PATIENT AND FAMILY WEBINAR:

From Best of ASH 2021 to 2022 COVID-19 Guidance

INTERNATIONAL MYELOMA FOUNDATION

Brian G.M. Durie, MD
International Myeloma Foundation
North Hollywood, CA

Thomas Martin, MD
University of California
San Francisco , CA

Saad Usmani, MD, MBA, FACP
Memorial Sloan Kettering
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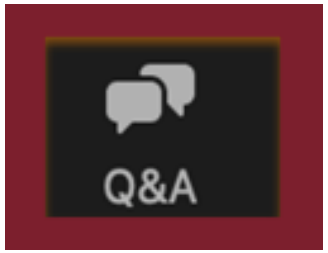
New York, NY

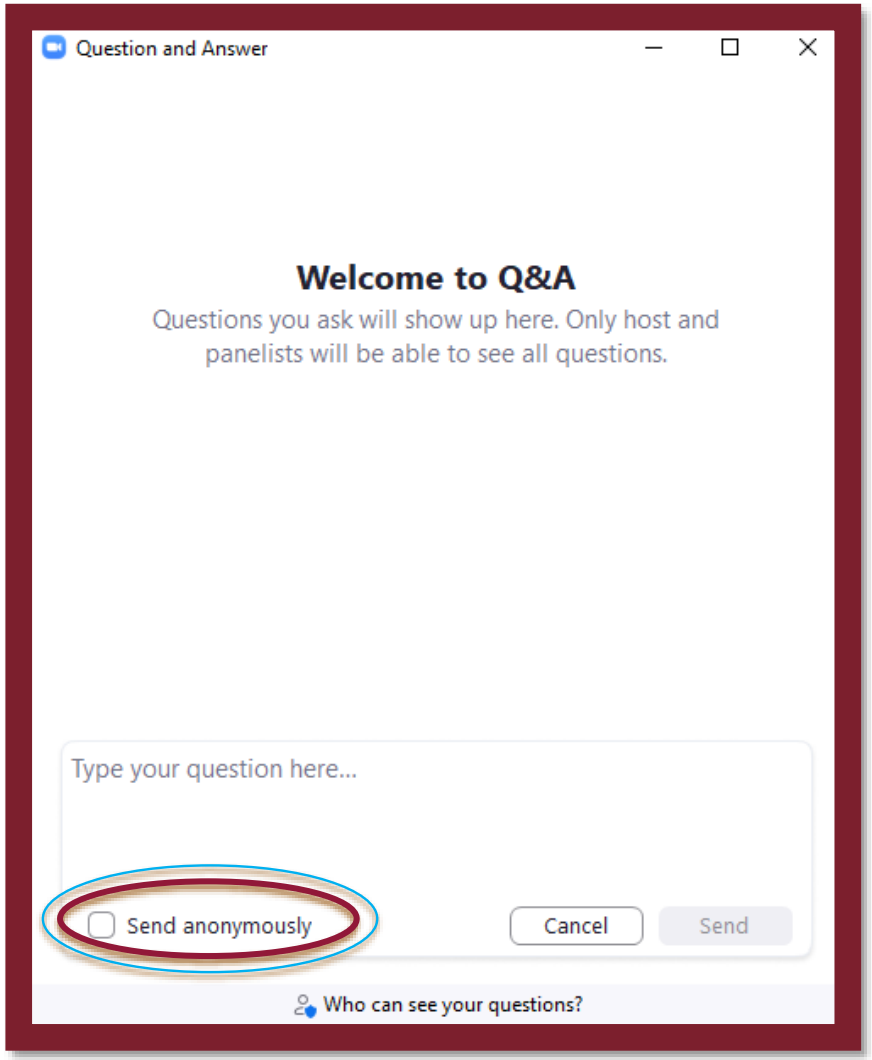
Donna Catamero, ANP-BC, OCN, CCRC
Icahn School of Medicine
at Mount Sinai Hospital
New York, NY

Thank you to our sponsors!

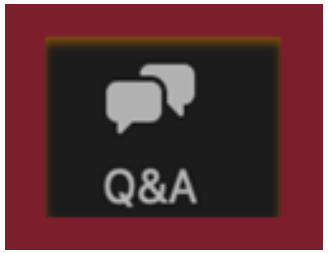
Audience Q&A



- **Open the Q&A window, allowing you to ask questions to the host and panelists. It will be sent to our moderator and panelists for discussion.**
- **If you have a question that does not get answered today, you can contact our Infoline at *800-452-CURE (2873) US & Canada, 1-818-487-7455*, or email infoline@myeloma.org.**

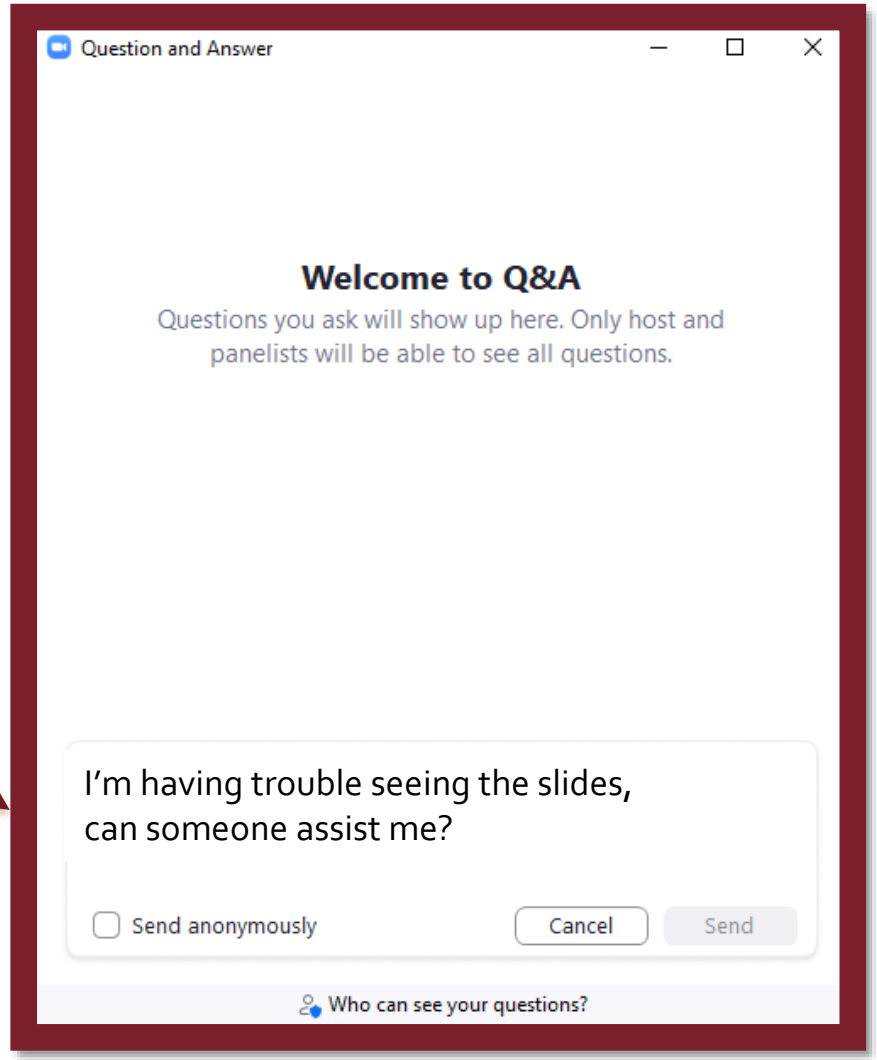


Technical Questions



- **If a technical issue arises – please use the Q&A to send questions to our support team who will reach out to assist you.**

- **You can also call the help desk at 765-633-4749 or email helpdesk@medipix.com**



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IMF Patient and Family Webinar

AGENDA *all times listed in US Eastern Standard

10:00 – 10:05 AM	Welcome Announcements with Robin Tuohy
10:05 – 11:35 AM	**Side Effects & Symptom Management** Donna Catamero, ANP-BC, OCN, CCRC
10:35 – 10:50 AM	**What Action Will You Take: *Myeloma Action Month*** Robin Tuohy
10:50 – 11:15 AM	**Myeloma 101** Dr. Brian G.M. Durie
11:15 – 11:45 AM	**Best of ASH 2021 & 2022 Covid Guidance** Dr. Brian G.M. Durie
11:45 – 11:55 AM	**Panel Discussion**
11:55 AM – 12:05 PM	**BREAK**

INTERNATIONAL MYELOMA FOUNDATION

IMF Patient and Family Webinar

AGENDA *all times listed in US Eastern Standard

12:05 – 12:35 PM	**Evolving Role of Immune Therapies:** ***A Focus on CAR T-cell Therapies*** Dr. Thomas Martin
12:35 – 1:05 PM	**Approaches to Relapsed Myeloma:** ***What are the Current Bispecifics & Novel Agents?*** Dr. Saad Usmani
1:05 – 1:25 PM	**Summary Panel Discussion** **Webinar Survey & Closing Remarks**

INTERNATIONAL MYELOMA FOUNDATION

Donna Catamero, ANP-BC, OCN, CCRC
Associate Director, Myeloma Translational Research
The Mount Sinai Health System
New York, NY

Side Effects and Symptom Management

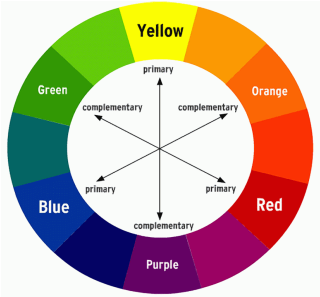
INTERNATIONAL MYELOMA FOUNDATION

February 26, 2022

LIFE IS A CANVAS, YOU ARE THE ARTIST

Donna D. Catamero, ANP-BC, OCN, CCRC
Mount Sinai Hospital
New York, NY

OBJECTIVES



COLOR WHEEL OF TREATMENT

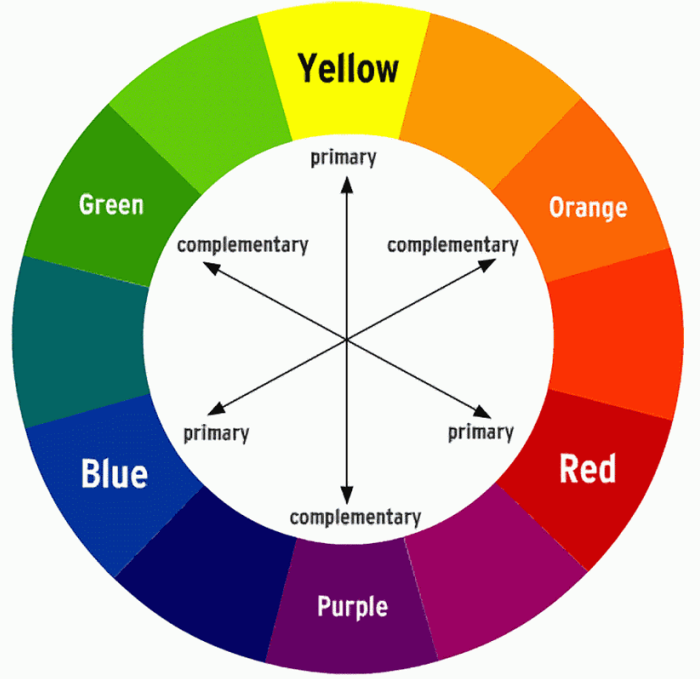
Myeloma and treatment side effects & symptom management

FRAMING YOUR CARE

Know your care team, Telehealth & Meeting Prep,
& Shared Decision Making

LIVE LIFE IN COLOR

Healthful Living, infection prevention,
renal and bone health



COLOR WHEEL OF TREATMENT

Treatment options, side effects, symptom management, & supportive care

GALLERY OF GOALS

MYELOMA TREATMENT

- Rapid and effective disease control
- Durable disease control
- Minimize side effects
- Allow for good quality of life
- Improved overall survival

SUPPORTIVE THERAPIES

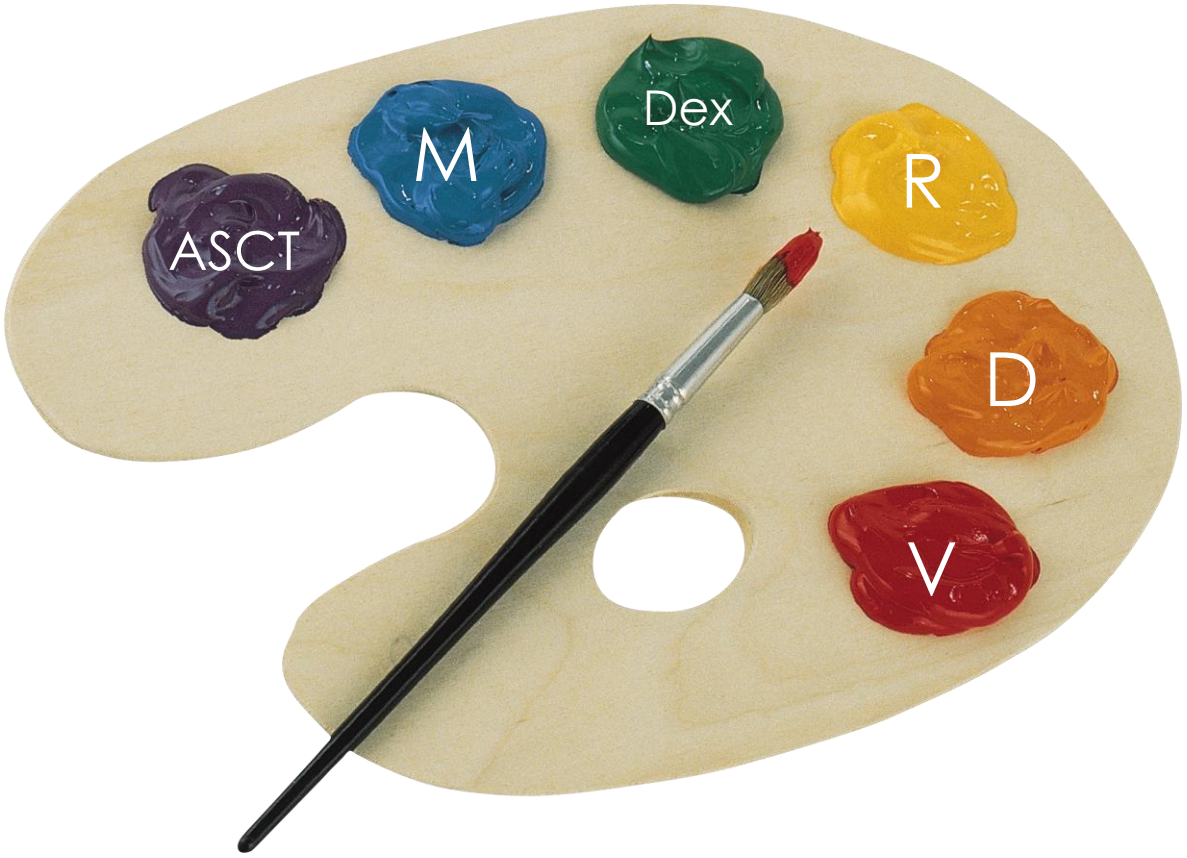
- Prevent disease- and treatment-related side effects
- Optimize symptom management
- Allow for good quality of life

DISCUSS GOALS AND PRIORITIES WITH YOUR HEALTHCARE TEAM

COLOR WHEEL OF TREATMENT OPTIONS

	-Mibs	-MAbs	-Mides	Steroids	Alkylators	Immuno-Therapy	Others	Cellular Therapies
Frontline	Velcade® (bortezomib)	Darzalex® (daratumumab)	Thalomid® (thalidomide) Revlimid® (lenalidomide)	Dexamethasone Prednisone Prednisolone SoluMedrol	Melphalan Cyclophosphamide			Melphalan + ASCT
Maintenance	Velcade® (bortezomib)		Revlimid® (lenalidomide)					
Relapse	Kyprolis® (carfilzomib) Ninlaro® (ixazomib)	Darzalex® (daratumumab) Empliciti® (elotuzumab) Sarclissa® (Isatuximab)	Thalomid® (thalidomide) Revlimid® (lenalidomide) Pomalyst® (pomalidomide)	Dexamethasone Prednisone Prednisolone SoluMedrol	Melphalan Cyclophosphamide Bendamustine	Blenrep® (Belantamab mafodotin) "Belamaf"	Xpovio® (Selinexor) Doxil (liposomal doxorubicin) Farydak® (panobinostat)	Melphalan + ASCT Ide-Cel (CAR-T)
Pending FDA Approval			CelMods • Iberdomide • CC-92480		Pepaxto (melphalan flufenamide) "Melflufen"	ADCs BSAs Ex: Teclistamab, Talquetamab Cevostamab	Venclexta® (venetoclax)	Other CAR-T • Cilta-Cel
Noted Side effects	Neuropathy Carfilzomib: Cardiac	Infusion reaction	DVT/PE	See steroid slide	Myelosuppression	Infusion reaction Blenrep: Keratopathy	Myelosuppression, GI Selinexor: Low sodium	Infection risk CAR-T: CRS and neurotoxicity

COMBINATIONS: MIX, MATCH, BLEND FOR DEPTH

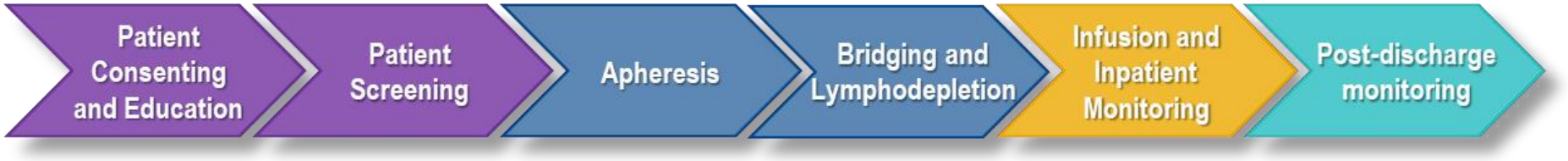


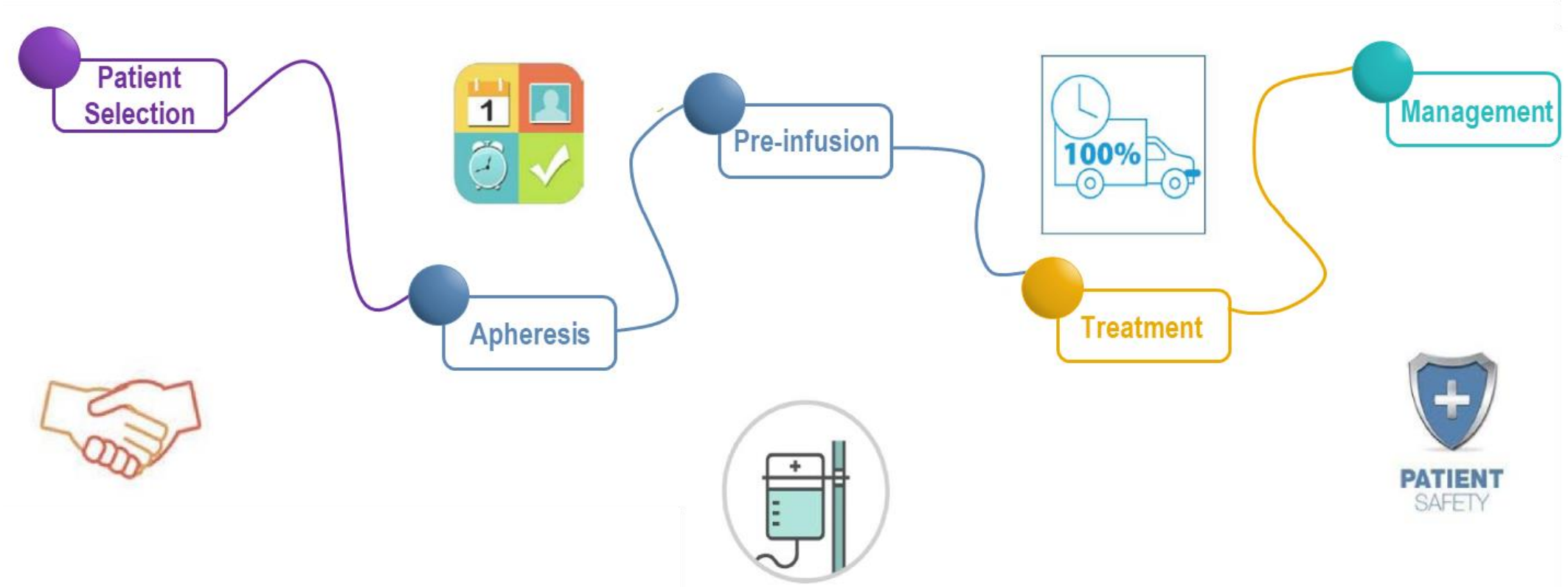
Myeloma Treatment Pallet	Common Combinations
Velcade® (bortezomib)	VRd, Vd
Lenalidomide	VRd, Rd
Kyprolis® (carfilzomib)	KRd, Kd, DKd, Isa-Kd
Pomalyst® (pomalidomide)	Pd, DPd, EPd, PCd, Isa-Pd
Darzalex® (daratumumab)	DRd, DVd, DPd, DVMP, DKd
Ninlaro®(ixazomib)	IRd
Empliciti® (elotuzumab)	ERd, EPd
Farydak® (panobinostat)	Panobinostat-Vd
Xpovio® (Selinexor)	Selinexor-Vd, Selinexor-dex
Sarclissa® (Isatuximab)	Isa-Kd, Isa-Pd
Blenrep® (Belantamab mafodotin)	Bela-d
Pepaxto (melphalan flufenamide)	--
Idecabtagene Vicleucel	--
Venclexta® (venetoclax)	Vd + ven
New agents or regimens in clinical trials are always an option	

ASCT = autologous stem cell transplant; Bela = belantamab; C = cyclophosphamide; D = daratumumab; d = dexamethasone; E = elotuzumab; Isa = isatuximab; I = ixazomib; K = carfilzomib; M = melphalan; P = pomalidomide; R = lenalidomide; V = bortezomib; ven = venetoclax.

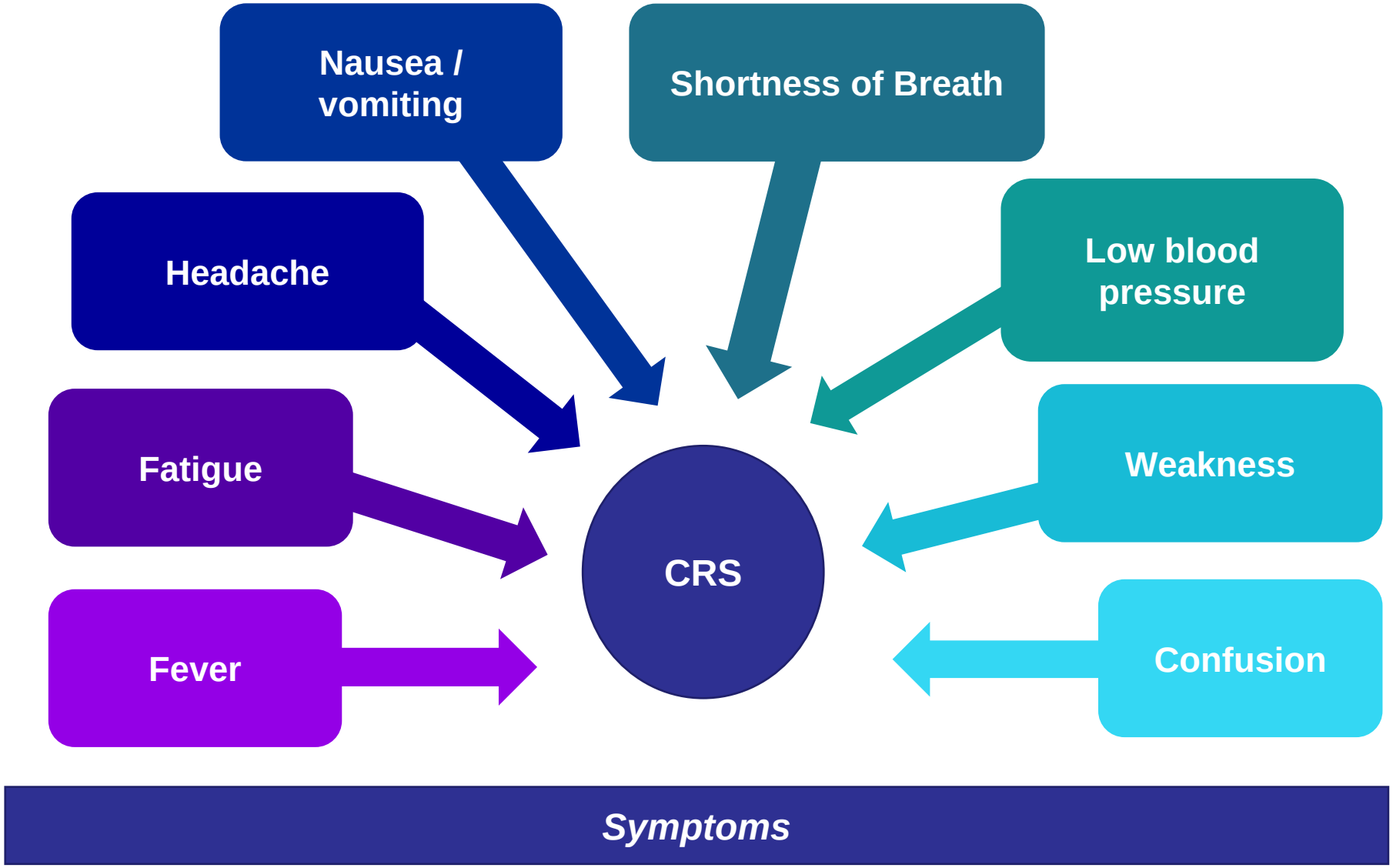
Prescribing information for each drug listed in the table. NCCN Guidelines. Multiple Myeloma. V3.2021. Accessed February 1, 2020.

CAR T: A NEW TREATMENT APPROACH

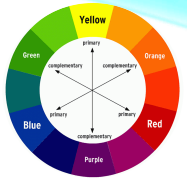




CAR T HAS UNIQUE SIDE EFFECTS



THE **BRIGHT** & **DARK** SIDE TO STEROIDS



Steroid Synergy

Steroids are a backbone and work in combination to enhance myeloma therapy

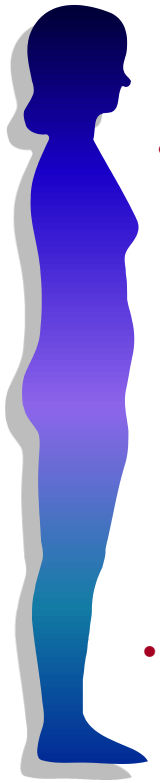
Managing Steroid Side Effects

- Consistent schedule (AM vs. PM)
- Take with food
- Stomach discomfort: Over-the-counter or prescription medications
- Medications to prevent shingles, thrush, or other infections

Do not stop or adjust steroid doses without discussing it with your health care provider

Steroid Side Effects

- Irritability, mood swings, depression
- Difficulty sleeping (insomnia), fatigue
- Increased risk of infections, heart disease
  - Muscle weakness, cramping
- Increase in blood pressure, water retention



- Blurred vision, cataracts
- Flushing/sweating
- Stomach bloating, hiccups, heartburn, ulcers, or gas
- Weight gain, hair thinning/loss, skin rashes
- Increase in blood sugar levels, diabetes

Rajkumar SV, Jacobus S, Callander NS, Fonseca R, Vesole DH, Williams ME, Abonour R, Siegel DS, Katz M, Greipp PR, Eastern Cooperative Oncology Group (2010) Lenalidomide plus high-dose dexamethasone versus lenalidomide plus low-dose dexamethasone as initial therapy for newly diagnosed multiple myeloma: an open-label randomised controlled trial. Lancet Oncol 11(1):29–37.

King T, Faiman B. Steroid-Associated Side Effects: A Symptom Management Update on Multiple Myeloma Treatment. Clin J Oncol Nurs. 2017 Apr 1;21(2):240-249. doi: 10.1188/17.CJON.240-249. PMID: 28315528.

ADDITIONAL TOOLS TO COMPLETE THE PICTURE

	DVT/PE Prevention	Bone Health	Renal Health	Infection Prevention	Peripheral Neuropathy	GI Symptoms
Medications	Blood thinners Ex: Aspirin, DOACs	Bone Strengthening Agents Calcium Vitamin D	**Med dose reduction** **Avoid harmful meds**	Antibacterial Antiviral Antifungal IVIG GCSF	Anti-depressants Anti-neuroleptic Analgesia Vitamins Dose adjustments	Anti-nausea Anti-diarrheal Laxatives & stool softners Fiber-binding agents
Non-medication Therapies	Compression stockings	Radiation Surgery Immobilization Physical therapy	Dialysis	Masking Activity	Massage Acupuncture Cocoa Butter	Dietary choices Relaxation
Lifestyle Options	Activity Stop smoking Weight loss	Activity	Hydration	Handwashing Avoid crowds & sick people Monitor for fever COVID precautions	Activity Diabetes management	Avoid greasy foods Activity Hydration

PATIENT-REPORTED SYMPTOMS

A meta-analysis identified the most common patient-reported symptoms and impact on QOL, and were present at all stages of the disease.

Symptoms resulted from both myeloma disease and treatment, including transplant, and were in these categories:

Physical

- Fatigue
- Constipation
- Pain
- Neuropathy
- Impaired Physical Functioning
- Sexual Dysfunction

Psychological

- Depression
- Anxiety
- Sleep Disturbance
- Decreased Cognitive Function
- Decreased Role & Social Function

Financial

- Financial burden (80%)
- Financial toxicity (43%)

Ramsenthaler, et al. 2016. https://doi.org/10.1111/ejh.12790.

GI SYMPTOMS: PREVENTION & MANAGEMENT

Diarrhea may be caused by medications and supplements

- Laxatives, antacids with magnesium
- Antibiotics, antidepressants, others
- Milk thistle, aloe, cayenne, saw palmetto, ginseng
- Sugar substitutes in sugar free gum

Avoid caffeinated, carbonated, or heavily sugared beverages

Take anti-diarrheal medication

- Imodium®, Lomotil®, or Colestid if recommended
- Fiber binding agents – Metamucil®, Citrucel®, Benefiber®
- Welchol® if recommended

Constipation may be caused by

- Opioid pain relievers, antidepressants, heart or blood pressure medications, others
- Supplements: Calcium, Iron, vitamin D (rarely), vitamin B-12 deficiency

Increase fiber

- Fruits, vegetables, high fiber whole grain foods
- Fiber binding agents – Metamucil®, Citrucel®, Benefiber®

Fluid intake can help with both diarrhea and constipation, and good for kidneys. Discuss GI issues with health care providers to identify causes and make adjustments to medications and supplements.

Smith LC, et al. *CJON.*2008;12(3)suppl:37-52. Faiman B. *CJON.* 2016;20(4):E100-E105.

Physical

PAIN PREVENTION AND MANAGEMENT

Pain can significantly compromise quality of life

Sources of pain include bone disease, neuropathy and medical procedures

Management

- Prevent pain when possible
  - Bone strengtheners to decrease fracture risk; anti viral to prevent shingles; sedation before procedures
- Interventions depends on source of pain
- May include medications, activity, surgical intervention, radiation therapy, etc
- Complementary therapies (Mind-body, medication, yoga, supplements, acupuncture, etc)

Tell your health care provider about any new bone pain or chronic pain that is not adequately controlled

Faiman B, et al. *CJON.* 2017;21(5)suppl:19-36.

PERIPHERAL NEUROPATHY MANAGEMENT

Peripheral neuropathy: damage to nerves in extremities (hands, feet, or limbs)

- Numbness
- Tingling
- Prickling sensations
- Sensitivity to touch
- Burning and/or cold sensation
- Muscle weakness

Report symptoms of peripheral neuropathy early to your health care provider; nerve damage from PN can be permanent if unaddressed

Prevention / management:

- Bortezomib once-weekly or subcutaneous administration
- Massage area with cocoa butter regularly
- Supplements:
  - B-complex vitamins (B1, B6, B12)
  - Folic acid, and/or amino acids but do not take on day of Velcade® (bortezomib) infusion
- Safe environment: rugs, furnishings, shoes

If PN worsens, your HCP may:

- Change your treatment
- Prescribe oral or topical pain medication
- Suggest physical therapy

Faiman B, et al. *CJON.* 2017;21(5)suppl:19-36. Tariman, et al. *CJON.*2008;12(3)suppl:29-36.

Physical

Psychological

FATIGUE, ANXIETY & DEPRESSION

All can affect quality of life and relationships

- Fatigue is the most common reported symptom (98.8%)
  Sources include anemia, pain, reduced activity, insomnia, treatment toxicity, bone marrow suppression

- Anxiety reported in >35%
- Depression nearly 25%
  Financial concerns, disease progression, end-of-life, and change in social and sexual function were highlighted sources

Often, people do not share these symptoms with their provider. Talk to your provider about symptoms that are not well controlled or thoughts of self harm. Help is available.

Ramsenthaler, et al. 2016. https://doi.org/10.1111/ejh.12790. Catamero D et al. *CJON.* 2017; 21(5)suppl:7-18.

REST AND RELAXATION CONTRIBUTE TO GOOD HEALTH

Adequate rest and sleep are essential to a healthful lifestyle

Short and disturbed sleep increase risk of

- Heart related death
- Increase anxiety
- Weaken immune system
- Worsened pain
- Falls and personal injury

Things that can interfere with sleep

- Medications : steroids, stimulants, herbal supplements
- Psychologic: fear, anxiety, stress
- Physiologic: sleep apnea, heart issues, pain

Sleep hygiene is necessary for quality nighttime sleep, daytime alertness

- Engage in exercise but not too near bedtime
- Increase daytime natural light exposure
- Avoid Daytime napping
- Establish a bedtime routine - warm bath, cup of warm milk or tea
- Associate your bed ONLY with sleep
- Sleep aid may be needed
- Avoid before bedtime:
  - Caffeine, nicotine , alcohol and sugar
  - Large meals and especially spicy, greasy foods
  - Computer screen time

Rod NH et al 2014. *PloS one. 9(4):e91965;* Coleman et al. 2011. *Cancer Nurs. 34(3):219-227.*
National Sleep Foundation. At: http://sleepfoundation.org/ask-the-expert/sleep-hygiene

Mustian et al. *Journal of clinical Oncology. Sep 10 2013;31(26):3233-3241.*
Stan DL, et al. *Clin J Oncol Nurs. Apr 2012;16(2):131-141.*
Zeng Y et al., *Complementary therapies in medicine. Feb 2014;22(1):173-186.*

FINANCIAL BURDEN

Financial burden comes from

- Medical costs
  - Premiums
  - Co-payments
  - Travel expenses
  - Medical supplies
- Prescription costs
- Loss of income
  - Time off work or loss of employment
  - Caregiver time off work

Contact the Social Services department at your hospital or clinic to talk to a social worker for assistance.

Funding and assistance may be available

- Federal programs
- Pharmaceutical support
- Non-profit organizations
- Websites:
  - Medicare.gov
  - SSA.gov
  - LLS.org
  - Rxassist.org
  - NeedyMeds.com
  - HealthWellFoundation.org
  - Company-specific website

FRAMING YOUR CARE

Know your care team, Telehealth & Meeting Prep, & Shared Decision Making

CARE TEAM COLLAGE

You are central to the care team

Be empowered

- Ask questions, learn more
- Participate in decisions

Communicate with your team

- Understand the roles of each team member and who to contact for your needs
- Participate in support network

PREPARE FOR VISITS & CONSIDER TELEMEDICINE

Come prepared:

- Bring a **list of current medications**, prescribed and over the counter
- Write down your **questions and concerns**. Prioritize them including financial issues
- Have there been any **medical or life changes** since your last visit?
- **Current symptoms** - how have they changed (improved, worsened, stable)? Keep a symptom diary. Bring it along
- **Communicate effectively**: your health care team can't help if they don't know
- Know the **"next steps"**, future appointments, medication changes, refills, etc

Check with your healthcare team –
Is telemedicine an option?

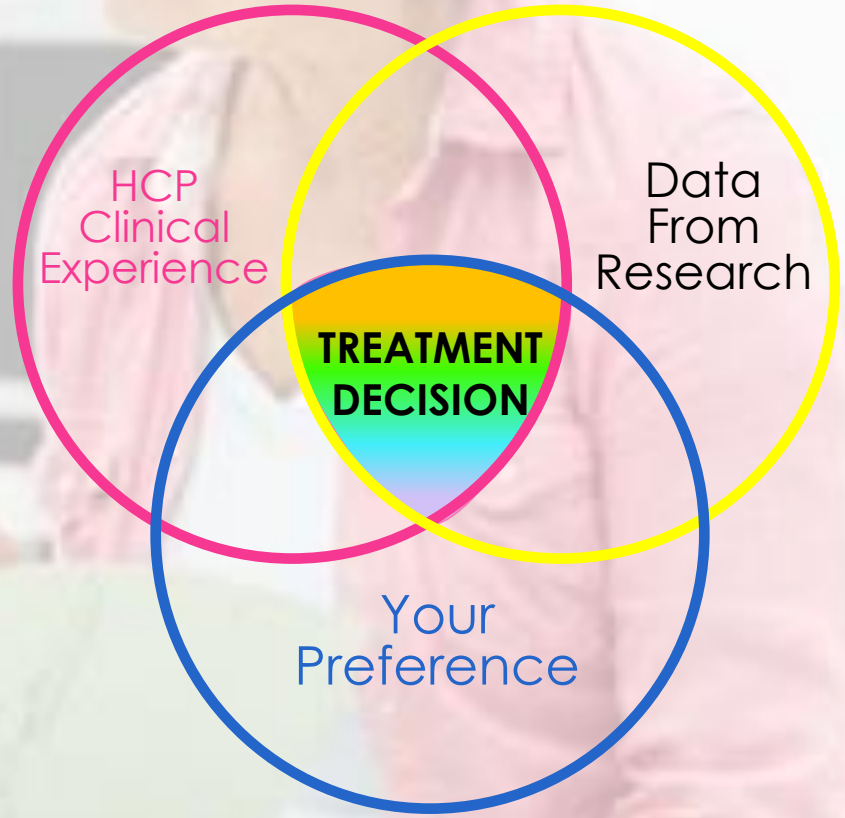
Similar planning for "in-person" appointment PLUS:

- What is the **process and what technology** is needed?
- **Plan your labs**: are they needed in advance? Do you need an order?
- 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

SHARED DECISION-MAKING

Be empowered to be part of the treatment decision-making

- **Ask for time to consider options (if needed/appropriate)**
- **Understand options; consider priorities**
  - Use reliable sources of information
  - Use caution considering stories of personal experiences
  - Consider your goals/values/preferences
- **Express your goals/values/preferences; create a dialog**
  - My top priority is [goal/value]; additional [preferences] are also important.
  - I think [treatment] may be a good choice given my priorities… What do you think?
- **Arrive at a treatment decision together**

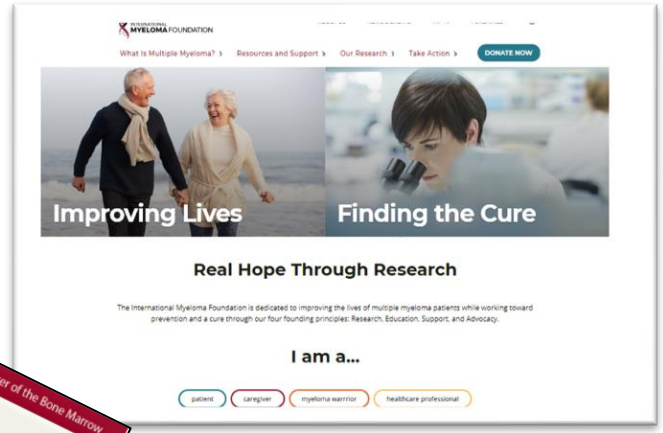


Philippe Moreau. ASH 2015.

