

IMF PATIENT AND FAMILY WEBINAR

Multiple Myeloma Patient Safety and the Coronavirus



Brian G.M. Durie, MD

Joseph Mikhael, MD

William Bensinger, MD

Joseph Tariman, PhD, RN

Saturday, May 9th, 2020

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ONCOLOGY

Today's Speakers

Saturday
May 9
2020

Patient and Family Webinar

MULTIPLE MYELOMA PATIENT SAFETY AND THE CORONAVIRUS

Watch the **LIVESTREAM**: 1:00 PM PT/2:00 PM MT/3:00 PM CT/4:00 PM ET



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with support from:

Amgen, Bristol-Myers Squibb, Genentech, GSK, Janssen Oncology, Karyopharm Therapeutics, The Binding Site, and Takeda Oncology

Structure of Webinar

- **Session One: COVID-19 Guidance**

SHORT STRETCH BREAK

- **Session Two: Ongoing myeloma care**

SESSION ONE

#1 Message



Stay at home

with

- **Hand washing**
- **Physical distancing**
- **Social networking**

COVID-19 BASIC INFORMATION

- Novel Coronavirus
- Highly infectious
- Spread by droplets from coughing/ sneezing
- Transmission in air and from surfaces
- Biggest risk: close person-to-person transfer
- Additional features such as: loss of smell; skin rashes;
GI symptoms; mental problems

Polling Question

Are you still sticking with “stay at home” guidelines?

1. Yes

2. No

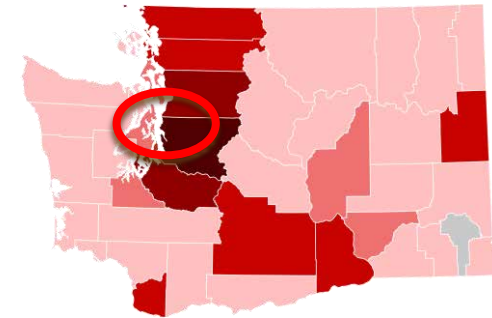
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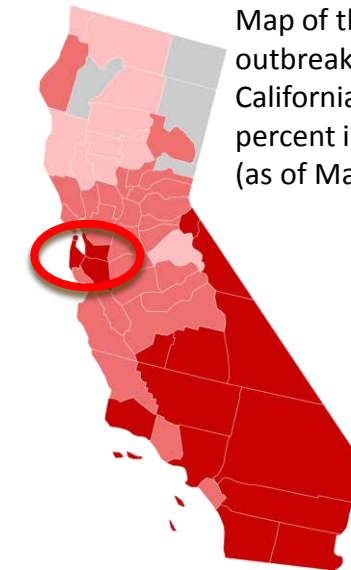
Timeline for spread of COVID-19



Likely spread since November 2019 in Wuhan, China



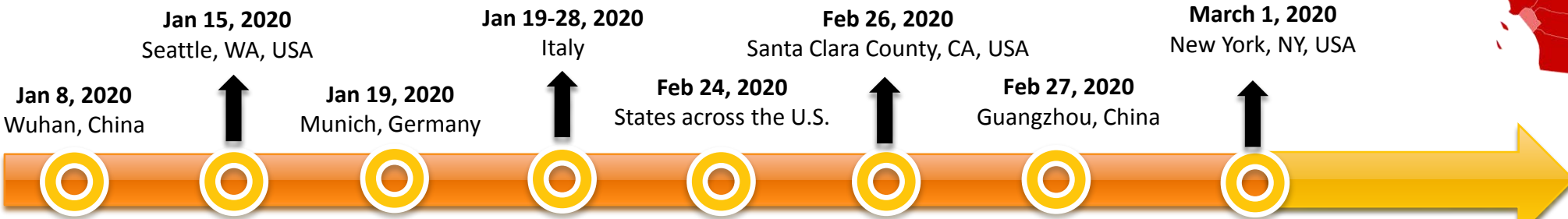
Map of the outbreak in Washington state by percent infected (as of April 23)



Map of the outbreak in California by percent infected (as of May 4)



Map of the outbreak in New York state by percent infected (as of May 4)



Sources of Infection

Sources

➤ Travel from Hotspot

- China, Europe, Other

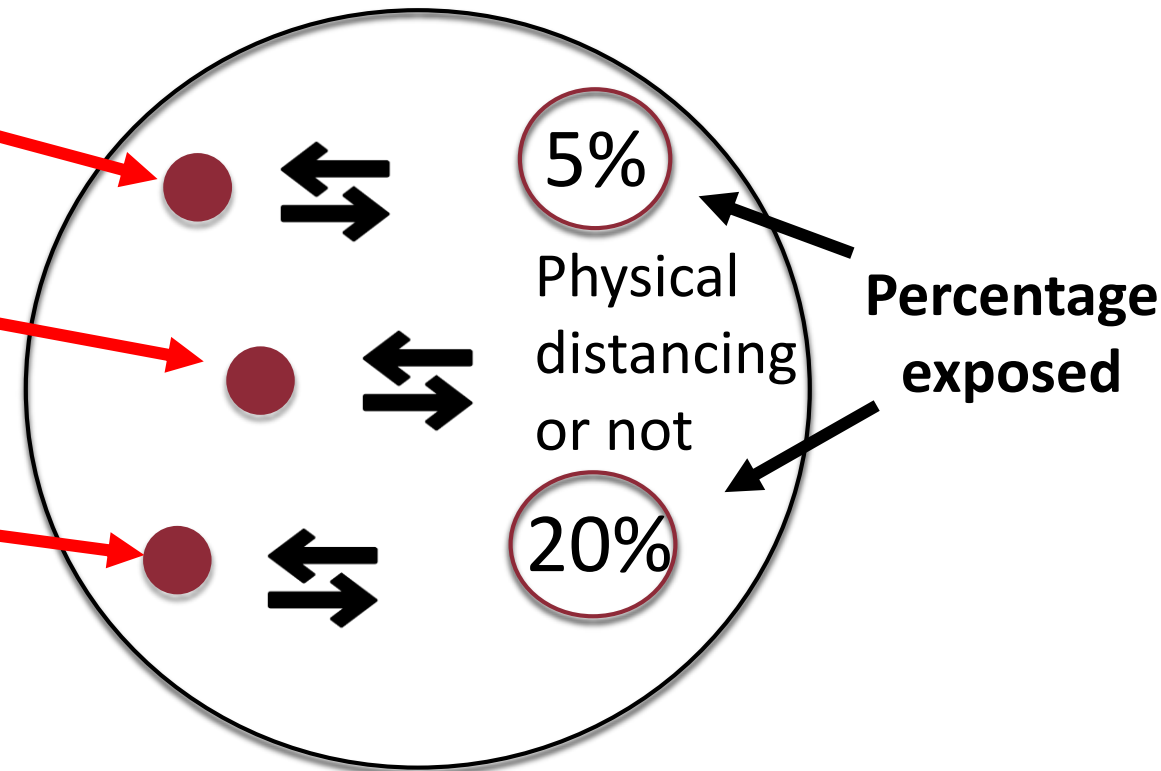
➤ Superspreader

- Especially in large group setting

➤ Spread within Risk Groups

- Nursing homes/ Medical settings
- High density living/ working
- Ships/ planes/ trains/ truck drivers
- Public places: religious, restaurants, stadiums, malls, large meetings
- Informal economy: poor/ immigrant

Local Population



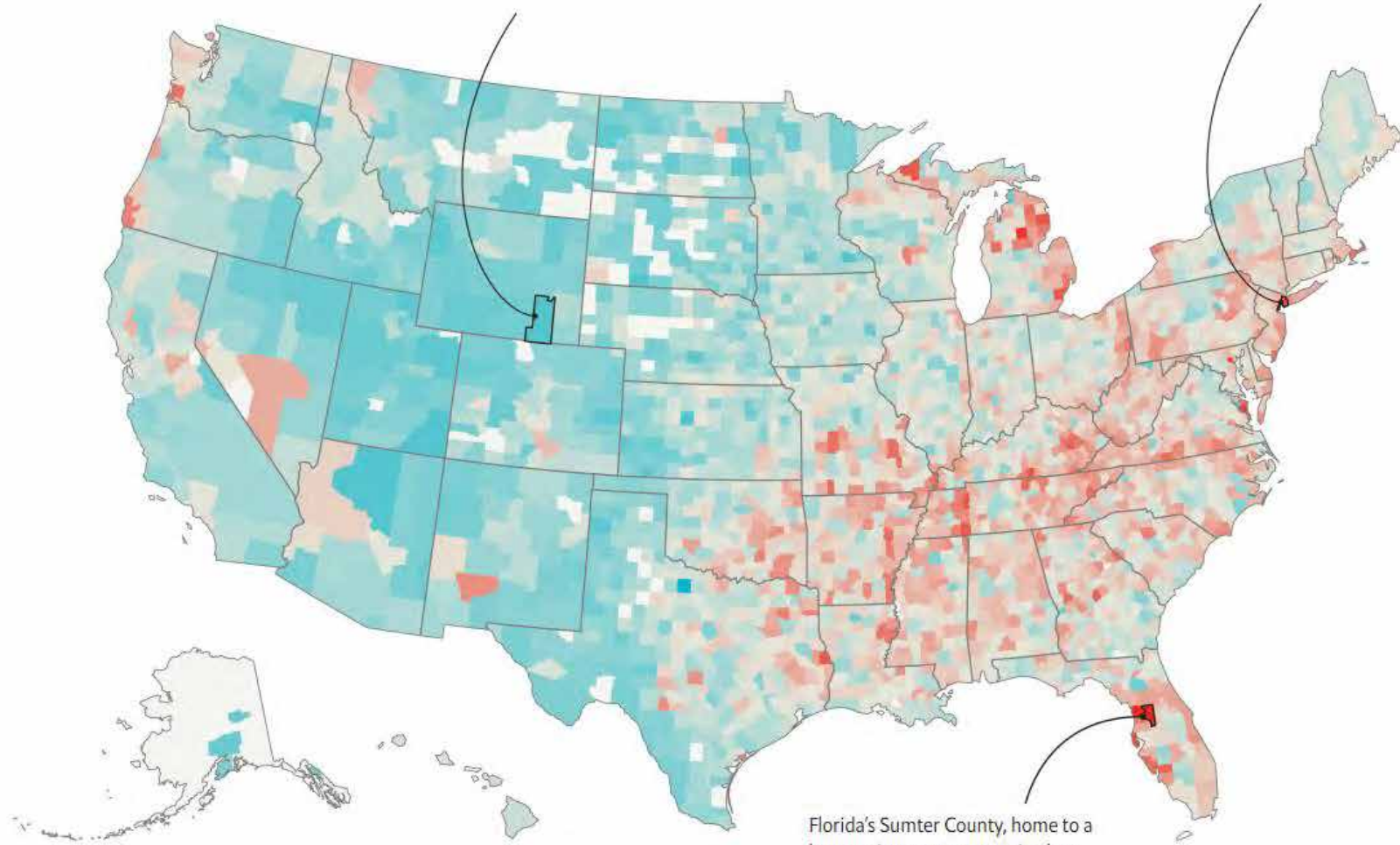
Graphic detail: Vulnerability to COVID-19

