Clinical Trials in MOGAD (anti-MOG antibody associated disease)

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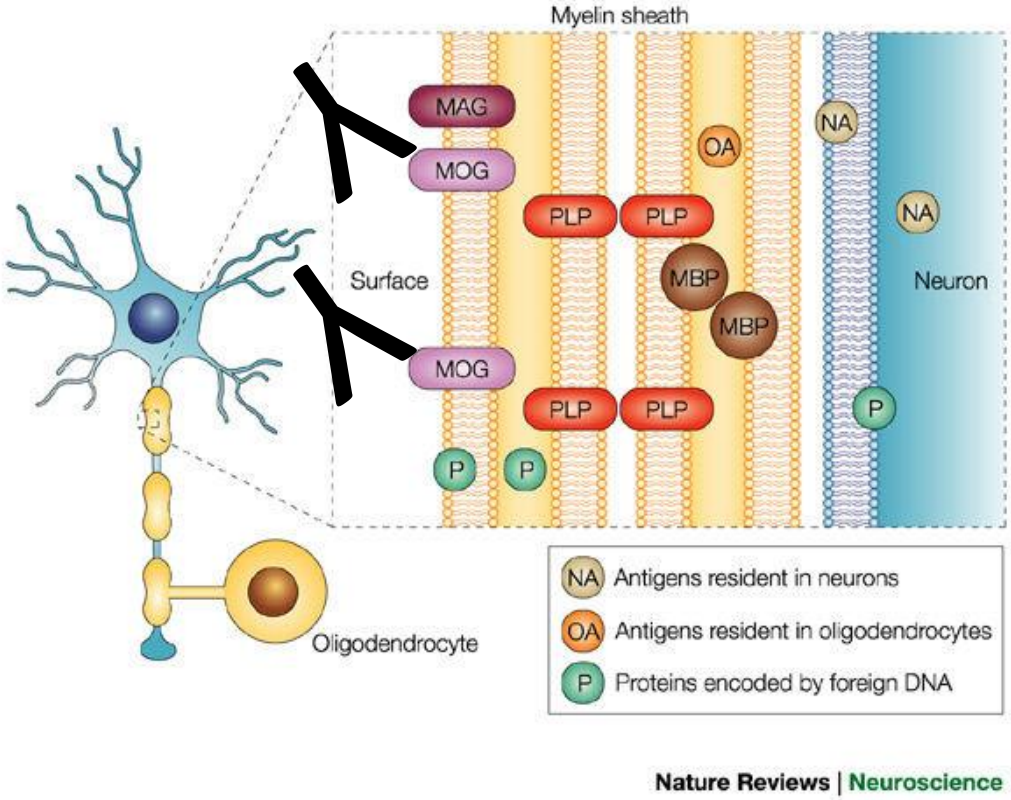
Disclosures

- Part-time salary support as consultant to the CDC for acute flaccid myelitis case review for disease surveillance
- Associate Editor for Annals of the Child Neurology Society (no honorarium)
- Off-label use of treatments may be discussed as no FDA approved medication for MOGAD
- No financial ties to any company discussed today

MOG = Myelin oligodendrocyte glycoprotein



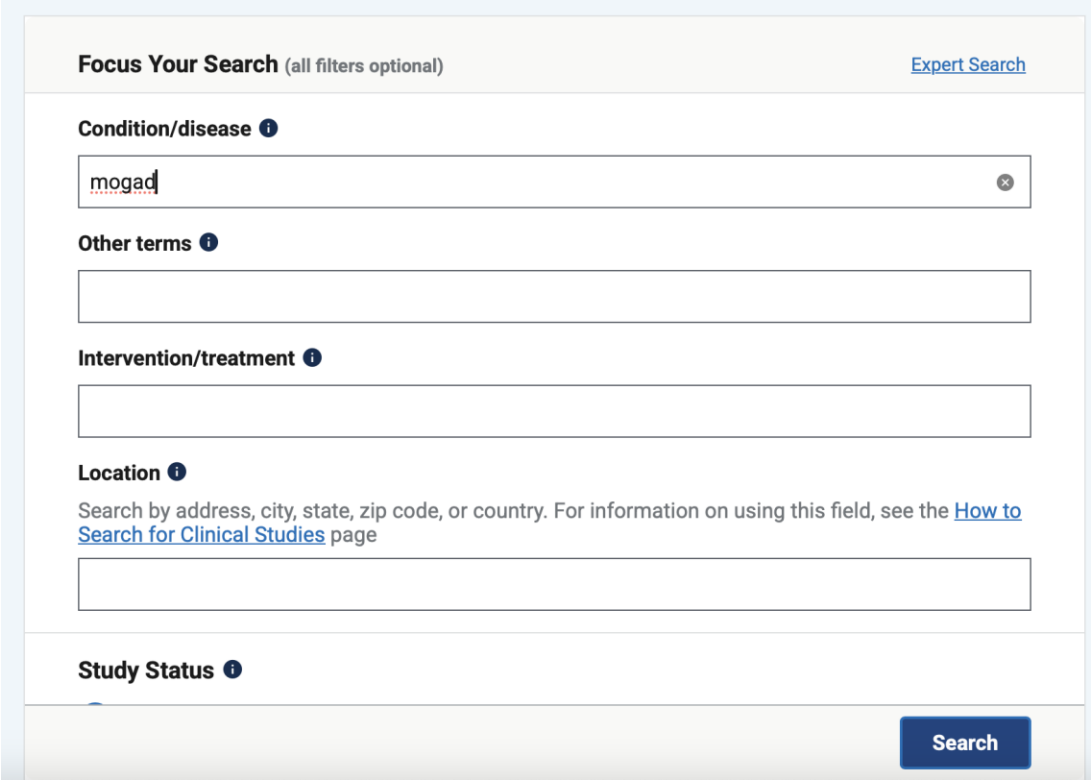
-Only expressed in central nervous system
-0.05% of myelin and on the surface of the myelin → exposed to antibodies

Hemmer B et al., Nat Rev Neurosci. 2002 Apr;3(4):291-301.

