Management of Multiple Myeloma: The Changing Paradigm

Relapsed/Refractory Disease

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Objectives

- Discuss use of standard myeloma therapies when used as therapy after relapse
- Consider patient and disease factors which might impact therapy decisions.
- Describe off-label options for patients who are not protocol candidates.
Line ≠ Line ≠ Line ≠ ...

POLICE LINE – DO NOT CROSS

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Define “Line”

• A pre-defined course of therapy utilizing agents either simultaneously or sequentially
  – Len/Dex
  – Len/Dex → ASCT
  – Vel/Dex → ASCT → Len/Dex
  – VDT-PACE → ASCT → TD → ASCT → VPT-PACE → LD

• Pts who have had the same # of “lines” of Rx may have had vastly different amounts of Rx
What Is Relapsed/Refractory Disease?

- **Relapsed**: recurrence after a response to therapy
- **Refractory**: progression despite ongoing therapy
What Do We Know About the Pt’s Myeloma?

- What prior therapy has been used?
- How well did it work?
- Did the myeloma progress on active therapy?
- High-risk cytogenetics/FISH/GEP?
What Do We Know About the Patient?

• Age
• Other medical problems
  – Diabetes
  – Blood Clots
• Lasting side effects from past therapies
  – Peripheral Neuropathy
• Personal preferences and values
# Choosing Therapy for Relapsed/Refractory Myeloma

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- **IMiDs**: Thalidomide, Lenalidomide, Pomalidomide
- **Proteasome Inhibitors**: Bortezomib, Carfilzomib, Ixazomib
- **Anthracyclines**: Doxil
- **Alkylators**: Melphalan, Cytoxan, Bendamustine
- **Steroids**: Dex, Pred
- **HDACs**: Panobinostat
- **Antibodies**: Elotuzumab, Daratumumab, Isatuximab

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**Note:** The table above outlines the main categories of therapies used for treating relapsed/refractory myeloma. Each category lists specific medications that can be used in combination therapy.
# Choosing Therapy for Relapsed/Refractory Myeloma

## IMiDs
- Thalidomide
- Lenalidomide
- Pomalidomide

## Proteasome Inhibitors
- Bortezomib
- Carfilzomib
- Ixazomib

## Anthracyclines
- Doxil

## Alkylators
- Melphalan
- Cytoxan
- Bendamustine

## Steroids
- Dex
- Pred

## HDACs
- Panobinostat
- Vorinostat

## Antibodies
- Elotuzumab
- Daratumumab
- Isatuximab

## Additional Drugs
- Bevacizumab
- Daratumumab
- Pomalidomide
- Ixazomib
- Lenalidomide
- Carfilzomib
- Bortezomib
- Dex
- Panobinostat
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- Lenalidomide, Ixazomib, Dex
- Bortezomib, Dex, Panobinostat
- Lenalidomide, Dex, Elotuzumab
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| Lenalidomide | Dex | Daratumumab |
## Apples to Apples: 1-3 Prior Lines

<table>
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<tr>
<th>Trial</th>
<th>Regimens</th>
<th>OS (mos)</th>
<th>ORR (%)</th>
<th>VGPR+ (%)</th>
<th>PFS</th>
</tr>
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<tr>
<td>Eloquent-2 (Abst #28)</td>
<td>Rd</td>
<td>39.6</td>
<td>66</td>
<td>29</td>
<td>3y: 18%</td>
</tr>
<tr>
<td></td>
<td>RdE</td>
<td>43.7</td>
<td>79</td>
<td>34</td>
<td>3y: 26%</td>
</tr>
<tr>
<td>Tourmaline (Abst #727)</td>
<td>Rd</td>
<td>NR</td>
<td>71</td>
<td>39</td>
<td>14.7 mos</td>
</tr>
<tr>
<td></td>
<td>Rd-Ixaz</td>
<td>NR</td>
<td>78</td>
<td>48</td>
<td>20.6 mos</td>
</tr>
<tr>
<td>ASPIRE¹</td>
<td>Rd</td>
<td>2y: 65%</td>
<td>66</td>
<td>9.3 (CR+)</td>
<td>17.3 mos</td>
</tr>
<tr>
<td></td>
<td>KRd (27)</td>
<td>2y: 73%</td>
<td>87</td>
<td>31.8 (CR+)</td>
<td>26.3 mos</td>
</tr>
<tr>
<td>PANORAMA²</td>
<td>Vd</td>
<td>30.4</td>
<td>54.6</td>
<td>15.7 (nCR+)</td>
<td>8 mos</td>
</tr>
<tr>
<td></td>
<td>Vd-Pan</td>
<td>33.6</td>
<td>60.7</td>
<td>27.6 (nCR+)</td>
<td>12 mos</td>
</tr>
<tr>
<td>ENDEAVOR³</td>
<td>Vd</td>
<td>NR</td>
<td>63</td>
<td>28.6</td>
<td>9.4 mos</td>
</tr>
<tr>
<td></td>
<td>Kd (56)</td>
<td>NR</td>
<td>77</td>
<td>54.3</td>
<td>18.7 mos</td>
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Takeaway Points

