ERKNet
The European Rare Kidney Disease Reference Network

WGIKD
Working Group on Inherited Kidney Disorders

WELCOME TO

ERKNet
Advanced Webinars on Rare Kidney Disorders

Date: 16 November 2021

Topic: Can we avoid using corticosteroids in glomerular diseases?

Speaker: Alan Salama (London, GB)

Moderator: Marina Vivarelli (Rome, Italy)

UCL
DEPARTMENT OF
RENAL MEDICINE

Can we (should we) avoid using corticosteroids in glomerular diseases?

Prof Alan Salama

UCL Department of Renal Medicine

Royal Free Hospital

What drug and dose would you use

- A 25 year old woman, weight 90Kg, with first presentation of minimal change disease and nephrotic syndrome ?

1. 1mg/Kg prednisolone tapering over 4 months
2. 0.5 mg/Kg prednisolone tapering over 6-8 months
3. Tacrolimus 2mg bd for 6-12 months
4. Rituximab 1 g x2
5. Methylprednisolone x3 followed by Tacrolimus

What drug and dose would you use

- A 60 year old woman, with lupus nephritis class IV/V, Creatinine 90mcmol/, UPCR 300, arthralgias, rash and mouth ulcers?

1. Methylprednisolone 500 mg x3 followed by 1mg/Kg prednisolone with MMF/cyclo
2. 1mg/Kg prednisolone with MMF/cyclo
3. Prednisolone 1 mg /Kg, Tacrolimus 2mg bd and MMF
4. Rituximab 1 g x2, and MMF

What drug and dose would you use

- A 75 year old woman, with ANCA associated vasculitis, MPO-ANCA, Creatinine 501 mcmol/l, rash and arthralgias, and osteoporosis.

1. Methylprednisolone 500 mg x3 followed by prednisolone with cyclo/RTX
2. prednisolone with cyclo/RTX
3. prednisolone with MMF
4. Rituximab 1 g x2 and Cyclo with 2 weeks of pred
5. PEX, MP, Pred and cyclo/RTX
6. PEX, Pred and cyclo/RTX

KDIGO Guidelines

Condition	Steroids	With
MCN/FSGS	Yes , 1mg/Kg	
Membranous*	Yes	CYC/RTX
SLE	Yes	MMF, CYC
AAV	Yes	CYC, RTX
IgAN*	Yes	
GBM	Yes	CYC, PEX
Immune Complex GN/C3GN	Yes	MMF

* At high risk of progression

Practice Point 1.13.3.	**Choose a glomerulonephritis treatment regimen that minimizes harmful side effects from immunosuppression**	• Disclose individual drug side effects (both short- and long-term) • Consider the patient's point of view in shared decision-making • Screen for latent infections, where appropriate, prior to initiation of certain immunosuppression protocols • Monitor therapeutic drug levels where clinically indicated • Prescribe prophylaxis for specific immunosuppressive drug side effects • Review vaccination status and update as required • Offer fertility preservation, where indicated • Monitor for development of cancers or infections • Prolonged immunosuppression or multiple rounds of immunosuppression is associated with more toxic drug exposure over time

Background

- Cortisone isolated 1930
- Used therapeutically in RA 1948
- Used to treat nephrotic syndrome and nephritis late 1940's and 1950's(ACTH, cortisone, prednisone)
- 0.9% of general US population prescribed steroids; 7% of hospitalised patients
- Mainstay of treatment for inflammatory renal diseases, but despite this…
- Dosing and duration of treatment poorly studied
- Significant side effects; universally hated by patients

How did we get to current steroid dosing ?

UCL DEPARTMENT OF RENAL MEDICINE

How did we get to current steroid dosing ?

- MCD: 31 patients ; prednisone vs placebo(although 4 controls treated with steroid)
- Dose not less than 20 mg
- Duration: at least 6 months

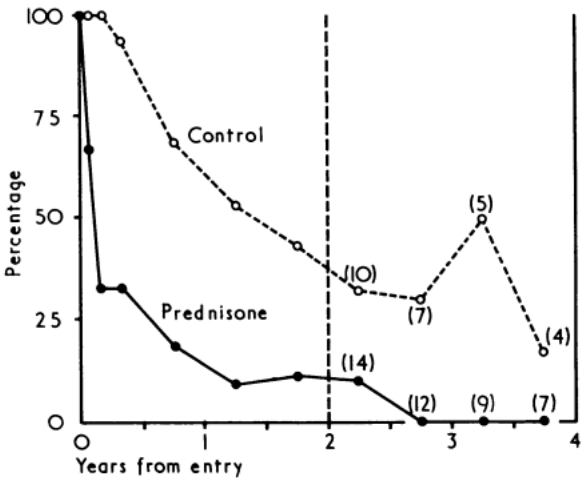
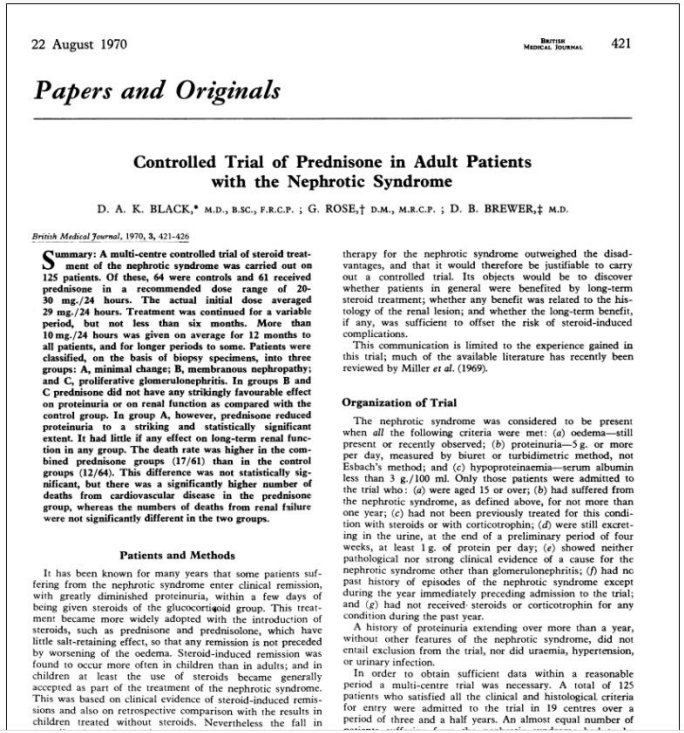


FIG. 2.—Group A patients (minimal change). Proportion of patients with proteinuria of more than 1 g./24 hours expressed as a percentage of those alive and in the trial (numbers of patients in trial after two years in parentheses).



22 August 1970 — British Medical Journal — 421

Papers and Originals

Controlled Trial of Prednisone in Adult Patients with the Nephrotic Syndrome

D. A. K. BLACK,* M.D., B.SC., F.R.C.P. ; G. ROSE,† D.M., M.R.C.P. ; D. B. BREWER,‡ M.D.

British Medical Journal, 1970, 3, 421-426

Summary: A multi-centre controlled trial of steroid treatment of the nephrotic syndrome was carried out on 125 patients. Of these, 64 were controls and 61 received prednisone in a recommended dose range of 20-30 mg./24 hours. The actual initial dose averaged 29 mg./24 hours. Treatment was continued for a variable period, but not less than six months. More than 10 mg./24 hours was given on average for 12 months to all patients, and for longer periods to some. Patients were classified, on the basis of biopsy specimens, into three groups: A, minimal change; B, membranous nephropathy; and C, proliferative glomerulonephritis. In groups B and C prednisone did not have any strikingly favourable effect on proteinuria or on renal function as compared with the control group. In group A, however, prednisone reduced proteinuria to a striking and statistically significant extent. It had little if any effect on long-term renal function in any group. The death rate was higher in the combined prednisone groups (17/61) than in the control groups (12/64). This difference was not statistically significant, but there was a significantly higher number of deaths from cardiovascular disease in the prednisone group, whereas the numbers of deaths from renal failure were not significantly different in the two groups.

Patients and Methods

It has been known for many years that some patients suffering from the nephrotic syndrome enter clinical remission, with greatly diminished proteinuria, within a few days of being given steroids of the glucocorticoid group. This treatment became more widely adopted with the introduction of steroids, such as prednisone and prednisolone, which have little salt-retaining effect, so that any remission is not preceded by worsening of the oedema. Steroid-induced remission was found to occur more often in children than in adults; and in children at least the use of steroids became generally accepted as part of the treatment of the nephrotic syndrome. This was based on clinical evidence of steroid-induced remissions and also on retrospective comparison with the results in children treated without steroids. Nevertheless the fall in therapy for the nephrotic syndrome outweighed the disadvantages, and that it would therefore be justifiable to carry out a controlled trial. Its objects would be to discover whether patients in general were benefited by long-term steroid treatment; whether any benefit was related to the histology of the renal lesion; and whether the long-term benefit, if any, was sufficient to offset the risk of steroid-induced complications.

