Updates in Multiple Myeloma

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November 8, 2025

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UPDATES IN MULTIPLE MYELOMA

INCIDENCE: Represents 1.8% of all new cancer diagnoses in US

36,110 new cases (20,030 in men, 16,080 in women) - 1.8%

Average lifetime risk < 1%

Average age at diagnosis: 69

SURVIVAL: 12,030 deaths (6,540 in men, 5,490 in women) - 1.9%

5-Year Survival: 62.4% (2015 - 2021)

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UPDATES IN MULTIPLE MYELOMA

Presentation/Diagnosis

Treatment

- Induction/Consolidation/Maintenance
- Autologous Stem Cell Transplantation
- CAR-T Cell/BiTE Therapy

Supportive Care

Survivorship

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CONCLUSIONS

Symptoms at presentation of MM are often nonspecific and diagnosis requires a high threshold of suspicion

Multi-drug regimens, ASCT, BiTE Therapy and CAR-T Cells are prominent treatment modalities in MM

Treatments in MM have resulted in significant improvement of overall survival

Survivorship and ongoing supportive care is crucial in patients after MM treatment, given prolonged remission duration but also high risk of relapse.

Case #1

HPI: 67 y/o woman presented to her PCP with worsening weakness/fatigue over the past 4 months. Dyspnea on exertion, though recovers with rest; no chest pain or palpitations. No nausea/vomiting, but appetite is down and she has lost 8 lbs in the past few months. No bone pain. No fevers/chills or night sweats.

LABS:
CBC - Hb 9.2 g/dL, Plt 477, MCV 78

CMP - Cr 1.6, Alb 3.1

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Case #2

HPI: 69 y/o woman presented to her PCP with worsening weakness/fatigue over the past 3 months. No dyspnea or chest pain, but her energy level is low and she is not able to exercise at her previous baseline. No nausea/vomiting, but appetite is down and she has lost 10 lbs in the past few months. No bone pain. No fevers/chills or night sweats.

LABS:
CBC - Hb 9.2 g/dL, o/w WNL

CMP - Cr 1.5, Ca 10.8, tProt 9.7, Alb 3.2

Common Presenting Symptoms/Signs

Symptoms	Labs
Fatigue	hyper**C**alcemia
Bone Pain/Fractures	**R**enal dysfunction
Nausea/vomiting/thirst	**A**nemia
Frequent infections	**B**one lytic lesions
Weight loss	Monoclonal gammopathy

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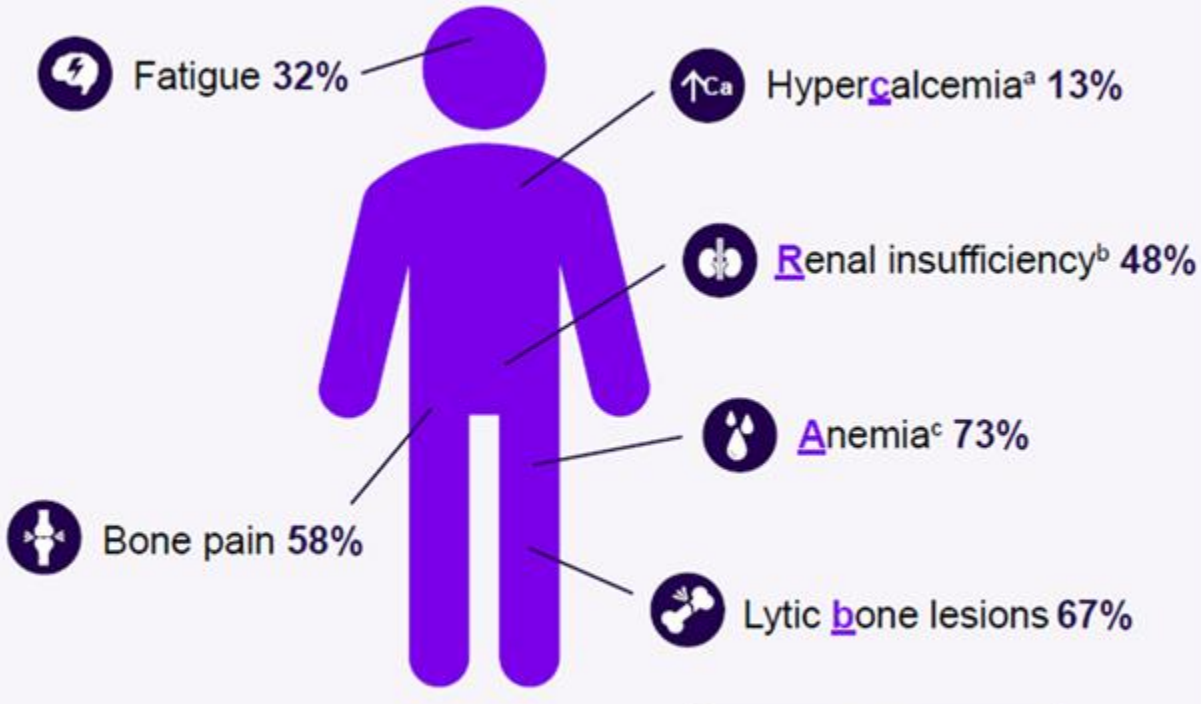
How to RECOGNIZE
Signs and Symptoms of Multiple Myeloma



Other: Neuropathy, repeated infections, bruising/bleeding

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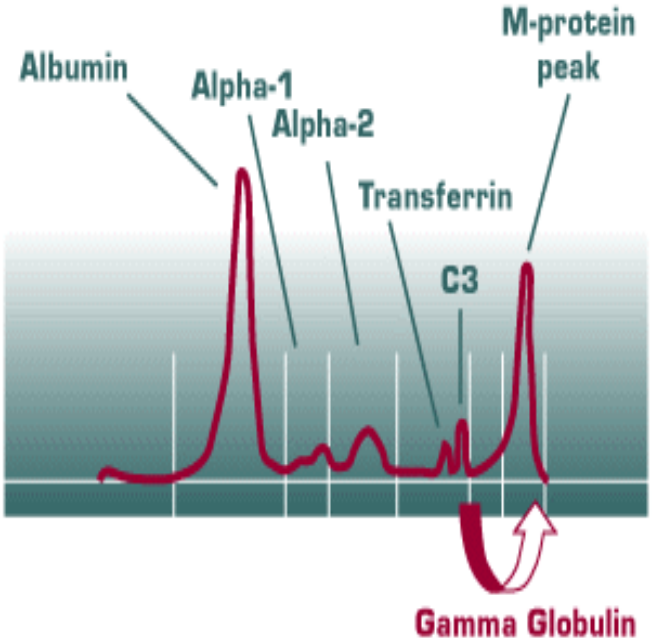

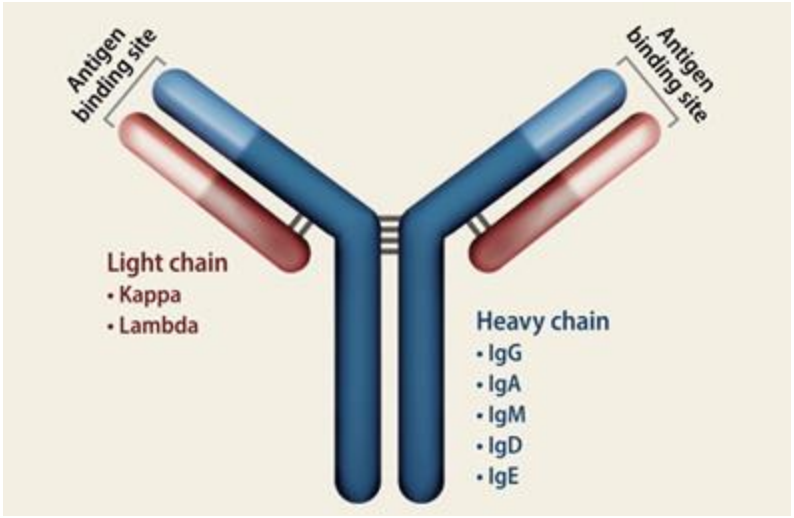

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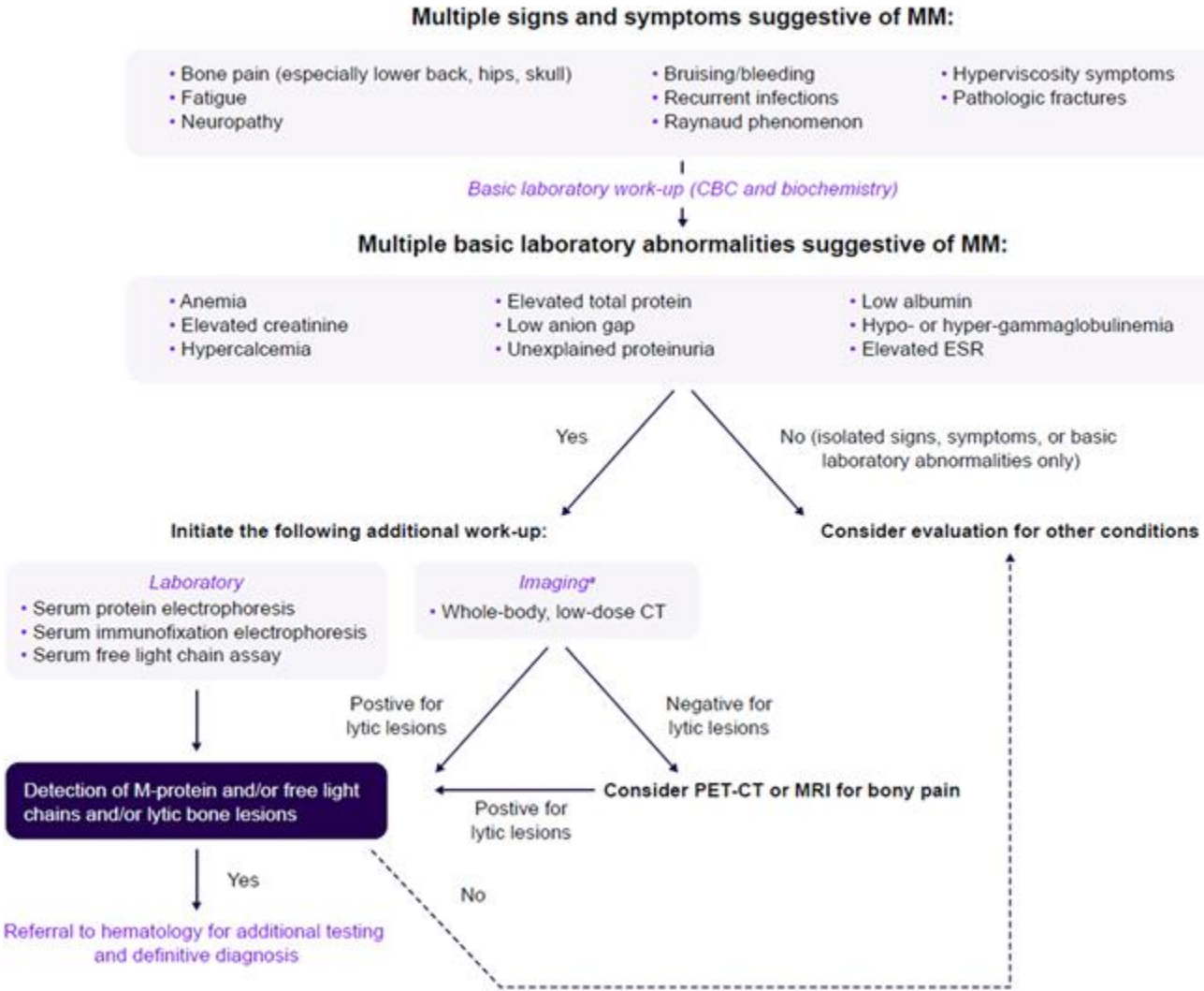

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Disease	Definition
Smoldering Myeloma[a,b] (Asymptomatic)	• Serum monoclonal protein ≥3 g/dL or • Bence-Jones protein ≥500 mg/24 h and/or • Clonal bone marrow plasma cells (BMPCs) 10%–59% and • Absence of myeloma-defining events or amyloidosis
Multiple Myeloma[a,c] (Symptomatic)	• Clonal BMPCs ≥10% or biopsy-proven bony or extramedullary plasmacytoma and any one or more of the following myeloma-defining events: • Myeloma-defining events: ▸ Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically: ◊ Hypercalcaemia: serum calcium >0·25 mmol/L (>1 mg/dL) higher than the upper limit of normal or >2·75 mmol/L (>11 mg/dL) ◊ Renal insufficiency: creatinine clearance <40 mL per min or serum creatinine >177 μmol/L (>2 mg/dL) ◊ Anaemia: haemoglobin value of >20 g/L below the lower limit of normal, or a haemoglobin value <100 g/L ◊ Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT ▸ Any one or more of the following biomarkers of malignancy: ◊ Clonal bone marrow plasma cell percentage ≥60% ◊ Involved:uninvolved serum free light chain ratio ≥100 ◊ >1 focal lesions on MRI studies
Solitary Plasmacytoma[a]	• Biopsy-proven solitary lesion of bone or soft tissue with evidence of clonal plasma cells • Normal skeletal survey and MRI (or CT) of spine and pelvis (except for the primary solitary lesion) • Absence of myeloma defining events • Normal bone marrow with no evidence of clonal plasma cells
Solitary Plasmacytoma with minimal marrow involvement[a]	• Biopsy-proven solitary lesion of bone or soft tissue with evidence of clonal plasma cells • Normal skeletal survey and MRI (or CT) of spine and pelvis (except for the primary solitary lesion) • Absence of myeloma defining events • Clonal bone marrow plasma cells <10%
Plasma Cell Leukemia	• Presence of ≥5% of plasma cells in circulation

Factors Considered as High Risk for Progression/Relapse	
For Those with Newly Diagnosed MM	**For Those with Relapsed MM**

• R-ISS III (MYEL-B 1 of 2)
• Extramedullary disease
• Circulating plasma cells
• Cytogenetic abnormalities[c]
  ▸ Del(1p32)
  ▸ t(4;14)
  ▸ t(14;16)
  ▸ t(14;20)
  ▸ Del(17p)/monosomy 17/*TP53* mutation
  ▸ 1q21 gain/1q21 amplification[d,4]
  ▸ MYC translocation[5]
• High-risk gene expression profile
• Markers of high proliferation rate
	• Disease relapse within 2 years of initial therapy when transplant and maintenance are used.
	
	• Relapse within 18 months in case of non-transplant–based treatment.
	
