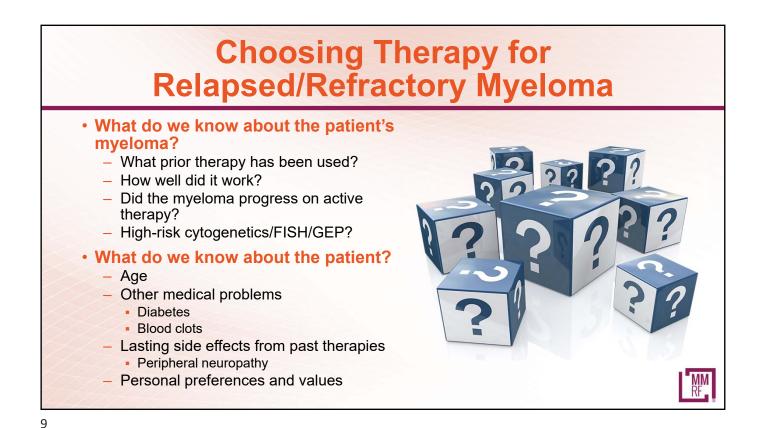


# Definitions: What is relapsed/refractory disease and a line of therapy?

- Relapsed: recurrence (reappearance of disease) after a response to therapy
- Refractory: progression despite ongoing therapy
- Progression: change in M protein/light chain values
- *Line of therapy:* change in treatment due to either progression of disease or unmanageable side effects
  - Note: initial (or induction) therapy + stem cell transplant + consolidation/ maintenance therapy = 1 line of therapy







### Factors to Consider in Treatment Selection

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#### **DISEASE-RELATED**

- DOR to initial therapy
- FISH/cytogenetics/genomics profile

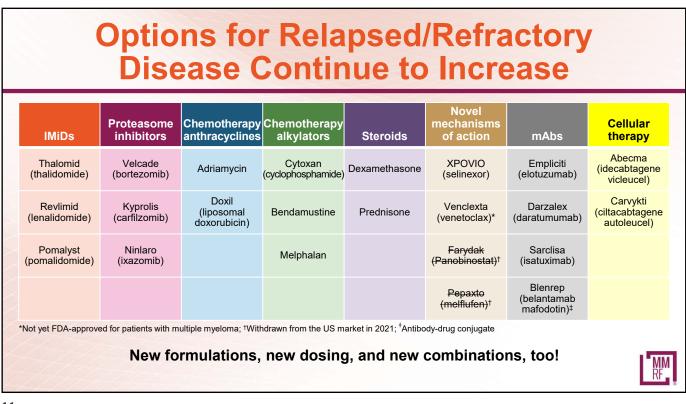
#### PRIOR TREATMENT-RELATED

- Prior drug exposure
- Toxicity of regimen
- Mode of administration
- Previous SCT

