Limited | AUTO2 (NCT0328780) | BCMA-TACI | NR | Terminated (Preliminary efficacy seen to date following treatment with AUTO2 has been determined not sufficient to warrant further development) | UK, Netherlands |
| University of Pennsylvania | CART-BCMA + huCART19 (NCT03549442) | BCMA-CD19 | LVV, 4-1BB/CD3ζ-based CARs transduced | Phase 1, recruiting | USA |
| iCell Gene Therapeutics | Compound CAR (NCT04156269) | BCMA-CS1 | LVV, an anti-BCMA CAR comprised of a CD8-derived hinge and transmembrane regions, and 4-1BB co-activation domains linked to the CD3ζ signaling domain is fused to a complete anti-CS1 CAR by a self-cleaving P2A peptide; a strong spleen focus forming virus promoter and a CD8 leader sequence were used for efficient expression of the BC1sCAR molecule on the T-cell surface | Phase 1, recruiting | China |
| Chinese PLA General Hospital | (NCT03767751, CHN-PLAGH-BT-037) | CD38-BCMA | NR | Phase ½, recruiting | China |
| Huazhong University of Science and Technology (Cellyan Therapeutics) | ChiCTR1800018143 | CD38-BCMA | 4-1BB signaling and CD3ζ domain | Phase 1, dose-climbing, recruiting | China |
| Chinese PLA General Hospital | BCMA-PD1-CART (NCT04162119) | BCMA-PD1 | BCMA CAR T cells which secrete the mutant PD-1Fc fusion protein | Phase 2, recruiting | China |
| Gracell Biotechnology | GC012F (NCT04236011, NCT04182581) | BCMA-CD19 | NR | Newly posted 22 January 2020, phase 1, recruiting | China |
| Hrain Biotechnology (Shanghai Zhongshan Hospital) | NCT03706547 | BCMA-CD19 | RVV | Phase 1, not yet recruiting | China |
| **Other** | | | | | |
| The First Affiliated Hospital of Soochow University | NCT03196414 | BCMA-CD38-CD19 (or more) | NR | Phase 1, recruiting | China |
| The First Affiliated Hospital of Soochow University | NCT03455972 | BCMA-CD19 | CD19 + or BCMA + high-risk MM after ASCT | Phase 1, recruiting | China |
| Shenzhen Second People's Hospital | NCT03767725 | BCMA and/or CD19 | NR | Phase 1, recruiting | China |


| Developer | Name (NCT) | Target antigen | Tools, technology, vectorization, or other notes | Status | Country |
|---|---|---|---|---|---|
| The First Affiliated Hospital of Nanchang University | NCT04194931 | BCMA-CD19 | Humanized, BCMA + and CD19 + patients | Phase 1, recruiting | China |
| The Sixth Affiliated Hospital of Wenzhou Medical University | NCT03778346 | CD138, integrin β7, CS1, CD38 and BCMA | NR | Phase 1, recruiting | China |
| Zhujiang Hospital | NCT03473496 | | single CAR-T or double CAR-T cells with BCMA, CD138, CD56, or CD38 | NR, recruiting | China |

# SAFETY AND EXPANSION OF MCARH109, A GPRC5D TARGETED CAR T CELL THERAPY IN OR REFRACTORY MULTIPLE MYELOMA

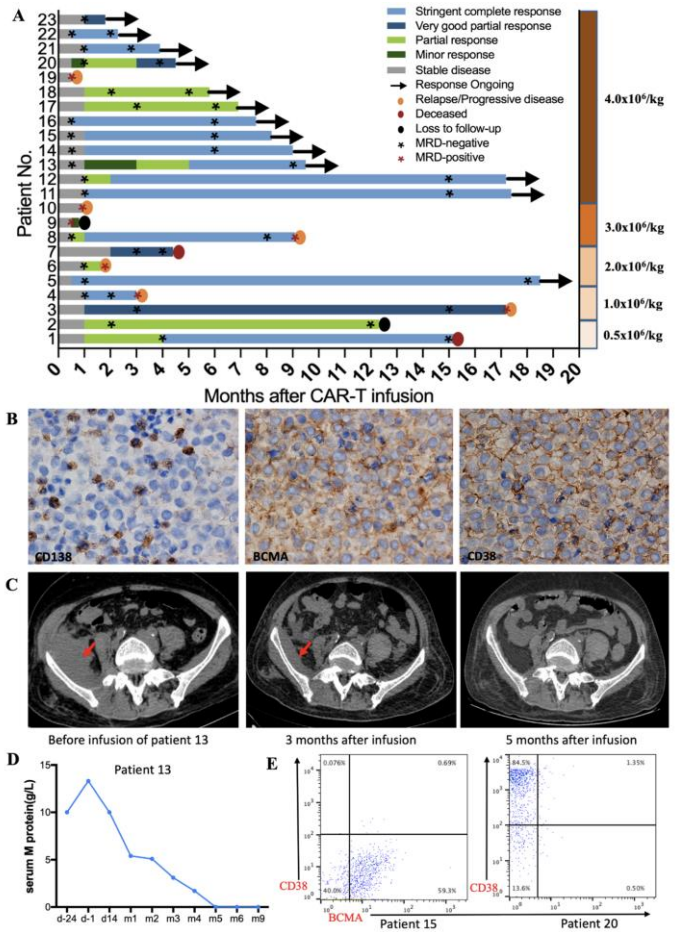
| Dose Level | 25 X10$^6$ CAR+ T cells (n=3) | 50 X10$^6$ CAR+ T cells (n=3) | 150 X10$^6$ CAR+ T cells (n=3) | 450 X10$^6$ CAR+ T cells (n=3) | All Doses (n=12) |
|---|---|---|---|---|---|
| Safety | | | | | |
| CRS any grade | 3 (100%) | 3 (100%) | 3 (100%) | 2 (67%) | 11 (92%) |
| Neurotoxicity any grade | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Nail changes (all grade 1) | 1 (33%) | 1 (33%) | 1 (33%) | 0 (0%) | 3 (25%) |
| MCARH109 expansion | | | | | |
| Median peak Expansion*, Vector copies/mL (range) | 56,357 (44,670-1,661,354) | 404,467 (162,947-770,785) | 1,277,092 (157,749-3,560,000) | NA | 404,467 (44,670-3,560,000) |
| Median time to peak expansion, weeks (range) | 2.0 (2.0-2.1) | 2.6 (1.9-3.9) | 3.1 (2.1-4.1) | NA | 2.1 (1.9-4.1) |