	• Acquisition of 1q gain/amplification and/or del(17p)/*TP53* mutation
	
	• Extramedullary disease at relapse and/or circulating plasma cells

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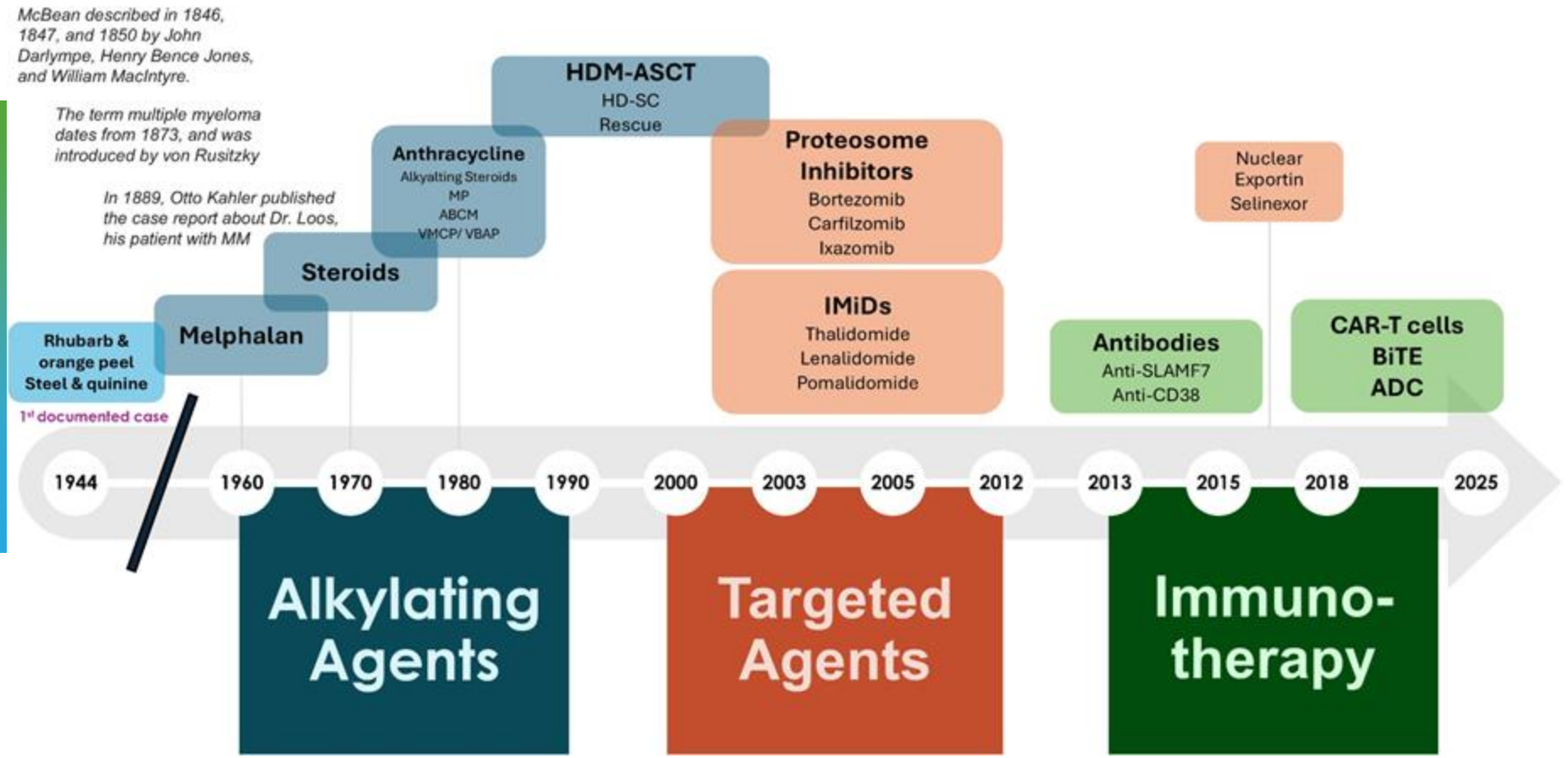
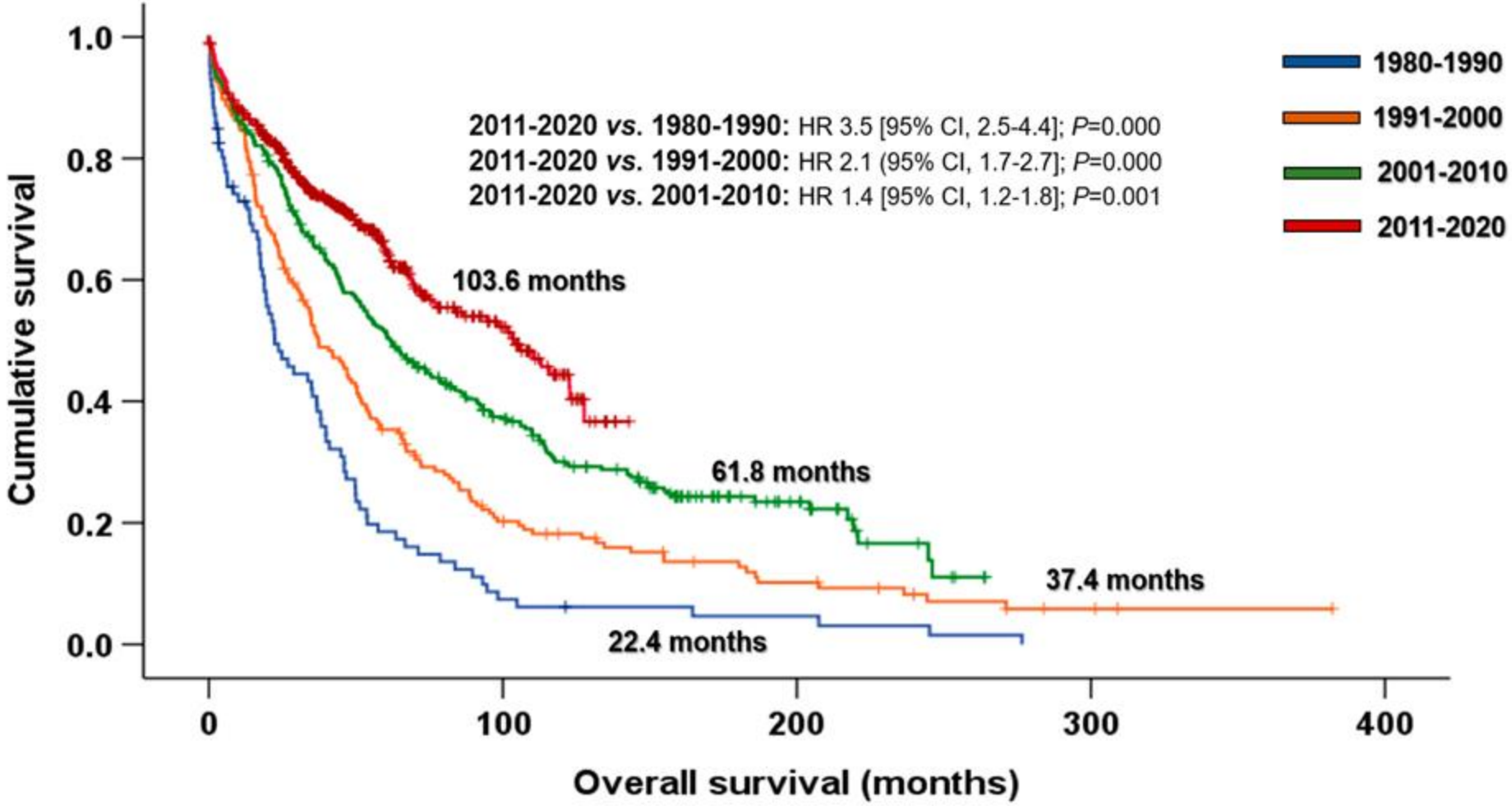
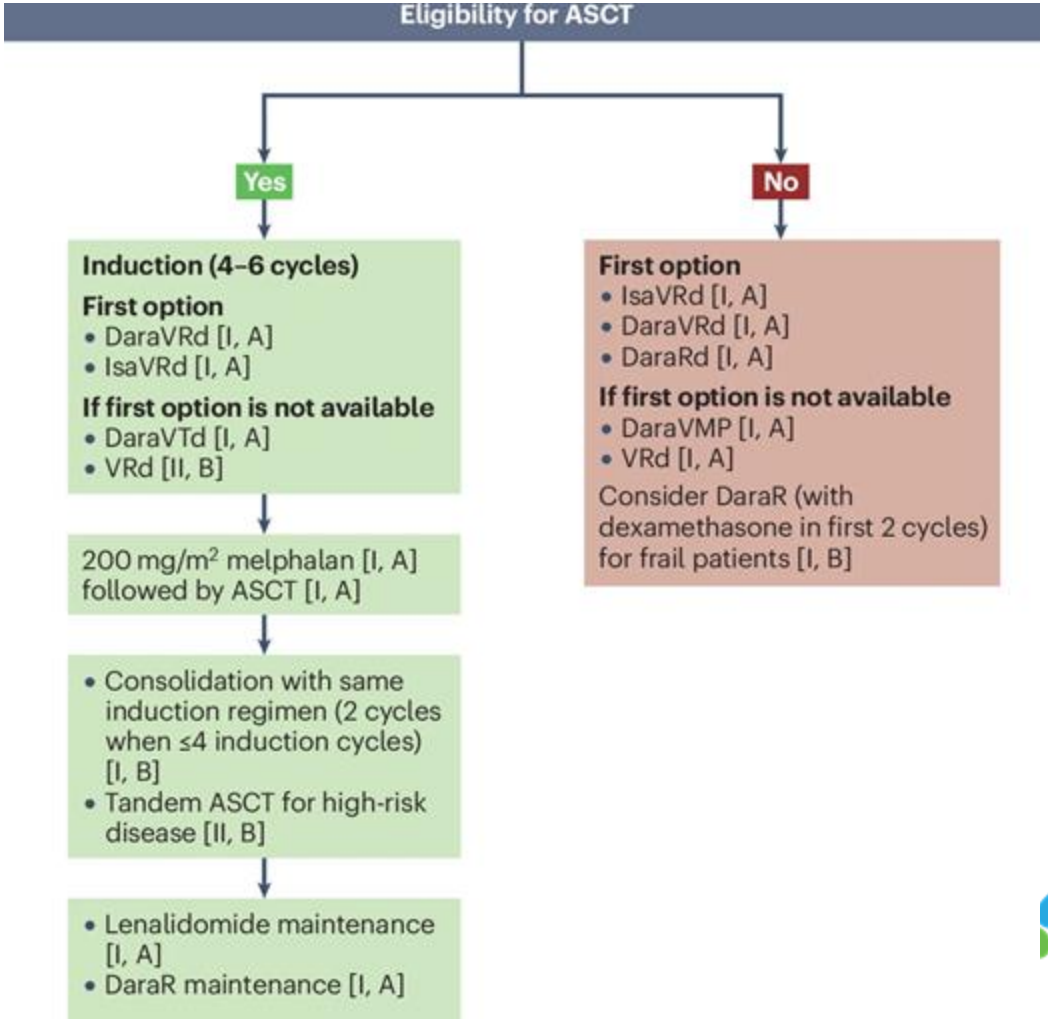
Eras of Multiple Myeloma Treatment




1.0
0.8
0.6
0.4
0.2
0.0
Cumulative survival
0
100
200
300
400
Overall survival (months)
2011-2020 vs. 1980-1990: HR 3.5 [95% CI, 2.5-4.4]; P=0.000
2011-2020 vs. 1991-2000: HR 2.1 (95% CI, 1.7-2.7]; P=0.000
2011-2020 vs. 2001-2010: HR 1.4 [95% CI, 1.2-1.8]; P=0.001
1980-1990
1991-2000
2001-2010
2011-2020
103.6 months
61.8 months
37.4 months
22.4 months



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IMiDs – Lenalidomide

T-cell and NK cell activation

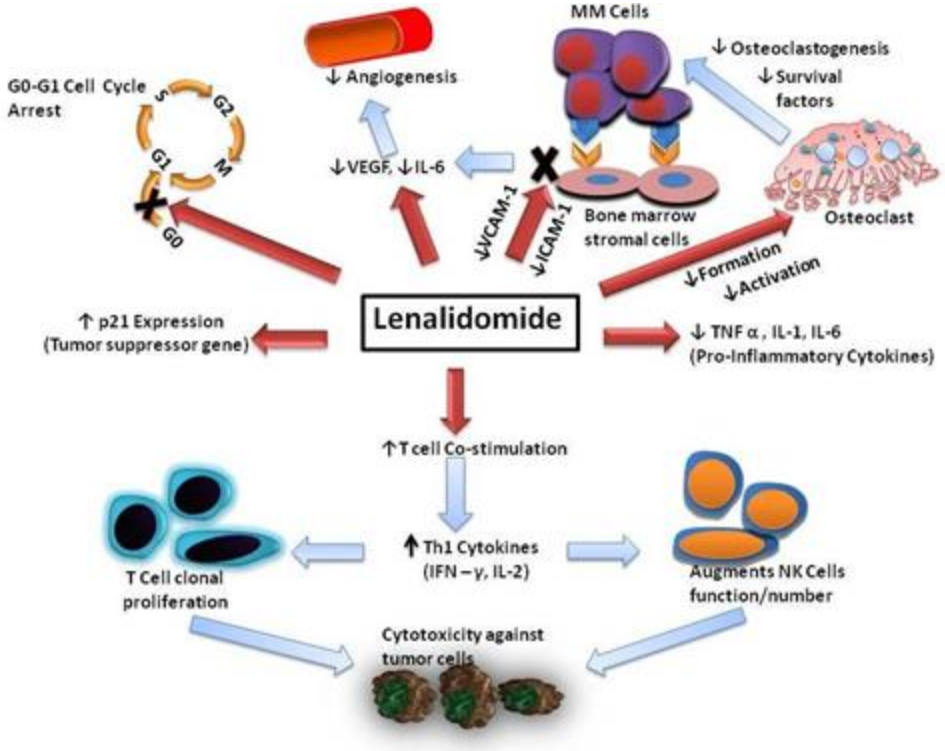
Anti-angiogenesis

Direct antitumor activity

Alters bone marrow microenvironment

Toxicities:

- Myelosuppression
- Hypercoagulable state
- Hepatotoxicity



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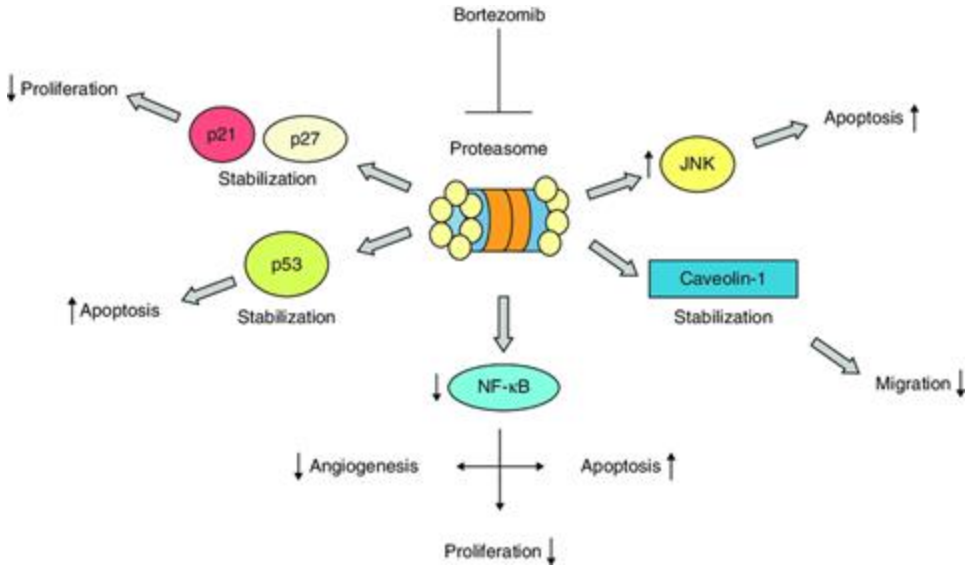
Proteosome Inhibitor – Bortezomib



Blocks NF-KB → protein accumulation

Induces apoptosis

Blocks cellular signaling

Cytokine inhibition

Toxicities:

- Neuropathy
- Autonomic dysfunction
- Myelosuppression

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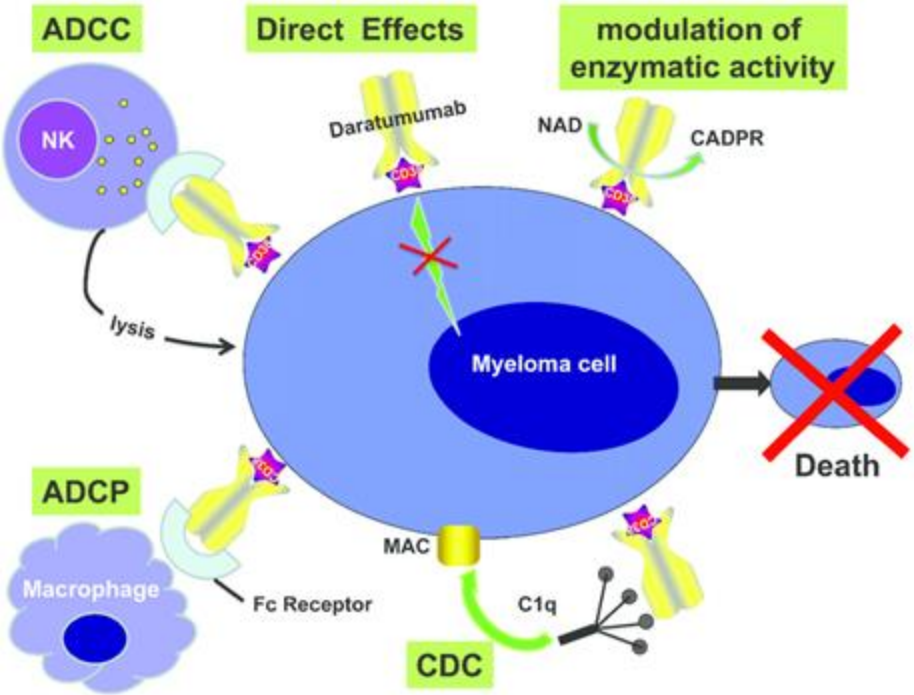
Monoclonal Antibodies – Daratumumab/Isatuximab

Binds CD-38

- Direct antineoplastic effects
- Recruits macrophages/NK cells
- Recruits complement

Toxicities:

- Infusion related reactions
- Myelosuppression
- GI symptoms
- Pulmonary toxicity



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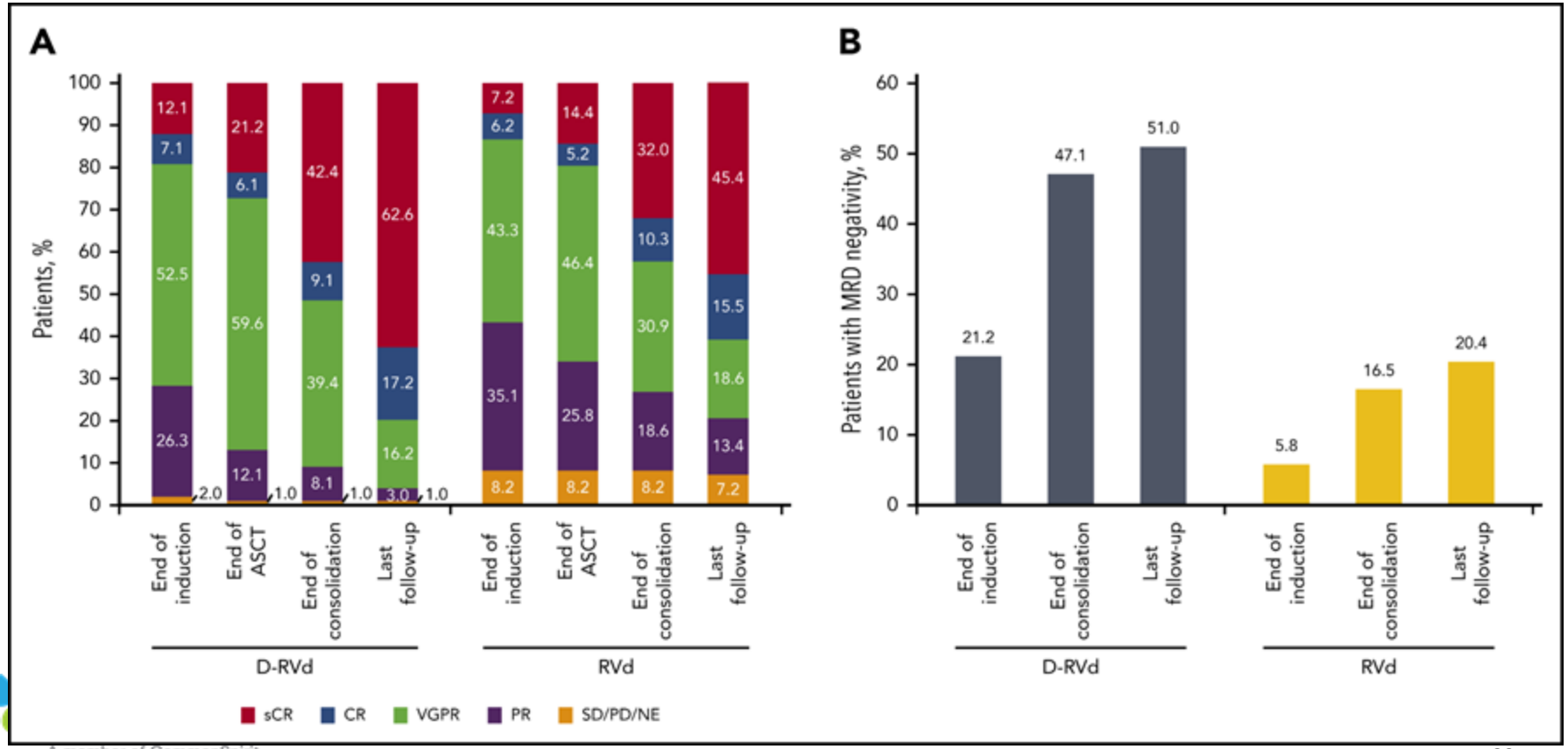
Dara/RVd


A
Patients, %
100
90
80
70
60
50
40
30
20
10
0
12.1
7.1
52.5
26.3
2.0
21.2
6.1
59.6
12.1
1.0
42.4
9.1
39.4
8.1
1.0
62.6
17.2
16.2
3.0
1.0
7.2
6.2
43.3
35.1
8.2
14.4
5.2
46.4
25.8
8.2
32.0
10.3
30.9
18.6
8.2
45.4
15.5
18.6
13.4
7.2
End of induction
End of ASCT
End of consolidation
Last follow-up
End of induction
End of ASCT
End of consolidation
Last follow-up
D-RVd
RVd
sCR
CR
VGPR
PR
SD/PD/NE
B
Patients with MRD negativity, %
60
50
40
30
20
10
0
21.2
47.1
51.0
5.8
16.5
20.4
End of induction
End of consolidation
Last follow-up
End of induction
End of consolidation
Last follow-up
D-RVd
RVd

Multiple Myeloma Response Criteria

Response category[†]	Criteria
Complete remission	All the following criteria: Negative IFE (serum and urine) <5% bone marrow plasma cells Disappearance of soft tissue plasmacytomas
Stringent complete remission	As above plus Normal serum free light chain ratio Absence of clonal plasma cells[‡]
Very good partial response	All the following criteria: ≥90% serum M-protein ⇓ Urine M-protein <100 mg/24 h
Partial response	All the following criteria: ≥50% serum M-protein ⇓ ≥90% urine M-protein ⇓ or <200 mg/24 h ≥50% ⇓ soft tissue plasmacytomas

[†]All response categories require two consecutive measurements made at any time.
[‡]Bone marrow plasma cells analyzed by immunohistochemistry and/or multiparametric flow cytometry.
IFE: Immunofixation electrophoresis.
Adapted from [11].

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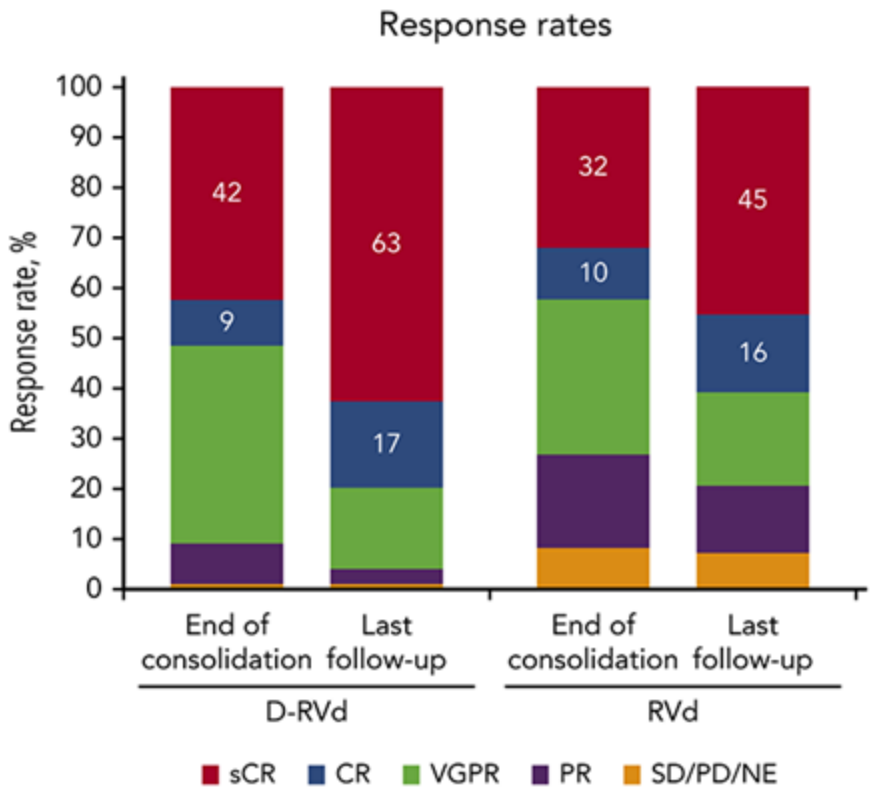
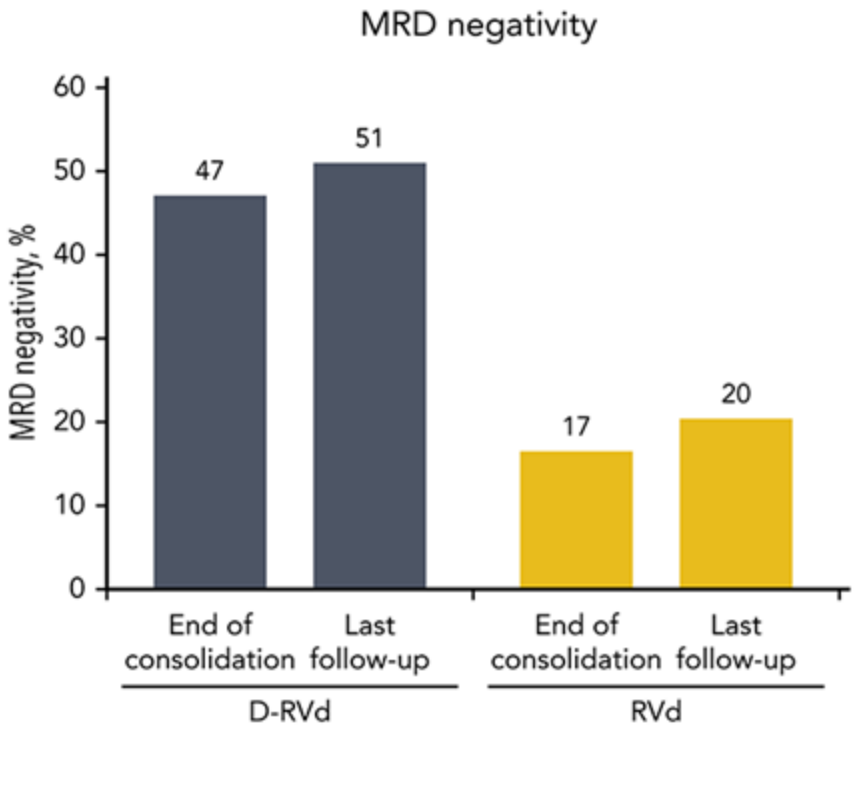
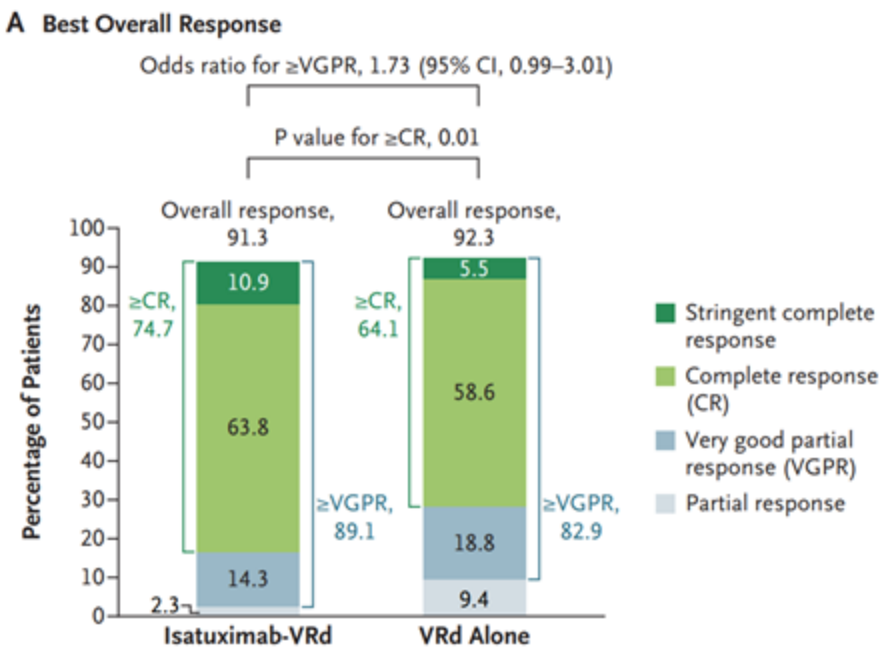
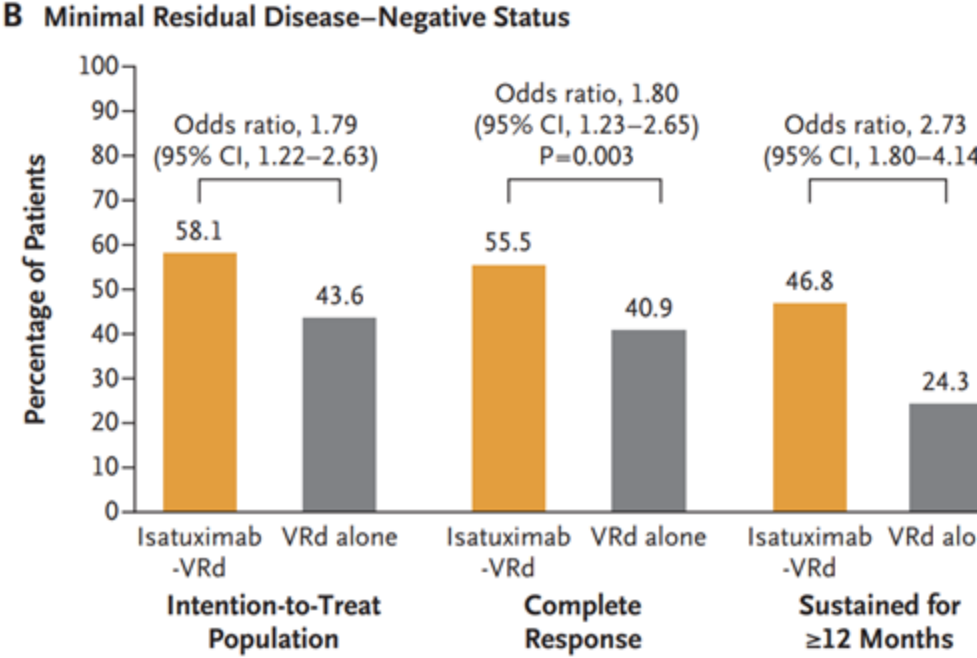
Daratumumab plus lenalidomide/bortezomib/dexamethasone (D-RVd) in transplant-eligible NDMM improves depth of response and MRD negativity (10^{-5}) over time.