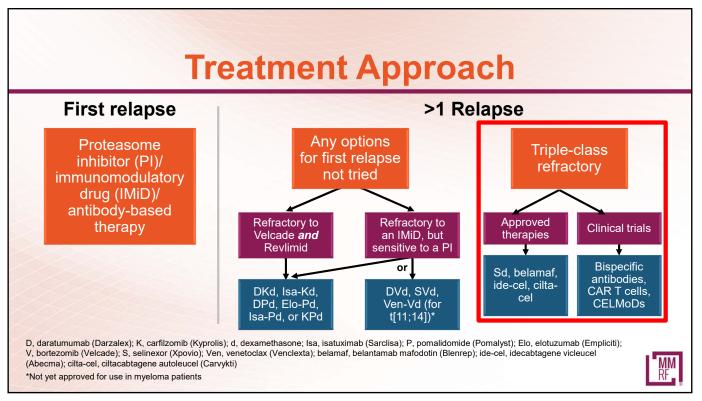
#### PATIENT-RELATED

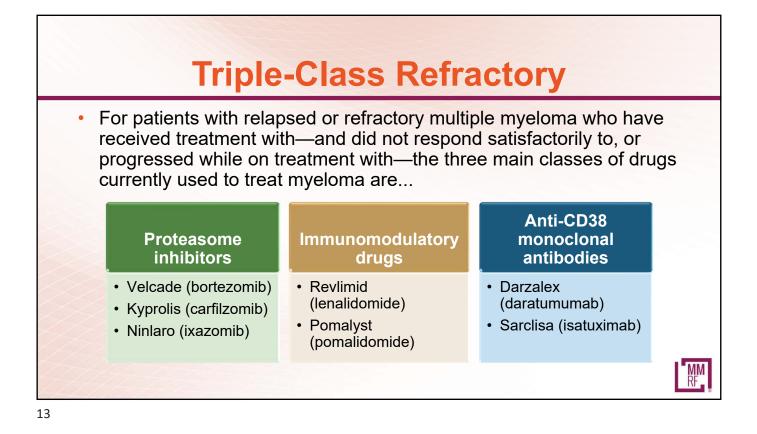
- Pre-existing toxicity
- Presence of other conditions
- Age
- General health
- Personal lifestyle and preferences

DOR, duration of response; FISH, fluorescence in situ hybridization; SCT, stem cell transplant Lonial S. *Hematology Am Soc Hematol Educ Program*. 2010;303.



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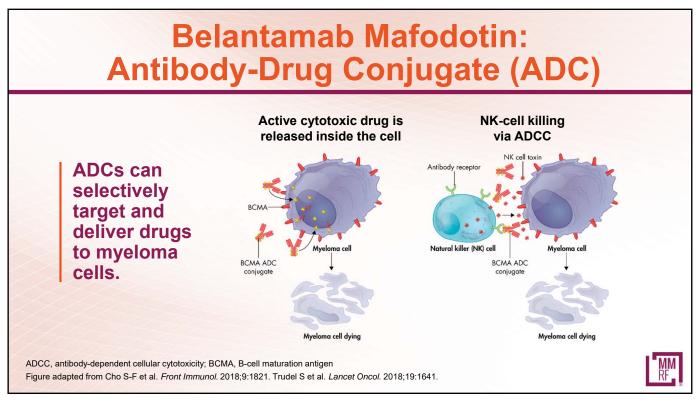


### Currently Available Drugs for Triple-Class Refractory Myeloma

Nuclear export inhibitor	XPOVIO			• For relapsed/refractory myeloma in combination with
	(selinexor)	<b>O</b>	Twice-weekly pill	dexamethasone (after at least 4 prior therapies and whose disease is refractory to at least 2 PIs, at least 2 IMiDs, and an anti-CD38 mAb
Antibody- drug conjugate	Blenrep (belantamab mafodotin)*	Ę	2.5 mg/kg IV over approximately 30 minutes once every 3 weeks	<ul> <li>For relapsed/refractory myeloma (after at least 4 prior therapies including an anti-CD38 mAb, a PI, and an IMiC</li> </ul>
Chimeric antigen receptor (CAR) T cell	Abecma (idecabtagene vicleucel) <sup>†</sup>	Ð	300 to 460 × 10 <sup>6</sup> genetically modified autologous CAR T cells in one or more infusion bags	<ul> <li>For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb</li> </ul>
CAR T cell	Carvykti (ciltacabtagene autoleucel)‡	Ð	0.5 to 1.0 × 10 <sup>6</sup> genetically modified autologous CAR T cells/kg of body weight	<ul> <li>For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb</li> </ul>