This communication is limited to the experience gained in this trial; much of the available literature has recently been reviewed by Miller *et al.* (1969).

Organization of Trial

The nephrotic syndrome was considered to be present when *all* the following criteria were met: (*a*) oedema—still present or recently observed; (*b*) proteinuria—5 g. or more per day, measured by biuret or turbidimetric method, not Esbach's method; and (*c*) hypoproteinaemia—serum albumin less than 3 g./100 ml. Only those patients were admitted to the trial who: (*a*) were aged 15 or over; (*b*) had suffered from the nephrotic syndrome, as defined above, for not more than one year; (*c*) had not been previously treated for this condition with steroids or with corticotrophin; (*d*) were still excreting in the urine, at the end of a preliminary period of four weeks, at least 1 g. of protein per day; (*e*) showed neither pathological nor strong clinical evidence of a cause for the nephrotic syndrome other than glomerulonephritis; (*f*) had no past history of episodes of the nephrotic syndrome except during the year immediately preceding admission to the trial; and (*g*) had not received steroids or corticotrophin for any condition during the past year.

A history of proteinuria extending over more than a year, without other features of the nephrotic syndrome, did not entail exclusion from the trial, nor did uraemia, hypertension, or urinary infection.

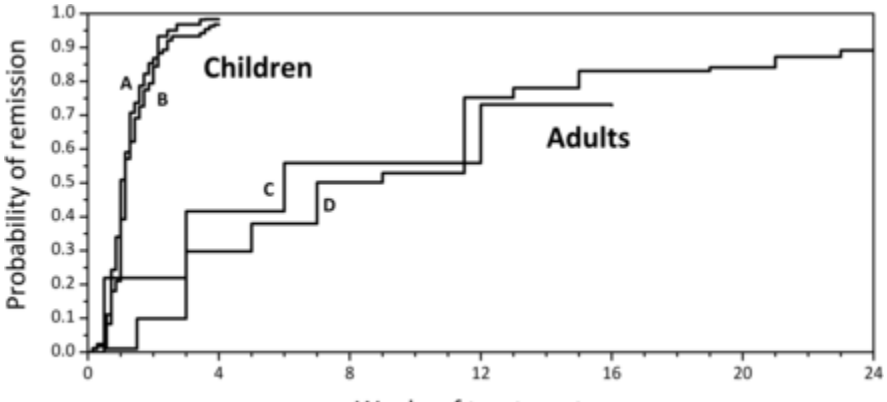
In order to obtain sufficient data within a reasonable period a multi-centre trial was necessary. A total of 125 patients who satisfied all the clinical and histological criteria for entry were admitted to the trial in 19 centres over a period of three and a half years. An almost equal number of

UCL DEPARTMENT OF RENAL MEDICINE

How did we get to current steroid dosing ?

- Adult nephrotic syndrome treatment extrapolated from some paediatric trials and adult cohorts: Despite differences in tempo

- 2-3 months no worse than 5-6 months of treatment in kids
- KDIGO 2021: max 16 weeks of high dose steroids



UCL
DEPARTMENT OF RENAL MEDICINE

The Journal of Laboratory and Clinical Medicine

VOL. 57 APRIL, 1961 No. 4

CLINICAL AND EXPERIMENTAL

EFFECT OF LARGE DOSES OF PREDNISONE ON THE RENAL LESIONS AND LIFE SPAN OF PATIENTS WITH LUPUS GLOMERULONEPHRITIS

VICTOR E. POLLAK, M.B., M.R.C.P.E.,* CONRAD L. PIRANI, M.D., AND ROBERT M. KARK, F.R.C.P., F.A.C.P.
CHICAGO, ILL.

Years	Number	Treatment	Outcome	notes
1953-55	N=10	Pred 10mg/day	10 died, 8 in renal failure median 13.8 months	Lower median creatinine at onset; More tubular damage and fibrosis on biopsy
1956-58	N=16	Pred 40-60 mg/day for 6 months	7 died (median 13.4 months), 9 alive at 34 months	More activity on renal biopsy

Saving daily oral steroids

BENEFICIAL EFFECTS OF METHYLPREDNISOLONE "PULSE" THERAPY IN DIFFUSE PROLIFERATIVE LUPUS NEPHRITIS

EDGAR S. CATHCART BELDON A. IDELSON
MORTON A. SCHEINBERG WILLIAM G. COUSER

Arthritis and Connective Tissue Disease and Renal Sections, Evans Department of Clinical Research, University Hospital; and Thorndike Memorial Laboratory and Division of Medicine, Boston City Hospital, Boston, Massachusetts 02118, U.S.A.

Summary Seven patients with diffuse proliferative lupus nephritis were subjected to high-dose intravenous methylprednisolone (pulse) therapy. Following the pulse, five patients with rapidly deteriorating renal function improved within three days and their serum-creatinine levels returned to baseline by one month. All seven patients demonstrated reversal of severe immunological abnormalities including increased serum D.N.A. binding, decreased serum C_3 levels, and reduced number of T lymphocytes in the peripheral blood. This form of therapy may make it possible to maintain patients with lupus nephritis on lower doses of steroids than is normally feasible.

Introduction

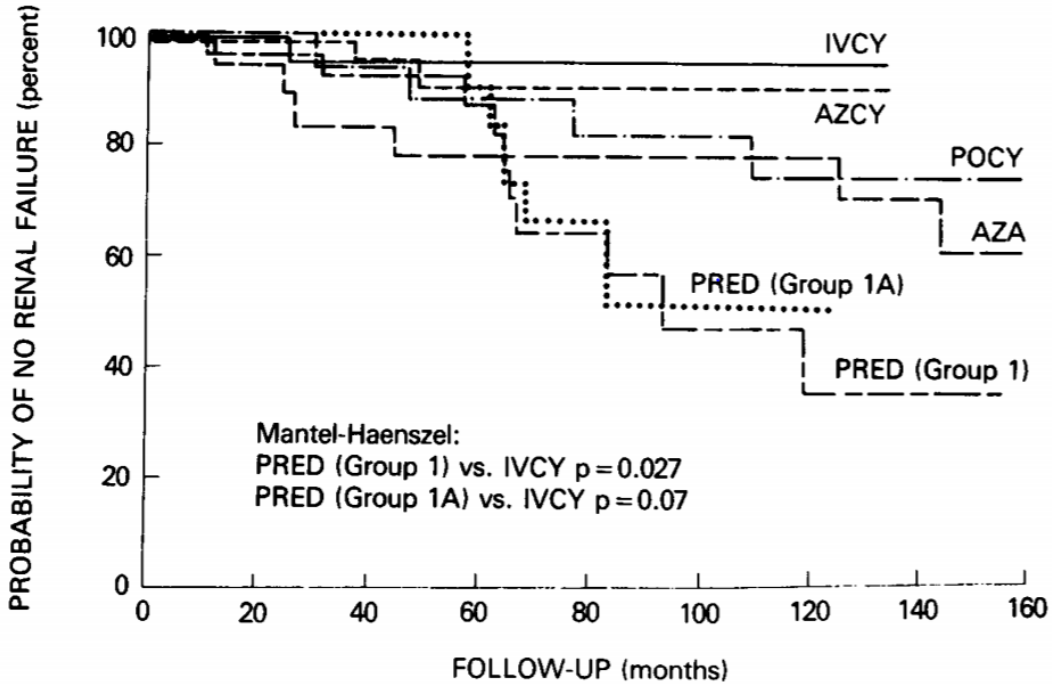
THE prognosis in patients with diffuse proliferative lupus nephritis is very poor and the majority of patients with this lesion and deteriorating renal function p gress rapidly to end-stage kidney disease.[1 2] In gen

3 pulses of 1g MP on consecutive days
Allowed reduction in daily oral prednisolone

Cathcart et al 1976

Combining steroids with other immunosuppressants

- Adding in cytotoxics or anti-proliferatives improved outcomes in SLE, anti-GBM, and vasculitis
- But despite adding in second agents, or using pulses of MP, high dose oral steroids were maintained

