REGIONAL COMMUNITY WORKSHOP

Welcome and Announcements

Kelly Cox

IMF Senior Director, Regional Community Workshops

REGIONAL COMMUNITY WORKSHOP

Thank you to our sponsors!

REGIONAL COMMUNITY WORKSHOP

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VIRTUAL REGIONAL COMMUNITY WORKSHOP

Saturday, November 21, 2020 | 9:00 AM-11:30 AM CT / 10:00 AM-12:30 PM ET

INTERNATIONAL MYELOMA FOUNDATION

with support from:
Amgen, The Binding Site, Bristol Myers Squibb, Janssen, Karyopharm Therapeutics, and Takeda Oncology

Craig Cole, MD

Assistant Professor, Division of Hematology and Oncology, MSU Breslin Cancer Center

Agne Paner, MD

Associate Professor, Division of Hematology, Oncology and Cell Therapy, Rush Medical College

Amy E. Pierre, RN, MSN, ANP-BC

Memorial Sloan Kettering Cancer Center

IMF Nurse Leadership Board

REGIONAL COMMUNITY WORKSHOP

Southern USA Virtual Regional Community Workshop (RCW)

Times listed are in Eastern Daylight Time (EDT)

10:00 - 10:10	Welcome and Announcements from Kelly Cox
10:10 - 10:50	"Myeloma 101 and Frontline Therapy"
	Craig Cole, MD – Michigan State University (MSU)
10:50 - 11:05	Question and Answer Session with Panel
11:05 - 11:10	Stretch
11:10 - 11:40	"Relapsed Therapy and Clinical Trials"
	Agne Paner, MD – Rush Medical College

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Southern USA Virtual Regional Community Workshop (RCW)

Times listed are in Eastern Daylight Time (EDT)

11:40 - 11:55	Question and Answer Session with Panel
11:55 - 12:15	"Health in the COVID Era" Amy Pierre, RN, MSN, ANP-BC – Memorial Sloan Kettering Cancer Center
12:15 - 12:30	Question and Answer Session with Panel Closing Comments Kelly Cox

REGIONAL COMMUNITY WORKSHOP

REGIONAL COMMUNITY WORKSHOP

“Myeloma 101”
“Frontline Therapy”

Craig Cole, MD
Michigan State University
(MSU) Breslin Cancer Center

REGIONAL COMMUNITY WORKSHOP

The Application of Science: Multiple Myeloma 101 and Frontline Therapy

International Myeloma Foundation

Great Lakes Virtual Regional Community Workshop

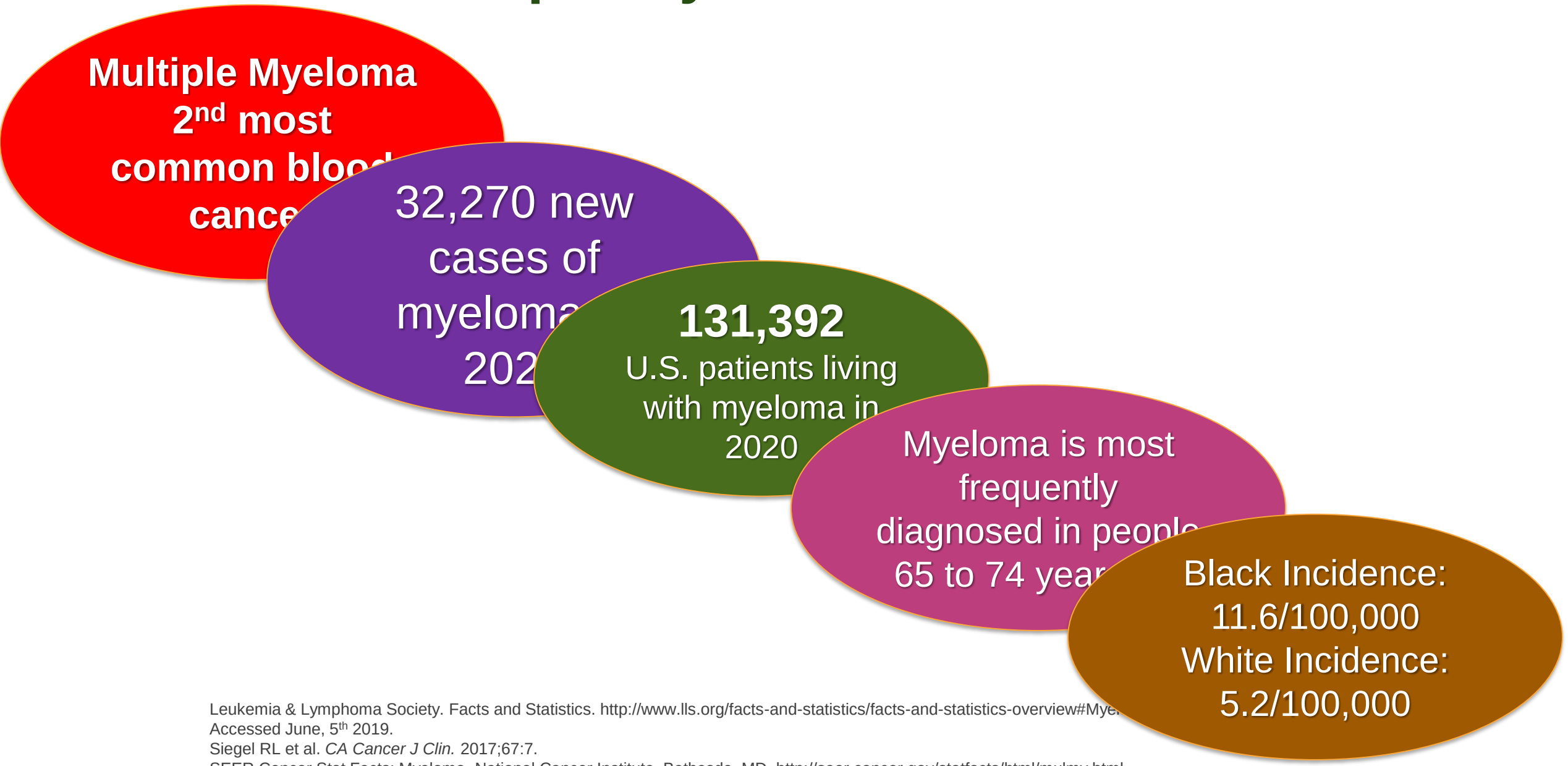
Craig Emmitt Cole, M.D.
Assistant Professor
Department of Internal Medicine
Division of Hematology/Oncology; Hematology Section
Breslin Cancer Center
Michigan State University

MICHIGAN STATE UNIVERSITY | College of Human Medicine
Breslin Cancer Center

Today's Discussion

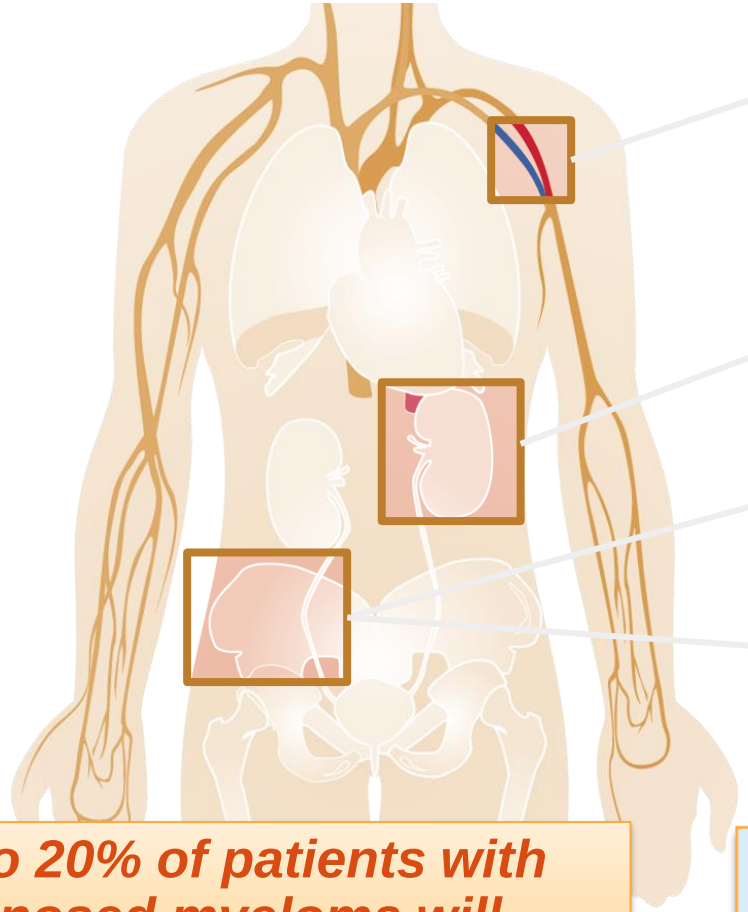
- How common is multiple myeloma
- Spectrum of plasma cell disorders
- Diagnosis of myeloma and labs
- Staging and risk stratification
- Treatment sequence and regimens
- Up front therapy strategies: induction, transplant, and maintenance
- Bone support
- "New Stuff" 4 drug induction therapy
- Perspectives in the advancement of myeloma science and survival

Multiple Myeloma Fast Facts



Leukemia & Lymphoma Society. Facts and Statistics. http://www.lls.org/facts-and-statistics/facts-and-statistics-overview#Mye
Accessed June, 5th 2019.
Siegel RL et al. *CA Cancer J Clin.* 2017;67:7.
SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/statfacts/html/mulmy.html

Common Symptoms Multiple Myeloma



Low Blood Counts
- Anemia is present in 60% at diagnosis
- May lead to anemia and infection

→ **Weakness**
Fatigue
Infection

Decreased Kidney Function
- Occurs in over half of myeloma patients

→ **Weakness**

Bone Damage
- Affects 85% of patients
- Leads to fractures

→ **Bone pain**

Bone Turnover
- Leads to high levels of calcium in blood (hypercalcemia)

→ **Loss of appetite**
Weight loss

About 10% to 20% of patients with newly diagnosed myeloma will not have any symptoms.

C: Calcium elevation (>11 mg/dL)
R: Renal- low kidney function; (serum creatinine >2 mg/dL)
A: Anemia –low red blood count (Hb <10 g/dL)
B: Bone disease (≥1 lytic lesions on skeletal radiography, CT, or PET-CT)

Campbell K. Nurs Times. 2014;110:12.

Spectrum of Plasma Cell Disorders and Myeloma

MGUS

M protein under 3 g/dL
AND
Plasma cells in Bone Marrow <10%
AND
No CRAB or "SLiM" high risk features

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

Observation
Clinical Trials

Smoldering Myeloma

M protein over 3 g/dL (serum) or over 500 mg/24 hrs (urine)
AND
Plasma cells in Bone Marrow 10%–60%
AND
No CRAB or "SLiM" high risk features

10% risk of progression/year to active myeloma

Observation
Clinical Trials

High Risk Smoldering

M protein over 2 g/dL
AND
Plasma cells in Bone Marrow 20%–60%
AND
Free Lt Chain Ratio >20

- "Evolving type"SMM Increase >10% protein w/in 6mo

AND
No CRAB or "SLiM" high risk features

>46% risk of progression in 2 yr to active myeloma

Close Observation
Clinical Trials
?? Treatment??

Multiple Myeloma

Malignant Plasma cells seen on any biopsy
AND ≥1 "CRAB" feature

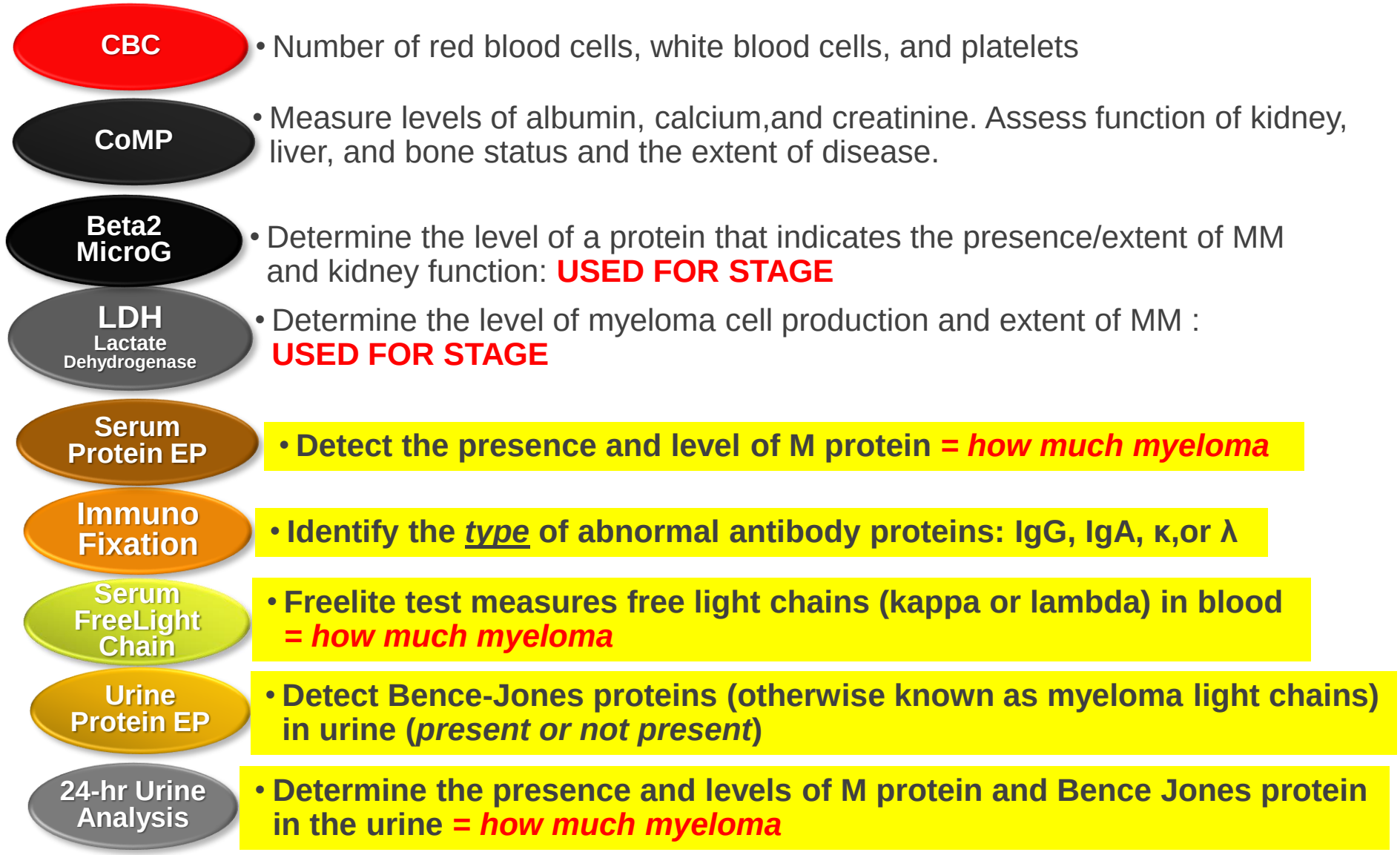
C: Calcium elevation (>11 mg/dL)
R: Renal- low kidney function; (serum creatinine >2 mg/dL)
A: Anemia –low red blood count (Hb <10 g/dL)
B: Bone disease (≥1 lytic lesions on skeletal radiography, CT, or PET-CT)

OR have ≥1 SLiM 'high risk" features:

S: >60% Plasma Cells on Bone Marrow biopsy
Li: Serum light chain ratio >100
M: >1 lytic lesions on MRI

Front Line Treatment
Clinical Trials

Diagnosing Myeloma: Learn Your Labs!