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

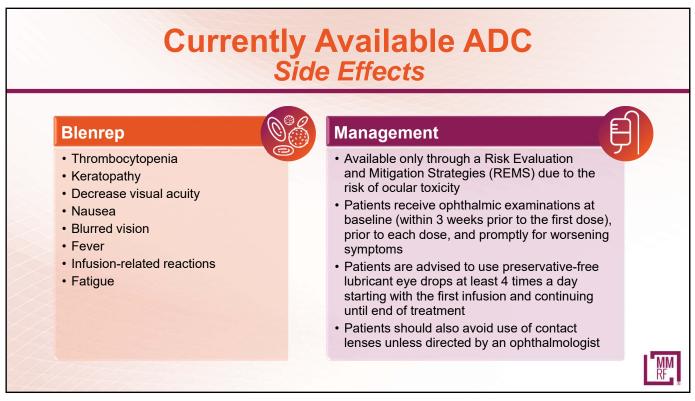




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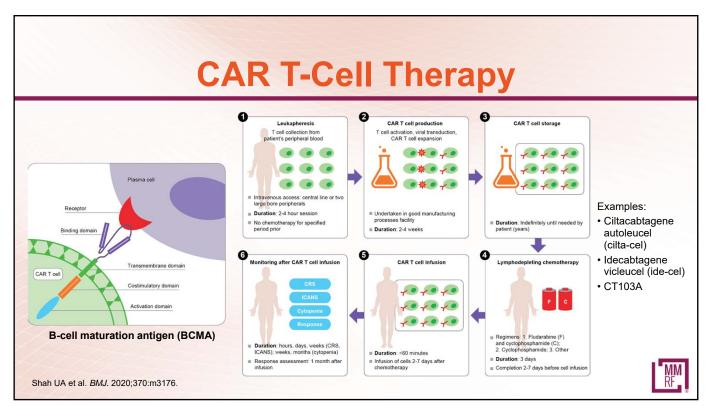
# **First ADC Approved in MM**

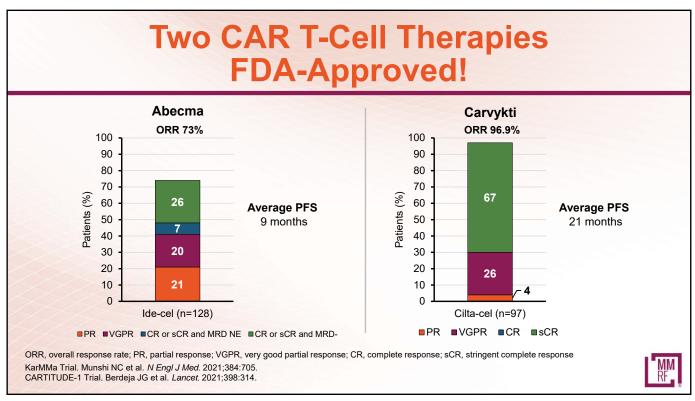
DREAMM-2 Study	Blenrep (2.5 mg/kg)	Blenrep (3.4 mg/kg)
Ν	97	99
Median no. lines of therapy, n (range)	7 (3–21)	6 (3–21)
Overall response rate (%)	31	34
Median progression-free survival (mos)	2.9	4.9
Median overall survival (mos)	Not reached	Not reached



