Myeloma remains one of the largest unmet medical needs within hematology

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MM is the Second Most Common Hematologic Malignancy After Lymphoma[1]

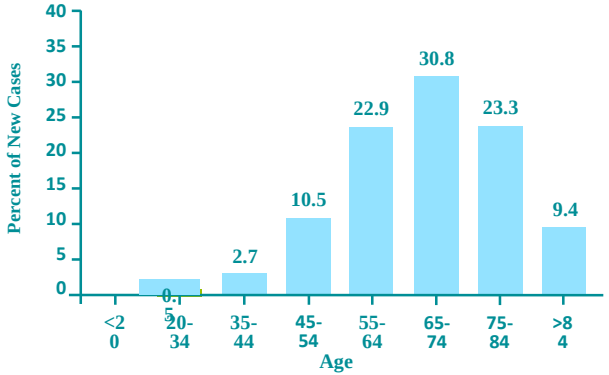
MM accounts for 1.8% of all new cancer cases in the US[2]

- Incidence of MM has steadily increased over the past 15 years in the US
- Estimated prevalence in US (2017) was 140,779[2]
- In 2020, an estimated 32,270 new cases and 12,830 deaths in the US were attributed to MM[2]
- Overall 5-year (2010-2016) relative survival rate: 53.9%[2]

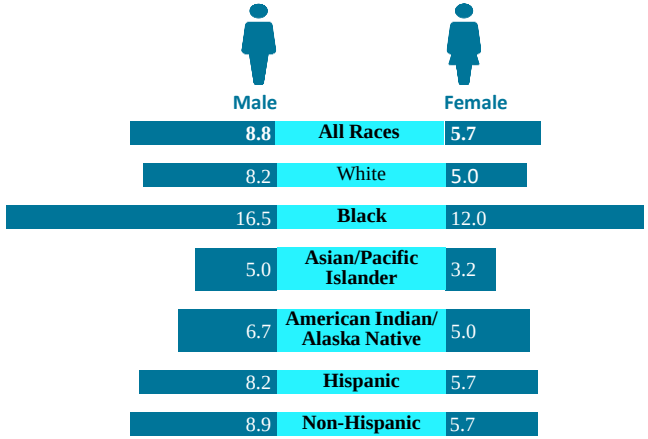
Although there is a lack of strong risk factors for MM, the incidence2:

- Increases with age (MM is most frequently diagnosed in patients aged 65-74 years; median age: 69 years)
- Is higher in males than females
- Is higher in individuals of African descent

Percent of new cases by age group (2013-2017)[2]

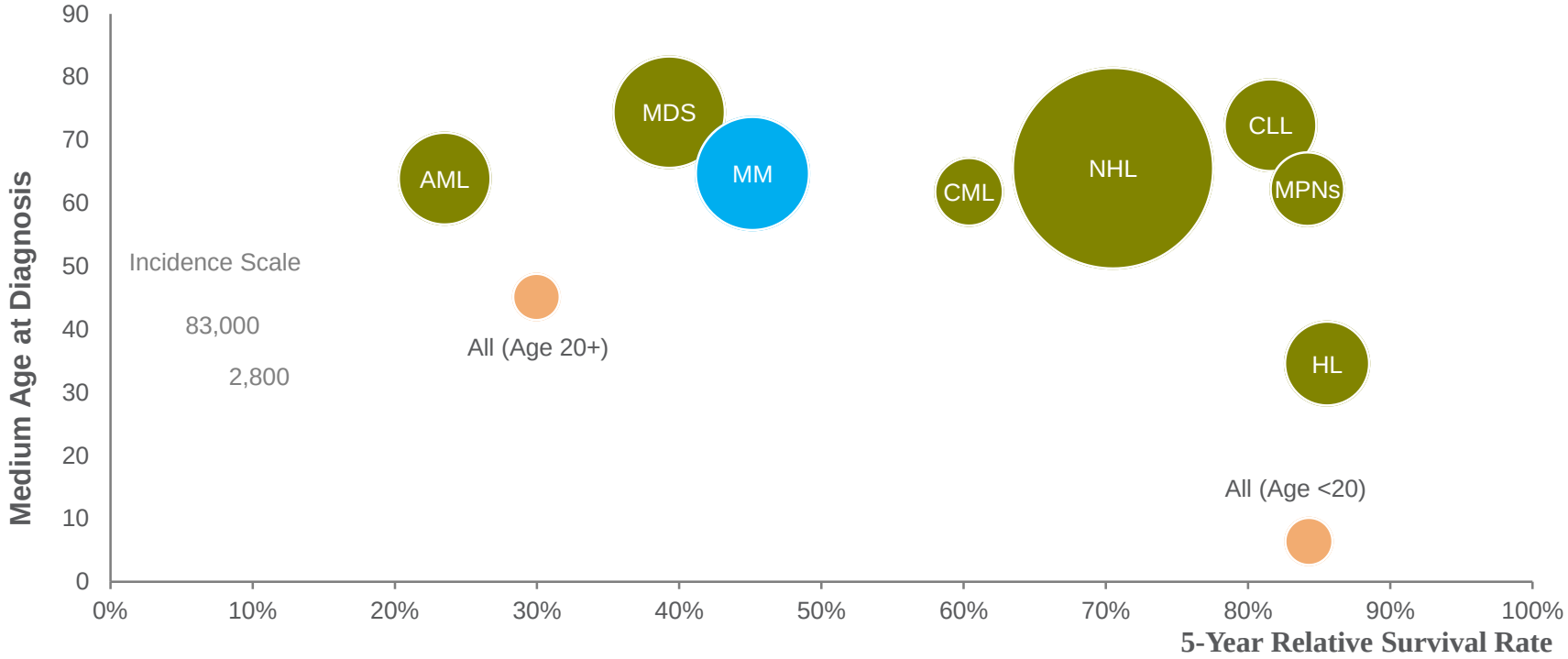


Number of new cases per 100,000 persons (2013-2017)[2]



- MM, multiple myeloma, US, United States.
- 1. Kazandijan D. *Semin Oncol*. 2016;43(6):676-681; 2. National Cancer Institute (NCI). Cancer Stat Facts: Myeloma. 2020. https://seer.cancer.gov/statfacts/html/mulmy.html. Accessed July 14, 2020.

Even with Advances in Treatment Myeloma Continues to Have One of the Worst Prognoses of Hematological Malignancies



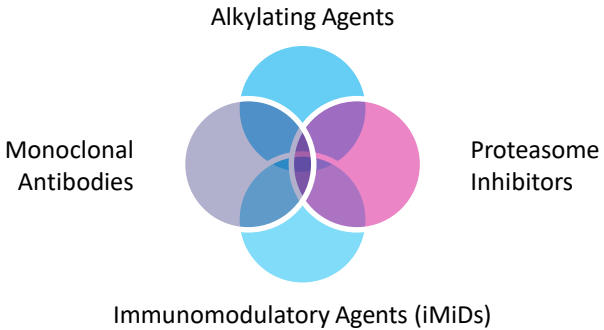
How Multiple Myeloma is Treated

Four therapeutic drug classes are used in the majority of treatments for patients with MM[1]

- Resistance to each subsequent line of treatment is inevitable, due to clonal selection

Most patients have been treated with all four drug classes after 2-3 lines of therapy[1]

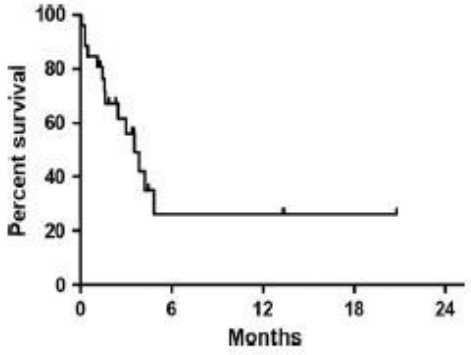
- These patients have limited treatment options



Triple-class refractory MM[1]

- Growing number of patients exposed to PIs, IMiDs, and anti-CD38 agents
- Eventually patients develop penta-exposed and triple-class refractory MM
- Associated with a poor prognosis [2]

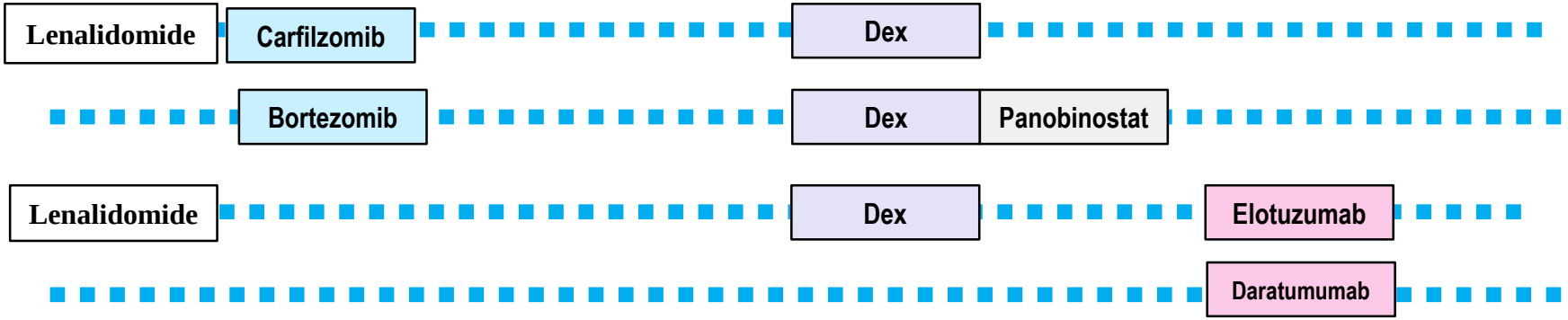
OS in Patients with triple-class refractory MM[2]