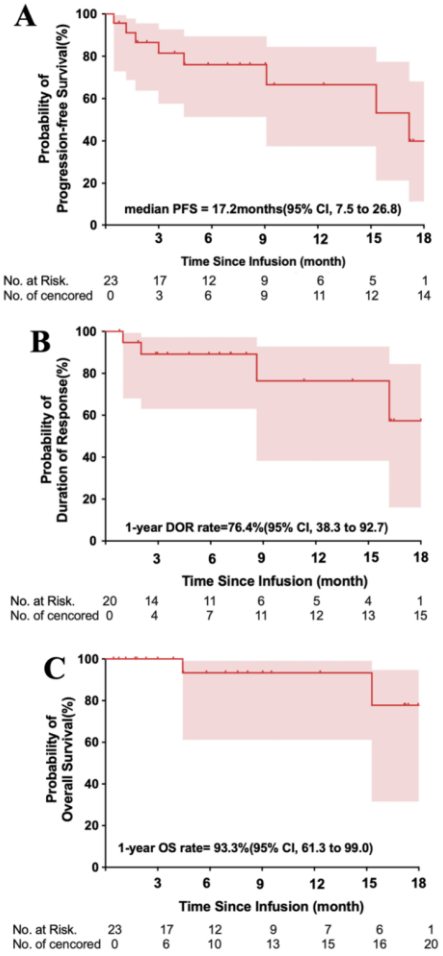
* Peak expansion is assessed using quantitative polymerase chain reaction (qPCR) and is available only for the first 3 dose cohorts.