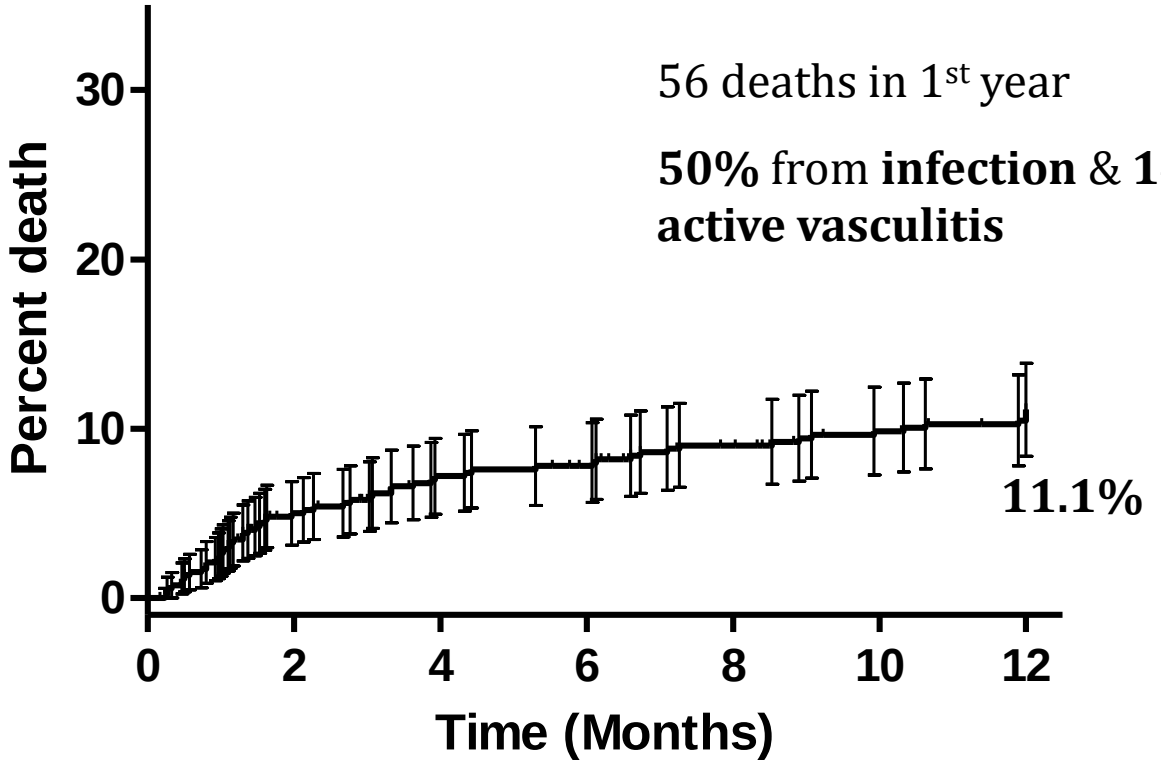


Pred 0.5 mg/Kg

Austin 1986

Modern protocols for AAV effective but problematic

EUVAS trials overall mortality

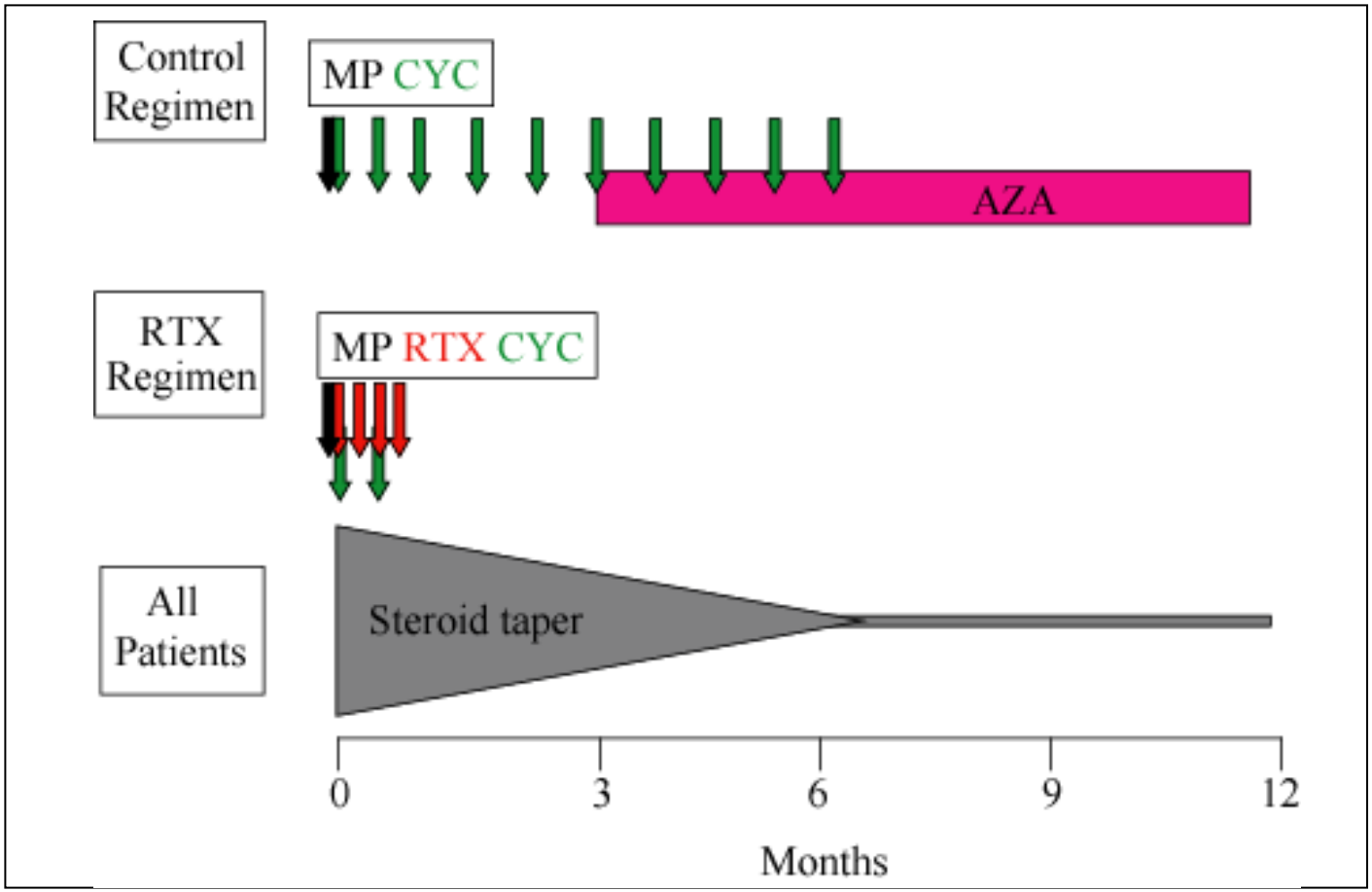


56 deaths in 1st year

50% from **infection** & **14%** from **active vasculitis**

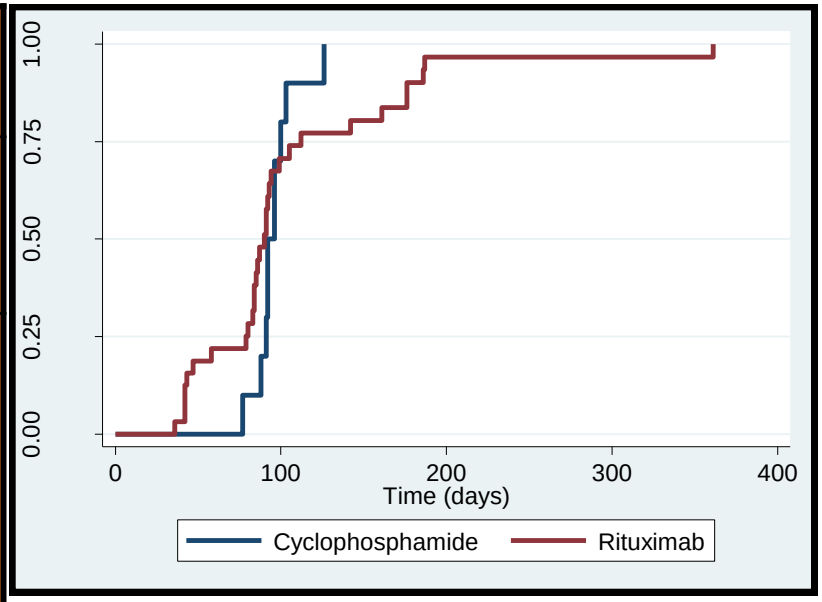
Little et al, Ann Rheum Dis, 2009

RITUXVAS: Trial Overview



Primary Efficacy End-point – Sustained remission (BVAS 0 maintained for 6 months)