Isa/RVd





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Autologous Stem Cell Transplant

Trial	Phase	Design	Follow Up	sCR (MRD) [a]	PFS
CASSIOPEIA [23,24]	3	VTd vs. D-VTd induction (4 cycles) and consolidation (2 cycles), with D maintenance or observation	Day 100 after ASCT	29% vs. 20% (64% vs. 44%)	NR vs. 47 mo [b]
GRIFFIN [25,26]	2	D-VRd induction (4 cycles) and consolidation (2 cycles) plus DR maintenance or VRd induction (4 cycles) and consolidation (2 cycles) plus R maintenance	50 mo	67% vs. 48% (64% vs. 30%)	87% vs. 70%
PERSEUS [27]	3	D-VRd induction (4 cycles) and consolidation (2 cycles) plus DR maintenance [c] or VRd induction (4 cycles) and consolidation (2 cycles) plus R maintenance	48 mo	88% vs. 70% [d] (75% vs. 48%)	84% vs. 68%
MASTER [28]	2	D-KRd induction (4 cycles) and consolidation (2 cycles), with R maintenance or observation [e]	42 mo	78% vs. 86% vs. 79% [f]	88% vs. 79% vs. 50% [f]
GMMG-HD7 [34]	3	Isa-VRd vs. VRd induction (3 cycles) with maintenance with Isa-R or R	After induction therapy	(50% vs. 36%)	Ongoing [g]
GMMG-CONCEPT [35]	2	Isa-KRd induction (6 cycles) and consolidation (4 cycles) with Isa-KR maintenance [h]	44 mo	73% (68%) [i]	NR

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THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA[a-d,l-o] Relapsed/Refractory Disease After 1–3 Prior Therapies		
Preferred* *Order of regimens does not indicate comparative efficacy*		
Anti-CD38 Refractory	**Bortezomib-Refractory**	**Lenalidomide-Refractory**
• Carfilzomib/Lenalidomide/Dexamethasone (category 1) • Carfilzomib/Pomalidomide/Dexamethasone • Pomalidomide/Bortezomib/Dexamethasone (category 1) ***After two prior therapies including lenalidomide and a proteasome inhibitor (PI)*** ▸ Elotuzumab/Pomalidomide/Dexamethasone ***After two prior therapies including an IMiD and a PI and with disease progression on/within 60 days of completion of last therapy*** ▸ Ixazomib/Pomalidomide/Dexamethasone	• Carfilzomib/Lenalidomide/Dexamethasone (category 1) • Daratumumab/Carfilzomib/Dexamethasone (category 1) • Daratumumab/Lenalidomide/Dexamethasone (category 1) • Isatuximab-irfc/Carfilzomib/Dexamethasone (category 1) • Carfilzomib/Pomalidomide/Dexamethasone ***After one prior therapy including Lenalidomide and a PI*** ▸ Daratumumab/Pomalidomide/Dexamethasone (category 1) ***After two prior therapies including Lenalidomide and a PI*** ▸ Isatuximab-irfc/Pomalidomide/Dexamethasone (category 1) ▸ Elotuzumab/Pomalidomide/Dexamethasone	• Daratumumab/Bortezomib/Dexamethasone (category 1) • Daratumumab/Carfilzomib/Dexamethasone (category 1) • Isatuximab-irfc/Carfilzomib/Dexamethasone (category 1) • Pomalidomide/Bortezomib/Dexamethasone (category 1) • Carfilzomib/Pomalidomide/Dexamethasone ***After one prior therapy including Lenalidomide and a PI*** ▸ Daratumumab/Pomalidomide/Dexamethasone (category 1) ***After two prior therapies including Lenalidomide and a PI*** ▸ Isatuximab-irfc/Pomalidomide/Dexamethasone (category 1) ▸ Elotuzumab/Pomalidomide/Dexamethasone ***After two prior therapies including an IMiD and a PI and with disease progression on/within 60 days of completion of last therapy*** ▸ Ixazomib/Pomalidomide/Dexamethasone
CAR T-Cell Therapy ***After one prior line of therapy including IMiD and a PI, and refractory to lenalidomide*** ▸ Ciltacabtagene autoleucel (category 1) ***After two prior lines of therapies including an IMiD, an anti-CD38 monoclonal antibody and a PI*** ▸ Idecabtagene vicleucel (category 1)		

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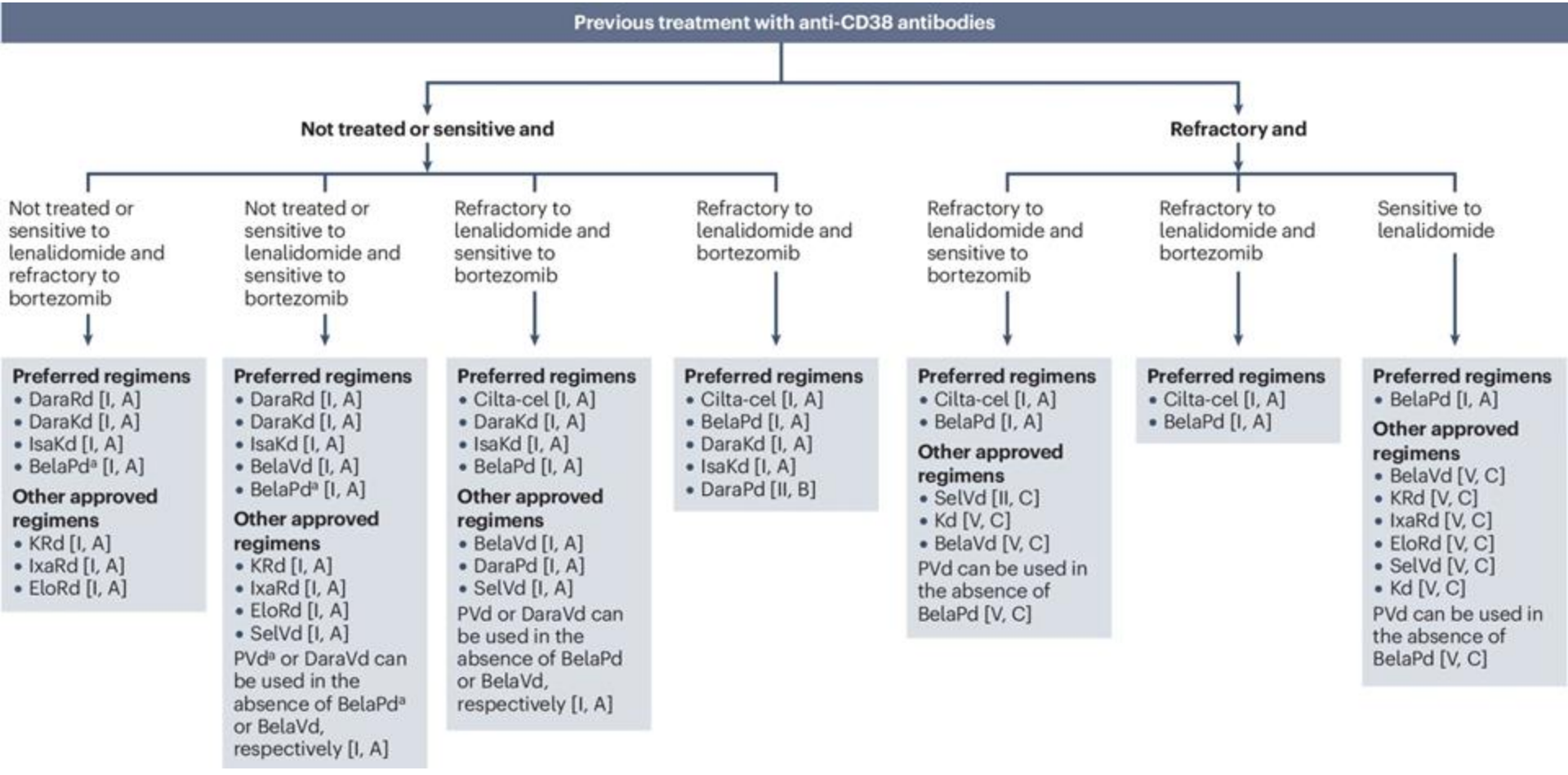
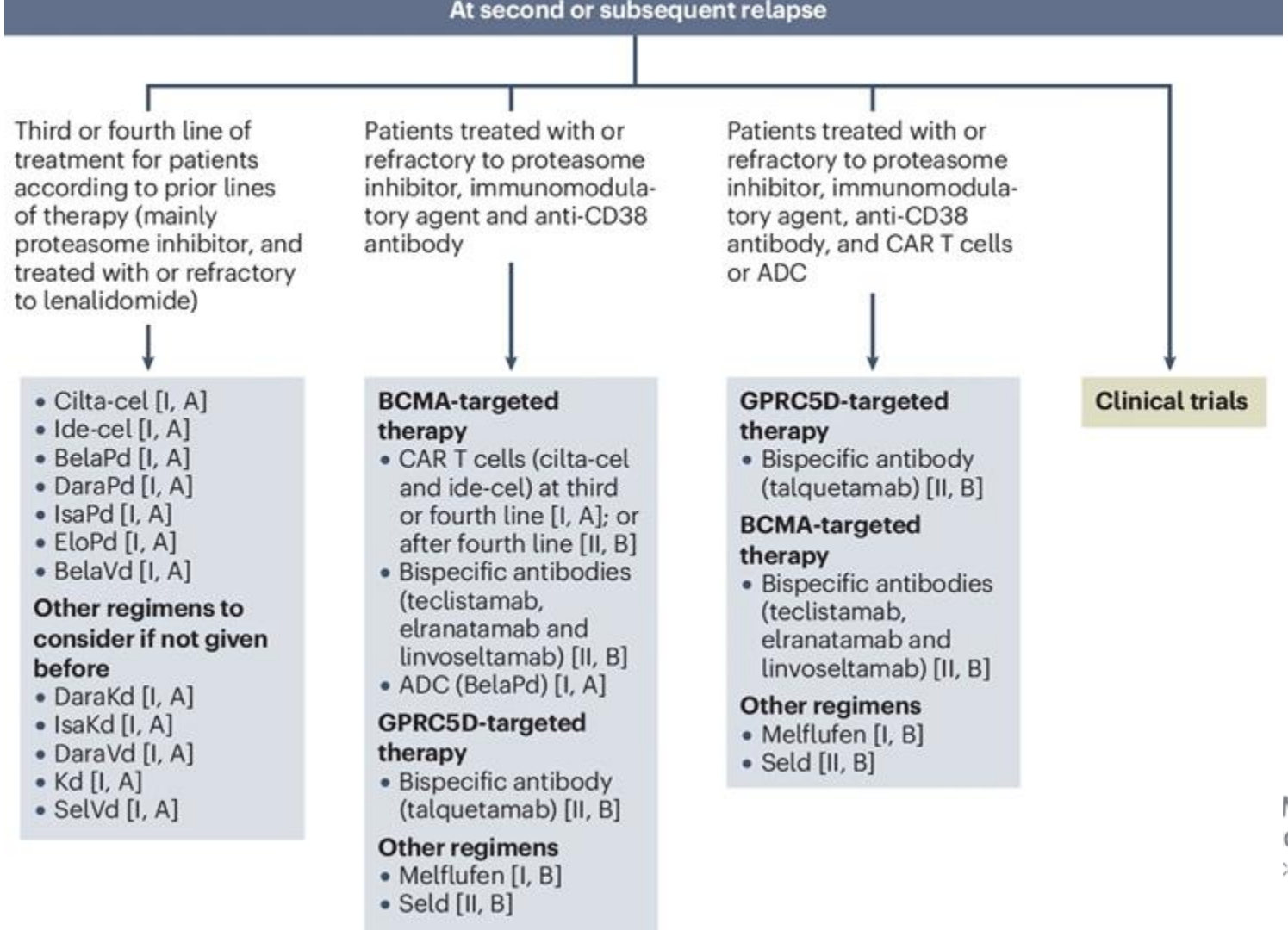

Previous treatment with anti-CD38 antibodies
Not treated or sensitive and
Refractory and
Not treated or sensitive to lenalidomide and refractory to bortezomib
Preferred regimens
• DaraRd [I, A]
• DaraKd [I, A]
• IsaKd [I, A]
• BelaPd[a] [I, A]
Other approved regimens
• KRd [I, A]
• IxaRd [I, A]
• EloRd [I, A]
Not treated or sensitive to lenalidomide and sensitive to bortezomib
Preferred regimens
• DaraRd [I, A]
• DaraKd [I, A]
• IsaKd [I, A]
• BelaVd [I, A]
• BelaPd[a] [I, A]
Other approved regimens
• KRd [I, A]
• IxaRd [I, A]
• EloRd [I, A]
• SelVd [I, A]
PVd[a] or DaraVd can be used in the absence of BelaPd[a] or BelaVd, respectively [I, A]
Refractory to lenalidomide and sensitive to bortezomib
Preferred regimens
• Cilta-cel [I, A]
• DaraKd [I, A]
• IsaKd [I, A]
• BelaPd [I, A]
Other approved regimens
• BelaVd [I, A]
• DaraPd [I, A]
• SelVd [I, A]
PVd or DaraVd can be used in the absence of BelaPd or BelaVd, respectively [I, A]
Refractory to lenalidomide and bortezomib
Preferred regimens
• Cilta-cel [I, A]
• BelaPd [I, A]
• DaraKd [I, A]
• IsaKd [I, A]
• DaraPd [II, B]
Refractory to lenalidomide and sensitive to bortezomib
Preferred regimens
• Cilta-cel [I, A]
• BelaPd [I, A]
Other approved regimens
• SelVd [II, C]
• Kd [V, C]
• BelaVd [V, C]
PVd can be used in the absence of BelaPd [V, C]
Refractory to lenalidomide and bortezomib
Preferred regimens
• Cilta-cel [I, A]
• BelaPd [I, A]
Sensitive to lenalidomide
Preferred regimens
• BelaPd [I, A]
Other approved regimens
• BelaVd [V, C]
• KRd [V, C]
• IxaRd [V, C]
• EloRd [V, C]
• SelVd [V, C]
• Kd [V, C]
PVd can be used in the absence of BelaPd [V, C]