NA, Not yet available

Mailankody, et al. ASH 2021: abstract 827

# BISPECIFC CAR-T CELL THERAPY TARGETING BCMA AND CD38

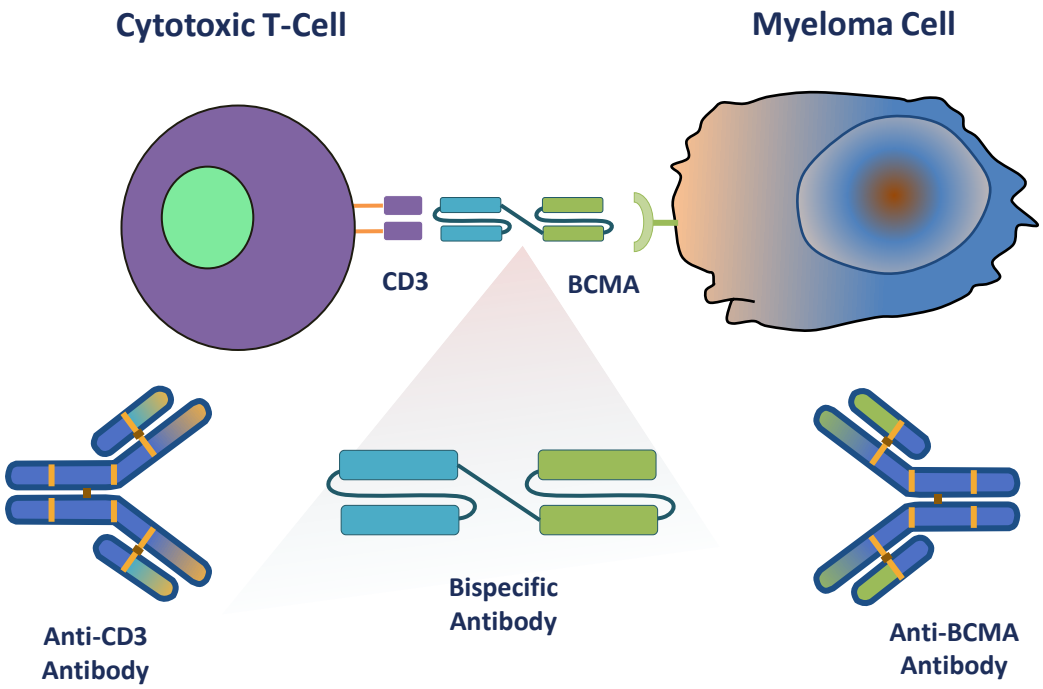



Mei et al. J Hematol Oncol (2021) 14:161

# BISPECIFIC T CELL ANTIBODIES IN MYELOMA: MECHANISM OF ACTION





# Bispecific Antibodies - BCMAxCD3

| Bispecific Antibody | AMG-701 | CC-93269 | Elranatamab | REGN5458 | Teclistamab | TNB-383B |
|---|---|---|---|---|---|---|
| Treatment | Weekly IV | Weekly IV | Weekly SC | Weekly IV | Weekly SC | IV q3w |
| Patients | N = 85 | N = 19 | N = 55 | N = 73 | N = 165 | N = 118 |
| Median prior lines | 6 | 6 | 6 | 5 | 5 | 5 |
| Triple-class refractory | 62% | IMiD/PI/Dara 84%/90%/89% | 50%; 22% prior BCMA-directed | 19% | 78% | 61% |
| ORR @ therapeutic dose | 26% all patients<br>5/6 (83%) most recent cohort | 10/12 (83%)<br>≥ 6mg IV | 9/13 (69%)<br>1000 µg/kg SC | 22/37 (75%)<br>200-800 mg IV | 93/150 (62%)<br>1500ug/kg SC (RP2D) | 60% in > 40<br>40-60 mg IV |
| Duration of Response | 17/21 (81%) ongoing at median 5.6 months | NR | NR | 90% @ median 8 months | 91% ≥ 6 mos | NR |
| **AEs, (All/(Gr 3+)** | | | | | | |
| CRS | 64% (9%) | 90% (5%) | 87% (0%) | 38% (0%) | 72% (1%) | 54% (3%) |
| Infections | (17%) | NR (26%) | NR | NR | 63% (35%) | 32% (17%) |
| Neutropenia | 25% | NR (53%) | 71% (67%) | 23% (22%) | 66% (57%) | 27% ( 22%) |
| Anemia | 42% | NR (42%) | 32% (23%) | 32% (23%) | 49% (35%) | 25% (14%) |
| Thrombocytopenia | 21% | NR (21%) | 21% (13%) | 21% (13%) | 38% (22%) | 22% (11%) |
| Deaths | 4 (5%) | 1 (5%) | 5 (7%) | 5 (7%) | 9, 7 COVID | 6, 3 COVID |
| Other | Neurotoxicity 8% (0%) | | ISR 56% (0%) | | ISR 35% (0%)<br>Hypogamma 72% | |

Harrison A et al. 2020 ASH. Abstract 1369. Costa LJ et al. *Blood*. 2019;134(suppl_1):143.
Sebag M et al. 2021 ASH. Abstract 1651. Zonder JA et al. 2021 ASH. Abstract 160.
Moreau P et al. 2021 ASH. Abstract 896. Kumar SK et al. 2021 ASH. Abstract 900.

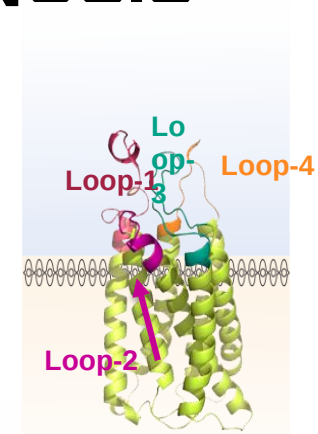
# GPRC 5D EXPRESSION AND PROGNOSIS

**G-protein–coupled receptor class 5member D (GPRC5D) is a type-C 7-pass transmembrane receptor protein**

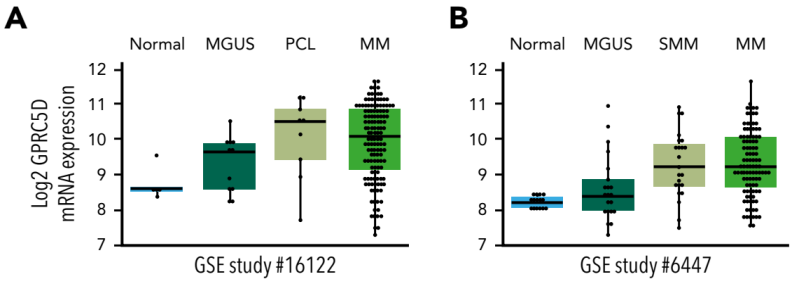
- Orphan receptor - ligand and signaling mechanism unknown
- No known shed peptides or extracellular domain shedding (reduced risk for sink effect)

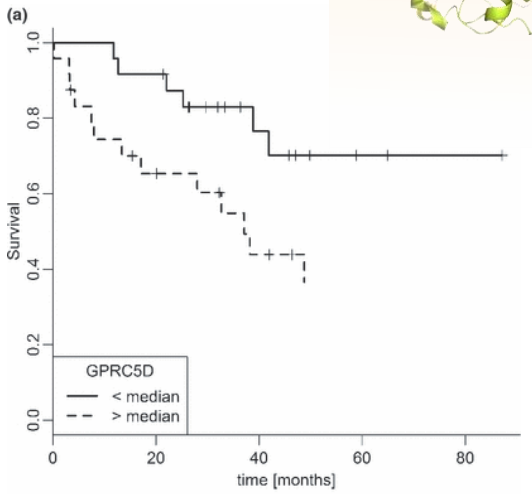
**Predominantly expressed in cells with a plasma-cell phenotype, including the majority of malignant plasma cells from patients with MM**

