Treatment for relapsed and/or refractory myeloma

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This talk will cover....

• What do the terms 'relapsed myeloma' and 'refractory myeloma' actually mean?
• Treatment options at relapse
• Treatment options for refractory disease

Take home messages

• Myeloma is a complicated cancer which can vary a lot between different patients
• With treatments available in 2014 in virtually all patients whose myeloma has responded to treatment the disease will come back some day although rapid improvements in treatment may change this.
• Most patients who relapse will respond to second line chemotherapy

Definitions of Response to Treatment in Myeloma

• Response= At least 50% reduction in the amount of paraprotein- means the treatment has killed at least half of the myeloma cells.
• Complete Response =Absence of paraprotein in blood and myeloma cells in bone marrow following treatment. (this level of response is only achieved in a minority of patients)

Definitions of Disease Status in Myeloma

Plateau: Stable but detectable disease after finishing treatment
Relapse: Myeloma getting worse again following a previously successful course of treatment
Refractory Myeloma: No response to a course of chemotherapy whether initial treatment or treatment at relapse OR the myeloma improves but then starts worsening again within 2 months of finishing treatment

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RELAPSE

Relapse often picked up by blood test showing rising paraprotein before any symptoms
• Relapse less commonly picked up by new symptoms
• If there is a rising paraprotein without symptoms or new organ damage, it can be difficult to know when to restart treatment
  Too early – risk unnecessary side effects
  Too late – risk bone pains or kidney problems from myeloma


… Because of disease heterogeneity and variability in patient-specific factors including co-morbidities and the persistence of toxicities related to previous therapy, there can be no standard approach recommended for the treatment at relapse…

Factors to consider in deciding next treatment.
• Length of first response/plateau
• Tolerability to previous treatments
• Patient wishes
• Existing illnesses (comorbidities)
• Number of previous relapses
• Type(s) of previous treatment
• What we are allowed to prescribe (NICE, Cancer Drugs Fund)
Current UK Myeloma Treatment

There are currently 3 main drugs
- Thalidomide
- Lenalidomide = Revlimid
- Bortezomib = Velcade

Standard treatment usually consist of giving one of these 3 drugs with something extra such as Dexamethasone

First relapse options

- Generally tend to try a different one of these 3 main drugs from that used at initial treatment unless there was very prolonged response to that treatment
- For example patients who have had a combination including thalidomide as initial treatment are often treated with Bortezomib Cylophosphamide and Dexamethasone when the disease comes back for the first time
- Increasingly treatment consists of giving at least 3 drugs at one time
- Need to consider non- chemotherapy parts of treatment blood transfusions, bone treatments such as Zoledronic acid, psychological support and pain relief

The National Institute for Health and Care Excellence (NICE) has issued a second draft guidance not recommending the use of Lenalidomide for myeloma patients at first relapse who have previously received Bortezomib and who are not eligible for high-dose therapy and autologous stem cell transplantation.

- They concluded that Lenalidomide is not considered to be cost-effective for use in this situation and that there is a lack of clinical trial evidence on its use in this patient group.

BUT The Cancer Drugs Fund will still pay for Lenalidomide in this situation

Second Transplant?

- Transplants only rarely done in patients over the age of 67 as the side effects get worse as the patient gets older
- The effect of second transplant will not usually last as long as the first but if there was a prolonged response to the first transplant, doing it again may still be worthwhile.
- A recent Medical Research Council trial showed a benefit to second transplant in patients whose myeloma had come back for the first time if they had had at least an 18 month response to their first transplant
- On average patients had an 8 month longer response with a second transplant compared to just giving chemotherapy

Second relapse options

If patient has previously had thalidomide and Bortezomib then the obvious choice may be lenalidomide (Revlimid®)

- Similar to thalidomide but less toxic
- Much less chance of numb toes (neuropathy)
- Not sedative but more risk of skin rash and low blood counts
- NICE approved with dexamethasone

Latest news (last week)

The Cancer Drugs Fund will still pay for Lenalidomide in this situation
Refractory options

Bendamustine available via Cancer Drugs Fund
• Chemotherapy drug but hair loss unusual
• Intravenous infusion, 2 days every 4 weeks
• Can be used in by itself but better in combination
  with other drugs e.g. thalidomide and/or
dexamethasone
• Potential side-effects:
  - nausea,
  - infections, low blood counts.

Try Bortezomib combination for a second
• Cancer Drugs Fund will fund this for
  time- patients who have had at least a six month
  response to Bortezomib previously

Strong chemotherapy drug combinations
generally only suitable for younger patients-
DT-PACE, or ESHAP

Similar to lenalidomide but can work in patient who
• have failed lenalidomide
• Access at relapse via Cancer Drugs Fund but only for
  patients who have failed both bortezomib and
  lenalidomide
• Daily tablet
• Better in combination with other drugs e.g.
dexamethasone
• Potential side-effects: infections, low blood counts.

Clinical trial – good option as large number of new
drugs are being developed and these may still be
effective even if conventional treatment isn’t
working. BUT
• Not all patients will be eligible
• Trials often work by comparing a new treatment
  with existing ones so there may only be a 50%
  chance of getting the new drug.
• Some trials may only be open in larger hospitals -
  may mean more travelling for treatment

Future strategies

- Daratumamab
  Kyprolis™ (carfilzomib)
  Ixazomib (MLN 9708)
  Elotuzumab
  Panobinostat

No standard best approach to treatment at relapse
- adapting to meet patients’ needs important
- identifying the best sequence of treatments is
  challenging
Relapse options
- Thalidomide-based treatment if not had it before
- Bortezomib -based treatment if previously treated
  with thalidomide
- Second transplant
- Lenalidomide-based treatment at subsequent
  relapse
- Clinical trials

Other options for Refractory Disease

Pomalidomide
This talk has covered

- What are relapsed and refractory myeloma
- Treatment options at relapse
- Treatment options for refractory disease

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MUK resources signpost

- Myeloma – your essential guide
- Revlimid Infoguide
- Bendamustine Horizons Infosheet
- Clinical Studies Infoguide
- Myeloma TV
- Infoline

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