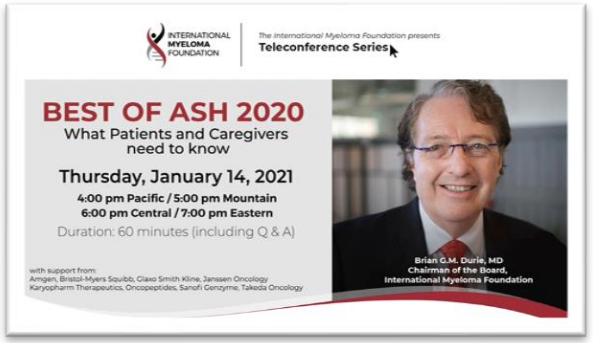
KNOWLEDGE IS POWER
USE REPUTABLE SOURCES

Download or order at myeloma.org

Website: http://myeloma.org



IMF TV Teleconferences



eNewsletter: Myeloma Minute

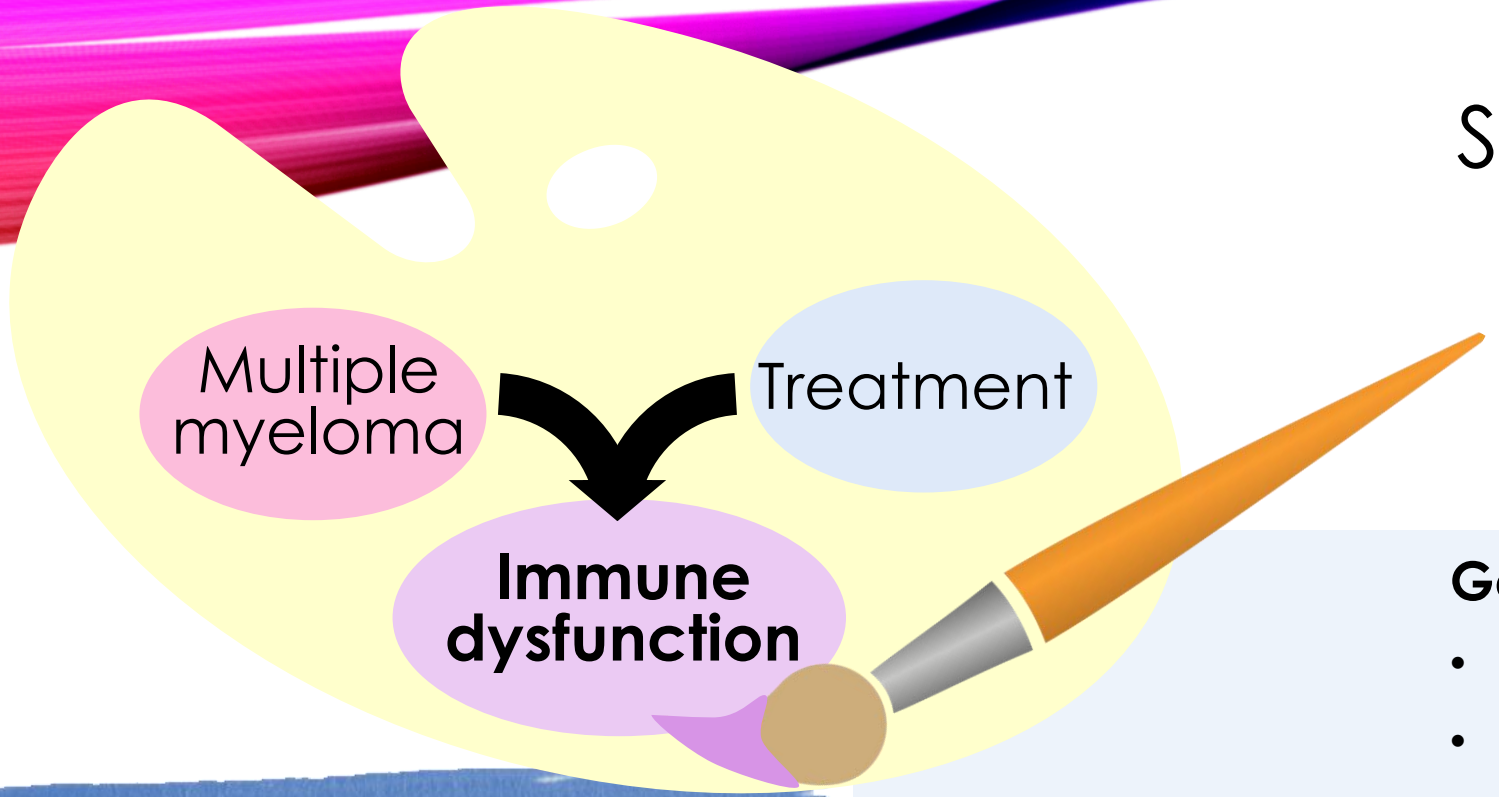
IMF InfoLine
1-800-452-CURE
9am to 4pm PST

LIVE LIFE IN COLOR

Healthful Living, infection prevention, renal and bone health

INFECTION PREVENTION AND COVID-19 IN PEOPLE WITH MULTIPLE MYELOMA

INFECTION CAN BE SERIOUS FOR PEOPLE WITH MYELOMA



7-10 fold increased risk of bacterial and viral infections for people with myeloma

Report fever of more than 100.4°F, shaking chills even without fever, dizziness, shortness of breath, low blood pressure to HCP as directed.

General Infection Prevention Tips

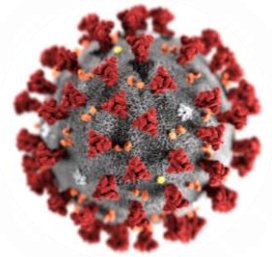
- Good personal hygiene (skin, oral)
- Environmental control (wash hands, avoid crowds and sick people, etc)

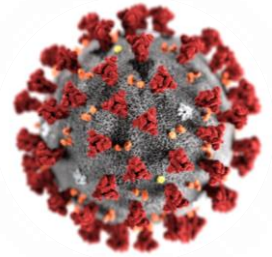
As recommended by your health care team

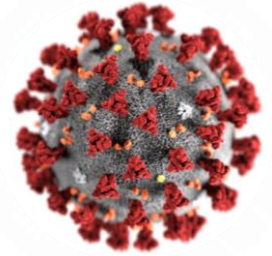
- Growth factor (Neupogen [filgrastim])
- Immunizations (NO live vaccines)
- Medications (antibacterial, antiviral)

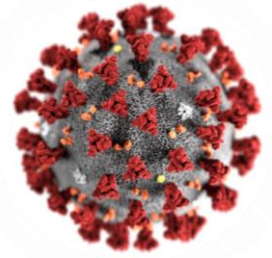
Brigle K, et al. *Clin J Oncol Nurs.* 2017;21(5)suppl:60-76. Faiman B, et al; IMF Nurse Leadership Board. *Clin J Oncol Nurs.* 2011;15(Suppl):66-76. Miceli TS, et al. *Clin J Oncol Nursing.* 2011;15(4):9-23.
ASH Website. COVID-19 Resources. Accessed January 30, 2022. https://www.hematology.org/covid-19/covid-19-and-multiple-myeloma

IMPORTANT WAYS TO SLOW THE SPREAD OF COVID-19









- Get a COVID-19 vaccine (and booster) as soon as you can
- Wear a mask (N95 is most protective) that covers your nose and mouth
- Stay 6 feet apart from others who don't live with you
- Avoid crowds and poorly ventilated indoor spaces
- Test to prevent spread to others
- Wash your hands often with soap and water. Use hand sanitizer if soap and water aren't available

CDC = Centers for Disease Control; FDA = Food and Drug Administration.

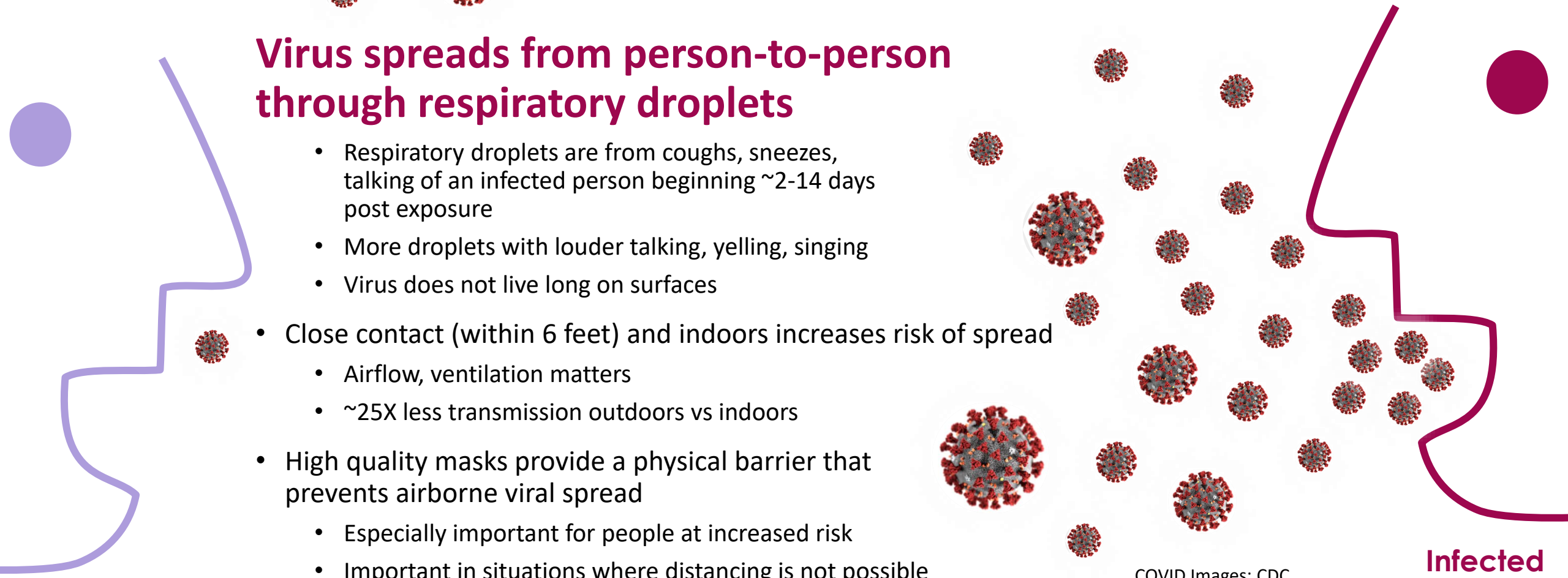
CDC website. Understanding Variants. Accessed January 30, 2022. https://www.cdc.gov/coronavirus/2019-ncov/variants/understanding-variants.html

PREVENTION: AVOID BEING EXPOSED TO THE COVID VIRUS

Virus spreads from person-to-person through respiratory droplets

- Respiratory droplets are from coughs, sneezes, talking of an infected person beginning ~2-14 days post exposure
- More droplets with louder talking, yelling, singing
- Virus does not live long on surfaces

- Close contact (within 6 feet) and indoors increases risk of spread
  - Airflow, ventilation matters
  - ~25X less transmission outdoors vs indoors
- High quality masks provide a physical barrier that prevents airborne viral spread
  - Especially important for people at increased risk
  - Important in situations where distancing is not possible

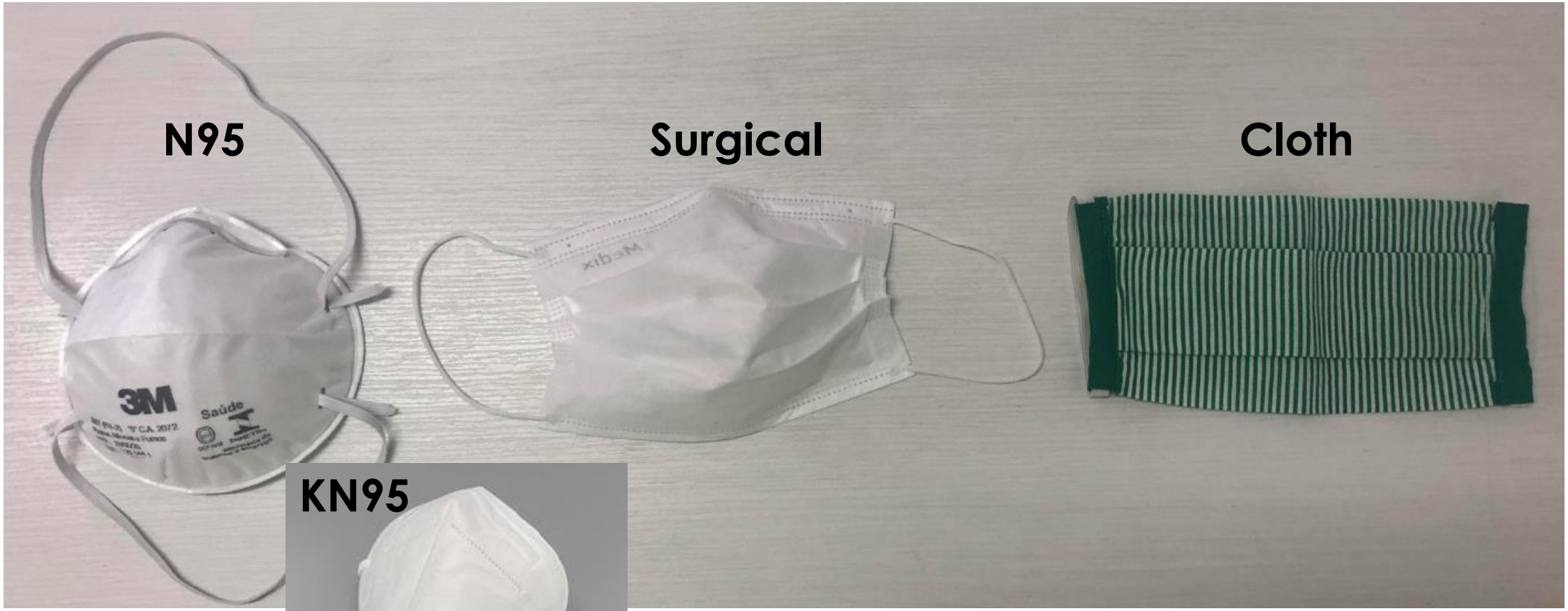


COVID Images: CDC

CDC = Centers for Disease Control; MIT = Massachusetts Institute of Technology

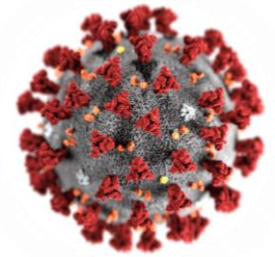
MIT Medical website. COVID-19 Updates. How safe are outdoor activities? Accessed January 30, 2022. https://medical.mit.edu/covid-19-updates/2021/08/how-safe-outdoor-activities
CDC website. Types of Masks and Respirators. Accessed January 30,2022, 2020.. https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/types-of-masks.html
CDC website. Your Guide to Masks. Accessed January 30, 2022. https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/about-face-coverings.html

CDC NOW RECOMMENDS HIGH QUALITY MASKS FOR THOSE AT RISK

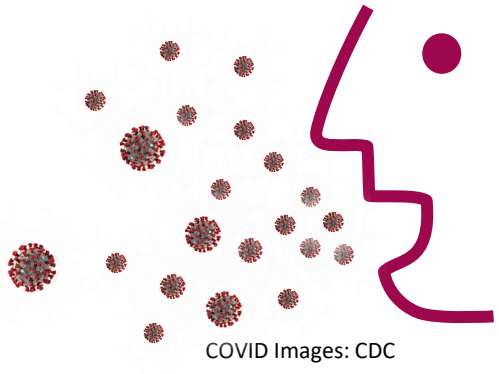


CDC website. Types of Masks and Respirators. Accessed January 30,2022, 2020.. https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/types-of-masks.html
CDC website. Your Guide to Masks. Accessed January 30,2022, 2020.. https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/about-face-coverings.html

TIME TO INFECTIOUS DOSE FOR SOMEONE NOT INFECTED WITH COVID-19

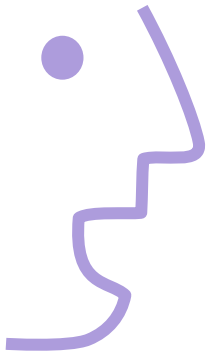


COVID Image: CDC



COVID Images: CDC

Person Infected Is Wearing



Person Not Infected Is Wearing

	Nothing	Cloth Mask	Surgical Mask	N95 Mask (10% leakage)
Nothing	<15 min*	20 min	30 min	**2.5 hrs**
Cloth Mask	20 min	27 min	40 min	**3.3 hrs**
Surgical Mask	30 min	40 min	60 min	**5 hrs**
N95 Mask (10% leakage)	**2.5 hrs**	**3.3 hrs**	**5 hrs**	**25 hrs**

*New research shows that 9.8 feet (3 meters) of social distancing are not enough to ensure protection from Covid-19. Even at that distance, it takes **less than five minutes** for an unvaccinated person standing in the breath of a person with Covid-19 to become infected with almost 100% certainty.

ACGIH website. COVID-19 Fact Sheet: Workers Need Respirators. Accessed January 30, 2022. https://www.acgih.org/covid-19-fact-sheet-worker-resp/
Cornell University website. Cornell Chronicle: Better-fitting masks offer better COVID protection. Accessed January 30, 2022. https://news.cornell.edu/stories/2021/12/better-fitting-masks-offer-better-covid-protection

HEALTHFUL LIVING STRATEGIES: PREVENTION

Manage stress
- Rest, relaxation, sleep hygiene
- Mental health / social engagement
- Complementary therapy

Maintain a healthy weight
- Nutrition
- Activity / exercise

Preventative health care
- Health screenings, vaccinations
- Prevent falls, injury, infection
- Stop smoking
- Dental care

Maintain renal health
- Myeloma management
- Hydration
- Avoid renally-toxic medications
  - Dose adjust to renal function
- Diabetes management

Protect your bones
- Nutrition, Calcium + D supplement
- Weight-bearing activity / walking
- Bone strengthening agents

"An ounce of prevention is worth a pound of cure." Benjamin Franklin

Faiman B, et al. *CJON.* 2017;21(5)suppl:19-36. Dimopoulous M, et al. *Leukemia.* 2009;23(9):1545-56.
Brigle K, et al. *CJON.* 2017;21(5)suppl:60-76. Faiman B, et al. *CJON.* 2017;21(5)suppl:19-36. Faiman B, et al. *CJON.* 2011;15suppl:66-76. Miceli TS, et al. *CJON.* 2011;15(4)suppl:9-23.

HEALTHFUL LIVING STRATEGIES: KEEP ACTIVE

Do

- Keep a log or journal of your activity
- Notify your healthcare provider about sudden onset of pain, progressive weakness, headaches, blurred vision, numbness, and tingling
- Dehydration can lead to low blood pressure, falls

Do Not:

- Overdo it
- Force exercise
- Try things without discussing with provider
- Consider weight lifting limits

Movement therapies can reduce stress, promote sleep

Yoga, Pilates, Tai Chi

- Shown to improve sleep and sleep quality,
- Improved quality of life & mood

Myeloma bone disease may affect your ability to do certain movement activities. Review your activity interests with your health care provider!

Boullosa DA, et al., *Jul 2013;45(7):1223-1228.*
Faiman B et al., *Clinical Journal of Oncology Nursing. 2008;12(0):53-62;* Rome S et al., *Clin J Oncol Nurs. Aug 2011;15 Suppl:41-52.*
Miceli T et al., *Clinical Journal of Oncology Nursing. 2011;15:9-23;* Coleman EA et al.,*Oncol Nurs Forum. May 2008;35(3):E53-61.*

YOU ARE NOT ALONE

Looking ahead with Robin Tuohy!

MYELOMA ACTION

MARCH IS MYELOMA **ACTION** MONTH

#MYELOMA**ACTION**

Robin Tuohy, Vice President, Support Groups

TAKE**ACTION**
#MYELOMA**ACTION**

#MYELOMAACTION
Join the Movement

Brian G.M. Durie, MD
Cedars-Sinai Outpatient
Cancer Center
Los Angeles, CA

Myeloma 101

INTERNATIONAL MYELOMA FOUNDATION

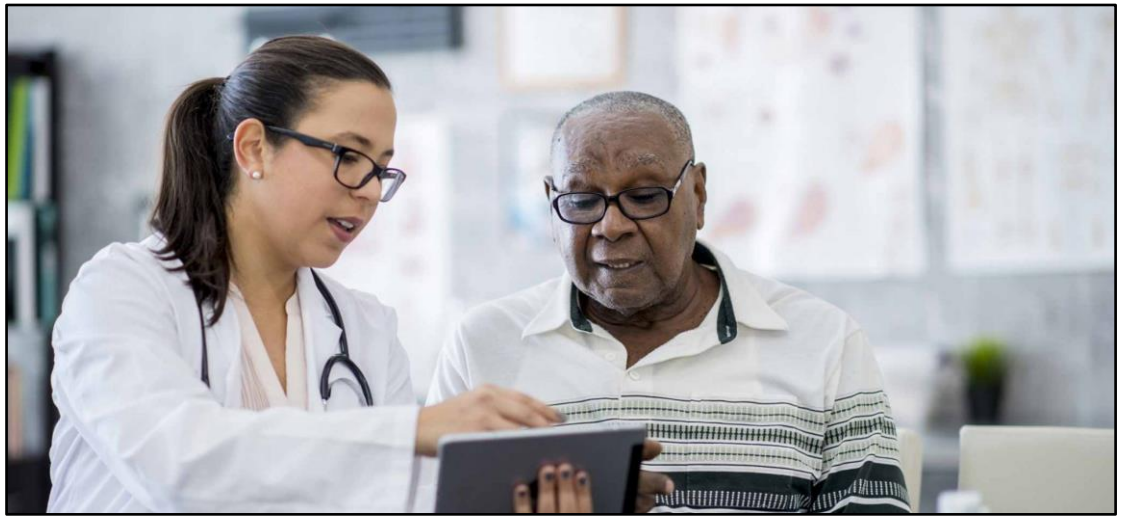
Myeloma is treatable

- **Over 90% of patients respond to current therapies**
- Average first remission is 4 years or more
- In 2021, average survival is at least 7-10 years
- Some patients live over 15-20+ years
- New therapies are constantly improving the outlook

INTERNATIONAL MYELOMA FOUNDATION

Myeloma Expert Consultation Helps!

- Good to do early!
- Virtual consults can be explored.
- Sets path for future
- Guides local doctor



SEE: Questions to ask your doctor

https://www.myeloma.org/resource-library/tip-card-ask-your-doctor-these-important-questions

INTERNATIONAL MYELOMA FOUNDATION

Smoldering Myeloma

New SMM Risk Score Tool*

2/20/20 Model

FLC Ratio 20

Serum M Protein 2 g/dl

Bone Marrow Plasma Cell % 20%

Risk Factor	Coefficient	Odds Ratio (95% CI)	P-value	Score
FLC Ratio				
0-10 (reference)	-	-	-	0
>10-25	0.69	1.99 (1.15, 3.45)	0.014	2
>25-40	0.96	2.61 (1.36, 4.99)	0.004	3
>40	1.56	4.73 (2.88, 7.77)	<0.0001	5
M protein (g/dL)				
0-1.5 (reference)	-	-	-	0
>1.5-3	0.95	2.59 (1.56, 4.31)	0.0002	3
>3	1.30	3.65 (2.02, 6.61)	<0.0001	4
BMPC%				
0-15 (reference)	-	-	-	0
>15-20	0.57	1.77 (1.03, 3.06)	0.04	2
>20-30	1.01	2.74 (1.6, 4.68)	0.0002	3
>30-40	1.57	4.82 (2.5, 9.28)	<0.0001	5
>40	2.00	7.42 (3.23, 17.02)	<0.0001	6
FiSH abnormality	0.83	2.28 (1.53, 3.42)	<0.0001	2

Risk Score

Low Risk

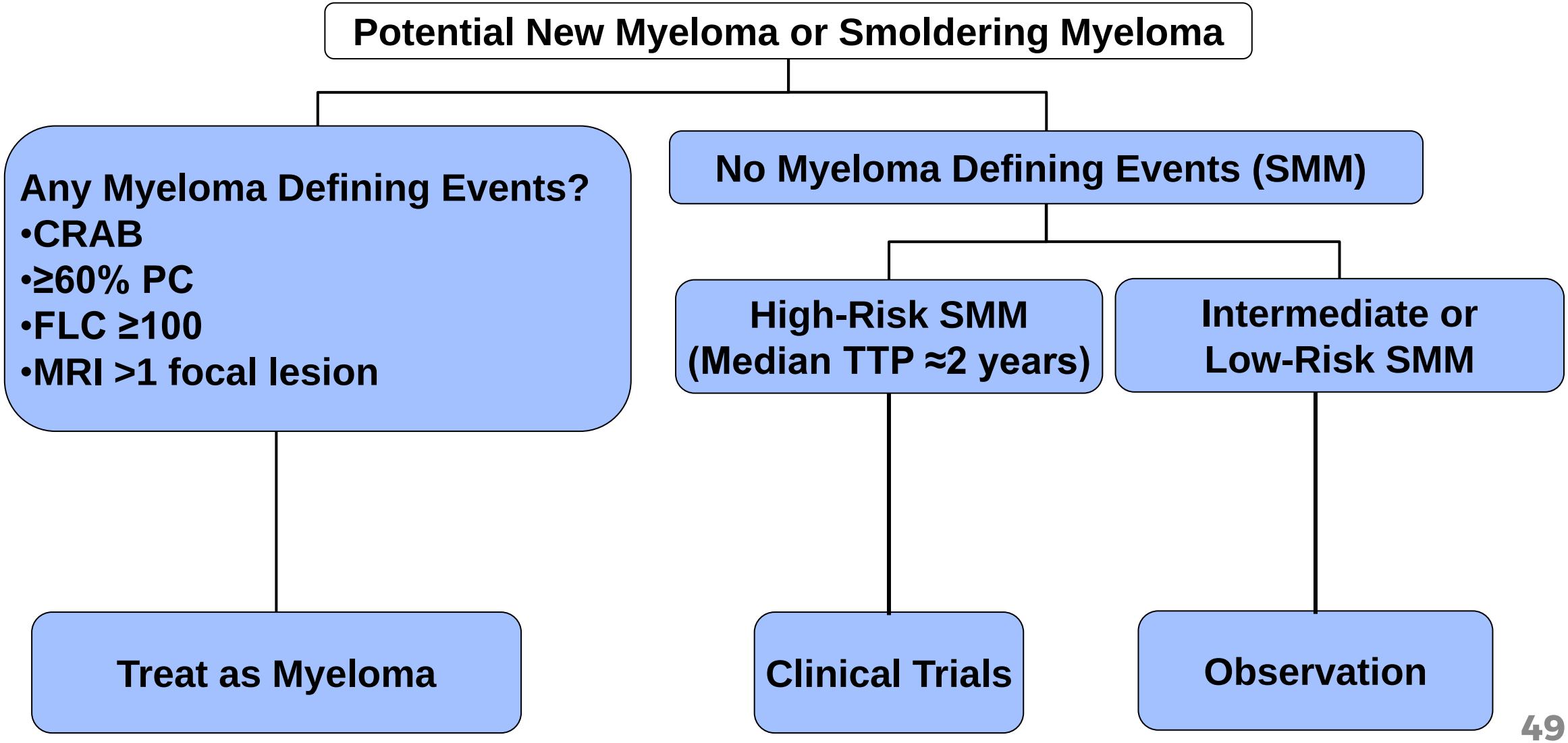
High Risk

*689 of the original 2286 had complete data for all risk factors. Logistic regression analysis was performed.
Principal Investigators: Mateos; Kumar; San Miguel; Durie.

International Myeloma Working Group risk stratification model for smoldering multiple myeloma (SMM)
Blood Cancer J. 2020 Oct 16;10(10):102. doi: 10.1038/s41408-020-00366-3.
https://www.nature.com/articles/s41408-020-00366-3

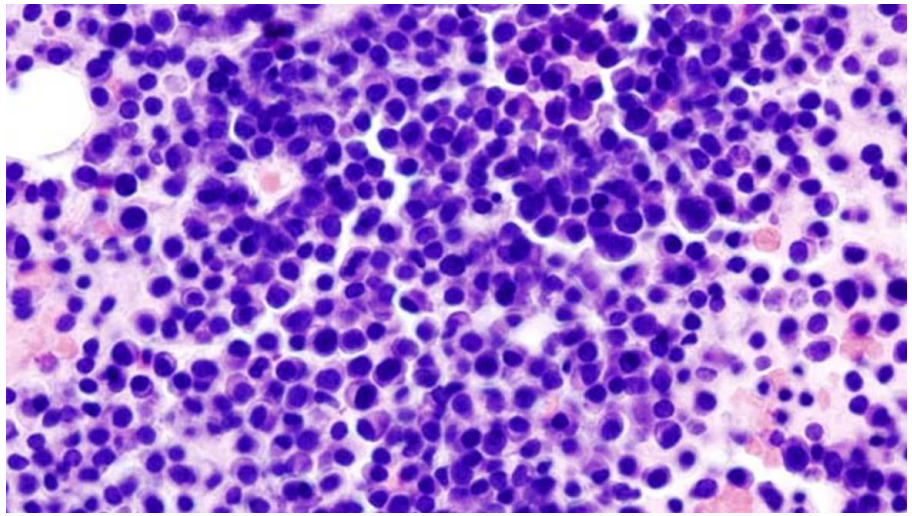
IMWG INTERNATIONAL MYELOMA WORKING GROUP
A Research Division of International Myeloma Foundation

When Should Treatment Be Initiated?



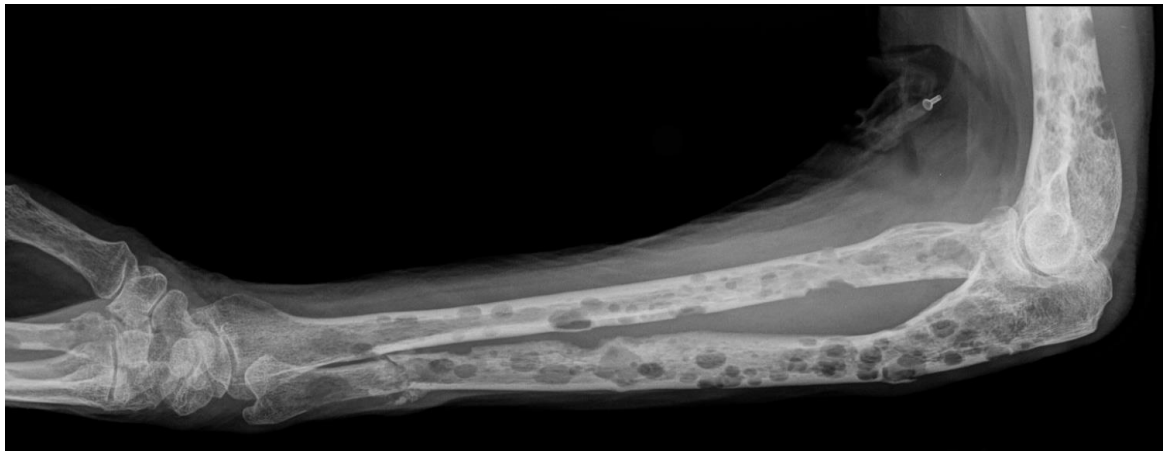
Careful testing required for diagnosis and monitoring

- **Bone marrow** indicates % myeloma
- **X-rays/ scans** show where lesions* are located



Myeloma cells as seen in a bone marrow aspirate

X-ray image of myeloma lesions in arm



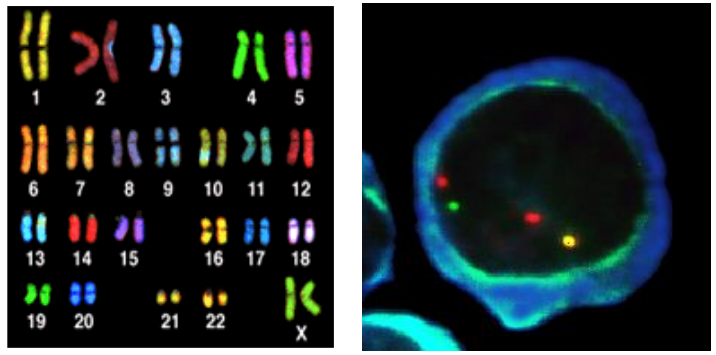
See further discussion: "What is a lesion?" https://www.myeloma.org/bone-disease

INTERNATIONAL MYELOMA FOUNDATION

More Test Details

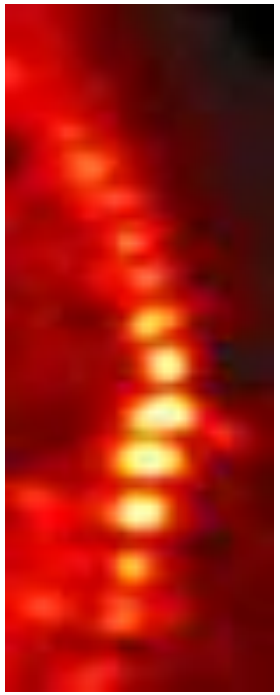
- **Bone marrow** FiSH shows chromosome results
- **MRI and PET/CT** show more lesions than x-rays

FISH

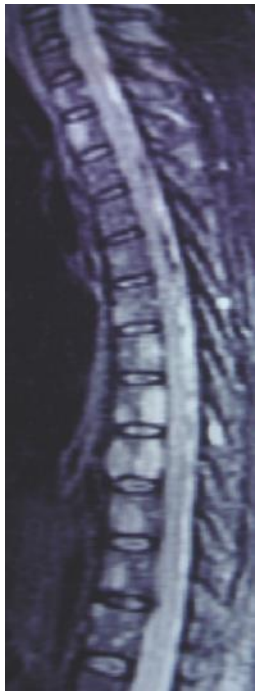


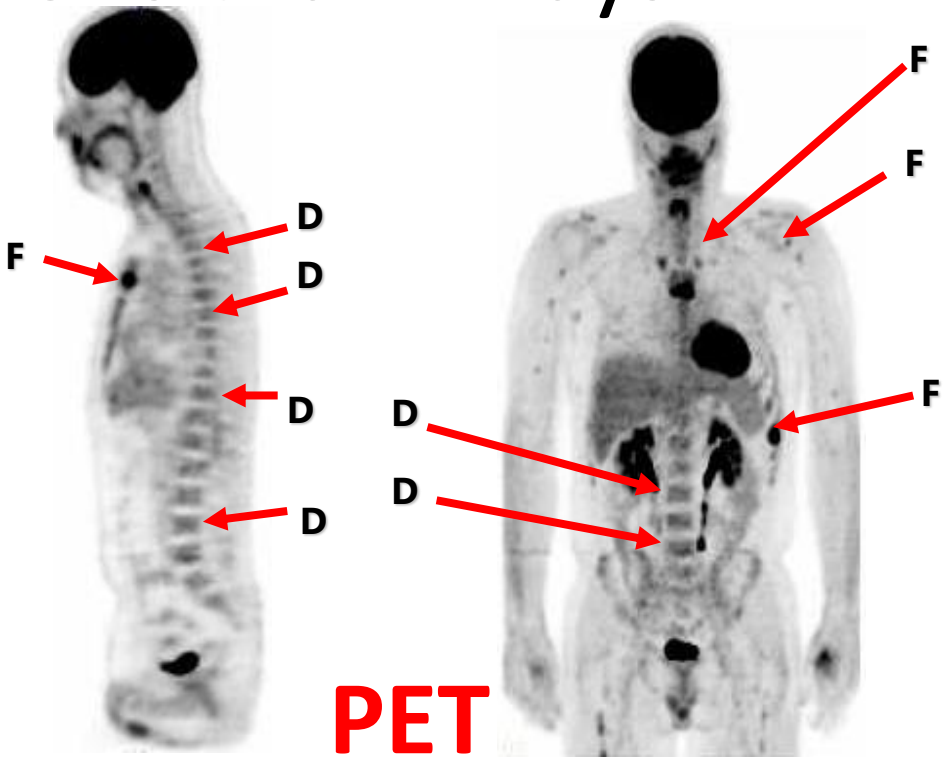
Colored spots show translocations: t(11;14)