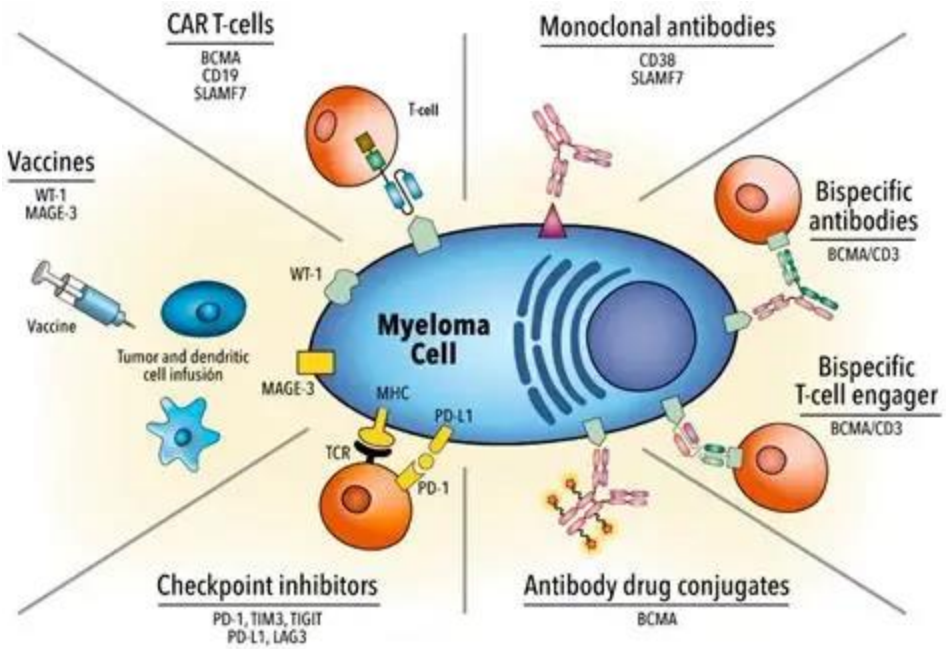
Treatment options for RRMM

Carfilzomib/Ixazomib

Pomalidomide

Elotuzomab

Selinexor - XPO1 inhibitor



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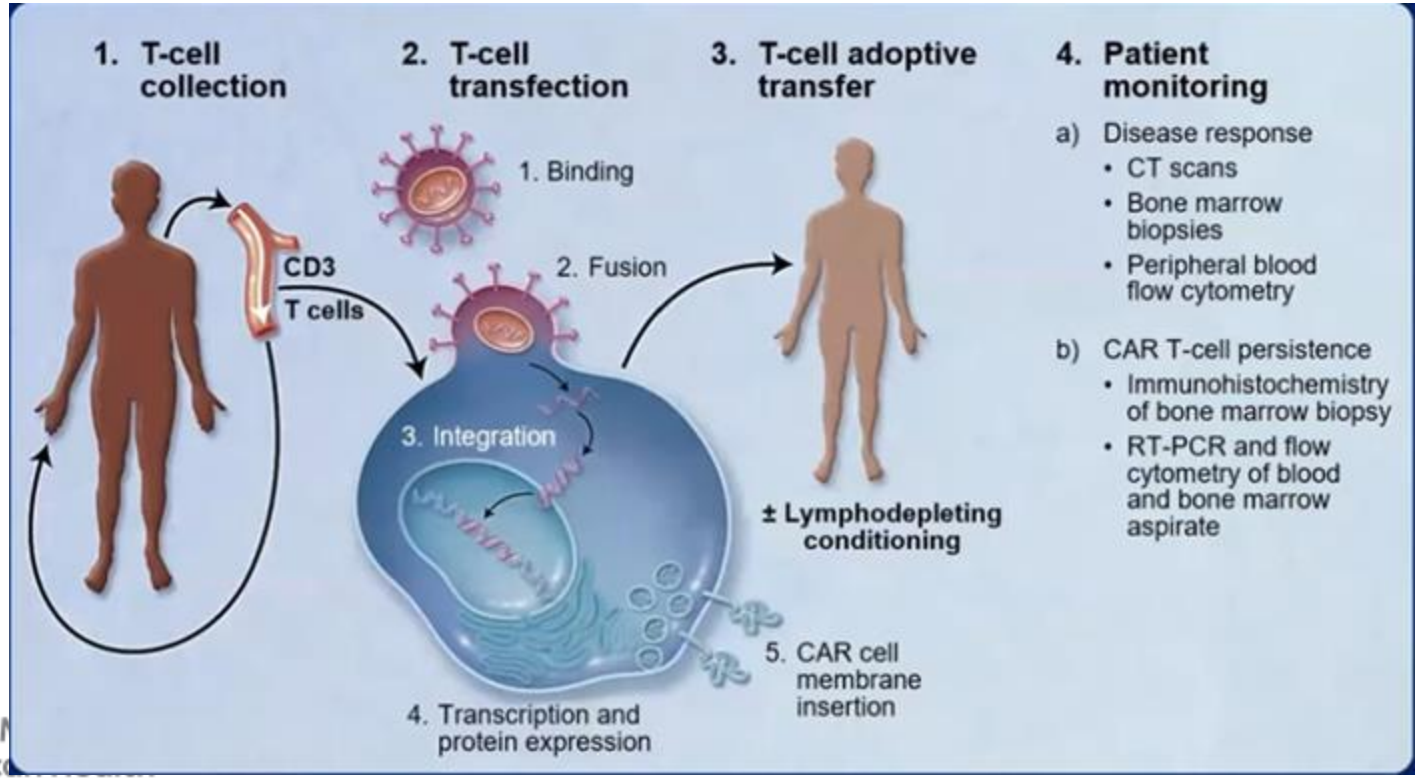
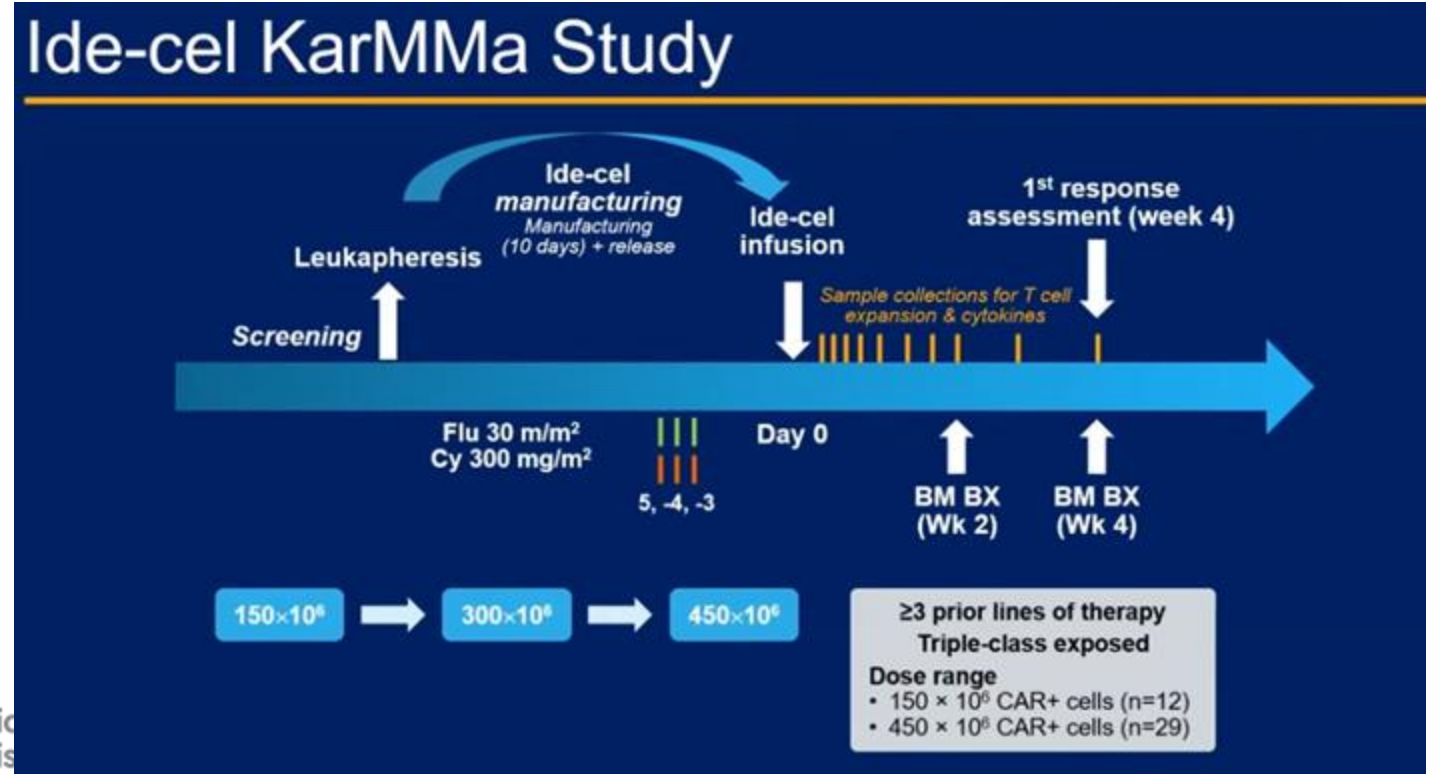
Chimeric Antigen Receptor (CAR)-T Cell

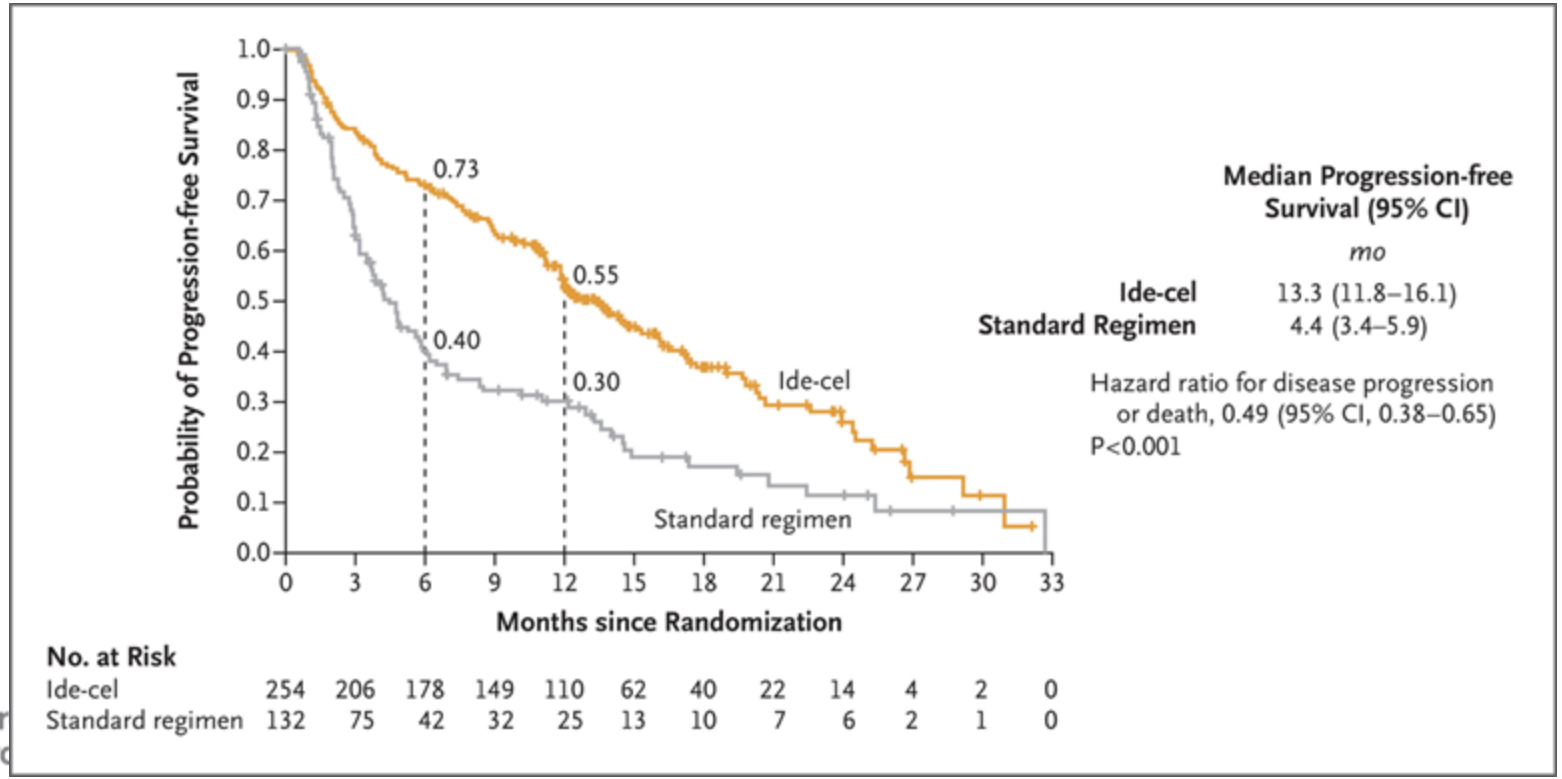


Antigen	Expression in nonmalignant cells	Expression in multiple myeloma	Clinical trial of CAR Ts in myeloma
CD38	Precursor B cells, **plasma cells**, T cells, NK cells, myeloid precursors, RBCs, prostate cells, nervous system, osteoclasts, muscle cells	Strong, uniform expression on myeloma cells	**Yes**
CD138	**Plasma cells**, salivary glands, liver, skin	Expressed on MM cells	**Yes**
CD19	Mature B cells	Minimal expression on MM cell surface (some exceptions).	**Yes**
Immunoglobulin κ light chain	Mature B cells	Potential target on B cells that represent MM stem cells and that express surface immunoglobulins	**Yes**
SLAMF7	**Plasma cells**, NK cells, $CD8^+$ cells, activated monocytes and B cells, dendritic cells	Expressed by MM cells	**Yes**
BCMA	**Plasma cells**, small subset of B cells	Expressed on MM cells	**Yes**
GPRC5D	**Plasma cells**	Expressed on MM cells	**Yes**

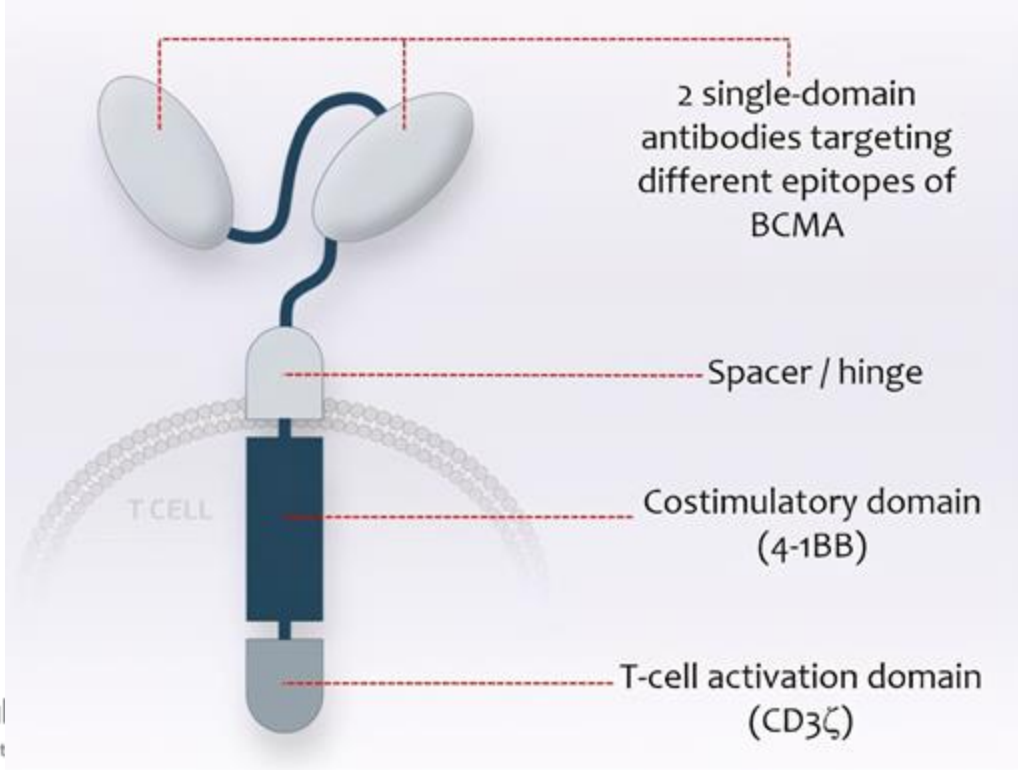
Idecaptagene-vicleucel (Ide-cel)