Serum Protein EP

- Detect the presence a… …protein = *how much myeloma*

Monoclonal protein

Treatment

Monoclonal gammopathy

IgG Kappa M-Protein

Treatment

Serum FreeLight Chain

- Freelite test measures fr… …ht chains (kappa or lambda) in blood = *how much myeloma*

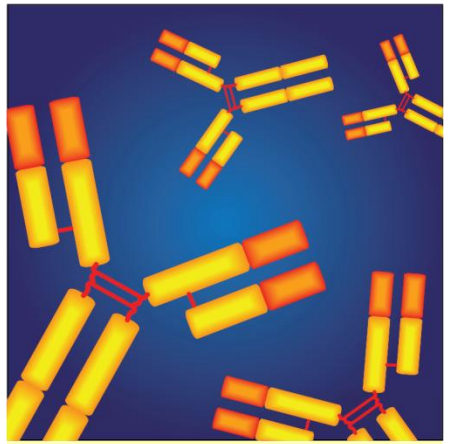
Kappa Lt. Chain MM

Lambda Lt. Chain

Positive Kappa Monoclonal Serum Light Chains

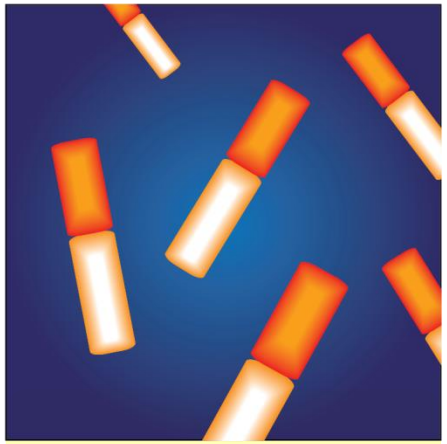
Ratio: 1

Types of Monoclonal Protein (M Protein) in Multiple Myeloma



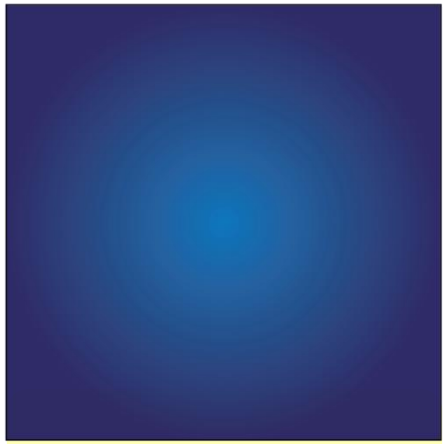
Intact immunoglobulin

- For example:
  - IgG+kappa
  - IgG+lambda
  - IgA+kappa
  - IgA+lambda
  - etc…
- 80% of myeloma cases



Light chain only

- Also known as Bence Jones protein
- 20% of all myeloma cases
- Renal failure more common in light chain multiple myeloma; creatinine >2 mg/dL in 1/3 of cases

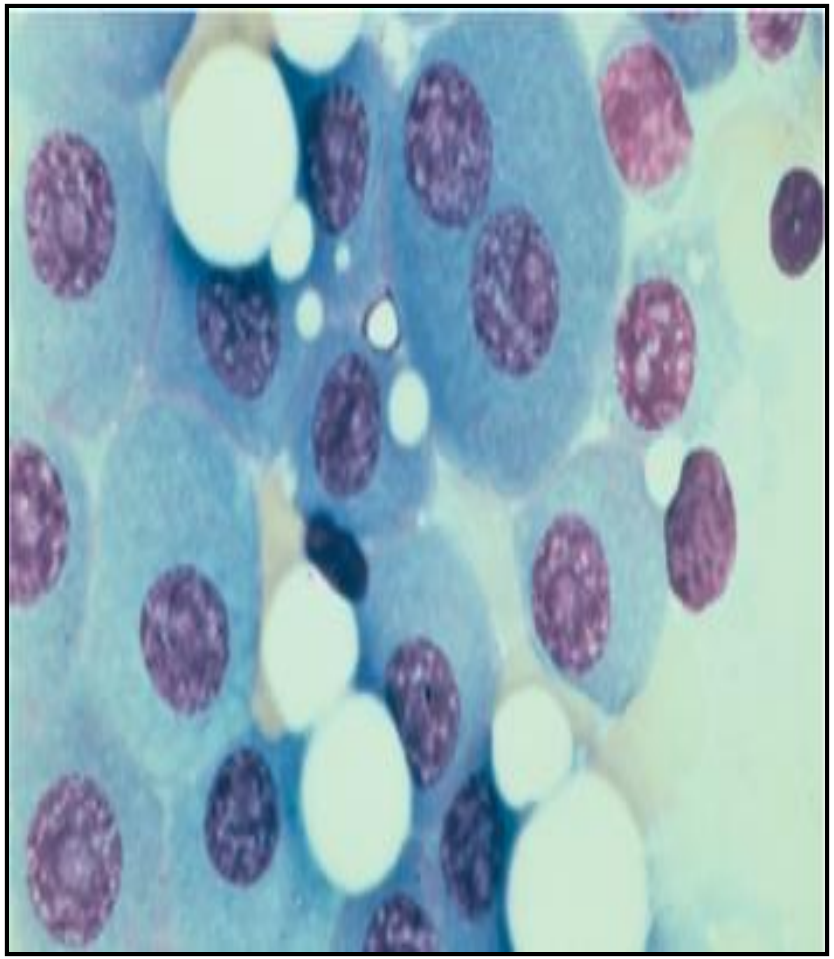


Non-secretory

- No monoclonal protein present
- 3% of cases of multiple myeloma

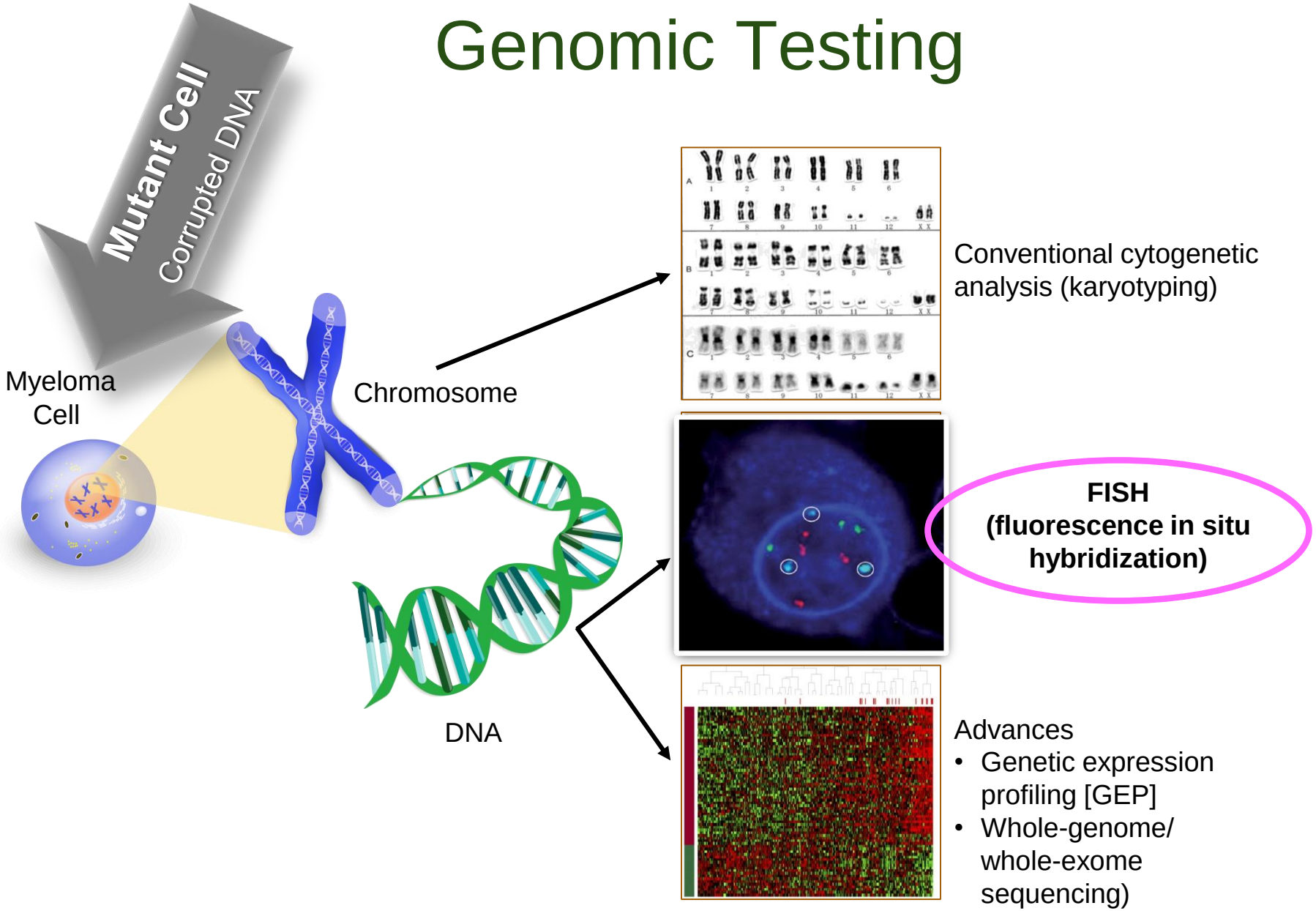
Diagnosis of Multiple Myeloma

- Conventional X-rays reveal punched-out lytic lesions, osteoporosis, or fractures in 75% of patients.
- FDG PET/CT appears to be more sensitive (85%) than skeletal survey for the detection of small lytic bone lesions.
- Diagnosis is confirmed with bone marrow demonstrating greater than **10% involvement by malignant plasma cells.**



Kyle RA et al. Mayo Clin Proc Jan;78(1): 2003. Nanni C et al. European Journal of Nuclear Medicine and Molecular Imaging Vol. 33:2006 Dimopoulos MA, et al. Leukemia. *2009*

Staging Myeloma: The Importance of Genomic Testing



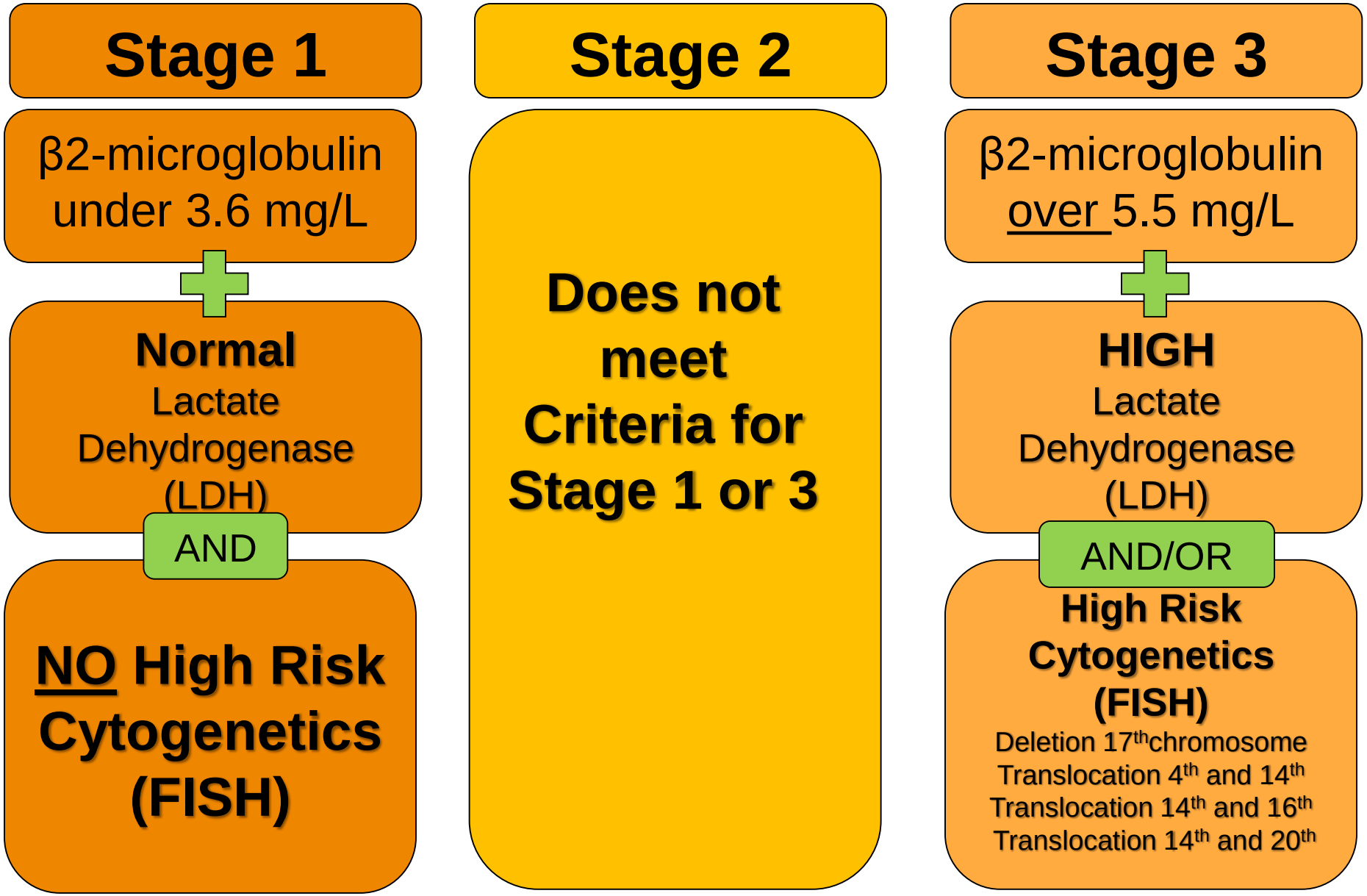
Staging Myeloma: FISH helps to Assign Risk in Myeloma

Risk Category	High Risk	Standard Risk
Findings on Chromosome (FISH) Analysis Results in the Bone marrow	**FISH:** • Deletion 17th chromosome • Gain of chromosome # 1 • Translocation 4;14 • Translocation 14 and 16 • Translocation 14 and 20 • Mutations in p53 gene on chromosome 17	**FISH:** • Hyperdiploid: *More than 1 pair of chromosomes* • Translocation 11;14 • Translocation 6;14 • Others • Normal

*Based on the Updated Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Guidelines 2013 Mikhael JR et al. *Mayo Clin Proc*. 2013;88:360.

Revised International Staging System for Multiple Myeloma

From International Myeloma Working Group



*Based on the Updated Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Guidelines 2013 Mikhael JR et al. *Mayo Clin Proc*. 2013;88:360.

Palumbo et al. *JCO*. September 10, 2015 vol. 33 no. 26 2863-2869

AND OTHER NOVEL THERAPIES:
Selinexor (Xpovio)
Belantamab mafodotin (Blenrep)
Farydak (panobinostat)

More to come…

Immunomodulatory Drugs (I

Thalomid(*Thalidomide*), Revlimid(*Lenalidomide*), Pomalyst(*Pomalidomide*)

Proteasome Inhibitors (Pis):

Velcade(*Bortezomib*), Ninlaro(*Ixazomib*), Kyprolis(*Carfilzomib*)

Antibodies Against Myeloma (Immunotherapy):

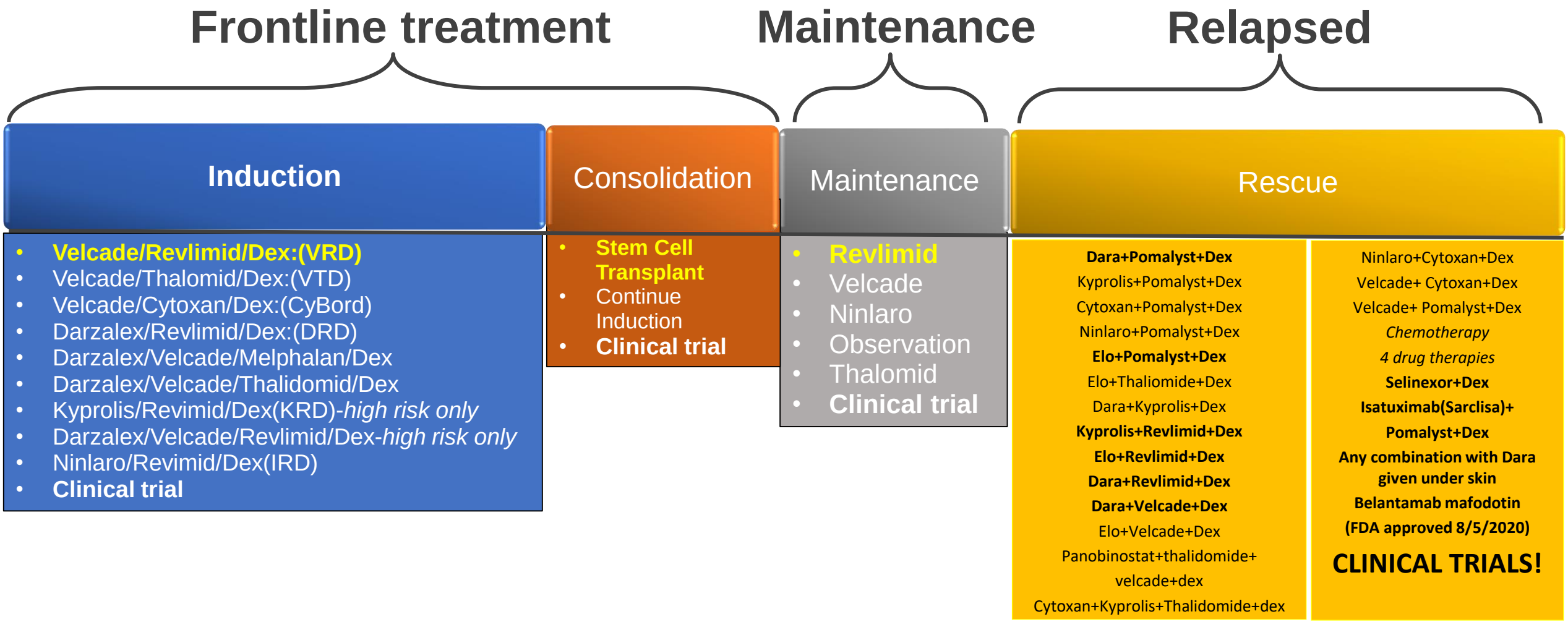
Darzelex (*Daratumumab*), Sarclisa(*Isatuximab*), Empliciti(*Elotuzumab*)