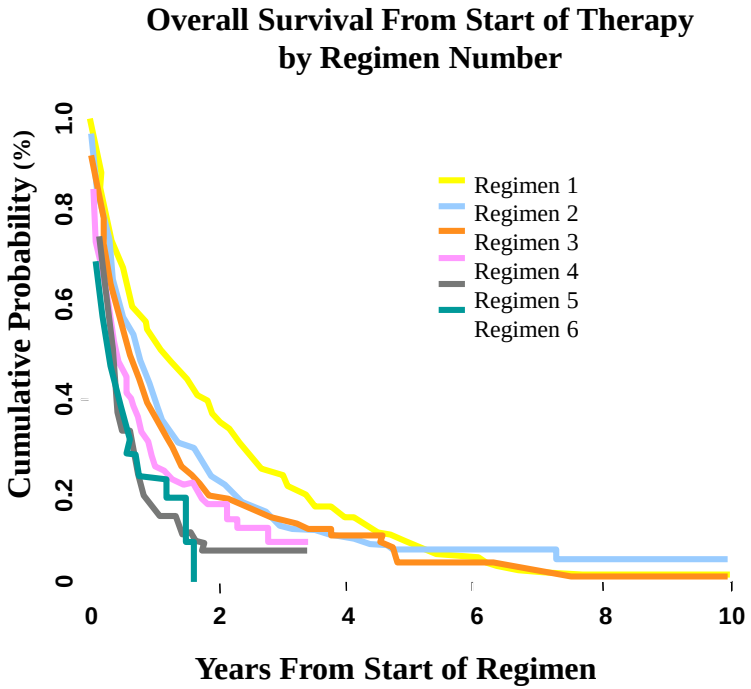
1. Mikhael J. *Clin Lymphoma Myeloma Leuk*. 2019;S2152-2650(19):32008-7.
2. Pick M, et al. *Eur J Haematol*. 2018;100:494-501.

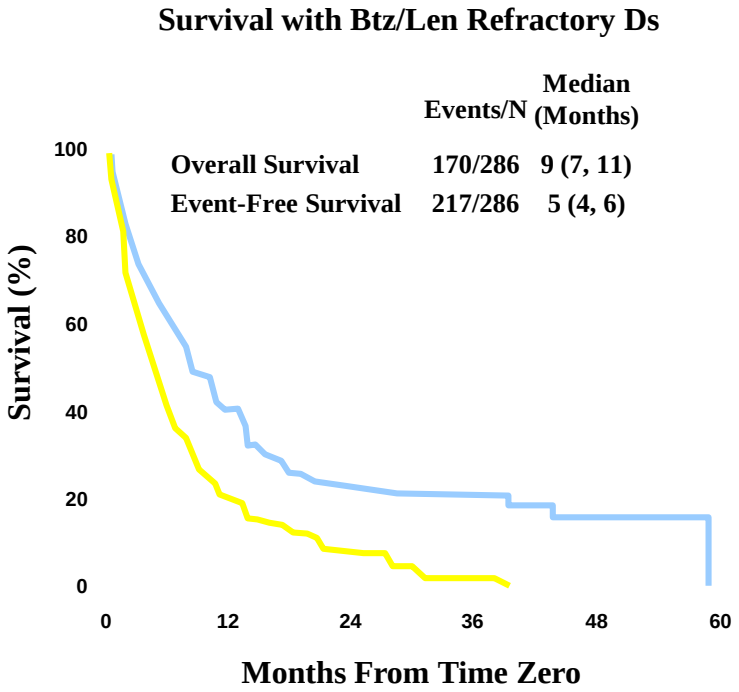
Choosing Therapies for Myeloma

IMiDs	Proteasome Inhibitors	Anthracyclines	Alkylators	Steroids	HDACi	Antibodies	SINE
Thalidomide	**Bortezomib**	**Doxil**	**Melphalan**	**Dexamethasone**	**Panobinostat**	**Elotuzumab**	**Selinexor**
Lenalidomide	**Carfilzomib**	**Doxorubicin**	**Cytoxan**	**Prednisone**		**Daratumumab**	
Pomalidomide	**Ixazomib**		**Bendamustine**	**Solumedrol**		**Isatuximab**	
						Belantamab	



