IMF PATIENT AND FAMILY WEBINAR

Brian G.M. Durie, MD
Rafat Abonour, MD
Paul Richardson, MD
Yelak Biru

Saturday, March 14\textsuperscript{th}, 2020
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TODAY’S SPEAKERS

Saturday
MARCH 14
2020

IMF PATIENT & FAMILY WEBINAR
Watch the LIVESTREAM: 8:00 AM PT/10:00 AM CT/11:00 AM ET

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Cedars-Sinai Medical Center, Los Angeles, CA

Paul Richardson, MD
Dana-Farber Cancer Institute, Boston, MA

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University of Indiana, Indianapolis, IN

Yelak Biru
Patient Advocate, NW Arkansas
TOPICS FOR DISCUSSION

• Coronavirus: COVID-19
• Frontline therapy
• Maintenance
• Approaches to Relapse
• Novel Therapies

Q&A after each topic
COVID-19
COVID-19

Symptoms of Concern

• Fever (90%)
• Dry Cough (70%)
• Extra Tiredness (30%)

Note: Cold/Flu Symptoms only 3%
COVID-19

Avoiding Exposure

- **Social Distancing:** Stay home for now
- Handwashing and don’t touch your face
- Clean surfaces including phones and screens
- Monitor family, friends and all contacts
- Avoid doctor’s offices, hospitals and large clinics
- Have a plan of action when symptoms emerge
COVID-19

Q&A
FRONTLINE THERAPY
Managing Myeloma: The Components

- Initial Therapy
- Transplant
- Maintenance
- Consolidation/Maintenance/Continued therapy
- Supportive Care

Transplant Eligible Patients

Transplant Ineligible Patients
Treatment Combinations Now and Then

**NEW**
- VD
- Rev/Dex
- CyBorD
- VTD
- VRD
- KRD
- DVTD

**OLD**
- Thal/Dex
- VAD
- DEX

**Induction**
- Thal/Dex
- VAD
- DEX
- SCT

**Consolidation**

**Post consolidation**
- Nothing
- Prednisone
- Thalidomide
- SCT
- VD/VRD

**Maintenance**
- Lenalidomide
- Bortezomib
- SCT

**Relapsed**
- Bortezomib
- Lenalidomide
- Thalidomide
- Carfilzomib
- Pomalidomide
- Dratumumab
- Elotuzumab
- HDAC
- Bendamustine

**Front line treatment**

**Rescue**
- Few options
• What is best?

• Are dara + triplet regimens the way forward?
## Daratumumab + VTD Produces Deeper Responses

Post-consolidation (D 100 Post-ASCT) Response and MRD-negative Rates: ITT.

<table>
<thead>
<tr>
<th></th>
<th>D-VTd, %</th>
<th>VTd, %</th>
<th>OR (95% CI)</th>
<th>P</th>
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<tbody>
<tr>
<td>sCR</td>
<td>28.9</td>
<td>20.3</td>
<td>1.60 (1.21-2.12)</td>
<td>0.0010</td>
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<tr>
<td>≥CR</td>
<td>38.9</td>
<td>26.0</td>
<td>1.82 (1.40-2.36)</td>
<td>&lt;0.0001</td>
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<tr>
<td>≥VGPR</td>
<td>83.4</td>
<td>78.0</td>
<td>1.41 (1.04-1.92)</td>
<td>0.0239</td>
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<table>
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<tr>
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<th>MRD-negative (10^-5)</th>
<th>MRD-negative (10^-5)</th>
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<tr>
<td></td>
<td>63.7</td>
<td>43.5</td>
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<tr>
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<td>2.27 (1.78-2.90)</td>
<td>&lt;0.0001</td>
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<tr>
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<th>≥CR + MRD-negative (10^-5)</th>
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<tr>
<td></td>
<td>33.7</td>
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<tr>
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<td>2.06 (1.56-2.72)</td>
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MYELOMA: FRONTLINE TREATMENT

Newly Diagnosed MM

Not Transplant Candidate
- Rd or VMP
- VMP-Dara or VRD followed by Len or DRd following approval

Transplant Candidate
- VRd or VTd or VCD if VRd not available or Dara-based quadruplet induction following approval
- Auto-SCT Maintenance (Len for std risk; Len+Pl-based for high risk)
- No Delayed Transplant Outside clinical trials
Q&A
What are recommendations for maintenance?
• Current Approaches
• Revlimid ± Proteasome Inhibitor
• Modifying for side effects
• Stopping for intolerance and/or MRD +/-
Q&A
What are current relapse options?
MYELOMA: FIRST RELAPSE

First Relapse

Not Refractory to Lenalidomide
- DRd or KRd
  - Alternatives including If Dara Refractory: KRd, IRd, Kd, ERd; Kd-dara after approval

Refractory to Lenalidomide
- PVd or DVd (DPd, DKd or KPd after approval)
  - Alternatives including If Dara Refractory: KPd, PVd, or EPd
    Frail: Pd, IPd
# 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 after approval

## Additional Options

- VDT-PACE like anthracycline containing regimens
- Melphalan/melflufen
- Adding Panobinostat
- Quadruplet regimens
- CART
- Bispecific
- Conjugated BCMA
- Selinexor
- Referral for clinical trials always if available
Q&A
NOVEL AGENTS OR COMBINATION AT RELAPSE

• dara/Kyprolis/dex (CANDOR): LBA-6
• dara/Pom/dex
• Kyprolis/Pom/dex
• iberdomide (CC-220)
• melflufen
• $^{131}$I CLR 1404 (lipid rafts target)
• CAR T Therapy

• Bispecific T Cell Engagers

• MoAb/drug conjugate: GSK 2857916 ("belamaf")
TIME FOR A PAUSE TO CONSIDER 100% RESPONSES!

CARTITUDE-1 Efficacy: Tumor Burden Reduction

- 100% of patients achieved a reduction in paraprotein

*Serum M-protein, urine M-protein, or difference between involved and uninvolved free light chain (dFLC). *Bence-Jones proteinuria at baseline, with a transient response during bridging therapy; output represents dFLC value.

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 (≤ 1/10^5) in the bone marrow on or before C4D1 by Euroflow®

Data as of October 20, 2019.

*MRD negativity by Euroflow analysis was reported only if a minimum sensitivity of ≤ 1 tumor cell in 10^9 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 ≤ 50% bone marrow plasma cells and ≤ 5 extramedullary lesions). MR, minimal response.

Luciano J. Costa, MD, PhD, et. al.
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
- Cassiopiea
- Griffin
- Dar KRd
- CESAR/ASCENT F/u

New Agent Data
- $^{131}$I CLR 140L
- Iberdomide
- Several others
Q&A
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