Tools of the Trade for Frontline Therapy

Standard Drug Overview

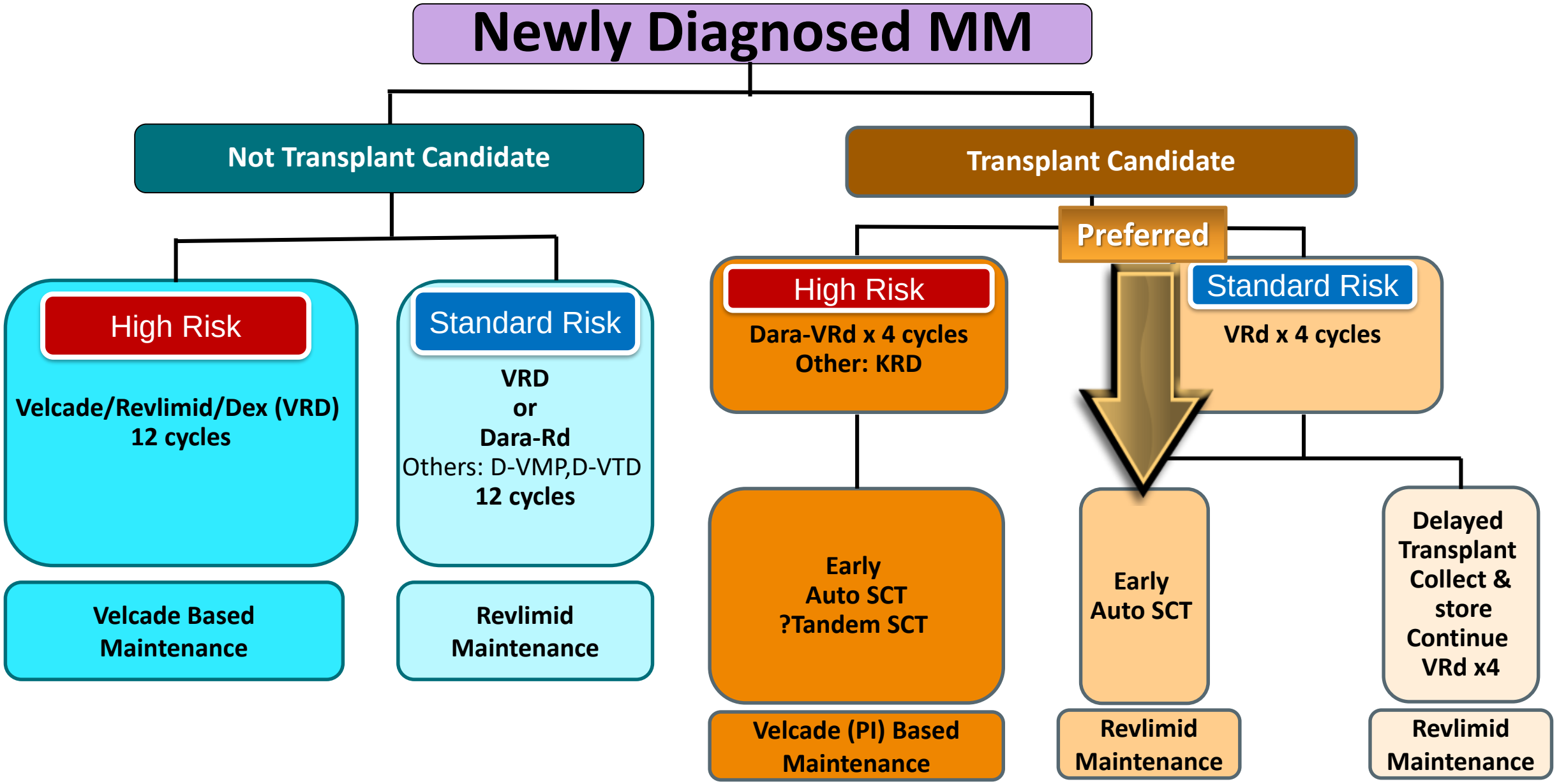
Class	Drug Name	Abbreviation	Administration
IMiD immunomodulatory drug	Revlimid (lenalidomide)	R or Rev	Oral
	Thalomid (thalidomide)	T or Thal	
Proteasome inhibitor	Velcade (bortezomib)	V or Vel or B	Intravenous (IV) or subcutaneous injection (under the skin)
	Kyprolis (carfilzomib)	C or K or Car	
	Ninlaro (ixazomib)	N or I	Oral
Chemotherapy	Cytoxan (cyclophosphamide)	C	Oral or intravenous
	Alkeran or Evomela (melphalan)	M or Mel	
Steroids	Decadron (dexamethasone)	Dex or D or d	Oral or intravenous
	Prednisone	P	
Monoclonal Antibodies	Daratumumab (Darzalex)	Dara	Intravenous (IV)

Treatment Sequence and Regimens for Active Myeloma



National Comprehensive Cancer Network. The NCCN Clinical Practice Guidelines in Oncology Multiple Myeloma (Version 1.2020). http://www.nccn.org/. Accessed September 6 2020

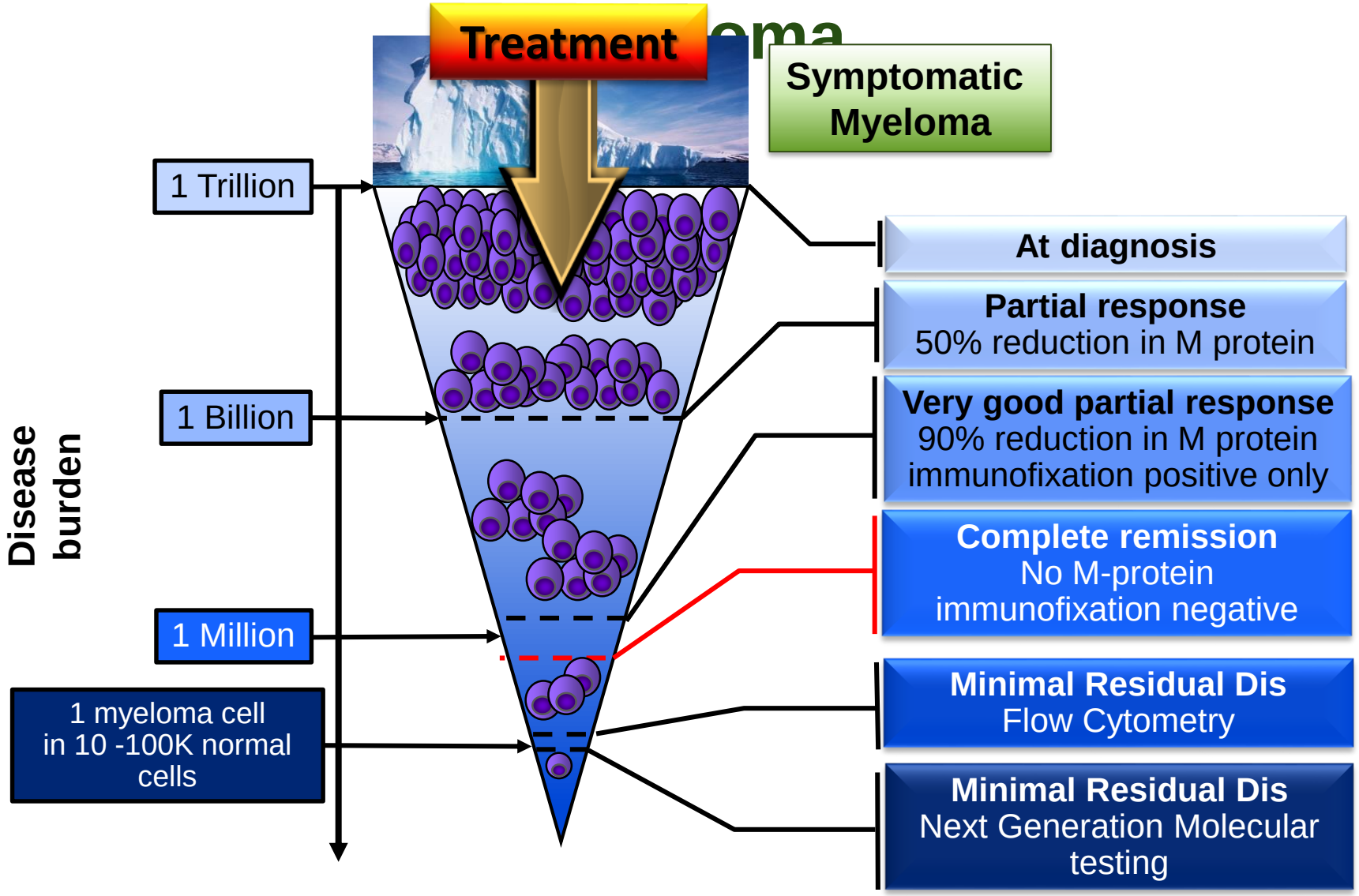
Newly Diagnosed MM



https://www.msmart.org/mm-treatment-guidelines

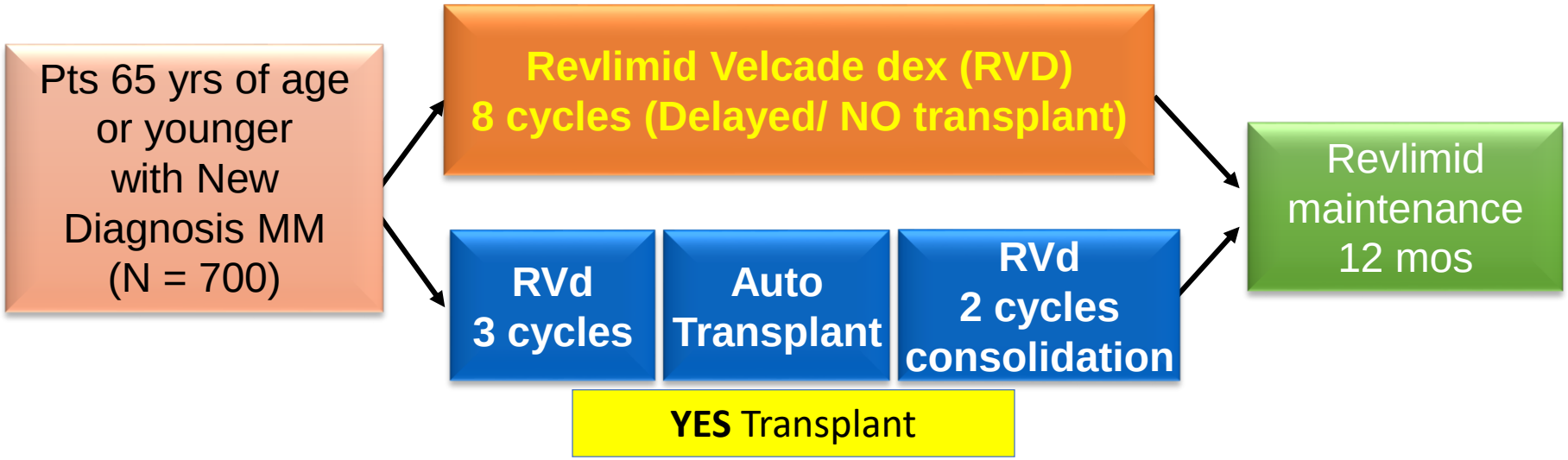
Dispenzieri et al. Mayo Clin Proc 2007;82:323-341; Kumar et al. Mayo Clin Proc 2009 84:1095-1110; Mikhael et al. Mayo Clin Proc 2013;88:360-376. v18 //last reviewed June 2020

Goals of Therapy: The Iceberg Model of oma



Stem Cell Transplant: Fighting Myeloma with the Left Hook!

RVD +Stem Cell Transplant vs. RVD with Late Transplant
IFM (Intergroupe Francophone du Myélome) 2009: Phase III Study Design



- Primary objective: Progress Free Survival (Time to next relapse)
- Revlimid Maintenance was only 1 year and stopped (not the standard in the US)
- At 1st relapse 76.7% of patients on the RVD only arm received a transplant at that time
- Follow-up was updated at in March 2020 with median f/u of 93 mos
- Study was done before routine use of carfilzomib and daratumumab tx at relapse

Attal M, et al. N Engl J Med 2017; 376:1311-1320 Perrot A, et al. ASH 2020, Abst:157

IFM 2009 : Response and Progression Free Survival

Parameter		RVd -Delayed Transplant- (n = 350)	Up Front Transplantation (n = 350)	P Value Is it Significant?
Grade 3 or 4 toxicities (%)	Blood	64	95	YES! P<0.001
	GI	7	28	
	Infection	9	20	
Median time to relapse (PFS), mos		35	47.3	YES! P<0.001
OVERALL SURVIVAL At 8 years (%)		60.2	62.2	NO
Very Good Partial Response and Complete Response (%)		77	88	YES! .001
Negative MRD		65	79	YES! .001

MDR negative was a strong predictor of PFS and OS

Attal M, et al. N Engl J Med 2017; 376:1311-1320 Perrot A, et al. ASH 2020, Abst:157

What to do After Transplant? STaMINA: Phase III Study Design

RESULTS

- **No difference in time to relapse (PFS) or Overall Survival in *standard risk* patients who have two transplants, consolidation RVD therapy, or just straight to maintenance after first BMT**
- **Straight to maintenance is the easiest!**
- **? If high risk patients benefit from two transplants**

Melphalan 200 mg/m² IV
Second ASCT
(n = 247)

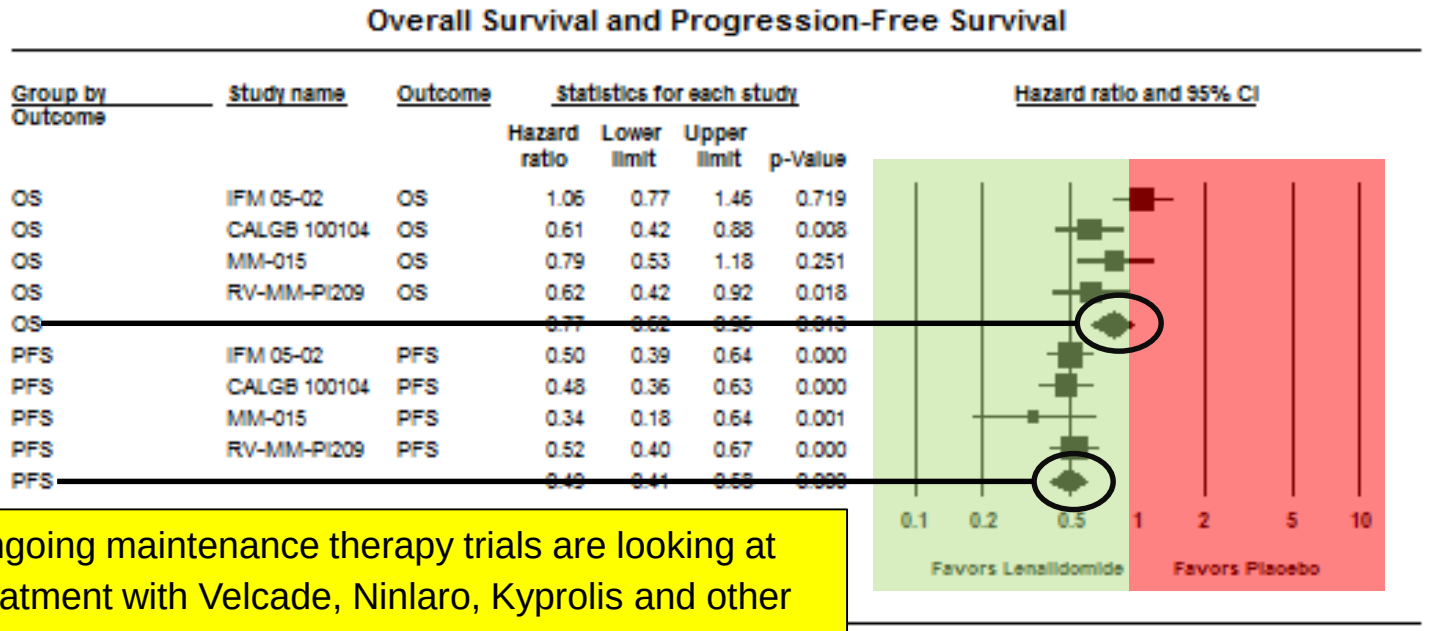
Induction regimens

- RVD
- CyBorD
- RD
- VD
- Others

Stadtmauer EA, et al. ASH 2016. Abstract LBA-1; Journal of Clinical Oncology 38, no. 15_suppl (ASCO May 20, 2020) 8506-8506

Analysis of the Maintenance Revlimid (Lenalidomide) Trials

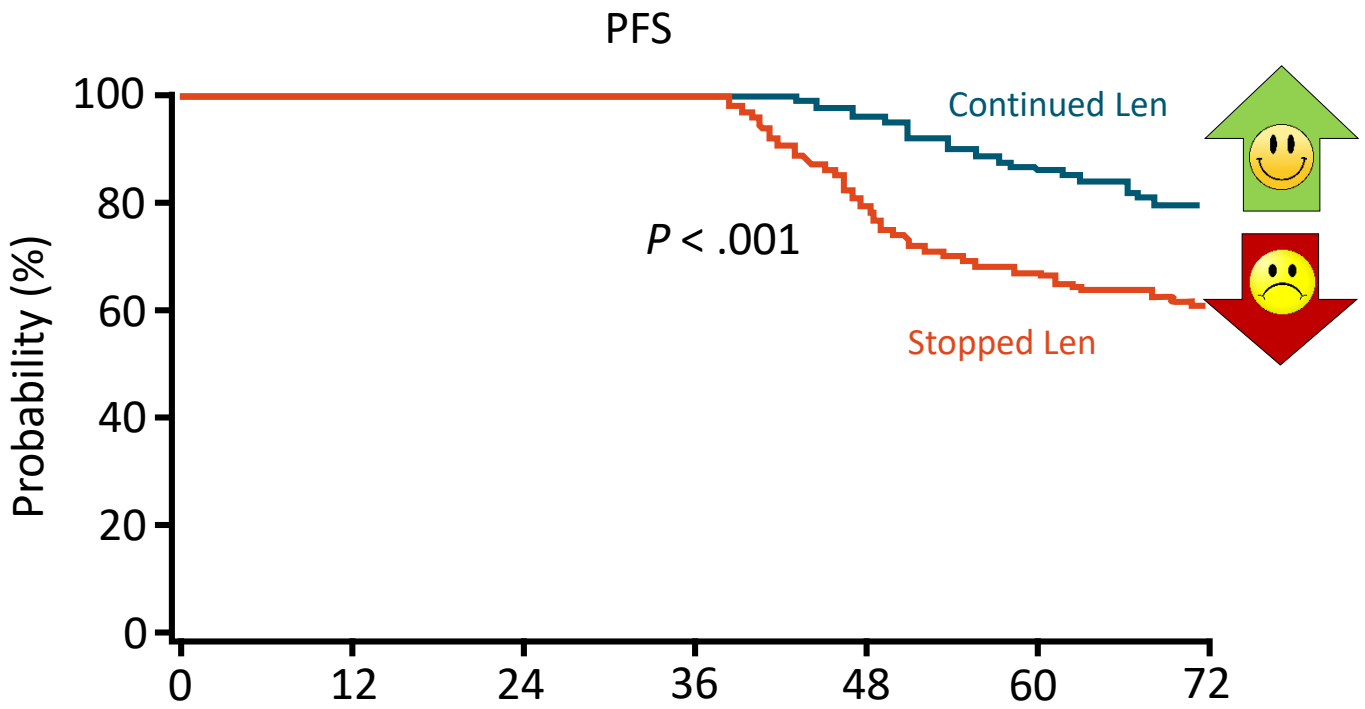
- Data from 4 randomized trials of Revlimid (lenalidomide) maintenance vs. no maintenance
  - Involving a total of almost **2,000** multiple myeloma patients
- The results of the analysis showed that Revlimid maintenance therapy is associated significant **improvement in progression-free survival and a modest improvement in overall survival**
- **Duration of maintenance is unknown**



- Ongoing maintenance therapy trials are looking at treatment with Velcade, Ninlaro, Kyprolis and other drugs used at treatment induction.

STaMINA Long-term Follow-up: Maintenance Therapy Time to elapse after transplant (PFS)

- **PFS benefit for lenalidomide continuation beyond 38 mos**



PFS, % (Range)	Continued Len (n = 215)	Stopped Len (n = 207)
4 yrs	95.8 (92-98)	80.1 (74-85)
5 yrs	86.5 (81-90)	67.2 (60-73)
6 yrs	79.5 (73-84)	61 (54-67)

5-Yr PFS, % (Range)	Continued Len	Stopped Len	*P* Value
High risk	86.7 (77-95)	67.8 (52-79)	.2
Std risk	86.3 (80-91)	66.7 (58-74)	< .001

- No OS benefit for lenalidomide continuation beyond 38 mos vs stopping in overall population (*P* = .353) or high-risk/standard-risk groups

Hari. ASCO 2020. Abstr 8506. Reproduced with permission.

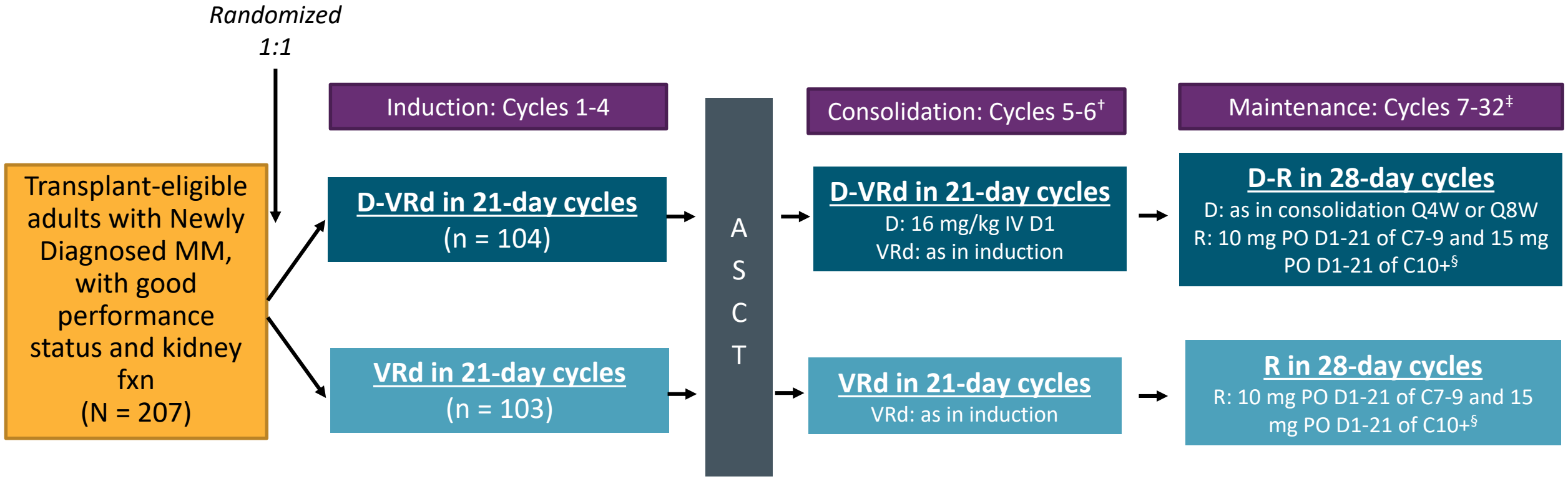
Bone Support & Control of Bone Pain

Multiple myeloma can cause weakened areas in the bone called osteolytic lesions
Plasma cell tumors can compress the spinal cord or cause bone destruction.

- Bone strengthening drugs: bisphosphonates (pamidronate & Zometa) or monoclonal antibodies (Xgeva) are given at diagnosis and continued for at least 2 years
- Vitamin-D and Calcium supplements to help bone healing
- Orthopedic support
  - Physical therapy, physical medicine consults, orthopedic/neuro surgery, radiation therapy, etc
- Drugs to control pain
- Anticonvulsants and antidepressants for treat relieve pain from nerve damage or numbness


NEW
STUFF

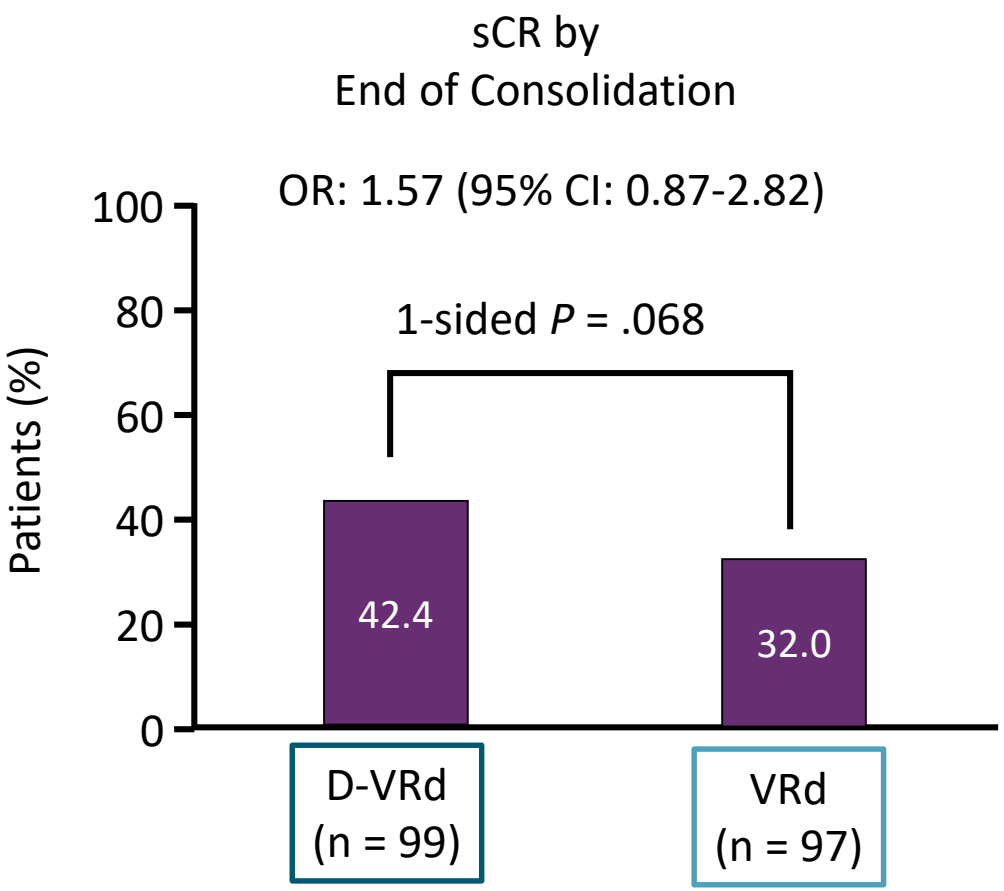
GRIFFIN Randomized Phase II: Dara-RVD vs. RVD in Newly Diagnosed Multiple Myeloma

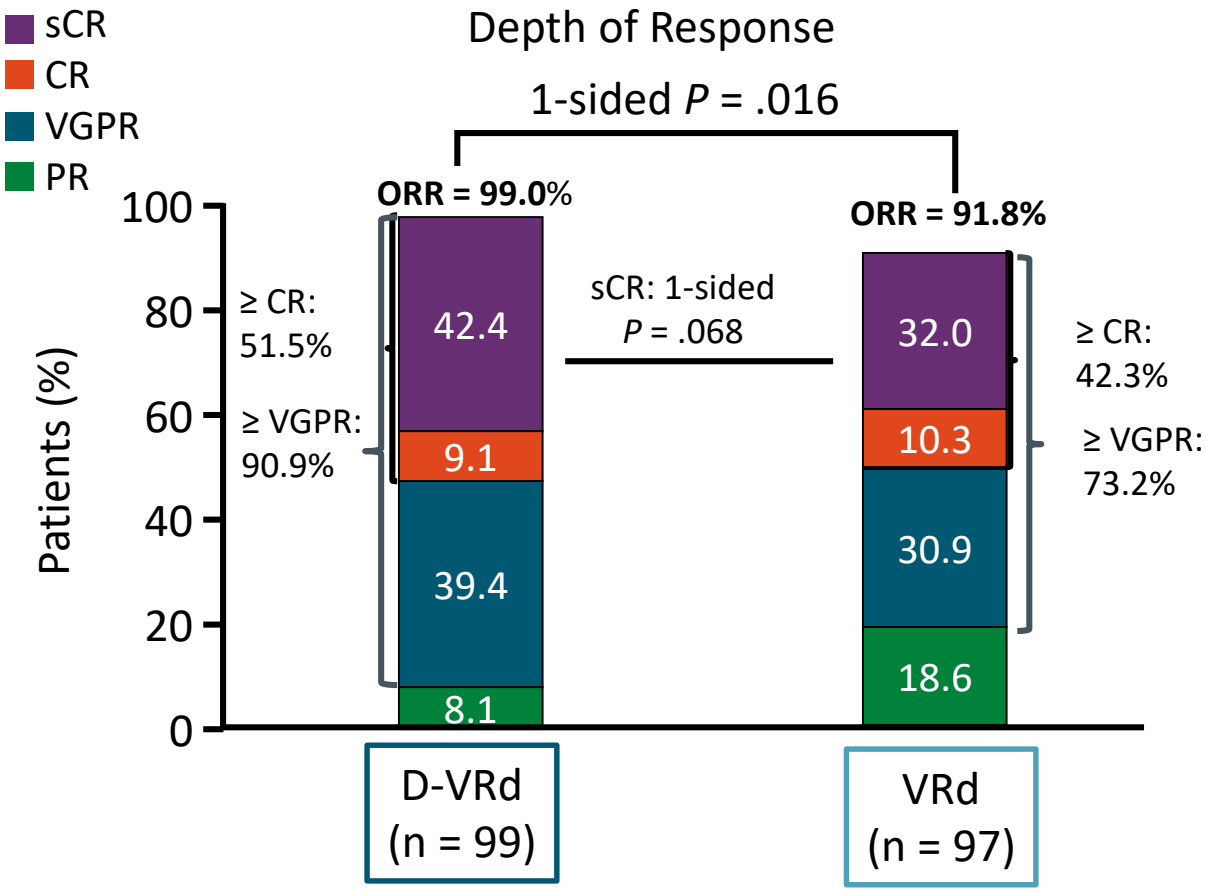


- Primary endpoint: sCR by end of consolidation with 1-sided $\alpha = .1$
  Secondary endpoints: MRD, CR, ORR, > VGP

Kaufman. ASH 2020. Abst.594; Voorhees PM etal. Blood. 2020 Aug 20;136(8):936-945.

GRIFFIN Update: Stringent Complete Response by End of Consolidation and Depth of Response

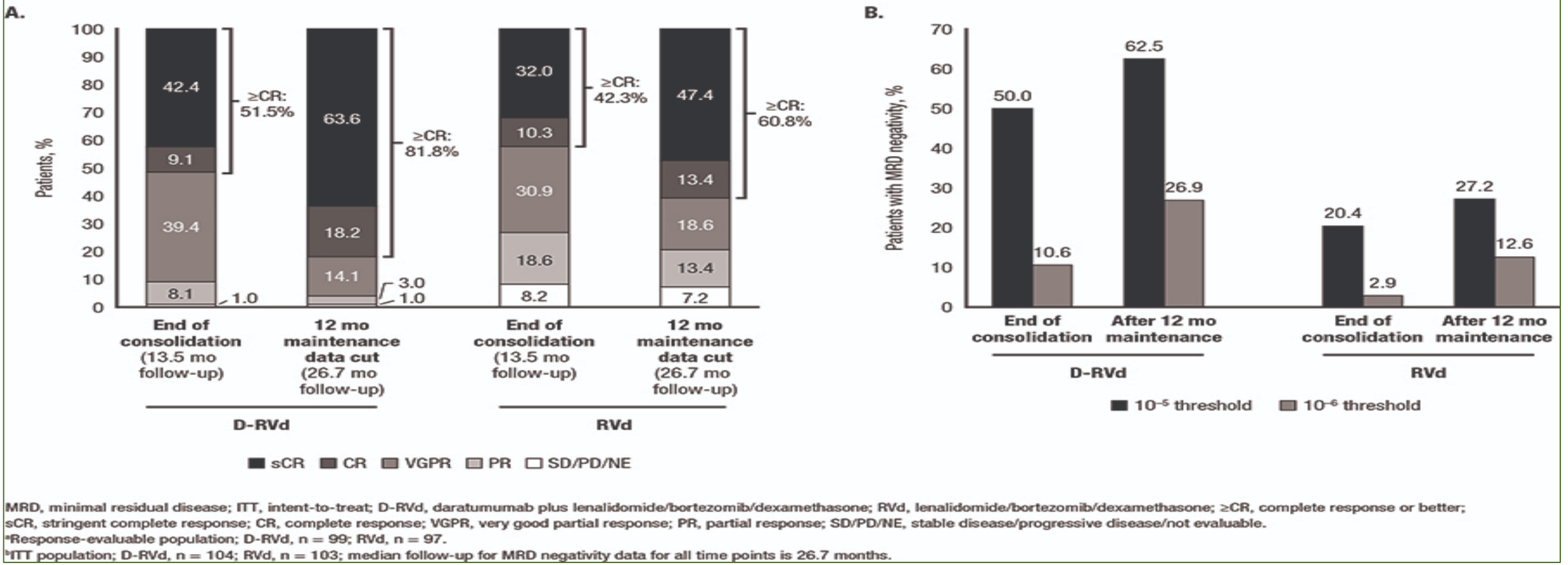




- Median follow-up: 13.5 months

Dara-RVD vs. RVD Responses Deepened Over Time

Figure. Summary of updated response rates[a] (A) and MRD-negativity rates[b] (B) over time in GRIFFIN.



MRD, minimal residual disease; ITT, intent-to-treat; D-RVd, daratumumab plus lenalidomide/bortezomib/dexamethasone; RVd, lenalidomide/bortezomib/dexamethasone; ≥CR, complete response or better; sCR, stringent complete response; CR, complete response; VGPR, very good partial response; PR, partial response; SD/PD/NE, stable disease/progressive disease/not evaluable.

[a]Response-evaluable population; D-RVd, n = 99; RVd, n = 97.

[b]ITT population; D-RVd, n = 104; RVd, n = 103; median follow-up for MRD negativity data for all time points is 26.7 months.

Response rates and depths were greater for D-RVd vs RVD at all time points

Estimated 24-month PFS rates were 94.5% for D-RVd and 90.8% for RVd

Kaufman. ASH 2020. Abst.594; Voorhees PM etal. Blood. 2020 Aug 20;136(8):936-945.