**High GPRC5D expression associated with poor prognosis**




## GPRC mRNA expression



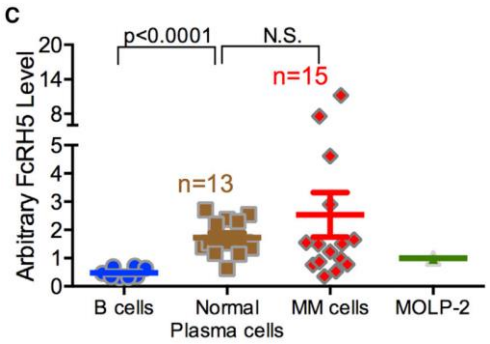




Pillarisetti K et al. *Blood*. 2020;135(15):1232-1243.
Atamaniuk J et al. *Eur J Clinical Invest*. 2012;42(9):953-960.

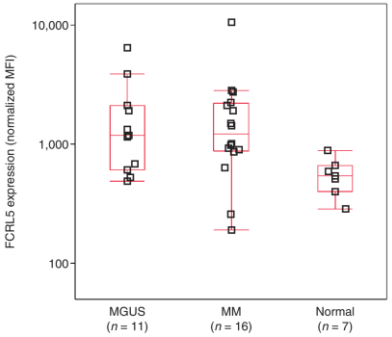
# FC RECEPTOR-HOMOLOG 5 (FCRH5) PROTEIN & MRNA EXPRESSION

- Surface protein in immunoglobulin superfamily, closely related to Fc receptors
- Ligand(s) for FcRH5 are unknown, but implicated in proliferation and isotype expression in the development of antigen-primed B cells
- FcRH5 protein and mRNA over-expressed in malignant plasma cells

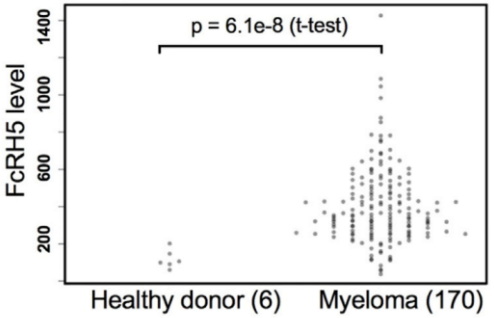
**FcRH5 protein expression by flow cytometry**




**FcRH5 protein expression by flow cytometry**




**FcRH5 mRNA expression in CD138+ plasma cells**




MGUS, monoclonal gammopathy of undetermined significance.

Li J et al. *Cancer Cell*. 2017;31(3):383-395.
Elkins K et al. *Mol Cancer Ther*. 2012;11(10):2222-2232.
Li J et al. *Cancer Cell*. 2017;31(3):383-395.

# NON-BCMA-TARGETED BISPECIFIC ANTIBODIES

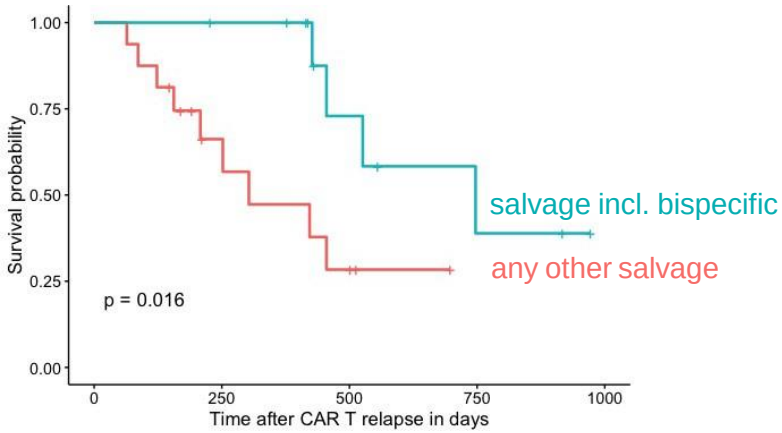
| Bispecific Antibody | Anti-GPRC5d Talquetamab[a] Phase 1 MonumenTAL-1 Study | | Anti-GPRC5d Talquetamab + Daratumumab Phase 1b TRIMM 2 Study[b] | Anti-FcRH5 Cevostamab[c] Phase 1 |
|---|---|---|---|---|
| Treatment | 405 µg/kg SC QW (RP2D) | 800 µg/kg SC QW | 400 qwk & 800 ug/kg q2wk | IV q3w |
| Patients | N = 30 | N = 25 | N = 29 | N = 161 |
| Median prior lines | 6 | 5 | 6 | 6 |
| Prior BCMA therapy | 27% | 16% | 55% | 33% |
| Triple-class refractory | 100% | 92% | 79% | 85% |
| Penta-drug refractory | 80% | 68% | 66% | 68% |
| ORR at therapeutic dose | 21/30 (70%) | 14/21 (67%) | 17/21 (81%) | 132-198 mg: (56.7%) |
| **AEs, (All/(Gr 3+)** | | | | |
| CRS | 77% (3%) | 72% (0%) | 55% (0%) | 80% (2%) |
| Infections | 33% (5%) | | 35% (10%) | 43% (19%) |
| Neutropenia | 67% (60%) | 44% (36%) | 41% (31%) | 18% (16%) |
| Anemia | 60% (27%) | 36% (8%) | 31% (21%) | 32% (22%) |
| Thrombocytopenia | 37% (23%) | 20% (8%) | 35% (21%) | % not reported |
| Deaths | 0% | | 0 | 6 (3.7%) |
| Dysgeusia | 60% (N/A) | 36% (N/A) | 48% (N/A) | Diarrhea 26% (1%) |
| Other | Skin-related & nail disorders 75%<br>G3 rash 7.5% | | Skin & nail 65%<br>G3 rash 10% | |