How to find current ongoing clinical trials

- Clinicaltrials.gov

- https://wearesrna.org → Research → Clinical Studies and Trials

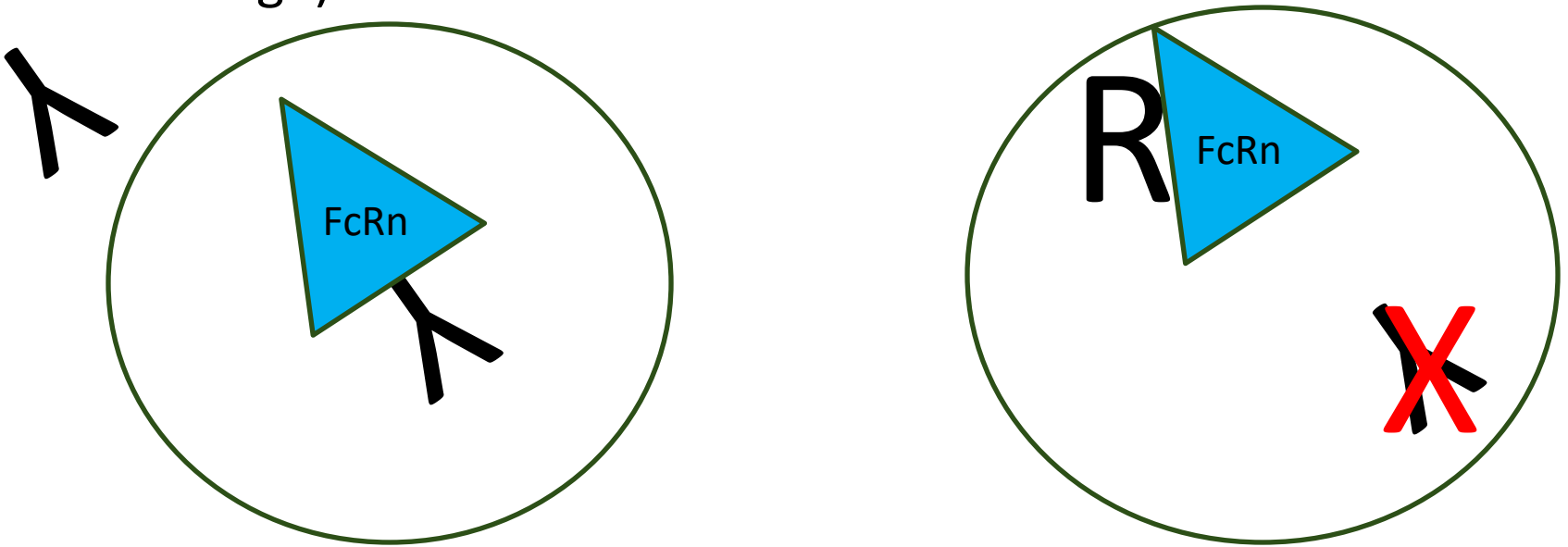


cosMOG clinical trial

- Clinical Trials number: NCT05063162
- Treatment: Rozanolixizumab (placebo – control)
- Double blind and then open label extension
- Inclusion criteria:
  - ≥18 to ≤89 years of age
  - Confirmed diagnosis of MOGAD
  - Relapsing MOG-AD with at least 1 documented relapse over the last 12 months
  - Positive serum MOG Ab test using a cell-based assay
  - No other immunotherapies

Rozanolixizumab mechanism of action

- Binds the neonatal Fc Receptor (works similarly to plasma exchange) → clears antibodies



Most common side effects

- Headache
- Upper respiratory infections
- Urinary tract infections

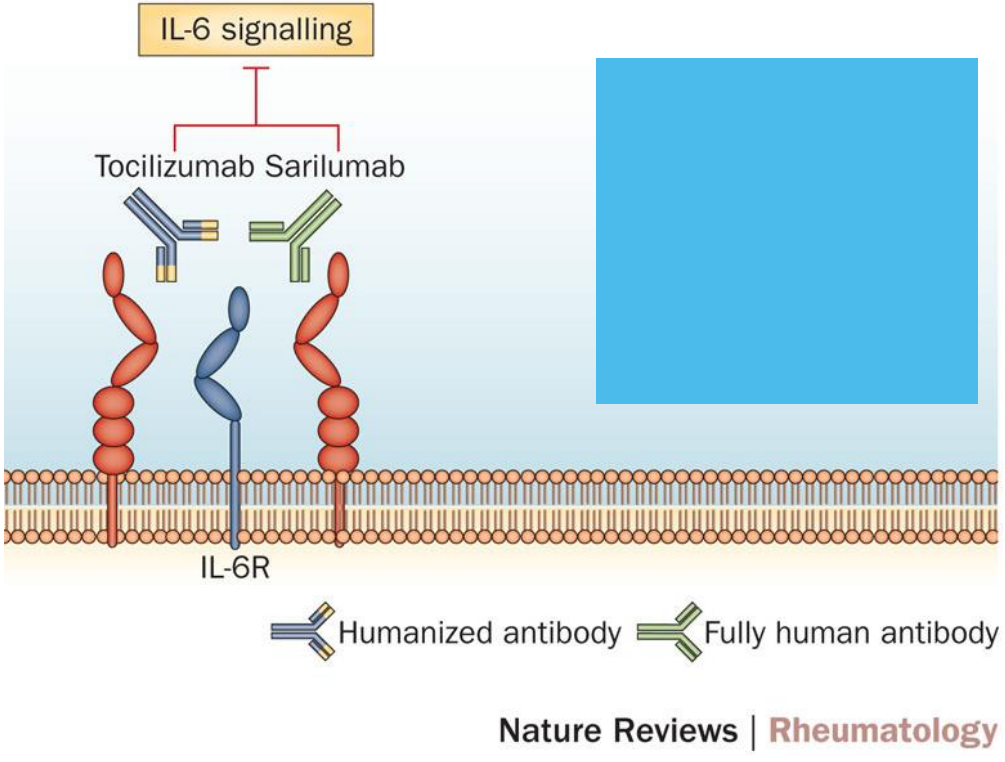
- For list of sites involved:
  - Clinicaltrials.gov: NCT05063162
  - https://wearesrna.org → Research → Clinical Studies and Trials

Meteroid

- Satralizumab (placebo-control)
- Double blinded (participants, researchers)
- >=12 years
- Confirmed diagnosis of MOGAD with a history of >=1 MOGAD relapse in the 12 months prior >=2 attacks in the 24 months prior to screening
- Can be on certain immune treatments

Mechanism of action for satralizumab

- IL-6 is a pro-inflammatory cytokine
- B cell activation
- Production of autoantibodies
- Blood-brain barrier dysfunction



Ruderman, E. M. (2015) IL-6 inhibition in RA—déjà vu all over again? Nat. Rev. Rheumatol. doi:10.1038/nrrheum.2015.58

