Future strategies for myeloma: new insights and treatments in development
Dr Cathy Williams
Consultant Haematologist
Nottingham University Hospitals
NHS Foundation Trust

Advancements in Science

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
  - Thalidomide
  - Revlimid
- IMiD Proteasome Inhibitor
  - Velcade
- Steroid
  - Dexamethasone
  - Prednisolone

New combinations

- Alkylating chemotherapy drug
  - Cyclophosphamide
- "Novel" drug
  - Thalidomide
  - Revlimid
- IMiD Proteasome Inhibitor
  - Velcade
- Steroid
  - Dexamethasone
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- New emerging drug
  - 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
- Immunovir (oralmidomide)
  - act on several different targets in myeloma
  - less toxic, more effective
  - still have marked side-effects
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

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
- Myeloma cells are particularly vulnerable
- Velcade, Kyprolis (carfilzomib), ixazomib

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
  - Seliciclib

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

Monoclonal antibodies

- Target different proteins on the surface of the myeloma cell
  - RANKL (denosumab)
  - CS1 (elotuzumab)
  - CD38 (daratumumab)
  - CD66
  - IL-6 (siltuximab)
  - DKK1 (BHQ 880)

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

This talk has covered...

Promising new treatments

Area where research needs to focus

Future prospects for myeloma treatment

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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