a. Krishnan A et al. 2021 ASH. Abstract 158. b. Chari et al. 2021 ASH. Abstract 161. c. Trudel S et al. 2021 ASH. Abstract 157.

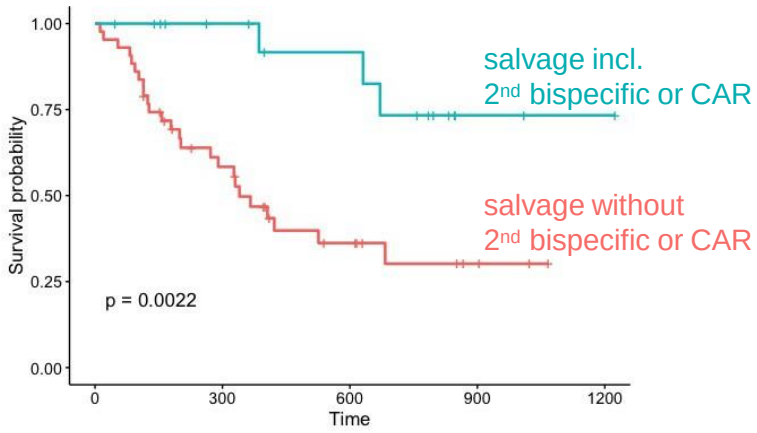
# CAR T – BISPECIFIC ANTIBODY SEQUENCE: DOES IT MATTER?

- Both approaches have resulted in **durable responses and are tolerable** anecdotally
- Important unanswered question as products go into market
- More data needed to interpret role **switch/sequencing of target antigen**

OS after CAR T relapse

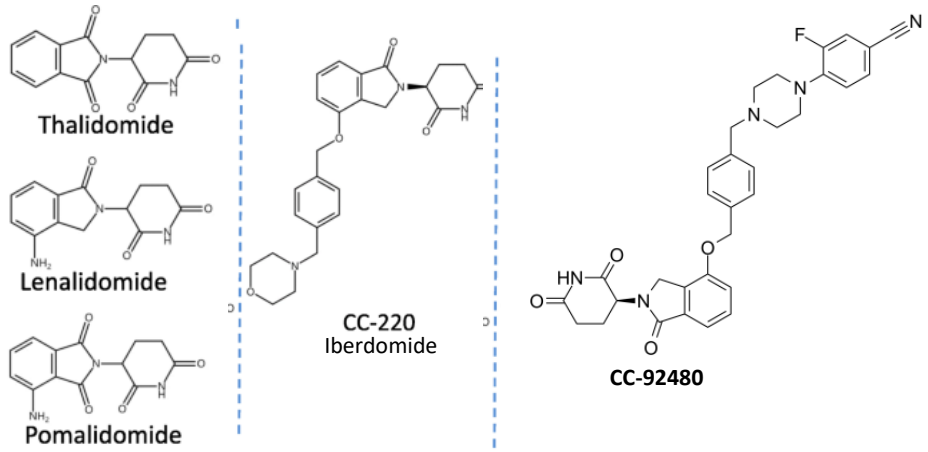


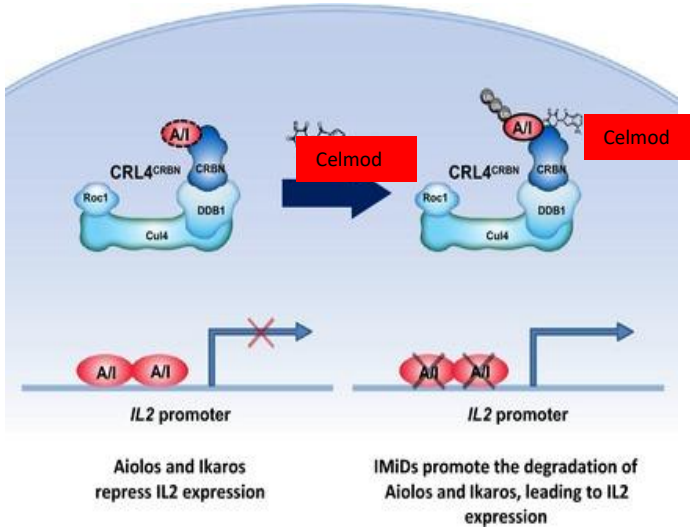

OS after bispecific relapse




Van Oekelen, et al. IMW 2021

# CEREBLON E3 LIGASE MODULATORS (CELMODS)




- Iberdomide (CC-220): novel small molecule inhibitor of cereblon E3 ligase – cereblon binding affinity 20* len and pom

Gao S et al. *Biomarker Res*. 2020;8(2):1-8; Sievers C et al. *Chemistry*. 2017; Gandhi AK et al. *Br J Hematology*. 2014;164(6):811-821.