Ide-Cel


Probability of Progression-free Survival
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0.73
0.55
0.40
0.30
Ide-cel
Standard regimen
0 3 6 9 12 15 18 21 24 27 30 33
Months since Randomization
No. at Risk
Ide-cel 254 206 178 149 110 62 40 22 14 4 2 0
Standard regimen 132 75 42 32 25 13 10 7 6 2 1 0
Median Progression-free Survival (95% CI)
mo
Ide-cel 13.3 (11.8–16.1)
Standard Regimen 4.4 (3.4–5.9)
Hazard ratio for disease progression or death, 0.49 (95% CI, 0.38–0.65)
P<0.001

Ciltacabtagene-autoleucel (Cilta-Cel)



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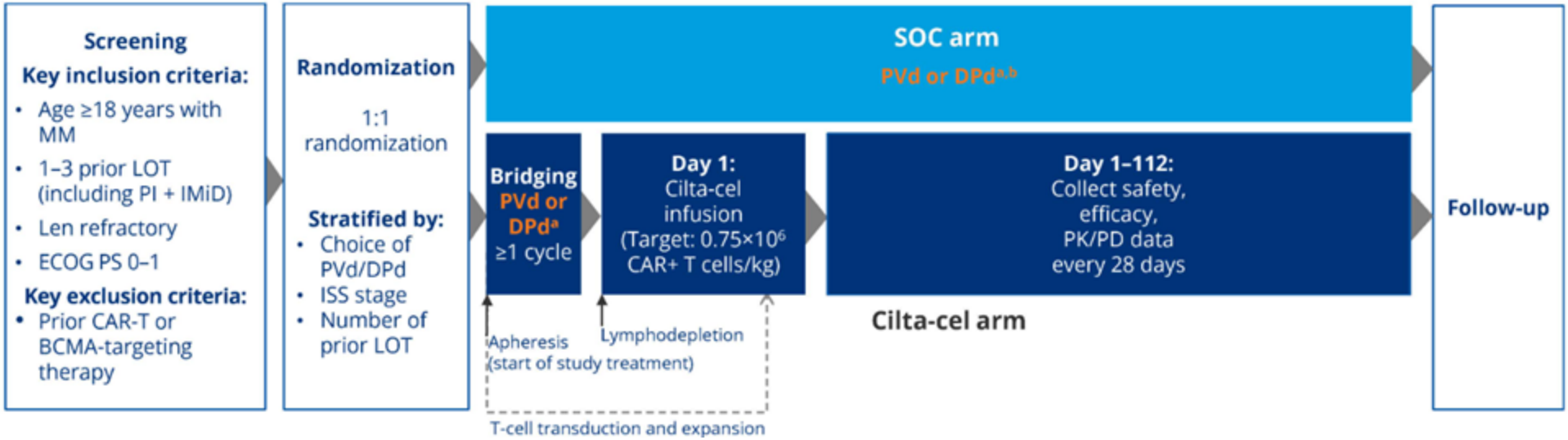
Cilta-Cel



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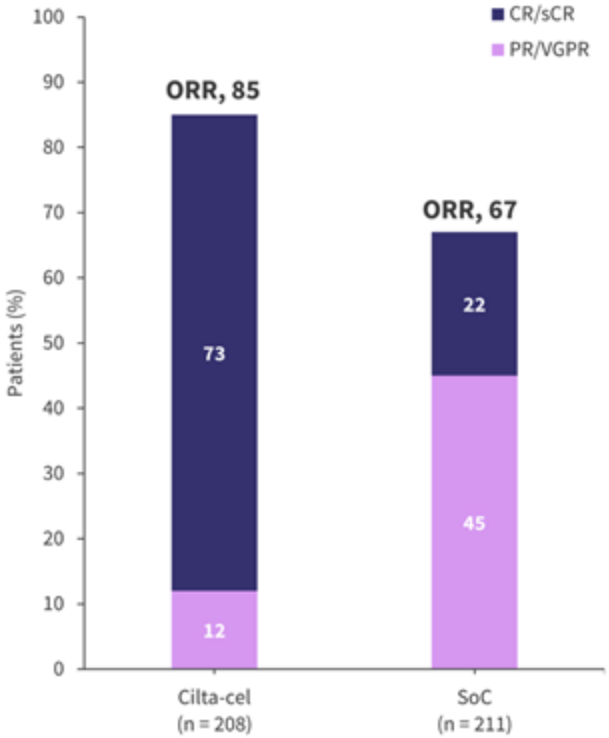
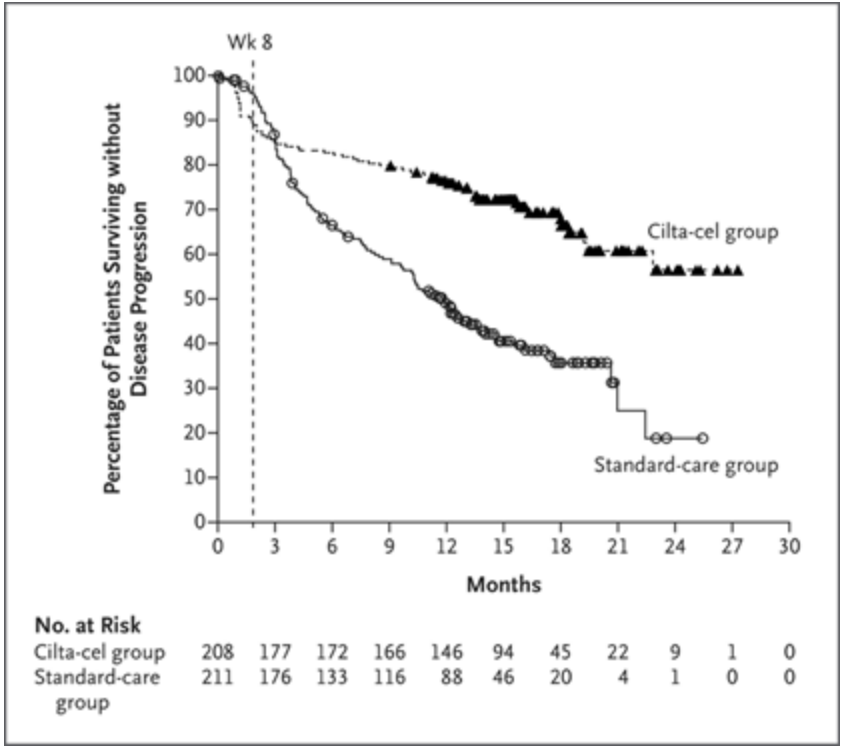
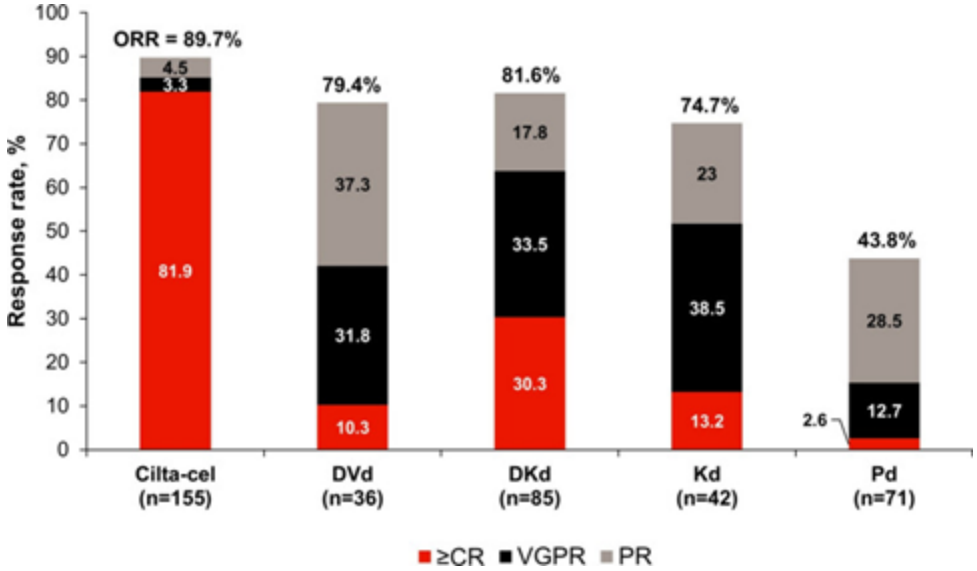
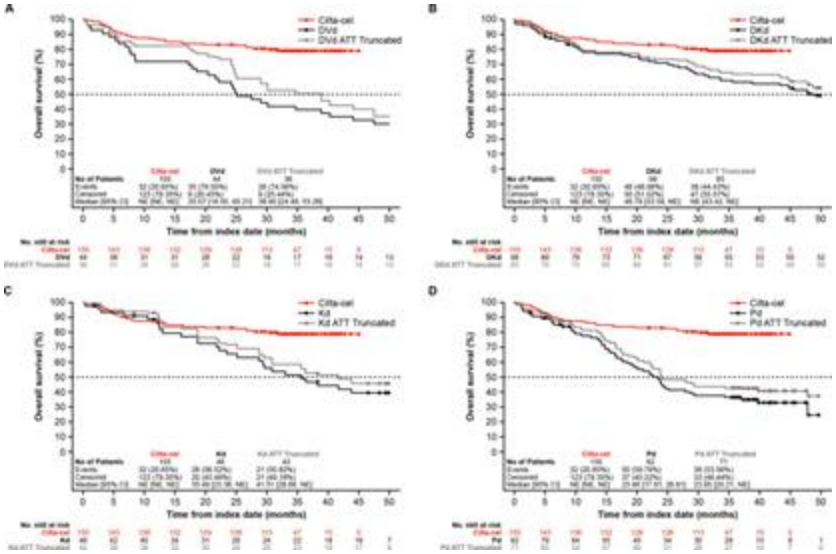
Cilta-Cel


CR/sCR
PR/VGPR
ORR, 85
ORR, 67
73
12
22
45
Patients (%)
Cilta-cel (n = 208)
SoC (n = 211)


Wk 8
Percentage of Patients Surviving without Disease Progression
Cilta-cel group
Standard-care group
Months
No. at Risk
Cilta-cel group 208 177 172 166 146 94 45 22 9 1 0
Standard-care group 211 176 133 116 88 46 20 4 1 0 0

Cilta-Cel





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CAR-T Cell Therapy – Toxicities

Cytokine Release Syndrome (CRS)

Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)

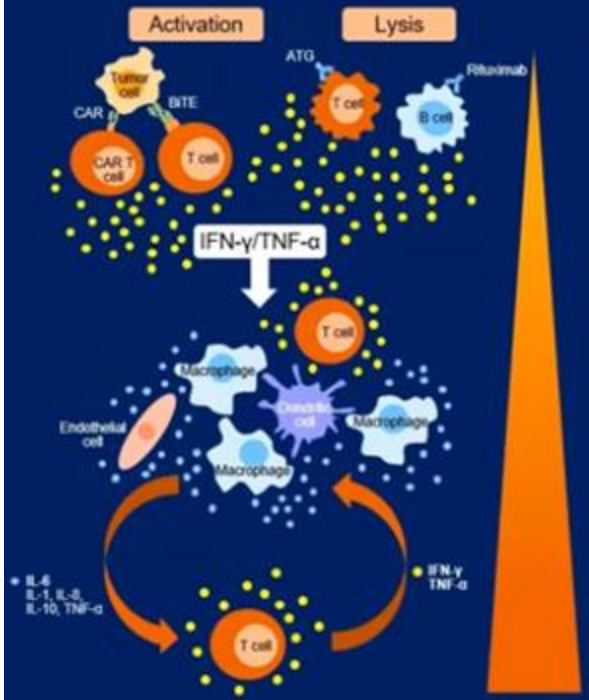
Immune Effector Cell-Associated Hematotoxicity (ICAHT)

Movement disorders

Infections

Cytokine Release Syndrome (CRS)

Stimulus



CRS Grading

Grade 1
- Fever
- Constitutional symptoms

Grade 2
- Hypotension responding to fluids/low dose vasopressors
- Grade 2 organ toxicities

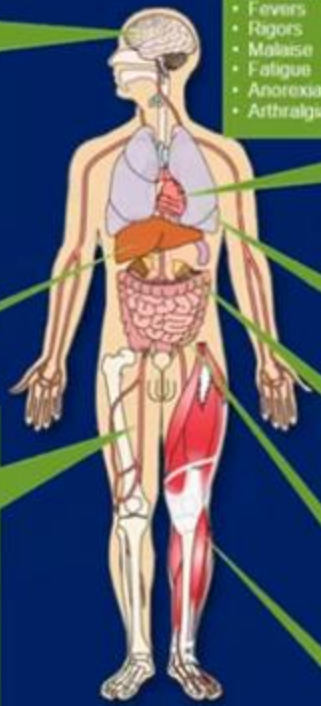
Grade 3
- Shock requiring high dose/multiple vasopressors
- Hypoxia requiring ≥40% FiO2
- Grade 3 organ toxicities, grade 4 transaminases

Grade 4
- Mechanical ventilation
- Grade 4 organ toxicities (excl. transaminases)

Neurologic
- Headaches
- Changes in level of consciousness
- Delirium
- Aphasia
- Apraxia
- Ataxia
- Hallucinations
- Tremor
- Dysmetria
- Myoclonus
- Facial nerve palsy
- Seizures

Hepatic
- Transaminitis
- Hyperbilirubinemia

Hematologic
- Anemia
- Thrombocytopenia
- Neutropenia
- Febrile neutropenia
- Lymphopenia
- B-cell aplasia
- Prolonged prothrombin time
- Prolonged activated partial thromboplastin time
- Elevated D-dimer
- Hypofibrinogenemia
- Disseminated intravascular coagulation
- Hemophagocytic lymphohistiocytosis



Constitutional
- Fevers
- Rigors
- Malaise
- Fatigue
- Anorexia
- Arthralgias

Cardiovascular
- Tachycardia
- Widened pulse pressure
- Hypotension
- Arrhythmias
- Decreased left ventricular ejection fraction
- Troponinemia
- QT prolongation

Pulmonary
- Tachypnea
- Hypoxia

Renal
- Acute kidney injury
- Hyponatremia
- Hypokalemia
- Hypophosphatemia
- Tumor lysis syndrome