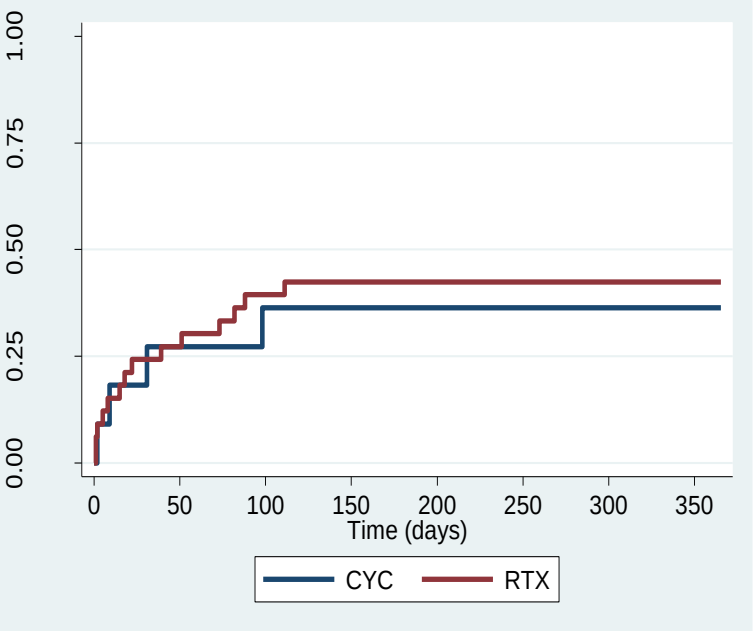
	RTX	CYC
Sustained remission	25/33 (76%)	9/11 (82%)
No sustained remission	2 incomplete response 6 deaths	1 incomplete response 1 death



Jones et al 2010 NEJM

Primary Safety End Point

	RTX	CYC
Severe Adverse Events	31 (42%) 1.0 / patient year	12 (36%) 1.1 / patient year
Infections	21 (39%) 0.66 / patient year	7 (21%) 0.60 / patient year
Death	6 (18%)	2 (18%)



Jones et al 2010 NEJM

Rituximab Versus Cyclophosphamide for Induction of Remission in ANCA-Associated Vasculitis: A Randomized Controlled Trial (RAVE)

- Non-inferiority study
- RTX (375 mg/m2 i.v. weekly x 4) vs oral CYC 2mg/Kg then Aza
- Steroids: 1-3 g i.v. methylprednisolone followed by prednisone 1 mg/kg/d p.o. reduced to 40 mg/d by month 1 and discontinued by month 6
- Endpoint remission off steroids at 6 months

- 197 patients;
- 1 European, 8 US centres

Stone et al 2010 NEJM

Rituximab Versus Cyclophosphamide for Induction of Remission in ANCA-Associated Vasculitis: A Randomized Controlled Trial (RAVE)

- 64% RTX vs 53% of CYC achieved primary endpoint (p=0.21)
- No difference in remission with Pulm haemorrhage or AKI
- Better outcome with RTX in those relapsing patients (67% vs 42% (p=0.01) regardless of ANCA type
- SAE Rate: 0.06 RTX vs 0.08 of CYC (p=NS), but fewer patients in RTX had 1 or more SAE (19 vs 32 pts, p=0.03)

What accounts for toxicity that persists despite avoidance of CYP?

- Common to all trials high doses of steroids with little data to support dosing regimen
- MP pulse doses vary a lot :
  - 250-1000mg x1-x3
  - 7-30 mg/kg vs 1g/m^2
- RAVE: mandated methylprednsiolone 1-3g, oral pred 1mg/Kg
- RITUXVAS: methylpred 500mg , oral pred 1mg/Kg

Role of MP in severe ANCA vasculitis

N=114 pts; 5 centres; severe AAV (Cr>500 or on dialysis) 52 additional MP vs 62 without

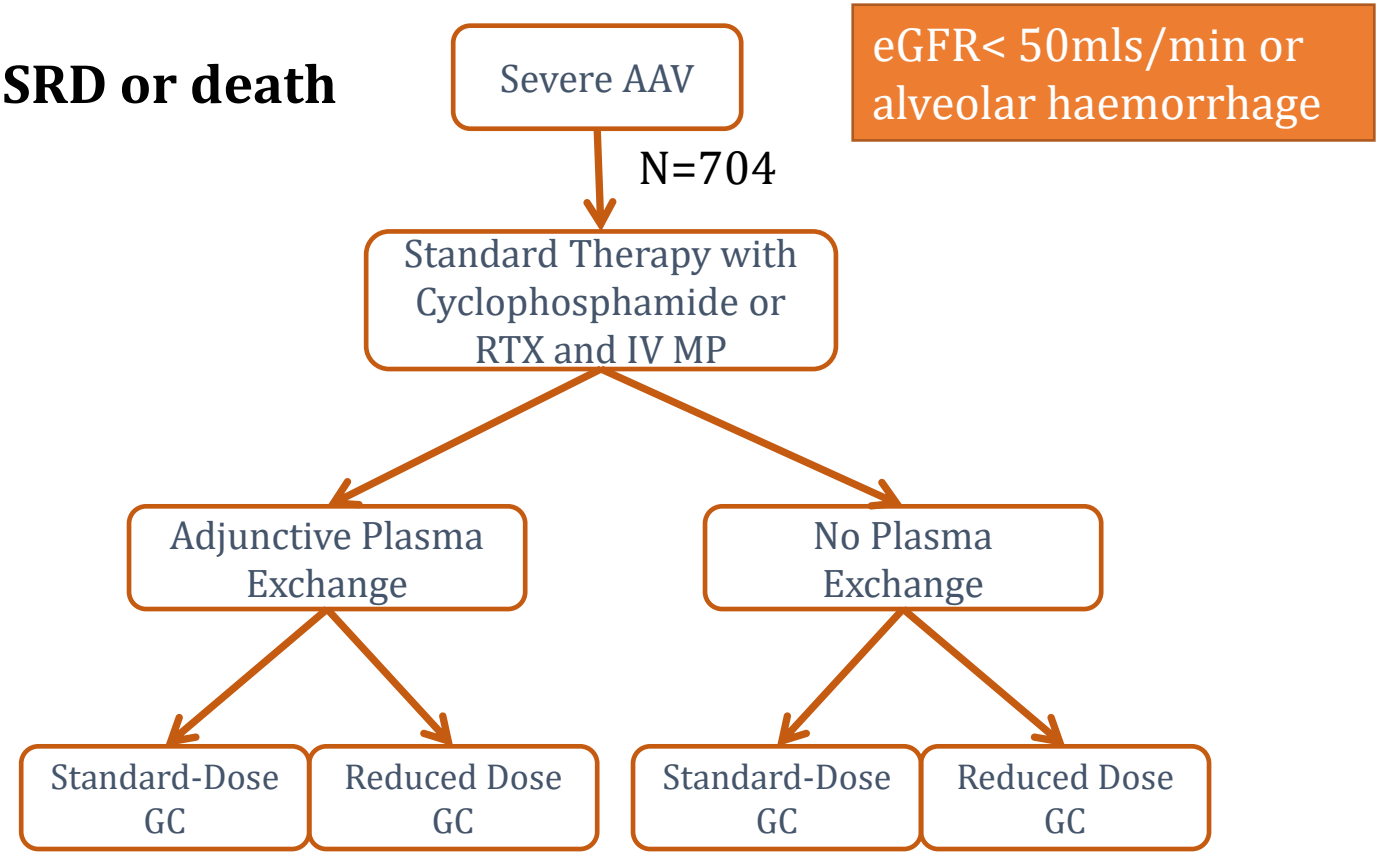
- No difference in renal recovery, survival or relapse
- Increased number of infections and rates of severe infection requiring hospitalisation(p=0.005)
- Increased risk of DM (28.6 vs. 6.6%; p=0.003)