PET



MRI



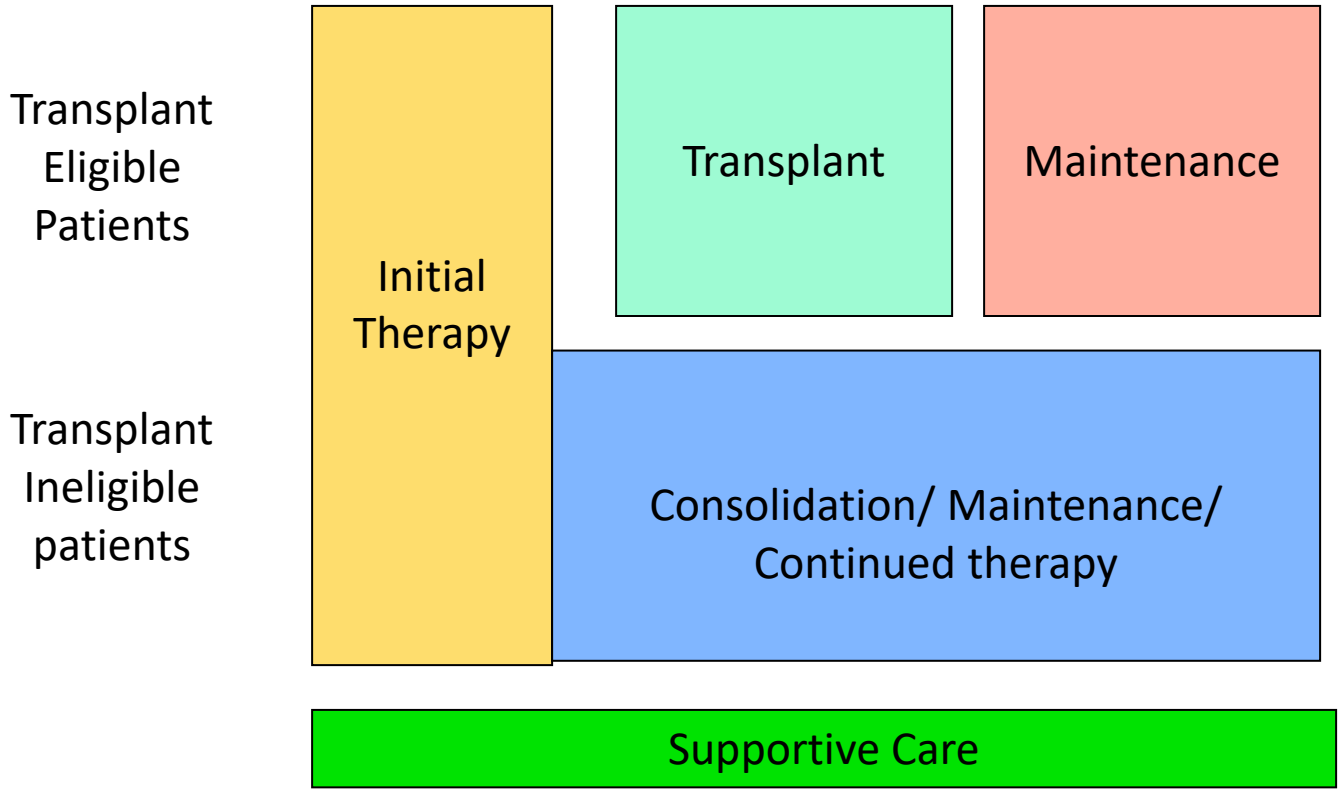


F = Focal
D = Diffuse

FiSH – **F**luorescent **i**n **S**itu **H**ybridization

INTERNATIONAL MYELOMA FOUNDATION

Managing Myeloma: The Components



Received: 12 March 2020 | Accepted: 18 March 2020
DOI: 10.1002/ajh.25791

ANNUAL CLINICAL UPDATES IN HEMATOLOGICAL MALIGNANCIES

AJH WILEY

Multiple myeloma: 2020 update on diagnosis, risk-stratification and management

S. Vincent Rajkumar

https://onlinelibrary.wiley.com/doi/full/10.1002/ajh.25791

INTERNATIONAL MYELOMA FOUNDATION

Treatment Combinations: Now and Then

NEW

Front line treatment	Maintenance	Relapsed
VD Rev/Dex CyBorD VTD **VRD** KRD IRD **Dara + triplet**	SCT VD/VRD	Lenalidomide Bortezomib Ixazomib Daratumumab Pomalidomide	Thalidomide Bortezomib Lenalidomide Carfilzomib Ixazomib Pomalidomide Daratumumab Isatuximab Elotuzumab Panobinostat Bendamustine Selinexor Belantamab Mafodotin **Melphalan Flufenamide (Melflufen)**
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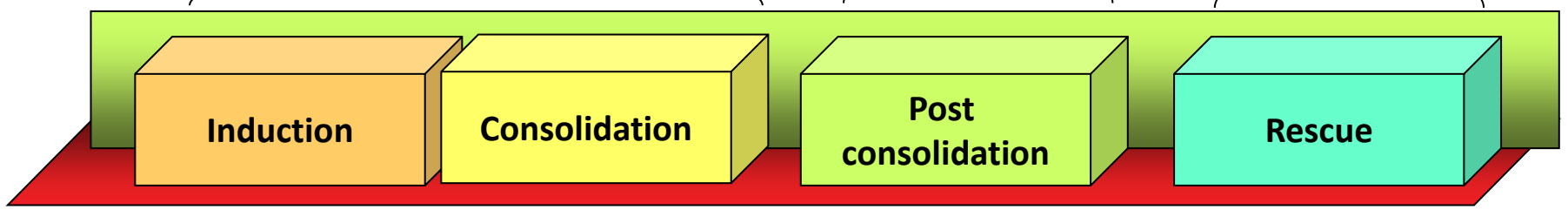
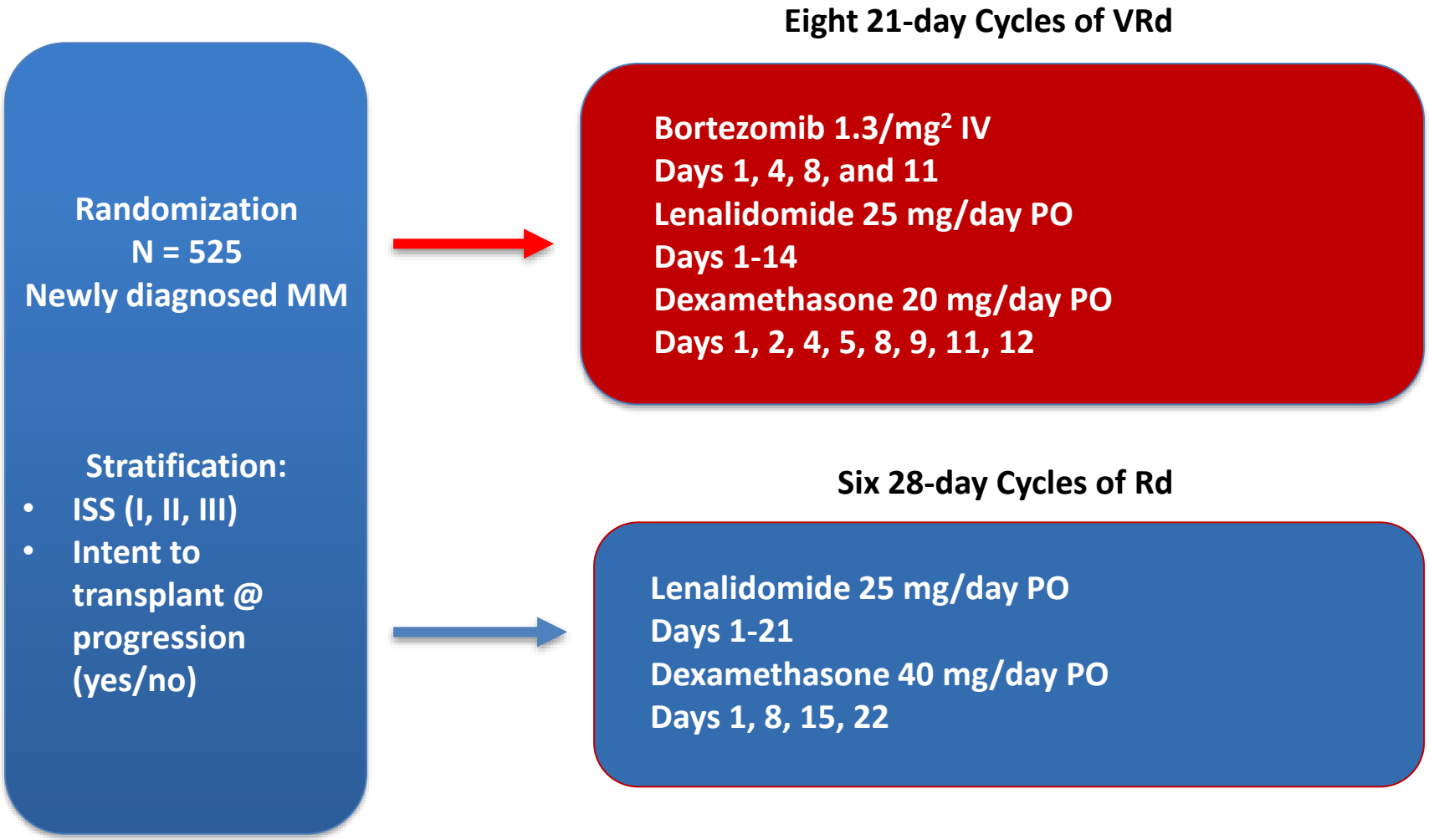


OLD

Thal/Dex VAD DEX	SCT	Nothing Prednisone Thalidomide	Few options

INTERNATIONAL MYELOMA FOUNDATION

S0777 Trial: VRd vs Rd



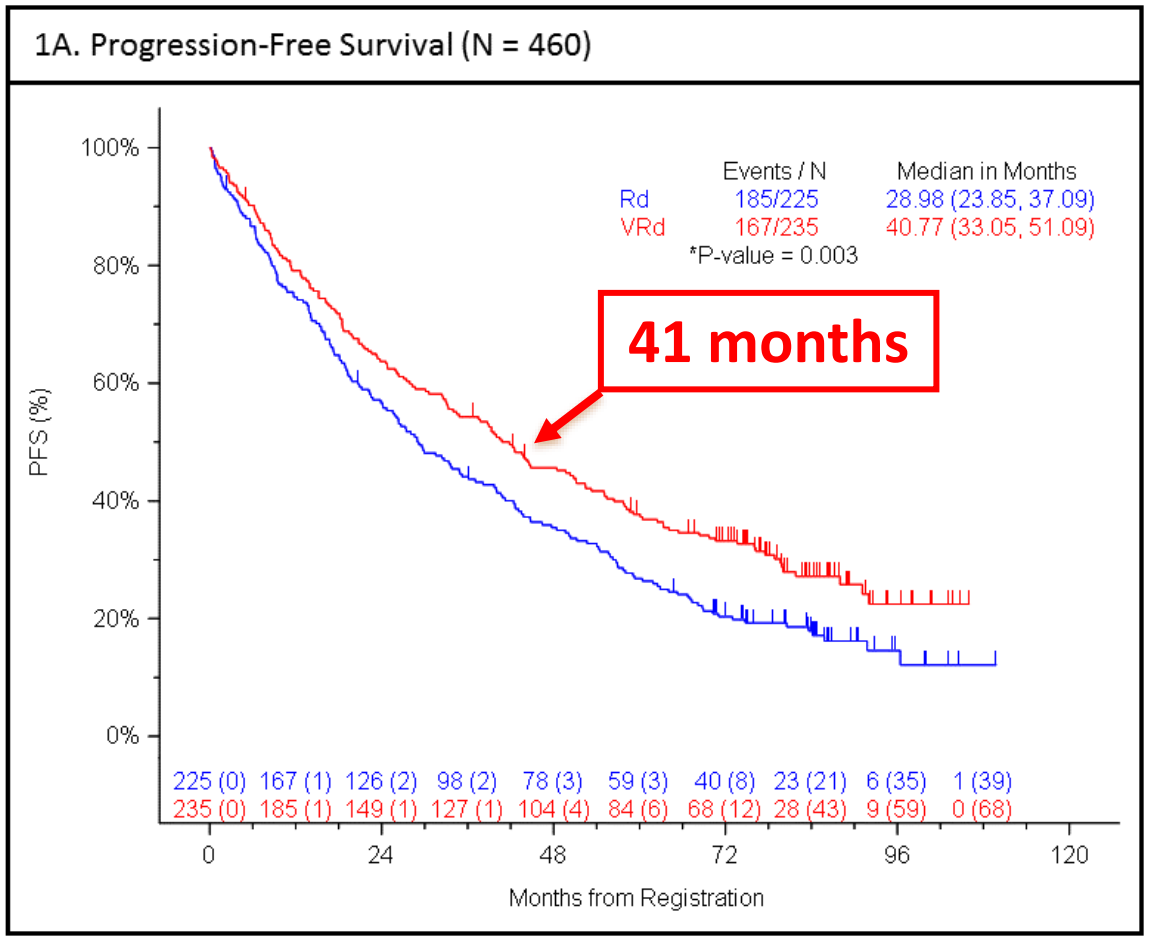
6 month of triplet followed by doublet

Durie BGM, et al. ASH 2015

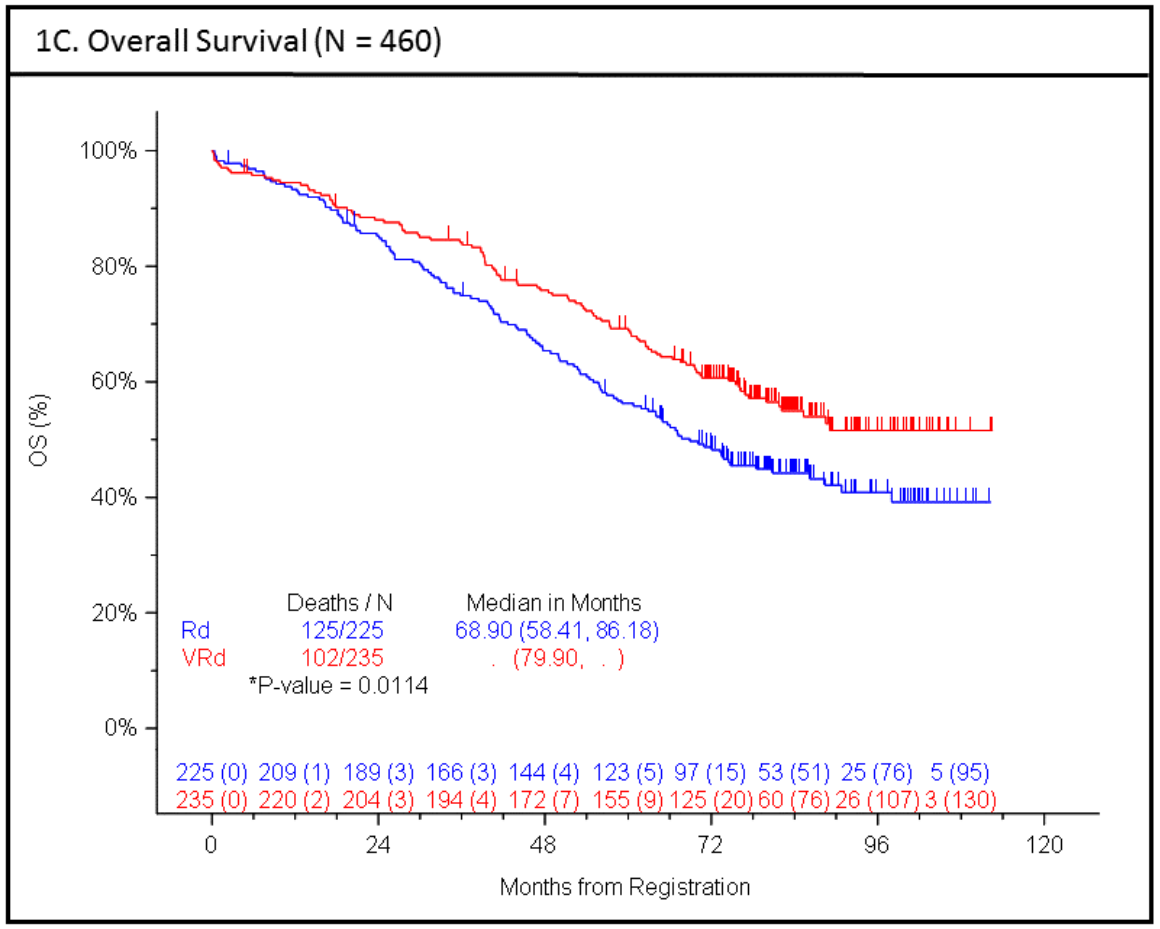
NCI National Clinical Trials Network
a National Cancer Institute program

INTERNATIONAL MYELOMA FOUNDATION

S0777 Trial: VRd vs Rd



*One-sided, stratified log-rank test



*Two-sided, stratified log-rank test.

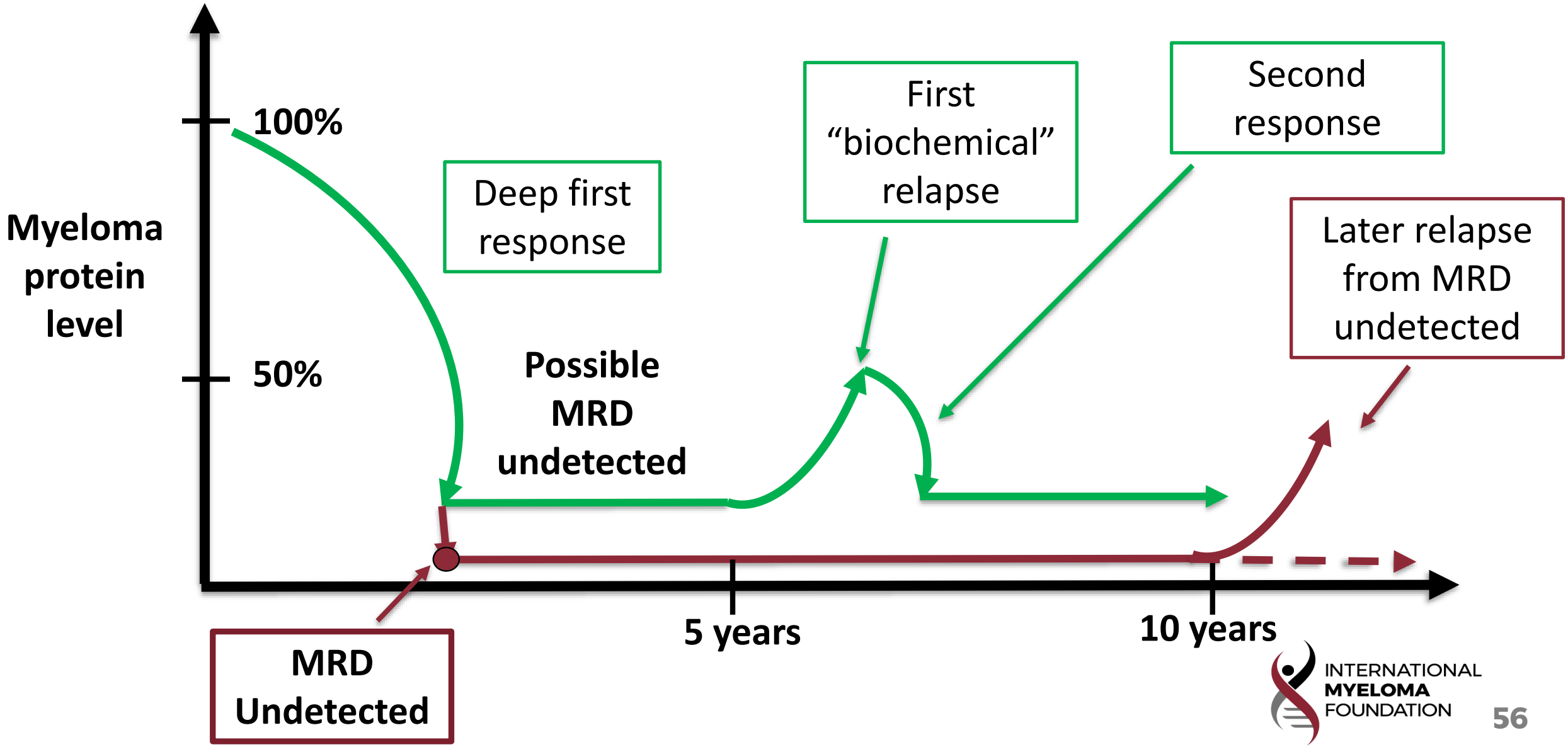
Blood Cancer Journal

Durie et al. Blood Cancer Journal (2020) 10:53
https://www.nature.com/articles/s41408-020-0311-8

OS 80% = 4 years
55% = 7 years

INTERNATIONAL MYELOMA FOUNDATION

What to Expect with Treatment



INTERNATIONAL MYELOMA FOUNDATION

Treatment Options

- **"Triple therapy":** 3 drugs recommended
  - Most common = VRd* [Rd for older/frail]

    (Velcade®/ Revlimid®/ dexamethasone)
- **ASCT** (**A**utologous **S**tem **C**ell **T**ransplant)
  - Can be considered to achieve better response (after 3-6 months of VRd)

Plus Zometa®/ Aredia or denosumab for bone lesions

* Other options include VCd (CyBorD); KRd; Dara + Rd; Vd

INTERNATIONAL MYELOMA FOUNDATION

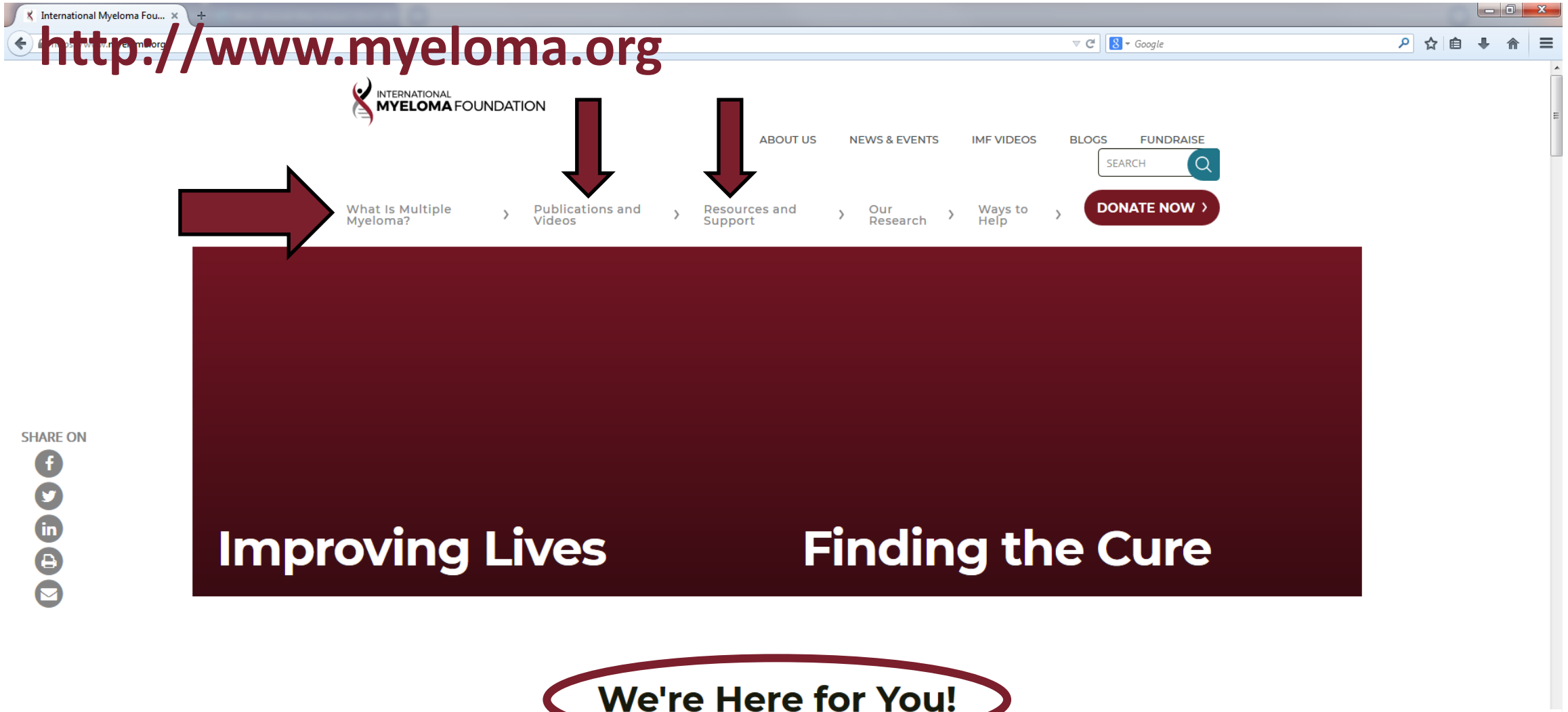
Treatment Strategies in 2022

- Triplets or quadruplets in frontline
- Maintenance based upon risk
- Decisive early relapse treatment

  (triplets if feasible)
- Earlier use of new immune therapies

INTERNATIONAL MYELOMA FOUNDATION

IMF Website – http://www.myeloma.org




INTERNATIONAL
MYELOMA
FOUNDATION

Brian G.M. Durie, MD
Cedars-Sinai Outpatient
Cancer Center
Los Angeles, CA

From Best of ASH 2021 to 2022 COVID-19 Guidance

INTERNATIONAL MYELOMA FOUNDATION

ASH 2021 OVERVIEW

ASH Annual Meeting & Exposition

- Virtual/ Live (hybrid)
- 879 “myeloma related” abstracts
- Many important reports on biology, diagnostics and trials follow-up

ASH 2021 – Hybrid (live & virtual)

ATTENDANCE

Live = **211**

Virtual = **647**

Total = 858

Slides and replay available:

ASH Friday Satellite Symposium

ASH 2021 – Hybrid (live & virtual)

IMWG
INTERNATIONAL MYELOMA WORKING GROUP
A Research Division of International Myeloma Foundation

MEETING SATURDAY DECEMBER 11

REGISTERED

Live = **120**

Virtual = **230**

Total = 360

INTERNATIONAL MYELOMA FOUNDATION | CELEBRATING 30 YEARS

iStopMM
Iceland Screens, Treats or Prevents Multiple Myeloma

iStopMM abstracts for ASH

- **6 ASH Abstracts for 2021**
- **4 oral presentations**
  - Overall results – Abstract #156
  - High prevalence of SMM – Abstract #151
  - No increased COVID with MGUS – Abstract #154
  - New FreeLite reference levels – Abstract #542

iStopMM
Iceland Screens, Treats or Prevents Multiple Myeloma

iStopMM abstracts for ASH

- **2 poster presentations**

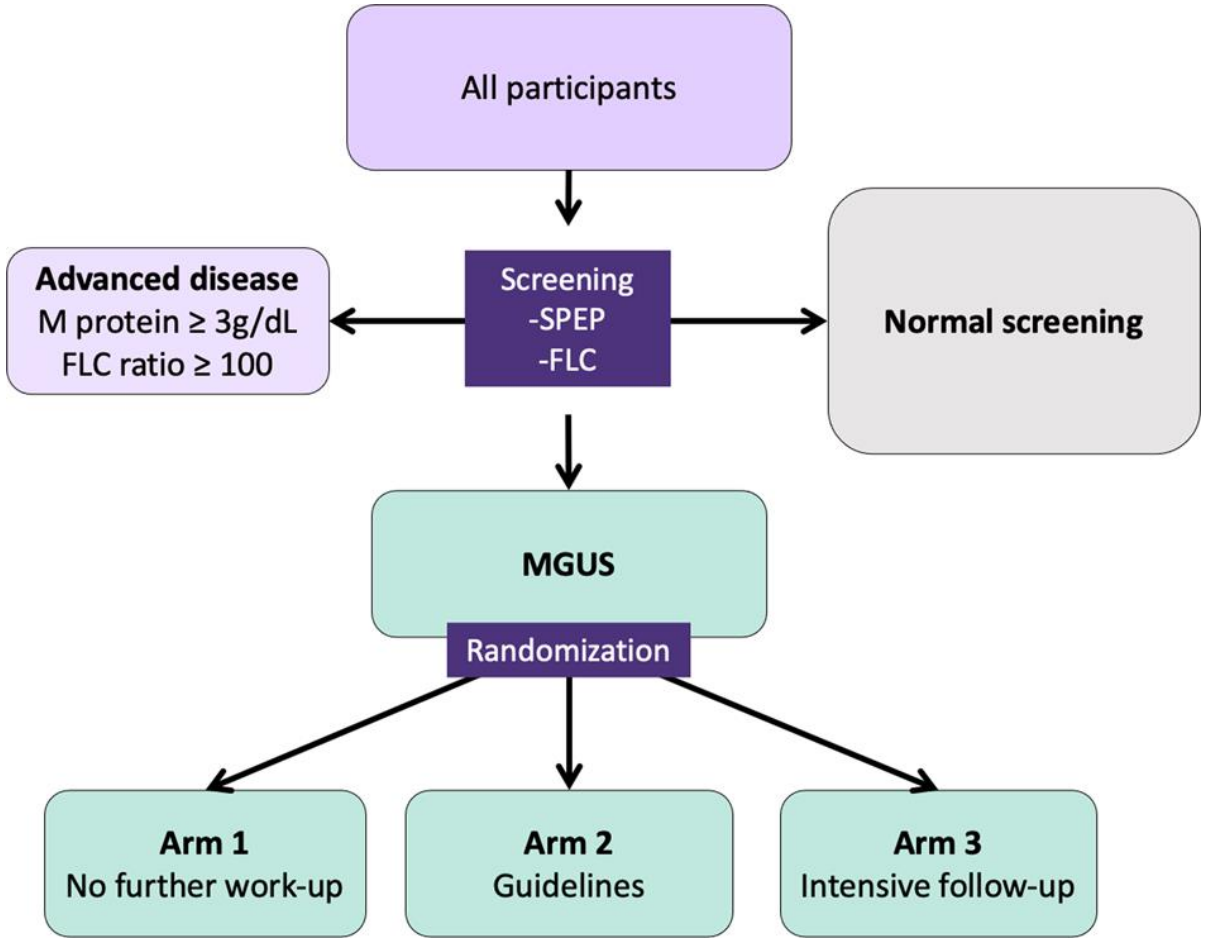
iStopMM
Iceland Screens, Treats or Prevents Multiple Myeloma

  - Circulating plasma cells – Abstract #2645
  - Selection bias in prior MGUS studies – Abstract #1618

iStopMM Overview

iStopMM
Iceland Screens, Treats or Prevents Multiple Myeloma

BLACK SWAN RESEARCH INITIATIVE
Signature Project of the International Myeloma Foundation



Rögnvaldsson S et al. Blood Cancer Journal 2021 –
"Monoclonal gammopathy of undetermined significance and COVID-19: a population-based cohort study"

iStopMM: Overall Results Abstract #156

- **Over 75,000** individuals screened
- "MGUS positive" patients randomized (3,725):
  - No further contact (1,164)
  - Periodic follow-up (1,159)
  - Intensive diagnostic testing/ monitoring (1,164)

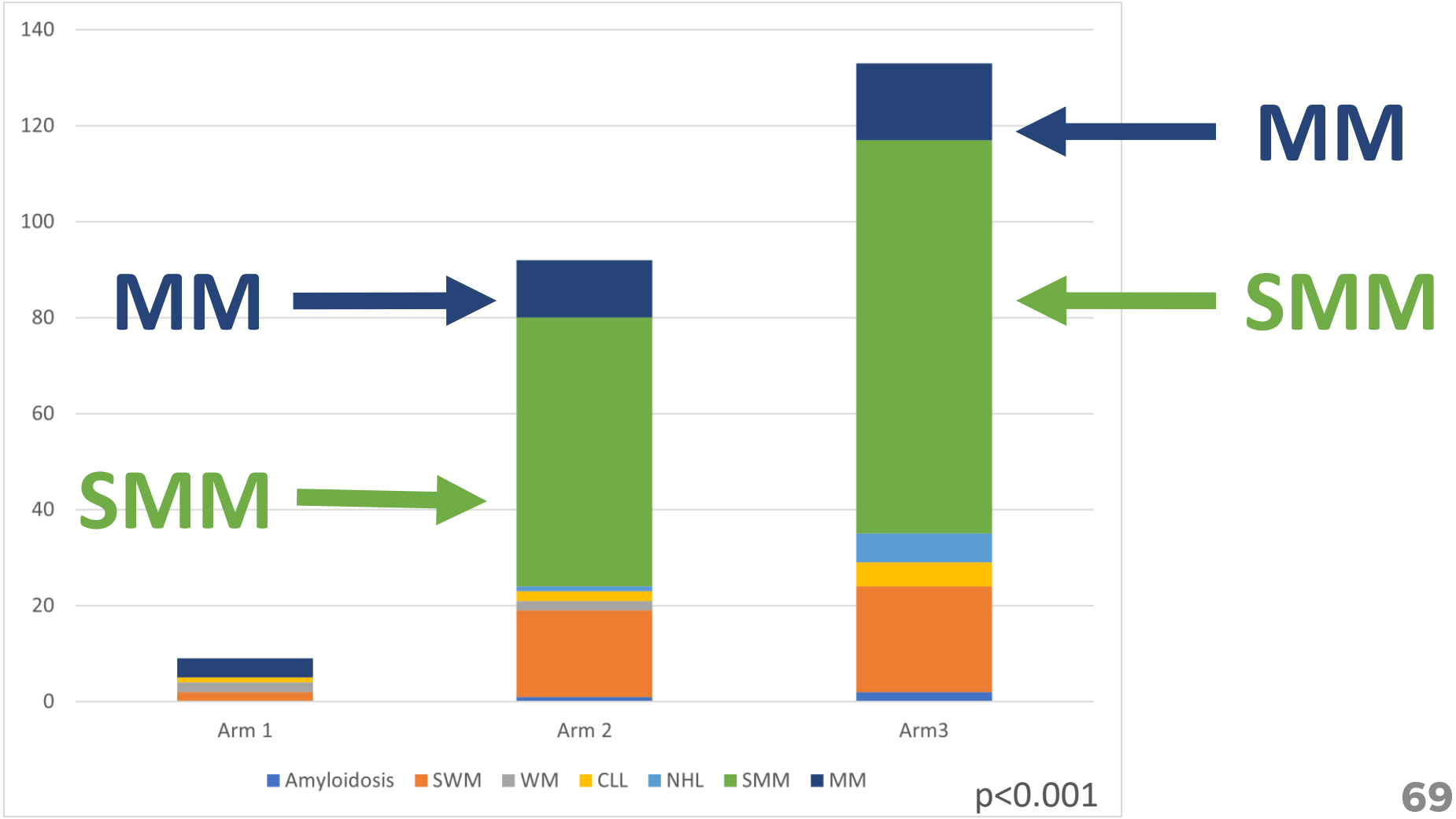
Abstract #156: Screening for Monoclonal Gammopathy of Undetermined Significance: A Population-Based Randomized Clinical Trial. First Results from the Iceland Screens, Treats, or Prevents Multiple Myeloma (iStopMM) Study

Diseases revealed by screening

RCT* OF MGUS SCREENING, WORK-UP, AND FOLLOW-UP

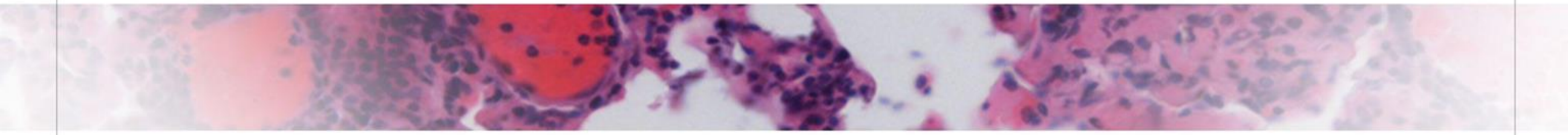
*RCT =
RANDOMIZED CLINICAL TRIAL

iStopMM
Iceland Screens, Treats or Prevents Multiple Myeloma



Abstract #151: ASH Abstract and Video Summary

American Society of Hematology
Helping hematologists conquer blood diseases worldwide



Definition and Clinical Significance of the MGUS-like Phenotype: A Study in 5,114 Patients (Pts) with Monoclonal Gammopathies

Leire Burgos*, Esteban Tamariz-Amador*, Noemi Puig*, Maria-Teresa Cedena*, Tomas Jelínek, Sarah Johnson, Paolo Milani, Lourdes Cordon, Jose J. Perez, Marta Lasa, Rosalinda Termini, Albert Oriol, Miguel-Teodoro Hernandez, Luis Palomera, Rafael Martinez-Martinez, Javier de la Rubia, Felipe de Arriba, Rafael Rios, Maria-Esther Gonzalez, Mercedes Gironella, Valentin Cabañas, Maria Casanova, Isabel Krsnik, Albert Perez-Montaña, Verónica González-Calle, Paula Rodriguez-Otero, Vladimir Maisnar, Roman Hajek, Fritz Van Rhee, Victor Jimenez-Zepeda, Giovanni Palladini, Giampaolo Merlini, Alberto Orfao, Laura Rosiñol, Joan Blade, Joaquín Martínez-Lopez, Juan-Jose Lahuerta, Maria-Victoria Mateos, Jesus F. San Miguel, Bruno Paiva

on behalf of the GEM (Grupo Español de Mieloma)/PETHEMA (Programa para el Estudio de la Terapéutica en Hemopatías Malignas) cooperative study group

PETHEMA GEM GRUPO ESPAÑOL DE MIELOMA

Universidad de Navarra | CIMA LAB DIAGNOSTICS

EuroFlow

Circulating tumor cells predict risk of progression in SMM patients

- 78% of SMM patients had CTC
- Untreated SMM patients with high CTC levels (**≥0.02%**) showed ultra-high risk of transformation (11 months) vs those with **<0.02% CTCs** and **undetectable CTCs**
- CTCs were selected as an independent prognostic factor for TTP, together with the M-protein and sFLC ratio (the % of BM tumor cells was not significant)
- *Additional Messages*: Evaluation of CTCs in PB outperformed quantification of BM tumor burden in SMM and the 2/20/20 model can be replaced by the 2/20/0.02% model. Allows frequent monitoring (evolving pattern)
- Thus, CTC assessment should be part of the diagnostic workup of SMM
- New SMM model 2/20/0.02% model

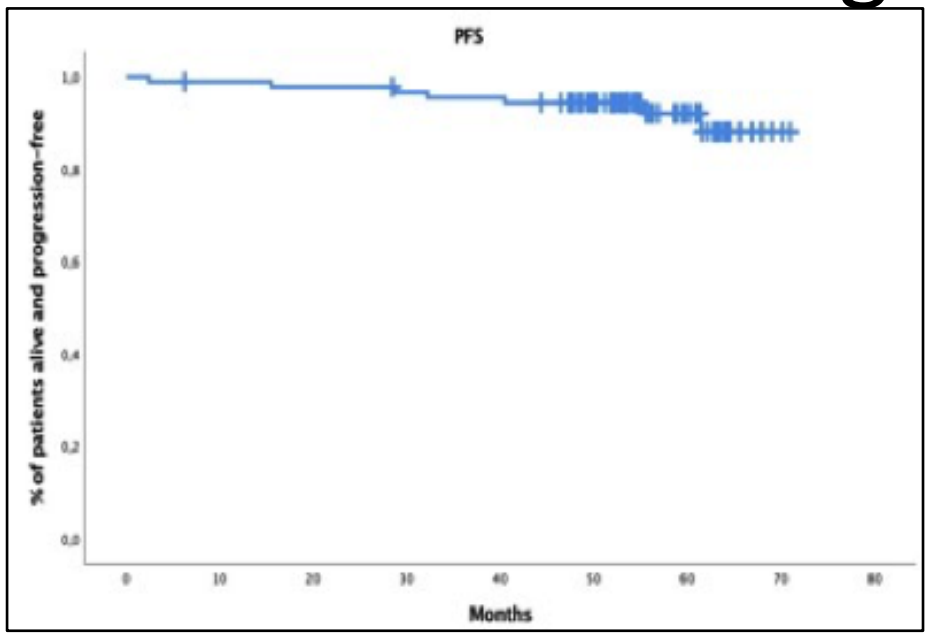
JJ Garcés ASH 2021 Abstr 76: TTP, time-to-progression; sFLC, serum free-light chain ratio

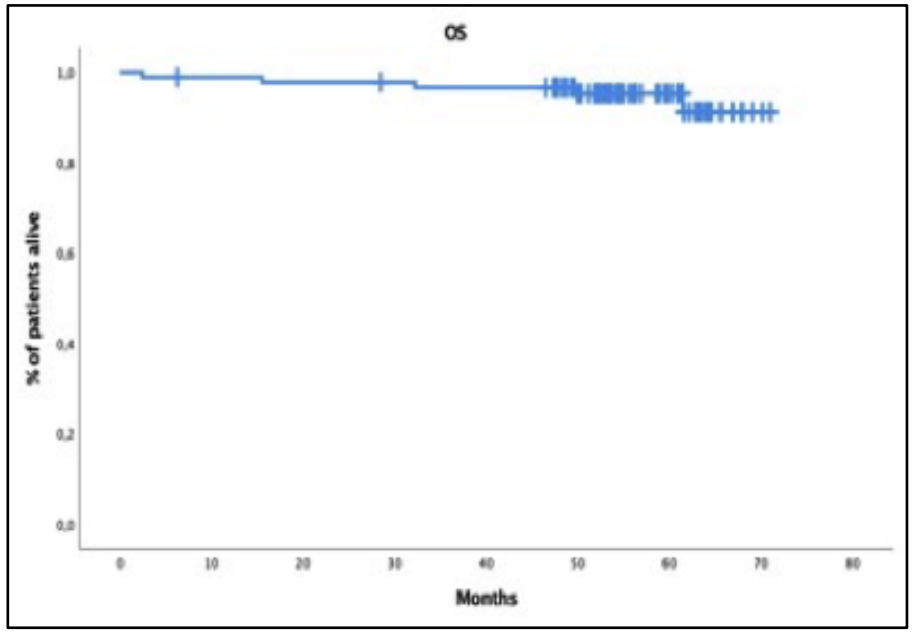
Abstract #76: Circulating Tumor Cells (CTCs) in Smoldering and Active Multiple Myeloma (MM): Mechanism of Egression, Clinical Significance and Therapeutic EndpointsClinically Relevant Abstract

CESAR Trial Update: Abstract #1829

Maria-Victoria Mateos, MD, PHD

- PFS = 94% @ 55 months and OS = 95%
- Sustained MRD negative 67% @ 12 months

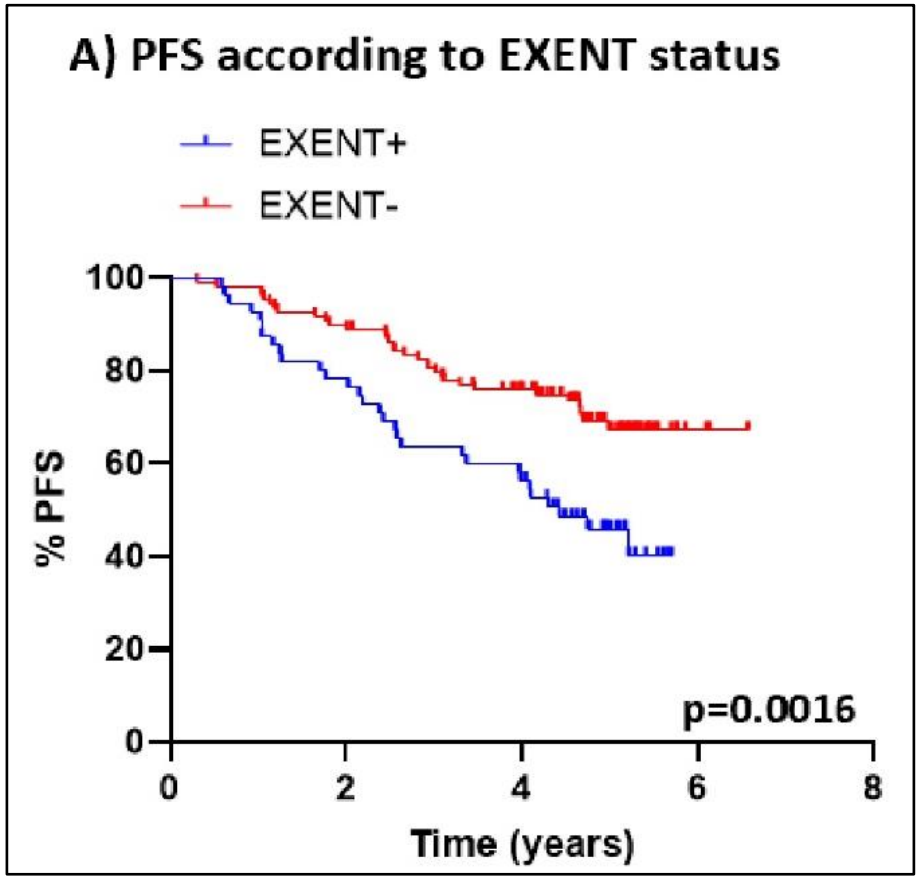


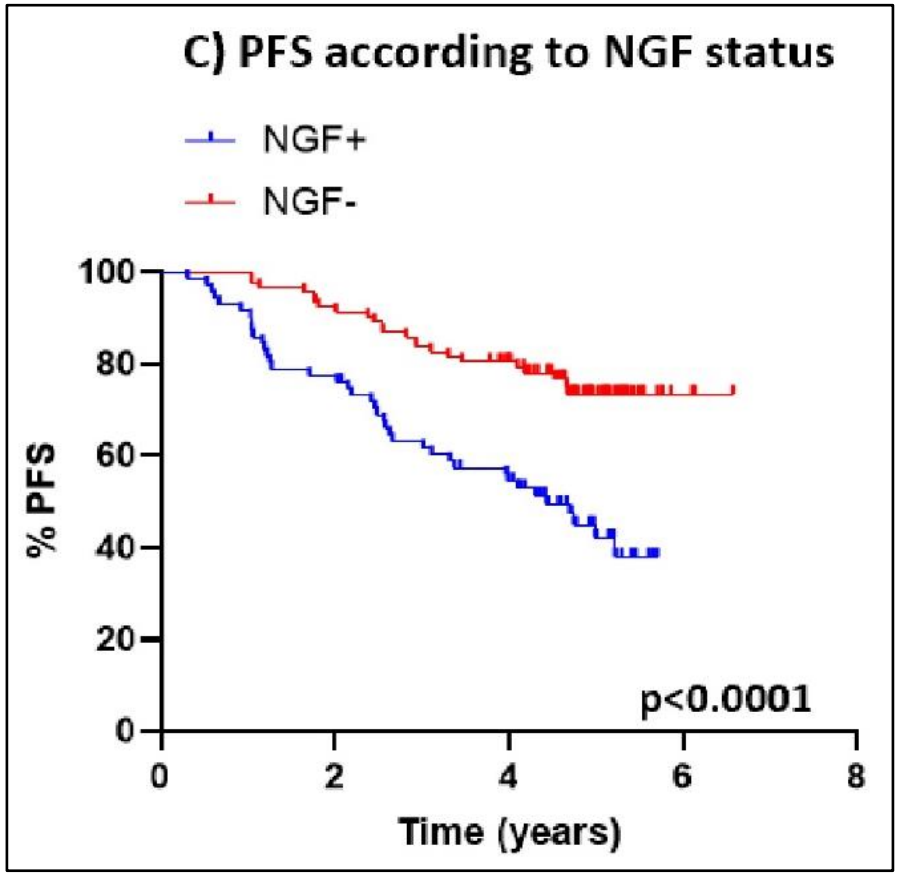


Abstract #1829: Curative Strategy (GEM-CESAR) for High-Risk Smoldering Myeloma (SMM): Carfilzomib, Lenalidomide and Dexamethasone (KRd) As Induction Followed By HDT-ASCT, Consolidation with Krd and Maintenance with Rd

NOTE: **Abstract # 2749:** IRd in HR SMM -- CR = 21.8%
A Phase II Trial of the Combination of Ixazomib, Lenalidomide, and Dexamethasone in High-Risk Smoldering Multiple Myeloma

Response assessed by IFE, NGF and Mass Spec (EXENT) - Abstract #544





Abstract #544: Assessment of Treatment Response By IFE, Next Generation Flow Cytometry and Mass Spectrometry Coupled with Liquid Chromatography in the GEM2012MENOS65 Clinical Trial

Daratumumab (DARA) Plus Lenalidomide, Bortezomib, and Dexamethasone (RVd) in Patients (Pts) With Transplant-eligible Newly Diagnosed Multiple Myeloma (NDMM): Updated Analysis of GRIFFIN After 24 Months of Maintenance

Jacob Laubach,[1,*] Jonathan L. Kaufman,[2] Douglas W. Sborov,[3] Brandi Reeves,[4] Cesar Rodriguez,[5] Ajai Chari,[6] Rebecca Silbermann,[7] Luciano J. Costa,[8] Larry D. Anderson Jr,[9] Nitya Nathwani,[10] Nina Shah,[11] Naresh Bumma,[12] Yvonne A. Efebera,[13] Sarah A. Holstein,[14] Caitlin Costello,[15] Andrzej Jakubowiak,[16] Tanya M. Wildes,[17] Robert Z. Orlowski,[18] Kenneth H. Shain,[19] Andrew J. Cowan,[20] Huiling Pei,[21] Annelore Cortoos,[22] Sharmila Patel,[22] J. Blake Bartlett,[23] Jessica Vermeulen,[24] Thomas S. Lin,[22] Paul G. Richardson,[1] Peter M. Voorhees[25]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Winship Cancer Institute, Emory University, Atlanta, GA, USA; [3]Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT, USA; [4]University of North Carolina – Chapel Hill, Chapel Hill, NC, USA; [5]Wake Forest University School of Medicine, Winston-Salem, NC, USA; [6]Tisch Cancer Institute, Mount Sinai School of Medicine, New York, NY, USA; [7]Knight Cancer Institute, Oregon Health & Science University, Portland, OR, USA; [8]University of Alabama at Birmingham, Birmingham, AL, USA; [9]Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX, USA; [10]Judy and Bernard Briskin Center for Multiple Myeloma Research, City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [11]Department of Medicine, University of California San Francisco, San Francisco, CA, USA; [12]Division of Hematology, The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [13]OhioHealth, Columbus, OH, USA; [14]Division of Oncology & Hematology, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, Nebraska, USA; [15]Moores Cancer Center, University of California San Diego, La Jolla, CA, USA; [16]University of Chicago Medical Center, Chicago, IL, USA; [17]Cancer & Aging Research Group, St. Louis, MO, USA; [18]Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [19]Department of Malignant Hematology, H. Lee Moffitt Cancer Center, Tampa, FL, USA; [20]Division of Medical Oncology, University of Washington, Seattle, WA, USA; [21]Janssen Research & Development, LLC, Titusville, NJ, USA; [22]Janssen Scientific Affairs, LLC, Horsham, PA, USA; [23]Janssen Research & Development, LLC, Raritan, NJ, USA; [24]Janssen Research & Development, LLC, Leiden, The Netherlands; [25]Levine Cancer Institute, Atrium Health, Charlotte, NC, USA.

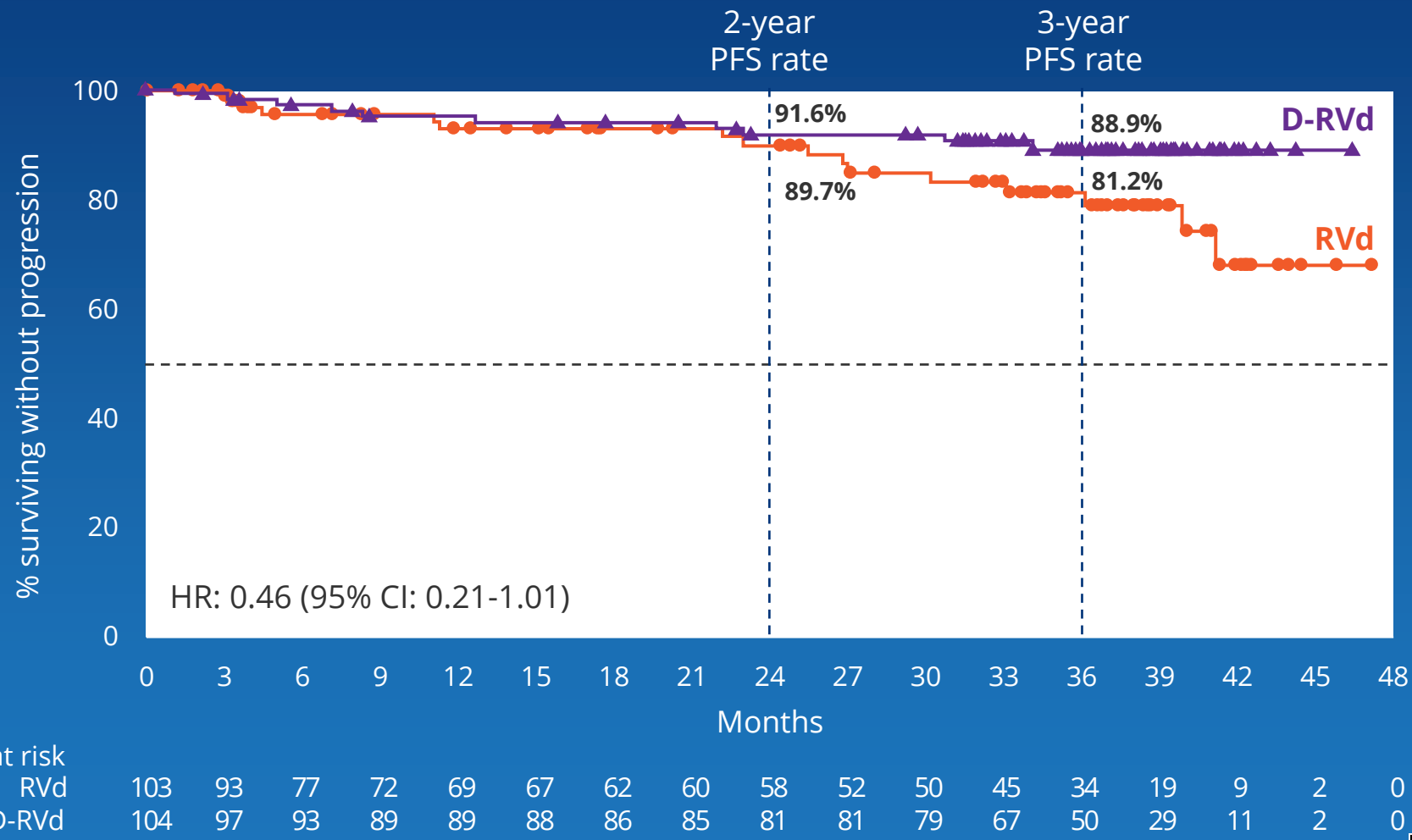
*Presenting author.

Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual

Additional information can be viewed by scanning the QR code or accessing this link: https://www.oncologysciencehub.com/ASH2021/Daratumumab/Laubach
The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.

GRIFFIN: PFS 88.9% vs 81.2%

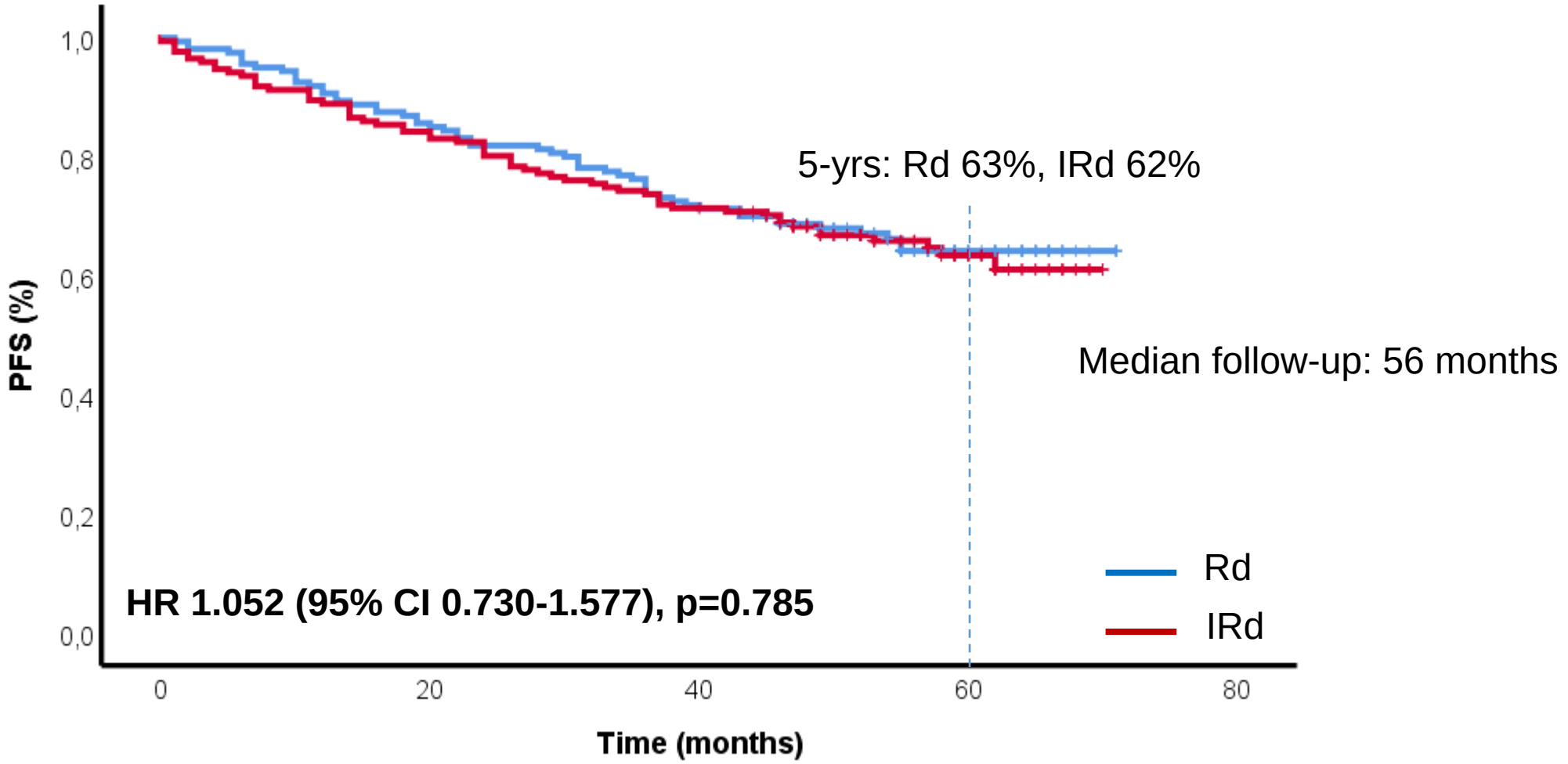
- Median follow-up: 38.6 months
- Median PFS was not reached in either group
- There is a positive trend toward improved PFS for D-RVd/DR versus RVd/R
- The separation of the PFS curves begins beyond 1 year of maintenance and suggests a benefit of prolonged DR therapy



HR, hazard ratio.

Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual

PFS from maintenance: Rd vs IRd

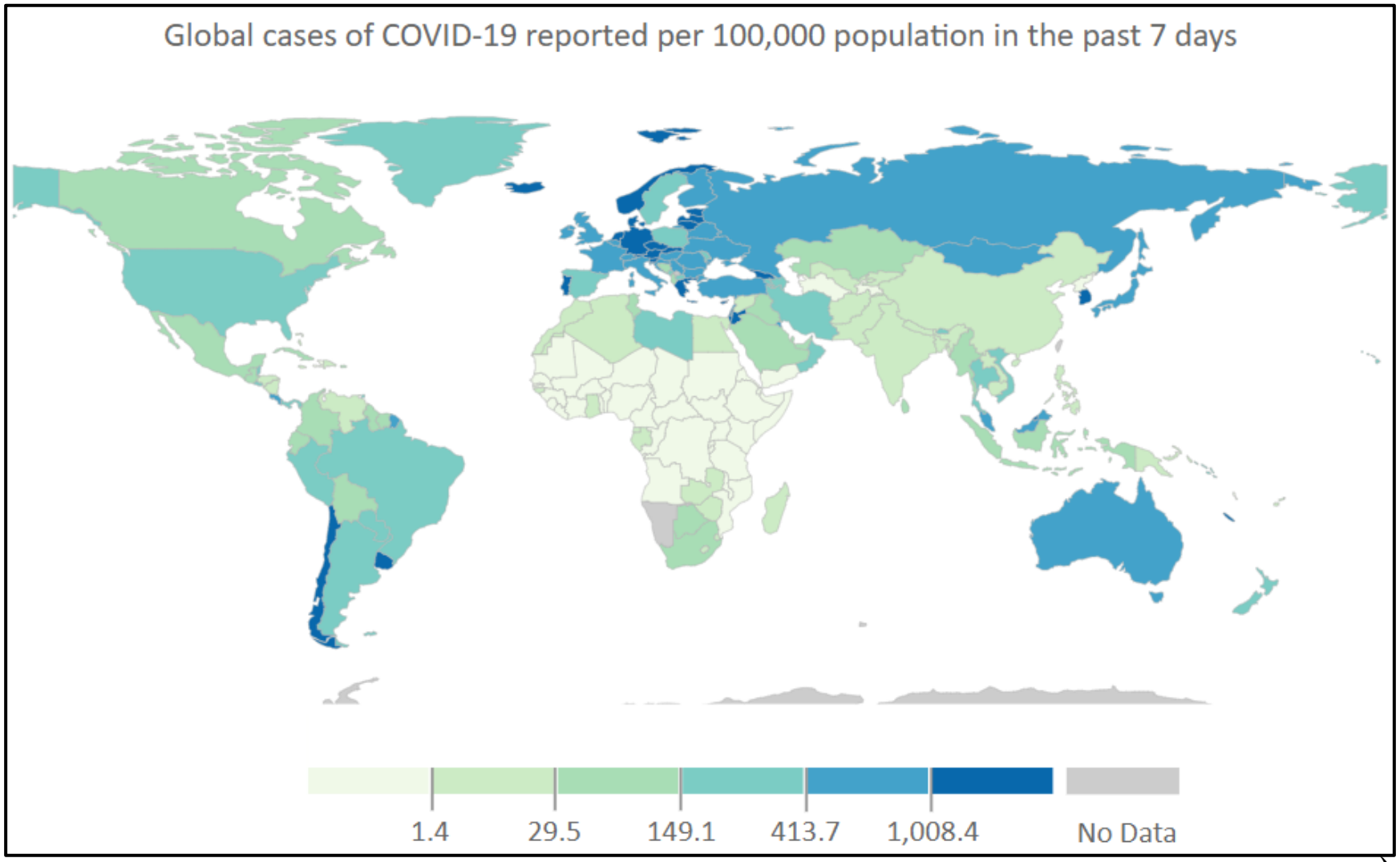


Triple Class Refractory: *When All Else Fails*

Chemotherapy	HDAC / *ADC* XPO inhibitors	**Approved BCMA**	**BCMA Abs** **TCEs/ADCs**	**BCMA CARs**
Doxorubicin, Liposomal doxorubicin	**Selinexor +** **Dexamethasone**	**Belantamab*** **Mafodotin**	**Teclistamab*** **Pavurutamab*** **TNB-383B***	**Cilta-cel (JNJ-4528)*** LCAR-B38M
Cyclophosphamide Bendamustine, Melphalan	**Venetoclax**	**Ide-cel*** **(bb2121)**	**REGN5458*** **Elranatamab*** **CC-93269**	**bb21217**
PACE, HyperCAD	Panobinostat/ Vorinostat		Non-BCMA [Talquetamab]* [Cevostamab]*	**Zevo-cel (CT053)** **ALLO-715** ALLO-605 (TurboCAR)

Blue = approved Orange = BCMA approved Green = ongoing clinical trials

Global cases of COVID-19 reported



Data from the CDC and WHO. The data includes cases as of February 20, 2022.

https://covid.cdc.gov/covid-data-tracker/#global-counts-rates and https://covid19.who.int/

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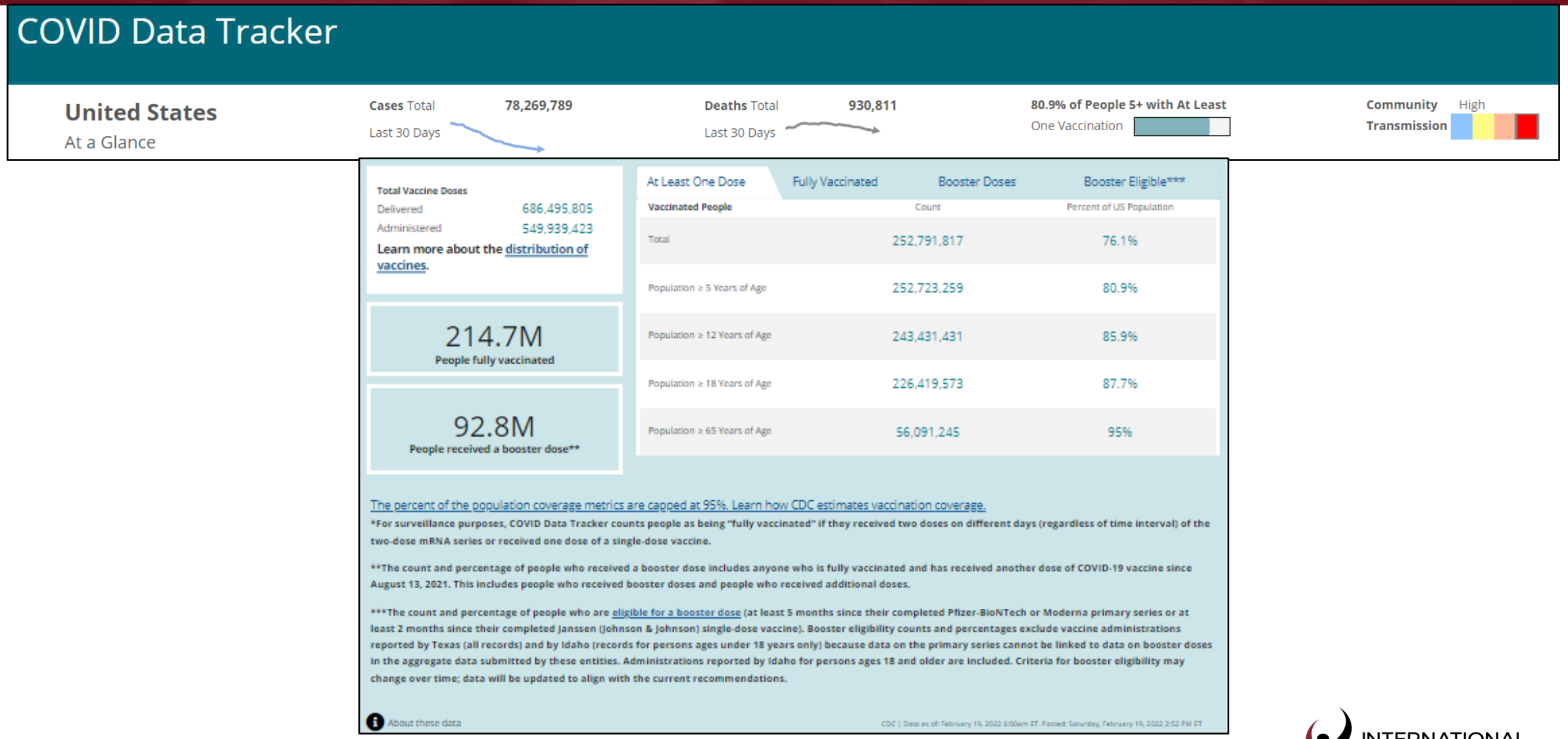
Overall U.S. COVID-19 Data Tracker



Overall US COVID-19 Vaccine | Deliveries and Administration – Data as of February 19, 2022

https://covid.cdc.gov/covid-data-tracker/#vaccinations and https://covid.cdc.gov/covid-data-tracker/#datatracker-home

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Updates on CDC COVID-19 Internal Guidelines

Summary of recent changes (last updated February 11, 2022):

- Updated guidance for moderately or severely immunocompromised people
  - Clarification of existing recommendation to receive a 3-dose mRNA vaccine primary series followed by a booster dose for a total of 4 doses
  - New guidance to shorten the interval between completion of the mRNA vaccine primary series and the booster dose to at least 3 months (instead of 5 months)
  - New guidance for those who received the Janssen COVID-19 Vaccine primary series to receive an additional dose and a booster dose, for a total of 3 doses to be up to date
- Updated guidance that it is no longer necessary to delay COVID-19 vaccination following receipt of monoclonal antibodies or convalescent plasma
- Updated guidance on receiving a booster dose if vaccinated outside the United States
- Updated contraindication and precaution section to include history of myocarditis or pericarditis after an mRNA COVID-19 vaccine as a precaution
- Reorganized and condensed multiple sections

Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the U.S.
(last updated Feb 11, 2022) https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

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Implications for New Variants for Myeloma Patients

- 3rd dose of vaccine (booster) recommended
- Continued use of masks essential
- Avoid **in-person** meetings for 2021
- Avoid crowds and indoor social/work gatherings
- Proactive COVID-19 therapy if positive test

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Current Vaccine Status

- 3rd dose (booster) approved for immunocompromised (myeloma patients)
- Pfizer has **full FDA approval**
- Follow-up for other vaccines pending

FDA U.S. FOOD & DRUG ADMINISTRATION

INTERNATIONAL MYELOMA FOUNDATION

Variants Summary – 22 February 2022

Variants of concern (VOC)

Working definition:

A SARS-CoV-2 variant that meets the definition of a VOI (see below) and, through a comparative assessment, has been demonstrated to be associated with one or more of the following changes at a degree of global public health significance:

- Increase in transmissibility or detrimental change in COVID-19 epidemiology; OR
- Increase in virulence or change in clinical disease presentation; OR
- Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics.

Currently designated variants of concern (VOCs)[+]:

WHO label	Pango lineage•	GISAID clade	Nextstrain clade	Additional amino acid changes monitored°	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2	GK	21A, 21I, 21J	+S:417N +S:484K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron*	B.1.1.529	GRA	21K, 21L 21M	+S:R346K	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

World Health Organization – "Tracking SARS-CoV-2 variants"
https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/

INTERNATIONAL MYELOMA FOUNDATION

Variants Summary – 22 February 2022

Variants of interest (VOI)

Working definition

A SARS-CoV-2 variant :

- with genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape; AND
- Identified to cause significant community transmission or multiple COVID-19 clusters, in multiple countries with increasing relative prevalence alongside increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health.

Currently designated variants of interest (VOIs):

WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Lambda	C.37	GR/452Q.V1	21G	Peru, Dec-2020	14-Jun-2021
Mu	B.1.621	GH	21H	Colombia, Jan-2021	30-Aug-2021

*Includes all descendent lineages. See the cov-lineages.org and the Pango network websites for further details.

World Health Organization – "Tracking SARS-CoV-2 variants"
https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/

Common Issues

- Pandemic fatigue/ stress
- Not feeling resilient
- Healthcare team not coordinated
- Not prepared for Zoom or appointments
- Need electronic help!
- Contacts with unknown COVID-19 status

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What does the future hold?

- Vaccination essential.
- Masks required.
- Caution in indoor spaces.

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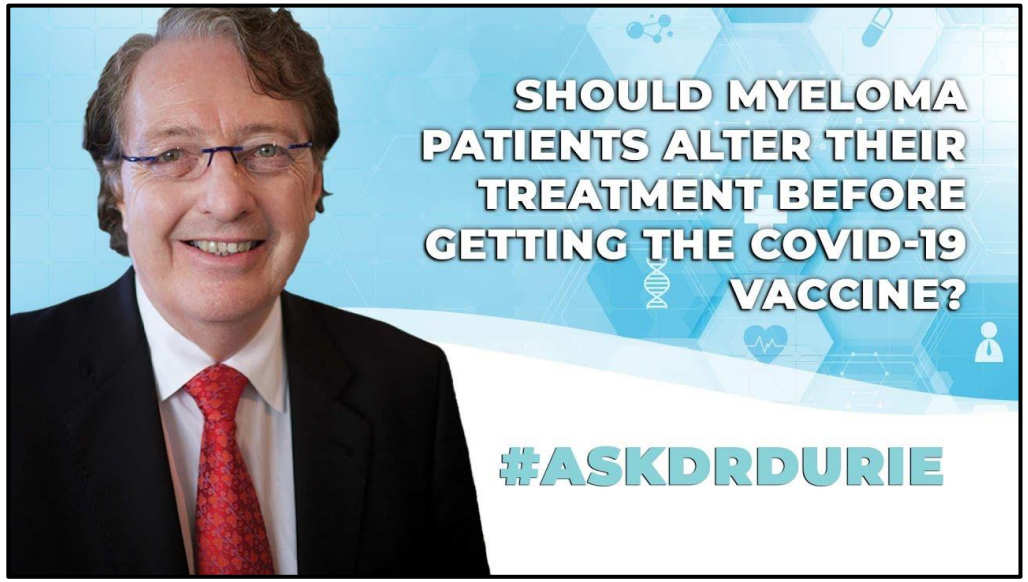
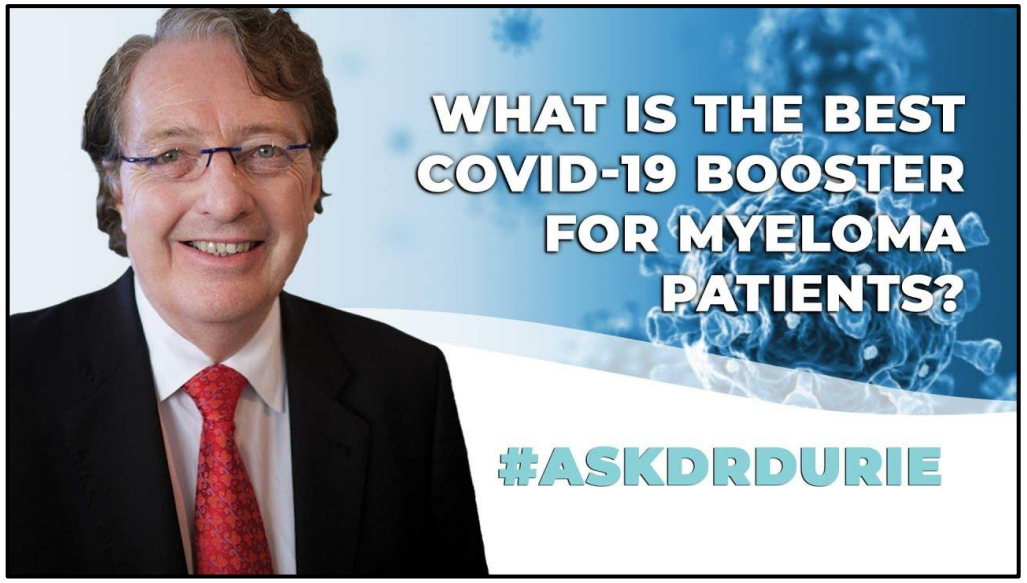
Other IMF Resources: Ask Dr. Durie Videos



Should myeloma patients alter their treatment before getting the COVID-19 vaccine?

https://www.myeloma.org/videos/should-myeloma-patients-change-their-treatment-try-improve-their-response-covid-19-vaccine



What is the best COVID-19 booster for myeloma patients?

https://www.myeloma.org/videos/which-covid-19-booster-best-myeloma-patients

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U.S. Support Group Virtual Meetings

Over 90 support groups are now holding monthly virtual GoToMeetings through the IMF

INTERNATIONAL MYELOMA FOUNDATION

U.S. Support Group Virtual Meetings

Over 90 support groups are now holding monthly virtual GoToMeetings through the IMF

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We will get through this together!

Myeloma has no borders

An apricot tree grows in Turkey

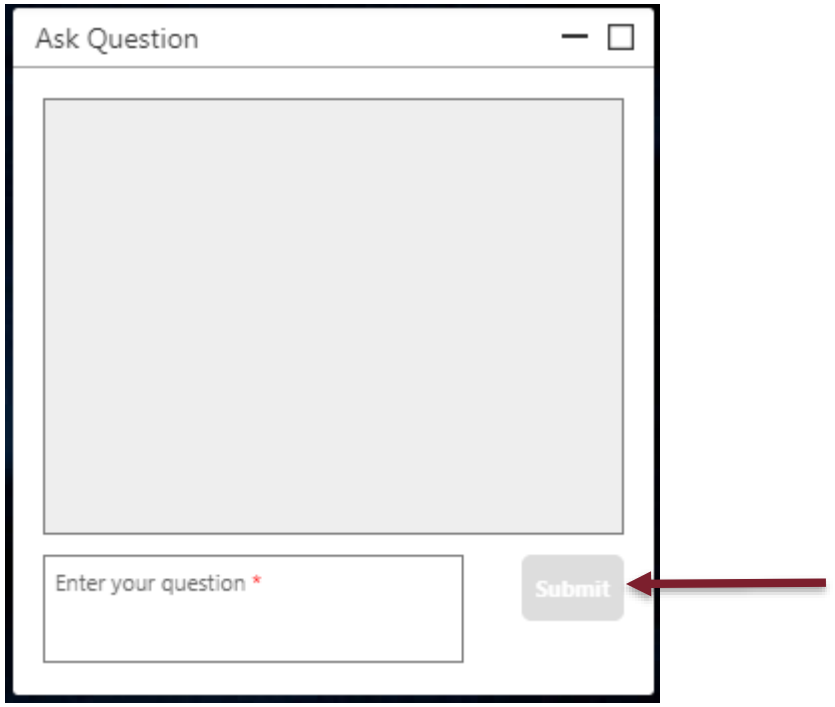
"Do Remember They Can't Cancel the Spring" – David Hockney

Support messages in the sky above Los Angeles

INTERNATIONAL MYELOMA FOUNDATION

IMF Patient and Family Webinar

Type your questions to the panel and press **Submit.**



INTERNATIONAL MYELOMA FOUNDATION

IMF Patient and Family Webinar

Dr. Tom Martin
Helen Diller Family
Comprehensive Cancer Center,
UCSF, San Francisco, CA

Evolving Role of Immune Therapies:

A Focus on CAR T-cell Therapies

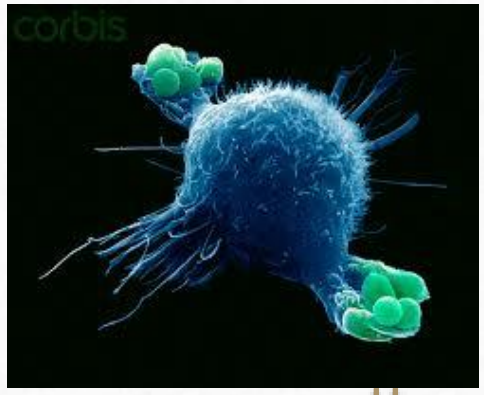
INTERNATIONAL MYELOMA FOUNDATION

Chimeric Antigen Receptor (CAR) T-Cell Therapy in Multiple Myeloma

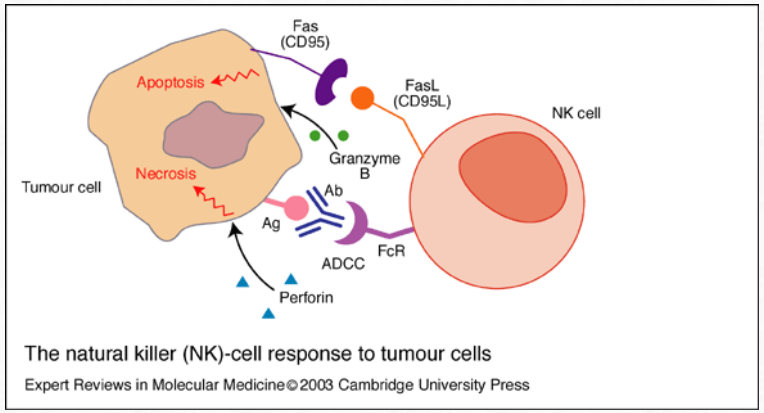
The next frontier

How will we cure multiple myeloma ?