# IBERDOMIDE WITH DEXAMETHASONE IN TRIPLE CLASS REFRACTORY MYELOMA

All patientts triple class-exposed:

- PIs 100%
- LEN 100%
- POM 100%
- Anti-CD38 mAbs 100%

- 97.2% triple-class refractory

**Survival outcomes:**

**mDOR 7.0 (4.5–11.3) mos**

**mPFS 3.0 (2.8–3.7) mos**

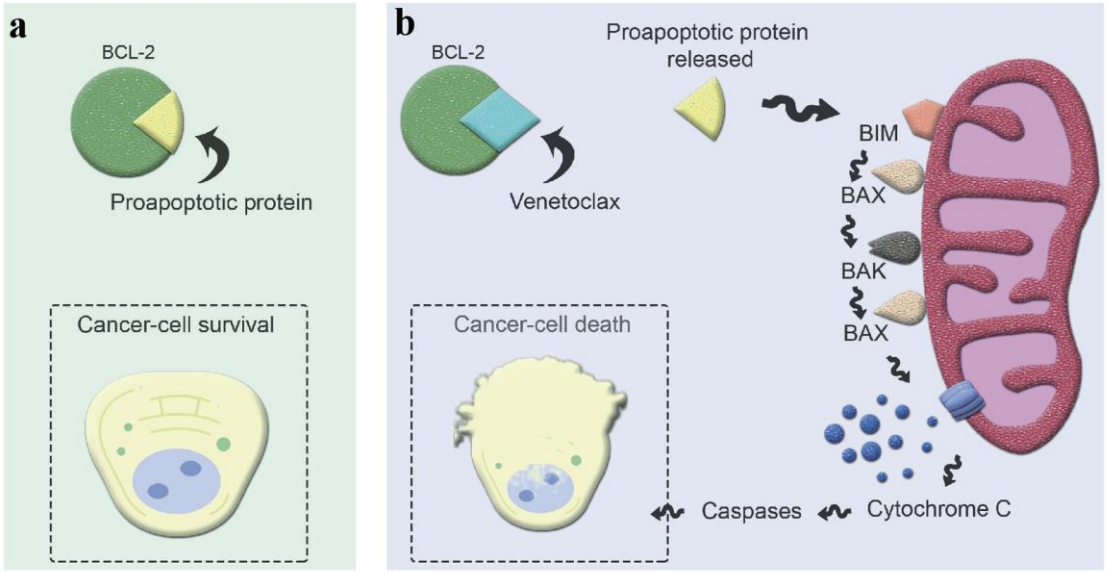
**mOS 11.2 (9.0–NR) mos**

| | IBER + DEX (N = 107) | IBER + DEX post anti-BCMA therapy (N = 24) |
|---|---|---|
| **Response, n (%)** | | |
| ORR[a] | 28 (26.2) | 6 (25.0) |
| sCR | 1 (0.9) | 0 |
| CR | 0 | 1 (4.2) |
| VGPR | 8 (7.5) | 1 (4.2) |
| PR | 19 (17.8) | 4 (16.7) |
| MR | 11 (10.3) | 4 (16.7) |
| SD | 46 (43.0) | 8 (33.3) |
| PD | 15 (14.0) | 4 (16.7) |
| NE | 7 (6.5) | 2 (8.3) |
| **Median DoR (95% CI), months** | 7.0 (4.5–11.3) | NA |

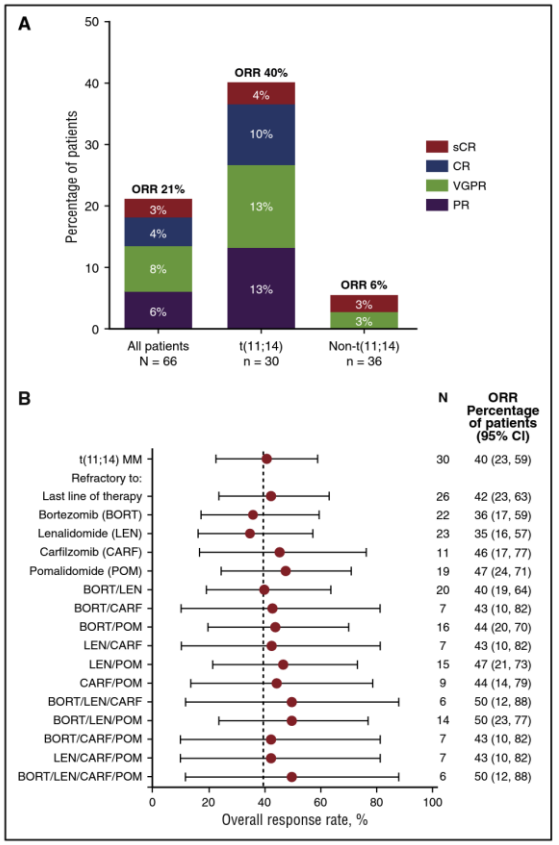
[a]Defined as PR or better.

Lonial S et al. 2021 ASH. Abstract 162.

# VENETOCLAX



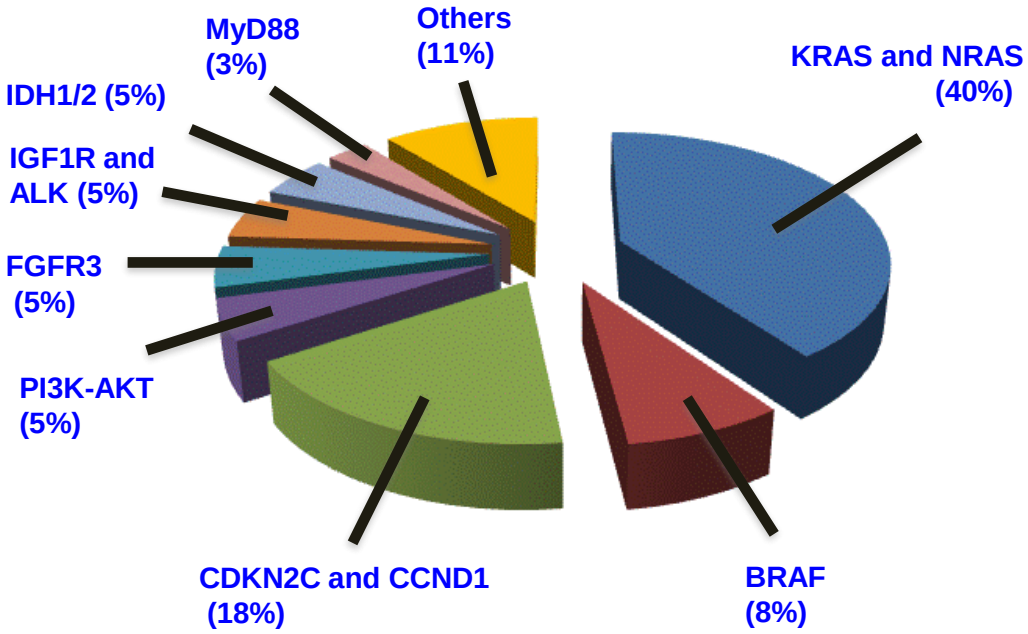

Ehsan, et al. J Hematol. 2021 Jun;10(3):89-97.