No benefit from additional MP; positive harm

Chanouzas 2019

PEXIVAS: 1st trial to test steroid dosing

Endpoint: ESRD or death



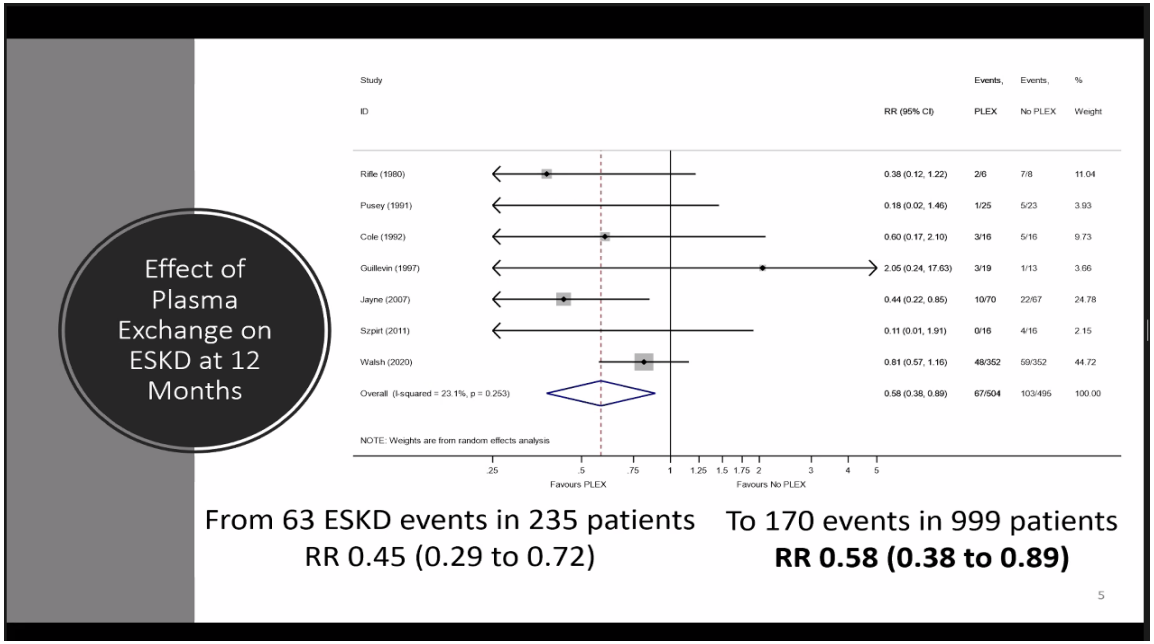
PEXIVAS outcomes

- Similar outcomes in lower/higher dose steroids
- Less infections in lower dose steroids HR 0.7(0.52-0.94) p=0.02
- **So we can use less steroids**

- No benefit from Pex on ESRD or death at 5 years
- Some potential signal in those with PH, so may still be beneficial

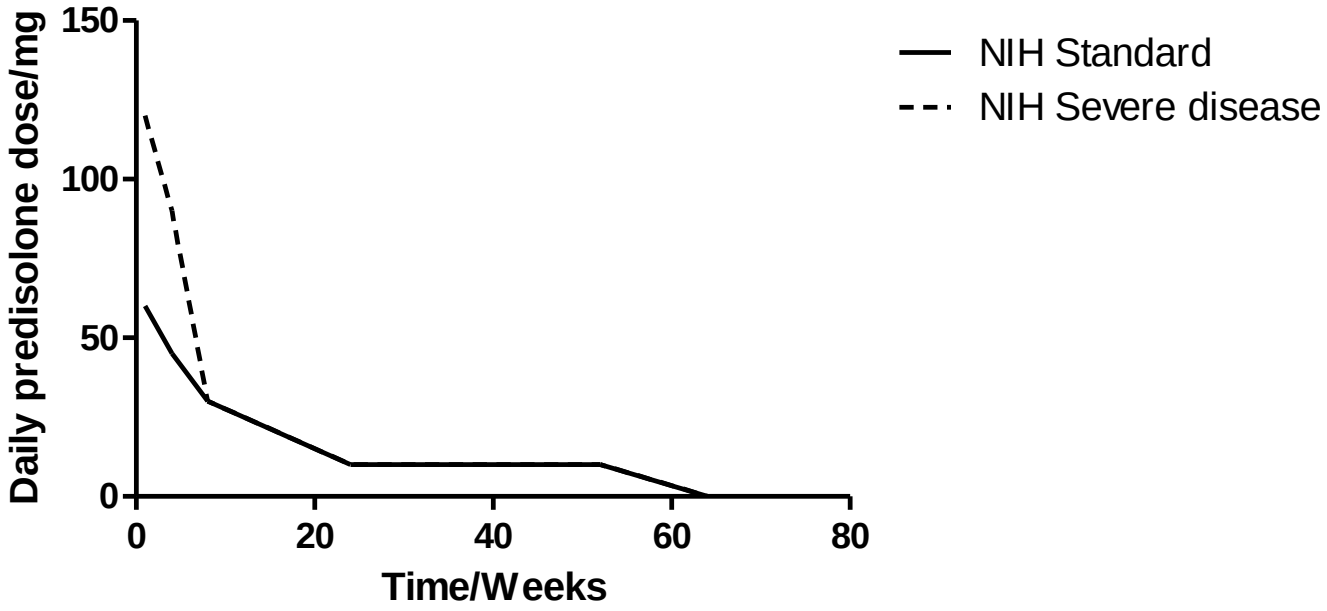
UCL DEPARTMENT OF RENAL MEDICINE

Meta analysis of PEX for severe AAV

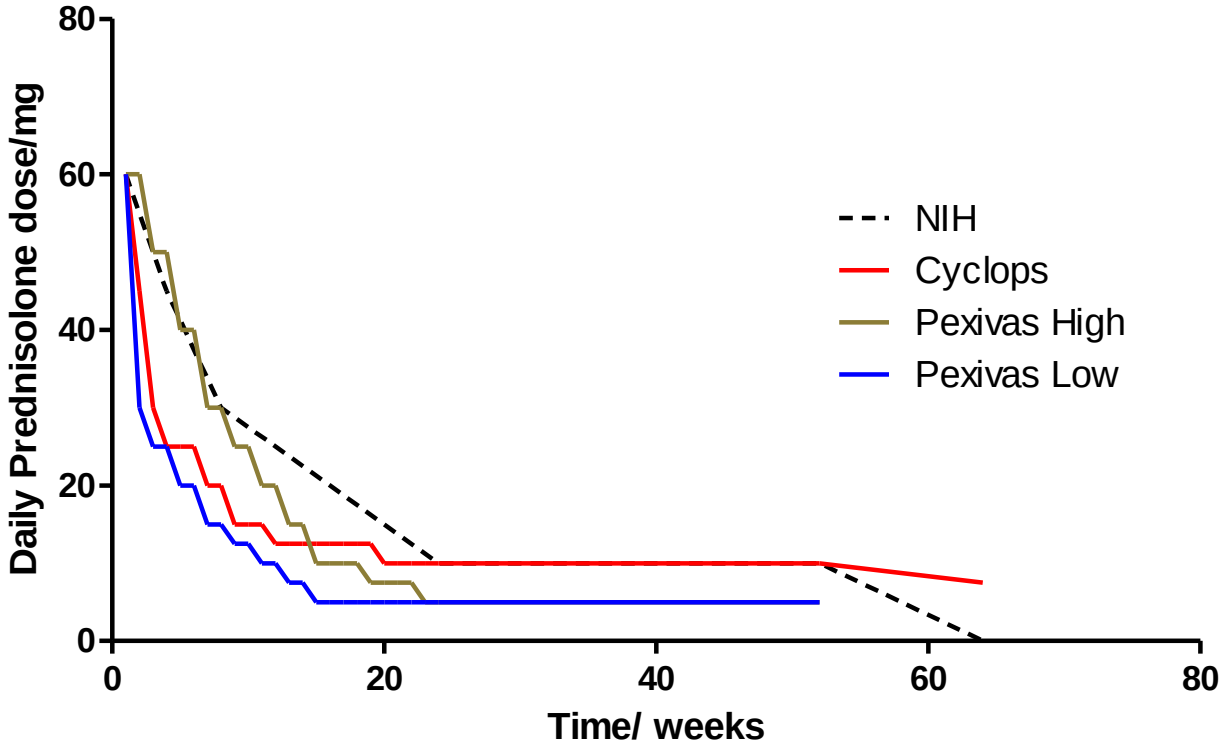


Serum Creatinine	Baseline Risk of ESKD	Risk of ESKD with PLEX	NNT	Recommendation
<200	1%	0.6%	250	Weak Recommendation **Against**
200 to 300	7.5%	4.3%	32	
>300 to 500	20%	11.6%	12	Weak Recommendation **For**
>500 or on dialysis	40%	23.2%	6	

