Cyclophosphamide IV in Autoimmune Disorders - Summary Clinical Guideline

Ref No. CG-RHEUM/2018/011

Introduction

There is an RCT evidence base for the use of pulse IV CYC in the following situations

- Remission Induction therapy in Systemic Vasculitis (e.g Granulomatosis with polyangitis; Eosinophilic granulomatosis with polyangitis; Microscopic polyangiitis and other forms of vasculitis)
- Lupus Nephritis (and other severe organ manifestations of Systemic Lupus Erythythematosus)
- CTD-ILD

Use in other situations e.g. Rheumatoid Vasculitis, Inflammatory Myopathy, is supported by an evidence base but no there are no RCT data.

The protocols for each condition are different, and should be adjusted by the treating Consultant according to disease and response to treatment.

Indications

1. Primary Systemic Vasculitis:

Pulsed IV Cyclophosphamide is preferred due to lower toxicity non-inferiority and reduced risk of infection. The following regime is in accordance with BSR ANCA positive vasculitis guidance https://doi.org/10.1093/rheumatology/ket445 :.

Adjunct steroids: IV Methylprednisolone 500-750mg 3 pulses followed by oral prednisolone 0.5mg/kg/day, reducing per clinicians discretion.

- 3 infusions at 2 weekly intervals then up to 7 infusions at 3 weekly intervals.
- 15mg/kg (reduce according to age & renal function- see below).
- Maximum single Cyclophosphamide infusion dose is 1.5 gm.

- Each individual course of Cyclophosphamide should be ≥3 months and ≤6 months.
- Lifetime exposure to Cyclophosphamide should be ≤25 g since the long-term toxicity of Cyclophosphamide is determined by cumulative dose.
- Patients on Cyclophosphamide should be monitored regularly and the dose should be reduced if there is Cyclophosphamide -induced leucopenia/neutropenia.
- Patients intolerant to Cyclophosphamide can be effectively treated with Rituximab.
- To be administered as per local practice.
- Give over a minimum of 30 minutes.

Dose adjustment according to age and renal function

Age (years)	**eGFR (ml/min/1.73m^2)**	
	>30	**<30**
< 60	15 mg/kg/pulse	12.5 mg/kg/pulse
> 60 and < 70	12.5 mg/kg/pulse	10 mg/kg/pulse
> 70	10 mg/kg/pulse	7.5 mg/kg/pulse

2. **CTD-ILD**

- Six 4-weekly infusions.
- 600mg/m$^{2.}$
- Dose adjustments: for eGFR<20 reduce dose by 25%; for eGFR<10 reduce dose by 50%.
- For systemic sclerosis patients use oral prednisolone: 10-20 mg alternate days.

3. **Lupus Nephritis**

Low dose regime (Euro-Lupus Nephritis Trial / St. Thomas' Hospital)

- Intravenous Cyclophosphamide; 500mg 2 weekly for 6 infusions.
- *Adjunct steroids:* IV Methylprednisolone 500-750mg 3 pulses followed by oral prednisolone 0.5mg/kg/day for 4 weeks, reducing to <10mg/day by 4-6 months http://doi.org/10.1093/rheumatology/kex286.

The high dose NIH regimen can also be used at the supervising consultant's discretion*:* Monthly IV Cyclophosphamide at 500-1000mg/m^2 BSA for 6 months followed by MMF/AZA as per ACR guidance: https://www.rheumatology.org/portals/0/files/ACR%20Guidelines%20for%20Screening,%20Treatment,%20and%20management%20of%20lupus%20nephritis.pdf.

The lower dose regimen has been proven to be as effective and safe yet less toxic for lupus nephritis in Europe in comparison to the high dose regimens.