United States, predicted covid-19 case-fatality rate, %



One-third of residents in thinly populated Albany County, Wyoming are university students

New York's high population density made it particularly vulnerable to covid-19



Florida's Sumter County, home to a huge retirement community, has the highest median age in America

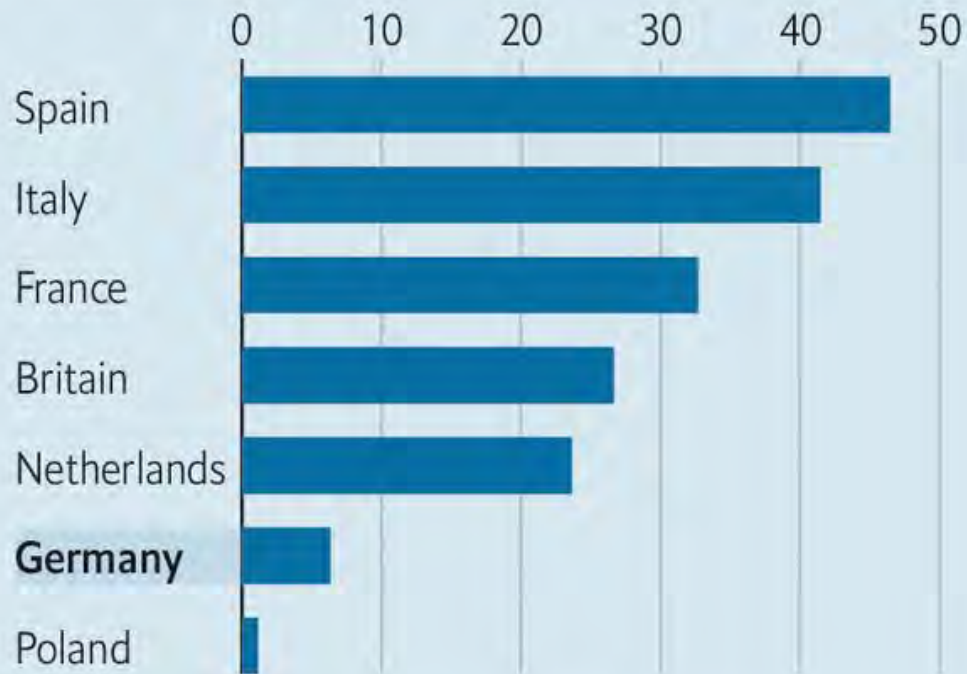
The South is likely to have America's highest death rate from COVID-19.

It has unusually unhealthy residents and few ICU beds.

Graphic detail: COVID-19 in different countries

Germany versus germs

Covid-19 deaths per 100,000 population
To April 22nd 2020



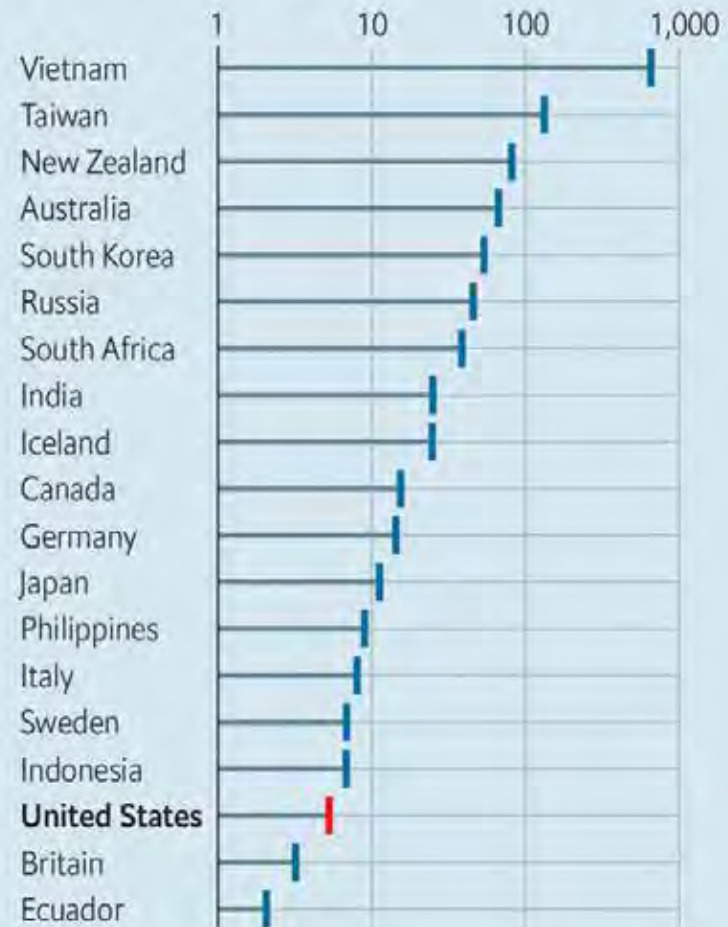
Sources: Johns Hopkins University CSSE; PHE/NHS

The Economist

Source: The Economist – April 25, 2020

Combing through haystacks

Tests per confirmed case of covid-19
To April 21st 2020*, log scale



Source: Our World In Data

*Or latest available

The Economist

Medical factors for serious COVID-19 infection

- Age > 65 years
- Hypertension/ cardiac issues
- Obesity
- Diabetes (Type-2)
- Underlying lung (\pm smoking/vaping) or kidney disease
- • Cancer diagnosis
- Contact with high risk sources (new mutations?)
- Nursing home
- High density living/ working
- African American, Hispanic or American Indian

Food Security

For Everyone

- Grocery trips
- Home Delivery

For Disadvantaged

- Home alone
- Disabled
- Lost job
- Poor/homeless



COVID-19 Emergency Food Assistance Program



A new program!



Team Rubicon will provide complimentary and contact-free delivery of food, groceries and critical supplies to your place of residence when you need it



\$500

One-time grant to pay for food, including groceries, food delivery or pickup, and medically tailored meals for qualified patients.



The patient, caregiver or member of the care team can apply and eligibility determinations are made at the point of application in most cases

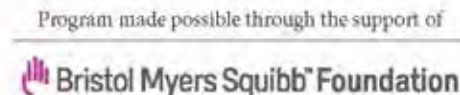


Apply online at
<https://teamrubiconusa.org/applynow>

COVID-19 Emergency Food Assistance Program

The program supports patients with cancer, multiple sclerosis or rheumatoid arthritis who are unable to afford or access food or nutritional needs due to COVID-19. Qualified patients will receive a one-time grant in the amount of \$500 to cover groceries, food delivery or pick up, and medically tailored meals and can request complimentary delivery of food and other critical supplies directly to their place of residence by one of TR's Greyshirt volunteers. Eligible patients include those who are undergoing active treatment, scheduled to begin treatment in 60 days, or have been in treatment in the last 6 months. Each patient must also be a US citizen or permanent resident, residing in the US or a US territory.

For people with
cancer
rheumatoid arthritis
multiple sclerosis
Who cannot access
or afford food due to
COVID-19



Polling Question

If you are a myeloma patient, have you tested positive for COVID-19?

1. Yes

2. No

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Risk factors for myeloma patients

- Need for urgent care (increased exposure risk)
- Active myeloma needing new therapy (at diagnosis/ relapse)
- Ongoing or recent ASCT
- Cellular therapies
- Poor bone marrow reserves
- Use of higher dose steroids
- Low vitamin D levels



Strategies to reduce risk during crisis

- Use telemedicine or equivalent
- Limit lab testing or do safely
- Temporarily reduce/ eliminate IV bisphosphonate (Zometa[®] / Aredia[®])
- Modify therapy to reduce risk of neutropenia
- Use more oral drugs such as ixazomib (Ninlaro[®])
- Limit ASCT and/or IV/subcutaneous therapies if possible
- Reassess pros/cons of daratumumab (Darzalex[®])
- Be aware that clinical trials can be modified

Polling Question

Have you used telemedicine or equivalent?

1. Yes

2. No

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Thinking of the way forward...

**What do we need
to know?**

What do we need now

- How many individuals have been exposed
 - In your community
 - Across the U.S.
 - Globally
- Risk factors for infection: congregate settings/ large gatherings with high population density (e.g. NY City), poverty, meat packing plants, exposure resulting from “essential” work ...
- Risk factors for serious consequences:
 - Hypertension/ obesity/ diabetes: ACE 2 related
 - Racial factors: African Americans, Hispanic, American Indian ...

Role of Antibody Tests

- The FDA just approved a new Roche antibody test method.
- “Roche gets emergency approval for COVID-19 antibody test as FDA vows closer oversight”
<https://www.cbsnews.com/news/roche-coronavirus-antibody-test-fda-approval-accuracy>
- Interesting new research with llamas indicating that they could become coronavirus heroes. Small llama antibodies can detect the key spike protein of COVID-19 better than larger human antibodies. These animal antibodies can be fused with human equivalents and perhaps be used for both testing and treatment. One never knows which research will turn out to be transformative!
- “Hoping Llamas Will Become Coronavirus Heroes”
- <https://www.nytimes.com/2020/05/06/science/llama-coronavirus-antibodies.html>
- **“Should You Get an Antibody Test?: A user’s guide to the immune system”**
- <https://www.theatlantic.com/health/archive/2020/05/coronavirus-antibody-test-immunity/611005/>

Dr. Durie Blog – May 7, 2020

<https://www.myeloma.org/cure-blog/re-focusing-myeloma-care-covid-19-world>

Question: Can I go for a walk?

- Yes!
- Respect “physical distancing”
- Enhance local “social” connections
- Many experts agree about the value

Bottom line: Regular exercise is helpful!



CT Support Group Virtual GoToMeeting



Over 75 support groups are now holding monthly virtual GoToMeetings through the IMF

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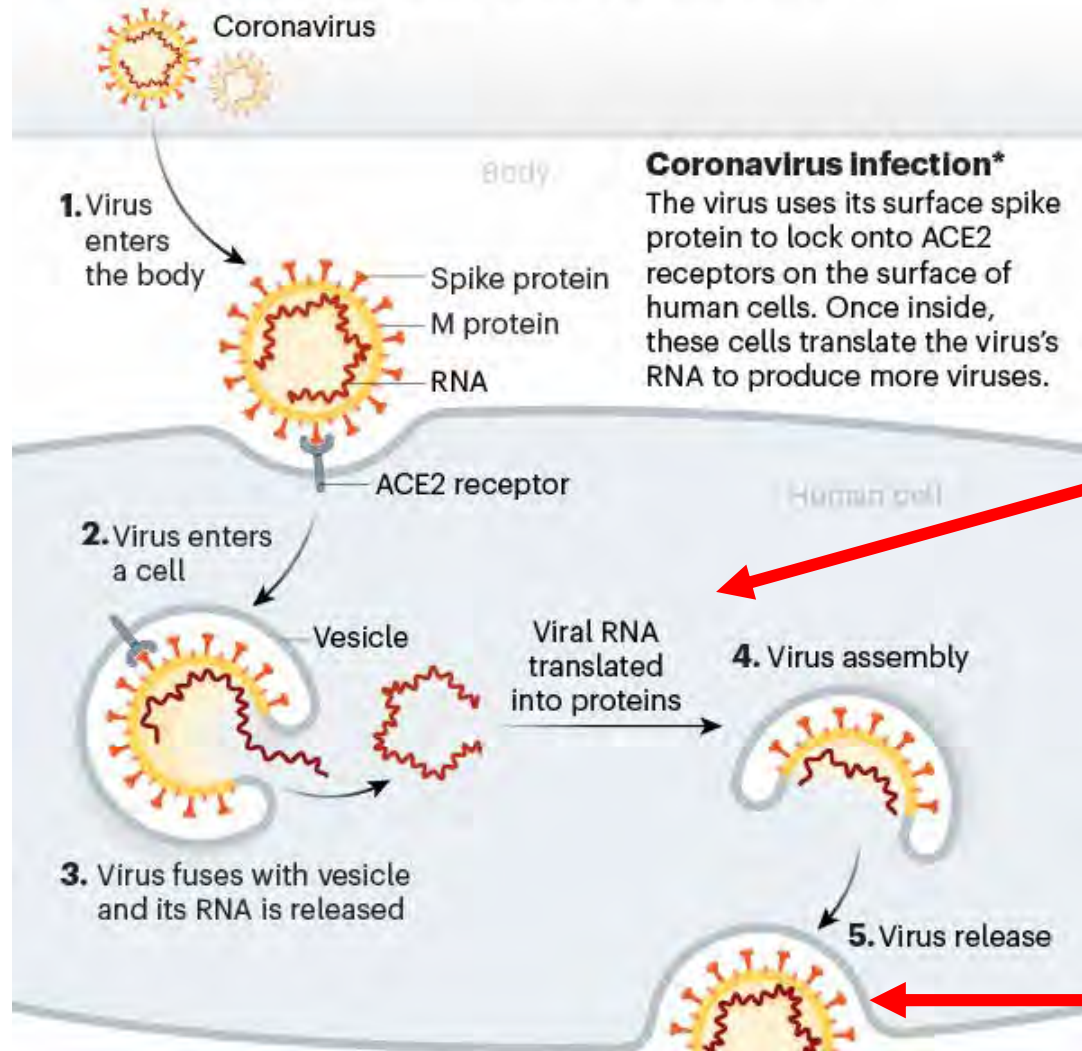
Potential treatments for COVID-19

- Remdesivir and other anti-virals
 - Selinexor (Xpovio[®])
 - Plasma infusions or hyperimmune immunoglobulin*
 - Tuberculosis vaccination (Bacillus Calmette–Guérin)
 - Vaccine: multiple developers including Oxford (UK) team, Janssen, Sanofi, GlaxoSmithKline, and biotech companies
- * Takeda joint partnership with Biotest and partners

Vaccine Basics: How We Develop Immunity

VACCINE BASICS: HOW WE DEVELOP IMMUNITY

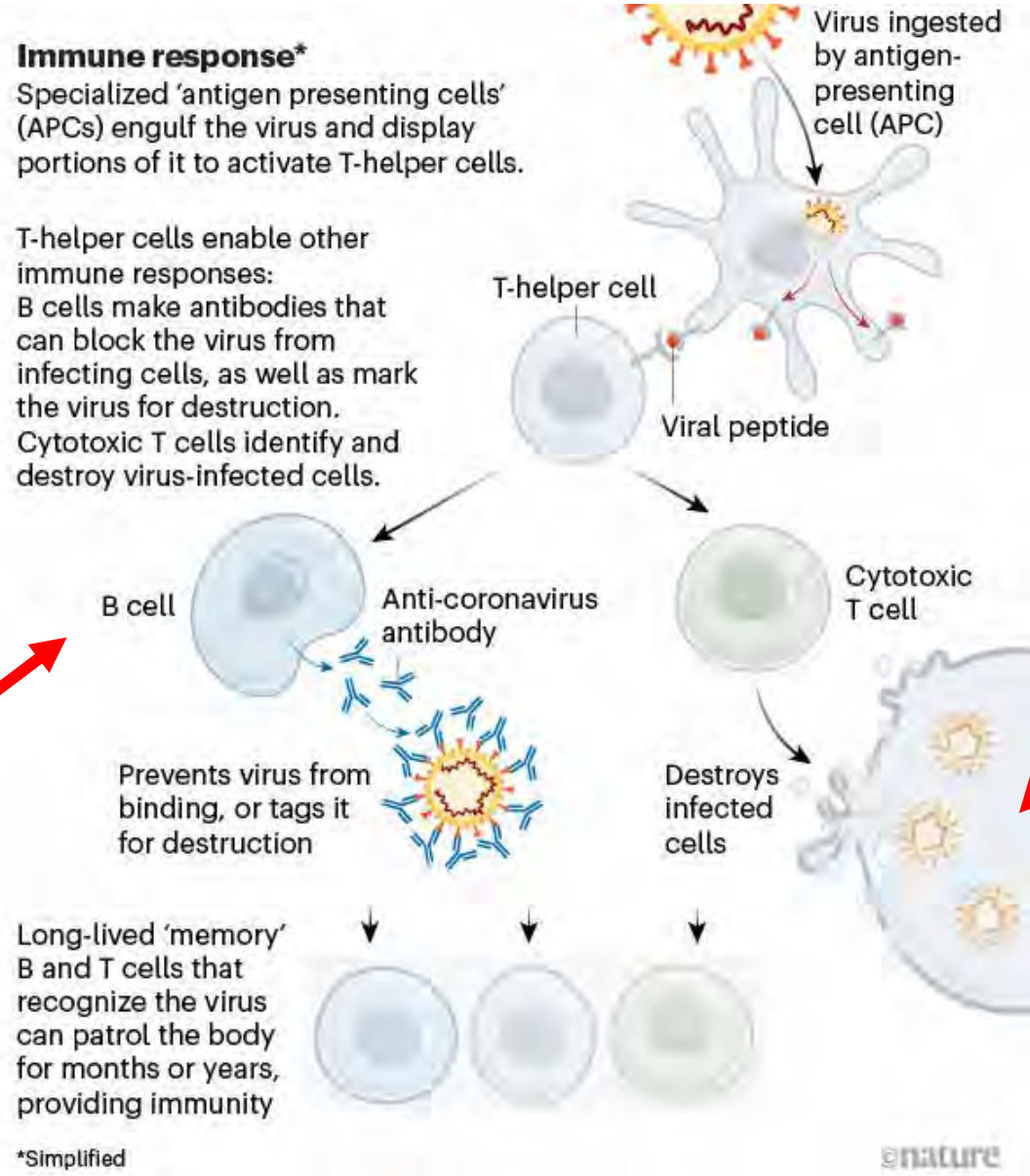
The body's adaptive immune system can learn to recognize new, invading pathogens, such as the coronavirus SARS-CoV-2.



Key RNA
from virus

New virus

Vaccine Basics: How We Develop Immunity



Destruction of COVID-19 virus!

COVID-19 antibodies

The New Abnormal

- Physical distancing continues
- Virtual social networking a requirement for everyone
- Antibody tests and COVID-19 testing required
 - Cluster testing essential
- Proper masks essential in public
- Telemedicine is new abnormal
- **For myeloma:** treatment paradigm evolves
- Traveling will be carefully selected if truly needed (or required for sanity – i.e. vacation!)

Question: Can I get through this without developing COVID-19 infection?

- Yes – with care and good luck!
- Population infection level = 2-5% or 10-20% in high risk community
- The key is to avoid becoming part of a local cluster!
- When local clusters are “contained,” the COVID-19 infection process subsides

The goal is to stay healthy until a vaccine is available (like in New Zealand)



Myeloma Patient Safety and the Coronavirus

As the COVID-19 respiratory virus spreads around the world, please know that the IMF is here for you.

People living with myeloma are at an increased risk. “Myeloma patients have compromised immune systems and are highly vulnerable to new infections,” says IMF Chairman Dr. Brian G.M. Durie.

“It is important to be proactive and guard against infection from unknown sources.”

On this page, you will find updated guidance to keep you safe. Featured are Dr. Durie’s blogs and FAQs, aimed specifically at myeloma patients, and links to the best sources of COVID-19 news.

There is currently no vaccine against COVID-19, so it is important for myeloma patients and their families to minimize their risk for contracting the virus. Practices to minimize your risk include:

<https://www.myeloma.org/covid19-myeloma-patients>

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Question: How can resilience help in the face of COVID-19 infections?