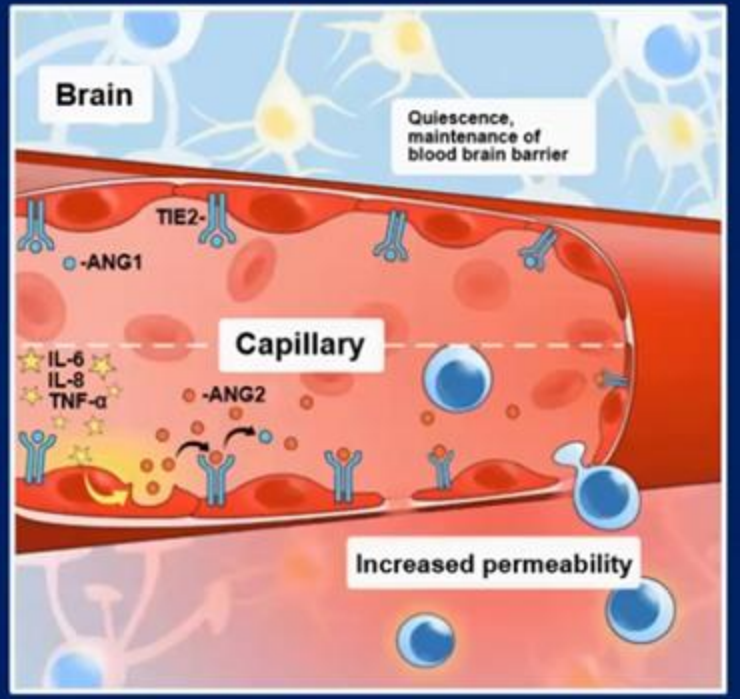
Gastrointestinal
- Nausea
- Emesis
- Diarrhea

Musculoskeletal
- Myalgias
- Elevated creatine kinase
- Weakness

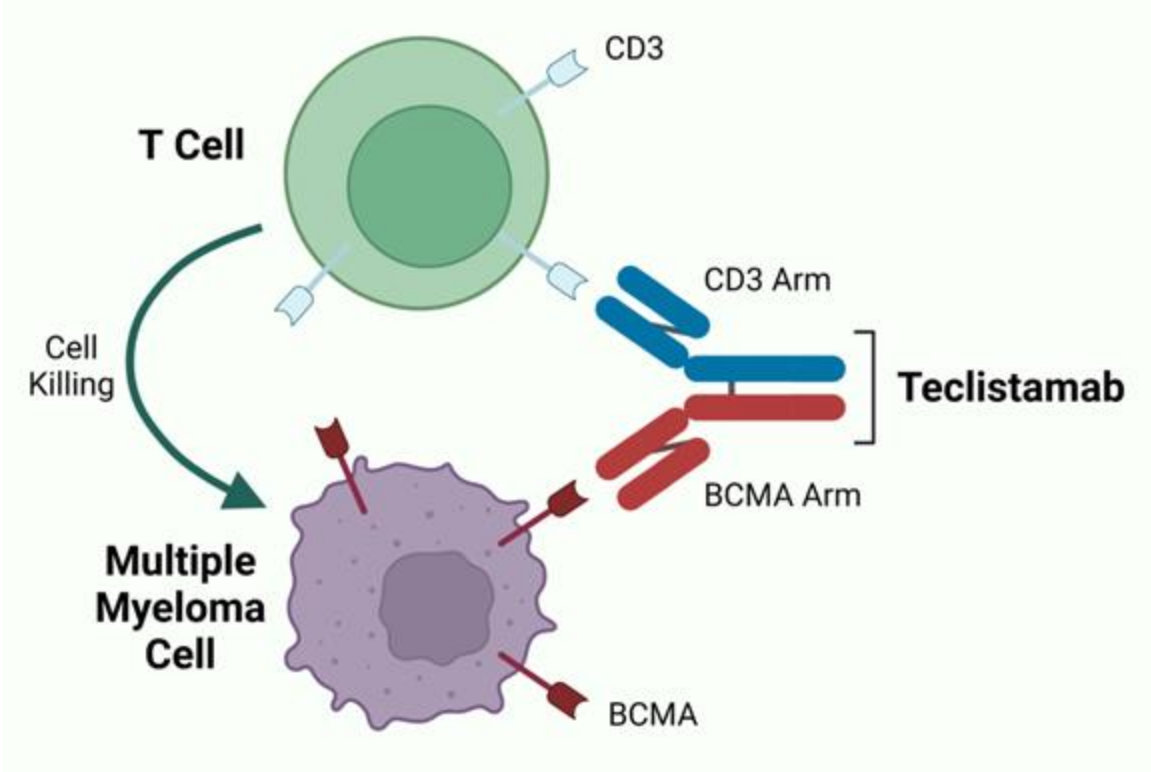
Shimabukuro-Vornhagen A et al. *J Immunother Cancer*. 2018;6:56.
Brudno JN, Kochenderfer JN. *Blood*. 2016;127:3321.

ICANS

- Associated with systemic inflammatory response
- Capillary leak
- Endothelial dysfunction
- Cerebral edema
- May be disconnected from grade of cytokine release syndrome (CRS)
- Appears to be less common/severe in multiple myeloma
- Late neurotoxicity can occur



Bi-Specific T-Cell Engager (BiTE) Therapy



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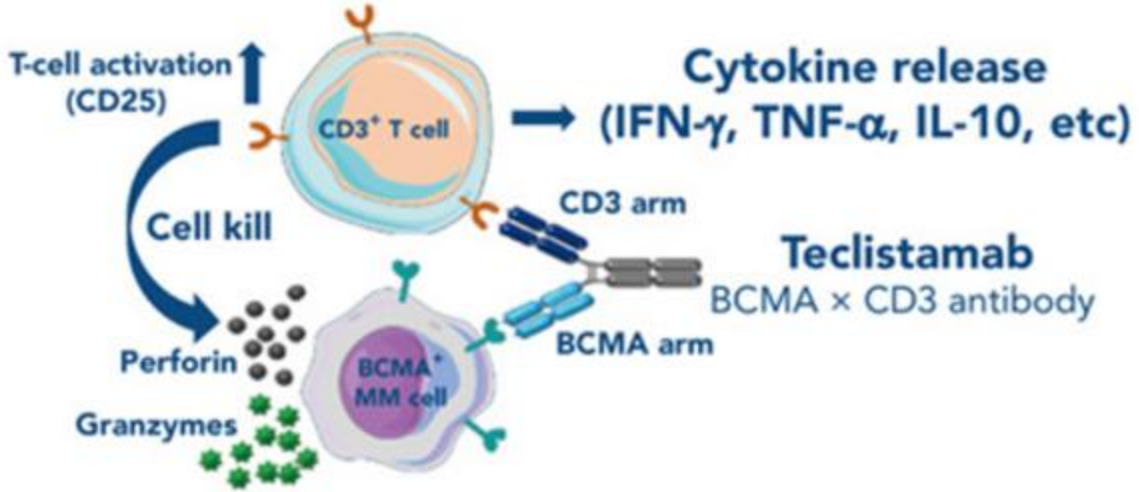
Bi-Specific T-Cell Engager (BiTE) Therapy

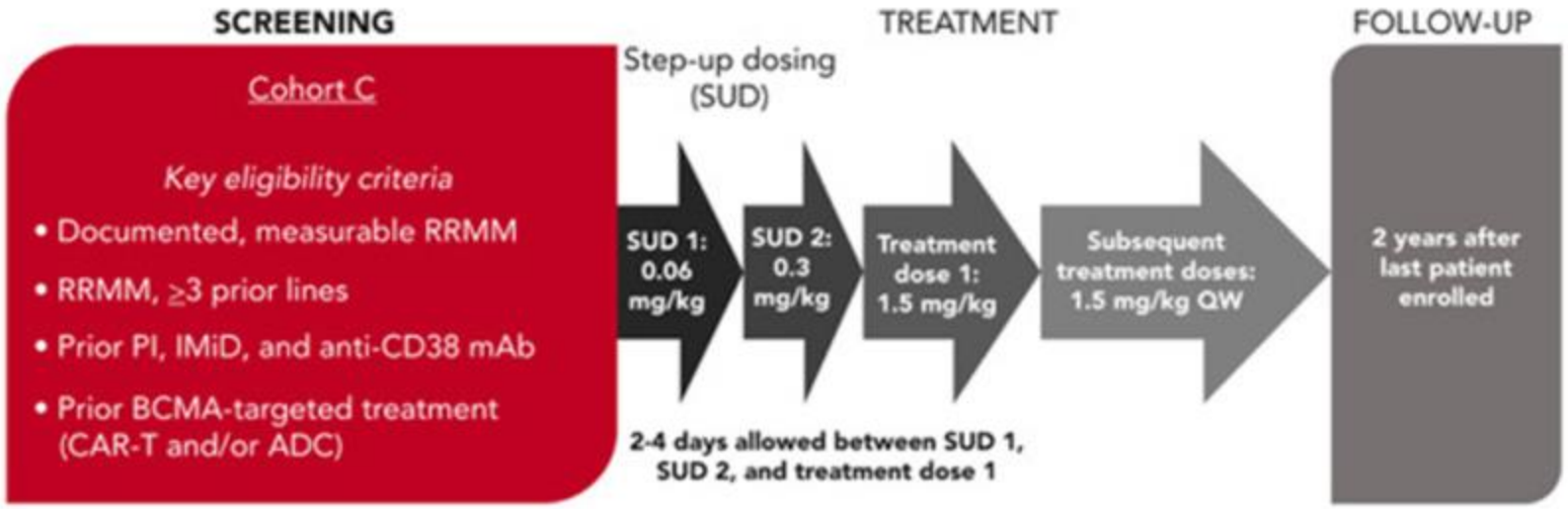
Background

In the phase 1/2 MajesTEC-1 study, a cohort of MM patients who had prior BCMA-targeted therapy (Cohort C) were treated with the BCMA × CD3 bispecific antibody teclistamab



Bi-Specific T-Cell Engager (BiTE) Therapy

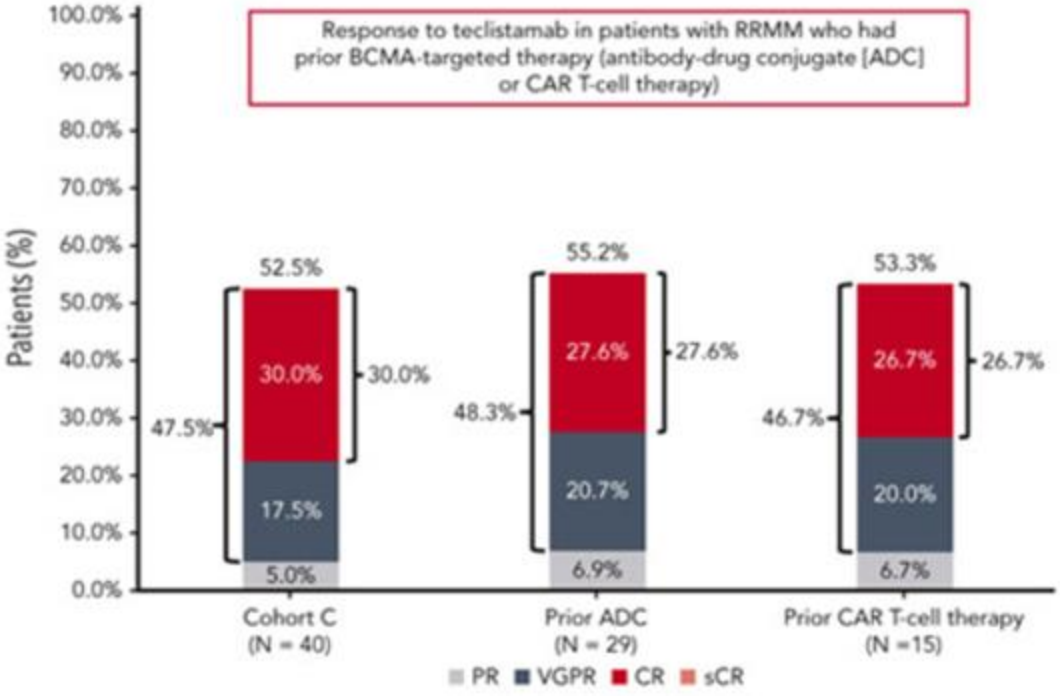
Materials and Methods



Primary endpoint: ORR
Key secondary endpoints: DOR, ≥VGPR, ≥CR, sCR, MRD status, PFS, OS, safety, PK, immunogenicity

Bi-Specific T-Cell Engager (BiTE) Therapy

Outcomes



Cohort C n = 40			
AEs >20%, n (%)	**Any Grade**	**Max Grade 3/4**	**Max Grade 5**
Hematologic			
Neutropenia	28 (70.0)	26 (65.0)	0
Anemia	20 (50.0)	14 (35.0)	0
Lymphopenia	18 (45.0)	17 (42.5)	0
Thrombocytopenia	18 (45.0)	12 (30.0)	0
Nonhematologic			
Infections and infestations	28 (70.0)	13 (32.5)	4 (10.0)
CRS	26 (65.0)	0	0
Diarrhea	15 (37.5)	1 (2.5)	0
Constipation	15 (37.5)	0	0
Pyrexia	14 (35.0)	0	0
Injection site erythema	13 (32.5)	0	0
Arthralgia	11 (27.5)	0	0
COVID-19	10 (25.0)	5 (12.5)	4 (10.0)
Dyspnea	10 (25.0)	2 (5.0)	0
Headache	10 (25.0)	0	0
Asthenia	9 (22.5)	2 (5.0)	0
Musculoskeletal chest pain	9 (22.5)	0	0

Bi-Specific T-Cell Engager (BiTE) Therapy

	Ide-cel	Cilta-cel	Teclistamab
Cell dose	150-450	0.75 × 10^6 / kg	N/A
Median f/u	13.3	33.4	14.1
Response rate			
ORR	73%	98%	63%
≥CR	33%	83%	39%
MRD			
Evaluable #	4 70 54	61	65
MRD- (%)	50% 31% 48%	92%	46%
Median DoR	10.7	33.9	18.4
Median PFS	8.8	34.9	11.3

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	Ide-cel		Cilta-cel		Teclistamab (bispecific antibody)	
	Any grade	Grade 3–4	Any grade	Grade 3–4	Any grade	Grade 3–4
Hematologic	91%	89%	100%	94%	71%	64%
CRS	84%	5%	95%	4%	72%	0.6%
Time to onset	1 days		7 days		2 days	
Median duration	5 days		4 days		2 days	
Neurotox	18%	3%	21%	9%	14.5%	0.6%
Time to onset	2 days		8 days		N/A	
Median duration	3 days		4 days		N/A	

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UPDATES IN MULTIPLE MYELOMA

Presentation/Diagnosis

Treatment

- **Induction/Consolidation/Maintenance**
- **Autologous Stem Cell Transplantation**
- **CAR-T Cell/BiTE Therapy**