Once Treatment Fails Trouble Begins

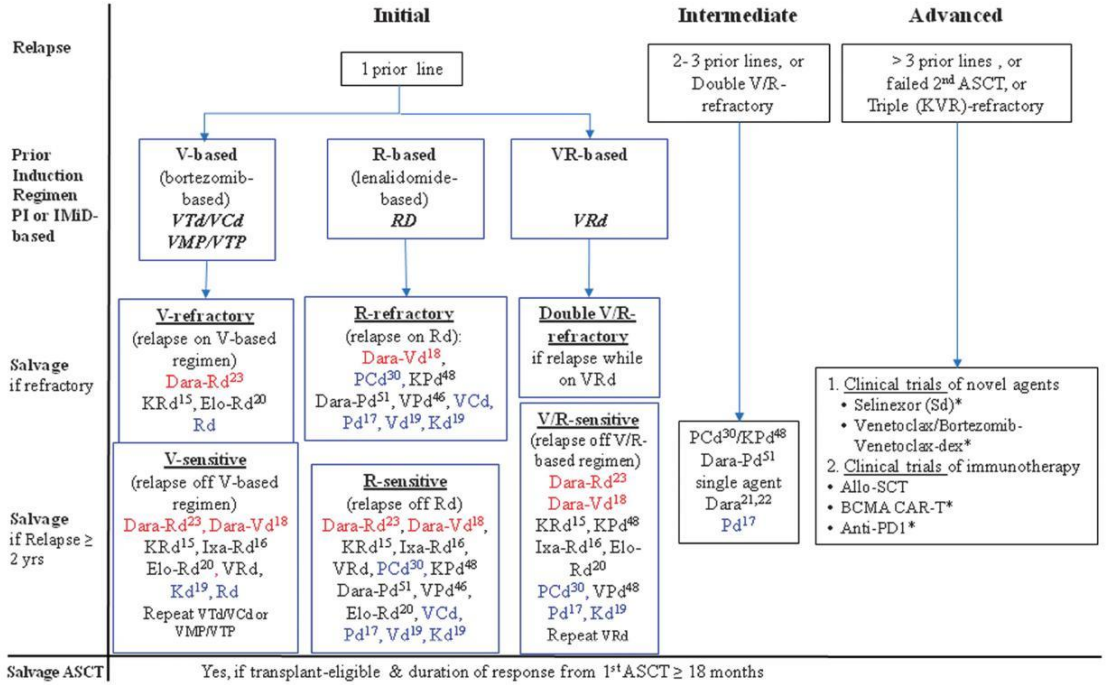




Kumar S. *Mayo Clin Proc.* 2004;79:867-874.

Kumar SK et al. *Leukemia.* 2012;26:149-157.

Sequencing Strategies

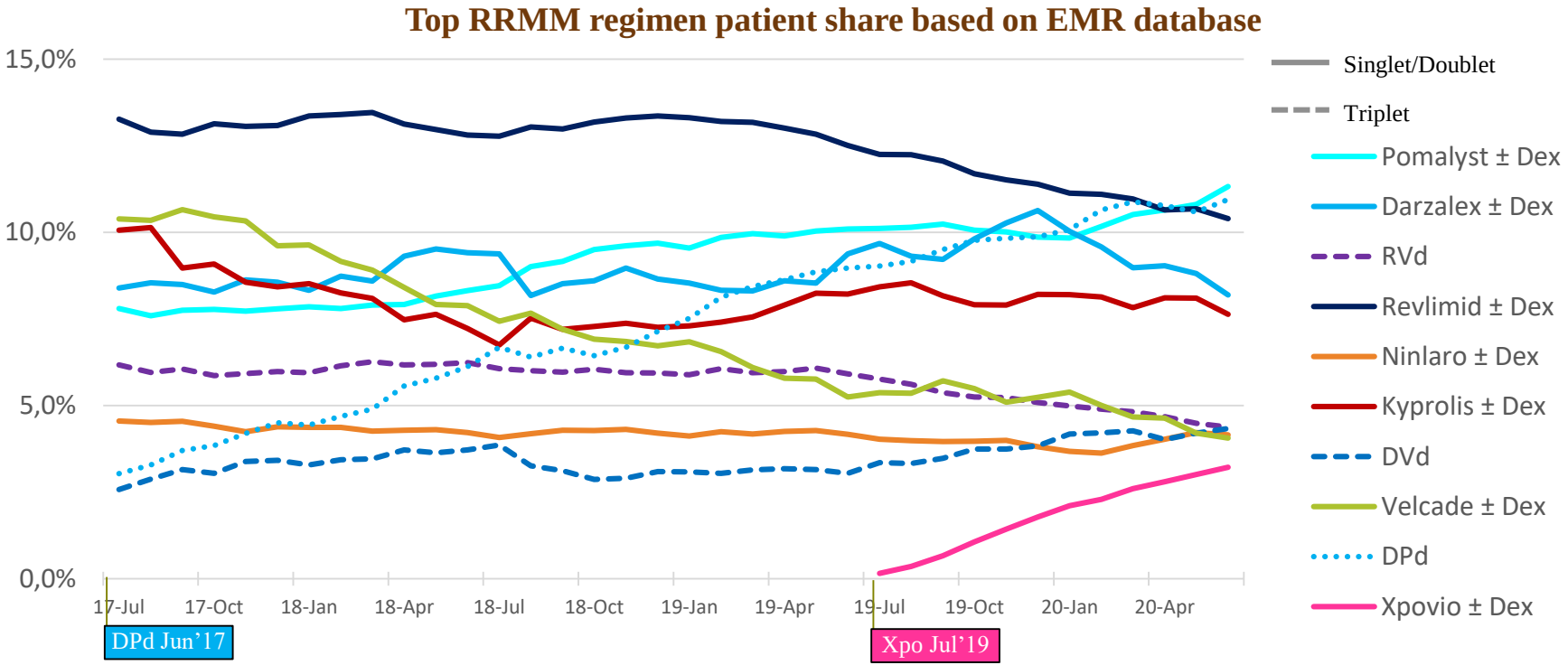


Abbreviations: Regimen in "red" font: most potent, 1st choice; "blue" font: less expensive regimens; PI: proteasome inhibitor, IMiD: immunomodulatory agent; V: bortezomib; R: lenalidomide; VTd: bortezomib-thalidomide-dexamethasone, VCd: bortezomib-cyclophosphamide-dexamethasone, VMP: bortezomib-melphalan-prednisolone, 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, *: ongoing clinical trials, number in superscript: reference in the manuscript

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

Fragmented RRMM Regimens Used in a Real-world Setting

55% Regimens are Singlet/Doublet Therapy (2L+)



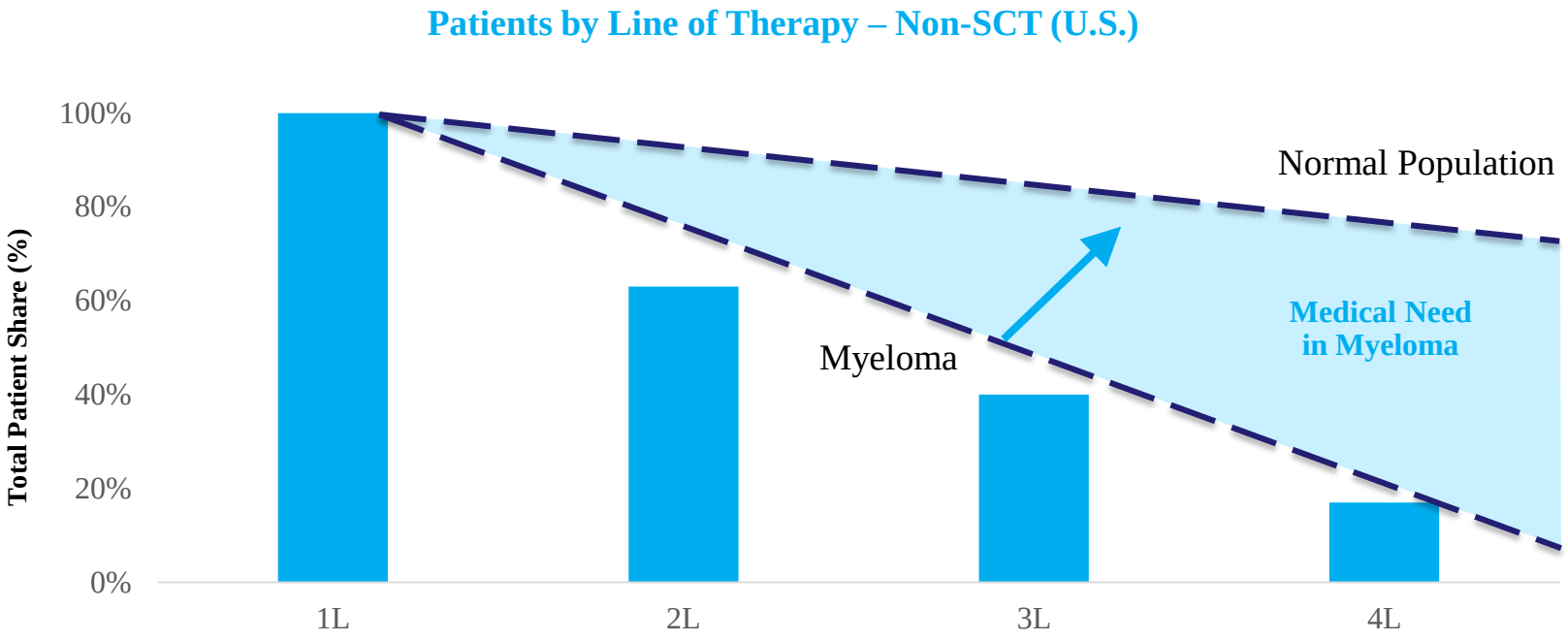
RRMM Approvals

Note: Assumed dexamethasone inclusion in regimens although not reported in data. Regimens <3% share not shown