Army (monocytes)



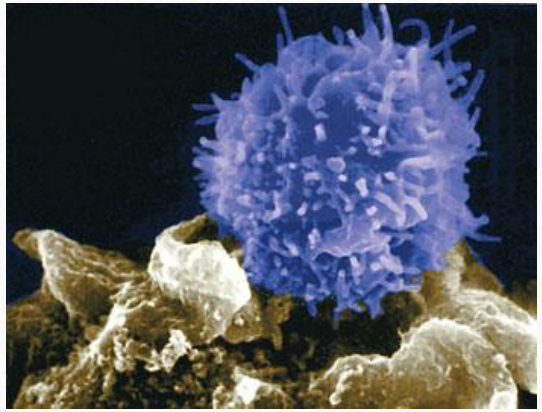
Navy (NK cells)



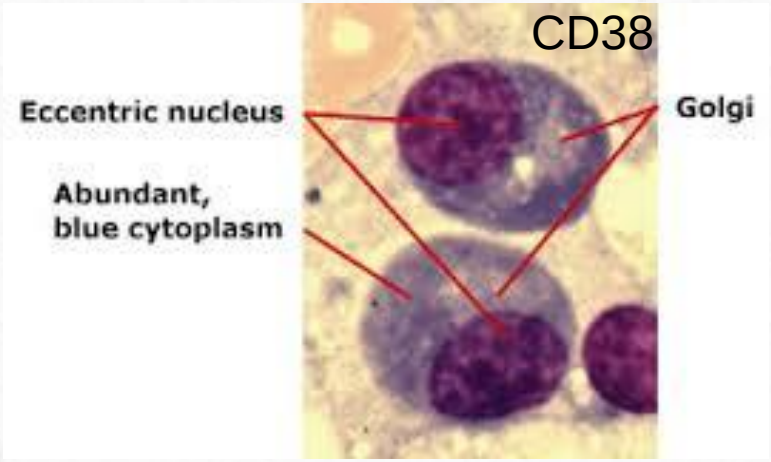
The natural killer (NK)-cell response to tumour cells

Expert Reviews in Molecular Medicine©2003 Cambridge University Press

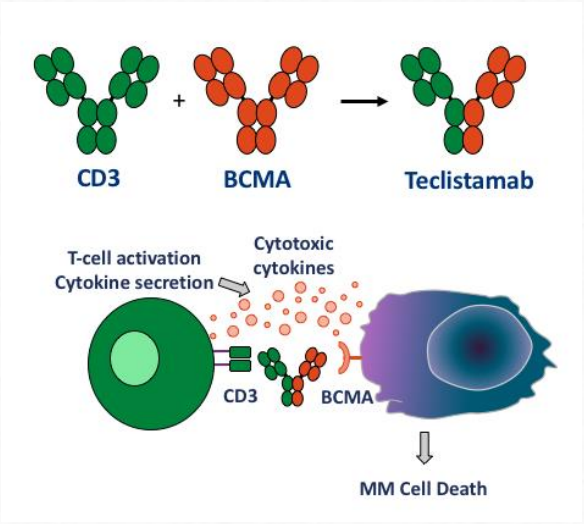
Marines (T cells)



Naked Abs

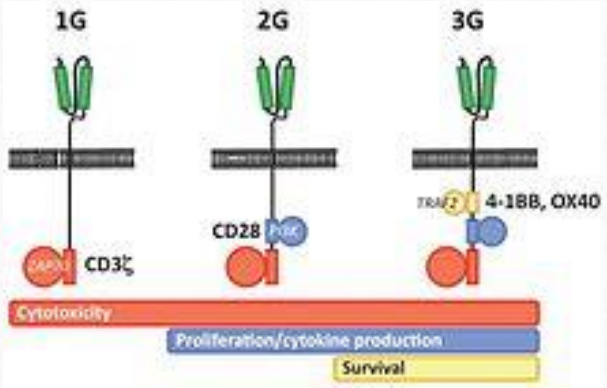


Bispecific/Trispecific Abs

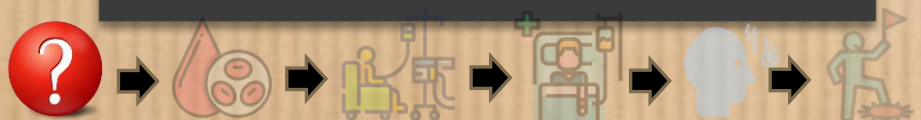


Cellular Therapies

CART



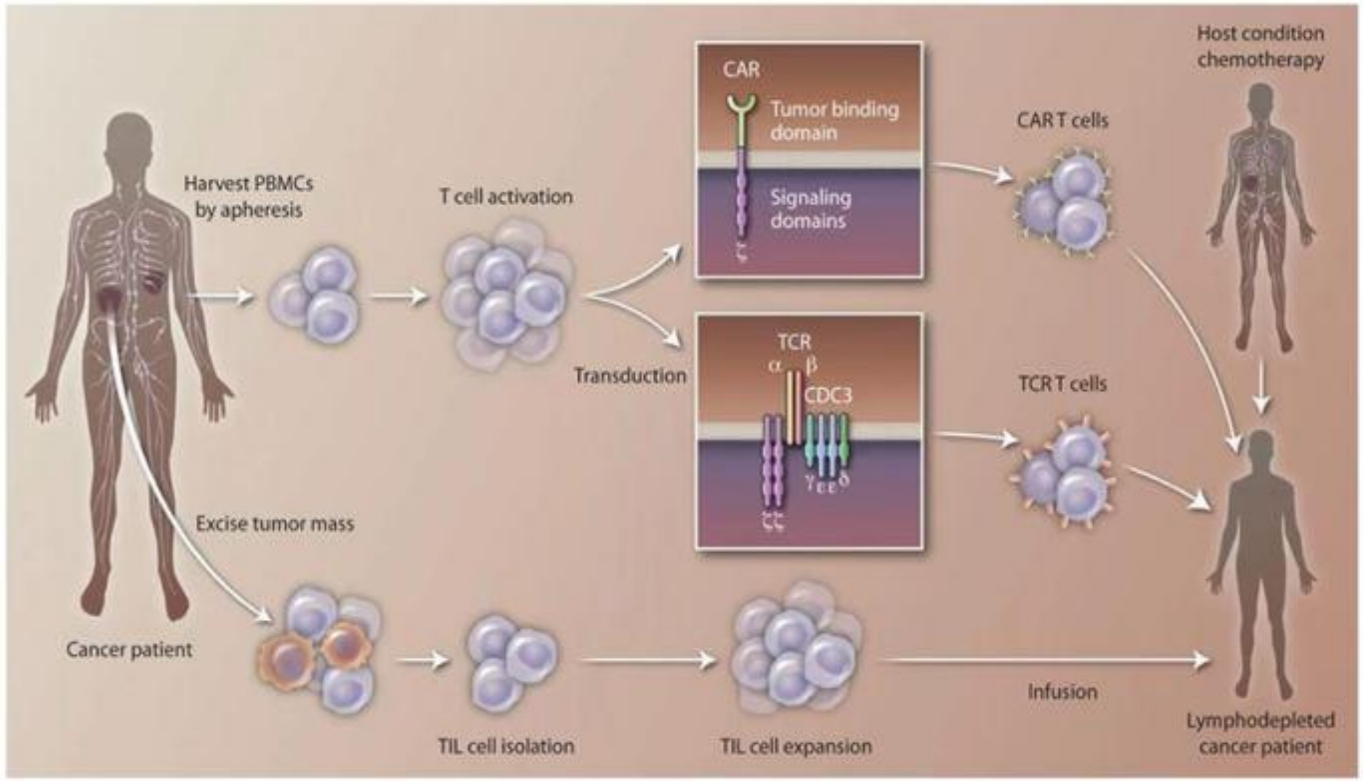
Understanding CAR-T Cell Therapy



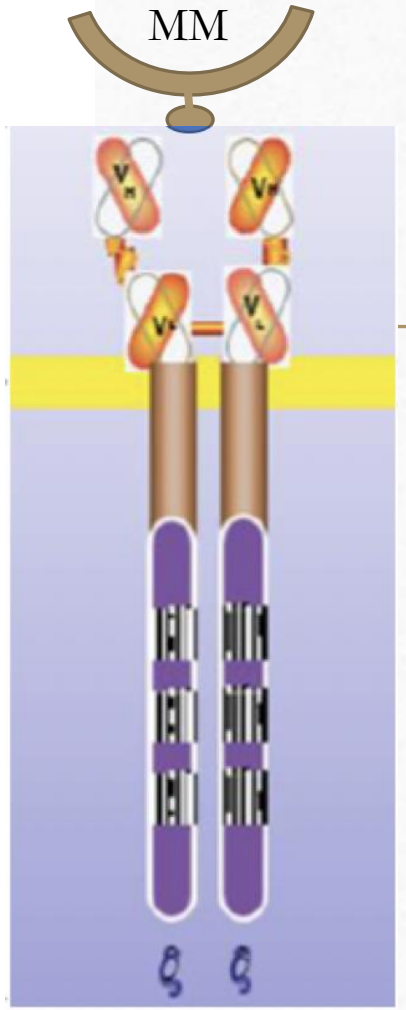
- Chimeric antigen receptor (CAR) T cell therapy, is an immune treatment that uses the body's own immunity to destroy cancer cells
- CAR-T cells are made from one's own T-cells that have been re-programmed to find and destroy cancer cells (MM)!

T-Cell Therapy for Cancer

Adoptive T cell therapy (three major approaches)



June et al *Sci Trans Med 2015*



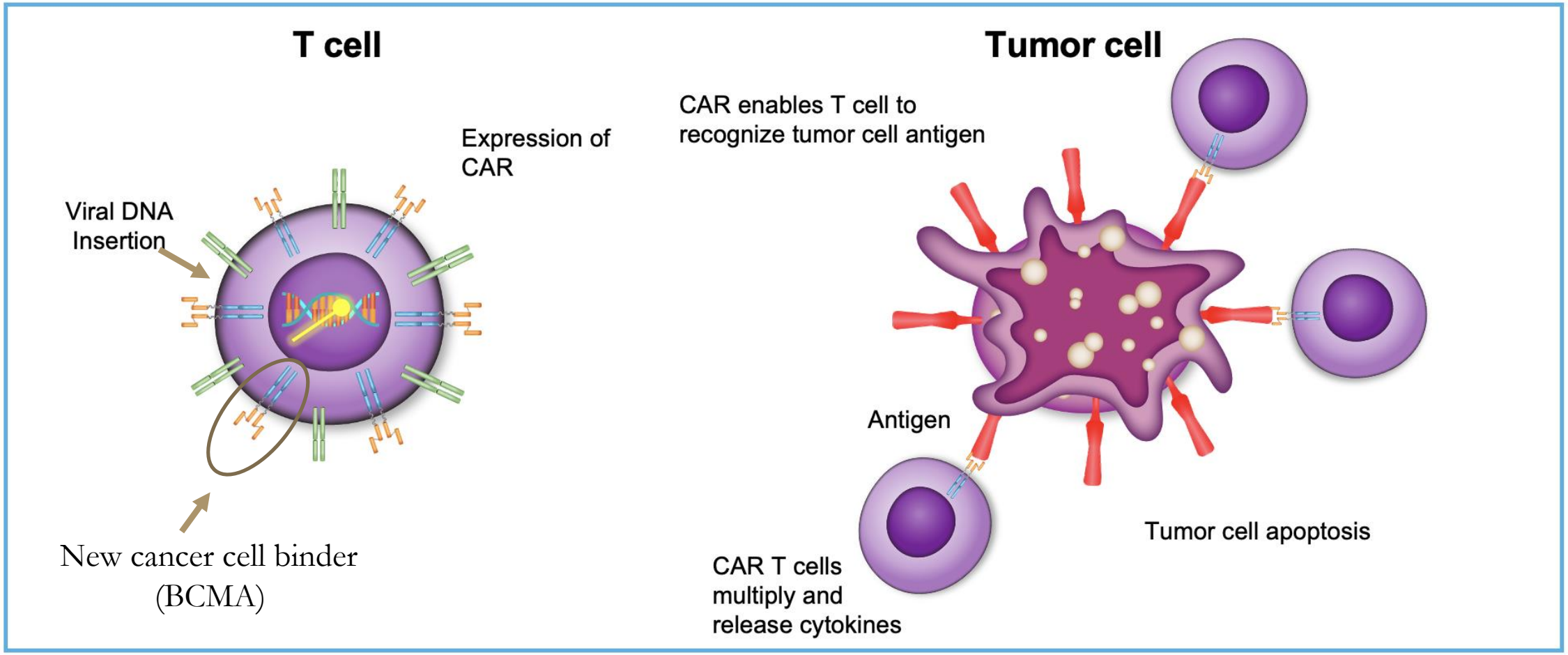
CAR Features

Cell targets

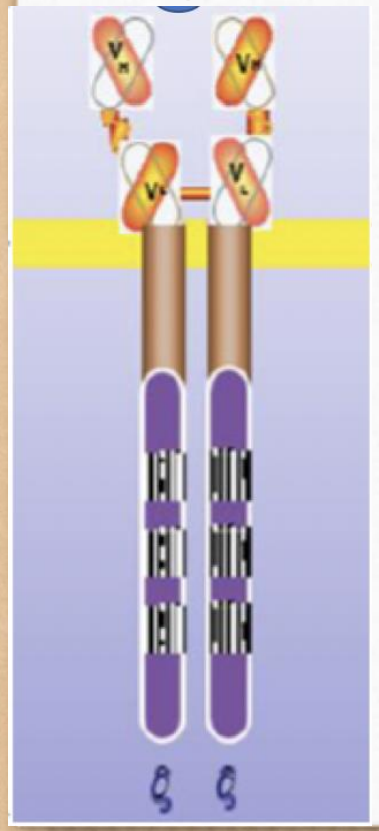
Binding domain

Transmembrane domain

Signaling Domain
-4-1BB, CD28
-CD3z


T cell
Expression of CAR
Viral DNA Insertion
New cancer cell binder (BCMA)
Tumor cell
CAR enables T cell to recognize tumor cell antigen
Antigen
Tumor cell apoptosis
CAR T cells multiply and release cytokines

Components of CAR T-Cell Therapy



CAR Features

Cell targets

Binding domain(s)

Transmembrane domain

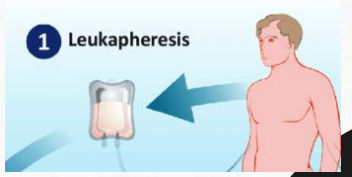
Signaling Domain
-4-1BB, CD28
-CD3z

Patient selection:

Are you eligible?

- RRMM ≥3 prior lines of therapy
- ECOG performance status 0/1
- Adequate cardiopulmonary and organ function

Patient



Test Tube

Apheresis ±cryopreservation

Gene transfer
T cell expansion

Manufacture CAR T-cells

Release testing

3-5 weeks

Bridging therapy

Lymphodepleting therapy

CAR T-cell infusion

Clinical management

CRS
Neurotox
Cytopenias

Roles of a caregiver

It's a 2+ person effort!!!

- **Medical support**
  - Medication management
  - Recognizing a change in condition and calling medical services
  - Checking and recording twice daily temperatures
- **Emotional support**
  - Checking in with your feelings
  - Listening to your needs
- **Practical support**
  - Driving and accompanying you to all appointments
  - Managing finances
  - Meal preparation
- Caregivers play an integral part in ensuring the success of the CAR-T

RECAP

Step 1
Pre-CART Evaluation
(2-3 weeks)

Step 2
T-Cell Collection
(1 day)

Step 3
CAR-T Cell Creation
(~4 weeks)

bridging therapy (per provider discretion)

Step 4
Lymphodepleting (LD) Chemotherapy
(~3 days)

Step 5
CAR-T Cell Infusion

Watch for side effects

Stay local for 30 days

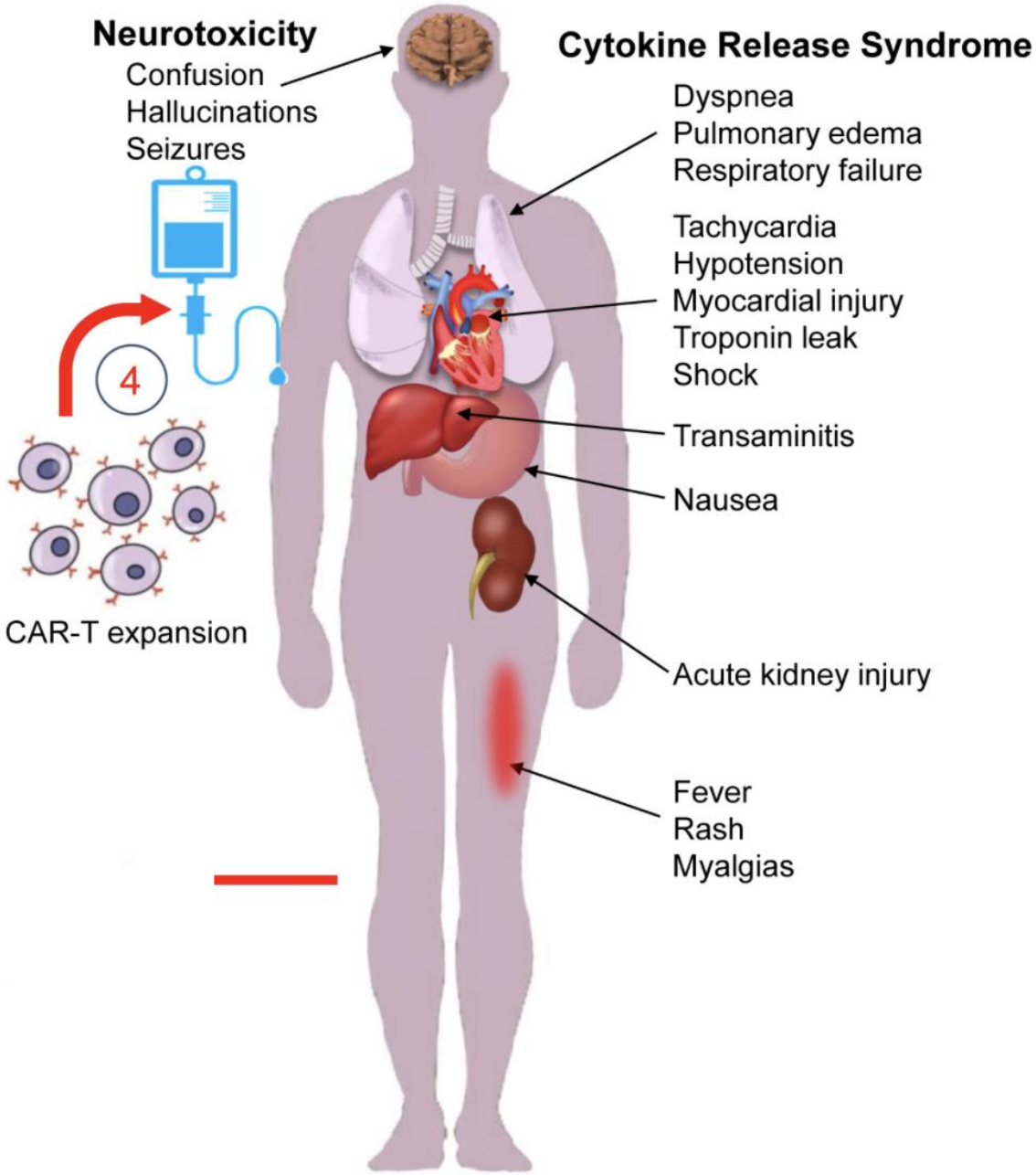
CAR T cell Toxicity

1. CRS – cytokine release syndrome (>80% of patients)
    1. Occurs between 1 hour and 10 days after infusion
    2. Lasts between 3-5 days (it is reversible/treatable)
    3. Symptoms:
        1. Fever, chills, HA, fatigue and malaise [flu-like symptoms]
        2. Low blood pressure, fast heart rate
        3. Shortness of breath, occasional need for oxygen,
    4. Treatment: tocilizumab +/- dexamethasone

2. Neurotoxicity (<30%; <10% G3-4)
    1. Occurs between 2 days to ~30 days, some later
    2. Lasts between 3-14 days, few have longer symptoms
    3. Symptoms
        1. Confusion, delirium, aphasia
        2. Tremor, Parkinson-like symptoms, nerve palsies
        3. Brain swelling is rare

3. Cytopenias (>90%)
    1. Low WBC
    2. Low platelets
    3. Anemia

4. Infections (~40-50%)
    1. Viral, Bacterial, fungal and unusual infections

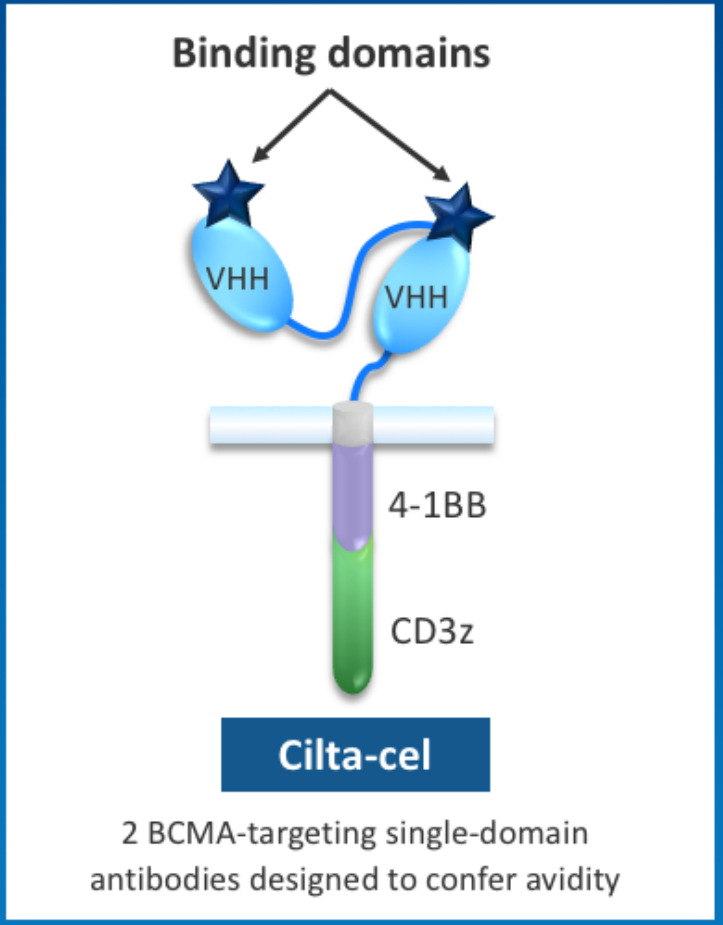


CARTITUDE-1: Introduction

Cilta-Cel => APPROVED??????

Ciltacabtagene autoleucel (cilta-cel; JNJ-68284528) is a chimeric antigen receptor T-cell therapy for the treatment of patients with RRMM[1]

- In the phase 1b/2 CARTITUDE-1 study, early, deep, and durable responses were observed with a single cilta-cel infusion in heavily pretreated patients with RRMM[1]
  - At a median follow-up of 12.4 months
    - Cilta-cel had a manageable safety profile
    - ORR and sCR were 97% and 67%, respectively
    - Overall 12-month PFS and OS rates were 77% and 89%, respectively
    - Median PFS and duration of response were not reached (95% CI, 16.8–not estimable and 15.9–not estimable, respectively)
- **Here, we report updated results from the CARTITUDE-1 study with a longer duration of follow-up (median ~2 years)[a]**



[a]Median 21.7 months, data cut-off July 22,2021

BCMA, B-cell maturation antigen; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; sCR, stringent complete response; VHH, single variable domain on a heavy chain

1. Berdeja JG, et al. *Lancet* 2021; 398:314-24.

Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual.

CARTITUDE-1: Demographics and Baseline Characteristics

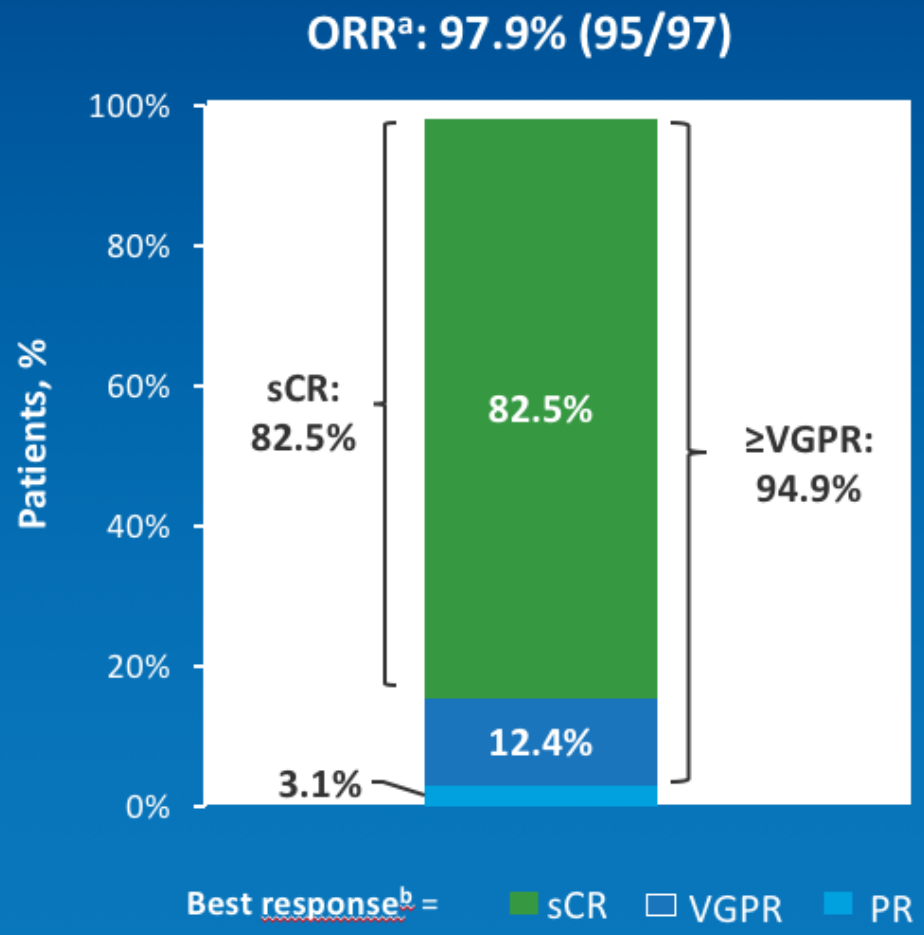
Characteristics	N=97
Age, median (range) years	61.0 (43–78)
Male, n (%)	57 (58.8)
Black/African American, n (%)	17 (17.5)
All plasmacytomas,[a] n (%)	19 (19.6)
Extramedullary plasmacytomas, n (%)	13 (13.4)
Bone-based plasmacytomas, n (%)	6 (6.2)
Bone marrow plasma cells ≥60%, n (%)	21 (21.9)
High-risk cytogenetic profile, n (%)	23 (23.7)
del17p	19 (19.6)
t(14;16)	2 (2.1)
t(4;14)	3 (3.1)
Tumor BCMA expression ≥50%, n (%)	57 (91.9)[a]

Characteristics	N=97
Prior lines of therapy, median (range)	6.0 (3–18)
Prior lines of therapy, n (%)	
3	17 (17.5)
4	16 (16.5)
≥5	64 (66.0)
Previous stem cell transplantation, n (%)	
Autologous	87 (89.7)
Allogeneic	8 (8.2)
Triple-class exposed,[b] n (%)	97 (100)
Penta-drug exposed,[c] n (%)	81 (83.5)
Triple-class refractory[b]	85 (87.6)
Penta-drug refractory[c]	41 (42.3)
Refractory status, n (%)	
Carfilzomib	63 (64.9)
Pomalidomide	81 (83.5)
Anti-CD38 antibody	96 (99.0)
Refractory to last line of therapy, n (%)	96 (99.0)
Years since diagnosis, median (range)	5.9 (1.6–18.2)

[a]The number of evaluable samples was 62; BCMA expression detected in all evaluable samples; [b]≥1 PI, ≥1 IMiD, and 1 anti-CD38 antibody; [c]≥2 PIs, ≥2 IMiDs, and 1 anti-CD38 antibody.
BCMA, B-cell maturation antigen; IMiD, immunomodulatory drug; PI, proteasome inhibitor

Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual.

ASH 2021 Updated Results:
CARTITUDE-1: Efficacy Response with Cilta-cel in RRMM



Responses deepened over time from the 1-year follow-up

Best response at any time	Median–1 year follow-up	Median–2 years follow-up
sCR, %	67	83

- Median time to first response was 1 month (range, 0.9–10.7)
- Median time to best response was 2.6 months (range, 0.9–17.8)
- Median time to CR or better was 2.9 months (range, 0.9–17.8)
- Median duration of response was not estimable (21.8 months–NE)
- 60.5% of patients are still progression-free at 2 years

[a]ORR assessed by independent review committee; [b]No patient had CR or stable disease as best response.

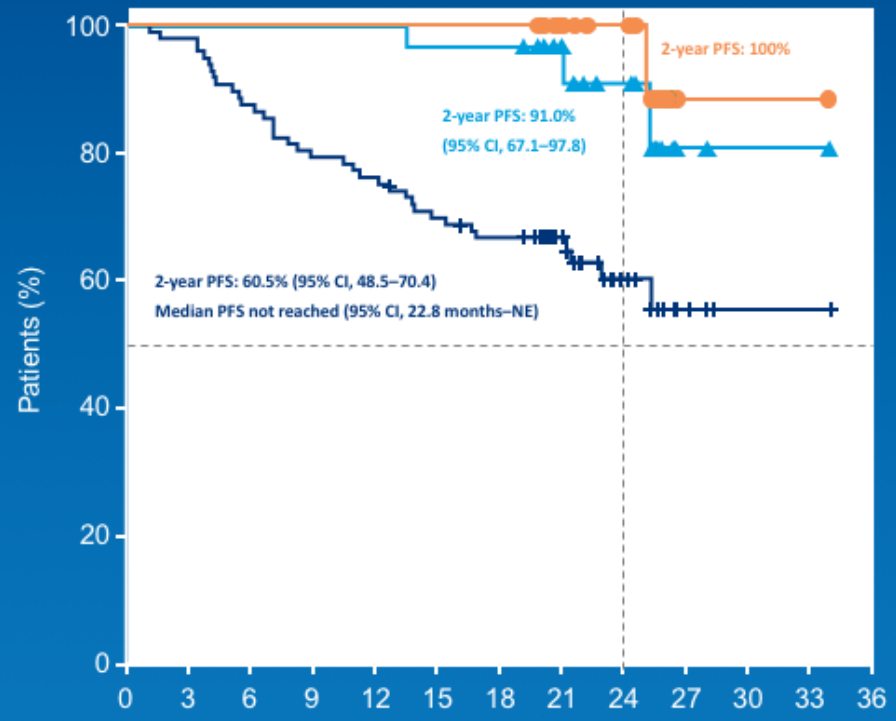
CR, complete response; NE, not estimable; ORR, overall response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual.

CARTITUDE-1: Progression-Free Survival and Overall Survival by MRD Negativity (10^{-5}) sustained for ≥ 6 and 12 months

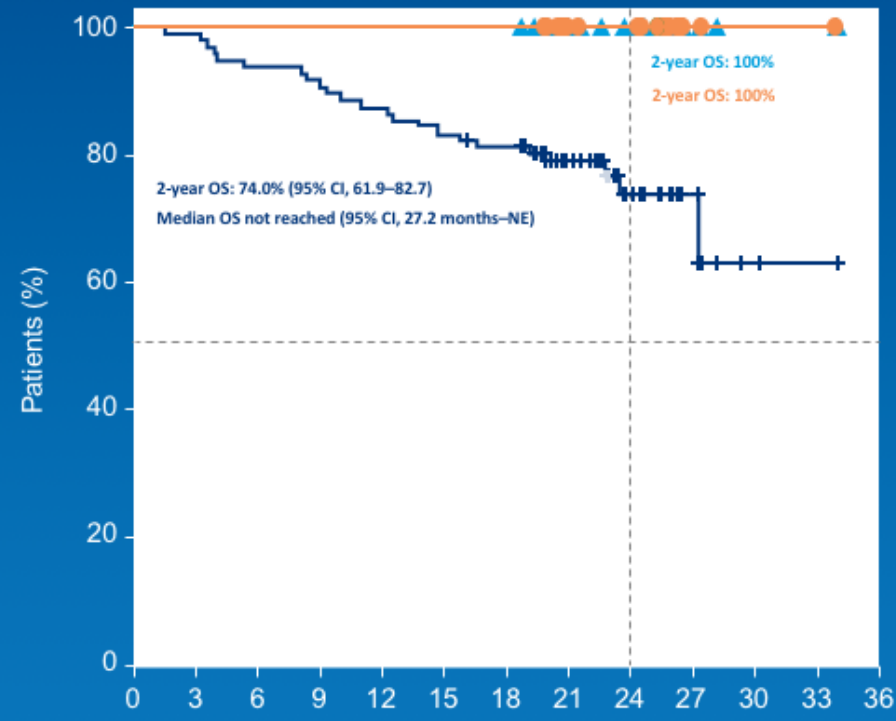
- Of the 61 patients evaluable for MRD, 92% were MRD-negative (at 10^{-5})

Progression-Free Survival



Patients at risk													
All patients	97	95	85	77	74	67	63	36	19	4	1	1	0
MRD negativity ≥6 months	30	30	30	30	30	29	29	17	12	2	1	1	0
MRD negativity ≥12 months	18	18	18	18	18	18	18	12	10	1	1	1	0

Overall Survival



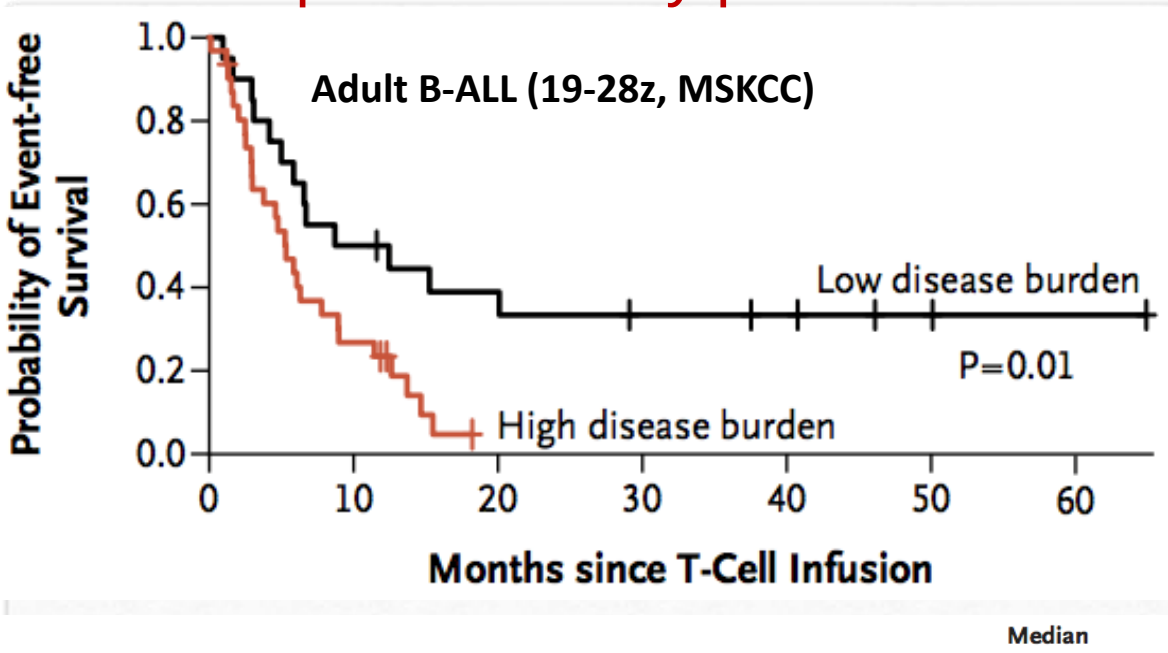
Patients at risk													
All patients	97	96	91	88	85	81	78	46	23	8	2	1	0
MRD negativity ≥6 months	30	30	30	30	30	30	30	17	13	3	1	1	0
MRD negativity ≥12 months	18	18	18	18	18	18	18	12	11	2	1	1	0

All patients | MRD negativity sustained ≥6 months | MRD negativity sustained ≥12 months

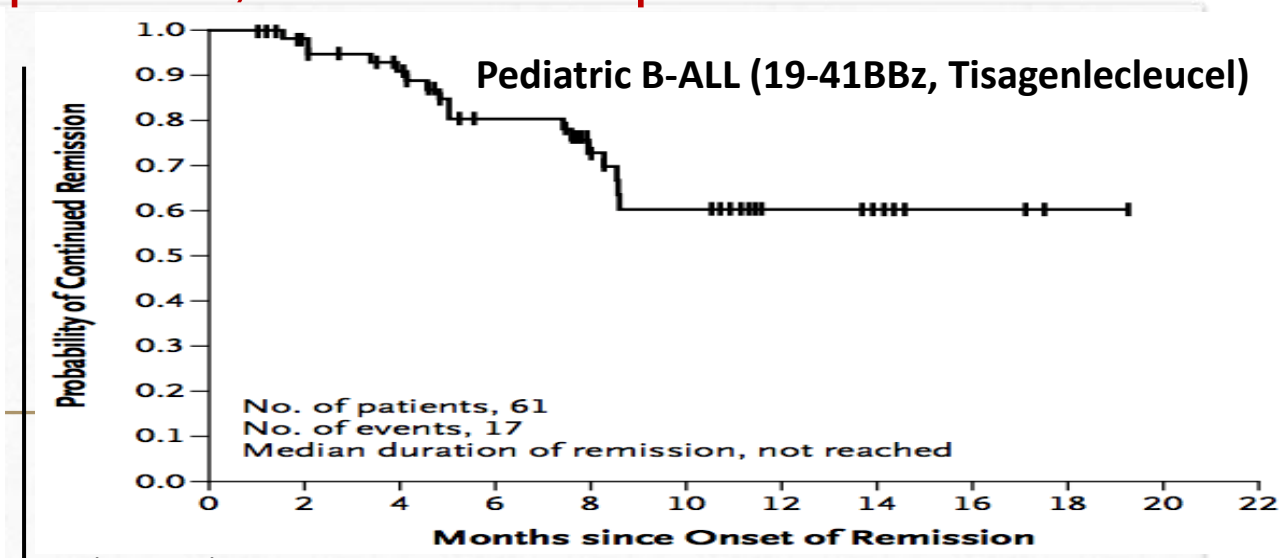
MRD, minimal residual disease; OS, overall survival; PFS, progression-free survival

Presented at the 63rd American Society of Hematology (ASH) Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual.

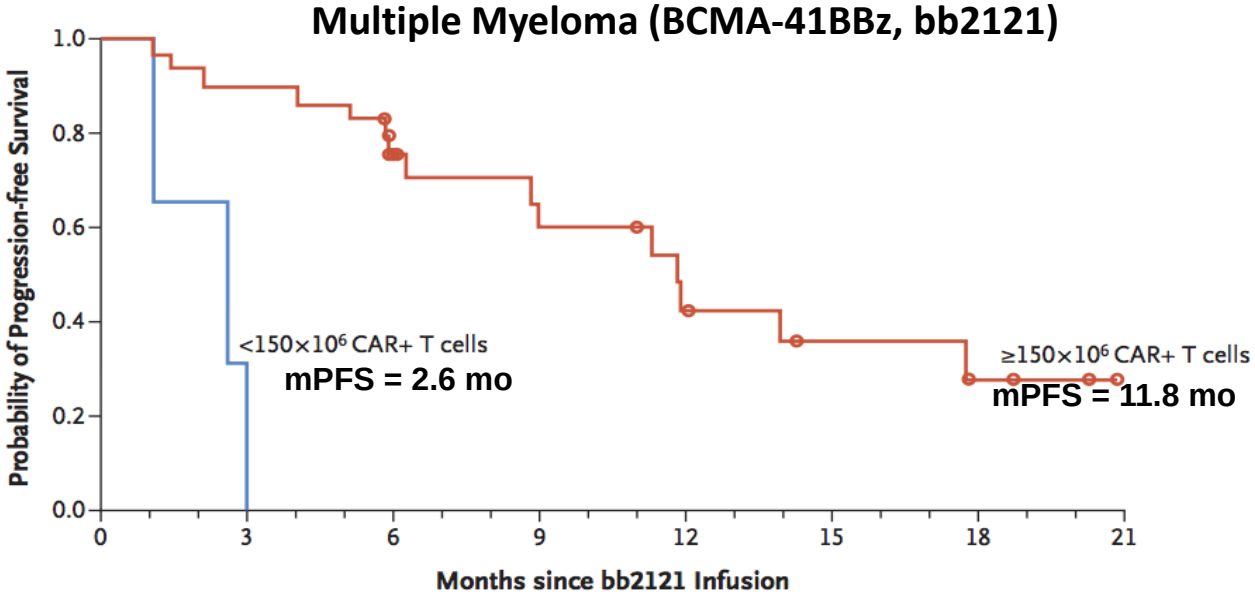
CAR T therapies in heavily pre-treated MM patients, however relapses still occur



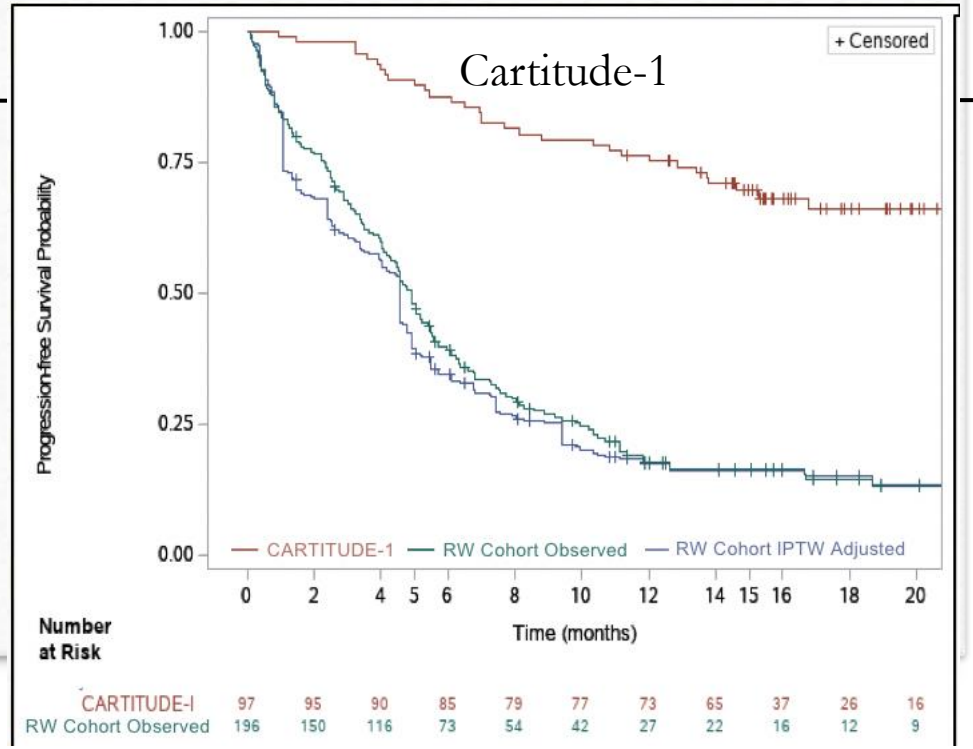
Park J et al. *NEJM* 2018



Maude SL et al. *NEJM* 2018



Raje N et al. *NEJM* 2019



Martin et al. ASCO2021

BCMA CAR T-Cell Therapies: Summary (ASH2020/ASCO2021)

	CARTITUDE-1[1] Cilta-cel Phase I	CRB-401[2] Ide-cel Phase I	CRB-402[3] bb21217 Phase I	LUMMICAR-2[4] CT053 Phase Ib	PRIME[5] BCMA-101 Phase I/II	GC012F[6] Dual CAR T-Cell BCMA + CD19
Patients	97	62	69	20	55	19
Median prior regimens, n	6	6	6	5	8	5
Triple refractory, %	87.6	69.4	64	85	60	NR
CAR T-cell therapy dose	0.75×10^6 ($0.5\text{-}1.0 \times 10^6$)	50, 150, 450, 800×10^6	150, 300, 450×10^6	$1.5\text{-}1.8/2.5\text{-}3.0 \times 10^8$	$0.75\text{-}15 \times 10^6$	$1.0\text{-}3.0 \times 10^5$
ORR, %	97.9	75.8	68/84*	94	67¶	94.7
CR/sCR, %	80.4	38.7	29/32*	25	NR	84.2
CRS (all grades), %	94.8	75.8	70	77/83§	17	95
CRS (grade ≥3), %	5.4	6.5	4‡	0/0§	0	11
Neurotoxicity (all grades), %	20.6	35.5	16	15/17§	3.8	0
Neurotoxicity (grade ≥3), %	10.3	1.6	4	8/0§	3.8	0

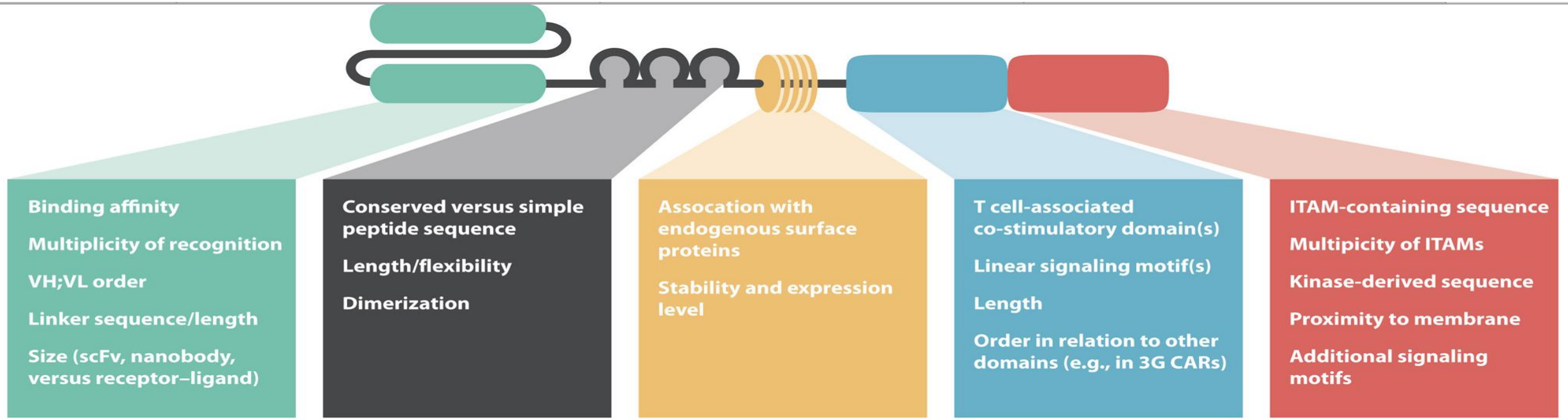
*After manufacturing change. ‡2 grade 5 events, 1 on Day 15 with grade 3 NT and 1 on Day 6 with afib and cardiac arrest. §Data for each dosing cohort. ¶ORR for patients receiving CAR T-cells manufactured using nanoplasmid technology (n = 6).

