Rituximab

a. Practical therapy

Rituximab should be administered under close supervision in a setting with full resuscitation facilities. Since transient hypotension may occur during infusion, consideration should be given to withholding anti-hypertensive medications 12 hours prior to and throughout infusion with rituximab. Treatment with paracetamol and H1 antihistamines is recommended before and throughout each infusion to reduce the risk of infusion reactions. Premedication with corticosteroids may also be considered in order to reduce the frequency and severity of infusion-related reactions. Patients should receive 100 mg IV methylprednisolone to be completed 30 minutes prior to each infusion.

For the first infusion, rituximab should be administered at an initial rate of 50 mg/hour. If hypersensitivity or infusion-related events do not occur, this can be increased in 50 mg/hour increments every 30 minutes, to a maximum of 400 mg/hour. If hypersensitivity or an infusion-related event develops, the infusion should be temporarily slowed or interrupted. The infusion can continue at half of the previous rate upon improvement of the patient's symptoms.

Subsequent infusions of rituximab can be administered at an initial rate of 100 mg/hour, and increased by 100 mg/hour increments at 30-minute intervals, to a maximum of 400 mg/hour as tolerated. No dose adjustment is required in elderly patients (aged greater than 65 years).

b. Contraindications

Rituximab is contraindicated in patients with known hypersensitivity to rituximab or to murine proteins, in patients with progressive multifocal leukoencephalopathy (PML) or viral hepatitis, those who are exposed to live virus vaccines, who are otherwise immuno-compromised or with severe infection.

c. Drug interactions

There is limited data on drug interactions with rituximab. It is unlikely that rituximab affects the pharmacokinetics of drugs that are used in combination with it.

Concomitant use of other immunosuppressive or immunomodulatory drugs can enhance the degree of immunosuppression and increase the risk of severe infections.

Patients may be immunised with non-live vaccines during treatment with Rituximab. However, the vaccine response may be attenuated.

d. Toxicity

Rituximab has a profound effect on B-cell populations and might thus be expected to have a major effect on risk of infection. As noted above however, the principal effect of rituximab

seems to be on autoantibody production rather than on protective immune responses.[1] The German Registry of Autoimmune Diseases reported safety data in 370 patients who had received rituximab therapy and in this group there were 11 deaths (3%), mostly related to infection; the rate of infection was reported to be 5.3 cases per 100 patient years of treatment.[2] There are particular concerns about the risk of reactivation of hepatitis B[3] and the precipitation of progressive multifocal leukoencephalopathy due to the JC virus.[4] Screening for viral hepatitis is mandatory prior to rituximab therapy and, whilst no patients with pemphigus have thus far been reported with rituximab induced PML and the risk seems lower in patients with autoimmune disease than in those with haematological malignancies treated with rituximab, the high case fatality rate in PML means that treatment should always weigh benefits against risk and patients should be counselled accordingly.

Infusion reactions are generally mild in patients with pemphigus treated with rituximab but full resuscitation facilities should be available during infusions. Premedication with H1 blockers, paracetamol and methylprednisolone is advised. Occasional patients develop antibodies against rituximab, which may be associated with less favourable treatment response.[5]

Hypogammaglobulinaemia is uncommon, but may be persistent and immunoglobulin levels should be monitored at follow-up.[6-8] Some patients develop late onset neutropenia,[9] the exact mechanism of which is uncertain.

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