Source: Intrinsiq MAT, Q2 2020

There is an Unmet Medical Need for Patients with RRMM

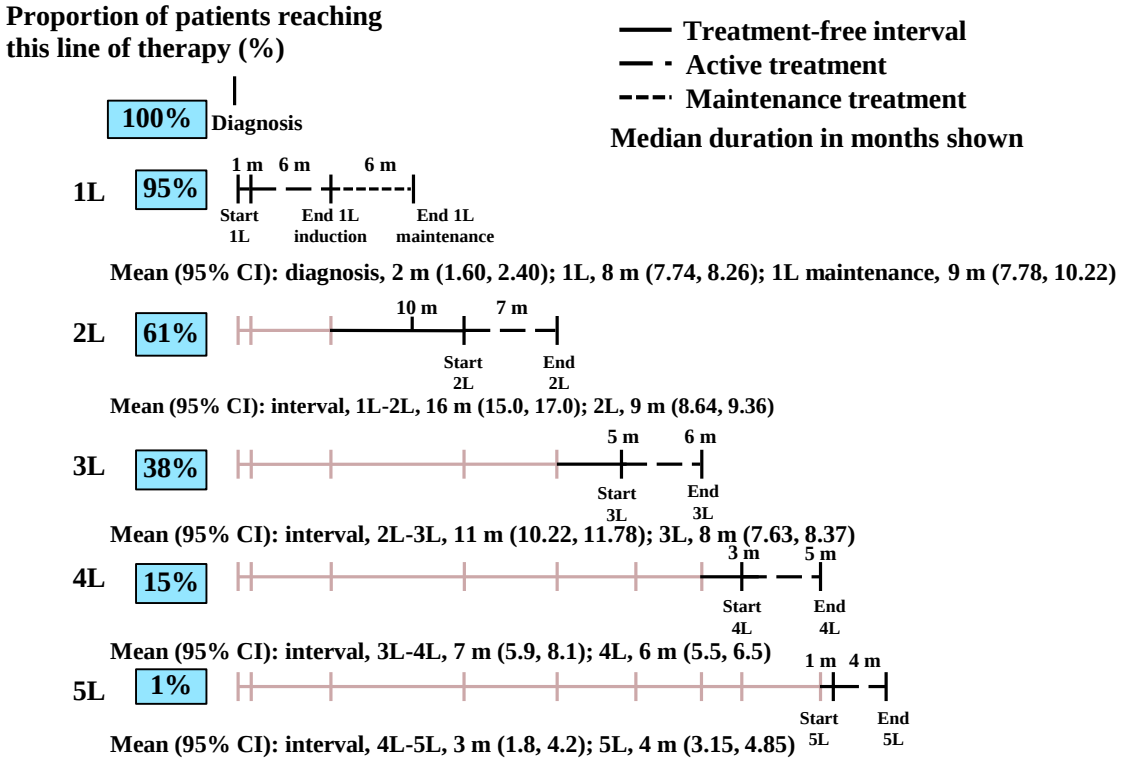
Later Line Patient Population Growing with Need for New Treatments



Source: Kantar Health 2018

Multiple Myeloma: Patient Outcomes in Real-World Practice

Treatment Duration and Treatment-Free Interval by Line of Therapy*



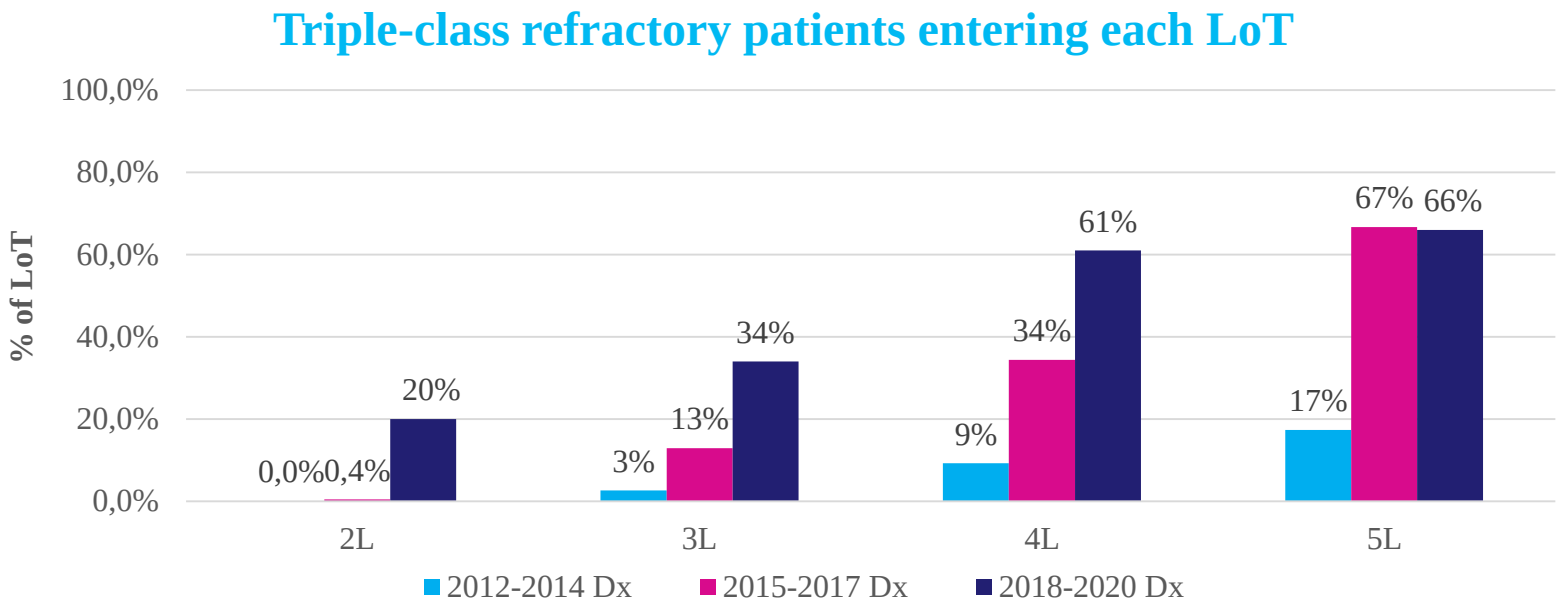
*Data from 4997 patient charts in Belgium, France, Germany, Italy, Spain, Switzerland, and the UK.