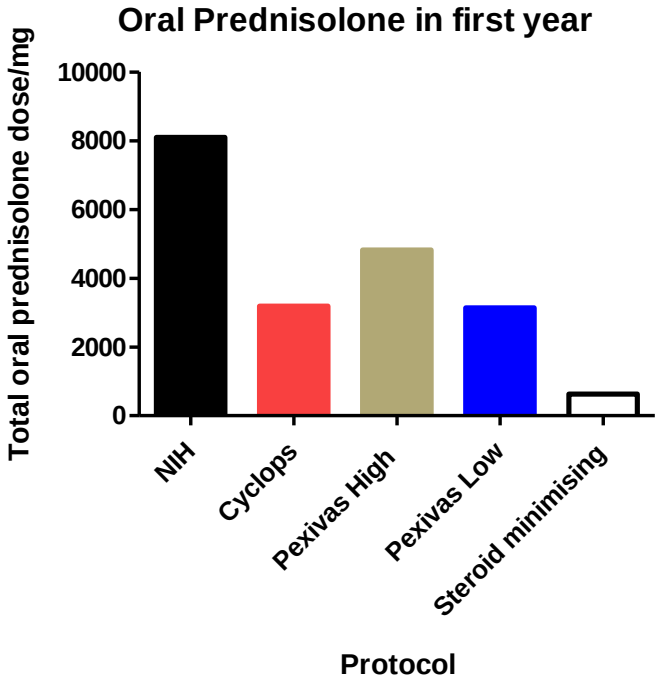
NIH prednisolone and cyclophosphamide for AAV

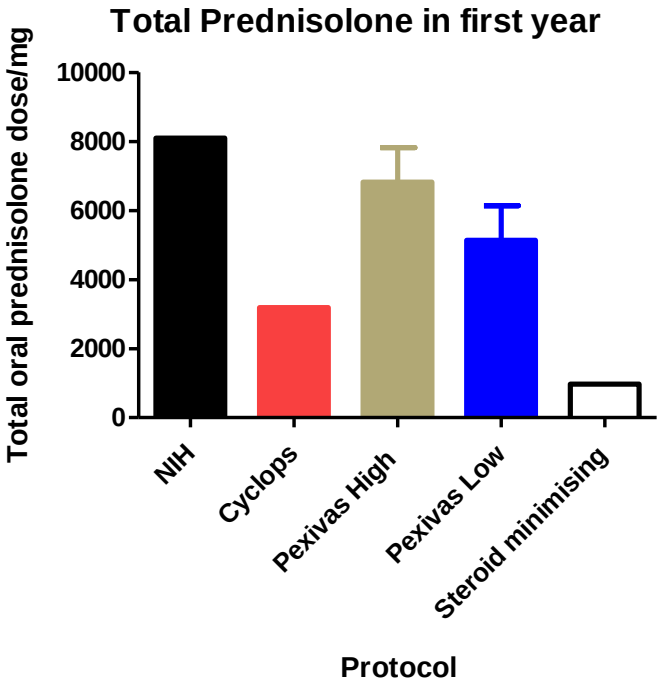


EUVAS steroid protocol refinement in AAV



Total steroid exposure in first year





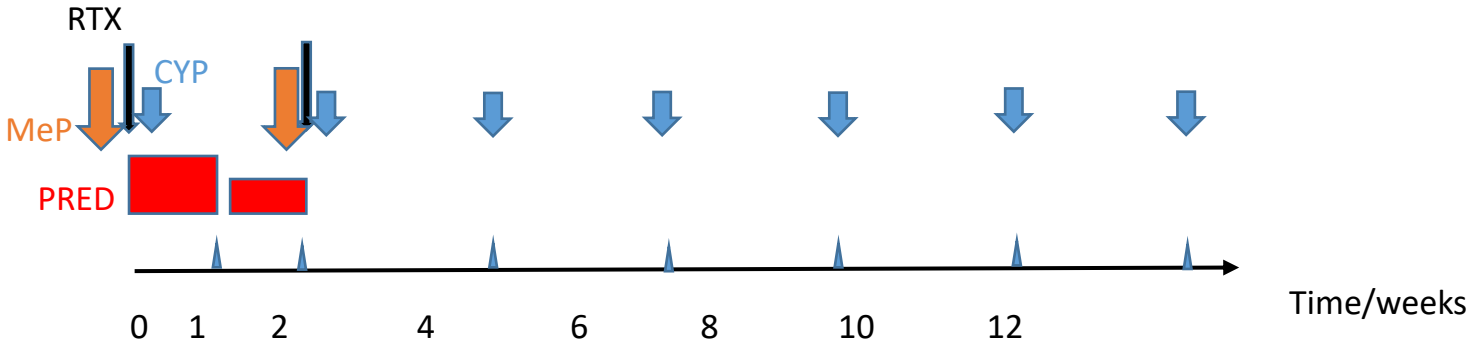
Steroid minimisation

- 8 weeks of steroids with 4 weeks of RTX ; N=20
- Allowed methylprednisolone (max 3 g)
- Excluded severe disease
- 70% achieved remission @6 months
- 30% relapse rate
- Fewer adverse events than RAVE

Miloslavsky et al 2018

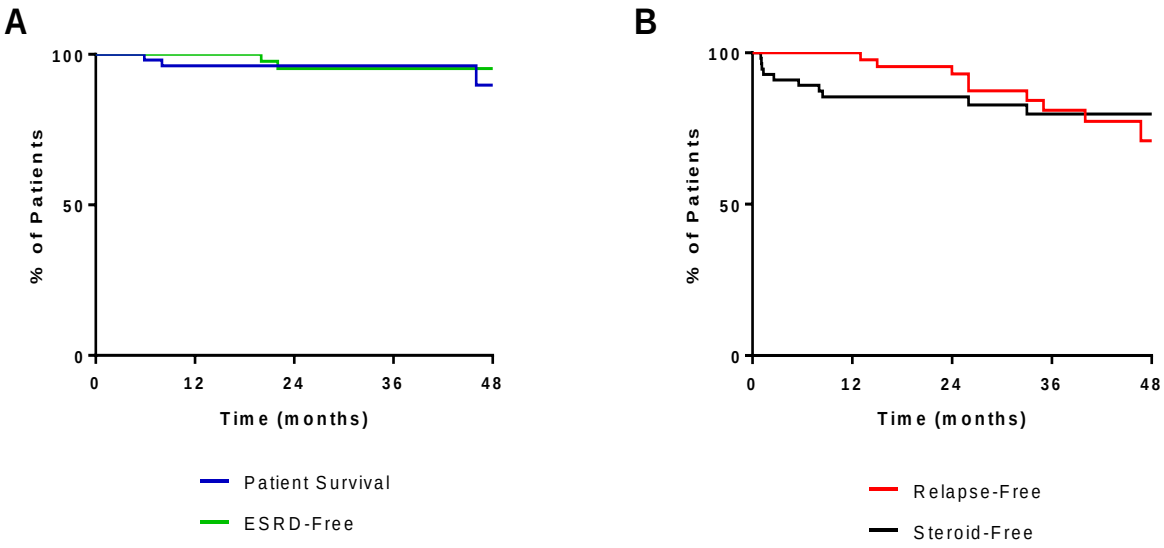
London extreme steroid minimization cohort n=58

Methylprednisolone
Rituximab 1gx2: 2 weeks apart
Cyclophosphamide 500mg x6/every 2 weeks
Prednisolone 60mg 1 week, 45mg 1 week or 30 mg for 1 week