1. Usmani. ASCO 2021. Abstr 8005. 2. Lin. ASH 2020. Abstr 131. 3. Alsina. ASH 2020. Abstr 130.
4. Kumar. ASH 2020. Abstr 133. 5. Costello. ASH 2020. Abstr 134. 6. Jiang. ASCO 2021. Abstr 8014.

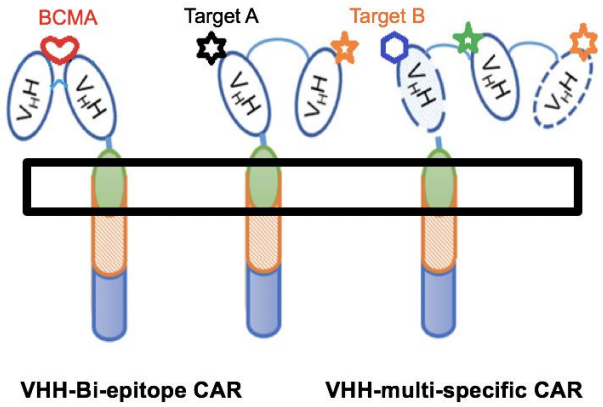
Long Term Side Effects

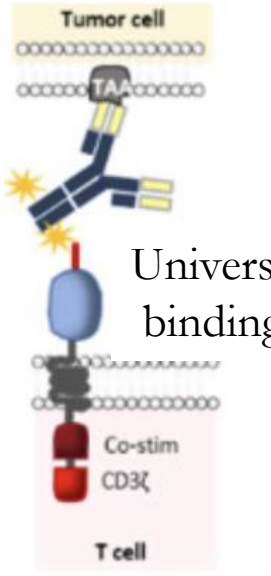
- Prolonged low blood counts
- Hypogammaglobulinemia - A condition in which the level of immunoglobulins (antibodies) in your blood is low and the risk of infection is increased
- Increased risk of infection
- Secondary Cancers

Next-Gen CARs



- Improving Binding
  - Synthetic receptors
  - Nanobodies
  - Universal CARs
    - BAT – CAR
  - GSIs/enrich target



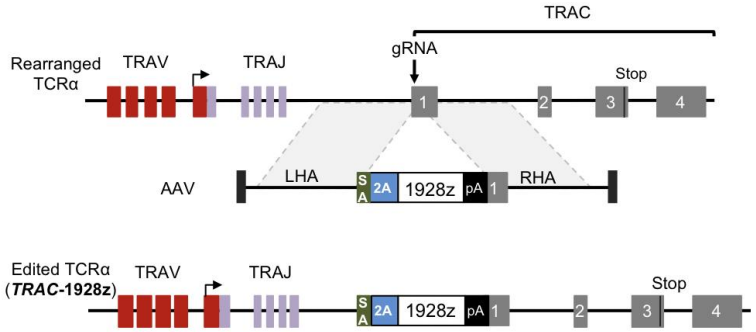


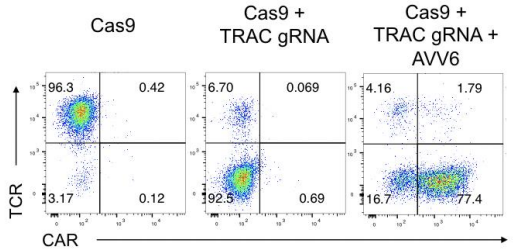
Universal binding

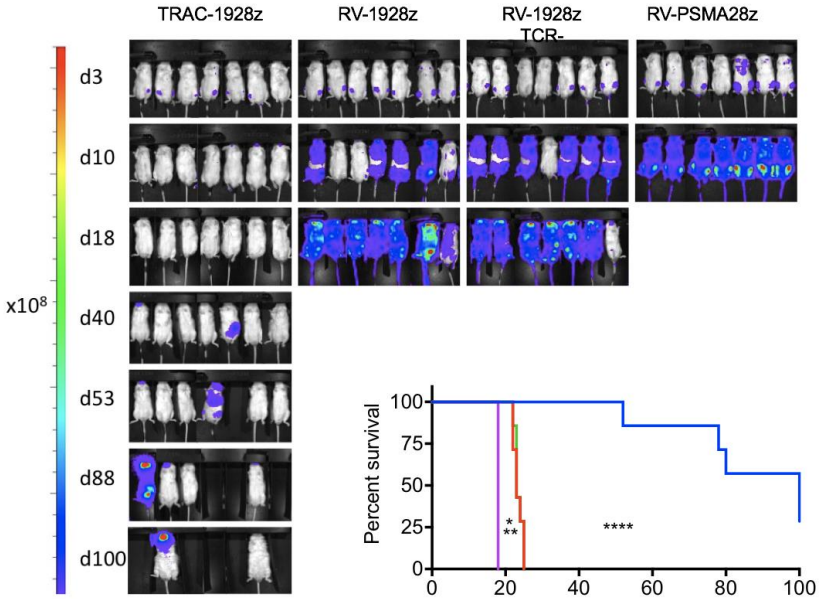
Hyrenius-Wittsten A, Roybal KT. Trends in Cancer 2019 Vol5:10; 583.

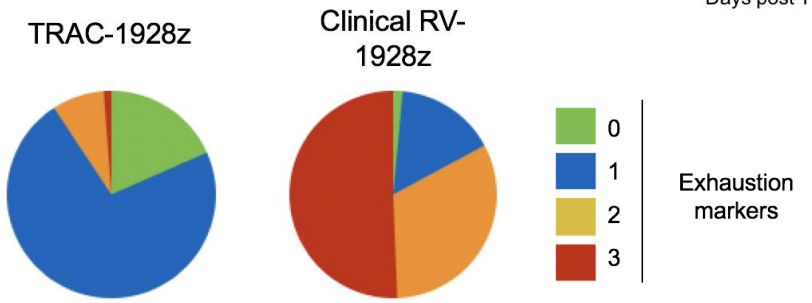
Improving CARs

- Improving integration
  - γ-retroviral vectors – <u>random</u>
    - Clonal expansion
    - Oncogenic transformation
    - Variable expression/silencing
  - Genome editing (CRISPR/Cas9)
    - <u>Site specific</u> targeting
    - T-cell receptor α constant (TRAC) locus
      - Uniform CAR expression
      - Enhanced CAR potency
      - Averts tonic signaling/exhaustion





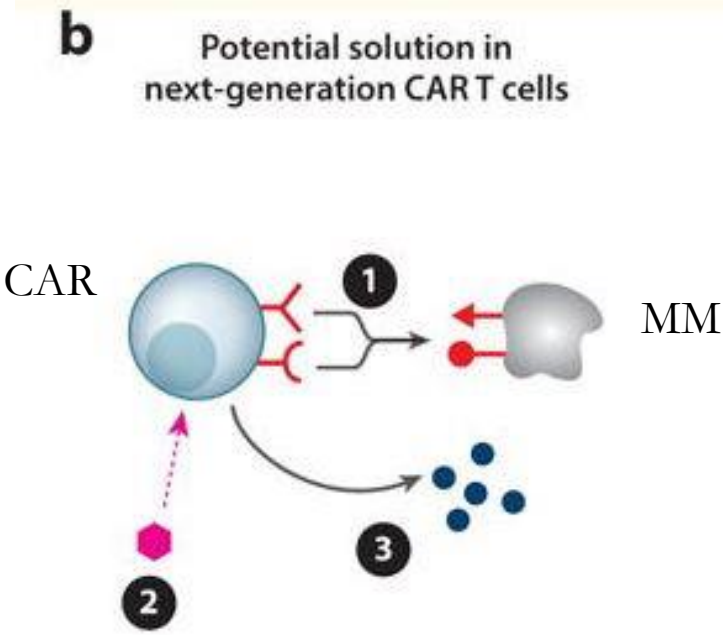




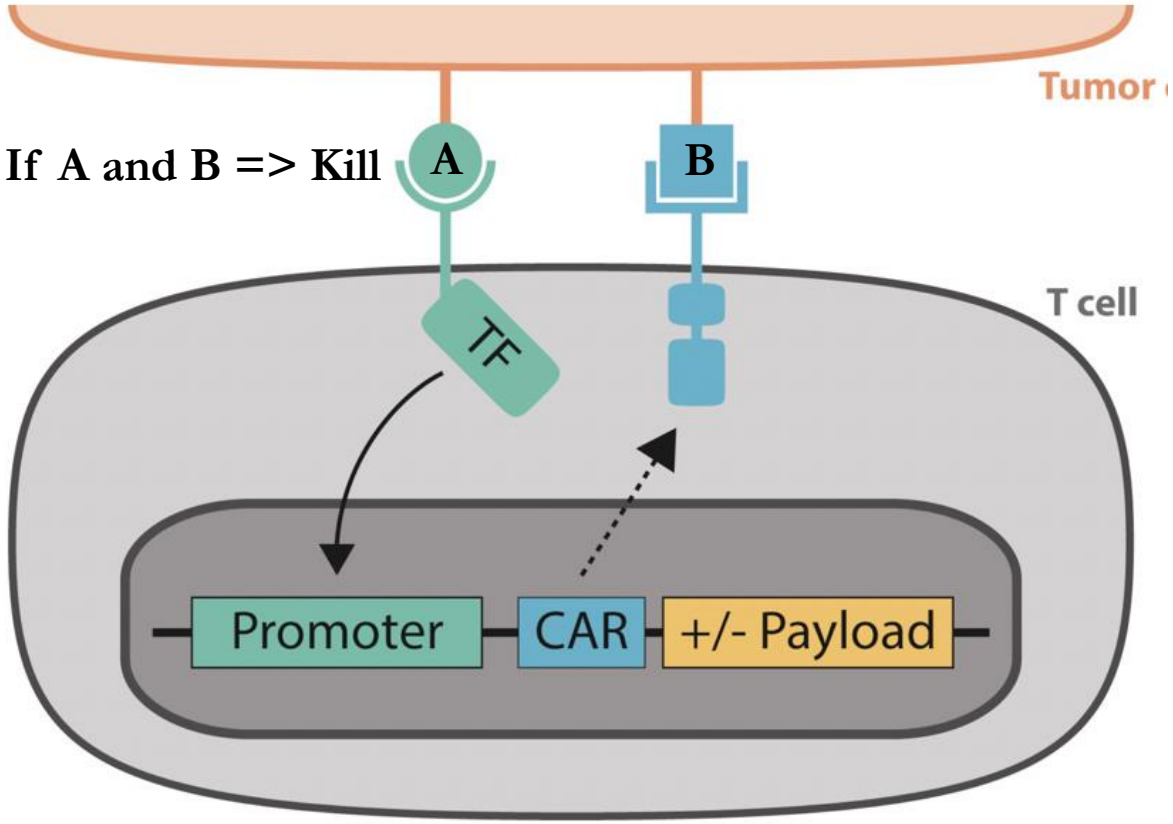
Eyquem et al., Nature 2017

Improving CARs

- Building Circuits (safety + efficacy)
  - Syn-Notch
  - Local Production
    - Therapeutic antibodies
    - Cytokines
  - Dummy receptors



Syn-Notch

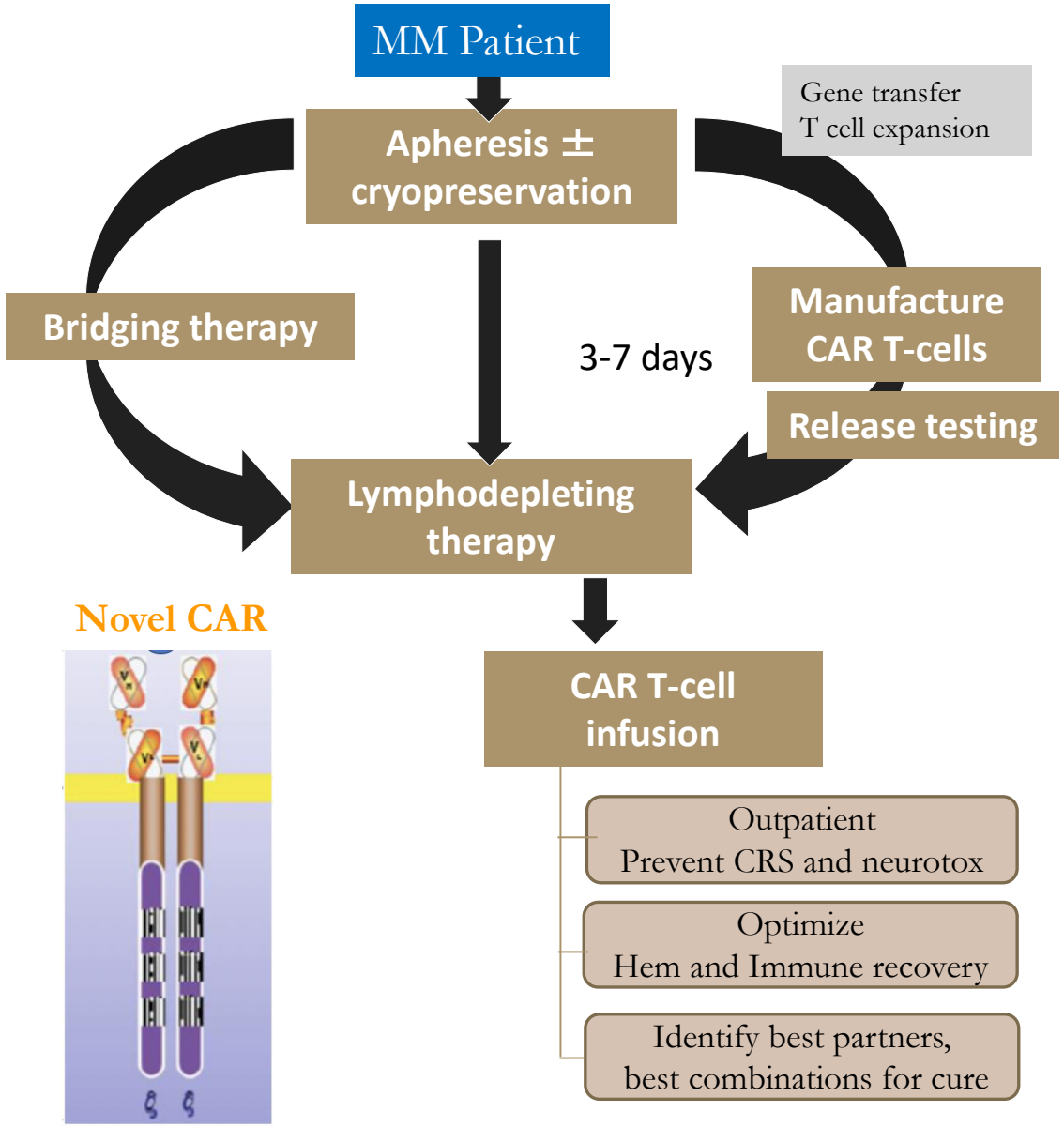


Roybal KT, Lim WA. Annu Rev Immunol. 2017 Apr 26;229-53

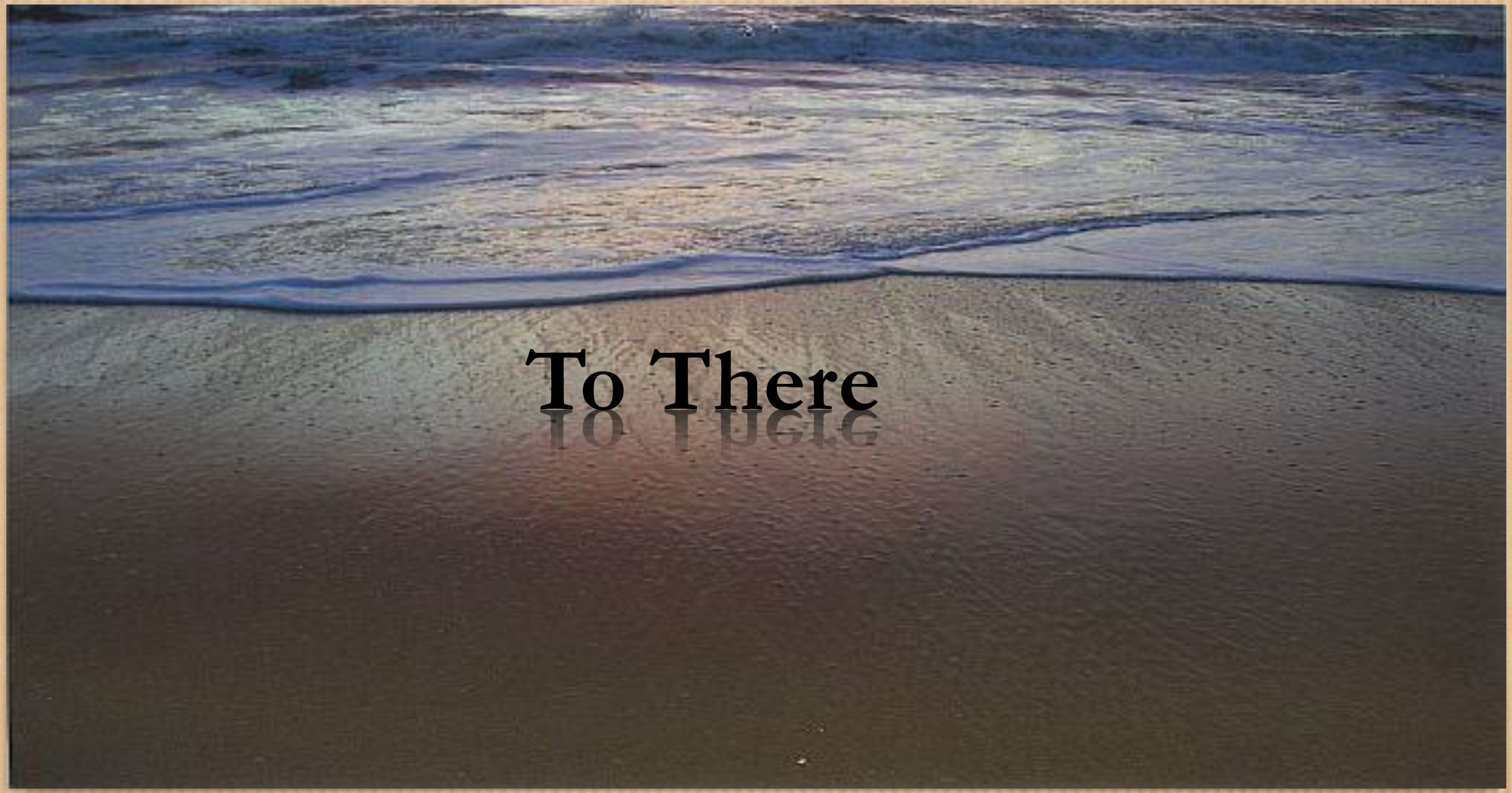
Hyrenius-Wittsten A, Roybal KT. Trends in Cancer 2019 Vol5:10; 583

Summary: Improving CAR T-Cell Therapy

- **Patient selection**
  - ND, <3 PLT
  - High Ag exp
  - Effective BT
- **Optimize manufacturing**
  - Faster (1-7d)
  - Better (Tscm)
  - *In vivo* expansion
- **CAR construct Optimization**
  - Gene Transfer
    - Transposon
    - Cispr/Integrate
  - Better Binders
    - Human/stealth
    - Dual targets
  - Novel Control
    - Switch tech
    - Optimize SD
- **Optimize T cell Fit/Fcn**
  - Freeze early
  - Use SC aliquots
  - Use Allo-T cells
- **Optimize LD therapy**
  - Chemo-Rad
  - Antibody-based
  - Allow serial Cars




From
HERE
Cancer

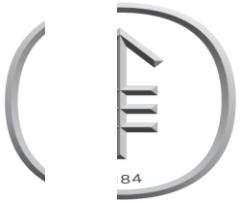

To There

Dr. Saad Usmani
Chief, Myeloma Service
Memorial Sloan Kettering
Cancer Center (MSKCC)
New York, NY

Approaches to Relapsed Myeloma:

What are the Current Bispecifics and Novel Agents?

INTERNATIONAL MYELOMA FOUNDATION



Memorial Sloan Kettering Cancer Center™

Bispecific Antibodies and Novel Agents in Multiple Myeloma

Saad Z. Usmani, MD MBA FACP

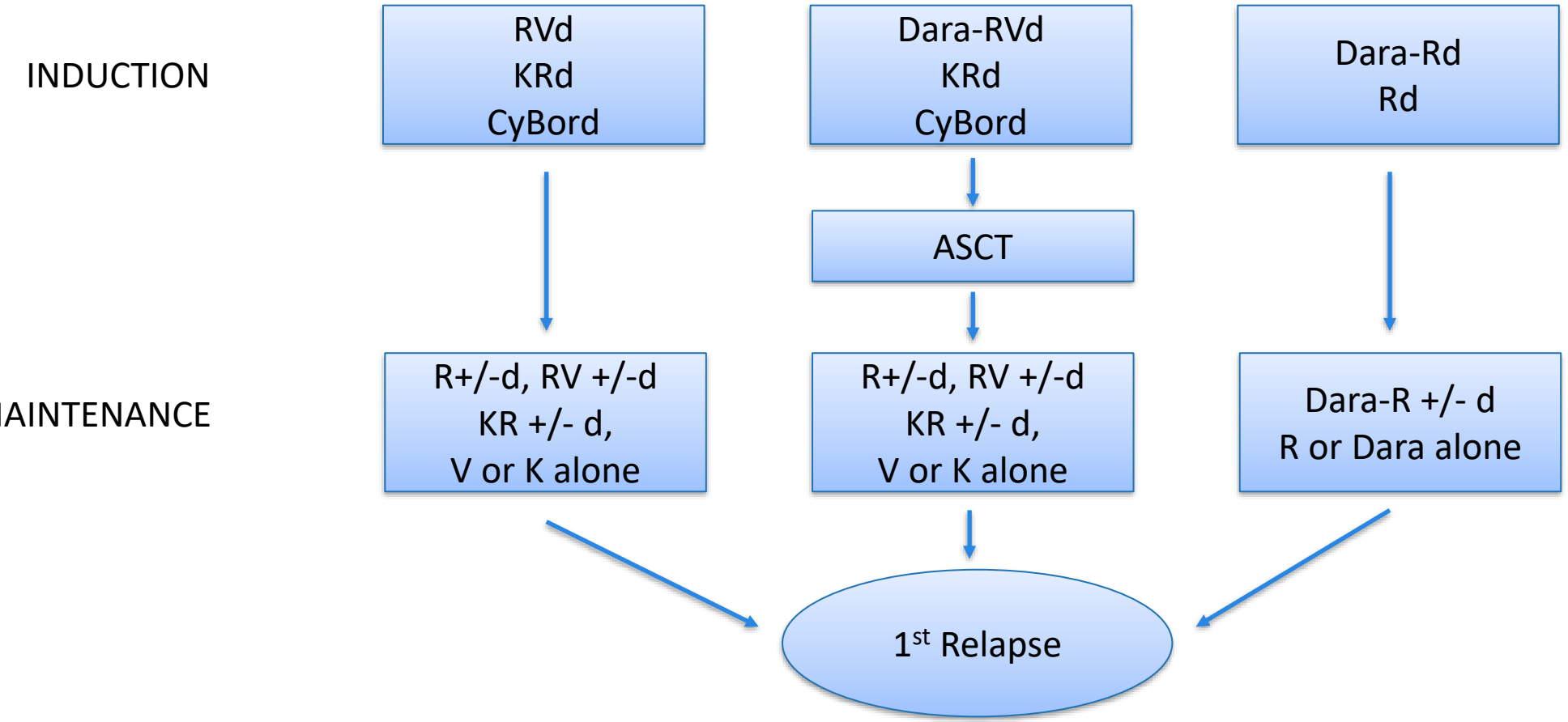
Chief of Myeloma Service

Memorial Sloan Kettering Cancer Center™

Disclosures

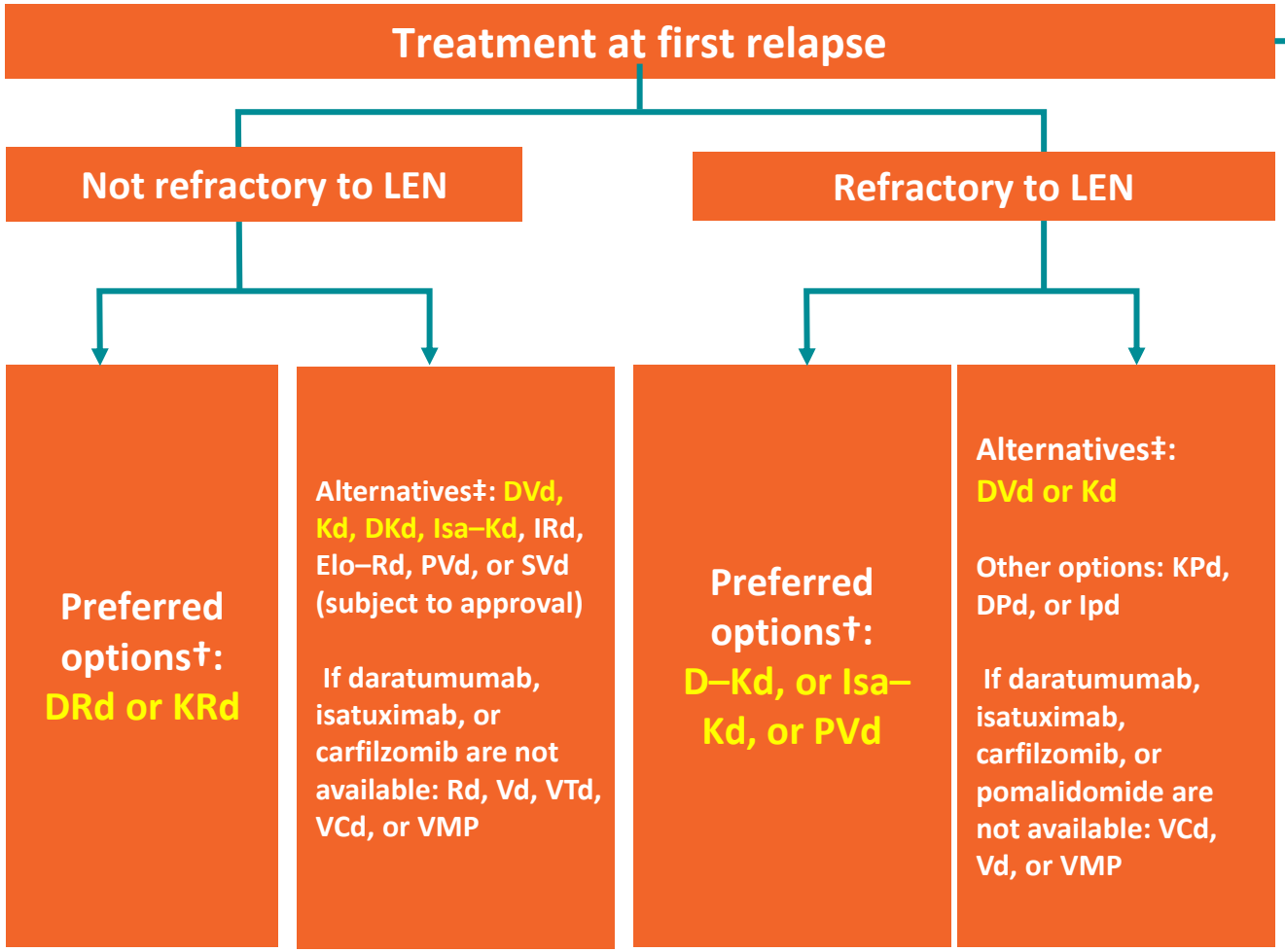
- Research funding: Amgen, Array Biopharma, BMS, Celgene, GSK, Janssen, Merck, Pharmacyclics, Sanofi, Seattle Genetics, SkylineDX, Takeda.
- Consulting: Abbvie, Amgen, BMS, Celgene, EdoPharma, Genentech, Gilead, GSK, Janssen,Oncopeptides, Sanofi, Seattle Genetics, SecuraBio, SkylineDX, Takeda, TeneoBio.
- Speaker: Amgen, BMS, Janssen, Sanofi.

The Landscape of MM in First Relapse



VRD (or VRd)=bortezomib + lenalidomide + dexamethasone; VCD=bortezomib + cyclophosphamide + dexamethasone; RD (or Rd)=lenalidomide + dexamethasone; SCT=stem cell transplantation; Len=lenalidomide; Btz=bortezomib

IMWG Guidelines: Treatment at Relapse



Treatment after multiple relapses

Any first relapse options not yet used (2 new drugs; triplet preferred)

Investigational options and clinical trial

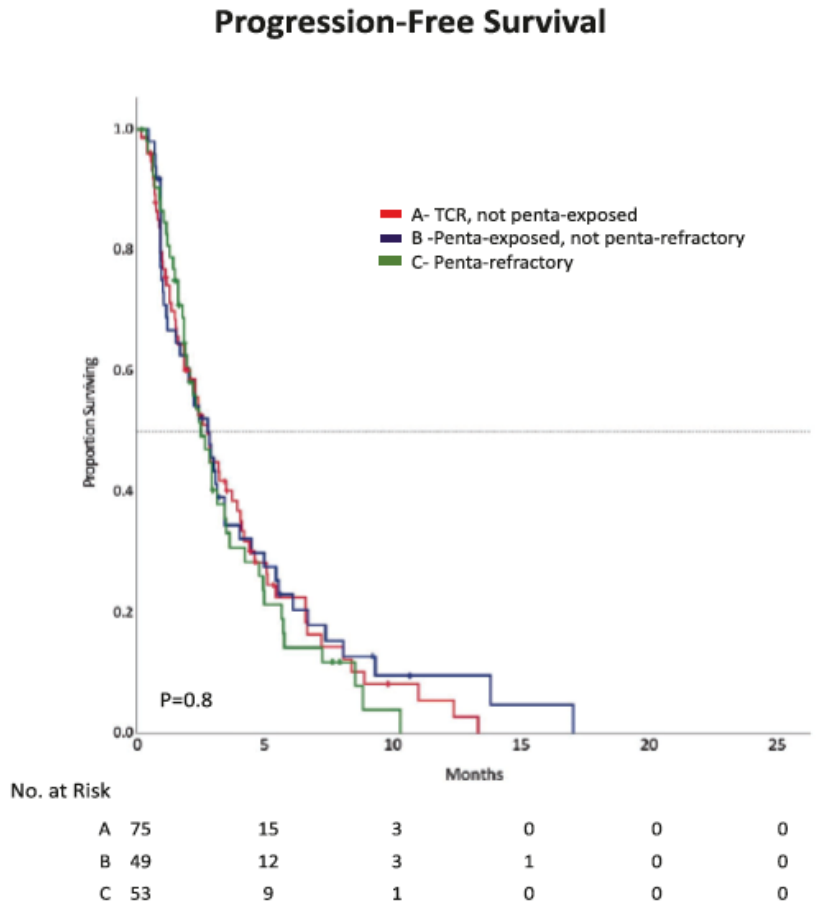
Autologous Stem Cell Transplant Candidate?

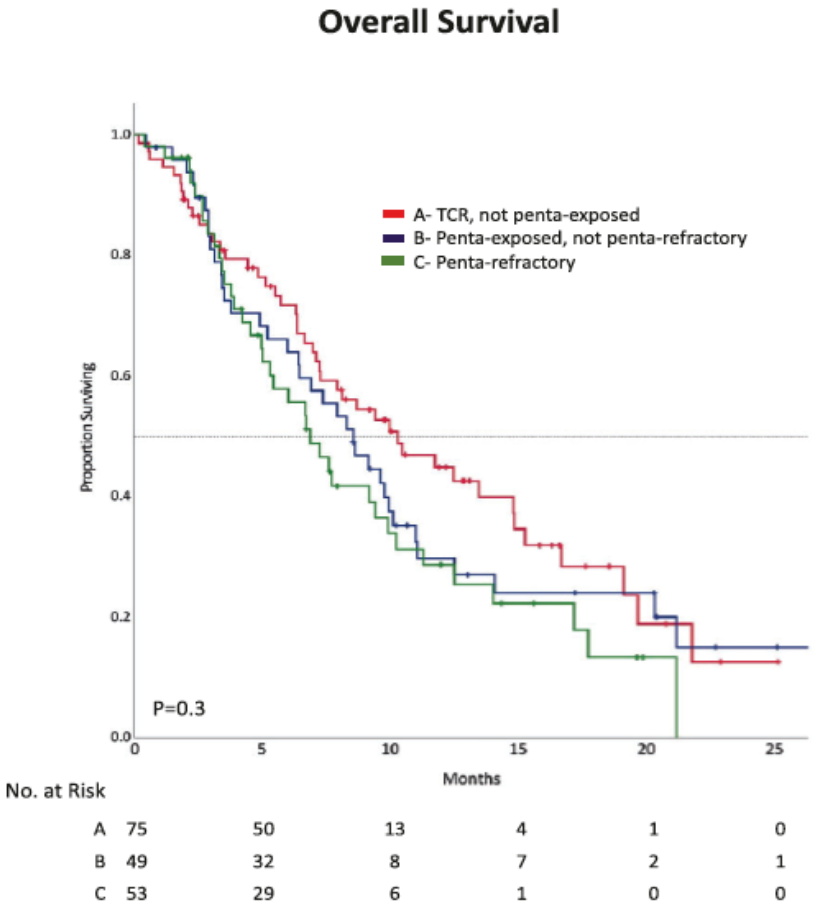
- SCT not performed as part of frontline therapySCT
- Durable remission after 1st SCT (≥24 months on no maintenance therapy, ≥36 months with maintenance therapy)

Memorial Sloan Kettering Cancer Center

Philippe Moreau,et al.Lancet Oncol 2021; 22: e105–18

Triple-Class Refractory (TCR) MM Outcomes





Bal S et al, Leukemia 2021

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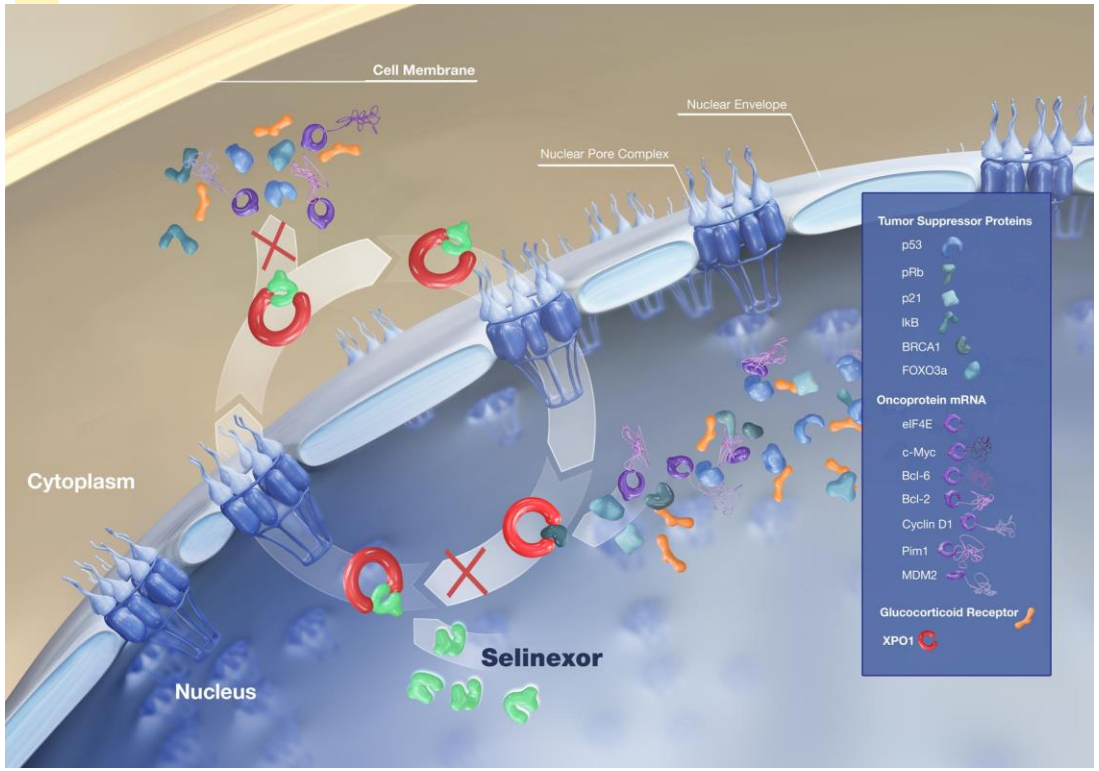
What is coming down the pike?

- Small Molecules
  - XPO1 inhibitors: Selinexor combinations
  - CelMods: Iberdomide, CC-480
  - BCL2/MCL1 Pathway: Venetoclax and its combinations, several MCL1 inhibitors
- Novel Antibody Drug conjugates
  - Belamaf combinations
- Bispecific Antibodies
- CARTs

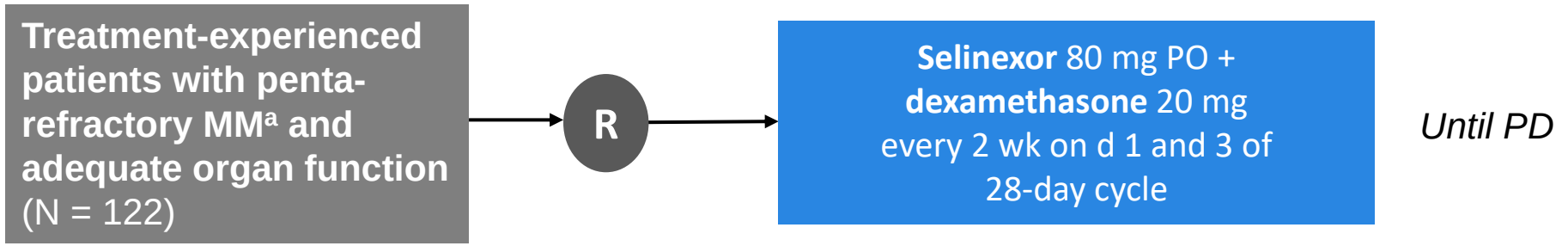
Selinexor: First-in-Class, Oral Selective Inhibitor of Nuclear Export (SINE)[1-4]



- Exportin 1 (XPO1) is the major nuclear export protein for
  - Tumor suppressor proteins (TSPs, e.g., p53, IkB and FOXO)
  - eIF4E-bound oncoprotein mRNAs (e.g., c-Myc, Bcl-xL, cyclins)
  - Glucocorticoid receptor (GR)
- XPO1 is overexpressed in multiple myeloma (MM)
  - High XPO1 levels enable cancer cells to escape TSP-mediated cell cycle arrest and apoptosis
  - XPO1 levels correlate with poor prognosis and drug resistance
- Selinexor is an oral selective XPO1 inhibitor that:
  - Reactivates multiple TSPs by preventing nuclear export
  - Inhibits oncoprotein translation
  - Reactivates Glucocorticoid Receptor (GR) signaling in presence of dexamethasone

1 Gupta A, et al. Therapeutic targeting of nuclear export inhibition in lung cancer. J Thorac Oncol. 2017;12(9):1446-1450. 2 Sun Q, et al. Inhibiting cancer cell hallmark features through nuclear export inhibition. Signal Transduct Target Ther. 2016;1:16010. 3 Gandhi UH, et al. Clinical implications of targeting XPO1-mediated nuclear export in multiple myeloma. Clin Lymphoma Myeloma Leuk. 2018;18(5):335-345. 4 Gravina GL, et al. Nucleo-cytoplasmic transport as a therapeutic target of cancer. J Hematol Oncol. 2014;7:85.

Phase 2 STORM Trial: Selinexor Plus Dexamethasone[1]



- PR achieved by two patients who had prior PD following CAR-T cell therapy
- 71% of evaluable patients had M protein reductions
- Patients with ≥ SD: 78.7%
- Median DOR: 4.4 mo
- Median PFS: 3.7; OS: 8.6 mo

Response, %	Selinexor + Dexamethasone
ORR	26.2
sCR	1.6
VGPR	4.9
PR	19.7

[a] Previously treated with bortezomib, carfilzomib, lenalidomide, pomalidomide, daratumumab, an alkylating agent, and glucocorticoid, with disease documented to be refractory to ≥1 PI, ≥1 IMiD, daratumumab, a glucocorticoid, and last therapy.

1. Chari A et al. ASH 2018. Abstract 598.

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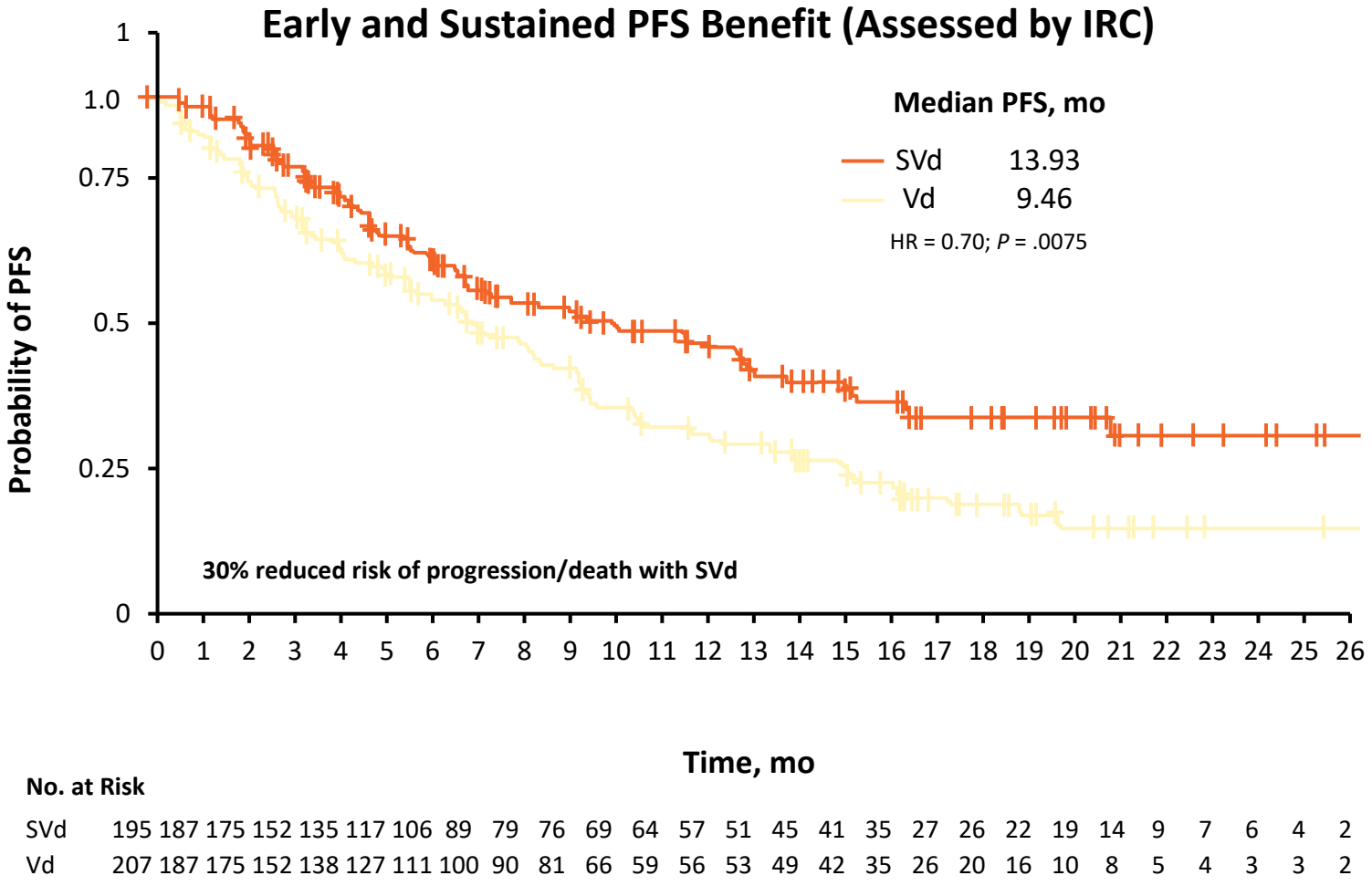
Phase 3 BOSTON Trial: Selinexor Plus Vd in RRMM[1]



Dimopoulos. ASCO 2020. Abstr 8501.

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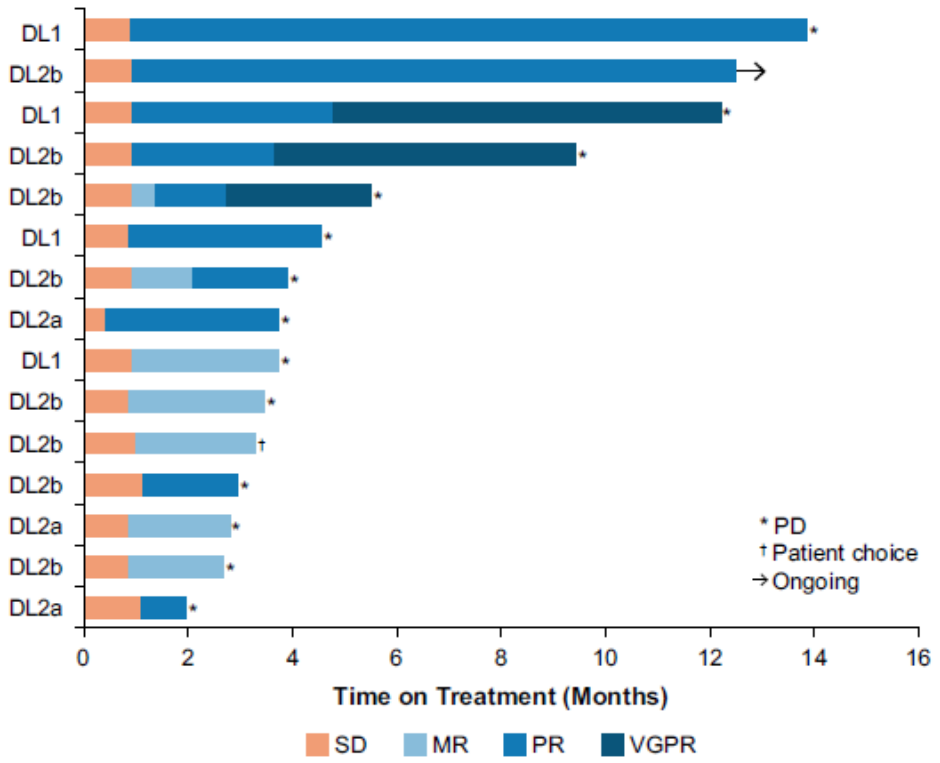
Phase 1 study: Selinexor Plus Kd in RRMM

- **Rates of ≥minimal response, ≥PR and VGPR were 71%, 48% and 14%, respectively;**
- **Similar response outcomes were observed for dual-class refractory (PI and IMiDs)/quad-exposed (K, V, R and P) patients (n = 17), and patients refractory to carfilzomib in last line of therapy (n = 13).**

Prior therapy	*N* = 21
Prior lines of therapy, median (range)	4 (2–10)
Prior PIs, *n* (%)	21 (100)
Carfilzomib	20 (95)
Bortezomib	20 (95)
Prior IMiDs, *n* (%)	21 (100)
Lenalidomide	20 (95)
Pomalidomide	17 (81)
Thalidomide	4 (19)
Other prior therapies, *n* (%)	20 (95)
Autologous stem-cell transplantation	20 (95)
Panobinostat	2 (10)
Daratumumab	1 (5)
Refractory to prior therapy, *n* (%)	21 (100)
Carfilzomib	20 (95)
Bortezomib	11 (52)
Pomalidomide	17 (81)
Lenalidomide	14 (67)
Dual-class refractory/quad-exposed†	17 (81)
Triple-class refractory/penta-exposed‡	1 (5)
Refractory in last line of therapy, *n* (%)	21 (100)
Carfilzomib	13 (62)
Pomalidomide	11 (52)
Carfilzomib and pomalidomide	9 (43)



DL, dose level

Br J Hematol 2019 Aug;186(4):549-560.

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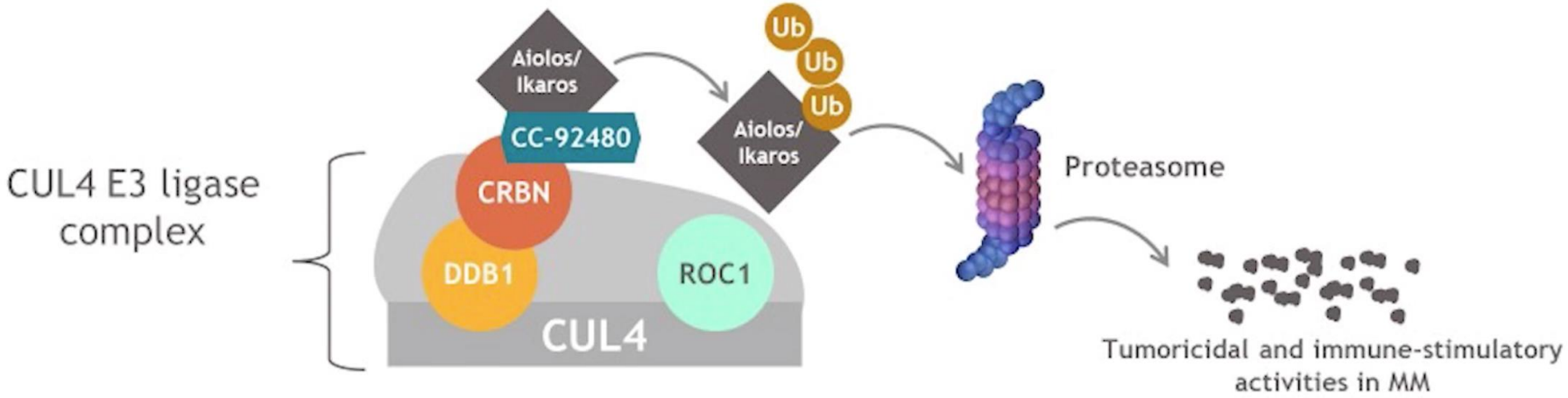
CELMoDs

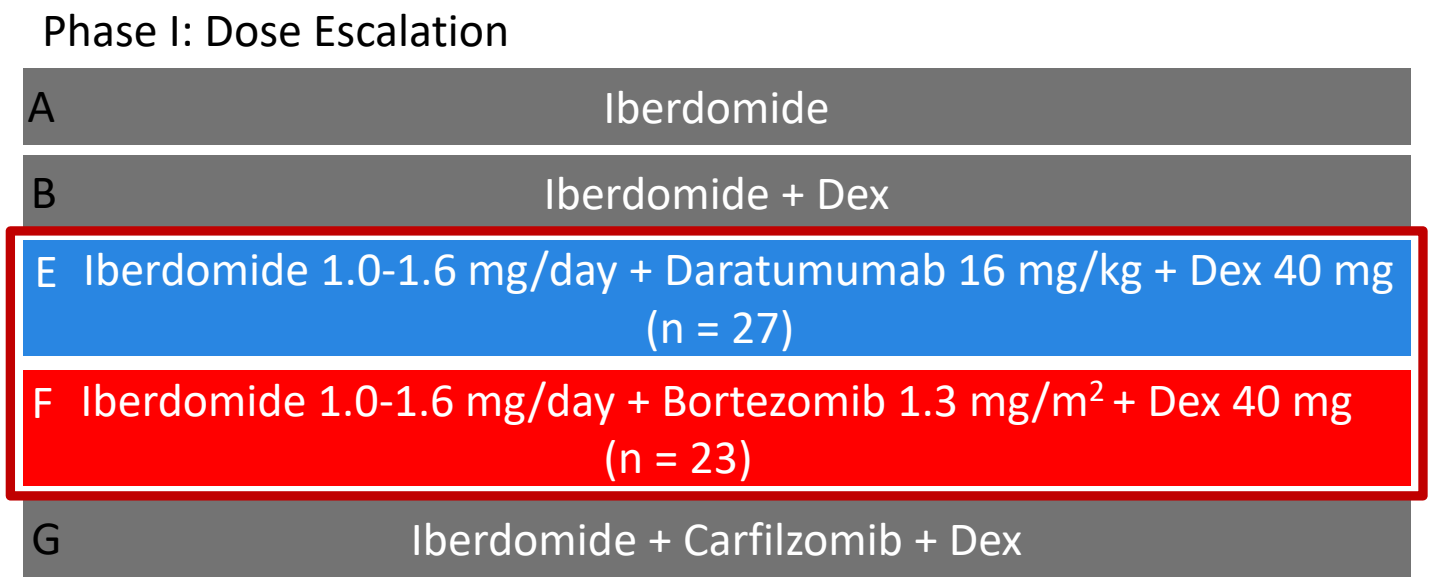
- Cereblon E3 ligase modulators
- Iberdomide and CC-480



CELMoD Iberdomide + Dd or Vd in R/R MM: Phase I/II Study Design

- Open-label, dose-escalation/dose-expansion trial

Patients with R/R MM and ≥2 prior regimens (≥1 in cohort F), including len/pom and PI) who progressed within 60 days of last therapy



Phase II: Dose Expansion

Cohort D at RP2D

Cohort I (post BCMA) at RP2D

Cohort J1 (ND MM, ASCT ineligible)

Cohort J2 (ND MM, ASCT eligible)

Dosing schedules

Cohort E (28-day cycles)

Iberdomide D1-21

Dexamethasone D1,8,15,22

Daratumumab C1-2: D1,8,15,22; C3-6: D1,15; C7+: D1

Cohort F (21-day cycles)

Iberdomide D1-14

Dexamethasone D1,8,15

Bortezomib C1-8: D1,4,8,11; C9+: D1,8

- Primary endpoints: identify MTD and RP2D, efficacy
- Secondary endpoint: safety
- RP2D of 1.6 mg/day determined for iberdomide with Dex; cohorts E, F continuing enrollment with 1.6-mg/day dose

Van De Donk. ASH 2020. Abstr 724.

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Iberdomide + Dd or Vd in R/R MM: Safety

Treatment-Emergent AE, n (%)	Iber + Dd (n = 27)		
	All Gr	Gr 3	Gr 4
Hematologic			
▪ Neutropenia	19 (70.4)	4 (14.8)	14 (51.9)
• Febrile neutropenia	1 (3.7)	0	1 (3.7)
▪ Thrombocytopenia	11 (40.7)	3 (11.1)	1 (3.7)
▪ Anemia	10 (37.0)	7 (25.9)	1 (3.7)
Nonhematologic			
▪ Fatigue	9 (33.3)	0	0
▪ Diarrhea	6 (22.2)	1 (3.7)	0
▪ Constipation	6 (22.2)	0	0
▪ Rash	3 (11.1)	0	0
▪ Peripheral neuropathy	2 (7.4)	0	0
▪ Infusion-related reactions	1 (3.7)	0	0
Infections	21 (77.8)	3 (11.1)	2 (7.4)
▪ Upper respiratory tract	10 (37.0)	0	0

Treatment-Emergent AE, n (%)	Iber + Vd (n = 23)		
	All Gr	Gr 3	Gr 4
Hematologic			
▪ Neutropenia	8 (34.8)	5 (21.7)	1 (4.3)
• Febrile neutropenia	0	0	0
▪ Thrombocytopenia	8 (34.8)	1 (4.3)	5 (21.7)
▪ Anemia	5 (21.7)	3 (13.0)	0
Nonhematologic			
▪ Peripheral neuropathy	7 (30.4)	0	0
▪ Diarrhea	7 (30.4)	1 (4.3)	0
▪ Decreased appetite	7 (30.4)	0	0
▪ Fatigue	6 (26.1)	0	0
▪ Rash	6 (26.1)	1 (4.3)	0
▪ Myalgia	5 (21.7)	0	0
▪ Insomnia	5 (21.7)	0	0
▪ Pruritus	5 (21.7)	0	0
▪ Constipation	5 (21.7)	0	0
Infections	14 (60.9)	13.0	0
▪ Upper respiratory tract	7 (30.4)	8.7	0

- No incidence of thrombotic events (including pulmonary embolism or deep vein thrombosis) reported in either cohort

Van De Donk. ASH 2020. Abstr 724.

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Iberdomide + Dd or Vd in R/R MM: Efficacy

Best Response, n (%)	Iber + Dd (n = 27)	Iber + Vd (n = 23)
ORR ▪ sCR ▪ CR ▪ VGPR ▪ PR	11 (42.3) 1 (3.8) 2 (7.7) 2 (7.7) 6 (23.1)	14 (60.9) 0 1 (4.3) 5 (21.7) 8 (34.8)
MR	2 (7.7)	2 (8.7)
SD	10 (38.5)	4 (17.4)
PD	3 (11.5)	2 (8.7)
NE	0	1 (4.3)
CBR (MR or better)	13 (50)	16 (69.6)
DCR (SD or better)	23 (88.5)	20 (87.0)
Median time to response, wks (range)	4.1 (4.0-12.0)	3.6 (3.0-13.1)

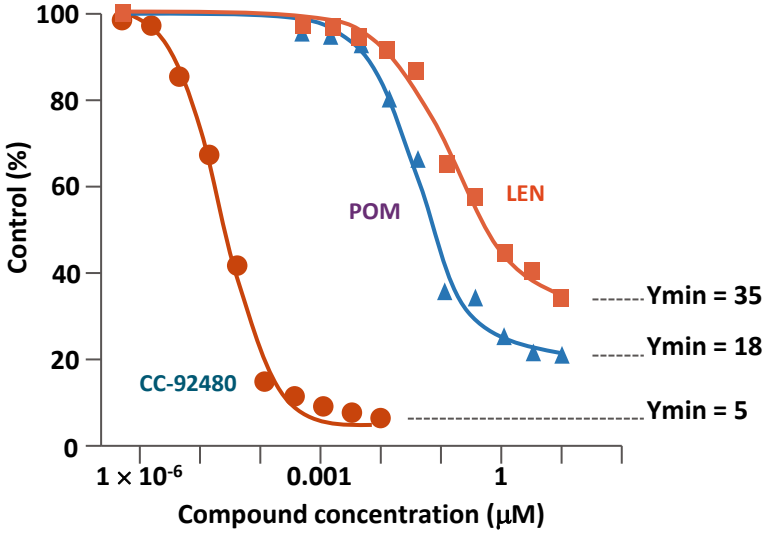
- High response rates in heavily exposed and highly refractory patient population
  - Among 27 patients in daratumumab cohort, 26 were IMiD refractory, 15 daratumumab refractory, 13 triple-class refractory; 4 patient refractory to daratumumab achieved PR
  - Among 23 patients in bortezomib cohort, 18 were IMiD refractory, 15 PI refractory, 9 bortezomib refractory, 9 triple class refractory; durable responses achieved in patients refractory or with prior exposure to bortezomib
- Addition of daratumumab or bortezomib to iberdomide + dexamethasone shows minimal effect on pharmacodynamics

Van De Donk. ASH 2020. Abstr 724.

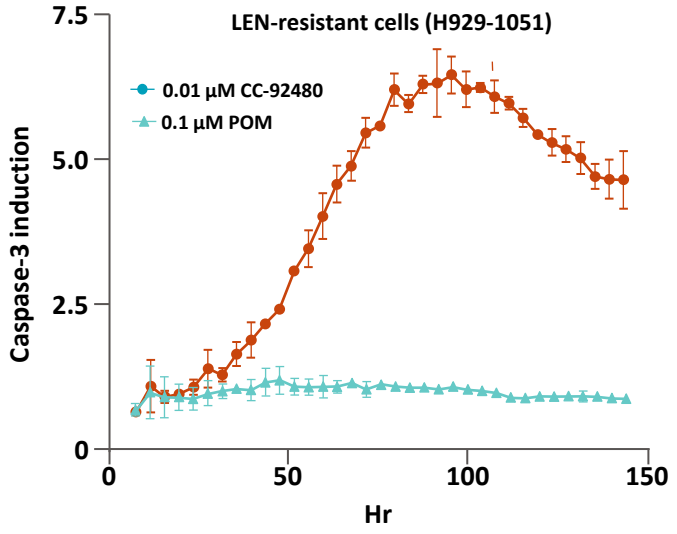
CC-92480 Is a Novel CELMoD Agent Specifically Designed for Rapid Protein Degradation[1,2]

Efficient substrate degradation leads to apoptosis, potent antiproliferative activity in LEN and POM resistance[3]

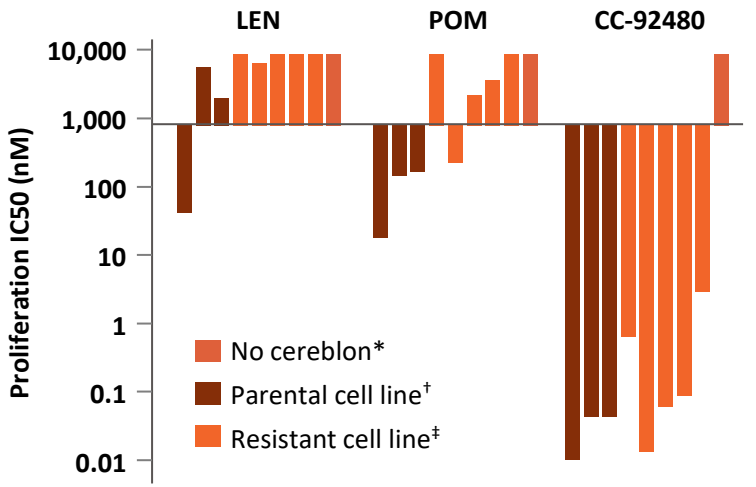
Aiolos degradation efficiency[1]



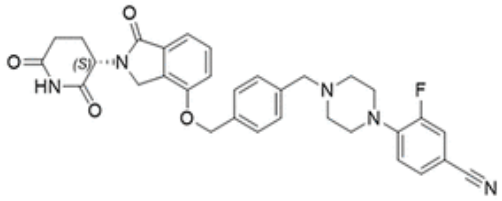
Apoptosis induction kinetics



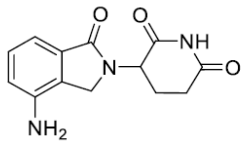
Antiproliferative activity in LEN/POM resistance



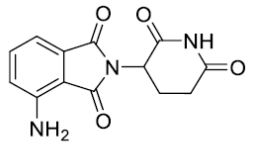
CC-92480, a potent CELMoD agent[1]



LEN[1]



POM[1]



*DF15R. †DF15, H929, and OPM-2. ‡H929R1, H929R2, OPM-2R1, OPM-2R2, and OPM-2R3.

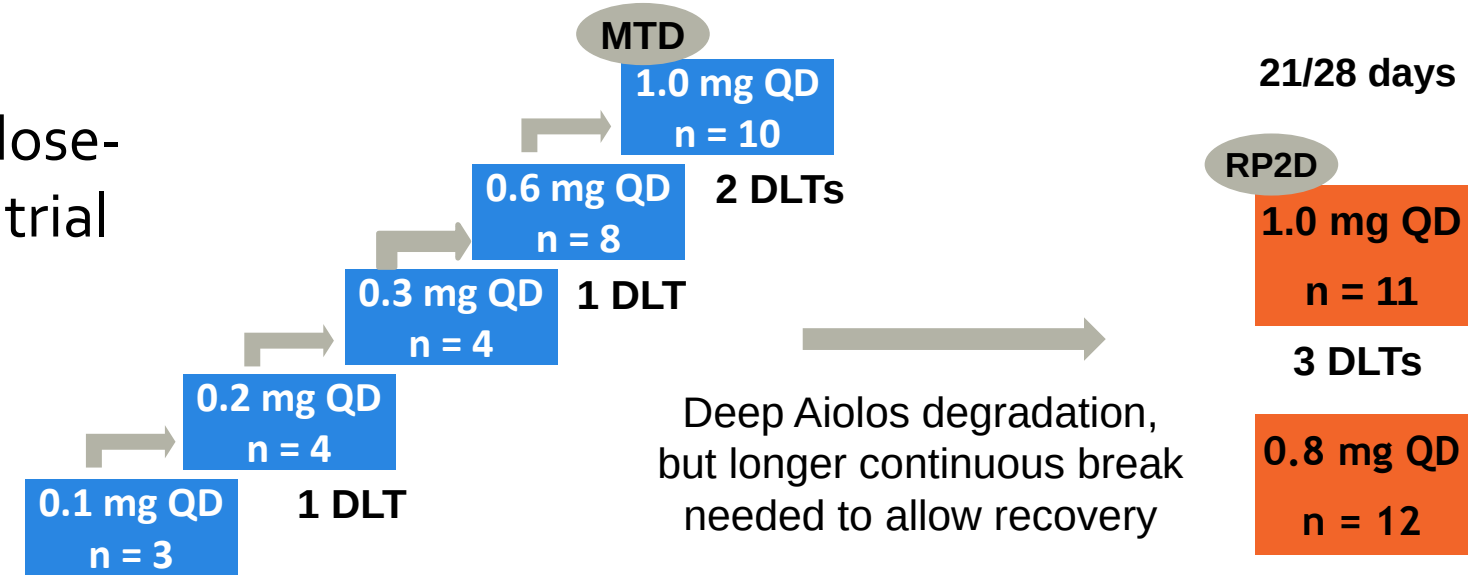
1. Hansen. J Med Chem 2020;63:6648. 2. Wong. ASH 2019. Abstr 1815. 3. Richardson. ASCO 2020. Abstract 8500.

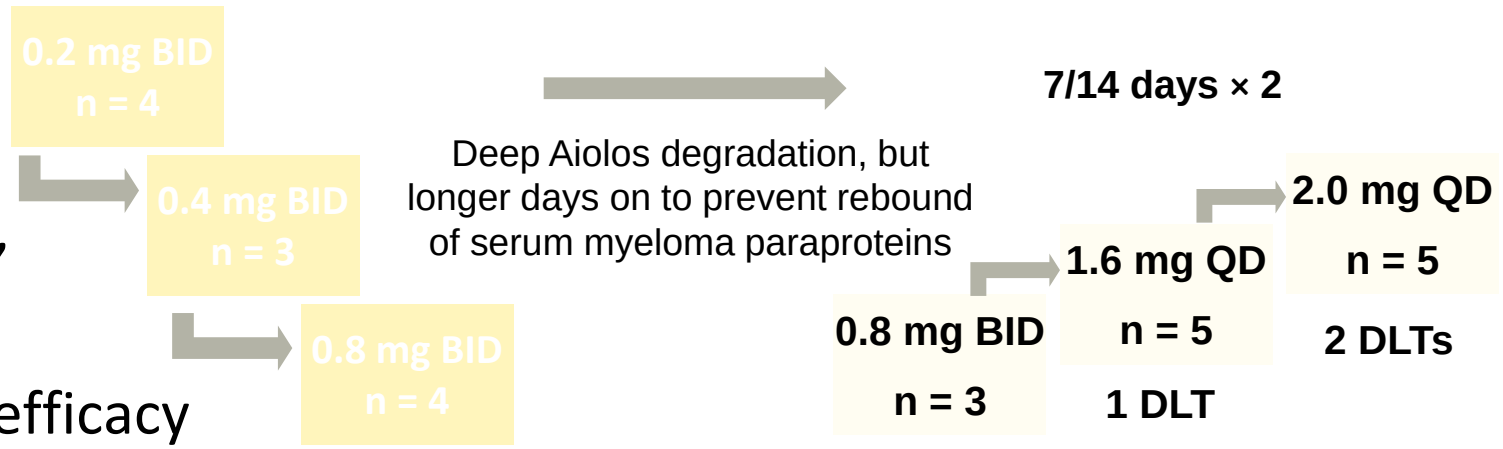
Memorial Sloan Kettering Cancer Center

Phase I CC-92480-MM-1 Trial: CELMoD CC-92480 + Dex in Patients With R/R MM

- First-in-human, multicenter, dose-escalation/-expansion phase I trial

Patients with R/R MM that is resistant or intolerant to established treatments;
PD ≤60 days of last MM tx
(N = 149)



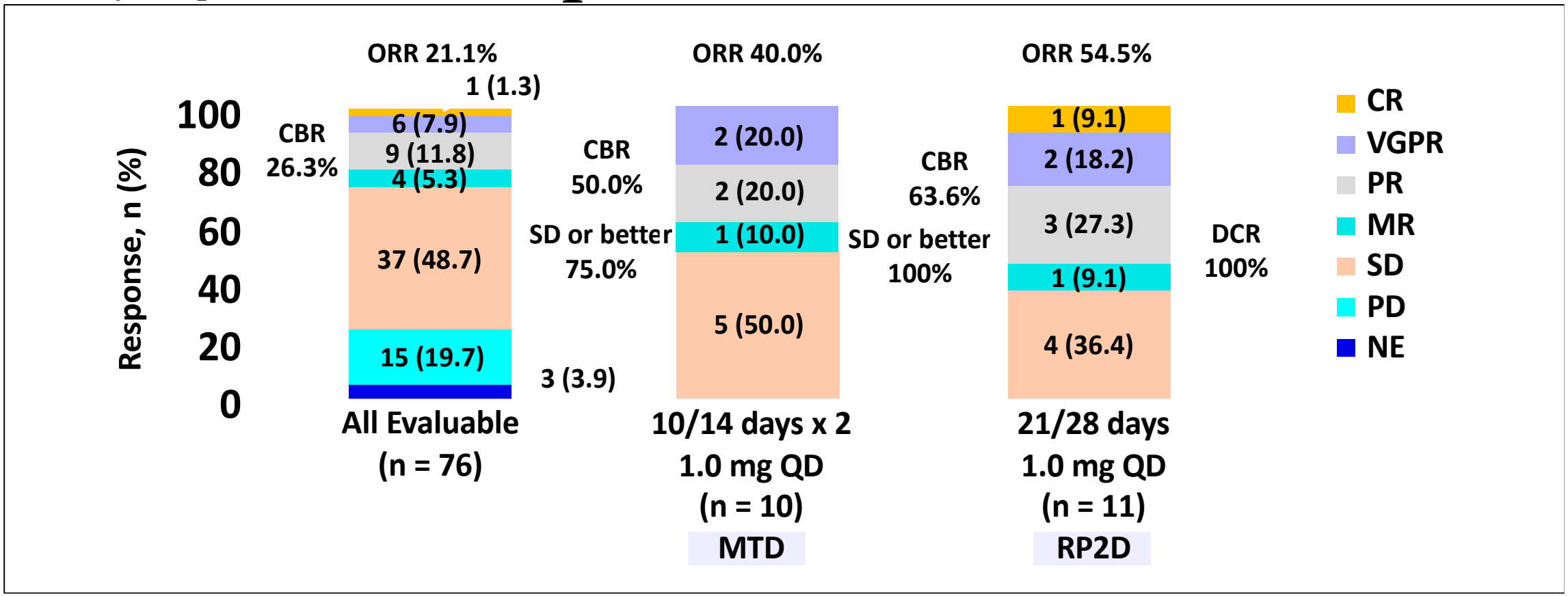


- Primary endpoints: PK, safety, MTD/RP2D
- Secondary endpoints: prelim efficacy

Richardson. ASCO 2020. Abstr 8500.

Memorial Sloan Kettering Cancer Center

CC-92480: Best Response



- 7 of 11 patients at RP2D of 1 mg QD 21/28 days were triple-class refractory (to ≥1 IMiD, 1 PI, and 1 anti-CD38 mAb)
  - Of these patients, 1 had CR, 1 VGPR, 2 PR, and 1 MR

Richardson. ASCO 2020. Abstr 8500.

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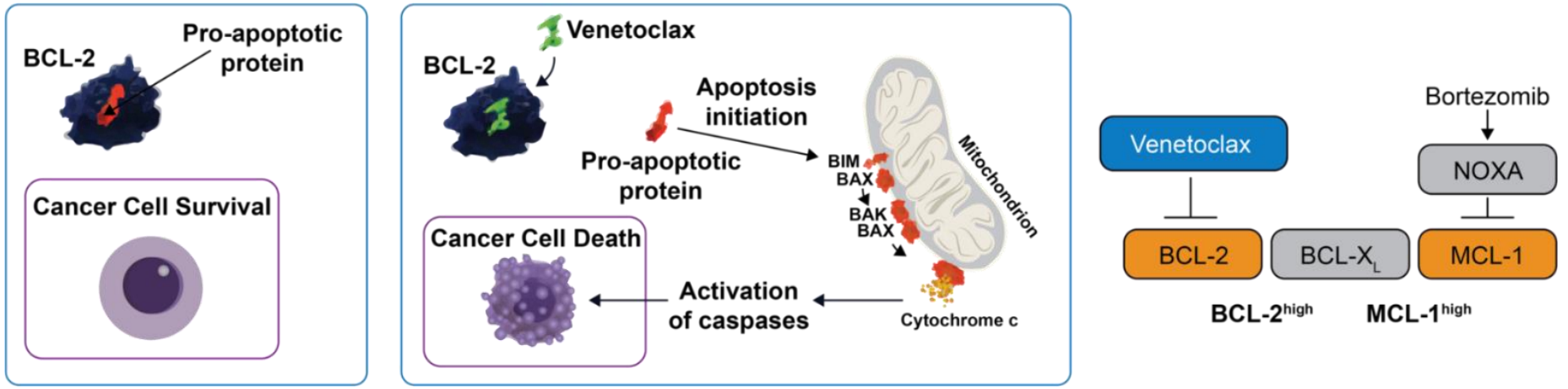
Targeting Apoptosis[1-3]

Venetoclax is a selective, orally available small-molecule BCL-2 inhibtor[1]; active in R/R MM[3]



Venetoclax (daily dose up to 1,200 mg) has an acceptable safety profile in R/R MM, predominantly in patients with t(11;14) abnormality and favorable BCL-2 family profile

In contrast to the CLL experience, TLS appears to be uncommon in MM; ramp-up dosing has not been necessary

1. Roberts AW et al. *N Eng J Med*. 2015;374:311-322. 2. Punnoose E et al. *Mol Cancer Ther*. 2016;15:1132-1144. 3. Kumar S et al. *Blood*. 2017;130:2401-2409.