Newly Diagnosed Myeloma

An Achievement of the Patient-Doctor Relationship

Regimen	Major Response ≥VGPR	All Reponses
Melphalan Prednisone (MP)	4%	35%
Vincristine Adriamycin Dex (VAD)	6%	63%
Thalidomide + Dex	4%	63%
Bortezomib + Dex	37%	78%
Lenalidomide + Dex	47%	94%
Melphalan+Prednisone+ Thalidomide	21%	62%
Velcade+ Revlimid + Dex	70%	98%
Ninlaro+ Revlimid +Dex	69%	92%
Kyprolis+ Revlimid+Dex	70%	100%
Dara+Melphalan+Prednisone+Thalidomide	72%	90%
Daratumumab+Velcade+Revlimid+Dex	100%	100%
Daratumumab+Revlimid+Dex	79%	92%
Elotuzumab+ Lenalid +Bort+Dex	71%	100%

Where We Are Going…4-Drug Induction for Newly Diagnosed Myeloma

Study	No. of patients	Phase of study	Efficacy Data	Safety Data
Dara-VMP vs VMP *Dimopoulos MA, 2018*	706	Phase III	**ORR = 90.9%** sCR = 22.3% VGPR = 27.7% PR = 18.0% ≥VGPR = 72.9% CR+ = 45.1% Median PFS (at 27.8 months) = NR	Grade 3 or 4 TEAEs = 23.7%
Dara-IRD *Kumar 2019*	40	Phase II	CR = 11% VGPR = 47% PFS = 97.5% **ORR = 95%**	Grade ≥3 AEs = 42%
Dara-RVD vs RVD followed by ASCT *Voorhees 2020*	D-RVD: 99 RVD: 97	Phase III	**ORR: DVRD=99.0%** vs VRD=91.8%; **22 mo sCR: DVRD 62.6% vs RVD 45.4%** **MRD negativity DRVD 51.0% vs RVD 20.4%** **24-mo PFS DRVD 95.8% RVD 89.8%**	Serious AEs were reported in 39 (39.4%) patients in the D-RVd group and 52 (51.0%) in the RVd group
Dara-CVD *Yimer 2018*	87 NDMM (101 total)	Phase II	≥VGPR = 56% CR = 9% **ORR = 81%** 12-month PFS = 87% OS = 99%	Grade ≥3 AEs = 56%
Dara-KRd *Costa 2019*	38	Phase II	**ORR = 100%;** ≥VGPR = 92% after induction CR/sCR = 91% before BMT; MRD negative 65% at best response.	Grade 3/4 AEs: neutropenia (n=7), infection (n=6), insomnia (n=4), hyperglycemia (n=2), rash (n=2)
Isatuximab-RVD *Ocio 2018*	22	Phase I	**ORR = 93%** MRD negativity = 38.5% sCR = 7.14% VGPR = 71.43% CR = 7.14% 7.5 mo PFS = 100%	Grade ≥3 AEs = 46%
Isatuximab-KRD for high-risk MM *Abstract S204. EHA 2020*	46	Phase II	**ORR = 100%,** with PR=10%, VGPR=44% and CR=46%; **20 of 33 pts were MRD negative** in ASCT eligible arm	Grade 3/4 AE: neutropenia 34%, anemia10%, thrombocytopenia 14%, hypertension 12%, infection 8%

It's important to know...

What are YOUR goals of therapy

How to read your M-protein level

What is your MM risk/ stage

What are your therapy options

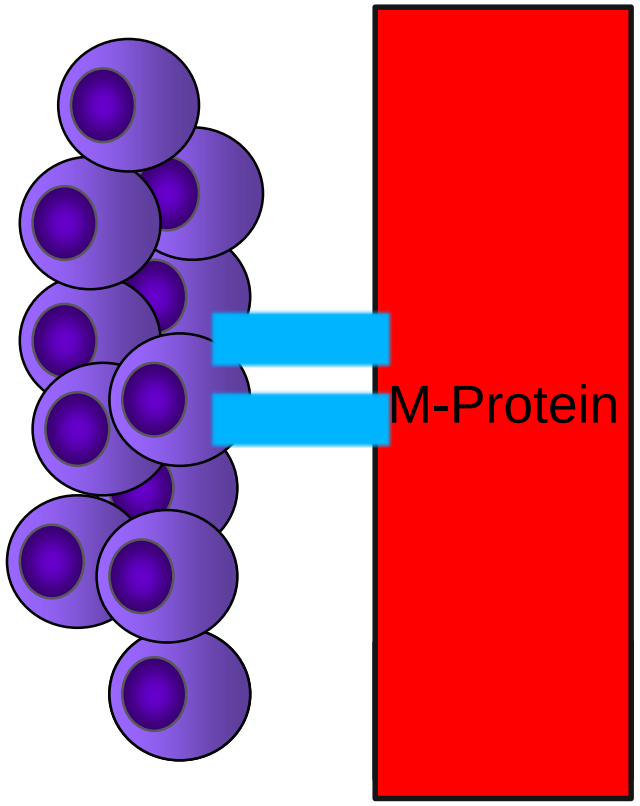
What is your response to tx

Know what side effects to expect so you can report them

Who is on your care team

Obtain a second opinion

Ask about clinical trials

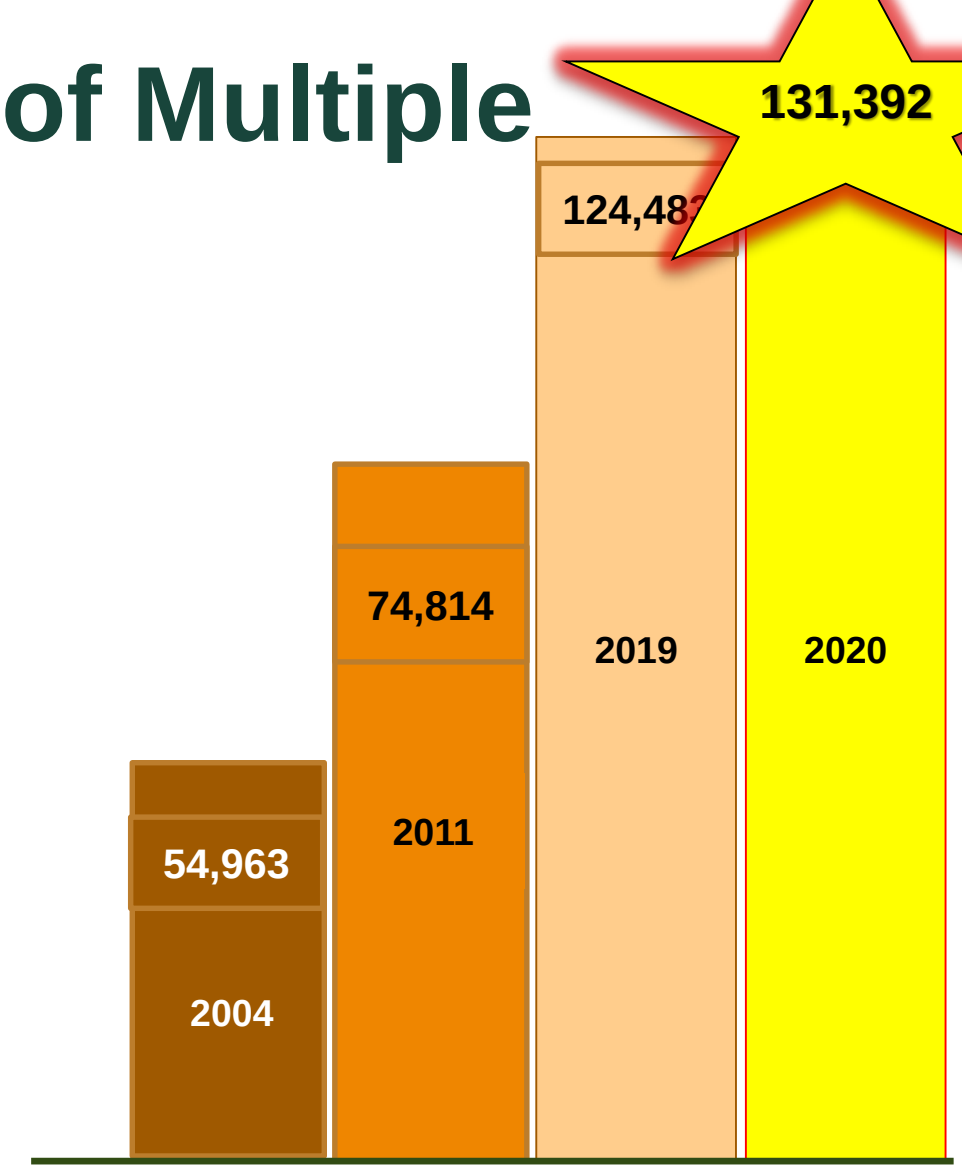


Advancements in Survival of Multiple Myeloma

- With new biology-based medication 3 drug regimens the response rates are now >98%
- We have had 5 drugs and tx indications FDA appovals for myeloma in this year!
  - 2 are new classes of drugs.
- When novel therapies are used at diagnosis, survival has improved dramatically
  - From 3.8 years to >8 years!
  - The 10yr relative survival rate has nearly doubled since in the past 20 years

Myeloma is not curable…yet.

But is survivable now!



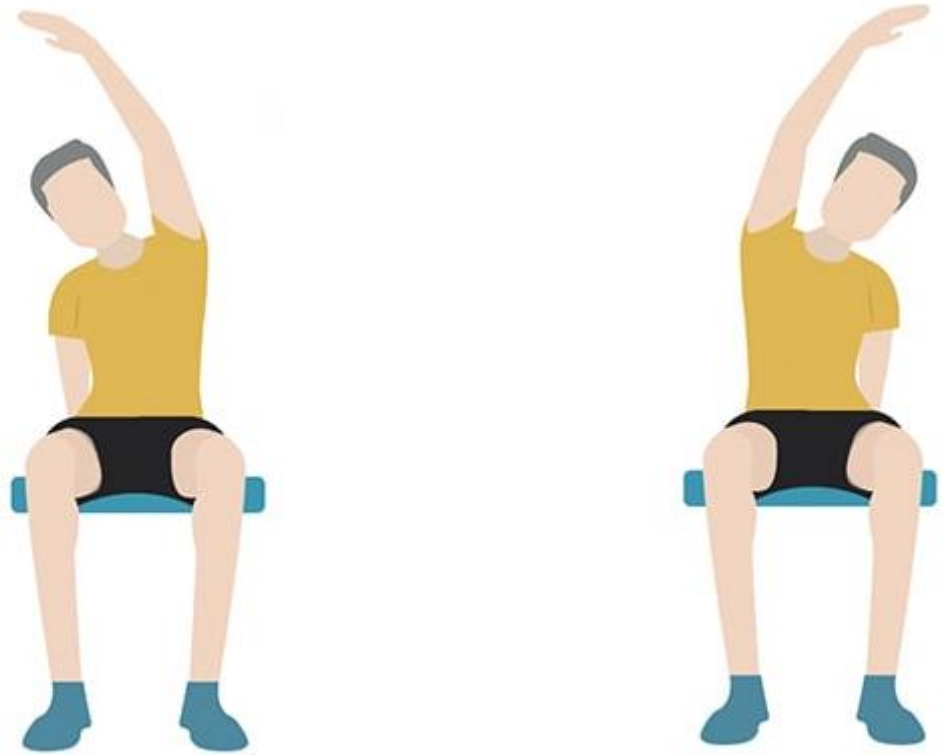
People in the United States living or in a Remission from Multiple Myeloma

Blood (ASH Annual Meeting Abstracts) 2011 118: Abstract 5070; Blood Advances, 2017 Vol1(4);p282-287.

colecrai@msu.edu

REGIONAL
COMMUNITY WORKSHOP

5 Minute Stretch



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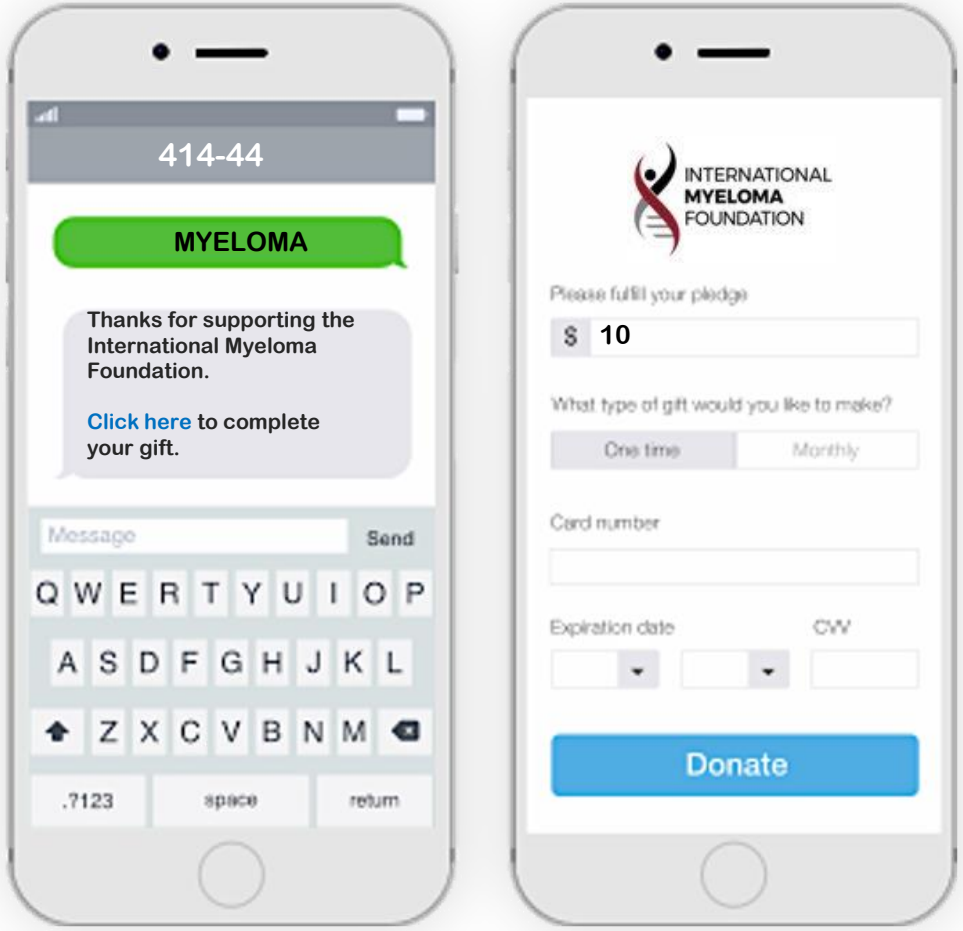
COMMUNITY WORKSHOP

Giving Tuesday: Text To Give

This #GivingTuesday 12/1/2020, you can MAKE A DONATION to the IMF From Your Smartphone

Step 1 Send a new text message to 41444
Step 2 Text MYELOMA
Step 3 Click the reply message to make a donation

Or scan the below QR code with your smart phone:



REGIONAL COMMUNITY WORKSHOP

“Relapsed Therapy and Clinical Trials”

Agne Paner, MD
Rush Medical College

REGIONAL COMMUNITY WORKSHOP

Clinical trials and treatment of relapsed Multiple Myeloma

Agne Paner, MD

Associate Professor of Medicine

Director of Multiple Myeloma and Amyloidosis Program

Rush University Cancer Center

November 21, 2020

What we will cover

- Why do we do clinical trials
- ABCs of clinical trials
- Updates in treatment of relapsed multiple myeloma

Why do we do clinical trials?

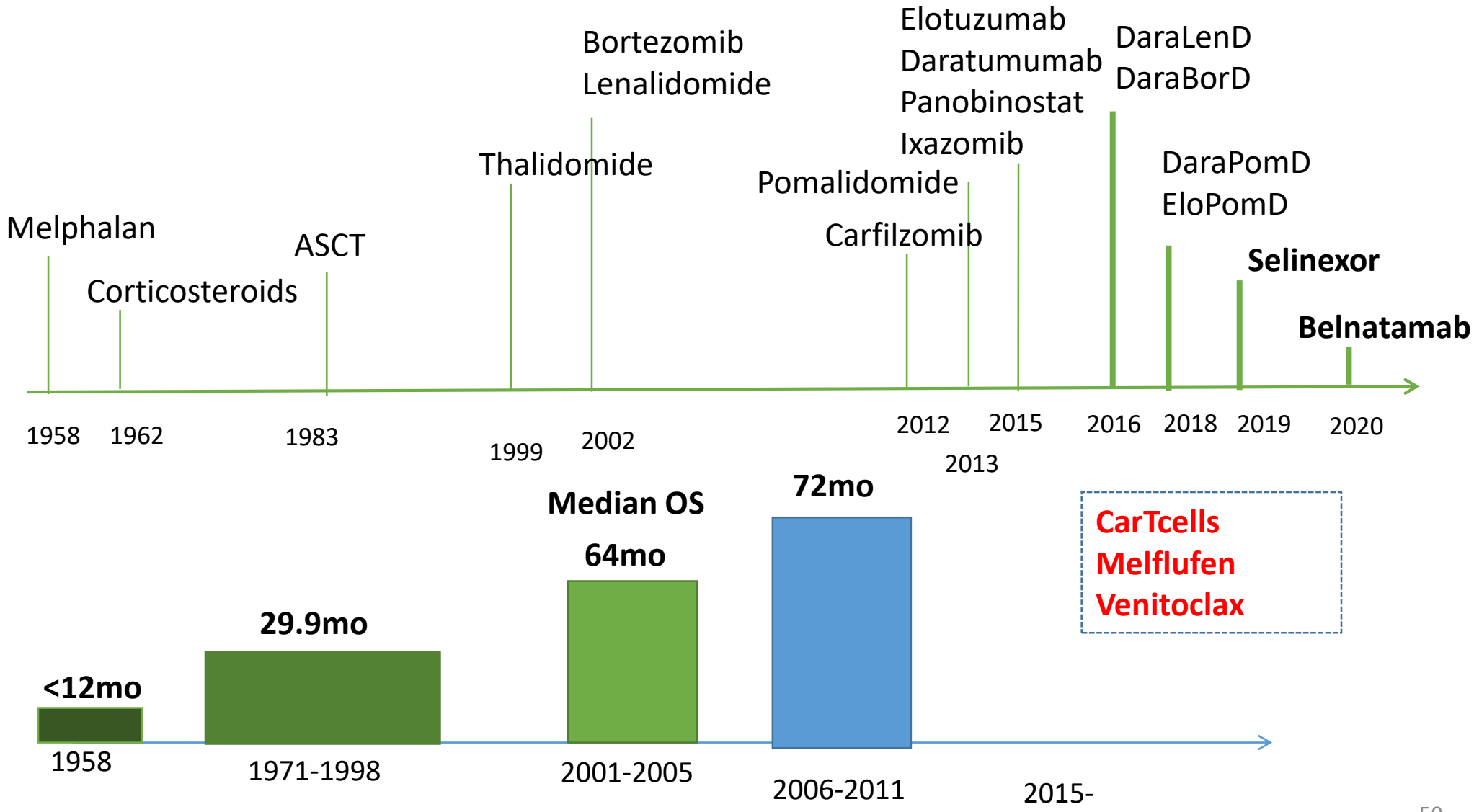
Patients ask…

- How did I get MM?
- What is my stage?
- Will I pass it to my children?
- What can I do about my cancer?
- Should I participate in a clinical trials?