- **A** ccept that this is a key challenge!
- **B** egin to asses how COVID-19 impacts you and your family/friends/groups
- **C** lear action plans are required!

Bottom line: By taking time to focus and come up with the best solutions, resilience can be enhanced

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

Additional IMF Resources

Acronyms & Abbreviations:

<https://www.myeloma.org/sites/default/files/resource/Acronyms.pdf>

Myeloma Terms & Definitions:

https://www.myeloma.org/sites/default/files/resource/glossary_0.pdf

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Take a quick stretch!

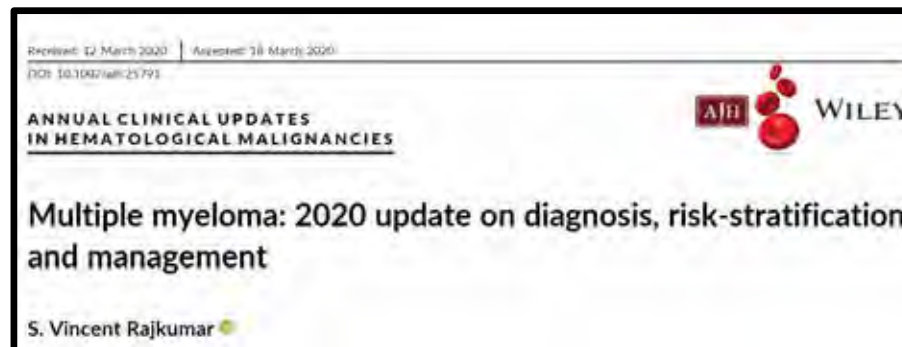
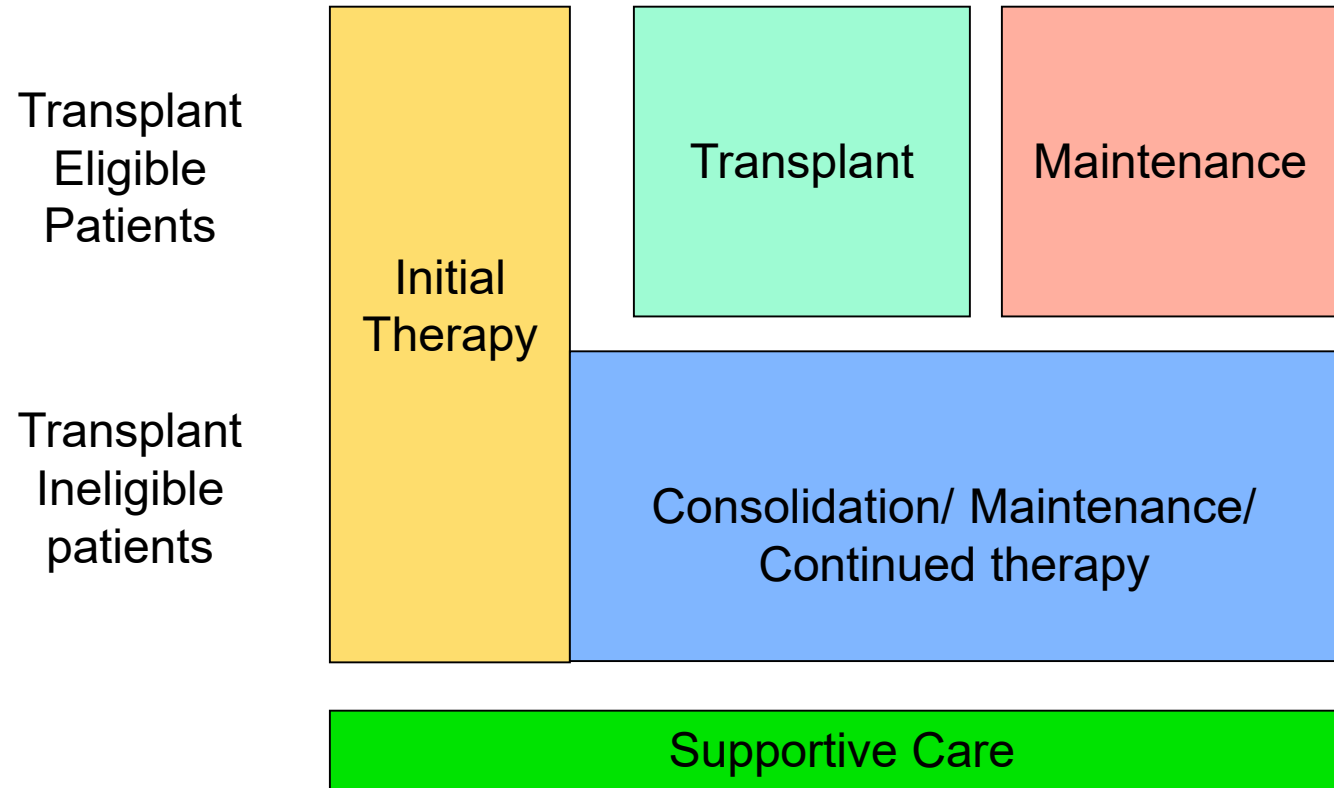


SESSION

TWO

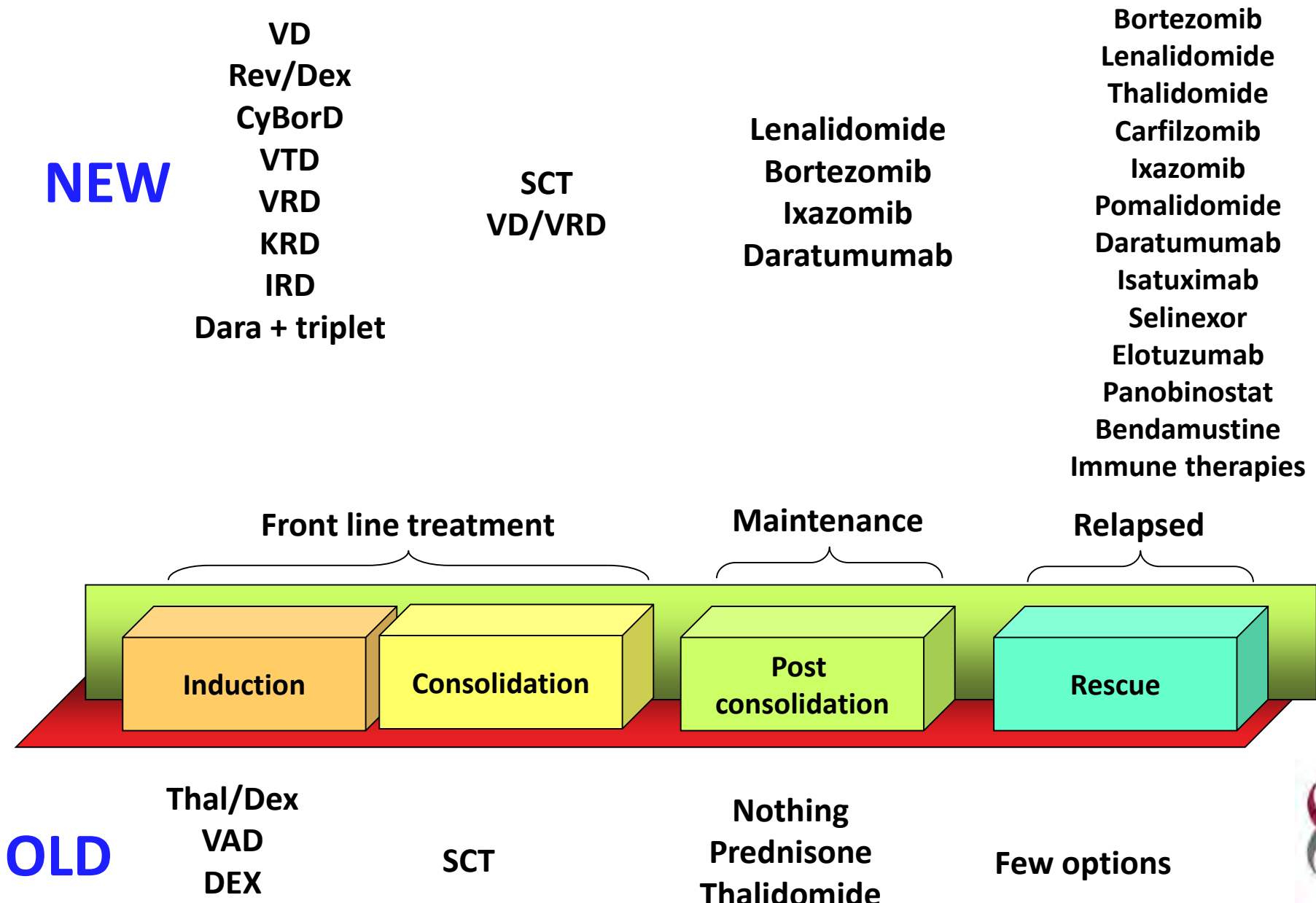
FRONTLINE THERAPY

Managing Myeloma: The Components



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

Treatment Combinations: Now and Then



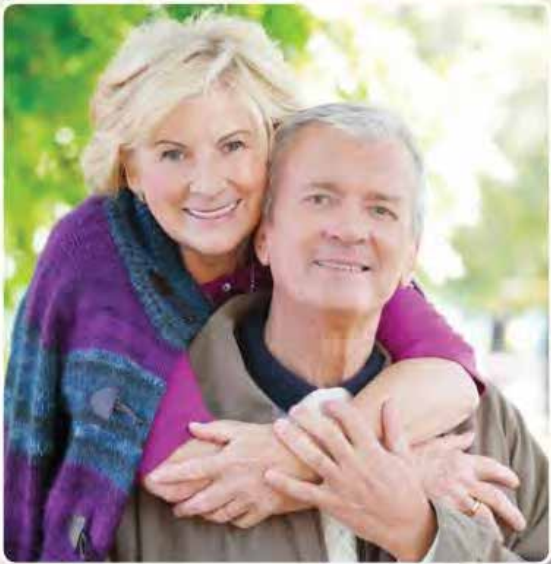
Frontline Therapy

- What is best?
- Are dara + triplet regimens the way forward?