More common side effects

- Headache
- Fatigue
- Rash
- Increased risk of infection
- Liver enzyme elevation

- Clinicaltrials.gov: NCT05271409

Azathioprine and MOGAD

- Medication taken by mouth
- Used in neuroinflammatory diseases
- Clinical trial in France to prevent relapses after a first attack in MOGAD
- Double blind
- Placebo control

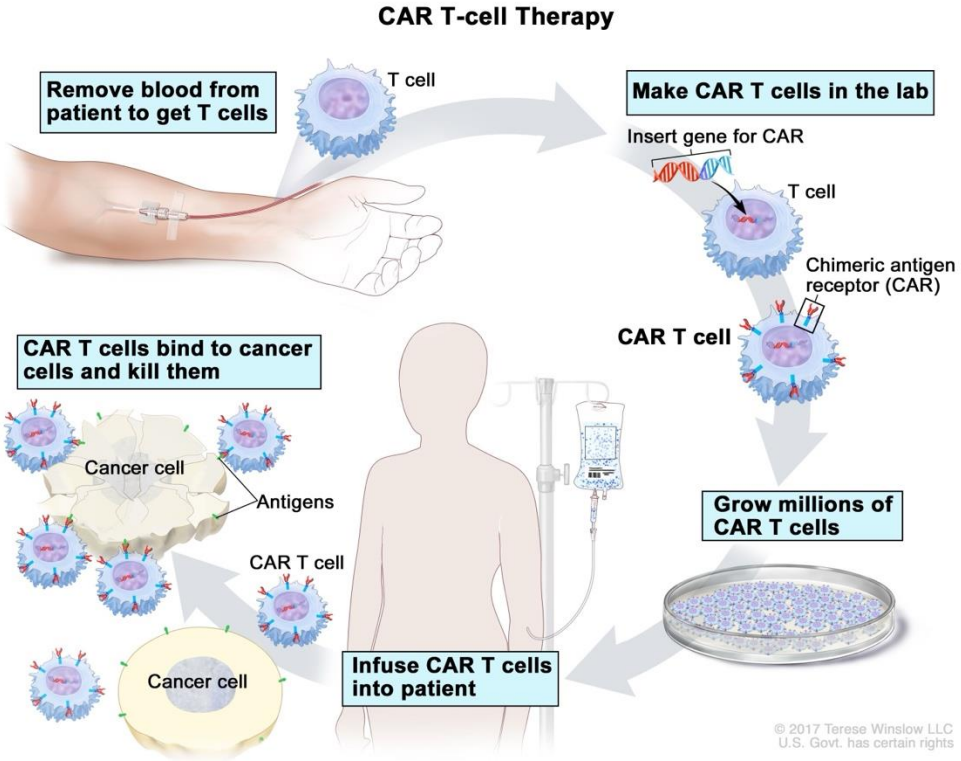
Clinical Trial number: NCT05349006

Safety and efficacy of tocilizumab in MOGAD

- Tocilizumab (similar action to satralizumab)
- Study is tocilizumab + prednisone vs prednisone only
- Confirmed diagnosis of MOGAD
- History of ≥1 MOGAD relapse in the 12 months or ≥2 attacks in the 24 months
- Randomized
- Open label
- China

Clinical Trial number: NCT06452537

CAR T-cell Therapy



https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy

MOGAD Clinical Trials

- Clinicaltrials.gov
- https://wearesrna.org → Research → Clinical Studies and Trials

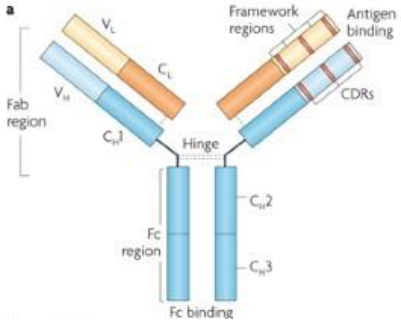
Treatments and side effects

Corticosteroids/steroids

- Prednisone, prednisolone, dexamethasone, methylprednisolone
- Suppress the immune system, can work quickly
- Side effects:
  - High blood sugars/diabetes
  - Acne
  - Bone density
  - Stomach irritation/stomach pain
  - Irritability/aggression/depression/mood changes
  - Insomnia
  - Glaucoma
  - Weight gain
  - Increased energy
  - High blood pressure
  - Suppress growth
  - Adrenal suppression – inhibit body's way to make steroids, which can cause problems in times of infection/stress