Research question…

- What causes MM?
- How can we predict prognosis?
- Is there genetic predisposition to MM?
- Which treatment option is the best?
- Can we improve current standard of care or explore new treatments?

Advances and Improvement in Survival in MM over the time



Kumar, et al. *Leukemia.* 2014;28:1122-1128. Kumar, et al. *Blood.* 2008;111:2516-2520.

All the treatments we have today are a result of clinical trials

Preclinical research:

Laboratory research

Animal models

Trials with humans:

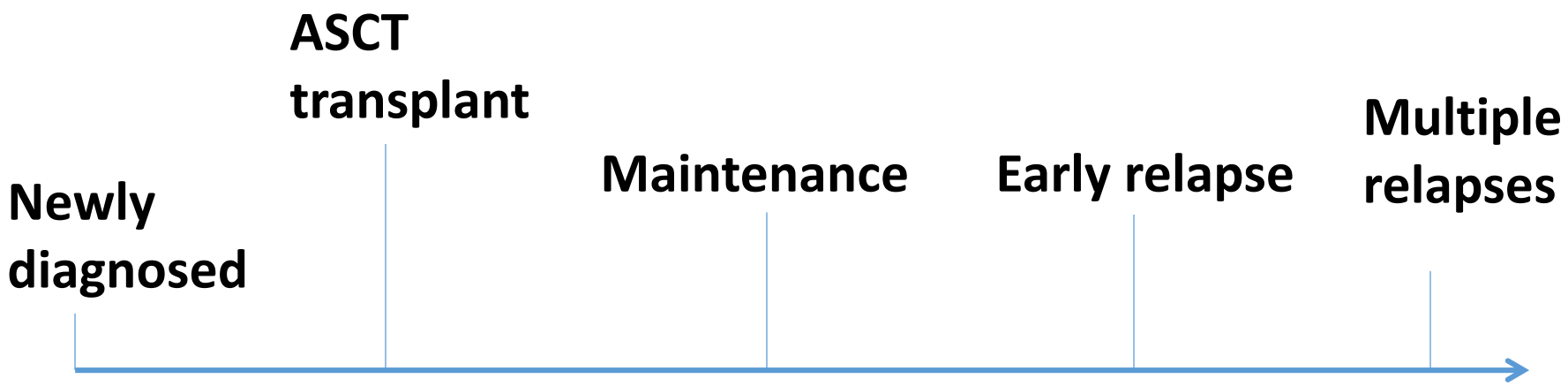
Phase I – is it safe?

Phase II – how many will respond?

Phase III –Is new treatment better than standard?

Road blocks in myeloma journey:

Natural history and treatment course of MM:



Nature of trials by timeline:

Phase III ← Phase I/II

Is new treatment better than what is standard?

Is it safe, do patients respond?

Terminology in the clinical trials

- What **phase** is the trial
- What **patient population** participated in the trial
- **Randomized**: computer decides which treatment patient will receive
- **Overall Response Rate:** how many patients had at least 50% reduction in tumor
- **Progression free survival:** how long patient remained in remission
- **Overall survival:** how long patients lived after starting this treatment
- **Adverse events:** side effects during clinical trial

Clinical trials to treat relapsed MM:

- New drugs for patients with relapsed and refractory disease (phase 1/2)
- Incorporating new drug into standard of care regimens (phase 1/2)
- Comparing new drugs to standard of care regimens (randomized phase 2/3)

Triple class refractory Multiple Myeloma:
Unmet medical need

Alkylators	Imids	Proteasome inhibitors	Anti-CD38 Monoclonal Abs	Anti-BCMA therapies	XPO1 inhibitor
Melphalan	Thalidomide	**Bortezomib**	**Daratumumab**	Belantamab mefadotin	Selinexor
Cyclophosphomide	**Lenalidomide**	**Ixazomib**		Car-T cells	
Bendamustine	**Pomalidomide**	**Carfilzomib**		BiTes	
Melflufen (melphalan flufenamide)	Iberdomide		Isatuximab		

Triple class refractory Multiple Myeloma

New agents within available drug class

Alkylators	Imids	Proteasome inhibitors	Anti-CD38 Monoclonal Abs	Anti-BCMA therapies	XPO1 inhibitor
Melphalan	Thalidomide	Bortezomib	Daratumumab	Belantamab mefadotin	Selinexor
Cyclophosphomide	Lenalidomide	Ixazomib		Car-T cells	
Bendamustine	Pomalidomide	Carfilzomib		BiTes	
Melflufen (melphalan flufenamide)	**Iberdomide**		**Isatuximab**		

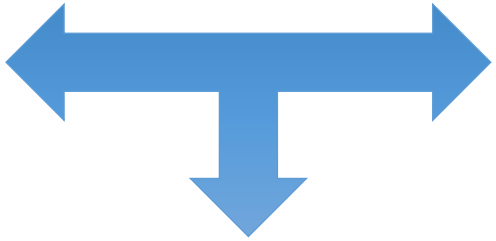
Triple class refractory Multiple Myeloma

Agents with new mechanism of action

Alkylators	Imids	Proteasome inhibitors	Anti-CD38 Monoclonal Abs	Anti-BCMA therapies	XPO1 inhibitor
Melphalan	Thalidomide	Bortezomib	Daratumumab	**Belantamab mefadotin**	**Selinexor**
Cyclophosphomide	Lenalidomide	Ixazomib		**Car-T cells**	
Bendamustine	Pomalidomide	Carfilzomib		**BiTes**	
Melflufen (melphalan flufenamide)	Iberdomide		Isatuximab		

B Cell Maturation Antigen, BCMA – new target in MM

BCMA



Cars:

38 trials registered at clinicaltrials.gov with anti-BCMA Car T-cells

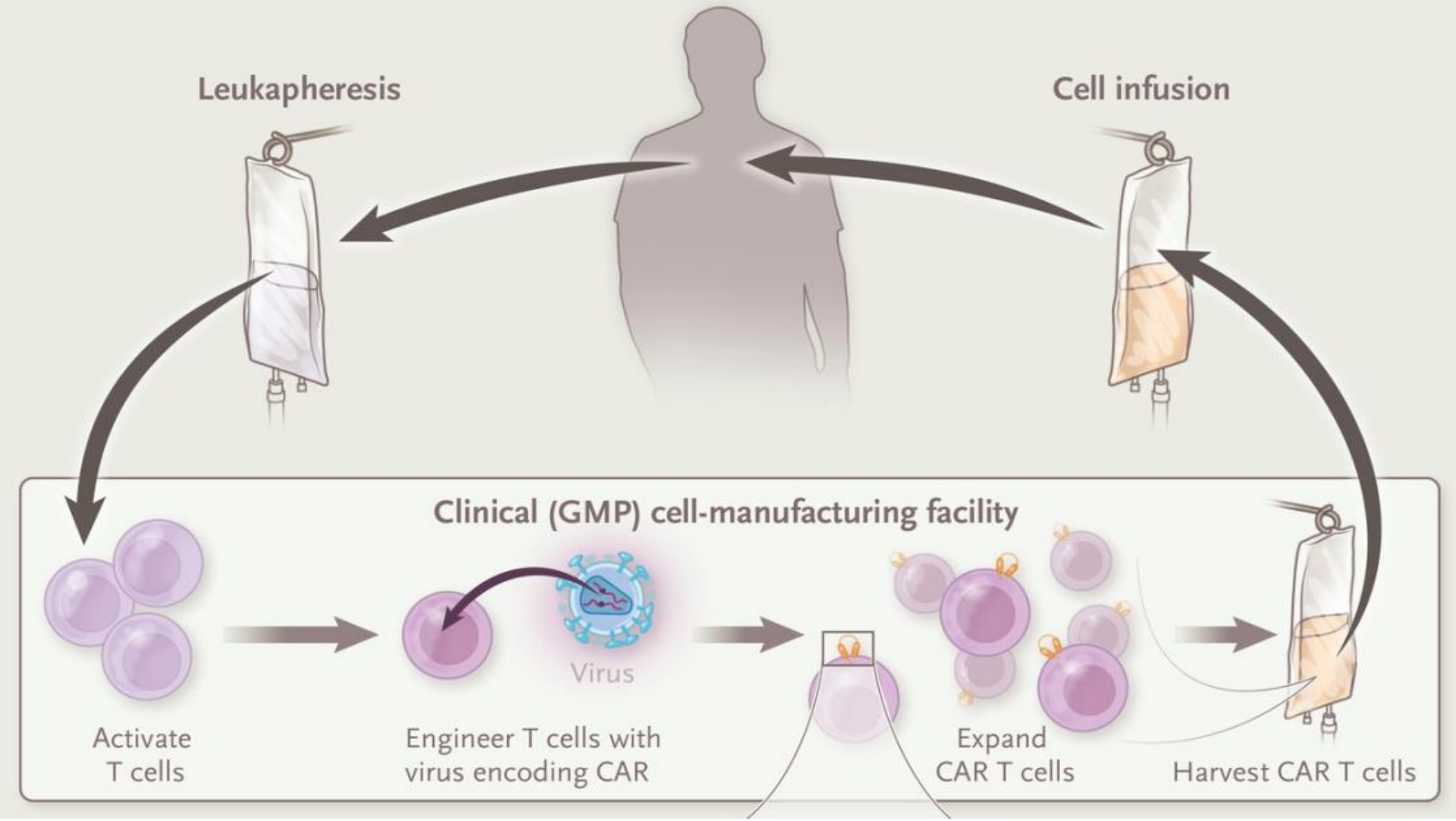
BiTes:

AMG 420, anti-BCMA Bispecific T-Cell Engager (BiTE®) Antibody Construct

DreaMM trials

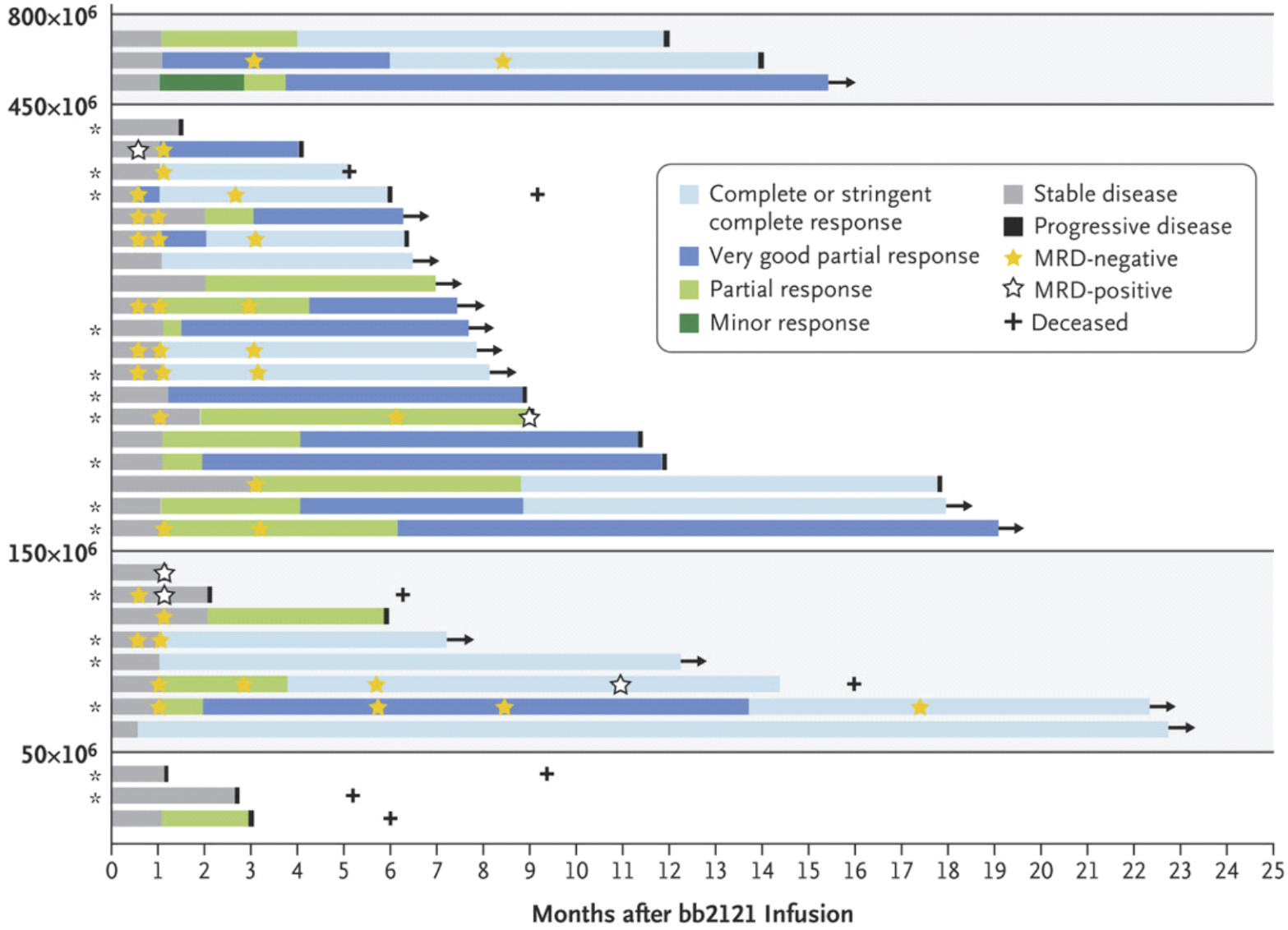
Anti-BCMA antibody drug conjugate, GSK2857916

Chimeric Antigen Receptor T-Cell Therapy



Tran E et al. N Engl J Med 2017;377:2593-2596.

Anti-BCMA CAR T-Cell Therapy bb2121 in Relapsed or Refractory Multiple Myeloma: response



Raje, N et al NEJM 2019

Table 2. Adverse Events, Cytokine Release Syndrome, and Neurologic Toxic Effects.

Variable	Total (N=33)		
	Any Grade	Grade 3	Grade 4
	number of patients (percent)		
Adverse event*			
Any	33 (100)	4 (12)†	28 (85)
Hematologic			
Neutropenia	28 (85)	2 (6)	26 (79)
Leukopenia	20 (61)	6 (18)	13 (39)
Anemia	19 (58)	15 (45)	0
Thrombocytopenia	19 (58)	5 (15)	10 (30)
Lymphopenia	6 (18)	3 (9)	3 (9)
Cytokine release syndrome‡	25 (76)	2 (6)	0
Neurologic toxic effect§	14 (42)	0	1 (3)

Belantamab mefadotin, DREAM-2 study,

Two arm phase 2 trial

N – 293
- **RRMM,**
- **Refractory to IMIDs, PIs, anti-CD38**
- **Three or more lines of therapy**

2.5mg/kg IV every 3 weeks
Till POD of intolerable toxicity

3.4mg/kg IV every 3 weeks
Till POD of intolerable toxicity

Primary endpoint:
- ORR

Secondary endpoint:
- PFS, OS, DoR, TTR

	2.5mg/kg	3.4mg/kg
ORR	**31%**	**34%**
PFS at 6.3mo of follow up	**6.9mo**	**NR**

Adverse events	2.5mg/kg arm	3.4mg/kg arm
Keratopathy	**27%**	**21%**
Thrombocytopenia	**20%**	**33%**
Anemia	**20%**	**25%**
Infusion reaction, grade 1-2	**18%**	**15%**