The proportion of patients who had received each line are from the cross-sectional review; data on durations of treatment and treatment-free intervals are from the retrospective review.

1L-5L = first line-fifth line treatment; CI = confidence interval; m = month.

Yong K, et al. *Br J Haematol*. 2016;175:252-264.

Triple-class Refractory Patients Are Growing Quickly and Occurring Earlier in RRMM



Source: Oncopeptides market research Q2 2020 and analysis; IQVIA patient data 2015-2018

Classical Chemotherapy in Quad- and Penta- Refractory Myeloma

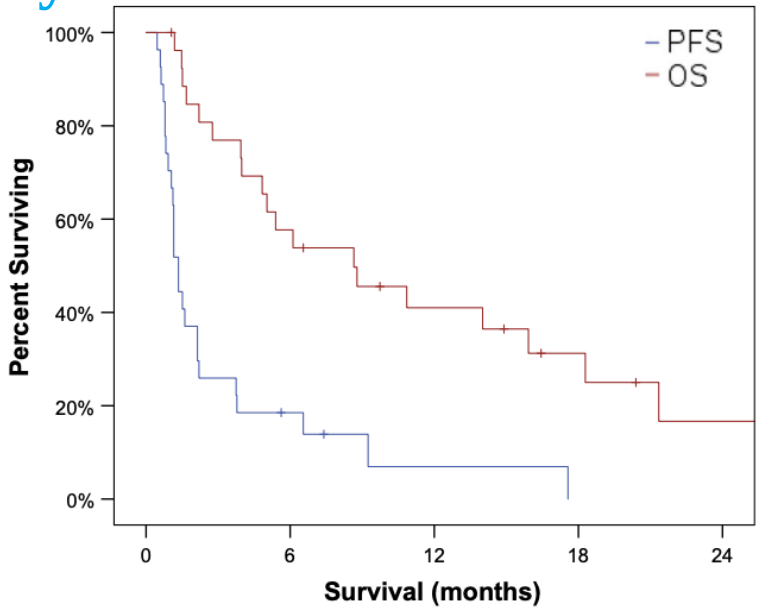


Fig. 1 Progression-free and overall survival of bendamustine-prednisone in quad- and penta-refractory myeloma. The median progression-free survival was 1.4 months (95% CI 1.1–1.6) and median overall survival was 8.7 months (95% CI 2.3–15.0)

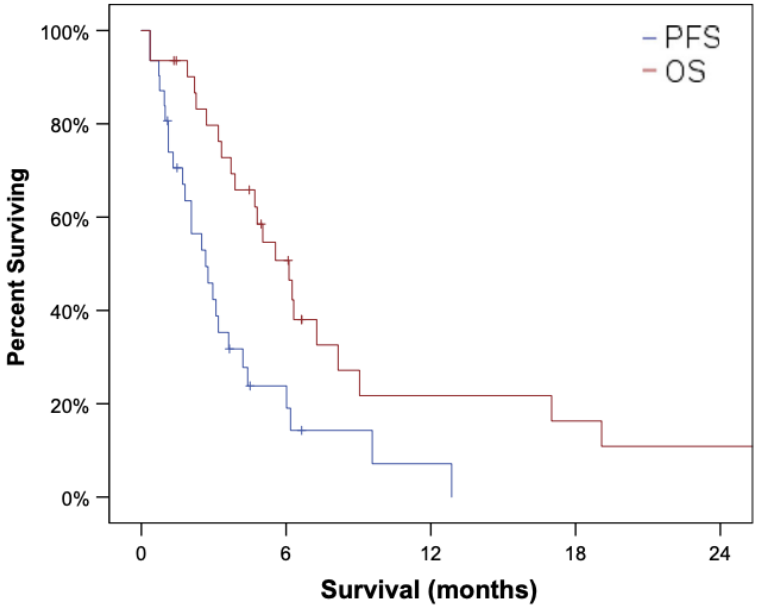


Fig. 2 Progression-free and overall survival of DCEP in quad- and penta-refractory myeloma. The median progression-free survival was 2.7 months (95% CI 1.5–3.8) and median overall survival was 6.2 months (95% CI 4.4–7.8)

Goldsmith, et al. Annals of Hematology (2020) 99:1041–1048

HORIZON: Registrational Trial for Accelerated Approval

Phase 2, Single-Arm, Open-Label, Multicenter Study

Adult patients with

RR MM refractory to pom or anti-CD38 mAb or both

≥2 prior lines of therapy, including an IMiD and a PI

ECOG PS ≤2

N=157

NCT02963493

Melflufen 40 mg + dex 40 mg[a]
(Until disease progression or unacceptable toxicity)

(EoT)