Intravenous immunoglobulin (IVIG)

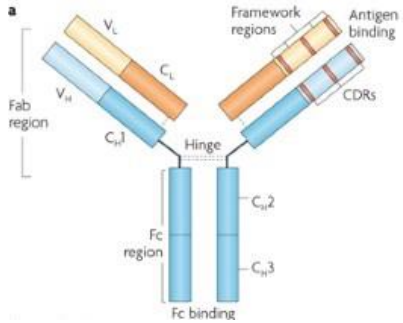
- Intravenous immunoglobulin is pooled from multiple of plasma, which comes from blood
- Different types of antibodies including IgG, IgA, IgM
- Antibodies are signals from immune cells that identify specific targets
- IVIG helps to block these targets or antibodies



https://giveplasma.ca/a-brief-history-of-ivig-therapy/

Side effects of Intravenous immunoglobulin (IVIG)

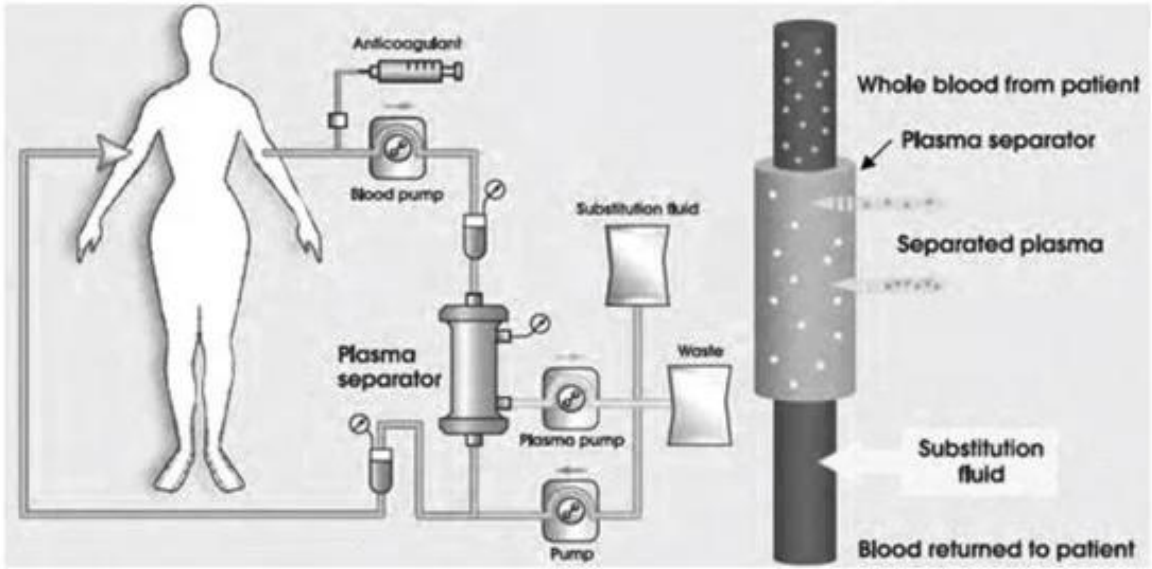
- Headaches
- Flu like symptoms
- Dizziness
- Nausea/vomiting
- Fevers
- Chills
- Aseptic meningitis
- Infusion reaction
- Allergic reaction
- Rash
- Fatigue
- Muscle soreness
- Blood clots
- Affects vaccine efficacy