Lonial S et al Lancet Oncol 2020 Feb;21(2):207-221

Anti-B-Cell Maturation Antigen BiTE Molecule AMG 420,
phase 1 trial

N – 42 patients
2 or more lines of prior therapy
No EMD

→

AMG 420 0.2-800 microgm/d, 4week/6weeks cycle, up to 10cycles

→

Primary endpoint:
- DLT and MTD

Secondary endpoint:
- ORR and DoR

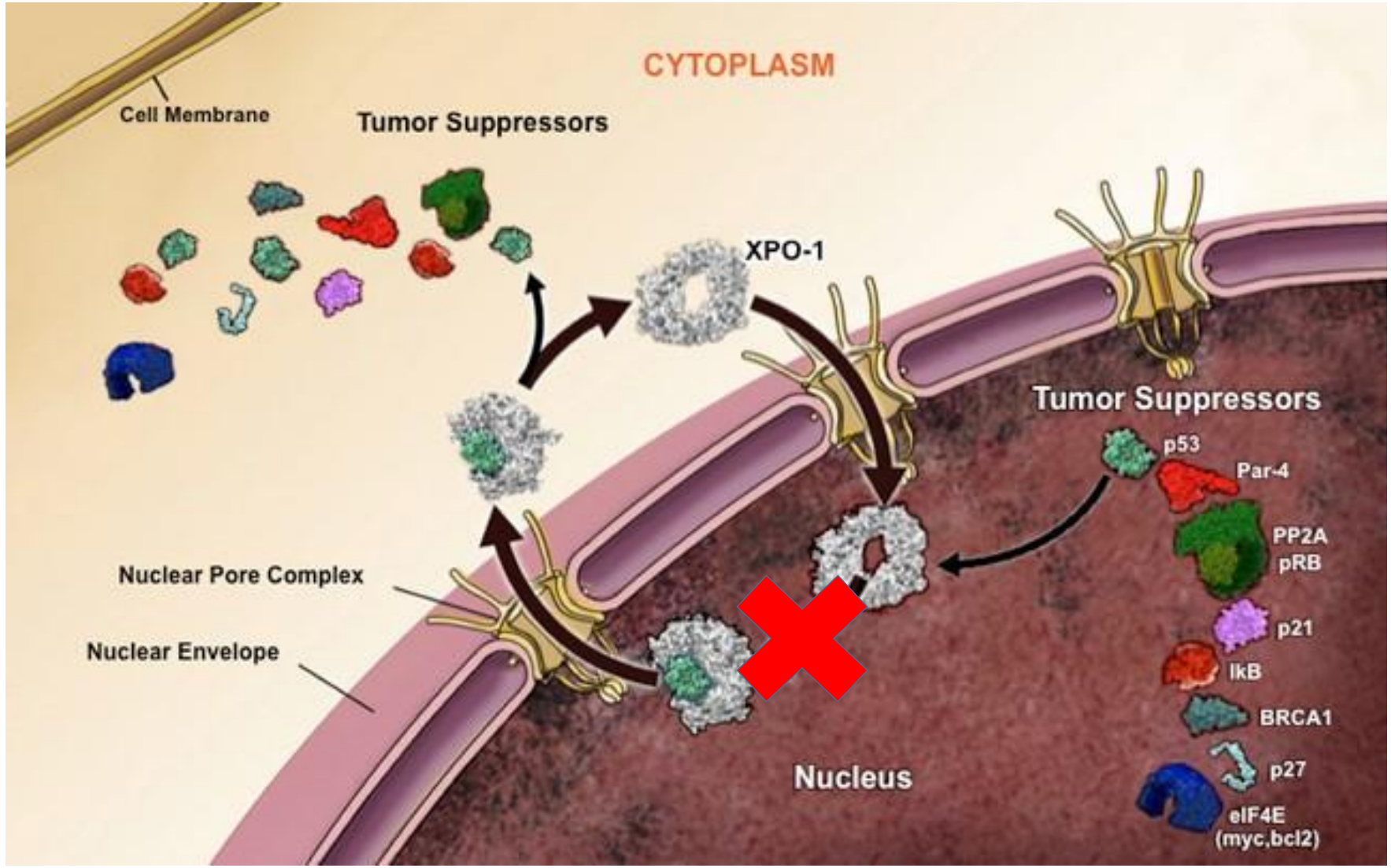
Maximum tolerated dose (MTD) was 400microgm/d

Dose limiting toxicity:
- CRS, grade 3
- polyneuropathy

	ORR	DoR
ITT	**31%**	**8.4 months**
MTD patients (n-7)	**70%:** **5/7 – MRD negative CR** **1/7 – VGPR** **1/7 - PR**	**9.6 months**

Topp, M et al 2020 Mar 10;38(8):775-783

SELINEXOR is a SELective Inhibitor of Nuclear EXport given ORally



- **Exportin 1 (XPO1):** nuclear exporter of tumor suppressor proteins (TSPs), glucocorticoid receptor (GR), and oncoprotein messenger RNAs (mRNAs)
- Overexpressed in MM
- Selinexor binds to Cys528 in the cargo-binding pocket of XPO1

Selinexor and dexamethasone for triple class refractory MM, STORM trial

Phase 2 trial

N-122
Triple class refractory
Exposed to IMIDs, PIs, Dara and alkylator
HR cytogenetics in 53%

→

Selinexor 80mg PO
Dexamethasone 20mg PO
twice weekly till POD or intolerable toxicity

→

Primary endpoint:
- ORR

Secondary endpoint:
- CBR, PFS, OS

ORR	**26%**
CBR	**39%**
PFS	**3.7 months**
DoR	**4.4 months**
OS	**8.6 months**

Chari et al N Engl J Med 2019; 381:727-738

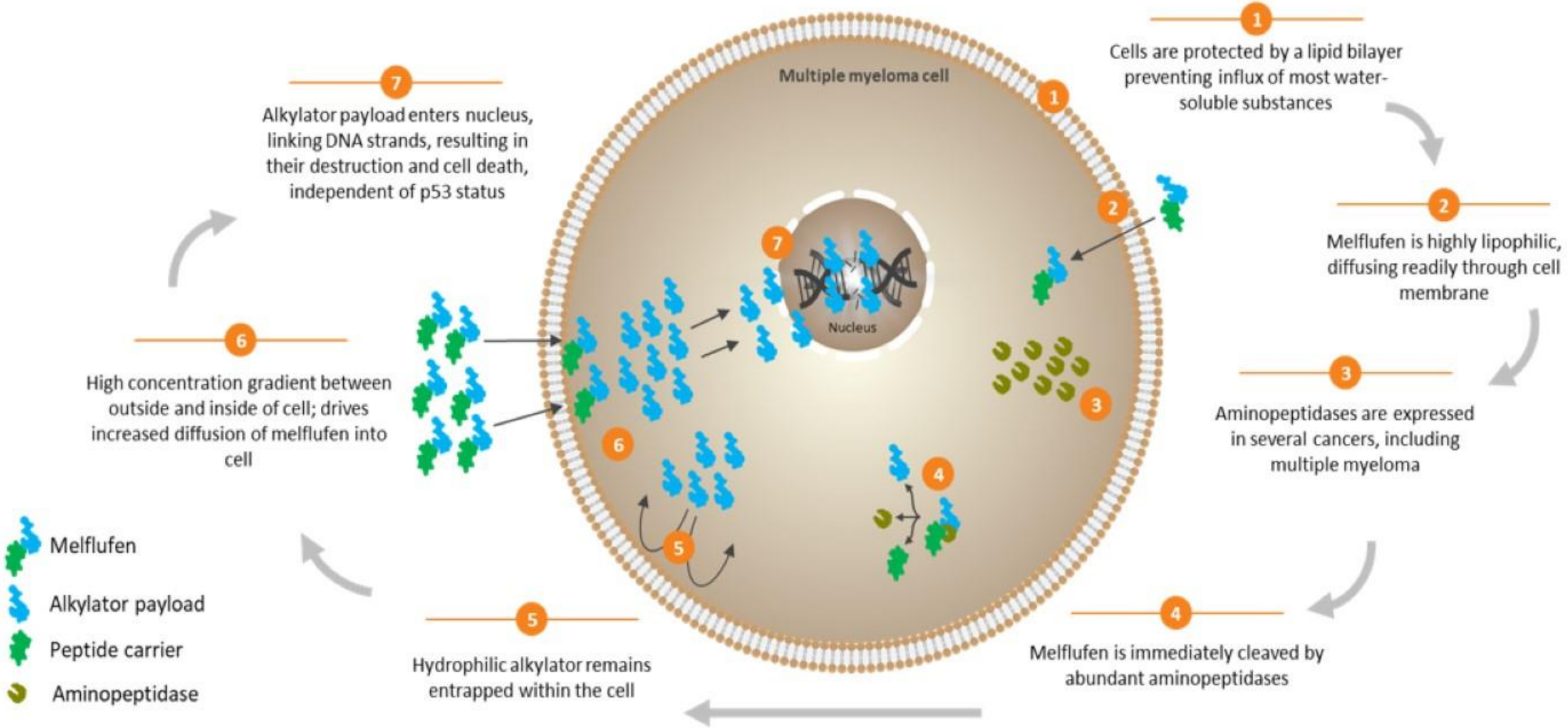
Supportive care for XPO1 inhibitor

Adverse event category	Symptom	Supportive care
Gastrointestinal	**Nausea 68%** **Vomiting 37%** **Diarrhea 41%**	**5-HT3 antagonists, Neurokinin 1 receptor antagonists, Olanzapine** **Cannabinoids** **Loperamide** **Bismuth subsalicylate**
Constitutional	**Fatigue 63%** **Decreased appetite 53%**	**Methylphenidate, Megestrol** **Cannabinoids, Olanzapine**
Hematologic	**Thrombocytopenia, 66%** **Neutropenia 37%**	**TPO agonists, dose reduction** **GCSF, dose reduction**
Biochemical	**Hyponatremia 32%**	**Sodium chloride tablets**

Most AEs occurred within 8 weeks, started as early as first week

Gavriatopoulou M Leukemia. 2020 Feb 24

HORIZON: Melflufen Mechanism of Action

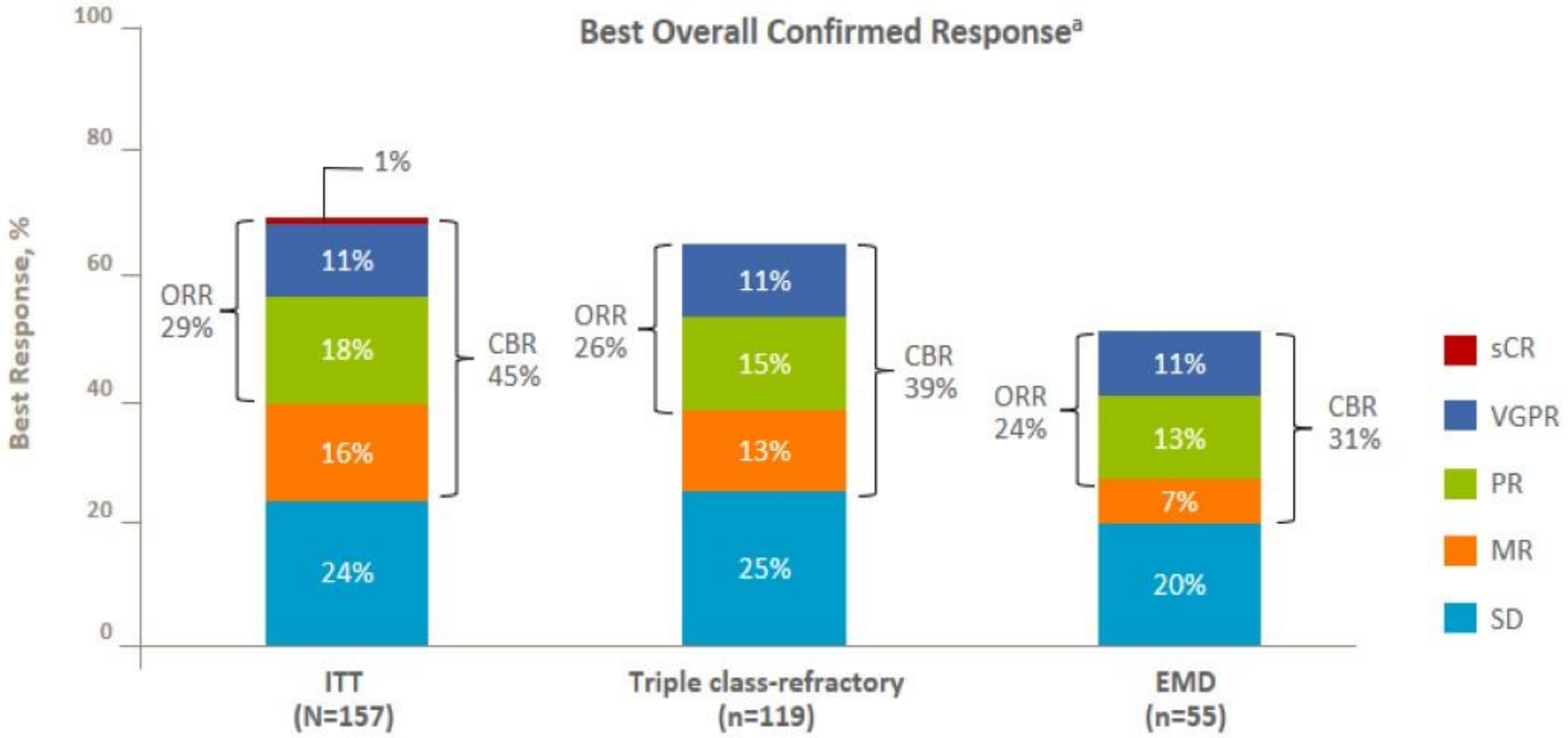


1. Chauhan D, et al. Clin Cancer Res. 2013;19(11):3019-3031. 2. Wickström M, et al. Invest New Drugs. 2008;26(3):195-204. 3. Ray A, et al. Br J Haematol. 2016;174(3):397-409. 4. Strese S, et al. Biochem Pharmacol. 2013;86(7):888-895. 5. Wickström M, et al. Oncotarget. 2017;8(39):66641-66655. 6. Slipicevic A, et al. Poster presented at: the American Association for Cancer Research (AACR) Annual Meeting; June 22-24, 2020; Virtual Annual Meeting II 2020:Abstract 1843.

HORIZON: Pivotal Phase 2 Study of Melphalan Flufenamide + Dex[1]

Melphalan Flufenamide + Dexamethasone Shows Activity in Patients With RRMM

ORR (Primary Endpoint)



- The ORR was 29% (95% CI, 22-37) in the ITT population, 26% (95% CI, 18-35) in the triple-class—refractory population, and 24% (95% CI, 13-37) in the EMD subgroup, and were consistent with the findings of the IRC

Data cutoff date: January 14, 2020.

[a]Investigator-assessed best overall response per International Myeloma Working Group uniform criteria.[2]

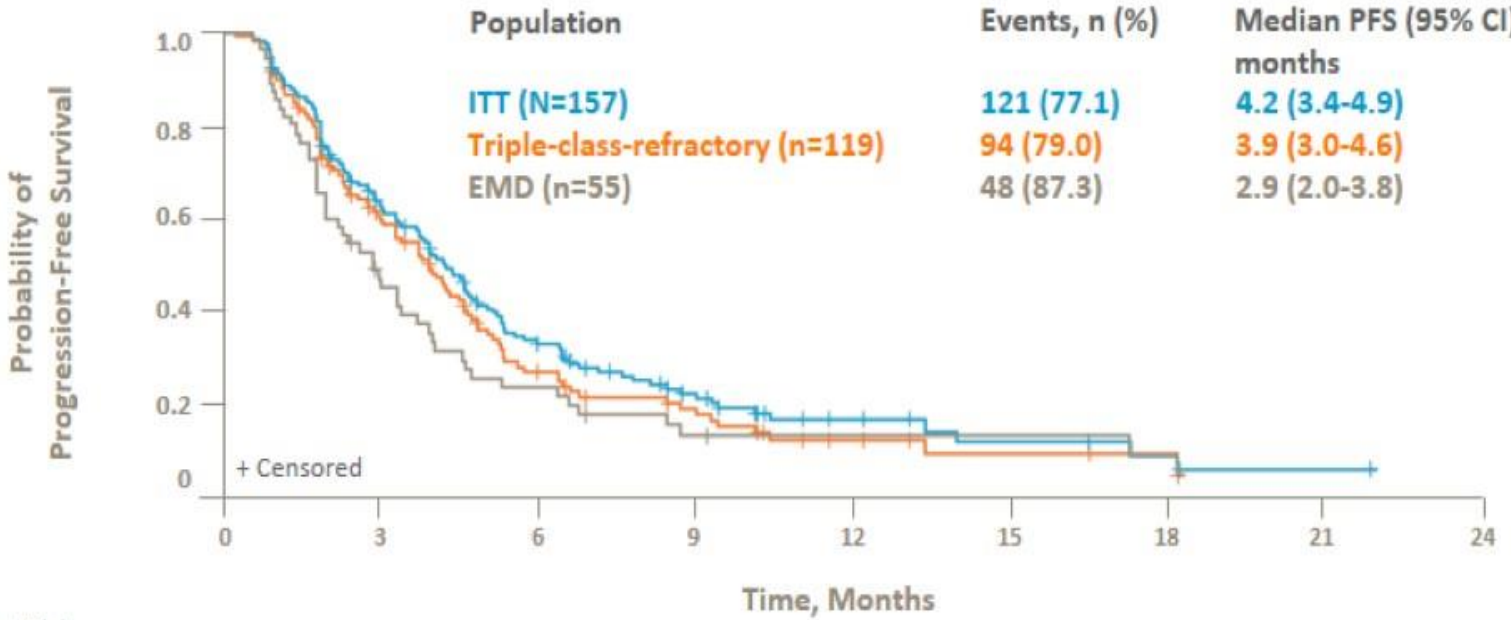
CBR, clinical benefit rate (≥MR); EMD, extramedullary disease; ITT, intent-to-treat; MR, minimal response; ORR, overall response rate; PR, partial response; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; SD, stable disease; VGPR, very good partial response.

1. Richardson PG, et al. EHA 2020. Abstract EP945. 2. Rajkumar SV, et al. *Blood*. 2011;117(18):4691-4695.

HORIZON: Pivotal Phase 2 Study of Melphalan Flufenamide + Dex

Melphalan Flufenamide + Dexamethasone in RRMM: PFS

PFS (Secondary Endpoint)



Population	Events, n (%)	Median PFS (95% CI), months
ITT (N=157)	121 (77.1)	4.2 (3.4-4.9)
Triple-class-refractory (n=119)	94 (79.0)	3.9 (3.0-4.6)
EMD (n=55)	48 (87.3)	2.9 (2.0-3.8)

Number at Risk

ITT	157	91	46	22	9	5	3	1	0
Triple-class Refractory	119	64	26	15	6	3	2	0	
EMD	55	24	12	6	5	4	2	0	

Among patients with a response (≥PR), median PFS (95% CI) was:

- 8.5 months (5.4-13.4) in the ITT population
- 8.5 months (5.3-13.4) in the triple class refractory population
- 17.3 months (5.3-NE) in patients with EMD

Data cutoff date: January 14, 2020.