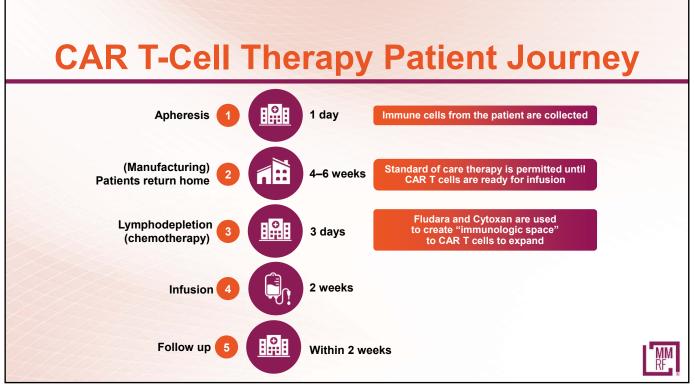


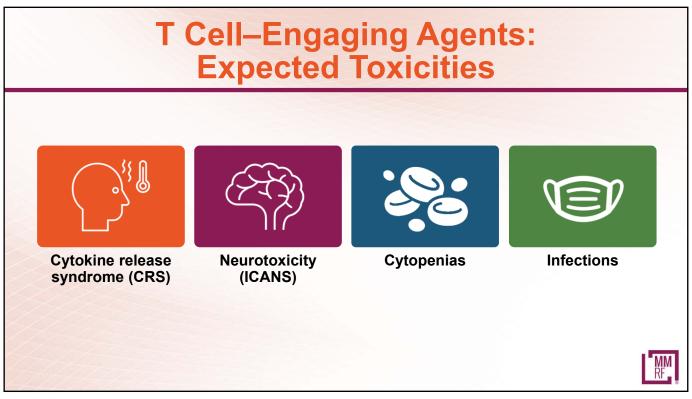






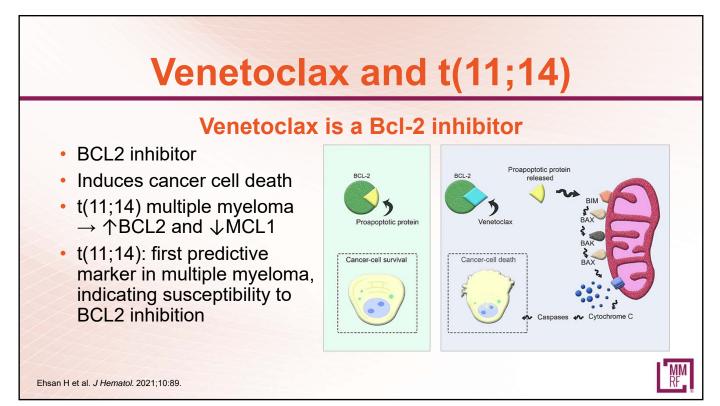


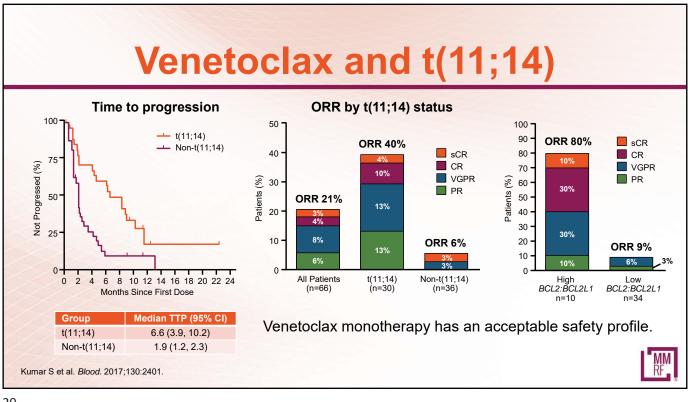




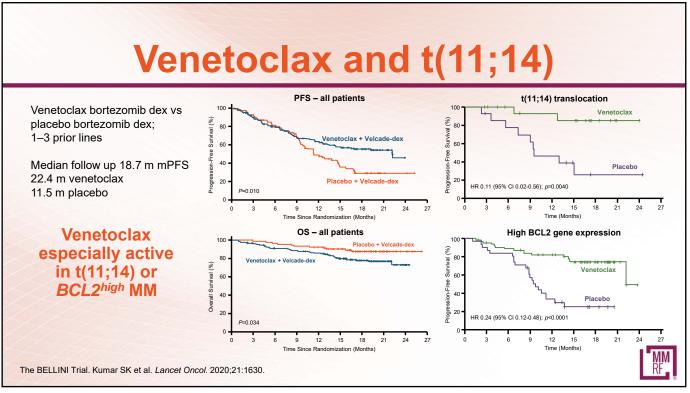
Cellular therapies	CAR T-cell therapy	Autologous stem cell transplantation
Patient's cells collected	Yes	Yes
Types of cells collected	T cells*	Stem cells <sup>†</sup>
Collected cells are genetically engineered in a lab	Yes	No
Patient given chemotherapy before cells are infused back into patient	Yes, lymphodepleting therapy	Yes, melphalan
When in the course of myeloma is this <i>usually</i> done?	After multiple relapses	As part of initial treatment
Side effects of treatment	Cytokine release syndrome; confusion	Fatigue, nausea, diarrhea