https://giveplasma.ca/a-brief-history-of-ivig-therapy/

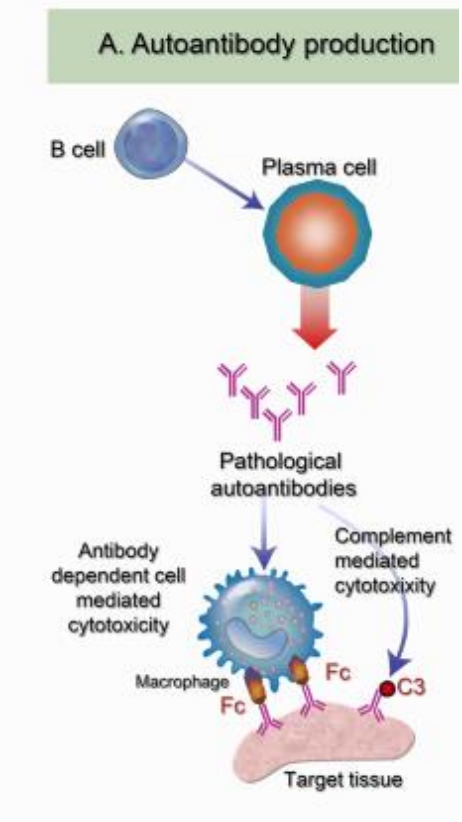
Plasma Exchange/Plasmapheresis

- Remove plasma which includes antibodies
- Large catheter cycles blood through a machine
- Every other day for 5-7 cycles
- Electrolyte imbalances, bleeding, low blood pressure, flushing, transfusion reactions



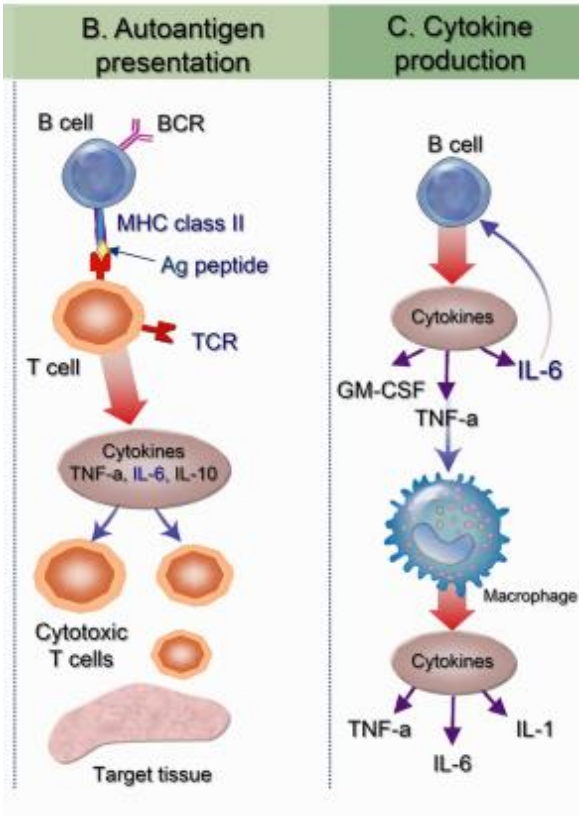
Tonev, Mochilova. Biomedicines. 2023 Jan25;11(2):328.

Rituximab: anti-CD20 monoclonal antibody



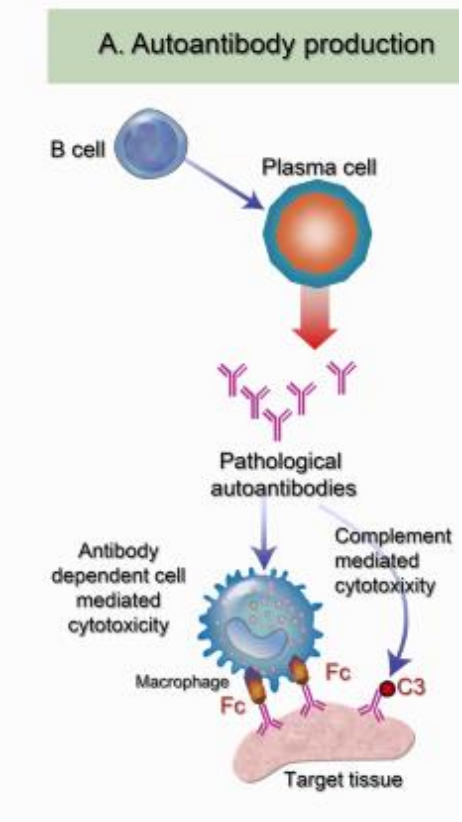
- Targets B cells which secrete antibodies
- Intravenously
- Side effects:
  - Infusion reactions
  - Rare allergic reactions
  - Immune suppression
  - Hepatitis and tuberculosis reactivation
  - Rare long term risk for cancer