Darzalex® (daratumumab)

Multiple Myeloma | Cancer of the Bone Marrow

 *Understanding*
DARZALEX[®]
(daratumumab) injection

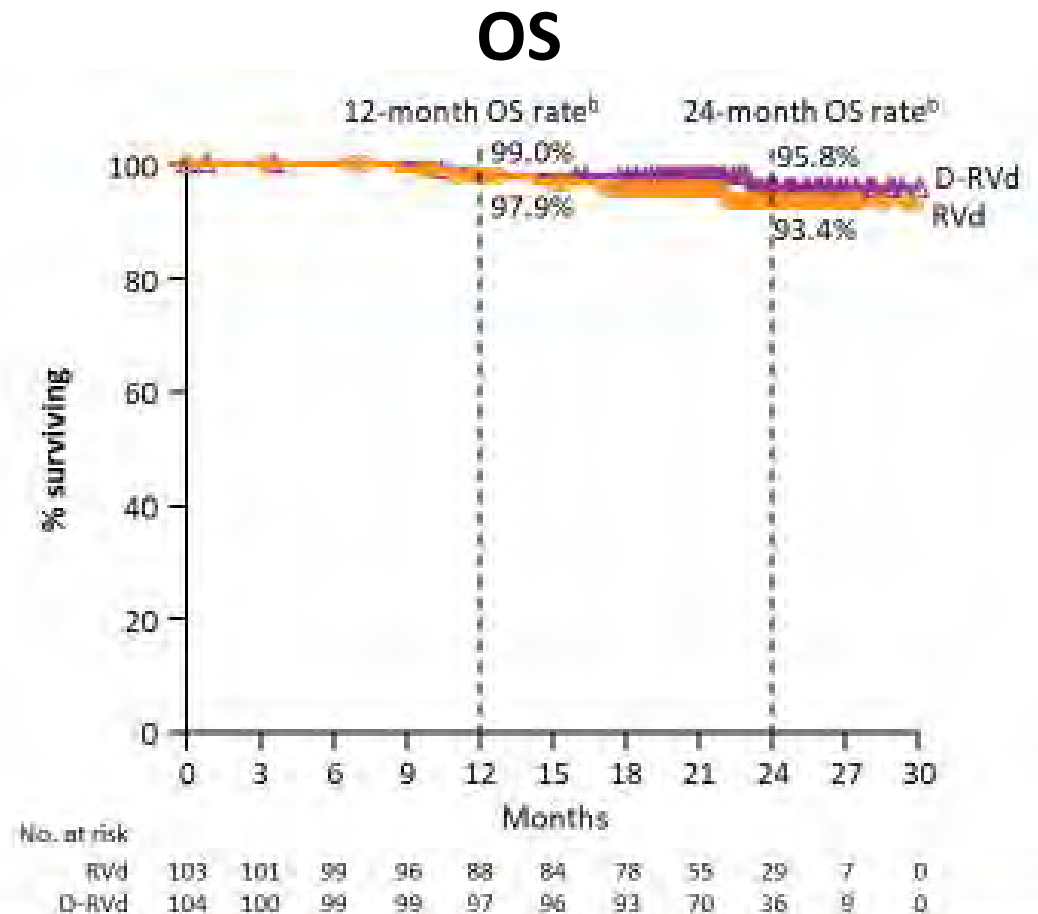
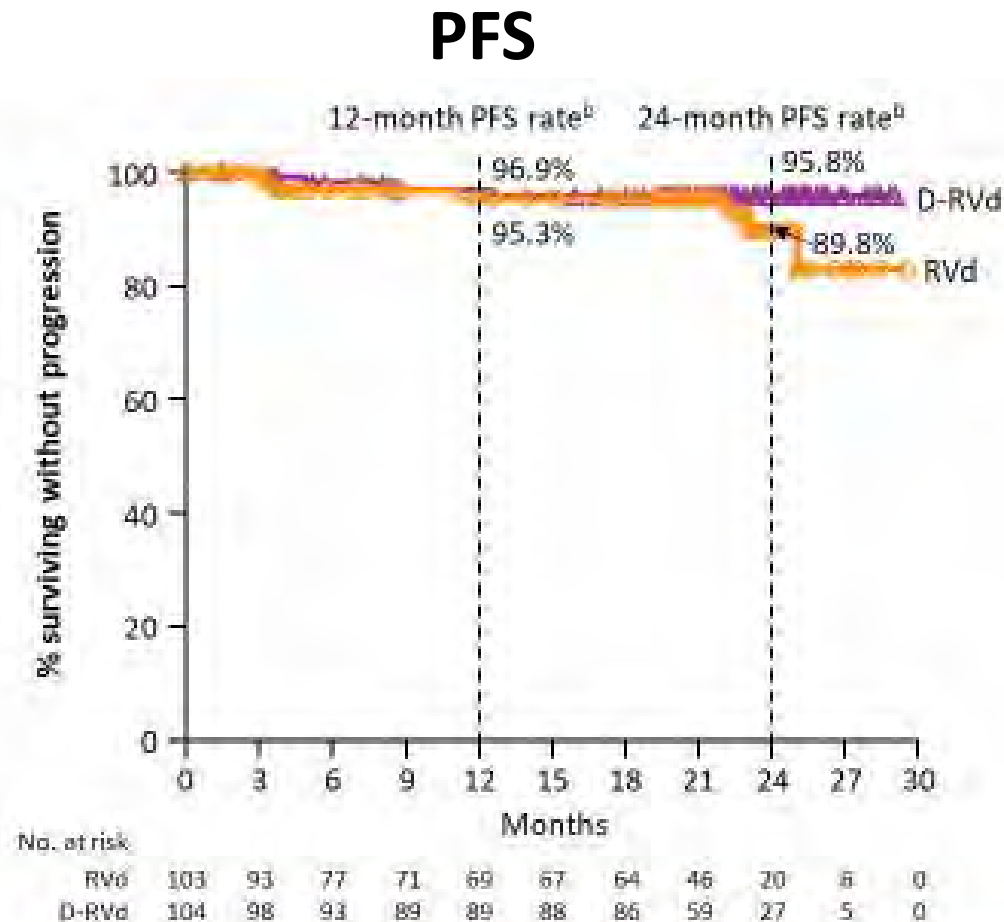


A publication of the International Myeloma Foundation

Improving Lives **Finding the Cure**

- Anti-CD38
- Now FDA approved as subcutaneous shot (DARZALEX FASPRO™)!
- Use broadly approved:
→ Frontline to relapse
- Combinations well tolerated/ manageable

ASH Abstract #691: Dara plus VRd v VRd: Griffin Study Update



Median PFS and OS not reached for D-RVd and RVd

^aITT population. ^bKaplan-Meier estimate.

Ninlaro® (ixazomib): Oral Proteasome Inhibitor

Multiple Myeloma | Cancer of the Bone Marrow

 *Understanding*
NINLARO[®]
(ixazomib) capsules

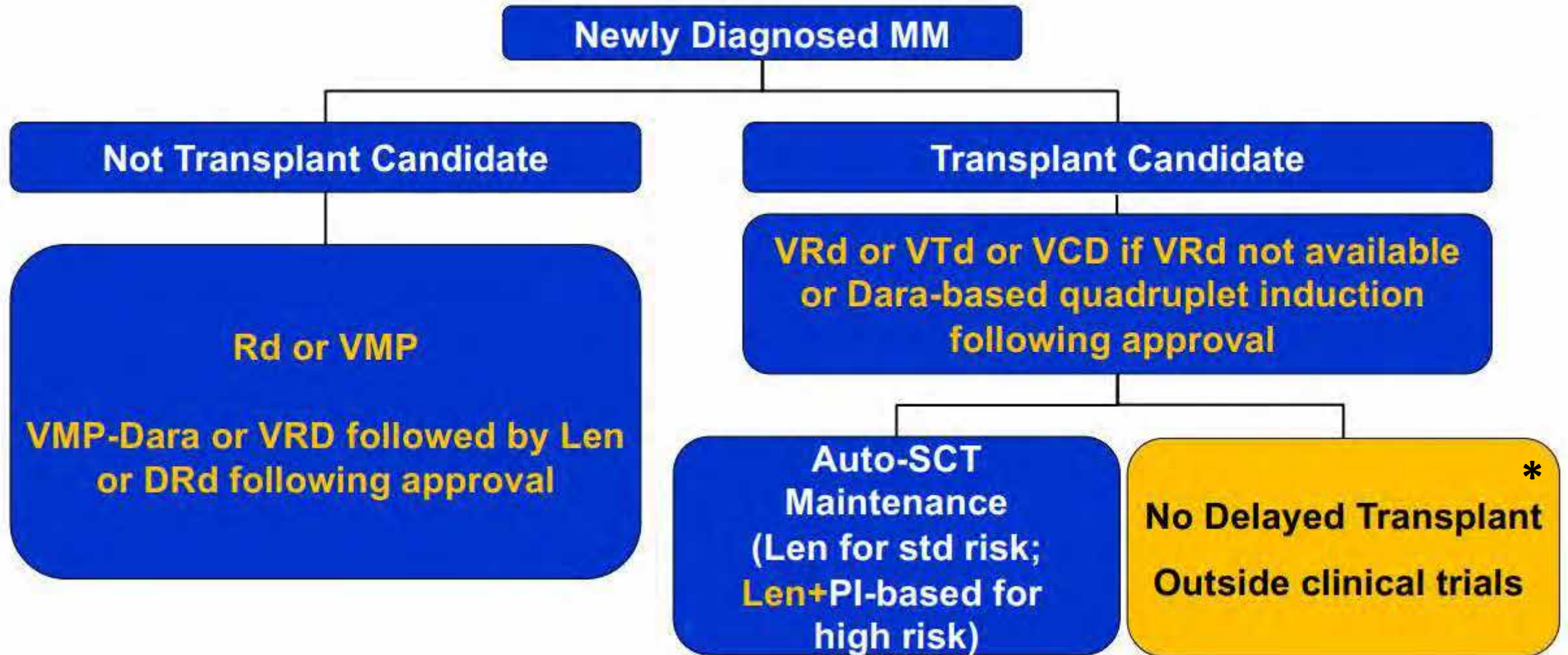


A publication of the **International Myeloma Foundation**

Improving Lives **Finding the Cure**

- Low level neuropathy
- Convenient weekly schedule
- Easily combine with other therapies
- Ongoing maintenance an advantage
- **Attractive during COVID-19 crisis**

Myeloma: Frontline Treatment



* Except for COVID-19 crisis!