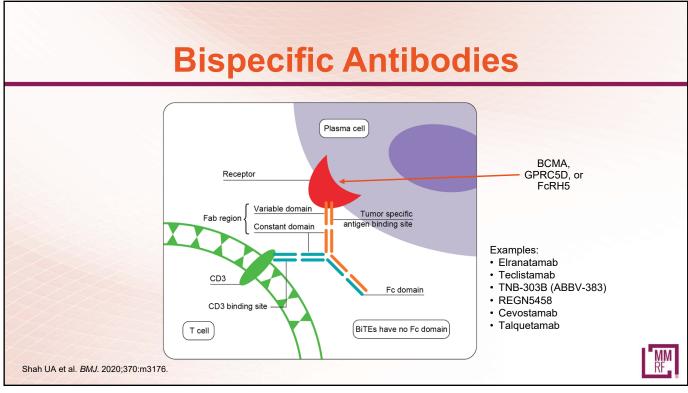
	Novel	agents			Immuno	therapies		
Clinical phase	Precision medicine	Novel mechanisms of action <sup>†</sup>	lmmuno- modulatory agents	Naked antibodies <sup>†</sup>	Antibody- drug conjugates	Bispecific antibodies and bispecific T-cell engagers <sup>†</sup>	CAR T-cell therapies <sup>†</sup>	Checkpoint inhibitors
Phase 3	Venetoclax*		Iberdomide			Teclistamab		
Phase 1, 2	Abemaciclib* Cobimetinib* Dabrafenib Enasidenib* Erdafitinib* Idasanutlin Trametinib Vemurafenib	AMG-176 AMG-232 APG-2575 Azacitidine CFT7455 Ciforadenant Citarinostat COM902 CYT-0851 Disulfiram Duvelisib	Avadomide Mezigdomide TAK-573	AB308 AEVI-007 ALT-803 AO-176 Relatlimab BMS-986207 Feladilimab GEN3014 GSK3174998 Lemzoparlimab Lirilumab	AMG-224 CC-99712 FOR46 HDP-101 Lintuzumab- Ac225 MED12228 MT-0169 STRO-001	AMG 420 AMG 701 Cevostamab CC-93269 Elranatamab HPN217 ISB 1342 Talquetamab REGN5459 REGN5459 TNB-383B	ALLO-605 ALLO-715 ATLCAR.CD138 CAR 2 CART-ddBCMA CART-TnMUC1 CC-98633 CS1-CART CT053 CTX120 CYAD-211	Abatacept Cemiplimab Dostarlimab Durvalumab Ipilimumab Nivolumab Pembrolizuma TTI-622 Zimberelimat











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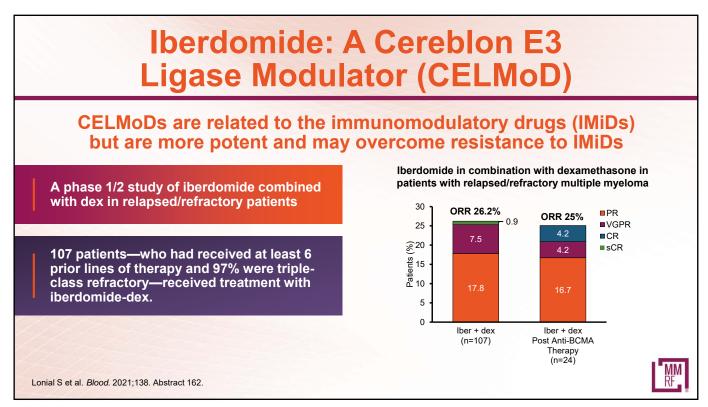
# **Bispecific Antibodies on the Horizon**