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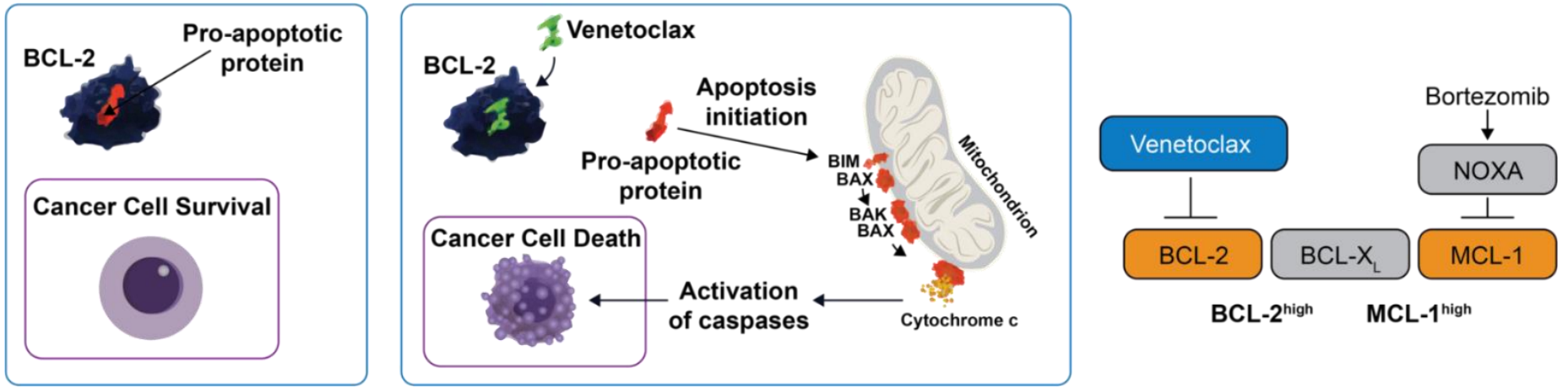

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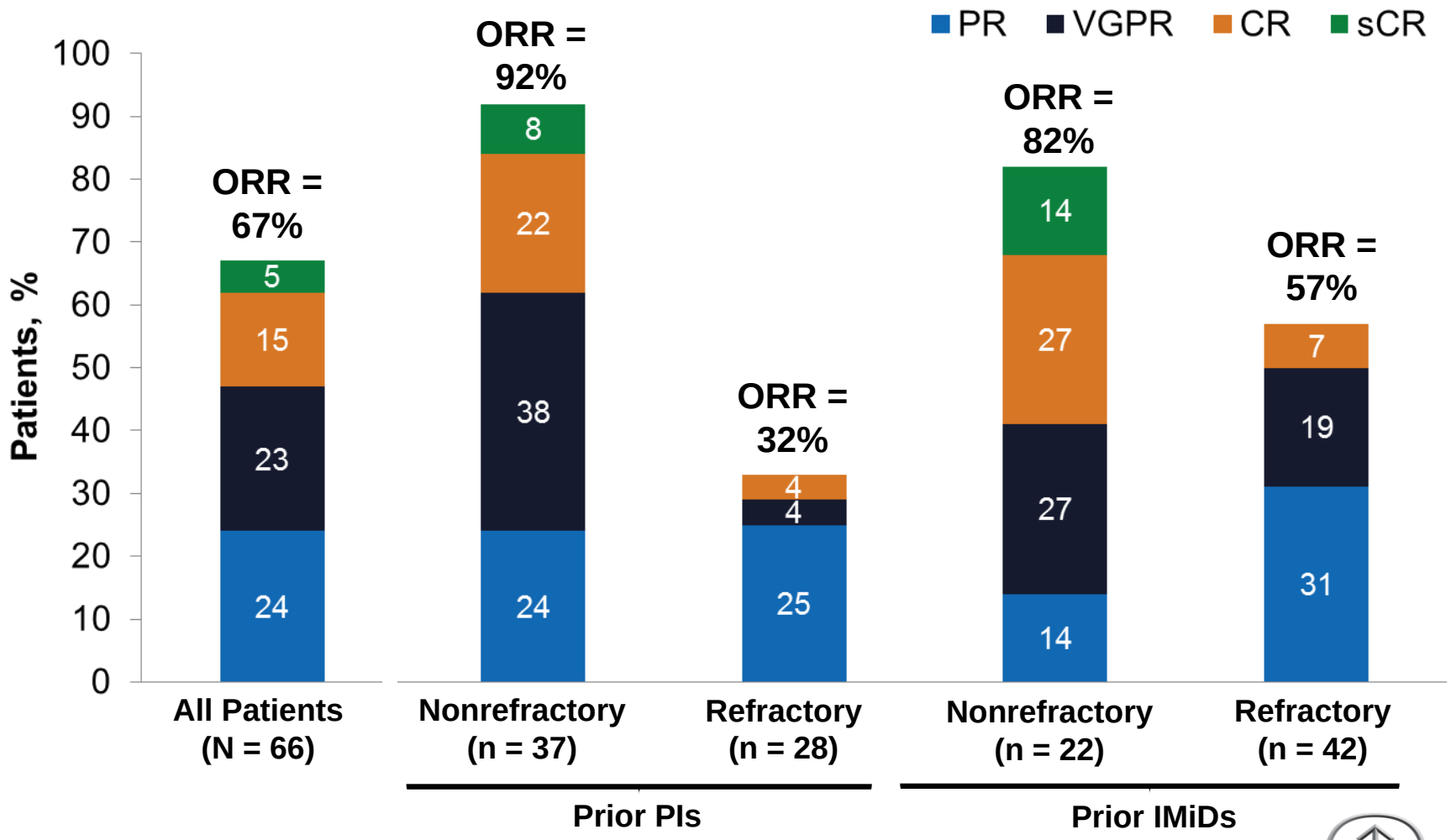
Venetoclax Is Active Combined With Bortezomib/Dexamethasone …[1]

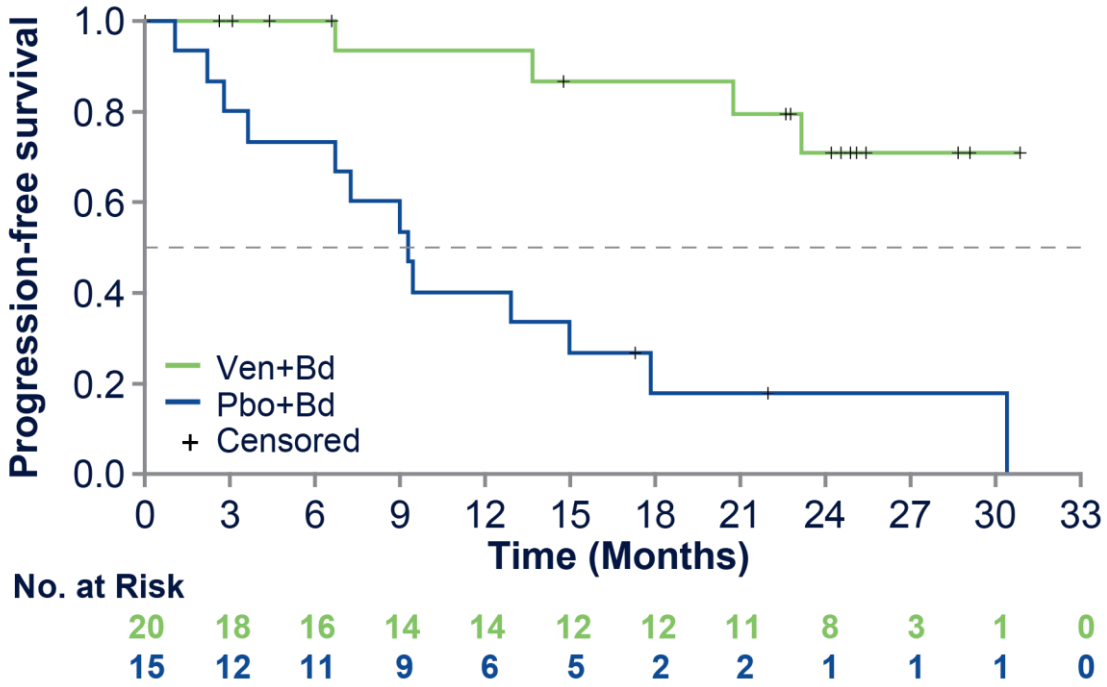
- N = 66 patients with R/R MM

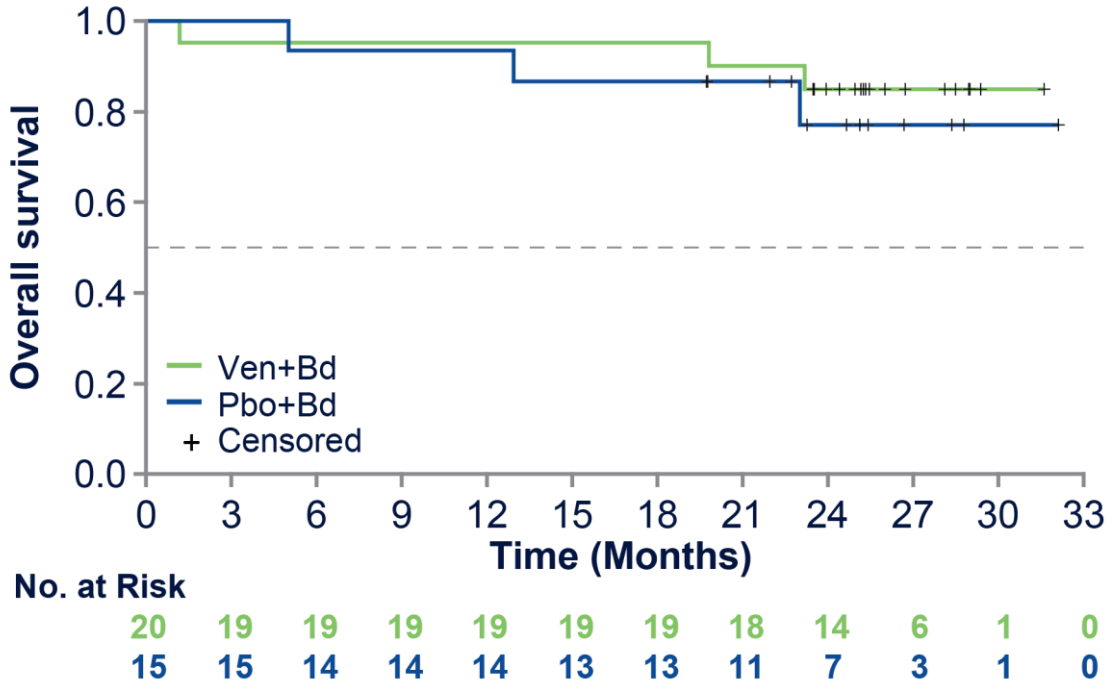


1. Moreau P et al. *Blood*. 2017;130:2392-2400.

Memorial Sloan Kettering Cancer Center

BELLINI Study: PFS and OS in Patients With t(11;14)[1]





PFS	VEN+BD	PBO+BD
Median, months	Not reached	9.3
HR (95% CI)	0.09 (0.02, 0.44)	
P value	0.003	

OS	VEN+BD	PBO+BD
Median, months	Not reached	Not reached
HR (95% CI)	0.68 (0.13, 3.48)	
P value	0.647	

Clinical Data Cutoff: September 13, 2019.

1. Kumar SK, et al. *Lancet Oncol.* 2020;21:1630-1642.

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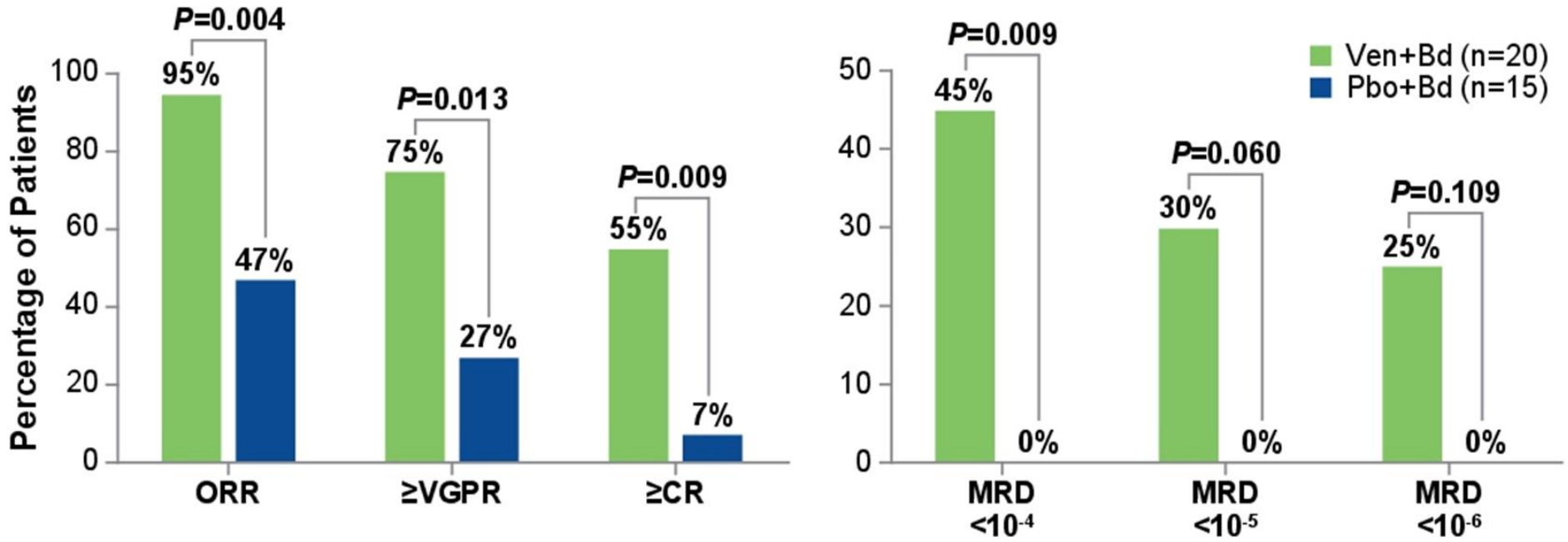
BELLINI Study: Clinical Response and MRD Rates in Patients With t(11;14)[1]



High rates of CR and MRD negativity were observed in the t(11;14) subgroup with VEN+BD.

Clinical Data Cutoff: September 13, 2019.

1. Kumar SK, et al. *Lancet Oncol.* 2020;21:1630-1642.

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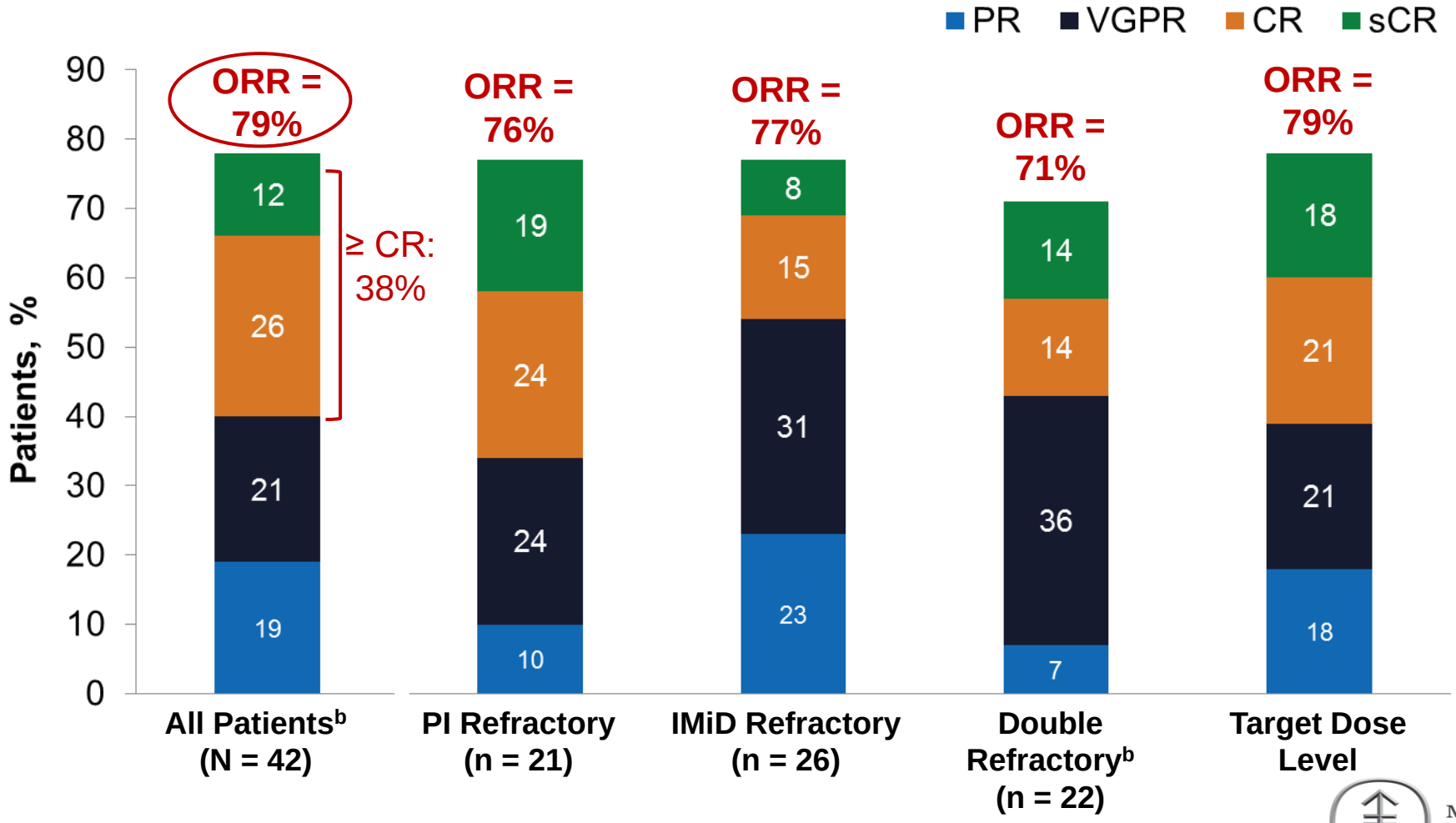
Active With Carfilzomib/Dexamethasone[1,a]

- N = 42 patients with R/R MM



[a] Data cutoff: September 17, 2018. [b] One patient died within the first 2 weeks of dosing; no data available.

1. Costa LJ et al. ASH 2018. Abstract 303.

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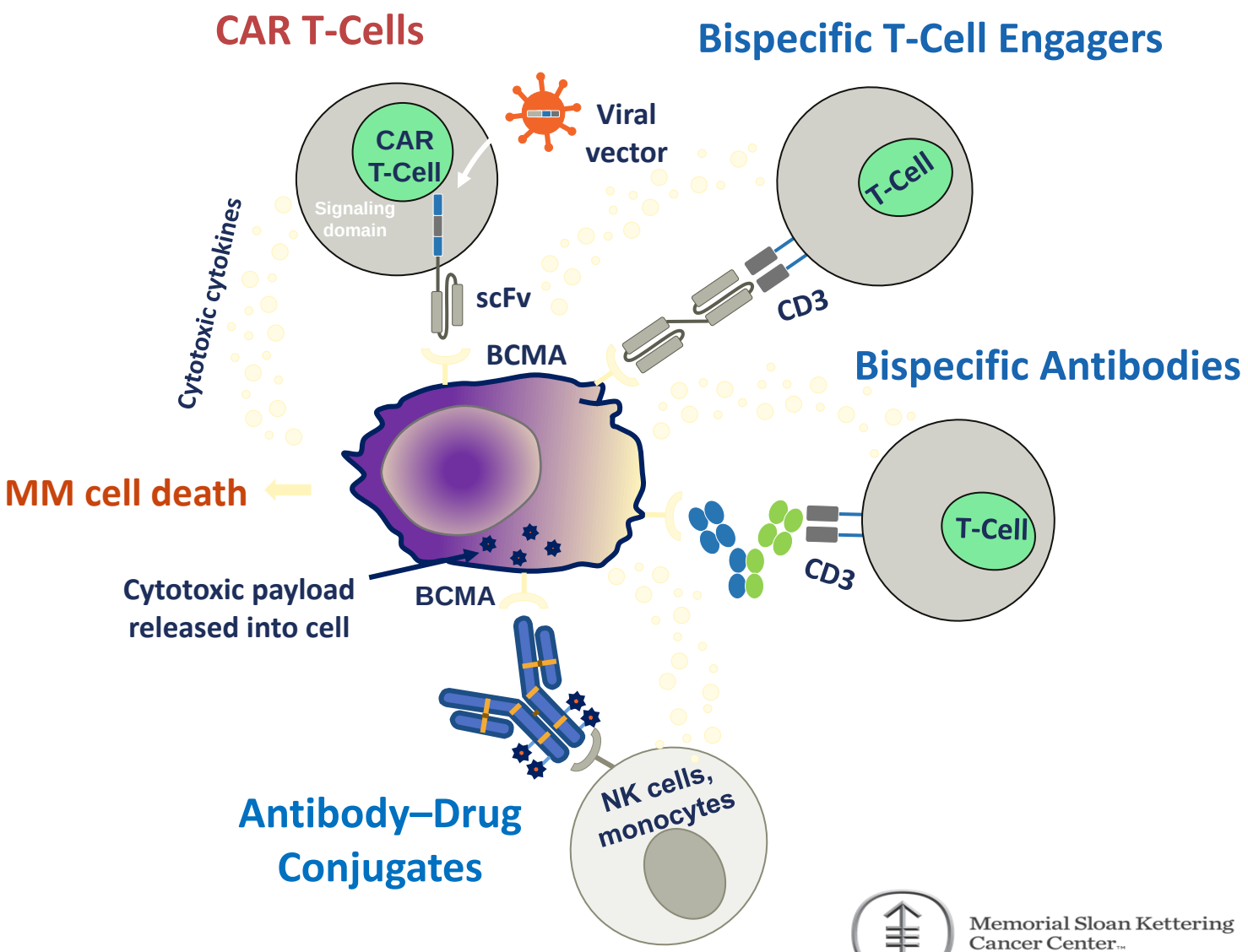
BCMA in Multiple Myeloma

- Expressed on late memory B-cells committed to PC differentiation and PCs
- BCMA plays a role in survival of long-lived PCs
- γ-secretase cleaves BCMA from the cell surface, yielding soluble BCMA
- Other targets under investigation
  - GPRC5D
  - FcHR5
  - SLAMF7
  - CD38/138



Cho. Front Immunol. 2018;10:1821.

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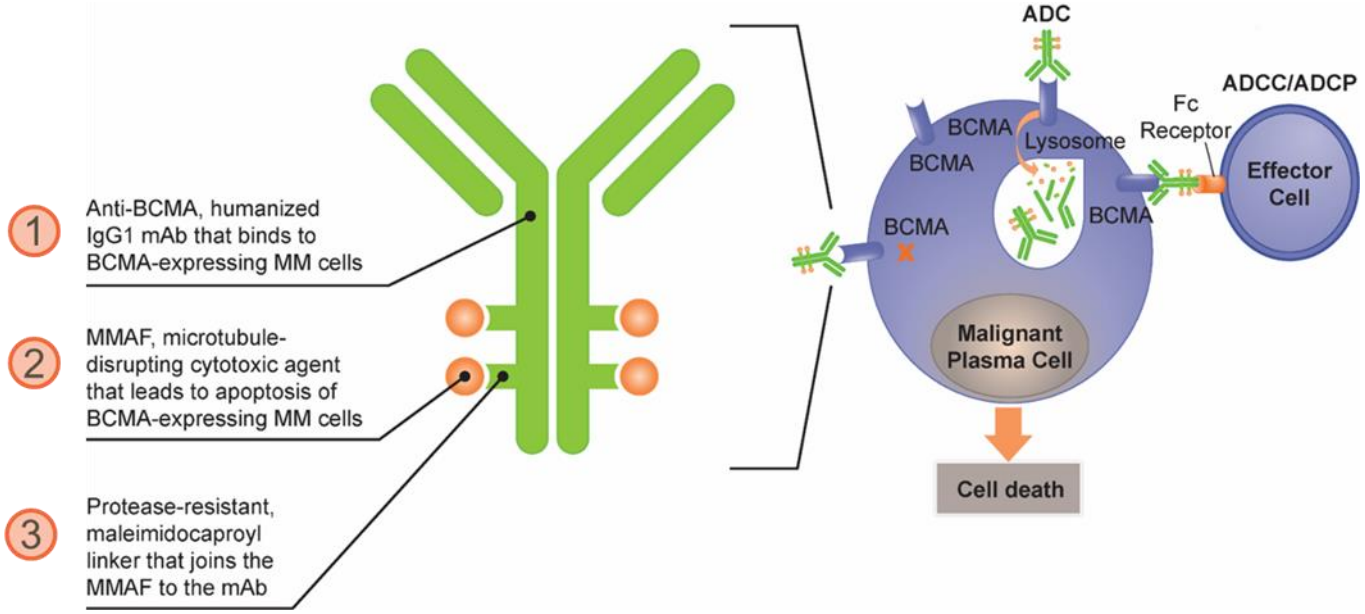
Bela-maf: Clinical Summary

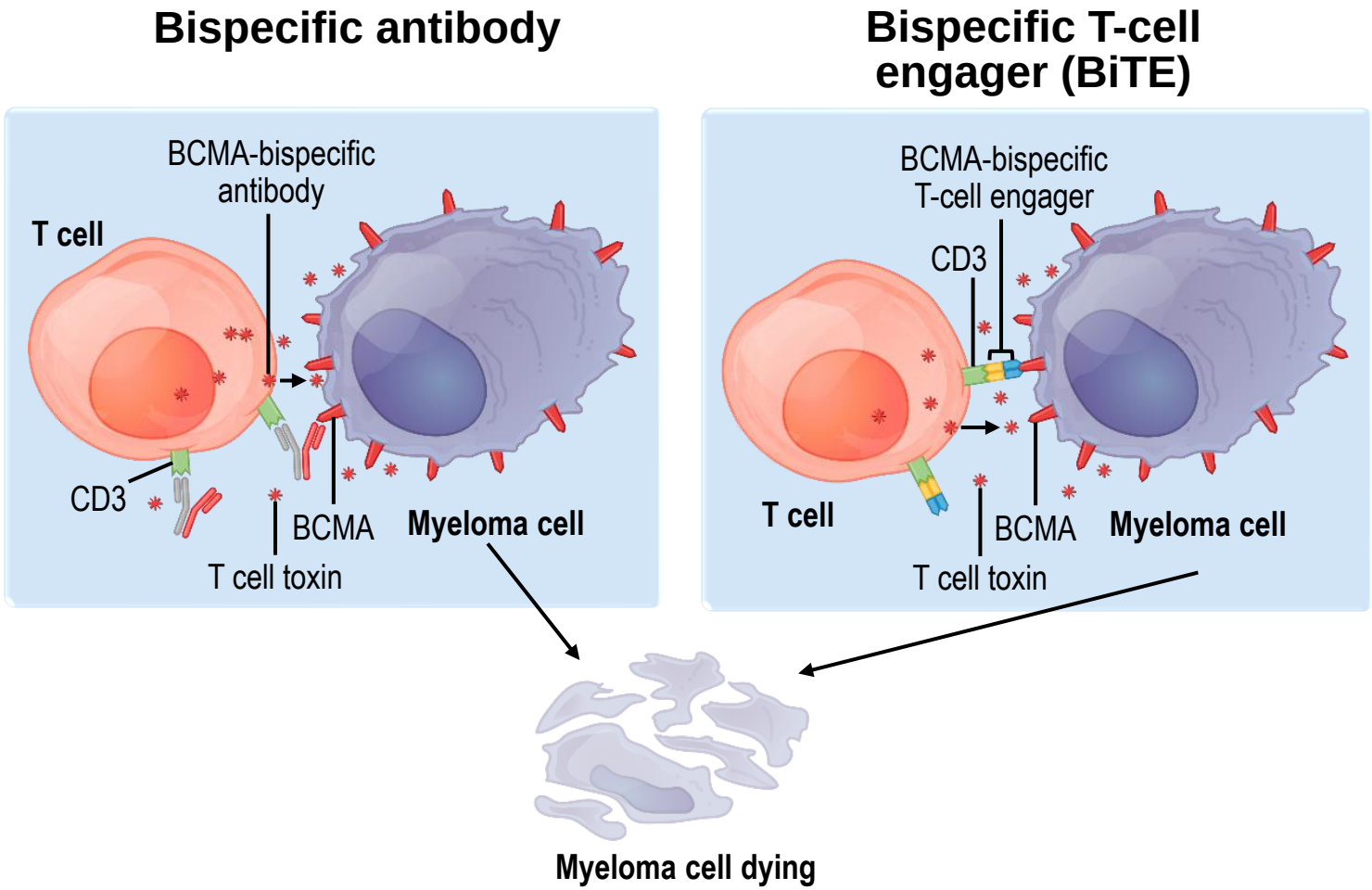
- Lessons from DREAMM2 Monotherapy Randomized Phase II Trial (Compared 2.5 mg/kg vs 3.4 mg/kg dosing):
  - 2.5 mg/kg: ORR 32%, median PFS 2.8 months, median DOR 11 months, median OS 13.7 months
  - Keratopathy: 71% all grade, 44% grade 3-4
  - Among pts with grade ≥2 keratopathy (N=60) :
    - Median time to onset of first occurrence was 37 days (range, 19-147 days)
    - Median duration of first event was 86.5 days (range, 8-358 days)
    - Most patients (77%) recovered from first occurrence[a,b]
  - Decreased visual acuity: 53% all grade, 28% grade 3-4
  - Best corrected visual acuity change ≥20/50: 18%



[a] Represents patients with events that recovered either prior to end of tx or after the end of study tx; recovery was defined as any grade 1 exam finding or no exam finding compared with baseline. [b]Lost to follow-up (n=4), withdrew (n=4), or died (n=9). After follow-up ended for some pts, no more data were available so it is not possible to say if their corneas recovered or not. [c]Better than 20/50 at baseline and 20/50 or worse postbaseline. [d]Recovery was defined as 20/40 or better in the better-seeing eye. After follow-up ended for some pts, no more data were available, so it is not possible to say if their eyesight recovered or not.

1. Farooq AV, et al. *Ophthalmol Ther.* 2020;9(4):889-911. 2. Lonial S, et al. Presented at ASH 2020. Abstract #3224.

Bispecific antibodies and Bispecific T-Cell Engagers (BiTEs)



Adapted from Cho S-F et al. *Front Immunol*. 2018;9:1821.

BCMA Bispecific Antibodies (ASH 2021 Updates)

	Teclistamab[1]	Elranatamab[2]	TNB-383B[3]	REGN5458[4]
Schedule	Weekly SC	Weekly SC or Q2W SC	IV q3W	Weekly IV
Patients	165	55	118	73
Median prior lines	5	6	5	5
Triple Class and Penta Refractory	78% and 30%	91% and NA	61% and NA	89% and 38%
Prior BCMA	No	22%	No	No
CRS, All (Gr 3/4)	72% (0.6%)	87% (0%)	54% (3%)	38% (0%)
ICANS, All (Gr 3/4)	3% (0%)	NA	2% (NA)	4% (0%)
ORR at higher doses	62%	69% 70% in prior BCMA	60%	75%
CR at higher doses	29%	Not reported	20%	16%

1. Moreau et al. Abstract #896; 2.Sebag et al. Abstract#895; 3. Kumar et al. Abstract #900; 4. Zonder et al. Abstract #160 (ASH 2021)

MSKCC Myeloma Service

Saad Z. Usmani (Chief)
MM Immunotherapy
High-Risk Disease Biology/Trials
Bispecific Antibodies
CAR T Cells
Checkpoint Inhibitors
Developmental Therapeutics

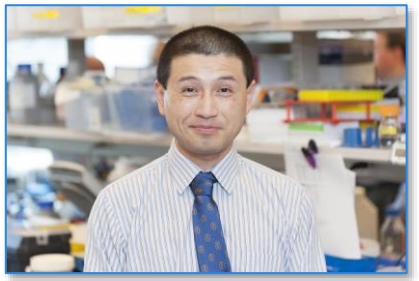
Alex Lesokhin
MM Immunotherapy
Bispecific Antibodies
Checkpoints Inhibitors
Neoantigens
Microbiota

Hani Hassoun
MM Supportive Care
Alliance Liaison
NDMM/RRMM Trials
Elderly and Frail

Sham Mailankody
MM Immunotherapy
CAR T Cells

Neha Korde
NDMM Clinical Trials
MRD Directed therapy
Supportive Care

Malin Hultcrantz
MM Precursor Disease
Antibody drug conjugates
Genetics/MRD



Sydney Lu
New molecular pathways
Mechanisms of resistance

Urvi Shah
Early Relapse
MM Precursor
Disease
Nutrition /CAR T cells

Carlyn Tan
MM Precursor diseases
Supportive Care

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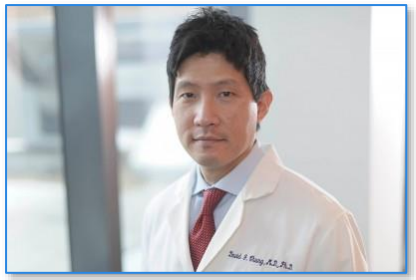
MSKCC Myeloma TCT Program

Sergio Giralt
Allo/Auto HCT for MM
New Regimens
CAR T Cells

David Chung
T Cell exhaustion
Auto HCT + Vaccines
MM Immunotherapies



Gunjan Shah
HCT Toxicities
Precision Drug Dosing
CAR T Cells
Salvage Auto and Allo HCT

Saad Z. Usmani
High-Risk Disease Biology/Trials
CAR T Cells
Auto HCT for MM

Michael Scordo
HCT Toxicities
Precision Drug Dosing
CAR T Cells

Heather Landau
Amyloidosis
HCT Toxicities
Homebound HCT
Precision Drug Dosing
Novel Regimens for Salvage Auto

Oscar Lahoud
Auto HCT and CAR T Cells
Post HCT Therapies

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Q&A Session

THANK YOU
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SUPPORT!

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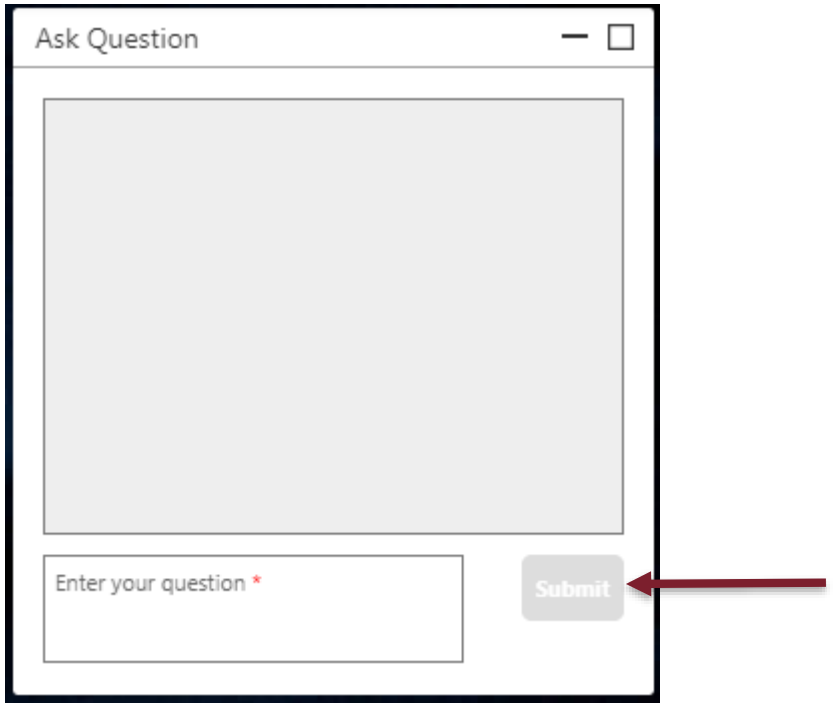
IMF Patient and Family Webinar

Type your questions to the panel and press **Submit.**



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IMF Patient and Family Webinar

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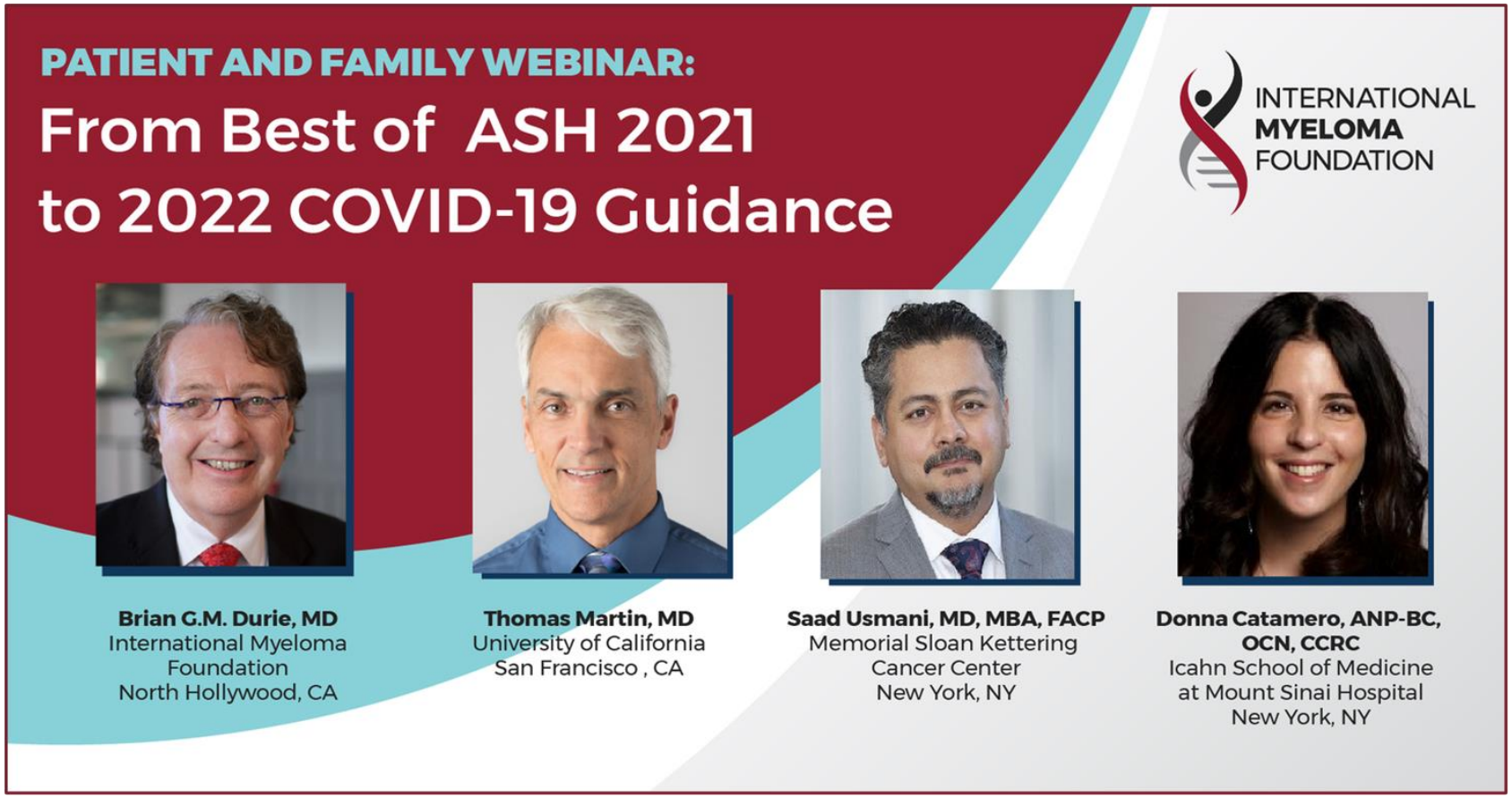
Webinar Video Replay and Slides



As follow up to today's webinar, we will have the speaker slides and a video replay available.

They will be provided shortly after the webinar concludes.

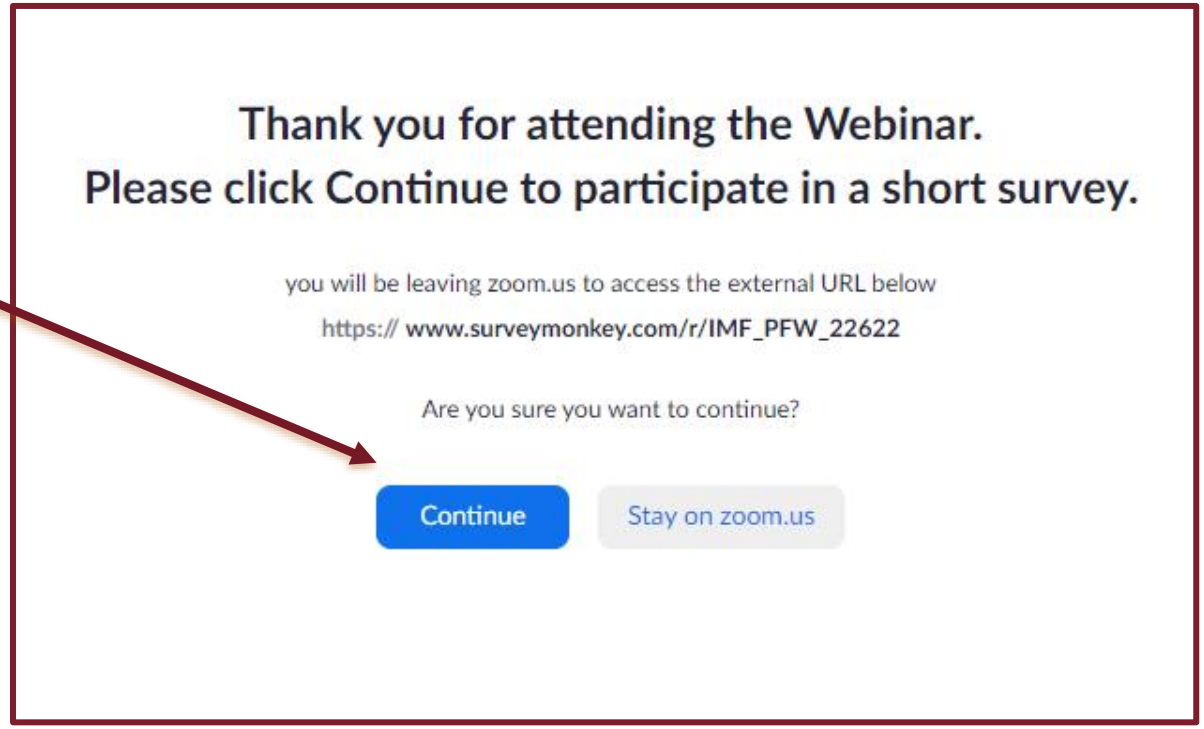
We Want to Hear From You!

Feedback Survey

At the close of the meeting a feedback survey will pop up. Click “continue” to complete the survey.

This will also be emailed to you shortly after the workshop.

Please take a moment to complete this survey.



Looking ahead!

What Is Myeloma Action Month?

Myeloma Action Month happens every year in March to encourage individuals and groups to take actions that positively impact the myeloma community. The International Myeloma Foundation (IMF) invites YOU to TAKE ACTION because every action makes a difference!

This year, the IMF is focusing on actions that individuals and groups can take for the myeloma community to better themselves and to foster community-building

TAKE ACTION
#MYELOMAACTION

#MYELOMAACTION
Join the Movement

IMF Patient and Family Webinar