Supportive Care

Survivorship

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SUPPORTIVE CARE

BONE HEALTH

INFECTION RISK

THROMBOSIS

PERIPHERAL NEUROPATHY

DERMATOLOGIC COMPLICATIONS

GI TOXICITY

OCULAR TOXICITY

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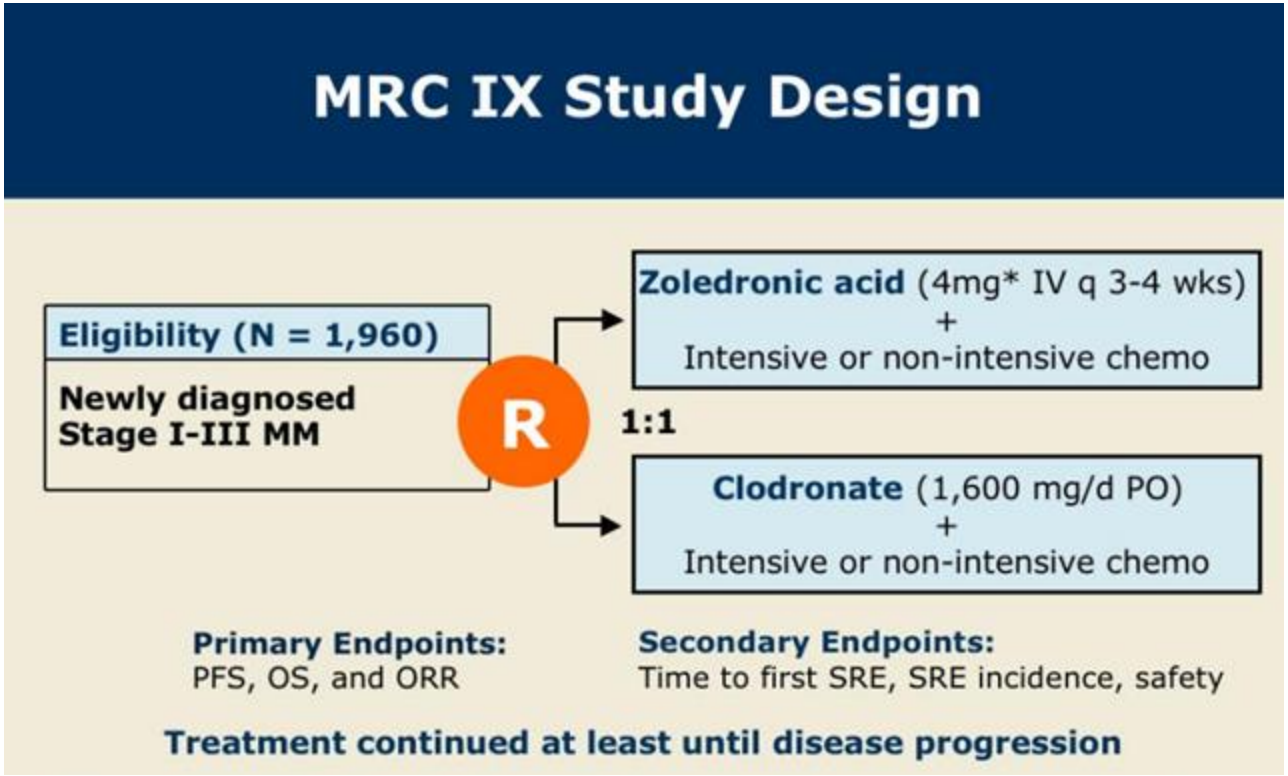
Bisphosphonate – Zoledronic acid



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Bisphosphonate – Zoledronic acid

Summary of Efficacy (Median Follow-Up: 3.7 Years)

Endpoint	Risk reduction (in favor of ZOL)	*p*-value
Overall survival (OS)*	16%	0.0118
Progression-free survival (PFS)*	12%	0.0179
Skeletal-related events (SREs)†	24%	0.0004
Improvement in median OS (ZOL vs CLO) = 5.5 mo, $p = 0.04$		
Is the observed OS improvement with ZOL due to SRE prevention, or does it represent an anti-myeloma effect?		
OS adjusted for SREs	15%	0.0178

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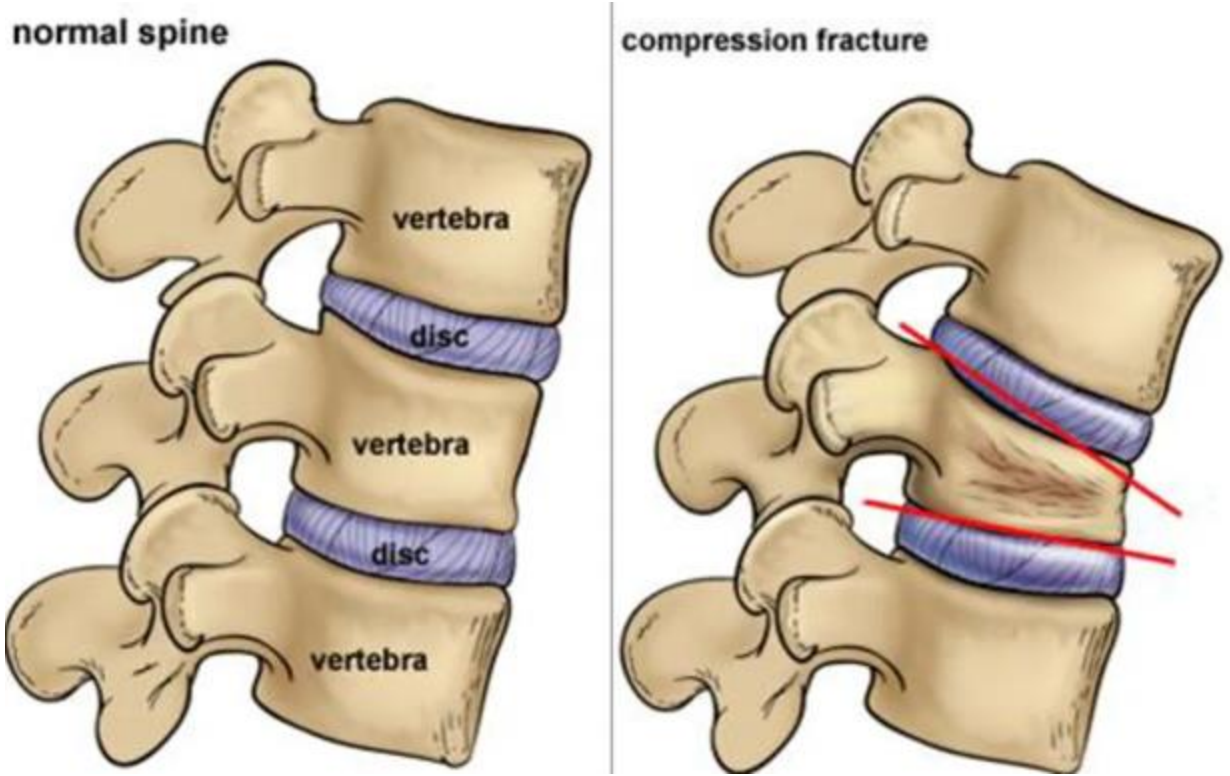
Kyphoplasty



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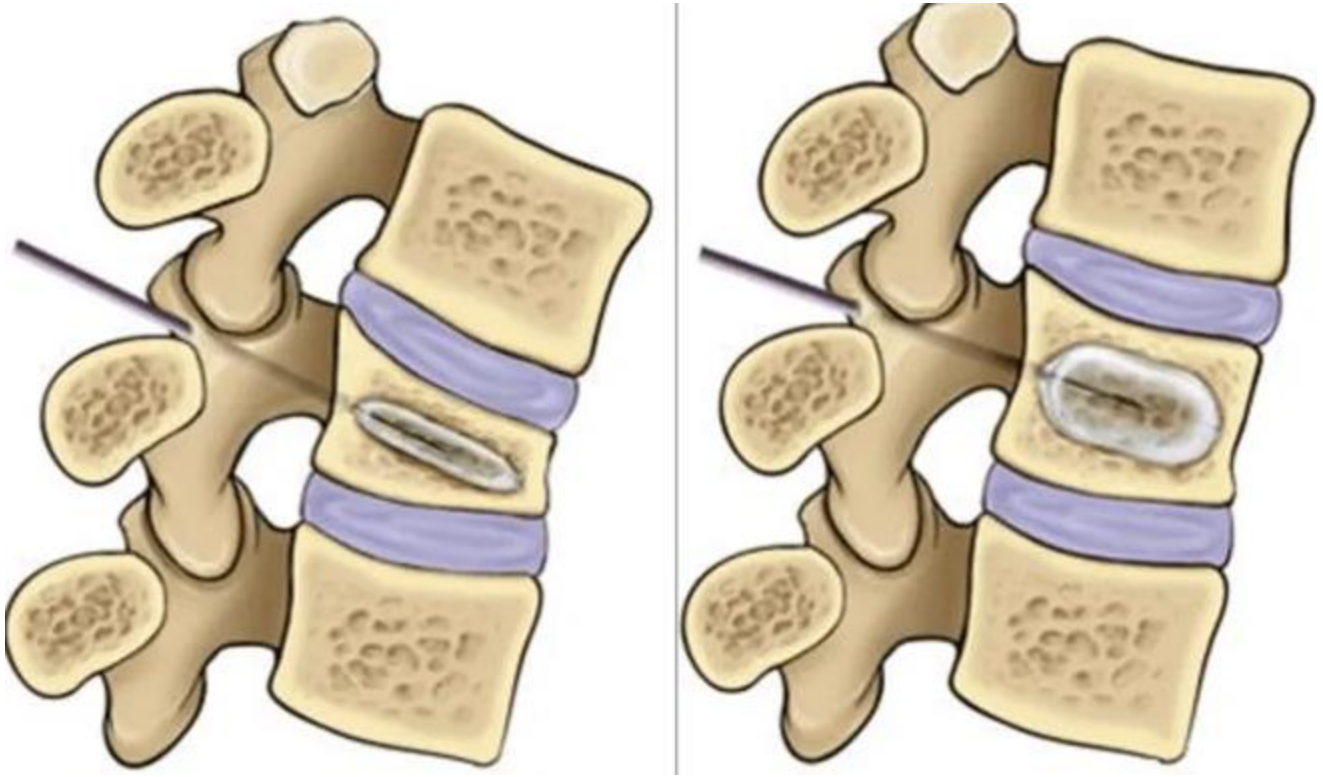
Kyphoplasty



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THROMBOSIS

Risk Factors	VTE prophylaxis regimen
Individual • Obesity (BMI >30 kg/m^2) • Prior VTE • CVAD or pacemaker • Co-morbidity (CAD, CKD, DM, acute infection, immobilization) • Surgery (general, any anesthesia, trauma) • Use of erythropoietin • Thrombophilia	0–1 Individual or myeloma-related risk factor • Aspirin 81–325 mg oral daily >1 Individual or myeloma-related risk factors • Enoxaparin 40 mg SQ daily (or LMWH equivalent) • Warfarin (INR 2–3) • DOACs (Apixaban 2.5 mg BID or rivaroxaban 10 mg daily)
Myeloma-related • Diagnosis of myeloma and being treated with and IMiD	

Myeloma therapy
• IMiD in combination with
  • High dose dexamethasone (≥480 mg/month)
  • Doxorubicin
  • Multiagent chemotherapy
  • Carfilzomib*
	• Enoxaparin 40 mg SQ daily (or LMWH equivalent)
	• Warfarin (INR 2–3)
	• DOACs (Apixaban 2.5 mg twice daily or rivaroxaban 10 mg daily)

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SURVIVORSHIP ISSUES

SECONDARY MALIGNANCIES

INFECTIOUS

CARDIOVASCULAR

NEUROLOGIC

VENOUS THROMBOEMBOLISM

BONE HEALTH

RENAL DYSFUNCTION

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SECONDARY MALIGNANCIES

MALIGNANCY	INCIDENCE
PRIOR MALIGNANCIES	
PROSTATE	25%
BREAST	13%
HEMATOLOGIC	4%
SECONDARY MALIGNANCY	
HEMATOLOGIC	21%
PROSTATE	7%
LUNG	7%

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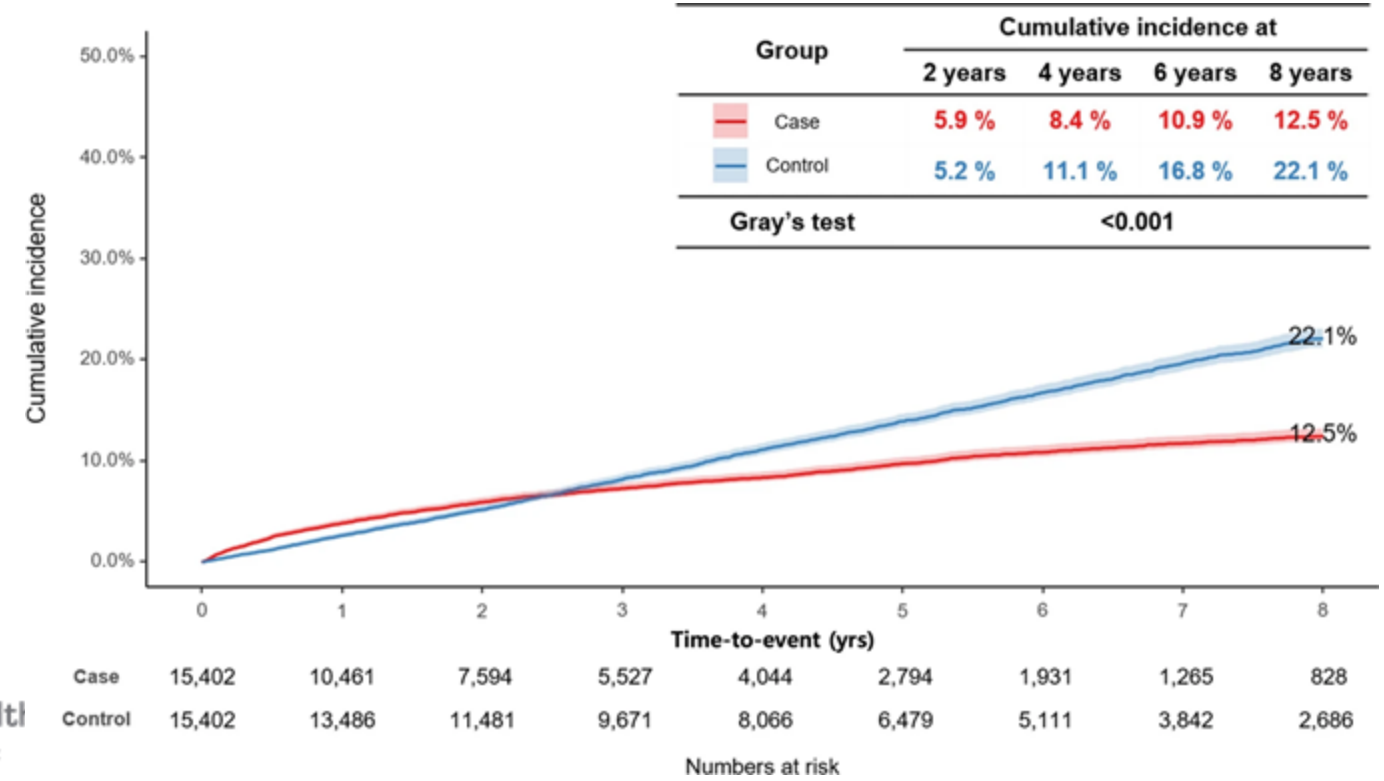
CARDIOVASCULAR DISEASE



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- Presentation/Diagnosis
- Treatment
  - Induction/Consolidation/Maintenance
  - Autologous Stem Cell Transplantation
  - CAR-T Cell/BiTE Therapy
- Supportive Care
- Survivorship

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CONCLUSIONS

Symptoms at presentation of MM are often nonspecific and diagnosis requires a high threshold of suspicion

Multi-drug regimens, ASCT, BiTE Therapy and CAR-T Cells are prominent treatment modalities in MM

Treatments in MM have resulted in significant improvement of overall survival

Survivorship and ongoing supportive care is crucial in patients after MM treatment, given prolonged remission duration but also high risk of relapse.

Thank you

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