**RITUXIMAB PROFORMA FOR INFLAMMATORY AND AUTOIMMUNE BRAIN DISEASE IN CHILDREN**

**Background:** Rituximab is a monoclonal antibody that binds to CD20+ lymphocytes resulting in depletion. Rituximab has been increasingly used off label by paediatric neurologists to treat inflammatory and autoimmune brain disorders. There is little literature to support its use other than in Opsoclonus myoclonus ataxia syndrome and NMDAR encephalitis. Given the rarity of the syndromes, it is unlikely that controlled trials will be performed. This survey aims to use international collaborative network to define the following:

* The clinical syndromes that clinicians are treating with rituximab
* The approximate effect (this is not a clinical trial so this is approximate effect only)
* The side effects incurred
* The general outcomes

This study aims to inform clinicians about practice and improve counseling of side effects to families, and form the basis of future studies.

**Completion of form:** Please add as much information as possible. Please print off form, complete by hand, scan and email back to: russell.dale@health.nsw.gov.au

Save each patient file individually and name as: Chief investigator, then number eg Dale1, Dale2 etc

Please add any extra details as required

**Demographics:**

Chief investigator (surname) and patient number (eg Dale1):

Name of clinician that you would like to be acknowledged in acknowledgements at end of paper if not yourself (please write full name):

Clinical site:

Patient DOB:

Age at illness presentation:

Age at rituximab administration:

Sex of patient:

**Rituximab regimen (please tick as appropriate):**

|  |  |
| --- | --- |
|  | 375mg/m2 weekly for 4 weeks |
|  | 500mg/m2 fortnightly for 4 weeks (2 doses) |
|  | Other dosage regimen. Please provide details…. |
|  | Prophylactic antibiotic prophylaxis (co-trim etc) |
|  | Concomitant antihistamine administration |
|  | Concomitant steroid administration |
|  | Routine viral screening pre-rituximab? including JC virus. Provide details…… |

**Clinical signs or symptoms at any stage of neurological illness**

|  |  |
| --- | --- |
|  | Headache |
|  | Reduced consciousness |
|  | Altered behaviour |
|  | Psychosis (hallucinations, delusions) |
|  | Disinhibition |
|  | Memory loss/cognitive decline |
|  | Aphasia/mutism |
|  | Dysautonomia (brady/tachycardia, hyper/hypothermia) |
|  | Sleep disturbance |
|  |  |
|  | Pyramidal signs |
|  | Movement disorder. Detail….. |
|  | Eye movement disorder. Detail….. |
|  | Cerebellar signs |
|  | Optic neuritis |
|  | Sphincter dysfunction |
|  | Myelitis |
|  | Brainstem syndrome |
|  |  |
|  | Seizures |
|  | Refractory seizures (unresponsive to 2 or more AED) |
|  | Status epilepticus |
|  |  |
|  | Intensive care admission |
|  | Other. Please provide details………….. |

Provide extra information if required………………………………………………………………

**Indication for rituximab:**

|  |  |
| --- | --- |
|  | Acute disseminated encephalomyelitis (monophasic) |
|  | Clinically isolated syndrome |
|  | Neuromyelitis optica spectrum monophasic (NMO IgG positive) |
|  | Neuromyelitis optica spectrum monophasic (NMO IgG neg) |
|  | Relapsing optic neuritis (NMO IgG negative) |
|  | Relapsing transverse myelitis (NMO IgG negative) |
|  | Neuromyelitis optica spectrum relapsing (NMO IgG positive) |
|  | Neuromyelitis optica spectrum relapsing (NMO IgG neg) |
|  | Multiple sclerosis relapsing remitting |
|  | Other inflammatory demyelinating disease……….. |
|  |  |
|  | NMDAR encephalitis |
|  | VGKC-complex encephalitis |
|  | Basal ganglia encephalitis |
|  | GAD antibody positive encephalitis |
|  | Glycine Receptor antibody positive encephalitis |
|  | Suspected autoimmune encephalitis (antibody negative). Please specify clinical syndrome if possible (eg NMDAR-like) |
|  |  |
|  | Cerebral lupus (definite cerebral disease in proven SLE) |
|  | Suspected cerebral lupus |
|  | Other systemic rheumatic condition. Please provide details…. |
|  |  |
|  | Cerebral vasculitis (pathology proven) |
|  | Cerebral vasculitis (angiography support) |
|  | Suspected cerebral vasculitis (no pathology, but suspected using radiology or clinical features) |
|  |  |
|  | Opsoclonus myoclonus ataxia syndrome |
|  | Autoimmune movement disorder not otherwise specified |
|  |  |
|  | Rasmussen encephalitis |
|  | FIRES (fever induced refractory epilepsy syndrome) |
|  |  |
|  | Other………………. |
|  |  |

**Abnormal or diagnostic investigations at any time (Please report most abnormal investigation at any time if tests performed on multiple occasions) :**

|  |  |
| --- | --- |
|  | MRI supportive of inflammatory demyelination syndrome |
|  | MRI supportive of autoimmune encephalitis syndrome as above |
|  | MRI abnormal but non-specific. Details….. |
|  |  |
|  | CSF pleocytosis (>4 white cells/mm3) |
|  | CSF protein elevated (>0.4g/dl) |
|  | CSF oligoclonal bands intrathecal |
|  | CSF oligoclonal bands mirrored (presence in both CSF and serum) |
|  | CSF elevated neopterin (>30pmol/l) |
|  | CSF pressure elevation (>25-28cm water). |
|  |  |
|  | NMO/AQP4 IgG serum positive |
|  | MOG IgG serum positive |
|  | NMDAR antibody CSF positive |
|  | NMDAR antibody serum positive |
|  | VGKC-complex antibody serum positive |
|  | Anti double stranded antibody positive |
|  | Other lupus or APL antibody positive…… |
|  | Other antibody positive. Please provide details……….. |
|  | Elevated inflammatory markers (ESR, crp etc). Please specify… |
|  |  |
|  | Neural crest tumour screening positive (MRI, CT, MIBG etc). Specify if positive… |
|  |  |
|  | Brain biopsy compatible with vasculitis |
|  | Brain biopsy compatible with encephalitis not otherwise specified |
|  |  |
|  | Other diagnostic investigation. Please provide details…………. |

