RITUXIMAB-FLASH CARD

Compiled by- Dr Ratnakar Shukla, Dr Vishalakshi Viswanath
IADVL TASKFORCE ON BIOLOGICALS AND SMALL MOLECULES

Rituximab (RTX) is a specific mouse and human chimeric immunoglobulin G1 (IgG1) kappa monoclonal antibody which targets the CD20 antigen.

MOA

- Complement-dependent CD20+ B cell lysis
- Antibody-dependent cell-mediated cytotoxicity of CD20+ B cells
- Apoptosis of CD20+ B cells

Indications

FDA approved:

- Pemphigus vulgaris
- Non-Hodgkin's lymphoma
- Chronic lymphocytic leukemia
- Rheumatoid arthritis
- Wegener's granulomatosis and microscopic polyangiitis

Off- label:

- Dermatomyositis, cutaneous lupus erythematosus, systemic sclerosis, Sjogren's syndrome
- Bullous pemphigoid, mucosal pemphigoid, epidermolysis bullosa acquisita
- Graft-versus-host disease
- Atopic dermatitis
- Churg–Strauss syndrome, ANCA positive vasculitis, cryoglobulinemia associated vasculitis
- Kimura's disease, Schnitzler's syndrome, Waldenstrom's disease
- Primary cutaneous B Cell lymphoma, intravascular large B cell lymphoma, melanoma

Contraindications

- Hypersensitivity to the drug or murine proteins
- Active Hepatitis B and hepatitis C infections
- Severe heart failure (NYHA Grade III/ IV)
- HIV infection with CD4 count <250/µl

Availability

- Injection: 100 mg/10 mL (10 mg/mL) and 500 mg/50 mL (10 mg/mL)
- Storage: Refrigerated at 2°C to 8°C.
- Diluted product: Prepared infusion solution is physically and chemically stable for 24 hours at 2°C-8°C and subsequently12 hours at room temperature (not more than 30 °C).

Dosage

- Lymphoma protocol: RTX 375 mg/$m^{2,}$ IV infusion once weekly with four infusions over a month.
- Rheumatoid arthritis: RTX 1 g, IV infusion, Two infusions, one on day 1 and the other on day 15 (commonly used in pemphigus)

Pre-treatment work-up

- Complete hemogram, Liver function tests, Renal function tests
- Chest X-ray, USG abdomen, Mantoux test or IGRA, HRCT chest (when indicated)
- Screening test for HBsAg, anti-Hep B core (total), anti-HCV, HIV 1 and 2
- ECG and echocardiography
- Baseline serum level of desmoglein 1 and 3 antibodies
- Baseline IgG levels / CD 19 levels (optional)

Use in Special situation

- Pregnancy: Category "C." Recommended to use effective contraception during treatment with rituximab and for a year after the last dose
- Lactation: Recommended not to breastfeed during treatment and for at least 6 months after last dose of rituximab.
- Paediatrics: Useful, alternative therapy in recalcitrant childhood pemphigus. (RA or lymphoma protocol) In patients ≥ 6 months to <18 years dosage of 375 mg/m2, six infusions approved as combination with chemotherapy (lymphomas/ leukaemia)
- Vaccination: undertaken at least 4 weeks before RTX therapy or after 6 months. Live vaccines not recommended

Administration

Preferably admitted and supervised closely in day care treatment unit/intensive care unit/ward with facilities for monitoring

Premedication:

- Injection hydrocortisone 100 mg IV stat
- Injection pheniramine maleate 22.75 mg IV stat
- Tablet paracetamol 500 mg PO; 30 min prior to RTX infusion

Preparation of the infusion: 2 vials would provide 1 g/100 ml, it is to be mixed with 400 ml of normal saline (after letting out 100 ml from the 500 ml bottle)

First infusion (Day 1):

- Initiate at a rate of 50 mg/hour, if there are no infusion reactions, increase rate by 50 mg/h increments every 30 minutes, to maximum 400 mg/h

Second infusion (Day 15) and subsequent infusions:

- Initiate at a rate of 100 mg/hour, if there are no infusion reactions, increase rate by 50 mg/h increments every 30 minutes, to maximum 400 mg/h

Intralesional rituximab: effective modality for refractory oral pemphigus (5 mg/cm^2)

Patient monitoring during infusion

- Check pulse, BP, and respiratory rate and do pulse oximetry every 30 min.
- Watch for infusion reactions, these can be managed by reducing the speed of infusion (half the flow rate and re-administer the premedication). After 30 min, consider re-infusion with RTX. Serious adverse effects such as angioedema and anaphylaxis require complete cessation of infusion

Maintainence Treatment

- Month 6: For patients not in complete remission at month 6, repeat dose of 2g; and For patients in complete remission, on / off therapy at month 6, repeat dose of 500 mg or 1g (especially in severe cases and high Dsg levels)
- Month 12 & 18: For patients in complete remission, on / off therapy, 500 mg at month 12 and at month 18 based on clinical evaluation and particularly in patients with high Dsg levels
- For Relapse cases: Dose of 1 g (not earlier than 4 months from previous infusion

Monitoring Guidelines during follow-up

- Complete hemogram, kidney function test, liver function tests, S. electrolytes
- Repeat serology for anti-desmoglein 1 and 3 antibodies at month 6, 12, and 18 and whenever there is clinical evidence of relapse

Drug Interactions:

- No significant drug interactions except cisplatin associated nephropathy

Adverse Effects:

- Infusion reactions: (fever, rigors, nausea, vomiting, headache, hypotension, abdominal pain, urticaria, anaphylaxis)
- Tumor lysis syndrome
- Severe life-threatening cardiac arrhythmias, myocardial infarction
- Cytopenia, late onset neutropenia
- Fulminant hepatitis, reactivation of infections (hepatitis B, herpes simplex, herpes zoster, cytomegalovirus, tuberculosis), progressive multifocal leukoencephalopathy, a JC polyoma-associated, potentially fatal infection of the central nervous system
- Cutaneous: SJS-TEN, lichenoid dermatitis, urticaria, paraneoplastic pemphigus, serum sickness, vasculitis

Average cost

- 500 mg/50 mL- 7500- 12000 INR
- 100 mg/10 mL -2500 – 3200 INR