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What are recommendations for maintenance?

Maintenance

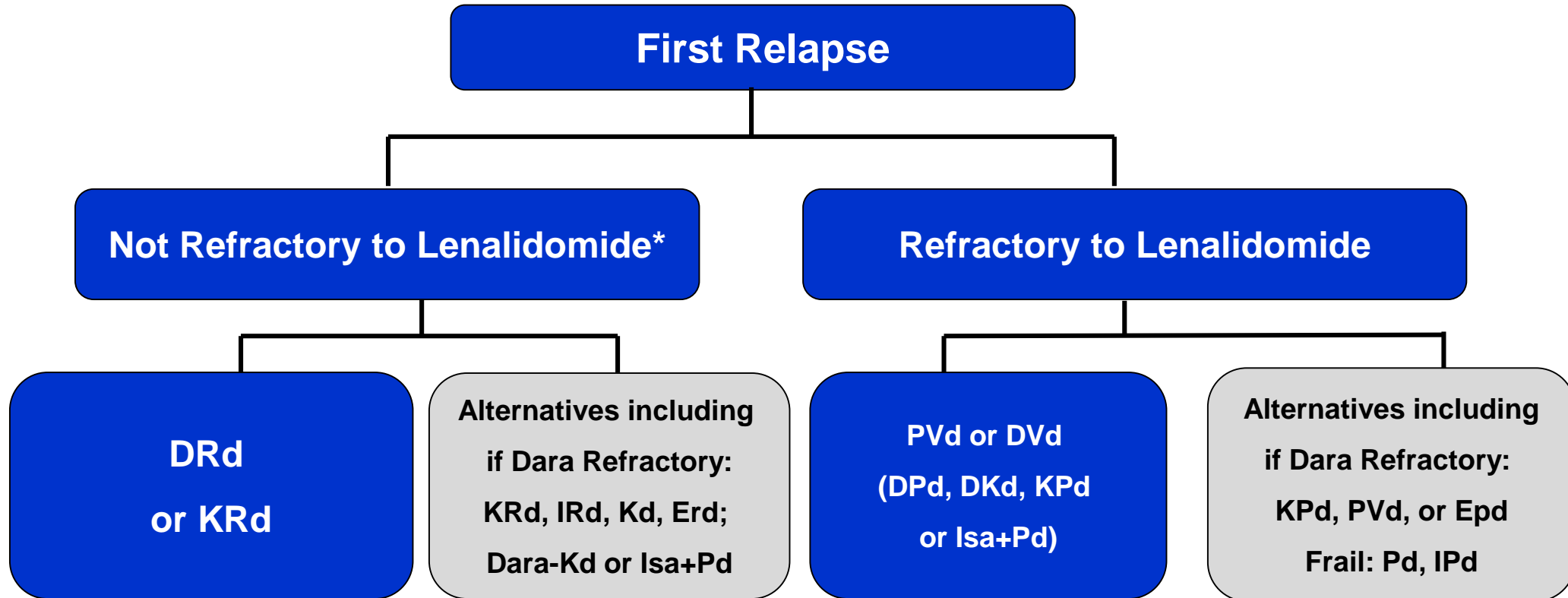
- Current Approaches
- Revlimid ± Proteasome Inhibitor
(Velcade[®] subcutaneous or Ninlaro[®])
- Modifying for side effects
- Stopping for intolerance and/or MRD +/-
or COVID-19 crisis!

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What are current relapse options?

Myeloma: First Relapse



Kyprolis® (carfilzomib)

Multiple Myeloma | Cancer of the Bone Marrow



A publication of the International Myeloma Foundation

Improving Lives **Finding the Cure**

- New combo with dara/dex
- Very active:
 - standard/ high risk
 - IMiD free!
 - Potent early
- Schedule can be
 - weekly Kyprolis
 - Dara now SQ

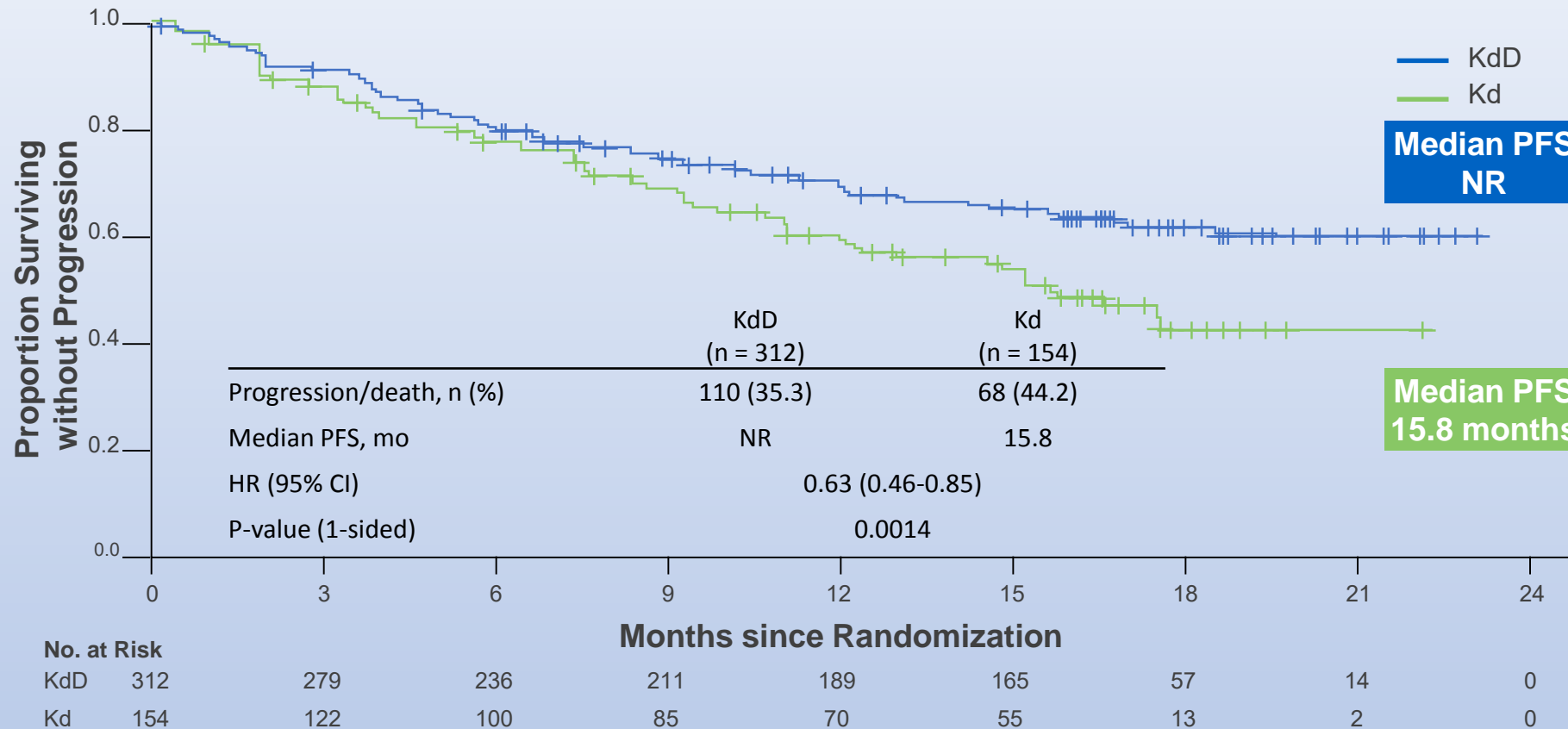
Polling Question

**Have you used the new
Kyprolis/daratumumab/dex treatment
(CANDOR Trial)?**

1. Yes

2. No

Dara Kd Demonstrated Significantly Longer Progression-Free Survival Versus Kd: CANDOR Study



Median OS was not reached in either arm at a median follow-up of 17 months (HR, 0.75; 95% CI, 0.49–1.13; P=0.08)

Treatment with KdD resulted in a 37% reduction in the risk of progression or death vs Kd in patients with RRMM

CI, confidence interval; Kd, carfilzomib and dexamethasone; KdD, carfilzomib, dexamethasone, and daratumumab; NE, not estimable; NR, not reached; PFS, progression-free survival; PI, proteasome inhibitor; RRMM, relapsed and/or refractory multiple myeloma.
 Usmani et al. Presented at: 61st American Society of Hematology Meeting and Exposition; December 7-10, 2019; Orlando, FL. Abstract LBA-6.

Sarclisa® (isatuximab)

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Improving Lives **Finding the Cure**