EMD, extramedullary disease; ITT, intent-to-treat; NE, not evaluable; PFS, progression-free survival; PR, partial response; RRMM, relapsed/refractory multiple myeloma.

Richardson PG, et al. EHA 2020. Abstract EP945.

Thank you

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COMMUNITY WORKSHOP

REGIONAL COMMUNITY WORKSHOP

“Health in the COVID Era”

Amy E. Pierre, RN, MSN, ANP-BC
Memorial Sloan Kettering
Cancer Center

NURSE LEADERSHIP BOARD
A Division of International Myeloma Foundation

REGIONAL COMMUNITY WORKSHOP

Be the Commander of Your Galactic Journey
Health in the COVID Era

Amy E. Pierre, RN, MSN, ANP-BC
Memorial Sloan Kettering Cancer Center

Great Lakes IMF Regional Community Workshop
November 21, 2020

You are in the Commander's Chair

Your Healthcare Team Is Here to Help You Stay Healthy

Subspecialists

General Hem/Onc

Primary Care Provider (PCP)

You and Your Caregiver(s)

Myeloma Specialist

Family/Support Network

Allied Health Staff

Preparation for Appointments in the COVID Era

Health in the COVID Era

Preparation

- Write down your questions and concerns including about COVID
- Bring current medications and supplements
- Any medical or life changes since your last visit?
- Current symptoms - how have they changed?

Appointment

- Remember your mask
- Ask your most important questions first
- Understand your treatment plan and next steps
- Have a list of who to contact and when
- Include a Caregiver for another “set of ears”

At Home

- Take precautions to stay healthy
- Communicate with other members of your health care team (pharmacist, others)
- Take your medications as directed, have supply on hand
- Update health care crew between visits

Consider Telemedicine Visits

- Check with your healthcare provider(s) to see if telemedicine is an option
- Similar planning for “in-person” appointment PLUS
  - Ask provider for telemedicine process (tips/info, how to make appt, if any copay needed, etc.)
  - Plan your labs: are they needed in advance? Do you need an order?
  - Plan your technology: smartphone or tablet with camera are preferred
  - Plan your location: quiet, well-lit location with strong wi-fi is best
  - Plan yourself: consider if you may need to show a body part and wear accessible clothing
  - Collect recent vital signs (blood pressure, temp, heart rate) self-serve blood pressure cuff is available at many pharmacies and for purchase
  - At the end of the visit: check future appointments (virtual or in-person), testing, medication refills

IMF Telemedicine Tip Sheet. In development.

Corona Virus: On a Scale of 1 to 10 How Risky Is…

- Opening mail

- Getting restaurant take out
- Pumping gasoline
- Playing tennis
- Camping

- Grocery shopping
- Going for a walk, run or bike ride with others
- Playing golf

- Having dinner at someone else's house
- Attending a backyard barbecue
- Going to a beach
- Shopping at a mall

- Staying in a hotel for 2 nights
- Sitting in a doctors waiting room
- Going to a library or museum
- Eating in a restaurant (outside
- Walking in a busy downtown
- Spending an hour at a playground

- Sending kids to school, camp, or day care
- Working a week in an office building
- Swimming in a public pool
- Visiting an elderly relative or friend in their house

- Going to a hair salon or barbershop
- Eating in a restaurant (inside)
- Attending a wedding or a funeral
- Traveling by plane
- Playing basketball
- Playing football
- Hugging or shaking hands when greeting a friend

- Eating at a buffet
- Working out at a gym
- Going to an amusement park
- Going to a movie theater

- Attending a large music concert
- Going to a sports stadium
- Attending a religious service with 500+ worshipers
- Going to a bar

Ranked by physicians from the Texas Medical Association COVID-19 Task Force and the Texas Medical Association Committee on Infectious Disease.
Texas Medical Association. www.texmed.org

Factors Contributing to Increased COVID Risk Among Minorities

- **Healthcare access** – Insurance , transportation, technology (virtual visits)
- **Healthcare utilization** – Health literacy/language, trust
- **Occupation** – Essential workers
- **Education, Income, and Wealth Gaps** – Can’t afford to miss work
- **Housing** – Crowded conditions or homelessness

CDC = Centers for Disease Control.

CDC website. Health Equity Considerations and Racial and Ethnic Minority Groups . Accessed October 25, 2020.

Disparities in Cancer Care During the COVID-19 Pandemic

- **Black** and **Hispanic** patients were **less likely** to have an increase in telehealth visits
- **Black** and **Hispanic** were **more likely** to have COVID-19
- **Hispanic** patients were **more likely** to have treatment delays
- **Minority** patients experienced **more** cancer care disruptions
- **Race/ethnicity** was the **most significant risk factor** for fatality among multiple myeloma patients hospitalized for COVID-19

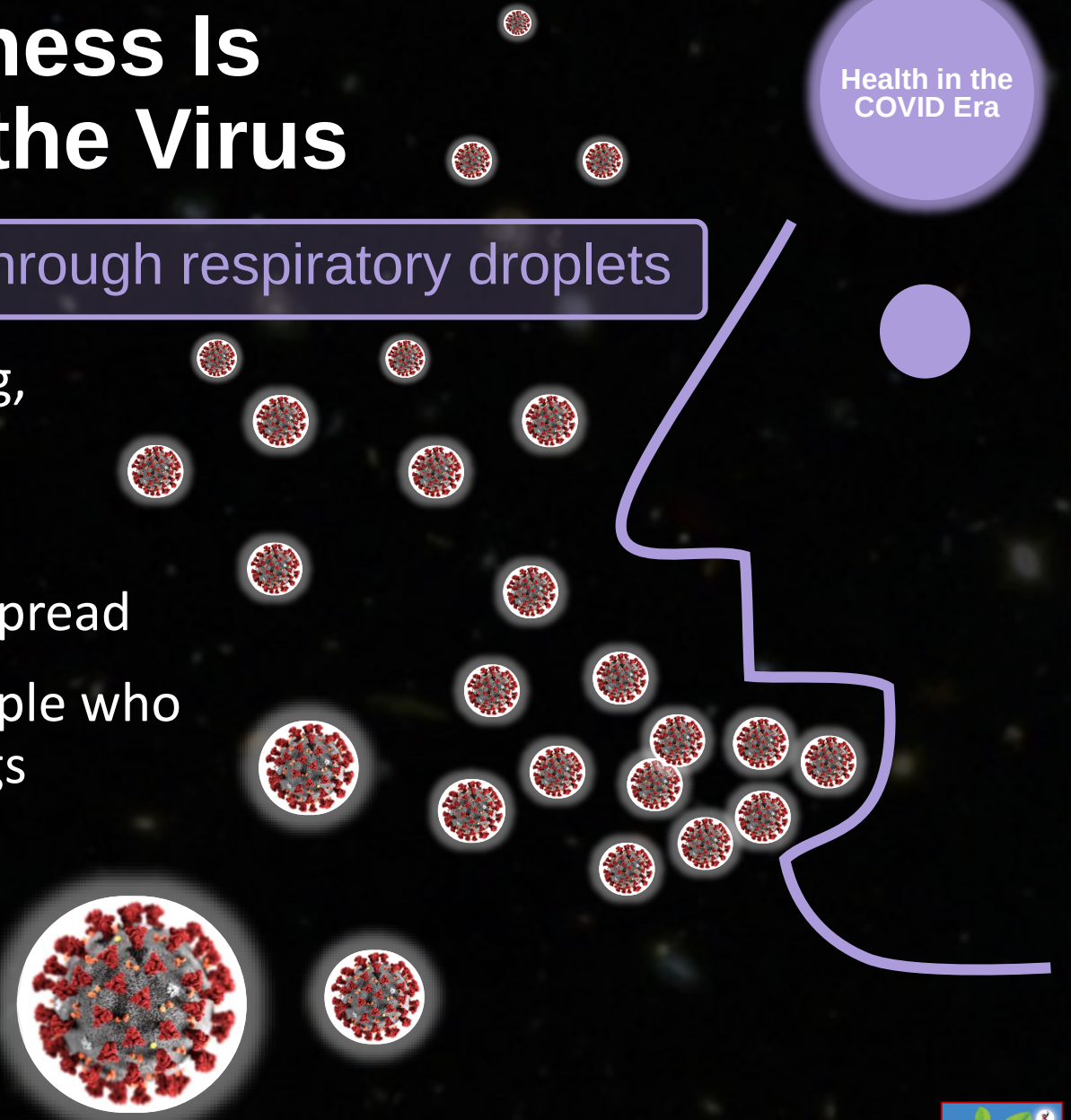
CDC = Centers for Disease Control; COVID-19 = coronavirus 2019.

Doroshow D, et al. *Ann Oncol.* 2020;31:S1204.; Hultcrantz M, et al. *Blood Cancer Discov.* 2020;1:1–10.

The Best Way to Prevent Illness Is to Avoid Being Exposed to the Virus

Virus spreads from person-to-person mainly through respiratory droplets

- Respiratory droplets are produced by coughing, sneezing, and talking
  - More droplets with louder talking, yelling, singing
- Close contact (within 6 feet) increases risk of spread
- Droplets can land in the mouth or nose of people who are nearby or possibly be inhaled into the lungs
- COVID-19 can be spread by people who are not showing symptoms
- Less common to get from a hard surface

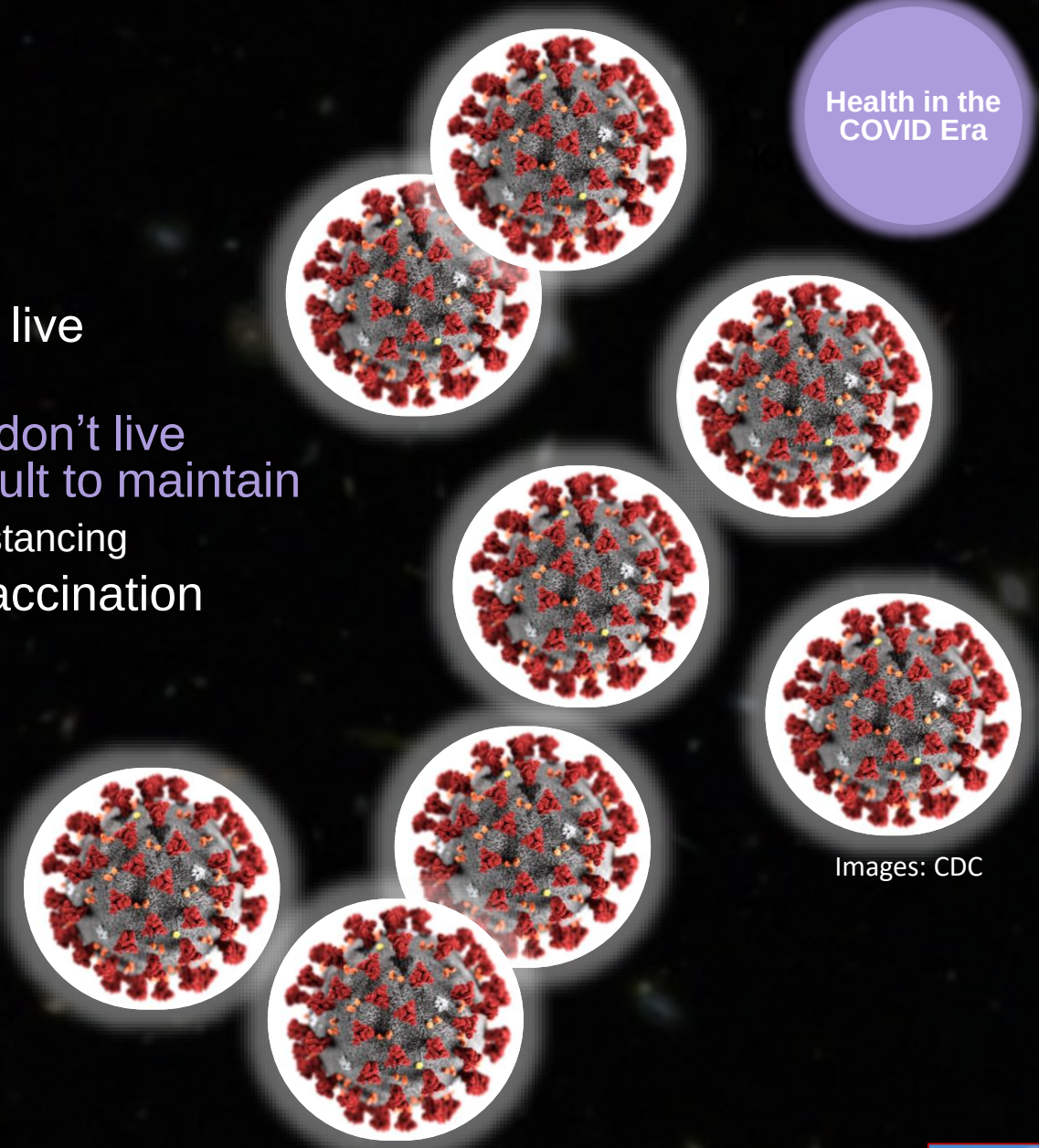


COVID Images: CDC

CDC = Centers for Disease Control; COVID-19 = coronavirus 2019.
CDC website. How to Protect Yourself & Others. Accessed October 22, 2020.

Reduce Your Risk

- Wash hands often
- Maintain 6-foot social distance with people who don't live in your household or sick people in your household
- Wear a mask in public and when around others who don't live in your household especially when distancing is difficult to maintain
  - Keep 6 ft of distance with mask; mask is not a substitute for distancing
- Prevent other illnesses: Get flu and pneumococcal vaccination
- Clean and disinfect frequently touched surfaces
- Avoid travel (cruises, airplanes)
- Choose activities outdoors (instead of indoors)



Images: CDC

And Protect Others

- Wear a mask in public
- Monitor your health: temperature, symptoms
- Quarantine (stay home away from others) if you think you've been exposed or are sick

CDC = Centers for Disease Control; COVID-19 = coronavirus 2019.
CDC website. How to Protect Yourself & Others. Accessed October 22, 2020.

Pick a Good Mask

DO choose masks that

Have two or more layers of washable, breathable fabric

Completely cover your nose and mouth

Fit snugly against the sides of your face and don't have gaps

DO NOT choose masks that

Are made of fabric that makes it hard to breathe, for example, vinyl

Have exhalation valves or vents, which allow virus particles to escape

Are intended for healthcare workers, including N95 respirators or surgical masks *Unless recommended*

CDC = Centers for Disease Control; COVID-19 = coronavirus 2019.
CDC website. How to Select, Wear, and Clean Your Mask. Accessed October 22, 2020.

Pick a Good Mask

Caution: Gaiters & Face Shields

Evaluation is on-going but effectiveness is unknown at this time

Evaluation is on-going but effectiveness is unknown at this time

Special Situations: Glasses

If you wear glasses, find a mask that fits closely over your nose or one that has a nose wire to limit fogging

"Anti-Fog" products to prevent fogging

CDC = Centers for Disease Control; COVID-19 = coronavirus 2019.
CDC website. How to Select, Wear, and Clean Your Mask. Accessed October 22, 2020.

And Wear It Right!

CDC = Centers for Disease Control; COVID-19 = coronavirus 2019.
CDC website. How to Select, Wear, and Clean Your Mask. Accessed October 22, 2020.

What about the Holidays?

Rising incidence of community spread from “safe” contacts (i.e. family, friends)

Are people taking precautions

- prior to the gathering
- during the gathering

Virtual celebrations or in-person with people in your household are low risk

Considerations for celebrations with people outside your household

- Where is the gathering (indoor, outdoor)?
- How many people at the gathering?
- Where are people traveling from (”hot spot”, air vs car)?

People who should not attend in-person holiday celebrations

- People with or exposed to COVID-19
- People at increased risk for severe illness

CDC = Centers for Disease Control; COVID-19 = coronavirus 2019.
CDC website. Holiday Celebrations. Accessed October 22, 2020.

Stress During a Pandemic

Health in the COVID Era

Stress during an infectious disease outbreak may sometimes cause the following:

- Fear and worry about your own health and the health of your loved ones
- Fear/worry about your financial situation or job, or loss of support services you rely on
- Changes in sleep or eating patterns
- Difficulty sleeping or concentrating
- Worsening of chronic health problems
- Worsening of mental health conditions
- Increased use of tobacco, and/or alcohol and other substances

Take care of your Mental Health

- Take breaks from watching, reading, or listening to news stories
- Take care of your body
  - Take deep breaths, stretch, or meditate
  - Try to eat healthy, well-balanced meals
  - Exercise regularly
  - Get plenty of sleep
  - Avoid excessive alcohol and drug use
- Make time to unwind
- Connect with others. While social distancing measures are in place, consider connecting online, through social media, or by phone or mail

CDC = Centers for Disease Control; COVID-19 = coronavirus 2019.
CDC website. How to Select, Wear, and Clean Your Mask. Accessed October 27, 2020.

You are Not Alone

Questions?

Closing Comments

Kelly Cox

IMF Senior Director, Regional Community Workshops

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