ANCA Induction and Maintenance in Severe Disease

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Background:

Induction:
- CYC and steroids have decreased mortality in AAV but both have significant toxicities.
- Oral and IV CYC have comparable efficacy (CYCLOPS) though lower cumulative dose in IV, with trend towards more relapses.
- RTX is effective in induction for AAV; noninferior to CYC, and superior in relapsing disease (but RAVE had no patients with Creat >4 or mechanical ventilation, and RITUXIVAS used 2 doses of IV CYC along with RTX)
- PEXIVAS: Plasmapheresis does not improve mortality or progression to ESRD in severe AAV. Low dose steroid regimen had equal efficacy and less infections than standard regimen.
- New drug: avacopan (oral): blocks C5a receptor on activated neutrophils reduces neutrophil activation, accumulation, adhesion and vascular permeability. Phase III trial (ADVOCATE)-results not published yet (treatment group for remission induction without use of any steroids). Promising preliminary results (tx group with avacopan was superior to standard of care). Avacopan as a possible steroid sparing agent in AAV.

Maintenance:
- Prone to flare: GPA dx, PR3 positivity, history of prior flare.
- MTX and AZA are both effective maintenance agents in AAV.
- RTX 500mg dose q6mo is superior to AZA in maintaining remission in PR3+ ANCA vasculitis patients.
- Currently recommend re-dosing RTX on a fixed schedule (500 iv q6mo) rather than monitoring ANCA and B cell repopulation

Q&A Pearls:
- When to use PLEX despite PEXIVAS: Presence of anti GBM Ab. Otherwise would not use PLEX as data convincing. Things to consider in PEXIVAS include low # of severe DAH with RTX induction. Lack of info on renal path on outcomes.
- When to use RTX vs CYC vs combination: Generally, use RTX for induction. IV CYC: when pt on mechanical ventilation; rapidly progressive GN as CYC may kick in faster.
- ANCA titers to monitor disease activity: upfront, after induction (did it remain positive? -->higher risk for relapse), and during maintenance, especially when trying to space out infusions.
- Usually uses 500mg q6mo for maintenance but if sicker patient may use 1g at initial maintenance dose. Or may start with 500mg and if improved but then worsening may increase to 1g. If flaring too soon, may dose at 4mo.
- Mononeuritis considered severe disease. Tracheal, subglottic involvement also may significantly affect quality of life. Treat aggressively, consider CTX too (especially if rapidly progressive as CTX works faster).
- Flares are not infrequent. May accrue damage. Maintenance tx for at least 2 years, usually for 5 years, then space out (checking ANCAs). May space out earlier if pt never had any flares, MPO+, intolerable issues with immunosuppression.