Cyclophosphamide



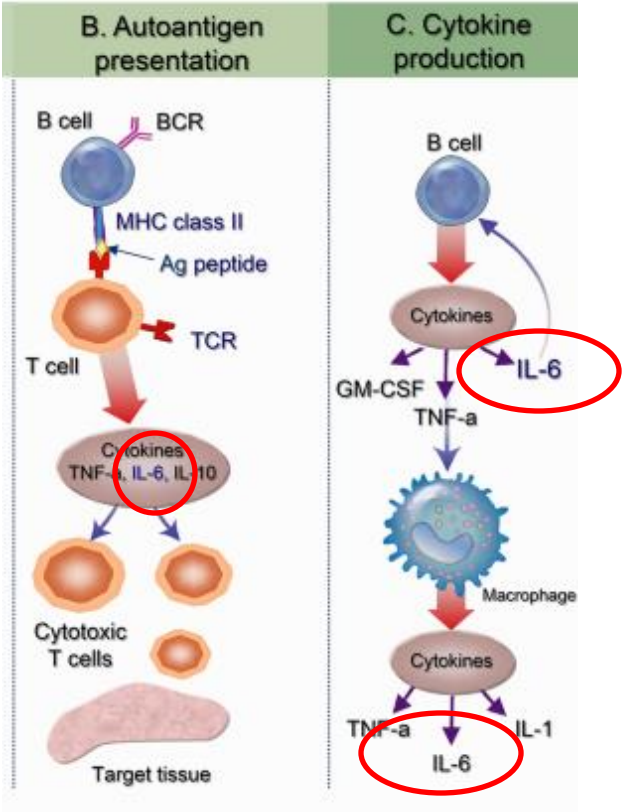
- Targets rapidly dividing cells, including B and T cells
- Usually given intravenously
- Given with Mesna and fluids to prevent hemorrhagic cystitis
- Nausea/vomiting
- Immune suppression, infection
- Urinary symptoms
- Can affect fertility, which is dose dependent
- Should not be given in pregnancy

Inebilizumab in autoimmune encephalitis



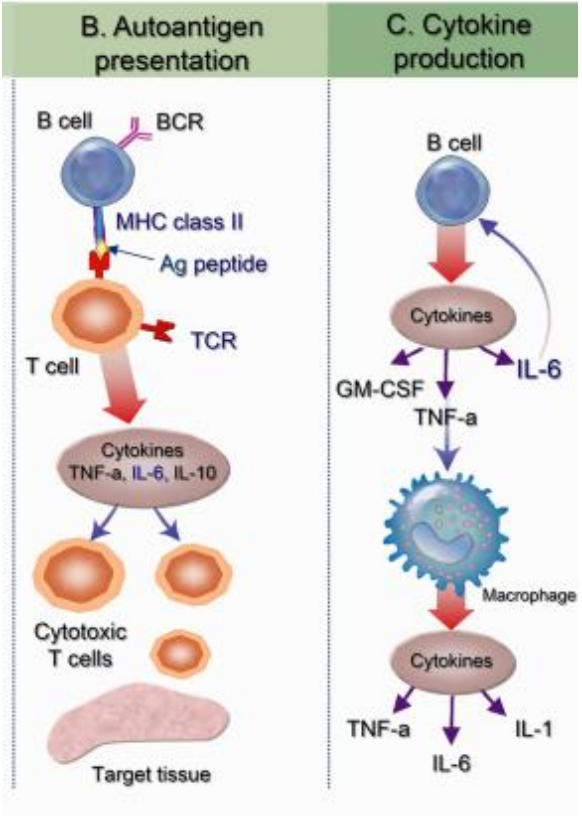
- Attaches to CD19, a marker of B cells including plasma cells and kills them
- Given intravenously
- Infusion reactions
- Low blood-cell counts
- Urinary tract infections
- Joint pain
- Headaches
- Back pain

Tocilizumab



- Blocks action of IL-6 by blocking IL-6 receptor
- Given intravenously (IV) or subcutaneously (under the skin)
- Increases plasma cholesterol
- Increases plasma AST or ALT
- Injection site reactions or infusion related reactions
- Do not start if: ANC < 2000, platelets < 100K, ALT or AST > 1.5 times ULN
- Hold therapy if ALT/AST 5x ULN, ANC < 500, platelets < 50K

Mycophenolate mofetil



- Inhibits replication of T and B cells
- Taken by mouth
- Nausea
- Infection
- Diarrhea
- Anemia
- Bleeding
- Bloating or swelling of the face, arms, hands, lower legs, or feet.
- Blood in the urine or stools