Current strategies for the treatment and management of myeloma

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When is treatment considered?

- If myeloma is active
- After previous treatment(s)
- To previous treatment(s)
Is treatment needed now?

Sometimes no treatment is the best treatment...

- Is myeloma causing symptoms?
  - Unwell, tiredness, pain

- Is myeloma causing organ impairment?
  - Kidneys, bones, anaemia, high calcium

- Are there other medical problems or individual issues to consider?

Asymptomatic myeloma...

Where action is not always needed

- Watchful waiting often appropriate

- Symptoms most often herald progression

- But......If only lab tests worse.....
  - Judgement when to start treatment
  - Negotiation
Aim of treatment

- Reduce myeloma activity
  - Chemotherapy

- Strengthen bones
  - Bisphosphonates

  - Alleviate symptoms
  - Improve quality of life
  - Prevent further bone and organ damage

Treatment Approach

- Chemotherapy
- ±Radiotherapy
- ±Surgery
- Supportive Care
- Bisphosphonates
Supportive care

Treatment approaches
- Pain relief
- Transfusions
- Antibiotics
- Haemodialysis

Non-treatment approaches
- Emotional Support
- Home help
- Social support
- Carers support

Improve quality of life

Choosing treatments...
Moving towards concordance

Doctor

Patient

Clinical evidence
Treatment jargon

**Paraprotein**
- Abnormal antibody or protein made by myeloma cancer cells

**Complete response (CR)**
- No abnormal protein (M-protein) detectable in blood or urine for ≥ 6 Weeks
- < 5 % Plasma cells in bone marrow

**Partial response (PR)**
- > 50 % reduction in blood M-protein and/or 90 % reduction in urine light chains

**Plateau**
- No evidence of continuing myeloma-related organ damage
- Stable M-protein levels for > 3 months

Bisphosphonates...
Reducing pain, preventing fractures

- **Intravenous** [pamidronate, zoledronate, (ibandronate)]
  - Monthly
  - Used for high calcium
  - Osteonecrosis of jaw reported

- **Oral** [clodronate, (ibandronate)]
  - Once or twice daily
  - No food 1 hr before & after
  - Nausea, diarrhoea

NNT: 8 over 2 years
Approach to treatment

Presentation → 1st Relapse → 2nd Relapse → Next Relapse

1st Line: Thalidomide (Velcade)
2nd Line: Velcade
3rd Line: Revlimid
Next Line: ?

- Autologous Stem cell Transplant

Clinical Trial Option

Intensive
- Younger
- Generally fit
Thalidomide...
Standard first line treatment in myeloma

• Used to modify immune response for decades, e.g. after bone marrow transplant
• First published paper in relapsed myeloma 1999
• Combinations more effective (e.g. CTD)
• Side effects
  – Thrombosis, neuropathy, constipation, drowsiness
### CTDa

**Day 1 4 8 15 18 22 28**

- **Cyclophosphamide**: ■ ■ ■ ■ ■
- **Thalidomide**: ■ ■ ■ ■ ■ ■ ■ ■ ■
- **Dexamethasone**: ■ ■■■■ ■ ■ ■

6-9 cycles

**Other medications required:**
- Thrombosis prevention (e.g. daily heparin injections)
- Supportive care meds

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### MPT

**Day 1 4 21 42**

- **Melphalan**: ■ ■ ■ ■
- **Thalidomide**: ■ ■ ■ ■ ■ ■ ■ ■ ■
- **Prednisolone**: ■ ■ ■ ■

**Improved responses to MP**

Most studies show improved survival

**Other medications required:**
- Thrombosis prevention (e.g. daily heparin injections)
- Supportive care meds
Intensive therapy.. is for those who can tolerate it

- Fitter
- Younger
- Few or non-severe co-existing medical problems
- Support network

1. Induction treatment (CTD)
2. Stem cell mobilisation
3. Stem cell collection
4. High-dose melphalan
5. Autologous stem cell transplant
Admit for transplant…
A stay of about 2 weeks

- IV fluids then high dose chemo (melphalan)
- Blood product support
- Gastrointestinal side effects
- Prevent/treat infection
- Home when blood counts safe
- A long recovery………months

Allogeneic stem cell transplant
Potentially curative?

- Suitable for a minority of patients (young, v. fit)
- High mortality with Cyclo/TBI
- Reduced intensity procedures safer (‘mini-allo’).
First relapse

- Increase of paraprotein by 25% or more from baseline
- Treatment required if there is a return of symptoms
- Current approved 2nd line of treatment - VELCADE

- Combined with dexamethasone
- Intravenous or subcutaneous
- Once or twice weekly
- 21-day cycle
- Between 4 – 8 cycles

Other options

- Consider same initial treatment if lengthy first remission
- Thalidomide combination if not previously received it
- Second transplant if remission > 18 months
- Consider entering a clinical study
Second relapse

Current approved treatment 3\textsuperscript{rd} line of treatment - REVLIMID

- Combined with dexamethasone
- Oral, day 1 – 21 of 28 day cycle
- Continue until myeloma progresses

Other options: - CTD or MPT if not received before
- Enter clinical study

Options:

- Consider previous treatments that have given lengthy remission
- Other strategies such as DT-PACE or ESHAP
- Non-approved drugs via access schemes
- Enter clinical study
Approach to treatment

Presentation → 1st Relapse → 2nd Relapse → 3rd Line → Next Line

1st Line:
- Thalidomide (Velcade)
- Autologous Stem cell Transplant
  - Clinical Trial Option

2nd Line:
- Velcade
- Autologous Stem cell Transplant
  - Clinical Trial Option

3rd Line:
- Revlimid
- Clinical Trial Option

Next Line:
- Clinical Trial Option

Clinical Trial Option

New ways with current treatments
- Myeloma XI
- PADIMAC
- Velcade consolidation
- LenaRIC

Novel drugs
- Pomalidomide
- Carfilzomib
- Panobinostat
- Elotuzumab
- KW-2478

Supportive
- TEAMM
- EuLITE
- CMV IMPACT
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
- Treatments and access to them have greatly improved
- But, it remains a difficult and challenging disease
- Lots more research required to understand and develop better treatments