Dedicated to improving the quality of life of myeloma patients while working towards prevention and a cure

ADVANCES IN THERAPY OF MULTIPLE MYELOMA

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Heidelberg, Germany

Brian GM Durie, MD
Cedars-Sinai, Los Angeles
MANAGING MYELOMA
THE COMPONENTS OF CARE

Transplant Eligible Patients

Transplant Ineligible patients

Initial Therapy

Consolidation

Maintenance

Consolidation/ Maintenance/ Continued therapy

Treatment of Relapsed disease

Supportive Care

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INCREASING NUMBER OF NEW DRUGS

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HDAC= HDAC inhibitors
ELOTUZ= Elotuzumab
POM = Pomalidomide
CAR = Carfilzomib
LEN [REVLMID]= Lenalidomide
BTZ [VELCADE] = Bortezomib
BISPH = Bisphosphonates
THAL = Thalidomide
SCT = Stem cell transplantation
HDC = High-dose chemotherapy
VAD = Vincristine, doxorubicin, dexamethasone

1950-1960s
1970-1980s
1990s
2000s

STEROIDS
RAD
ME

STEROIDS
RAD
ME

MINI-ALLO
1° SCT
BISPH
THAL

MINI-ALLO
1° SCT
BISPH
THAL

SCT
HDC
VAD

SCT
HDC
VAD

In Trials
Approved
Improving Overall Survival in Myeloma

Impact Of Transplant And Novel Therapies

Overall survival 1971–2006

- Last decade: 45 months
- Before last decade: 30 months


50% improvement

...further increase for 2007-2012

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TREATMENT SEQUENCE

NEW

Front line treatment

Induction

Consolidation

Maintenance

Post consolidation

Relapsed

Old

VAD

DEX

SCT

Nothing

Prednisone

Thalidomide

Few options

NEW

Thal/Dex

Rev/Dex

Cyclo/vel/dex

VD

RevVel

VTD

SCT

VD/VRD

MPT?

VMP?

Nothing

Thalidomide?

Bortezomib?

Lenalidomide?

Bortezomib

Lenalidomide

Carfilzomib

Pomalidamide

Elotuzumab

HDAC

Bendamustine

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YOU NEED GOOD COMBINATIONS

WHICH ONES ARE BEST?

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WHAT’S BEST IN 2012?

Rd: LENALIDOMIDE/DEX
VD: BORTEZOMIB/DEX
KD: CARFILZOMIB/DEX
CD: CYCLOPHOSPHAMIDE/DEX

2 DRUG

VRd
VCd
KCd
CTD or VTD
“PAD”

3 DRUG
INDIVIDUALIZING CARE

Important Factors

- Age
  - High Risk cytogenetics
  - Renal disease
  - Convenience/location
  - Blood counts
    - Steroid “status”
  - Previous therapy

and PATIENT PREFERENCE

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New Drug Trial Example

ELOTUZUMAB/LENALIDOMIDE/DEX

ELOQUENT 1 @ clinicaltrials.gov- NCTO1335399

Randomized Study
- Len/dex ± Elotuzumab
- Previously untreated myeloma
- Non-ASCT candidates
ISSUES WITH CURRENT OPTIONS

1. Toxicity
2. Convenience
3. Cost
4. Ability to collect stem cells
5. Long term risks (?)

KEY POINT

Does DEPTH of response predict DURATION of response?
### KEY DECISION FACTORS

<table>
<thead>
<tr>
<th>SITUATION</th>
<th>CHOICE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Renal impairment</td>
<td>Bortezomib</td>
</tr>
<tr>
<td>2. Convenience</td>
<td>Lenalidomide</td>
</tr>
<tr>
<td>3. Cytopenias</td>
<td>Bortezomib or thal</td>
</tr>
<tr>
<td>4. Neuropathy</td>
<td>Lenalidomide</td>
</tr>
<tr>
<td>5. High risk disease</td>
<td>Bortezomib</td>
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</tbody>
</table>
Will cure come from

....an extra piece for the puzzle?

or

....something different entirely?
KEY ROLE OF IMWG

Moving Research Forward

Chairs:
• Brian G.M. Durie
• S. Vincent Rajkumar
• Antonio Palumbo
• Jésus San-Miguel
• Philippe Moreau

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IMWG PAPERS ON THE IMF WEBSITE

International Myeloma Working Group (IMWG)

Mission of the IMWG

- To conduct basic clinical and translational research in a collaborative manner to improve outcomes in myeloma, and to provide scientifically valid and clinically appraised consensus opinions on the diagnosis and treatment of myeloma and related disorders.

In further pursuit of this mission, IMWG holds an annual summit to identify, support, and implement the most promising research to prevent onset of active disease, improve treatment, and find a cure for myeloma.

IMWG Publications

The IMWG has a two-fold task: to conduct translational research—from lab bench to patient bedside—under the auspices of the IMF and to publish consensus statements and guidelines for the management of myeloma. These publications represent both the work of the IMWG and the work of individual IMWG members who have based their papers on IMWG data sets that were made available to them.

IMWG Guidelines

These guidelines from the International Myeloma Working Group (IMWG) represent a capsule summary, capturing the main points of, but not intended to replace the publications from which they came. As with all guidelines, they are informational and may contain issues to be discussed with your treating physician. To see the full list, click on "view all" in the bottom right hand corner.

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We welcome our international partners:

Australia, Brazil, Canada, China, Czech Republic, Europe, Israel, Italy, Japan, Latin America
MAINTENANCE
• Ludwig, Attal, IMWG consensus on maintenance therapy in multiple myeloma BLOOD (Impact Factor- 9.8)

TRANSPLANT
• Cavo, Lonial, International Myeloma Working Group (IMWG) consensus statement on the treatment of multiple myeloma patients who are candidates for autologous stem-cell transplantation BLOOD (Impact Factor- 9.8)

RELAPSE
• Kumar, S. et al 'Risk of Progression and Survival in Multiple Myeloma Relapsing After Therapy with IMiDs and Bortezomib: A Multicenter International Myeloma Working Group Study‘ Leukemia (Impact Factor- 9.5)

NEUROPATHY
• Richardson, “IMWG Recommendations on the Management of Treatment-Emergent Peripheral Neuropathy in Multiple Myeloma” Leukemia (Impact Factor- 9.5)
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MODEL OF MYELOMA OVER TIME

EARLY  RELAPSE

CLONES
- Original Clone

NEW SUBCLONES

FEWER  MULTIPLE CLONES  MORE

CURATIVE Rx  salvage Rx
Improving 10-year survival

- **1950-1990**: Chemo 5-15%
- **1990-2000**: Transplant 15-25%
- **2000-2010**: New Agents 25-50%
- **Beyond 2010**: New Combos 50-80%

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