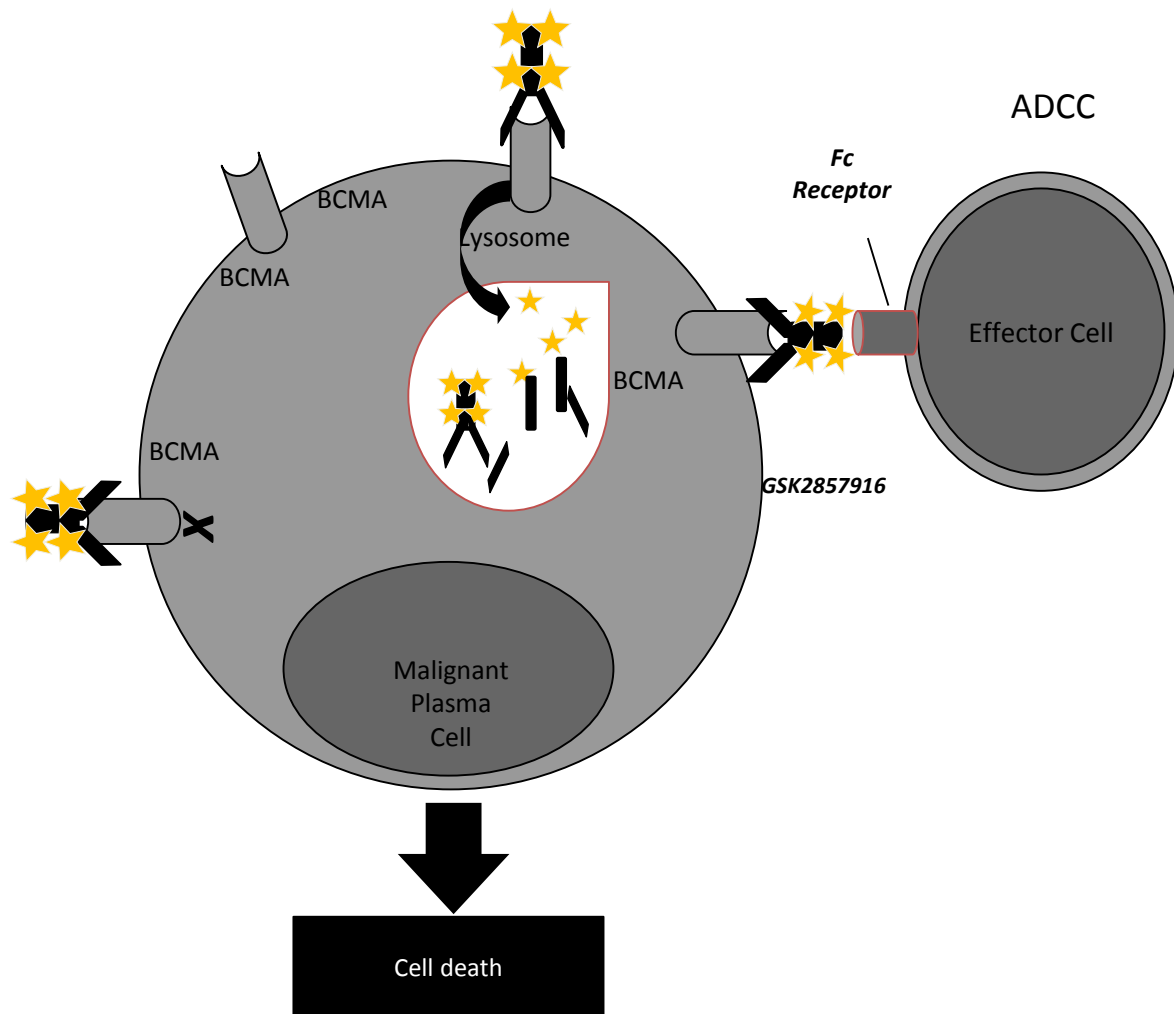
- Alternate anti-CD38 MoAB
- Well tolerated IV infusion protocol
- Approved in combo with pom/dex (ICARIA study)
- Early use post IMiD (Revlimid®)/ PI beneficial

Belantamab mafodotin

- Anti-BCMA MoAB – drug conjugate
- Active even if lower BCMA expression
- Recruits local anti-myeloma immune response
- Off-the-shelf anti-BCMA product
- Corneal toxicities manageable
- Many combos tested/ feasible
- FDA approval expected soon

Belatamab Mafodotin (GSK2857916): a BCMA-Targeted Antibody Drug Conjugate

**EPA
open**

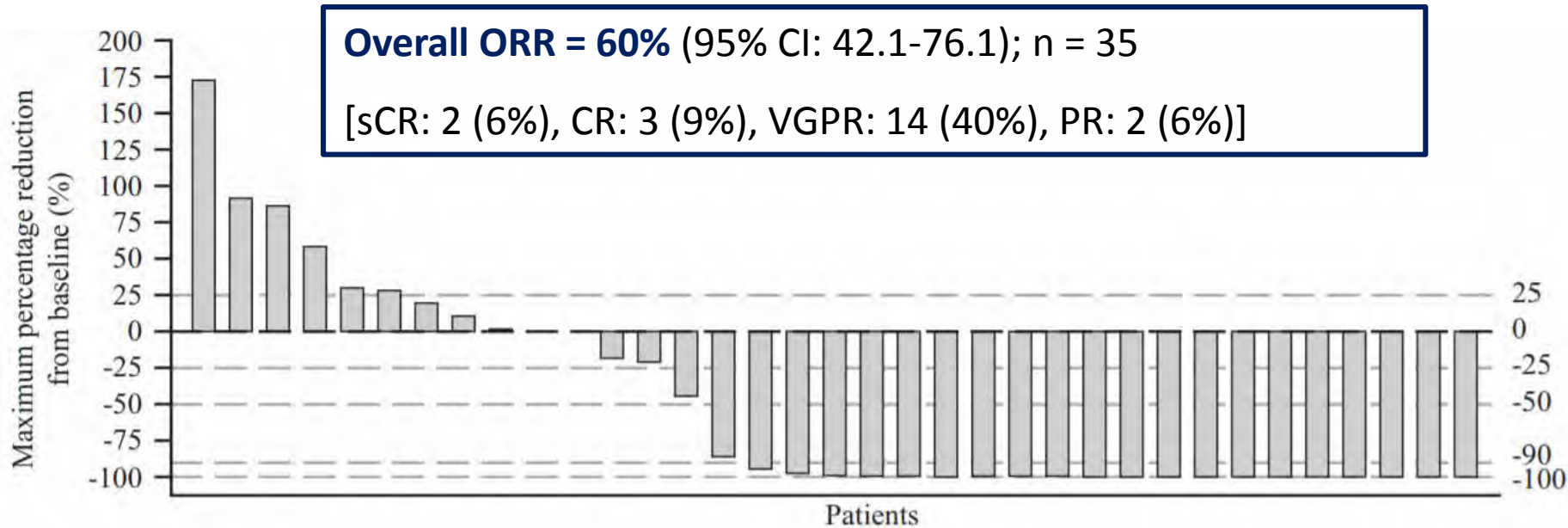


- Fc region of the Antibody**
 - Target specific
 - Enhanced ADCC
- Linker**
 - Stable in circulation
- Drug**
 - MMAF (non cell permeable, highly potent auristatin)

- Mechanisms of Action:**
1. ADC mechanism
 2. ADCC mechanism
 3. Immunogenic cell death

Belantamab Mafodotin: Efficacy in Multiple Myeloma

DREAMM – 1: single agent dose expansion results
Dose 3.4 mg/kg every 3 weeks, 1hr infusion



Heavily pretreated - 89% double refractory;
- 34% double + dara refractory
29% with high-risk cytogenetics

Efficacy in refractory populations

Patients refractory to IMiD and PI (n = 32)

ORR: 56.3%
(95% CI: 37.7-73.6)

Patients previously treated with dara AND refractory to IMiD and PI (n = 13)

ORR: 38.5%
(95% CI: 13.9-68.4)

Empliciti® (elotuzimab)

Multiple Myeloma | Cancer of the Bone Marrow



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Improving Lives **Finding the Cure**

- Best tolerated MoAB!
- Synergistic with IMiDs
- Impressive results with pom/dex combo
- Attractive in resistant setting

Xpovio® (selinexor)

Multiple Myeloma | Cancer of the Bone Marrow



A publication of the **International Myeloma Foundation**

Improving Lives **Finding the Cure**

- Novel mechanism: also anti-viral
- Active in triple refractory
- Oral dosing convenient
- Unique side effects require proactive care
- Can broadly be partnered
- BOSTON data support early/ combo benefit



Polling Question

Have you taken Xpovio[®] (selinexor)?

1. Yes

2. No

Myeloma: Second or higher relapse

First Relapse Options



- Any first relapse options that have not been tried

(2 new drugs; triplet preferred)

Isa-PD, or DPd, or DKd, or KPd

Additional Options



- VDT-PACE like anthracycline containing regimens
- Melphalan/ melflufen
- Adding Panobinostat
- Quadruplet regimens
- CAR T: bb2121, J&J Legend
- Bispecific
- Conjugated BCMA
- Selinexor

Referral for clinical trials always if available

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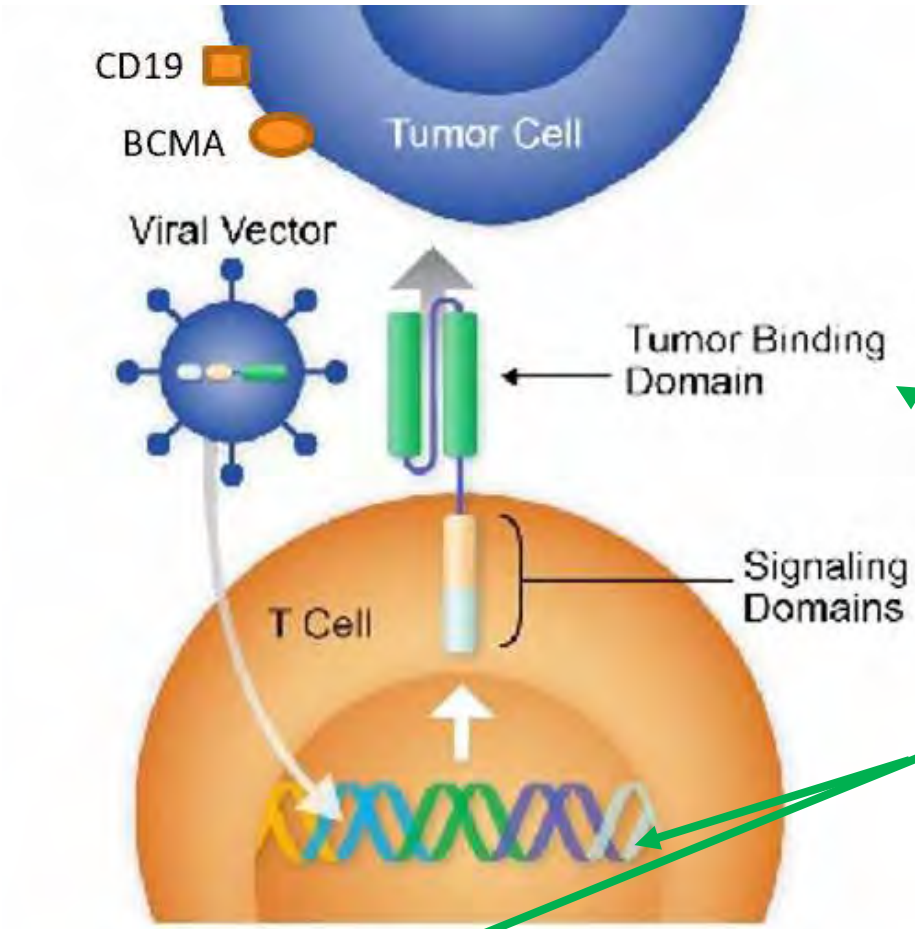


