Future strategies for myeloma: new insights and treatments in development
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This talk will cover...
- Promising new treatments
- Area where research needs to focus
- Future prospects for myeloma treatment

Take home messages
- Survival and quality of life has improved for myeloma patients
- New drugs attack new targets
- Myeloma treatment will become more personalised in the future

Developments to date

Average survival after relapse from transplant has doubled since the introduction of new drugs (Thalidomide, Velcade and Revlimid)

Mayo Clinic, Blood Journal, March 2008
More to be done

Survival rates have improved but:
- Less toxic treatments are needed
- Newer drugs have specific targets so may not all be effective for all patients
- Relapsing and remitting – need for next treatments
- Need to target effective early treatment for patients with high risk of progression
- Need to know which combinations of drugs are best, and for which type of patient

Which combinations are best?

Current combinations

- Alkylating chemotherapy drug
  - Cyclophosphamide
  - Melphalan
- Novel drug
  - IMiD
    - Thalidomide
    - Revlimid
  - Proteasome inhibitor
    - Velcade
- Steroid
  - Dexamethasone
  - Prednisolone

New combinations

- Alkylating chemotherapy drug
- Novel drug
  - Next generation IMiD
  - Next generation proteasome inhibitor
- New emerging drug
  - IMMUNE modulation
    - HDAC inhibitor
    - Monoclonal antibody
    - Cell cycle inhibitor

Promising new treatments

Categories or types of new treatments:
- New IMiDs and new proteasome inhibitors
- Monoclonal antibodies
- Cell-cycle inhibitors
- HDAC inhibitors

Plus new treatments to improve:
- Quality of life, supportive care

Immunomodulatory drugs (IMiDs)

IMiDs are derived from thalidomide
- Newer versions are more easily tolerated
- Imnovid (pomalidomide)
- Less toxic, more effective
- Still have marked side-effects
Pomalidomide

• Closely related to Thalidomide and Revlimid
• More potent and generally well tolerated, works in patients refractory to Velcade and Revlimid
• Latest data shows that it enhances survival

Clinical study in UK:
• Pomalidomide plus low-dose dex (relapsed and refractory patients)

Proteasome inhibitors

• Proteasomes get rid of worn-out or unwanted proteins from cells
• Blocking proteasomes poisons the cell
• Myeloma cells are particularly vulnerable
• Velcade, Kyprolis (carfilzomib), ixazomib

MLN 9708 (Ixazomib)

• First oral proteasome inhibitor
• Effective on its own in multiply-relapsed patients
• Response rate of 90% in newly diagnosed patients in combination with Revlimid and Dexamethasone
• Reduced incidence of neuropathy

Clinical studies in UK:
• MLN 9708 plus Rev/dex vs Rev/dex (relapsed patients)
• MLN 9708 plus Melphalan/prednisolone (newly diagnosed patients)

Study Interventions

UK Myeloma Research Alliance
Myeloma XII (ACCoRD study):
Augmented Conditioning & Consolidation in Relapsed Disease

• Proposal for Myeloma XII Relapsed Intensive Study

• Re-induction therapy: Ixazomib/Thalidomide/Dexamethasone (ITD) as an oral version of VelThalDex
• ASCT: A comparison of HD Melphalan with HD Melphalan augmented by the proteasome inhibitor, Ixazomib.
• Consolidation/Maintenance: ITD for 2 cycles as consolidation. Ixazomib as monotherapy until progression.
Monoclonal antibodies

- Mimic antibodies produced naturally by the immune system
- Monoclonal antibodies recognise and attach to specific proteins on the surface of cancer cells
- This enables the immune system to target and destroy the cancer cells

Cell-cycle inhibitors

- Stop myeloma cells dividing (increasing)
- Dividing cells go through stages with "checkpoints"
- Cell-cycle inhibitors block the cell cycle in dividing myeloma cells
  - Arry-520
  - MLN8237
  - Seleciclib

HDAC inhibitors

- Histones are part of DNA scaffolding and switch off genes
- Allow myeloma cells to grow and multiply
- HDAC inhibitors keep good genes switched on
- Stops myeloma cells growing and surviving
- Panobinostat

Quality of life

- As patients live longer, improving quality of life is even more important
- This includes effects of the myeloma and its treatment on you as a person

Supportive care

- A key factor in prolonging life is better supportive care
- Specific studies looking at e.g. benefits of exercise, infection control, better management of complications (e.g. pain and peripheral neuropathy)
Areas for improvement

Myeloma is a very individual cancer, treatment needs to be personalised

Approval/access
- Drugs can only help when patients have access to them
- Health Technology Assessment bodies

Increased role of genetics and diagnostics

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MUK resources

- Clinical Trials Infoguide
- Clinical Trial Tracker and
- New Drug Scanner
- Horizons Infosheets
- Myeloma TV
- Infoline

** please visit the Myeloma UK Patient Information stand in the foyer area for further information