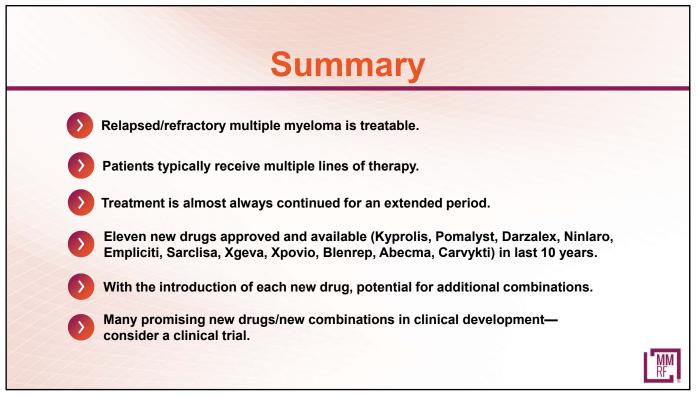
Study	MagnetisMM-1 (Phase 1)	MajesTEC-1 (Phase 1/2)	Phase 1	Phase 1	Phase 1	MonumenTAL-1 (Phase 1)
Agent	Elranatamab <sup>1</sup>	Teclistamab <sup>2</sup>	TNB-383B (ABBV-383) <sup>3</sup>	REGN5458 <sup>[4]</sup>	Cevostamab⁵	Talquetamab <sup>6</sup>
Targets	BCMA × CD3	BCMA × CD3	BCMA × CD3	BCMA × CD3	FcRH5 × CD3	GPRC5D × CD3
No. patients	55	165	118	73	161	55 at 2 RP2D
Median no. prior therapies	6 (2–15)	5 (2–14)	5 (1–15)	5 (2–17)	6 (2–18)	6 (2–17)
Efficacy						
Overall response rate (%)	69	62	81 (≥40 mg)	75 (200–800 mg)	56.7 (132–198 mg)	69
Complete response or better (%)	30	29	39	16	8	16
Median duration of response (mos)	Not reported	Not reached	Not reported	Not reached	11.5	Not reached
Median progression-free survival (mos)	Not reported	59% at 9 mos	Not reported	Not reported	Not reported	Not reported
Safety						
CRS, all grades (G3/4), %	87 (0)	72 (1)	54 (3)	38 (0)	80 (1.2)	75 (5)
Neurotoxicity, all grades (G3/4), %	Not reported	13 (0)	Not reported	4 (0)	14 (1)	Not reported

RP2D, recommended phase 2 dose

1. Sebag M et al. *Blood*. 2021;138. Abstract 895. 2. Moreau P et al. *Blood*. 2021;138. Abstract 896. 3. Kumar SK et al. *Blood*. 2021;138. Abstract 900. 4. Zonder JA et al. *Blood*. 2021;138. Abstract 160. 5. Trudel S et al. *Blood*. 2021;138. Abstract 157. 6. Krishnan AY et al. *Blood*. 2021;138. Abstract 158.





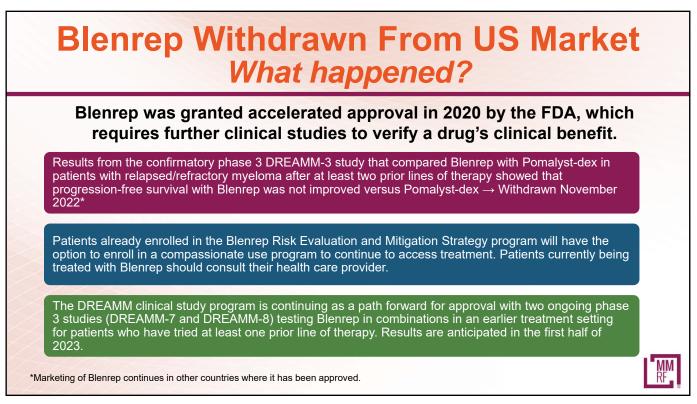


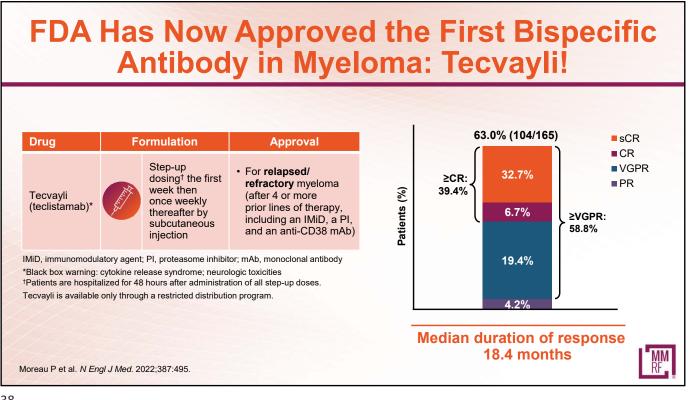


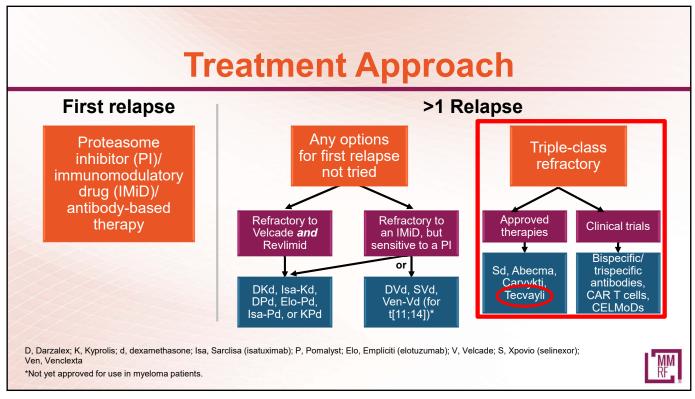
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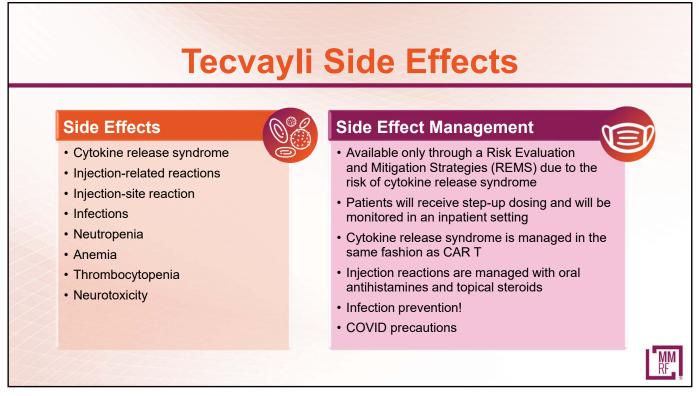
## Options for Relapsed/Refractory Disease Continue to Increase

IMiDs	Proteasome inhibitors	Chemotherapy anthracyclines	Chemotherapy alkylators	Steroids	Novel mechanisms of action	Monoclonal antibodies	Cellular therapy
Thalomid (thalidomide)	Velcade (bortezomib)	Adriamycin	Cytoxan (cyclophosphamide)	Dexamethasone	XPOVIO (selinexor)	Empliciti (elotuzumab)	Abecma (idecabtagene vicleucel)
Revlimid (lenalidomide)	Kyprolis (carfilzomib)	Doxil (liposomal doxorubicin)	Bendamustine	Prednisone	Venclexta (venetoclax)*	Darzalex (daratumumab)	Carvykti (ciltacabtagene autoleucel)
Pomalyst (pomalidomide)	Ninlaro (ixazomib)		Melphalan		<del>Farydak</del> <del>(Panobinostat)</del> †	Sarclisa (isatuximab)	
					<del>Pepaxto</del> <del>(melflufen)</del> †	<del>Blenrep</del> <del>(belantamab</del> <del>mafodotin)<sup>‡§</sup></del>	
						Tecvayli (teclistamab) <sup>∥</sup>	
Not yet FDA-approve Bispecific antibody	ed for patients with m	ultiple myeloma; †With	ndrawn from the US m	arket in 2021; <sup>‡</sup> Antibo	ody-drug conjugate; <sup>§</sup> V	Vithdrawn from US ma	arket in 2022
44/2	New fo	rmulations,	new dosing	g, and new o	combinatio	ns, too!	M









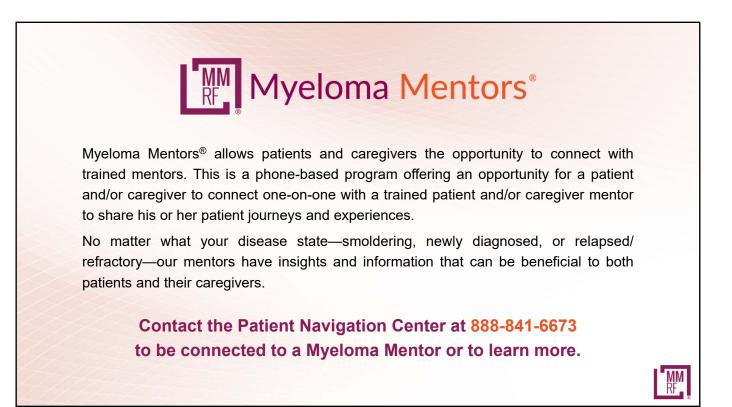
## Similarities and Differences Between CAR T-Cell Therapy and Bispecific Antibodies

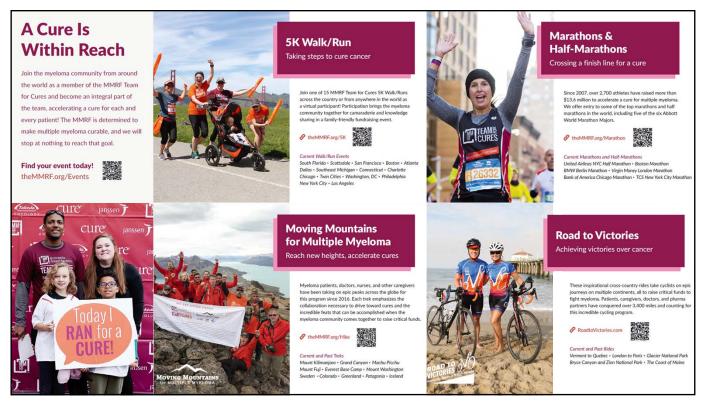
	CAR T-cell therapy	Bispecific antibody
Approved product	Abecma, Carvykti	Tecvayli
Efficacy	++++	+++
How given	One-and-done	IV or SC, weekly to every 3 weeks until progression
Where given	Academic medical centers	Academic medical centers
Notable adverse events	CRS and neurotoxicity	CRS and neurotoxicity
Cytokine release syndrome	+++	++
Neurotoxicity	++	+
Availability	Wait time for manufacturing	Off-the-shelf, close monitoring for CRS and neurotoxicity





**MMRF Patient Resources MMRF** Patient Navigation Center You and your care team will have many decisions to make along your treatment journey. The Patient Navigation Center is a space for multiple myeloma patients and their caregivers to connect with patient navigators — who are professionals specializing in oncology – for guidance, information, and support. You can conn with a patient navigator via phone, or email. Whatever questions you may have, our patient navigators are here to help. EXPECT GUIDANCE. MMRF Patient Navigators include: Grace Allison, RN, BSN, OCN, RN-BC Brittany Hartmann, RN-BSN Erin Mensching, RN-BSN, OCN THE RIGHT TRACK MMRF Patient Navigation Center Get on the right track for you The MMRF's Right Track pr ogram puts you on the path to the best results for you (A) (A) Juni 副 Right Team **Right Tests Right Treatment** Work with your team to consider the best treatment plan and dentify clinical trials that Get the information, tests, and precise diagnoses to make the right treatment decisions. Expert Advice Contact the Patient Navigation Center Today Looking for guidance? We're here to help. Monday – Friday | 9:00AM – 7:00PM ET hone: 1-888-841-MMRF (6673) Online: TheMMRF.org/PatientNavigationCen Email: patientnavigator@themmrf.org Supported By Adaptive AMGEN ( Bristol Myers Squibb' CUTC MM MULTIPLE MYELOMA RF Research Foundation MM RF Alberber of the Render Green Janssen Sonofi Cakedas ONCOLOGY





# **Upcoming Patient Education Events**

### Save the Date

Торіс	Date and Time	Speakers
<i>Patient Summit</i> (live and online)	Friday, December 9 12:00 рм – 4:30 рм (СТ) New Orleans, Louisiana	Laura Finn, MD—Host Ambuga R. Badari, MD Amrita Y. Krishnan, MD Paul G. Richardson, MD A. Keith Stewart, MBChB
Facebook Live Session	Thursday, December 15 4:00 Рм – 5:00 Рм (ET)	Nitya Nathwani, MD
Expert Session: Multiple Myeloma Highlights From the 2022 American Society of Hematology Meeting	Tuesday, December 20 1:00 рм – 3:00 рм (ЕТ)	Hearn Jay Cho, MD, PhD Joshua Richter, MD
	For more information or to re it themmrf.org/resources/edu	



