CHEMOTHERAPY PROTOCOL: VAD

INDICATION

VAD is a possible option for initial chemotherapy for symptomatic patients who may later be considered for high-dose therapy if CTD is for some reason thought to be inappropriate.

PRE-ASSESSMENT (see Lenalidomide with Dexamethasone protocol)

1. Ensure all the following staging investigations are done:
   - FBC & film
   - Clotting screen
   - U&Es
   - LFTs
   - Calcium
   - Albumin
   - Uric acid
   - CRP
   - Urine collection for creatinine clearance (CrCl), total protein, light chain (Bence Jones)
   - Electrophoresis and immunofixation for quantitation of serum paraprotein and immunoglobulins.
   - If light chain myeloma or non-secretory disease, serum free light chain assay (freelite)
   - β_2 microglobulin
   - Group and save
   - Skeletal survey (skull, whole spine, pelvis, all proximal limbs, CXR)
   - MRI if suspicion of spinal cord compression, or significant pain present in the absence of plain Xray changes
   - Bone marrow aspirate and trephine (with immunophenotyping for kappa/lambda if appropriate)
   - Consider sending cytogenetics to Dr. Fiona Ross, UKMF, Salisbury if new diagnosis < 60 yrs and not in a trial. Her lab should be phoned before sending the sample to:-

     LRF UK Myeloma Forum Cytogenetics Database
     Wessex Regional Genetics Laboratory
     Salisbury District Hospital
     Salisbury
     Wilts SP2 8BJ
     Tel: 01722 429087

     (NB: Cost of this test is ca. £350)

     Additional investigations:
   - Plasma viscosity if hyperviscosity suspected
   - If allogeneic transplant an option: Tissue typing of patient and siblings and CMV serology
2. Fertility - all relevant patients should be offered fertility advice and sperm storage if appropriate.
3. Hydration - fluid intake should be at least 3 litres per day.
4. Central venous access should be used, e.g. Hickman line.
5. Document patient's height and weight.
6. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent on the day of treatment.

DRUG REGIMEN

Vincristine	1.6 mg iv by continuous infusion (0.4 mg per day)	Days 1 to 4
Doxorubicin	36 mg/m^2 by continuous infusion (9 mg/m^2 per day) (Vincristine & doxorubicin may be mixed together & infused via a CADD or 6060 Sabraset made up to 96 ml with sodium chloride 0.9%)	Days 1 to 4
Dexamethasone	40 mg oral per day	Days 1 to 4 Days 12 to 15

CYCLE FREQUENCY

21 days. Repeat until maximum response. It is unusual to require more than 6 courses of treatment.

DOSE MODIFICATIONS

- Neutrophil count should be > 1.0 x 10^9/L and platelet count should be > 50 x 10^9/L before giving treatment at any stage unless low counts are thought to be due to myeloma per se.
- Vincristine should be omitted if significant neuropathy, likely to be due to this drug, occurs.
- Consider reduced dose of vincristine and doxorubicin if bilirubin > 50 µmol/L.
- If severe steroid related side effects develop, days 12 to 15 dexamethasone may be omitted from subsequent courses.

INVESTIGATIONS - First Cycle

- FBC.
- U&Es, Ca^{++}, LFTs, glucose, urate.
- Others - as per staging investigations (as listed under the PRE-ASSESSMENT heading above).

INVESTIGATIONS - Subsequent Cycles

- FBC.
- U&Es, Ca^{++}, glucose, LFTs.

ADDITIONAL INVESTIGATIONS - Alternate Cycles

- Monitor disease response (PP, free light chain assay or BM in non-secretory myeloma as appropriate).

CONCURRENT MEDICATIONS

- Allopurinol 300 mg daily for first week of first cycle only.
- Bisphosphonates as per protocol.
- Consider proton pump inhibitor and /or fluconazole.
- Consider aciclovir 200 mg three times a day if previous herpetic infection on chemotherapy.
- The incidence of pneumocystis infection in this situation is low and prophylactic co-trimoxazole should not generally be necessary.

ANTI-EMETICS

Metoclopramide 10 mg qds for 5 days - use as required. A $5HT_3$ antagonist may be needed if this is ineffective.

REFERENCES

1. Smith A, Wisloff F, Samson D; UK Myeloma Forum; Nordic Myeloma Study Group; British Committee for Standards in Haematology. Guidelines on the diagnosis and management of multiple myeloma 2005. Br J Haematol. 2006 Feb;132(4):410-51.
2. Cavenagh JD, Oakervee H; UK Myeloma Forum and the BCSH Haematology/Oncology Task Forces. Thalidomide in multiple myeloma: current status and future prospects. Br J Haematol. 2003 Jan;120(1):18-26.