• Combinations (triplets, particularly) are more active than sequential single agents in relapsed/refractory myeloma
  – Switching drug classes often done, but may not be required to obtain response

• Duration of response is likely to be shorter than in initial therapy
  – Possibly MUCH shorter
Second ASCT an Option

- 69% Response Rate, **Med EFS: 14.8 mos**
- More likely to work if pt responded to 1st ASCT

Frame the Issue Correctly

- The question is not whether one can get as much out of a second transplant as the first one.
- It's whether any other therapy left is likely to be better (and less toxic) than transplant.
Clinical Trials as an Option

• ALWAYS ask your doctor whether a clinical trial is potentially available

• Promising therapies in development
  – Ricolinostat
  – Selinexor
  – Pembrolizumab
  – CAR-T cell therapy
  – Many, many others….

• www.clinicaltrials.gov
Typical Obstacles to Trials

• *Peripheral Neuropathy*
• *Kidney Dysfunction*
• Low Platelets
• Low White Blood Cells
• # of Prior Therapies
• Lacking Molecular Target
• Travel Distance
• Insurance Coverage
“A Little of This, a Little of That…”

- CyBorD-Rev
- Car-Cy-Dex
- Car-Pom-Dex
- Car-Fary-Dex
- Car-Dara
- VR-PACE
- HyperC(Vel)AD

- Benda-Dex
- Benda-Rev-Dex
- Rev-Dex-Vorinostat
- Vel-Dex-Vorinostat
- Pom-Cy-Dex
- Pom-Dara-Dex
- Pom-Ixa-Dex
- Vemurafenib
The MMRF CoMMPass Study

**MMRF CoMMPass Study℠**

**ACCELERATING A CURE**

The Multiple Myeloma Research Foundation CoMMPass Study is the most comprehensive long-term genomic study ever conducted in myeloma. With 1,000 patients now participating, the study offers unprecedented promise to accelerate the understanding of disease progression and provide increased insights for the development of personalized treatments. This is one of the ways the MMRF is helping to cure cancer now.

**MMRF IS CREATING SOLUTIONS THROUGH PRECISION MEDICINE**

For the past 10+ years, MMRF has led the effort to treat multiple myeloma based on an individual's genetic makeup. One example of MMRF's discoveries through precision medicine research is the identification of the BRAF mutation, which has transformed multiple myeloma care by inspiring a new class of innovative treatments.

**MULTIPLE MYELOMA**

A cancer with significant unmet needs

Multiple myeloma is a devastating disease that affects 230,000 patients around the world. As the second most common type of blood cancer, we need precise and individualized treatments now.

230,000

patients around the world with multiple myeloma

2nd most common blood cancer

**10+ YEARS**

leading precision medicine efforts

**8 YEARS**

leading precision medicine efforts

**THE MMRF COMMPASS STUDY WILL PRODUCE A GOLDMINE OF PUBLICLY AVAILABLE DATA**

VISIT THEMMRF.ORG FOR MORE INFO

With 1,000 patients involved in the study, equivalent to 1.23 million type 2 diabetes patients, and more than 100 trial sites in the United States, Canada, and Europe, the study will have significant and meaningful reach.

The MMRF CoMMPass Study will evaluate 20,000 genes at the molecular level per patient. $40 million is needed to fund the study.
Summary: Relapsed/Refractory Myeloma

- Relapsed/refractory multiple myeloma is treatable
- Patients typically receive multiple lines of therapy
- Treatment may sometimes be continued for an extended period of time
- Six new drugs (Carfilzomib, Pomalidomide, Panobinostat, Daratumumab, Elotuzumab, Ixazomib) introduced in last 4 years
- With the introduction of each new drug, potential for additional combinations
- Many promising new drugs/new combinations in clinical development—consider a clinical trial