**Other immune drugs used (please tick box as appropriate for ‘before rituximab’ or ‘at any time’:**

|  |  |  |
| --- | --- | --- |
| Before rituximab | At any time |  |
|  |  | Steroids |
|  |  | IVIG |
|  |  | Cyclophosphamide |
|  |  | Azathioprine |
|  |  | Mycophenolate mofetil |
|  |  | Beta-interferon |
|  |  | Glatiramer acetate |
|  |  | Vitamin D |
|  |  | Other…… |

**Haematological effects of rituximab – please tick only if haematological side effect was considered likely** to rituximab

|  |  |
| --- | --- |
|  | No haematological effects |
|  | Transient lymphopenia (resolve within 12 months) |
|  | Persistent lymphopenia >12 months |
|  |  |
|  | Transient B cell lymphopenia |
|  | Persistent B cell lymphopenia >12 months |
|  | Transient hypogammaglobulinaemia |
|  | Persistent hypogammaglobulinaemia |
|  | Hypogammaglobulinaemia requiring IVIg replacement |
|  |  |
|  | Anaemia |
|  | Thrombocytopenia |
|  | Pancytopenia |

**Side effects attributed to rituximab (please tick box as appropriate).**

|  |  |
| --- | --- |
|  | No notable side effects |
|  | Infusion related headache (transient) |
|  | Infusion related skin rash (transient) |
|  | Infusion related fever |
|  | Infusion related flu like symptoms (chills) |
|  | Infusion related anaphylaxis |
|  | Other infusion reaction……….. |
|  | Serious infection probably related to rituximab. Provide detail and time relative to rituximab………… |
|  | Serious infection possibly related to rituximab. Provide detail and time relative to rituximab…………. |
|  | Progressive multifocal leukoencephalopathy (JC virus positive) |
|  | Other side effects probably related to rituximab………. |
|  | Other side effects possibly related to rituximab but other reasons possible…………. |

**Apparent ‘benefit’ of Rituximab. Please complete to best of your ability.**

|  |  |
| --- | --- |
|  | Definite benefit (clear improvements associated with use that were attributable to rituximab) |
|  | Probable benefit (clear improvements which could have been due to rituximab, natural improvements or related to other drugs used) |
|  | Possible benefit (modest improvements which could have been due to rituximab or other reasons) |
|  | No benefit (no clear effect on disease course) |
|  |  |

**Worst modified Rankin score at any stage of illness:**

**(Please report the level of disability for the patient’s illness as a whole, rather than just motor aspects)**

|  |  |
| --- | --- |
|  | Score 0- no symptoms at all |
|  | Score 1- no significant disability despite some residual symptoms, behavior and development appropriate for age |
|  | Score 2- slight disability: unable to carry out previous activities, but same independence as other age and sex matched children. |
|  | Score 3- moderate disability: (e.g. requiring some help but able to walk without assistance). |
|  | Score 4- moderately severe disability; (e.g. unable to walk without assistance). |
|  | Score 5- Severe disability; (e.g. bedridden, requiring constant  nursing care and attention) |
|  | Score 6- Dead |
|  |  |

**Modified Rankin score at time of initiation of rituximab**

|  |  |
| --- | --- |
|  | Score 0- no symptoms at all |
|  | Score 1- no significant disability despite some residual symptoms, behavior and development appropriate for age |
|  | Score 2- slight disability: unable to carry out previous activities, but same independence as other age and sex matched children. |
|  | Score 3- moderate disability: (e.g. requiring some help but able to walk without assistance). |
|  | Score 4- moderately severe disability; (e.g. unable to walk without assistance). |
|  | Score 5- Severe disability; (e.g. bedridden, requiring constant  nursing care and attention) |
|  | Score 6- Dead |
|  |  |

**Outcome of patient’s illness using modified Rankin score:**

|  |  |
| --- | --- |
|  | Score 0- no symptoms at all |
|  | Score 1- no significant disability despite some residual symptoms, behavior and development appropriate for age |
|  | Score 2- slight disability: unable to carry out previous activities, but same independence as other age and sex matched children. |
|  | Score 3- moderate disability: (e.g. requiring some help but able to walk without assistance). |
|  | Score 4- moderately severe disability; (e.g. unable to walk without assistance). |
|  | Score 5- Severe disability; (e.g. bedridden, requiring constant  nursing care and attention) |
|  | Score 6- Dead |

**Ongoing problems:**

Length of follow-up……………………………….(years)

|  |  |
| --- | --- |
|  | No ongoing problems |
|  | Ongoing cognitive or learning problems |
|  | Ongoing behavioural problems |
|  | Ongoing motor problems |
|  | Ongoing visual impairment (specify Visual acuity) |
|  | Ongoing epilepsy |
|  | Other ongoing problem. Please provide details…. |

**Ongoing treatments:**

|  |  |
| --- | --- |
|  | None |
|  | Repeat Rituximab regardless CD20 B cell counts (please specify time interval) |
|  | Repeat Rituximab when B cells repopulate (please specify threshold of B cell %) |
|  | Repeat Rituximab if clinical relapse |
|  | Other ongoing immune therapy required. Please provide details…. |

Thank you for completing this form.

Please write full name as required for authorship:

Please write highest degree:

Please write affiliation: