Initial treatment for myeloma and stem cell transplantation

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Treatment overview

- When to treat?
- Emergency treatment
- Aim of treatment
- Treatment of bone disease
- Chemotherapy basics
- Which treatment is best for you?
- Treatment complications & avoidance
- Monitoring response to treatment

At presentation

- 15% no symptoms - watch & Wait
- 38% Emergency presentation
  - Kidney failure
  - Spinal cord compression
  - Fracture
- Remainder have symptoms
  - Backache or bone pain
  - Tiredness/anaemia

Emergency treatment

- Steroids
- Radiotherapy
When to treat?

- Calcium increased
- Renal Impairment
- Anaemia
- Bone disease
- Hyperviscosity
- Spinal Cord compression

Symptomatic myeloma

Aims of treatment

- Anti-myeloma treatment: Reduce myeloma activity and related damage
- Supportive treatment: Relieve symptoms and complications

- Reduce symptoms and complications
- Improve quality of life
- Prevent further bone and other organ damage
- Prolong survival

Treatment of bone disease

BISPHOSPHONATES
- Sodium clodronate tablets
- Zoledronate intravenously
- Pamidronate intravenously

- Strengthen bones
- Stop myeloma driven bone breakdown
- Direct anti-myeloma effect

Balloon Kyphoplasty

- 70 % patients
  - Vertebral fractures at diagnosis
- Multiple fractures
  - reduced height
- Kyphoplasty
  - Indicated for persistent pain
Chemotherapy basics

• Myeloma is treatable but not curable
• Repeated cycles of treatment needed
• Given as outpatient

Drugs used to treat myeloma

- Melphalan and prednisolone
- Thalidomide
- Revlimid
- Pomalidomide
- Carfilzomib

The pace of change.....era of novel agents

Improved survival with new drugs (novel agents)

- Combination treatment
  - Novel agents
  - Steroid
  - Chemotherapy
  - Consider treatment in clinical trial

Myeloma microenvironment
Which treatment is best for you?

Patients fall into two groups:

- Younger patients (<70 years) who are candidates for High Dose therapy and stem cell transplant
- Older patients & other patients not fit for transplant

Treatment options:

**Non-transplant patients**

- **Thalidomide-based**
  - CTD
    - Cyclophosphamide
    - Thalidomide
    - Dexamethasone
  - MPT
    - Melphalan
    - Prednisolone
    - Thalidomide
    - 6-8 cycles

- **Velcade-based**
  - VMP
    - Velcade
    - Melphalan
    - Prednisolone
    - Max 8 cycles

**Supportive**

- Bisphosphonates
  - Zometa, pamidronate, Bonefos
- Blood transfusions/EPO
- Pain-killers

As per NICE guidance

### MP vs MPT: Response rate

<table>
<thead>
<tr>
<th>Regimen</th>
<th>n</th>
<th>Response Rate %</th>
<th>Remission length (months)</th>
<th>Reference</th>
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<tbody>
<tr>
<td>MPT vs MP</td>
<td>120</td>
<td>76</td>
<td>21.8</td>
<td>Palumbo et al Blood 2008</td>
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<td>124</td>
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<td>MPT vs MP (&gt;75 yrs)</td>
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<td>Hulin et al ASH 2007</td>
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<td>31</td>
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<tr>
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<td>MPT vs MP</td>
<td>152</td>
<td>66</td>
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<td>Wijermans et al ASH 2008</td>
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<tr>
<td>MPT vs MP</td>
<td>149</td>
<td>47</td>
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</table>

5/5 studies, MPT superior to MP

### VMP: Response

Remission longer with VMP

Survival better with VMP

Home Treatment

Velcade at Home
• Started 2008
• Feasible
• Better QOL?
  Velcade at home QOL trial
• zoledronate at Home

Treatment options:
Transplant patients:

Step 1: Induction treatment
  ➢ Induce remission
  ➢ spare stem cells

Step 2: High-dose therapy and stem cell transplant
  ➢ Autologous (own stem cells) – vast majority
  ➢ Allogeneic (donor stem cells) – very small minority

Step 1: Induction treatment

Thalidomide-based
• CTD
  Cyclophosphamide
  Thalidomide
  Dexamethasone
  normally 4-6 cycles – must have partial response or better

Velcade-based
• VD or CVD
  Cyclophosphamide
  Velcade
  Dexamethasone
  Max 6 cycles

Supportive
• Bisphosphonates
  Zometa, pamidronate, Bonafos
• Blood transfusions/EPO
• Pain-killers

Avoiding complications

➢ Anti-sickness
➢ Anti-gout
➢ Antibiotics
➢ Anti-virals
➢ Anti-fungals
➢ Stomach protection
➢ Laxatives
➢ Blood thinners
### Novel Agents: Side effects

<table>
<thead>
<tr>
<th>Novel Agent</th>
<th>Tablets</th>
<th>Side Effects</th>
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<tbody>
<tr>
<td>Thalidomide</td>
<td>Tablet daily</td>
<td>Drowsiness, Constipation, Peripheral neuropathy, Thrombosis</td>
</tr>
<tr>
<td>Velcade</td>
<td>s/c injection</td>
<td>Low platelets, Constipation, Peripheral neuropathy, Dizziness</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>Tablet day 1-21</td>
<td>Fatigue, Diarrhoea, Anaemia, Low WCC</td>
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### Treatment decisions: Summary

- **Treatment recommendation:**
  - Patient needs & priorities
  - Evidence & Guidelines
  - Treatment side effects

- **Treatment decisions: Summary**
  - One size does not fit all!
  - Remission – current practice
    - No treatment, most drugs stopped
    - Maintenance treatment – not standard
    - Bisphosphonates for at least 2 years
    - Minimal effective pain management
  - Myeloma XI study
  - Randomise
  - CTD, CCRD, RCD
  - Assess response
  - SD + PD, CR + VGPR, PR + MR
  - Randomise
  - VCD, No maintenance, Revlimid maintenance
  - Transplant if appropriate
  - Randomise
  - Assess response
  - Further 1989 patients
- **Evidence & Guidelines**
  - Is Revlimid superior to thalidomide? Is Revlimid/Carfilzomib better?
  - For patients achieving sub-optimal response, can VCD improve response rates?
  - Does Revlimid or Rev + vorinostat maintenance improve survival?
Preparation for Peripheral Stem Cell Harvest

- On completion of your initial treatment your Consultant will discuss the next step of your treatment plan. This may include collecting your stem cells and a stem cell transplant.
- Both verbal and written information will be given to you.
- A venous assessment will be carried out.
- Blood tests will be taken including Mandatory Virology Screening.
- You will be asked to sign consent forms at a later appointment.

Mobilisation Chemotherapy

- May be given on the day ward. Some patients may require an overnight stay so bring in an overnight bag.
- Input and output recorded throughout the day. Diuretics may be administered if required.
- Potential side effects from the chemotherapy may include nausea, vomiting, bladder irritation and infection.
- Growth factor injections may cause some bone pain, headaches and flu-like symptoms.

Day Of Harvest Procedure

- Verbal consent obtained
- Blood test
- Medical Assessment
- Cannulation or femoral line insertion
- Vital Signs
- Procedure lasts approx 4/5hrs.
The Purpose of Transplantation

- The aim is to prolong remission.
- Patients can be transplanted in complete remission (CR), VGPR, PR or in plateau phase.
- Transplantation allows higher doses of toxicity limiting chemotherapy to be administered.

Pre Transplant Assessment

- Re-staging of disease: Bone marrow, PET scan etc
- Blood tests
- Cardiac: Echo
- Respiratory: Pulmonary function studies, CXR, Sinus Xray
- Renal: GFR
- Medical Assessment

Pre Transplant Assessment

- Psychological: Preparation, transplant discussion, Information leaflets
- Dental: Check-up and dental work done pre-procedure
- Fertility: Discuss infertility post-procedure, sperm/ova collection, early menopause

Consent

- Transplant morbidity and mortality
- Release of Data to EBMT database

Admission Procedure

- Single room
- Venous access: Central Venous Line
- Start IV fluids D-2, Chemotherapy D-1
- Pentamidine nebuliser
- Commence mouth care
- Bring in photos, cards, pictures laptops books etc.
- Baby wipes.
Stem Cell Infusion

- >24 hours post-chemo completion (D0)
  - Anti-histamine and hydrocortisone pre-med
  - Bags thawed in sterile water bath
  - Each Infusion over approx 15 mins

- Potential Side effects
  - Allergic reaction to DMSO
  - Chest tightness
  - Pink urine
  - Smell! (sweetcorn, asparagus)
Infusing the Stem Cells

Potential Complications
- Mortality nationally 3-5%
- Nausea/vomiting
- Gastro-intestinal side-effects mucositis and diarrhoea
- Infection
- Anaemia, risk of bleeding.
- Hair Loss
- Nutritional Status
- Psychological

Post-PBSCT Follow Up
- Immediate post-discharge
  - You will be allowed home when your neutrophils > 1x10⁹/l, apyrexial, bowels settling.
  - Central Lines are removed prior to discharge.
  - You will be seen regularly for a medical assessment which will include blood tests.
  - Continue antibiotic, antiviral and anti fungal prophylaxis until stable engraftment
  - Continue with monthly pentamidine nebulisers

Long-term post-discharge
- Commence co-trimoxazole prophylaxis for Pneumocystis infection > 6 months
- Antibiotics for 6 mths
- Day 100 assessment of disease response to transplant.
- Vaccines at 12 mths
- Check female hormone levels +/- HRT
- Long-term disease follow up
Summary

• Myeloma is an individual cancer - requires a personalised approach
• Patients should have a role in their treatment plan - important to discuss goals and perceptions
• Various treatment combinations are effective and generally well tolerated
• More research required to understand and develop better treatments and better ways of using existing treatments

For information:

- www.myeloma.org.uk
- 0800 980 3332