

CHEMOTHERAPY PROTOCOL: C-VAMP

INDICATION

Initial chemotherapy for symptomatic patients who may later be considered for high-dose therapy and stem cell rescue. CTD is usually preferred for initial treatment unless there is a contraindication to this combination.

PRE-ADMINISTRATION

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. Allopurinol 300 mg daily for 7 days for first cycle only.
5. Central venous access should be used, e.g. Hickman line.
6. Document patient's height and weight.

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7. 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

Cyclophosphamide	500 mg iv bolus daily.	Days 1, 8 and 15
Vincristine	1.6 mg iv by continuous infusion (0.4 mg per day).	Days 1-4
Doxorubicin	36 mg/m ² by continuous infusion (9 mg/m ² per day) (Vincristine and doxorubicin may be mixed together and infused via a CADD or 6060 Sabraset made up to 96 ml with sodium chloride 0.9%).	Days 1-4
Methylprednisolone	1 g/m ² (max 1.5 g) daily iv OR orally - use iv preparation - dissolve the contents of the vials in water or fruit juice and take every morning.	Days 1-5

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 10⁹/L and pl count > 50 x 10⁹/L before giving treatment at any stage unless low counts are thought to be due to myeloma per se.

The day 8 and/or 15 cyclophosphamide should be omitted rather than delayed if the blood counts do not reach these criteria.

In presence of renal insufficiency (creatinine > 300 µmol/L) cyclophosphamide should be omitted and VAMP only (or VAD) given.

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.

INVESTIGATIONS - First Cycle

- FBC.
- U&Es, Ca⁺⁺, LFTs, glucose, urate.
- Others - as per staging protocol.

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).

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CONCURRENT MEDICATIONS

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

Days 1, 8 and 15 are moderate emetic risk.

REFERENCES

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2. Raje N, Powles R, Kulkarni S, Milan S, Middleton G, Singhal S, Mehta J, Millar B, Viner C, Raymond J, Treleaven J, Cunningham D, Gore M. A comparison of vincristine and doxorubicin infusional chemotherapy with methylprednisolone (VAMP) with the addition of weekly cyclophosphamide (C-VAMP) as induction treatment followed by autografting in previously untreated myeloma. *Br J Haematol*. 1997 Apr;97(1):153-60.
3. 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.

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