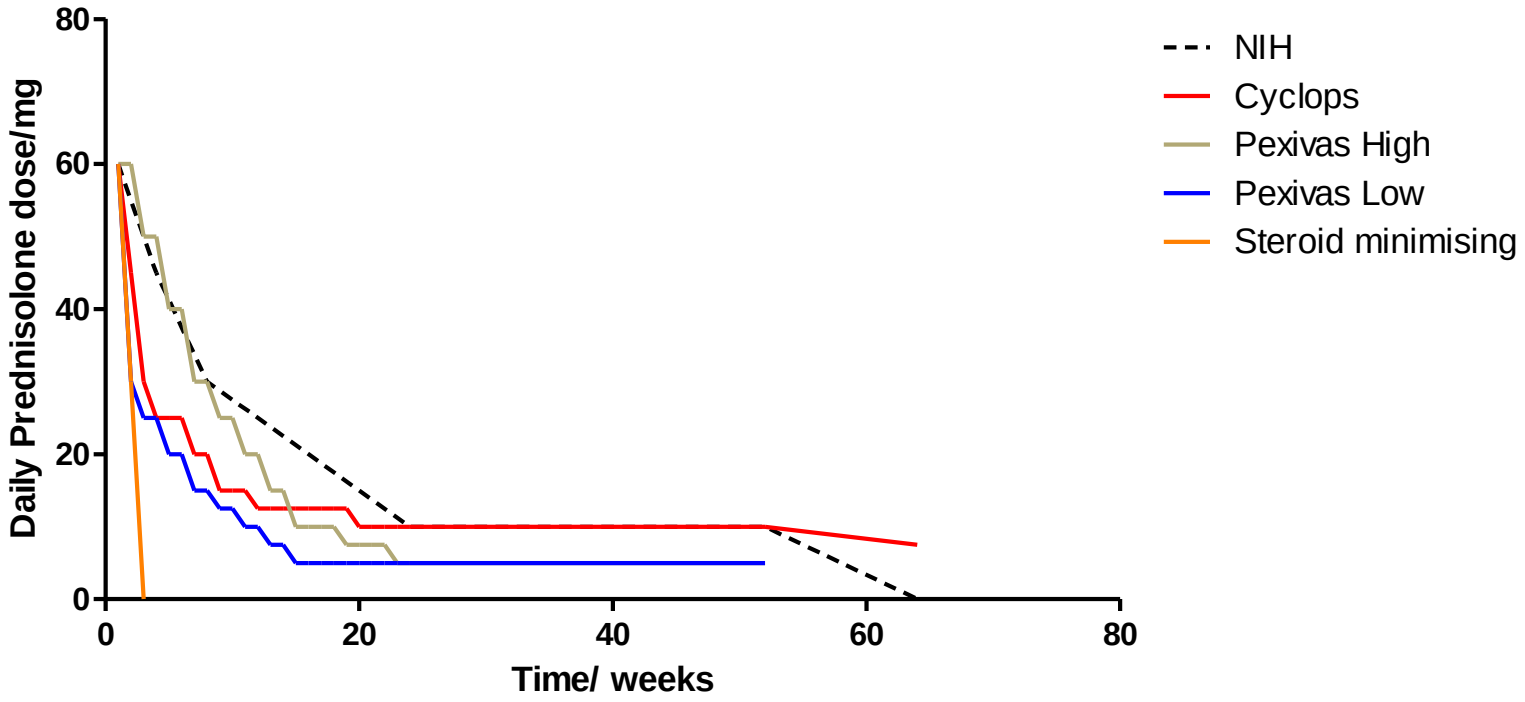


Long term outcomes of steroid minimising protocol

- n=58, 84% new presentation
- 65% MPO-ANCA, 29% PR3-ANCA, 5% ANCA negative
- 9% required steroid re-introduction in 1st 6 months for disease; by 3 years 80% remain steroid-free with relapse of 19%

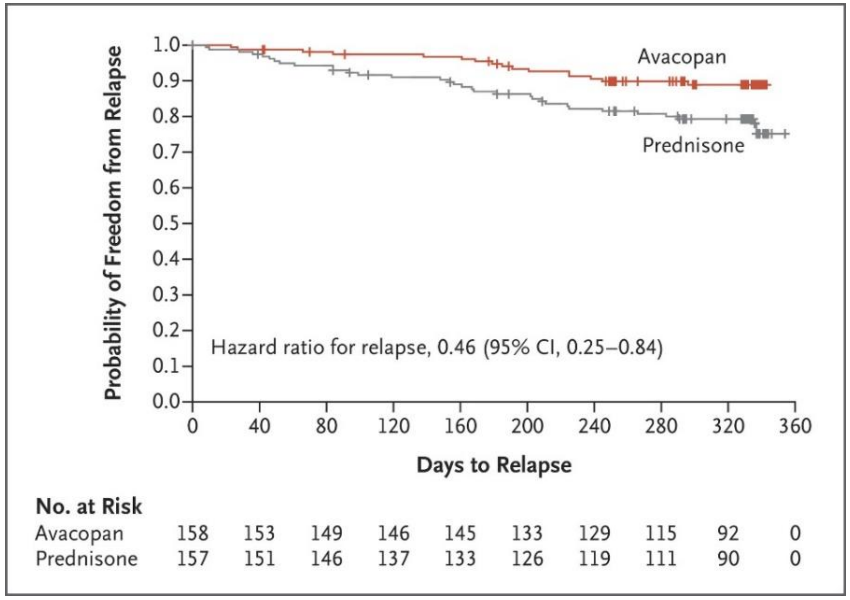


Extreme Steroid Minimisation



Avacopan: Advocate trial

- C5aR inhibitor; N=331;
- 43% PR3-ANCA, 57% MPO-ANCA
- Similar remission outcomes with Avacopan and prednisolone at 6 months(non inferior)



Jayne et al 2021 NEJM

Steroid minimisation in SLE

- Rapid taper with Voclosporin (AURORA trial)- but no difference in infectious complications vs control arm
- Steroid free with RTX and MMF (RITUXILUP cohort)- single dose MP with RTX but no maintenance steroids

Figure S1 Phase 3 AURORA 1 clinical trial study design

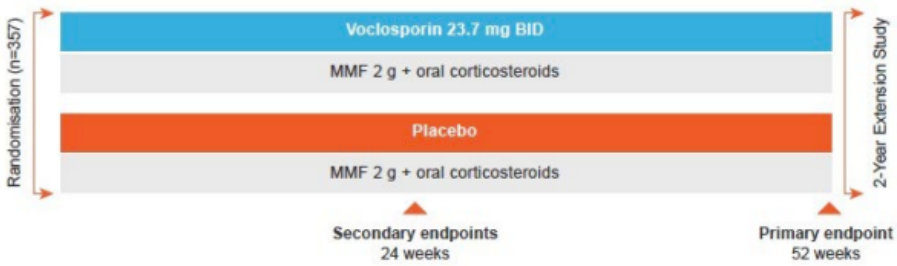


Table S3 Dosing Schedule for IV Methylprednisolone and Daily Oral Prednisone

	Patients <45 kg	Patients ≥45 kg	In Case of Prior IV Steroids During Screening (pre-randomisation)
Weeks 1-2*	0·25 g (IV)	0·5 g (IV)	1 g minus prior IV steroids mg or 0·5 g minus prior IV steroids mg for patients who weigh <45 kg‡
Days 1-2†			
Days 3-13	20 mg (oral)	25 mg (oral)	
Week 2 (Day 14)	15 mg (oral)	20 mg (oral)	
Week 4 (Day 28)	10 mg (oral)	15 mg (oral)	
Week 6 (Day 42)	10 mg (oral)	10 mg (oral)	
Week 8 (Day 56)	5 mg (oral)	5 mg (oral)	
Week 12 (Day 84)	5 mg (oral)	5 mg (oral)	
Week 16 (Day 112)	2·5 mg (oral)	2·5 mg (oral)	

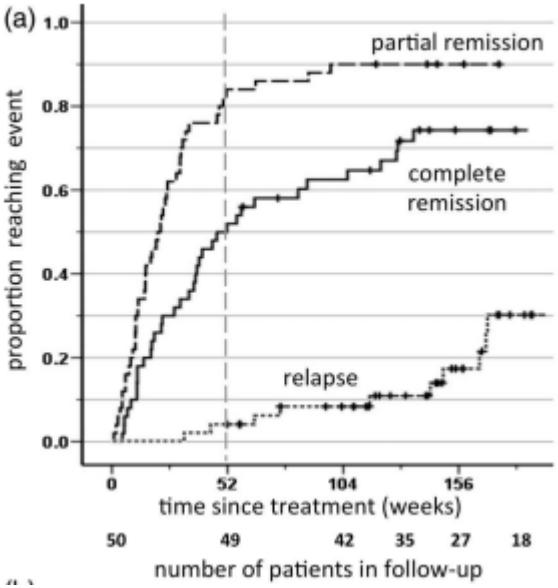


TABLE 1. **Adverse Somatic Effects of Corticosteroid Therapy**

Cardiovascular
Hypertension
Accelerated atherosclerosis
Dermatologic
Acne
Alopecia
Hirsutism
Striae
Skin atrophy
Purpura
Endocrine
Obesity
Diabetes mellitus
Adrenal-pituitary axis suppression
Hyperlipidemia
Fluid and sodium retention
Loss of potassium, calcium, and nitrogen
Delayed growth
Gastrointestinal
Peptic ulcer disease
Pancreatitis
Fatty liver
Hematologic
Leukocytosis
Neutrophilia
Lymphopenia
Infectious
Oral candidiasis
Increased risk of systemic infection
Musculoskeletal
Myopathy
Osteoporosis
Avascular necrosis
Neurologic
Pseudotumor cerebri
Ophthalmologic
Cataracts
Glaucoma

Adapted from Keenan G. Management of complications of glucocorticoid therapy. *Clin Chest Med.* 1997;18:507-520, with permission from Elsevier.

Psychiatric side effects

Meta analyses of >2500 pts, 13 studies

- Mild-moderate reactions 28%; Severe reactions 6%
- Short term: **Euphoria, hypomania** commonest
- Long term: **Depression**
- In children: 50% some behavioural and affective disorders- depression, anxiety, insomnia, irritability, argumentative...

