Vienna, Austria

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New Development in Diagnosis & Treatments

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International Myeloma Foundation
What information is required to make a decision?

- Age
- Sex
- Details of myeloma
  - Type
  - Stage
  - Chromosomes
- Immediate medical issues: pain; infection;
- Other medical problems: diabetes; heart disease;
- Work/ family situation: job; children;
- Personal preferences
PROS & CONS: MRI / PET

MRI
- Very accurate
- Gadolinium enhancement shows active disease
- Very slow to improve with 6-9 month “lag”
- Cumbersome to screen whole body

PET
- Also accurate
- Shows active myeloma
- Some false negatives
- MGUS negative
- Shows early response to treatment
- Maybe too sensitive
- CT-PET ideal for whole-body monitoring
**Anatomic/ functional staging**

## Integration of Imaging

<table>
<thead>
<tr>
<th>DURIE/SALMON STAGE</th>
<th>PLUS upstage</th>
<th>MRI/PET Number of lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>I B</td>
<td></td>
<td>0 - 4</td>
</tr>
<tr>
<td>II A or B*</td>
<td></td>
<td>5 - 20</td>
</tr>
<tr>
<td>III A or B*</td>
<td></td>
<td>&gt; 20</td>
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</tbody>
</table>

* B: creatinine > 2
  EMD on PET or MRI

DURIE
Ideal Baseline Diagnostic Evaluation for Staging and Prognosis

Full Radiographic Skeletal Survey

Other Imaging

Outcome

Whole body CT-PET* or MRI of spine/pelvis and/or symptomatic sites

NEGATIVE

Recommended

RECOMMENDED

D/S Plus Staging

DIFFUSE DISEASE

Optional to confirm D-Plus stage and assess prognosis

Identification of MGUS or smoldering myeloma

CLASSIFIED D/S Plus I-III A/B
Initial Treatment Strategy

Induction Frontline

- Induction:
  - VAD or VDD
  - Thal + Dex
  - MP or MPT

Consolidation Transplant

- High dose chemotherapy
- Double transplant
  - Novel consolidation
- Revlimid + Dexamethasone
  - Velcade combo’s…others

Maintenance or Monitoring

- Prednisone / Dexamethasone
- Thalidomide + Dexamethasone
- Revlimid + Dexamethasone
**Initial Decisions 2006**

**Chromosome Testing**

**If normal**

- **Age < 65**
  - VAD
  - Thal/Dex
  - Rev/Dex
  - Velcade/ Dex

  - Transplant 1 or 2
  - Or not

**Age ≥ 65**

- MP or MPT
  - OR
  - Modified Thal/Dex/CTD/ other combos

  - Full Transplant
  - Or not

  - ½ Transplant
  - DURIE

**If abnormal**

- Chromosome 13q-
- 4;14
- Or other “high risk” features

Consideration of new trial including Velcade
# Frontline Options

<table>
<thead>
<tr>
<th>THERAPY</th>
<th>CR + PR</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAD</td>
<td>65%</td>
</tr>
<tr>
<td>Thal/Dex</td>
<td>68%</td>
</tr>
<tr>
<td>Dex</td>
<td>46%</td>
</tr>
<tr>
<td>Revlimid/ Dex</td>
<td>91%</td>
</tr>
<tr>
<td>Velcade/ Dex</td>
<td>88%</td>
</tr>
</tbody>
</table>
### Phase III Trial: Thal/Dex vs Dex in Patients With Newly Diagnosed MM

**Adverse Events Reported During 4 Cycles of Treatment**

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Thal/Dex (N=102)</th>
<th>Dex (N=101)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT (Grade ≥3)</td>
<td>16 (16%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Neuropathy (Grade ≥3)</td>
<td>6 (6%)</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Total of any Type (Grade ≥3)</td>
<td>45 (44%)</td>
<td>19 (19%)</td>
</tr>
</tbody>
</table>

21% achieved best response in ≥ 4 cycles
10% achieved best response in ≥ 6 cycles

* All patients received velcade alone for the first 2 cycles of treatment.
- **Median overall survival**: not reached
- **Estimated survival rate at 12 months**: 91%

DURIE
So What’s the Answer for patients < 65

- Thal/ Dex
- Velcade/ Dex
- Rev/ Dex (or BiRD)

OR Attempt even higher CR?
New Trials

Frontline Induction

- Velcade/ Dex vs VAD
- Velcade/ MP vs MP (Vista)
- Velcade/ AD vs VAD
- Velcade/ Thal/ Dex vs Thal/ Dex
- Velcade/ Cytoxan/ Dex

IFM
Spain
HOVON
SWOG
Aptium
Is Transplant Needed?

High-Dose Therapy/AutoSCT Is Superior to Conventional Chemotherapy in Myeloma

Overall Survival According to Response Following Single Transplant

1 versus 2 transplants
How About for an Older Patient?

- MP
- MPT
- VAD + MEL 100mg/ m² x2
MP vs MPT

Event-free survival

Overall survival


DURIE
Velcade for Patients with 13q- Chromosome Deletion

In Summit and APEX Velcade trials 13q- did not do worse

Conclusions

- Velcade equally effective for 13q- patients
- Dexamethasone patients with 13q- did not do as well (p=0.002)
Many New Drugs Are in Trials

Heat Shock Protein 90 Inhibitors

Diagram showing the interaction between ribosomes, ATP, ADP+, Pi, HSP-90, 17-AAG, and the outcome of viable cells versus cell death.
The Future of Myeloma Therapy

- New Drugs
- New Combinations
- Longer Remissions
- Longer and Better Survival
- Cure!