PFS and OS follow-up for ≤24 mo

	28-Day Cycle			
	D1	D8	D15	D22
Melflufen (IV)	✓			
Dex (oral)	✓	✓	✓	✓

Primary endpoint

- ORR

Secondary endpoints

- DOR
- CBR
- TTNT
- PFS
- TTR
- Safety
- OS
- TTP
- HRQOL

Data cutoff date: January 14, 2020

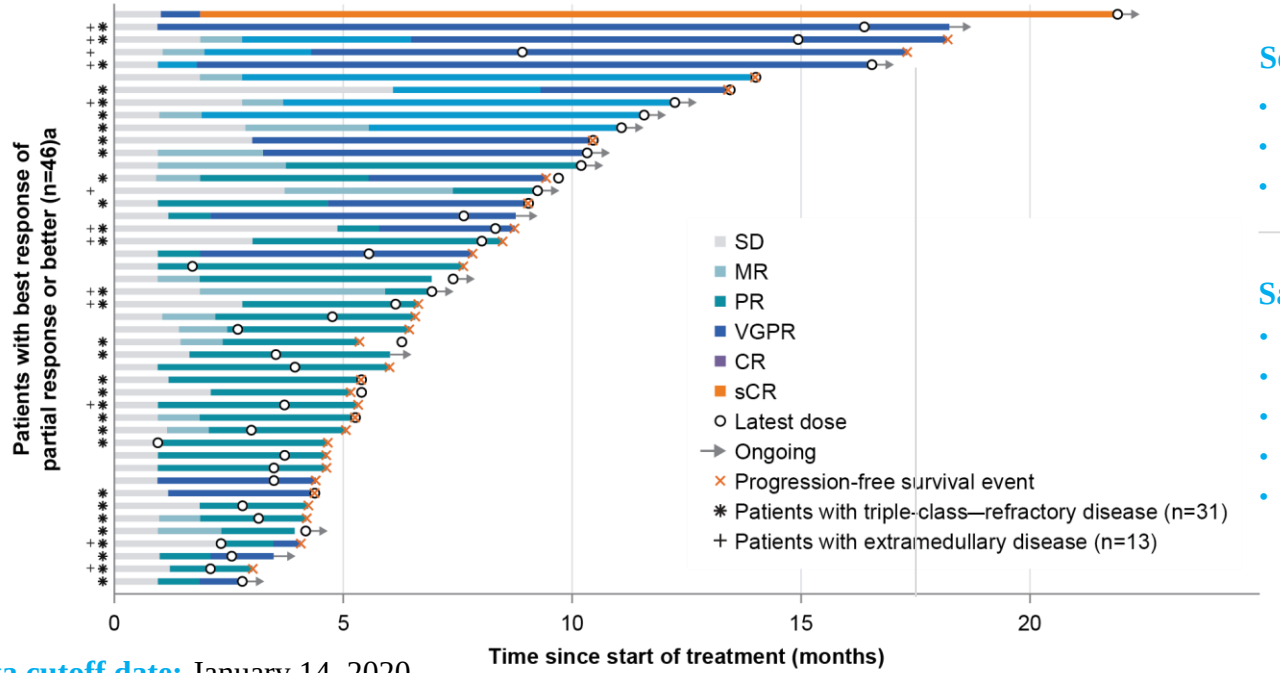
[a] Patients aged ≥75 years received dex 20 mg.

CBR, clinical benefit rate; dex, dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; EoT, end of treatment; HRQoL, health-related quality of life; IMiD, immunomodulatory agent; IV, intravenous; mAb, monoclonal antibody; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PI, proteasome inhibitor; RR MM, relapsed/refractory multiple myeloma; TTNT, time to next treatment; TTP, time to progression; TTR, time to response.

Richardson P, et al. Oral Presented at the 24th EHA Annual Congress, June 13-16, 2019. Abstract S1605; Richardson P, et al. Oral (Late Breaker) Presented at the 17th International Myeloma Workshop, September 12-15, 2019. Abstract OAB-86; Richardson P, et al. ePoster at the virtual edition of the 25th EHA Annual Congress, June 11-21, 2020. Abstract EP945.

HORIZON Study Results: Summary of Outcomes (ITT)

ORR: Patients in the Who Achieved a PR or Better



Data cutoff date: January 14, 2020

Primary endpoint (95%CI)

- **ORR: 29% (22-37)**

Secondary endpoints (95%CI)

- **DOR: 5.5m (3.4-7.6)**
- **PFS: 4.2m (3.4-4.9)**
- **mPFS in responders 8.5m**
- **CBR: 45% (37-53)**
- **OS: 11.6m (9.3-15.4)**

Safety (% all Grade /Gr 3/Gr 4)

- **Neutropenia: 82/ 32/ 47**
- **Thrombocytopenia: 82/ 25/ 51**
- **Anemia: 71/ 42/<1**
- **Nausea: 32/ <1/ 0**
- **Fatigue: 29/ 3/ 0**

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What a New Treatment Option Would Mean For My Clinic

- In the Horizon Trial, Melphalan Flufenamide demonstrated clinically meaningful efficacy and a manageable safety profile in heavily pretreated relapsed refractory multiple myeloma patients

- An effective alkylator-based option for patients who enter the more advanced relapsed setting
- An option for RRMM with limited non-hematologic toxicity
- At its core alkylators, including melphalan, remain one of best anti-myeloma therapies in existence. Current approaches as follows
  - Sometimes too much: High-dose with ASCT
  - Sometimes not enough: oral alkeran

- Goldilocks alkylator? : Mid-range dosing that is cyclable, tolerable and effective