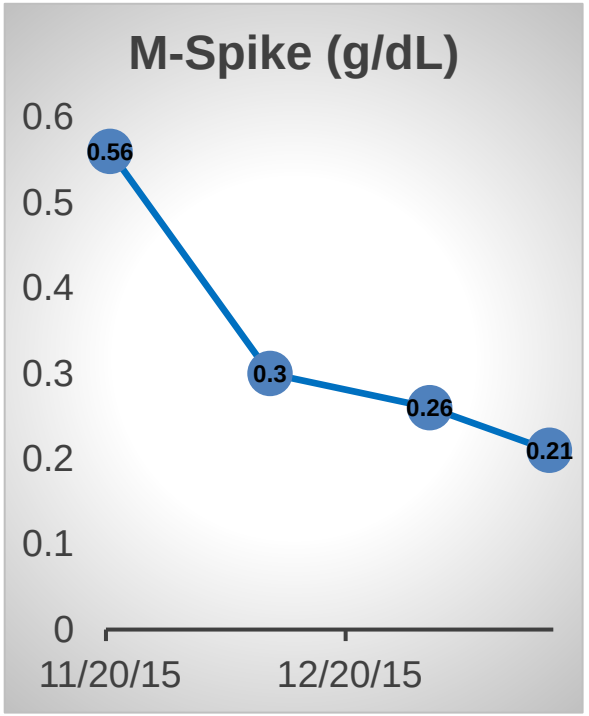



Kumar, et al. Blood. 2017 Nov 30;130(22):2401-2409

# MEK INHIBITOR "REPURPOSED" FOR MYELOMA

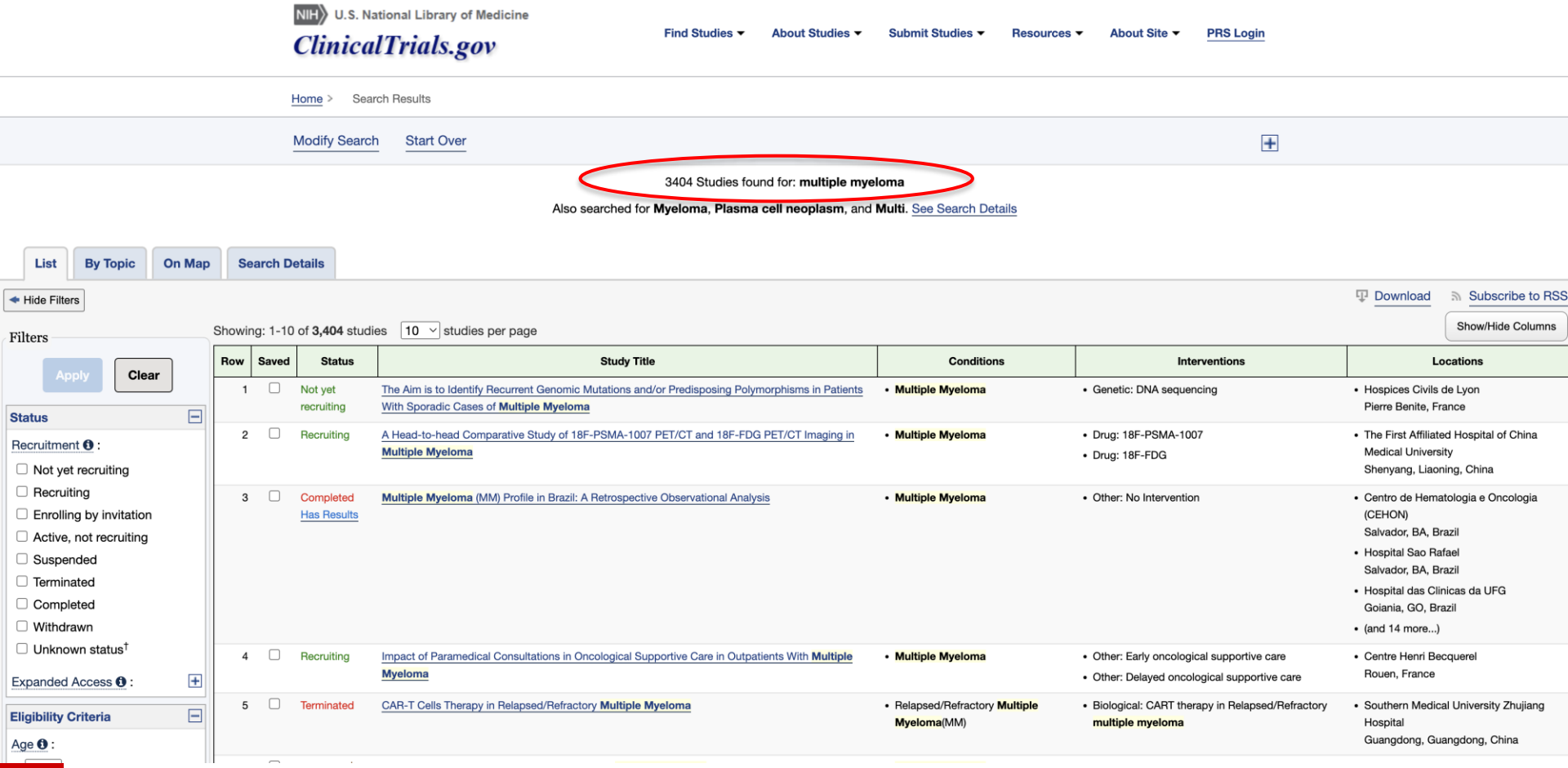
"Actionable" Genomic Alterations: occur in ~50% of patients




Lohr et al. Cancer Cell. 2014; 25: 91-101

# A PATH TO CURE!!!



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Also searched for **Myeloma**, **Plasma cell neoplasm**, and **Multi**. See Search Details

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**Status**

Recruitment :

- Not yet recruiting
- Recruiting
- Enrolling by invitation
- Active, not recruiting
- Suspended
- Terminated
- Completed
- Withdrawn
- Unknown status†

Expanded Access :

**Eligibility Criteria**

Age :

Showing: 1-10 of **3,404** studies 10 studies per page

| Row | Saved | Status | Study Title | Conditions | Interventions | Locations |
|---|---|---|---|---|---|---|
| 1 | ☐ | Not yet recruiting | The Aim is to Identify Recurrent Genomic Mutations and/or Predisposing Polymorphisms in Patients With Sporadic Cases of **Multiple Myeloma** | • **Multiple Myeloma** | • Genetic: DNA sequencing | • Hospices Civils de Lyon<br>Pierre Benite, France |
| 2 | ☐ | Recruiting | A Head-to-head Comparative Study of 18F-PSMA-1007 PET/CT and 18F-FDG PET/CT Imaging in **Multiple Myeloma** | • **Multiple Myeloma** | • Drug: 18F-PSMA-1007<br>• Drug: 18F-FDG | • The First Affiliated Hospital of China Medical University<br>Shenyang, Liaoning, China |
| 3 | ☐ | Completed<br>Has Results | **Multiple Myeloma** (MM) Profile in Brazil: A Retrospective Observational Analysis | • **Multiple Myeloma** | • Other: No Intervention | • Centro de Hematologia e Oncologia (CEHON)<br>Salvador, BA, Brazil<br>• Hospital Sao Rafael<br>Salvador, BA, Brazil<br>• Hospital das Clinicas da UFG<br>Goiania, GO, Brazil<br>• (and 14 more...) |
| 4 | ☐ | Recruiting | Impact of Paramedical Consultations in Oncological Supportive Care in Outpatients With **Multiple Myeloma** | • **Multiple Myeloma** | • Other: Early oncological supportive care<br>• Other: Delayed oncological supportive care | • Centre Henri Becquerel<br>Rouen, France |
| 5 | ☐ | Terminated | CAR-T Cells Therapy in Relapsed/Refractory **Multiple Myeloma** | • Relapsed/Refractory **Multiple Myeloma**(MM) | • Biological: CART therapy in Relapsed/Refractory **multiple myeloma** | • Southern Medical University Zhujiang Hospital<br>Guangdong, Guangdong, China |



https://clinicaltrials.gov/ct2/results?cond=multiple+myeloma&term=&cntry=&state=&city=&dist Access date 9/16/22

# THANK YOU