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Protocols for Pulsed IV Cyclophosphamide Immunosuppression

Pre-treatment checklist ☑

- ☐ Patient counseled about risks and benefits
- ☐ Document completion of immunosuppression risk management assessment – see protocol
- ☐ Fertility risk assessment when indicated, including sperm and oocyte preservation.
- ☐ Contraception is essential for both male and female recipients, lactation contraindicated
- ☐ Patient should have access to a thermometer and have a "Fever plan"
- ☐ Bladder care counselling
- ☐ Patient receives
    1. Patient Information Sheet
    2. Schedule of appointments (infusion dates and clinic appointments)
    3. Corticosteroid weaning strategy (if applicable)
- ☐ Schedule of infusions dates arranged with Nursing Team Leader, Concord Cancer Centre (aka B60-CCC), on ext 77893
- ☐ IV access satisfactory (if not, discuss with Nursing staff in Concord Cancer Unit)
- ☐ Surface area Mostellar Body Surface Area: available in "Powerchart Clinical Calculator"
- ☐ Use pre-printed chemotherapy order form
- ☐ Consider Bactrim prophylaxis (see protocol)
- ☐ Documented cessation of other forms of immunosuppression - excluding corticosteroids
- ☐ Consider drug interactions: Allopurinol, carbamazepine, phenytoin, rifampicin, others
- ☐ Outpatient script for take home anti-emetics completed for each cycle which is given by Oncology Pharmacy

1. **Cyclophosphamide: Standard Protocol (NIH)**

   - Cyclophosphamide 0.75 g/m^2 4-weekly for 6 cycles. Max dose 1500mg.
     - *GFR <30% normal*: Reduce dose to 0.5 g/m^2
     - *Severe disease*: Increase dose by 200mg per cycle (maximum 1.0g/m^2) unless neutrophils fall below normal at the day 10-14 nadir
   - Subsequent maintenance immune intervention strategies are generally required

2. **Cyclophosphamide: EUVAS ANCA-Vasculitis protocol** (Ann Intern Med 2009, 150, 670)

   Note: the 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of ANCA–associated Vasculitis recommends RTX in favour of cyclophosphamide for the initial treatment of GPA/MPA including severe disease

   1. Cyclophosphamide 15mg/kg IV (or as adjusted below) every **2 weeks for 3 doses** followed by 15mg/kg IV (or as adjusted below) **every 3 weeks until remission, and then for a further 3 months.**
   2. Remission is defined as a BVAS score of 1.0 or less. In the trial, treatment followed local practice for patients who did not achieve remission at 9 months.
   3. Maximum dose per pulse = 1.2g
   4. **Dose adjustments**:
      a. Age between 60 - 70 years: reduce dose by 2.5 mg/kg per pulse
      b. Age >70 years: reduce dose by 5 mg/kg per pulse
      c. Serum creatinine 300 to 500 µmol/L: reduce by 2.5 mg/kg per pulse
      d. Nadir total WBC between 2.0 and 3.0 x 10^9/L: reduce the next dose by 20%
      e. Nadir total WBC between 1.0 and 2.0 × 10^9/L: reduce dose by next dose by 40%

   - Subsequent maintenance with Azathioprine 2mg/kg daily until 18 months of therapy completed
   - PJP prophylaxis was standard for all patients

3. **Cyclophosphamide: Euro-lupus Nephritis protocol**

   - Cyclophosphamide 500mg (fixed dose) every TWO weeks for 6 cycles only.

Corticosteroids

- Please see PEXIVAS reduced dose corticosteroid dose reduction plan. Bone protection may be required.

Hydration

- Patients should be encouraged to drink at least 2000ml of fluid the day before and the day after treatment to maintain a brisk urine output

Mesna

- Mesna will not be prescribed routinely due to lack of evidence of benefit for patients receiving CYP doses in these protocols. Mesna should be considered for patients with obstructive bladder symptoms, micro/macroscopic haematuria or prolonged past oral cyclophosphamide therapy.

Full blood count monitoring

Each infusion will be subject to a satisfactory neutrophil count: > 1.5 x 10^9/L in the 2 weeks before treatment.

- FBC collected on the day of the infusion will tend to prolong the day-stay visit
- It is acceptable to proceed using the day 10-14 nadir neutrophil count from the previous pulse if this count is greater than 1.5 x 10^9/L..
- It is preferable if the FBC is arranged through Concord Hospital. If done privately, results should be faxed to 9767 8315 as well as sent by mail.

Medical review

- The patient should be discussed at the following Tuesday Patient Care Meeting
- The patient should be reviewed by the consultant or the registrar in the Immunology Clinic with the day 10-14 nadir neutrophil count depending on the protocol, and a urine dipstick for haematuria, in the middle of each cycle (NIH, EUVAS). Alternative arrangements may apply for patients located out of area.
- Confirmation for treatment form to proceed to next cycle to be completed
- The patient will be seen by the Immunology Registrar and/or resident in the Oncology Day Unit as required on the day of the infusion.

Premature ovarian failure - POV

- Breast cancer studies, 50% risk of POV is linked to cumulative CYP doses of
  - 20g for women in their twenties,
  - 10 g for women in their thirties,
  - 5 g for women in their forties

Bactrim

- Cotrimoxazole SS or DS daily or alternatives should be considered for all patients

Other monitoring

- Blood pressure (preference for early ACEI use), Body weight, Fasting lipids, BSL, intra-ocular pressure, BMD (see “Immunosuppression risk management”)