Immune therapy results dominated ASH 2019

- **CAR T Therapy**
 - Bb2121
 - J&J Legend product
- **Bispecific T Cell Engagers**
- **MoAb/drug conjugate: GSK 2857916 (“belamaf”)**

Chimeric Antigen Receptor (CAR) Therapy for Multiple Myeloma

*Is CAR T
Therapy a
Game Changer
in MM?*

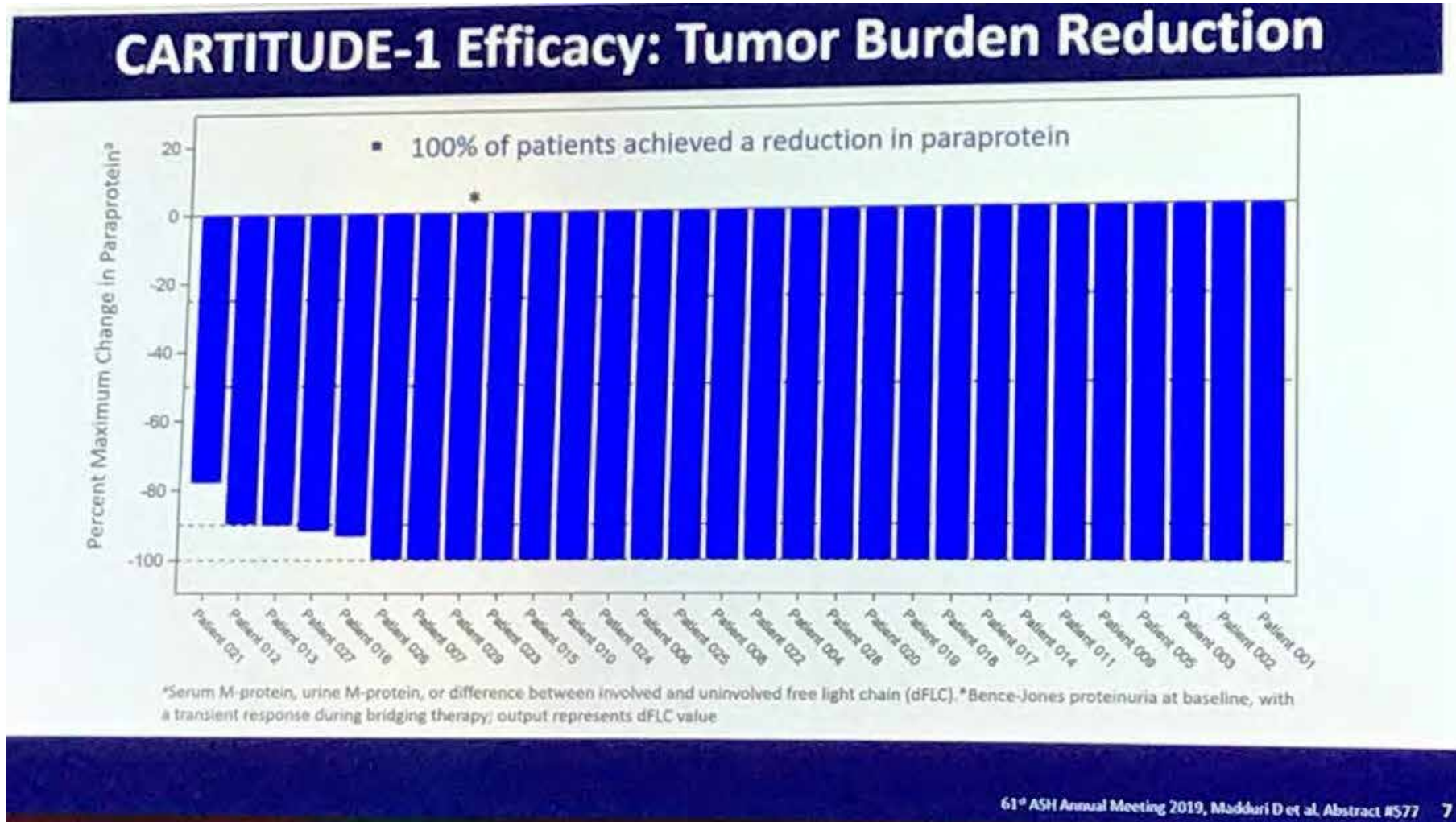


**BCMA
sequence
inserted
into DNA**



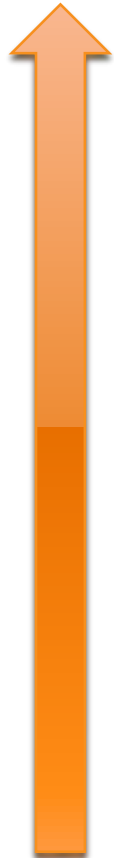
Kochenderfer, et al. 2016.
Ali. Blood. 2016;128:1688.

Time for a pause to consider 100% responses!

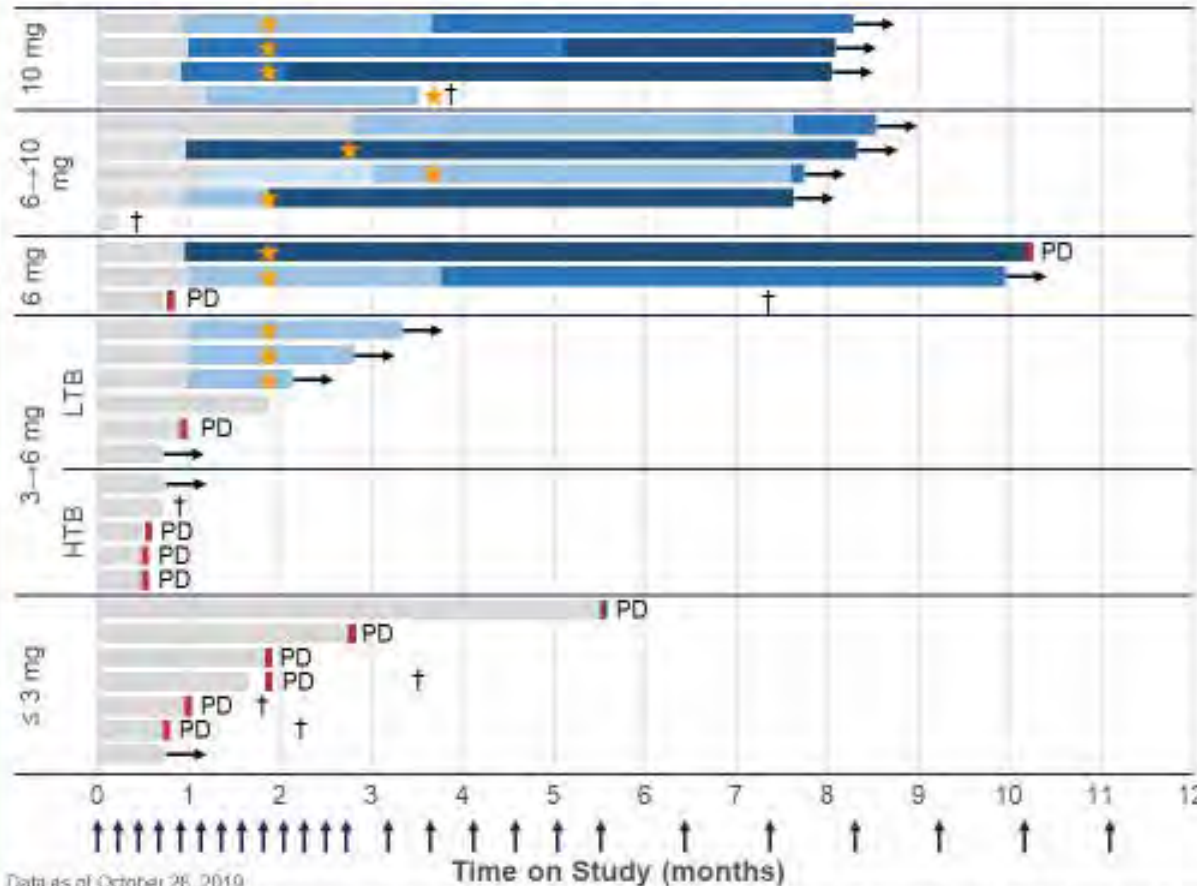


ASH Abstract #143: Anti-BCMA [2] T Cell Engager (TCE): Phase 1 Trial of CC 93249

Dose Response



RESPONSE OVER TIME



- Median time to first response was 4.1 weeks (range 4.0–13.1)
- 5 of 30 (16.7%) patients achieved an MRD-negative sCR/CR
 - Of 13 responding patients, 92.3% achieved MRD negativity ($\leq 1/10^5$) in the bone marrow on or before C4D1 by Euroflow^a



Data as of October 26, 2019

^a MRD negativity by Euroflow analysis was reported only if a minimum sensitivity of ≤ 1 tumor cell in 10^5 nucleated cells was achieved and in patients who had ≥ 1 baseline and ≥ 1 post-baseline MRD assessment: HTB, high tumor burden (defined as $> 50\%$ bone marrow plasma cells or > 5 extramedullary lesions); LTB, low tumor burden (defined as $\leq 50\%$ bone marrow plasma cells and ≤ 5 extramedullary lesions); MR, minimal response.

ROLE OF IMMUNE THERAPIES

Clearly active in relapsed patient population

How should BCMA targeted therapy be used and sequenced?

Is earlier use the best approach?

- **For consolidation?**
- **At first relapse?**

2020 EXPECTATIONS

Potential New Approvals

- GSK
- bb 2121 CAR T
- Legend CAR T
- Melflufen

Longer Term Results

- Cassiopeia
- Griffin
- Dara KRd
- CESAR/ASCENT follow-up

New Agent Data

- Venetoclax
- I¹³¹ CLR 140L
- Iberdomide
- Several others

Additional IMF Resources

Acronyms & Abbreviations:

<https://www.myeloma.org/sites/default/files/resource/Acronyms.pdf>

Myeloma Terms & Definitions:

https://www.myeloma.org/sites/default/files/resource/glossary_0.pdf

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