- **Dose related**: 1.3% <40 mg pred, 4.6% 41-80 mg, 18% >80 mg
- But dose doesn't predict onset, duration or severity
- More common in women

Warrington 2006

Metabolic/CV consequences in steroid treated patients with AAV

From AAV trials and long term follow up :

- Weight gain : 22% >10Kg
  Persists >1 year, does not regress during one year of remission; Most marked in new patients
- HT: 17% in five years
- New onset diabetes: 4-8%
- Cardiovascular disease: 2-4 fold increase CAD; 14% @ least one CV event in first 5 years ; 6% CV deaths, 8% MI, 5% stroke

Westman 2015

Cardiovascular disease and renal inflammation

- In SLE and AAV patients with nephritis, cardiovascular disease 3-8 times more common than age, and renal function matched controls
- Not explained by traditional risk factors
- Pexivas CV events 16-19% (high and standard dose)
- Does therapy play a role?

SLE and CV disease: role of steroids

- Post Mortem series aged 8-62 years
- 36 patients with SLE; 19 treated with prolonged steroids vs 17 with <12 months treatment compared to 20 non-steroid pts
- Prednisolone 20-120 mg a day in prolonged treatment
- Various changes: increased HT, cardiac fat deposition, greater coronary atheroma in those >1 year treatment (42%, had 50% stenosis in one c/artery)

Bulkley and Roberts 1975

Cardiovascular disease and renal inflammation

- In trial of patients with nephrotic syndrome and Cr<150 mcmol/l, n=125
- Minimal change, membranous or proliferative GN
- 61 treated prednisolone 20-30 mg a day for 6 months; 10 mg/day for further 6 months
- 64 supportive care
- 17/61 died in pred group vs 12/64
- Cardiovascular deaths: 7/17 vs 1/12

Mostly in those with proliferative nephritis

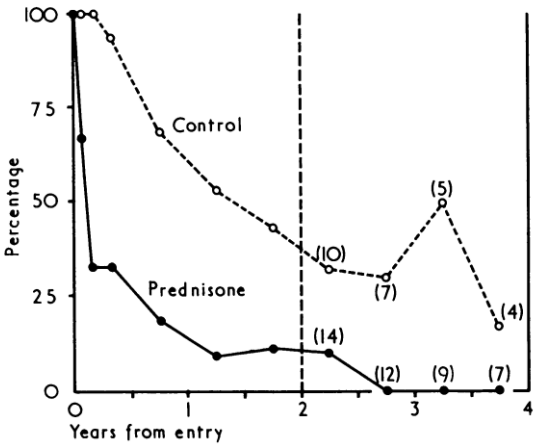


FIG. 2.—Group A patients (minimal change). Proportion of patients with proteinuria of more than 1 g./24 hours expressed as a percentage of those alive and in the trial (numbers of patients in trial after two years in parentheses).

Black 1970

Impact of Steroid Exposure

- Population study using linked data to GP and hospital datasets in UK, 1998-2017
- N=70,638 on steroids vs 41,166 matched non-steroid users, >18 years old
- Spanned various inflammatory diseases including vasculitis, SLE, RA, GCA/PMR and IBD*
- Outcomes: Death, Cushing's and adrenal insufficiency; mean 5 year f/u

Outcome	Steroid use	No steroid use	HR
Cushing's	248		1.09 for every 5 mg /day increase Or 2.31 for every 1000mg/year
Adrenal Insufficiency	183		1.07 for every 5 mg /day Or 2.25 for every 1000mg/year
Death**	22,317(31.6%)	7,544(18.3%)	**1.26 for every 5 mg /day or 2.05 for every 1000mg/year**

*Highest rates of exposure in SLE and AAV; ** CVD, infections highest cause of mortality

Mebrahtu et al 2019

Cardiovascular disease and renal inflammation

- Those with greatest degree of inflammation have the greatest need for therapy and may have greatest dose of steroids
- So is cardiovascular disease due to inflammation or treatment or both?

UCL DEPARTMENT OF RENAL MEDICINE

Modelling renal inflammation and atheroma

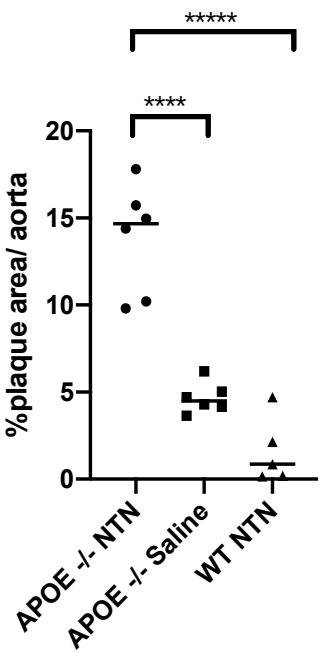
- Modified NTN model in ApoE-/- mice fed a high fat diet

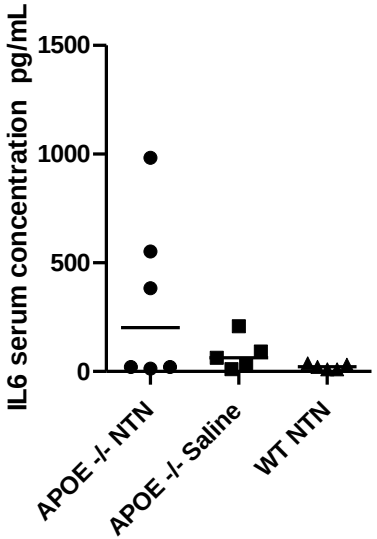
2 weeks

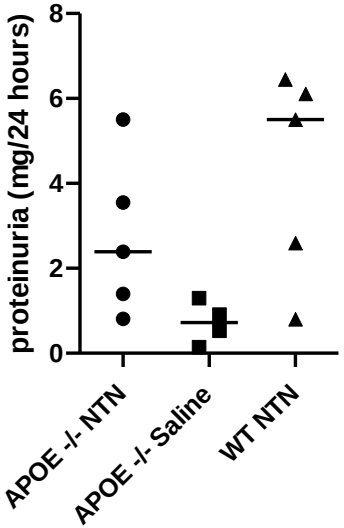
11 weeks

APOE-/- NTN APOE-/- Saline WT NTN

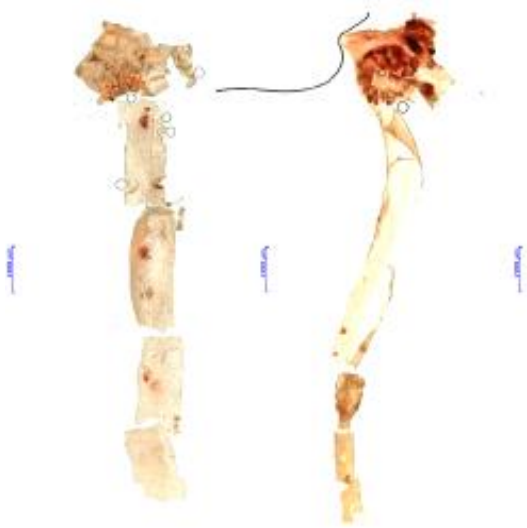
In atheroma-susceptible mice, nephritis increases degree of atheroma



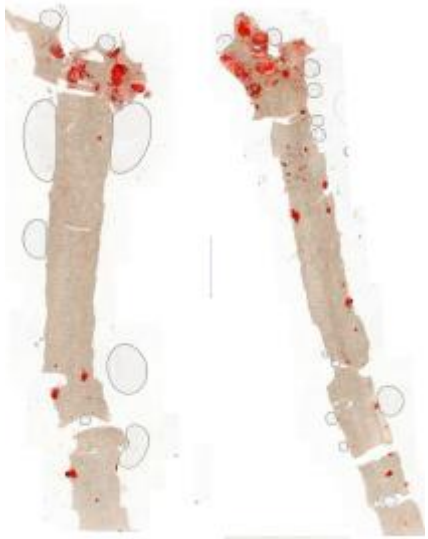




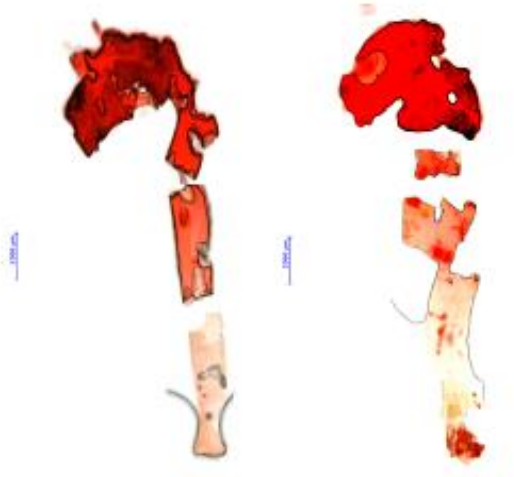
WT NTN



APOE-/- Saline



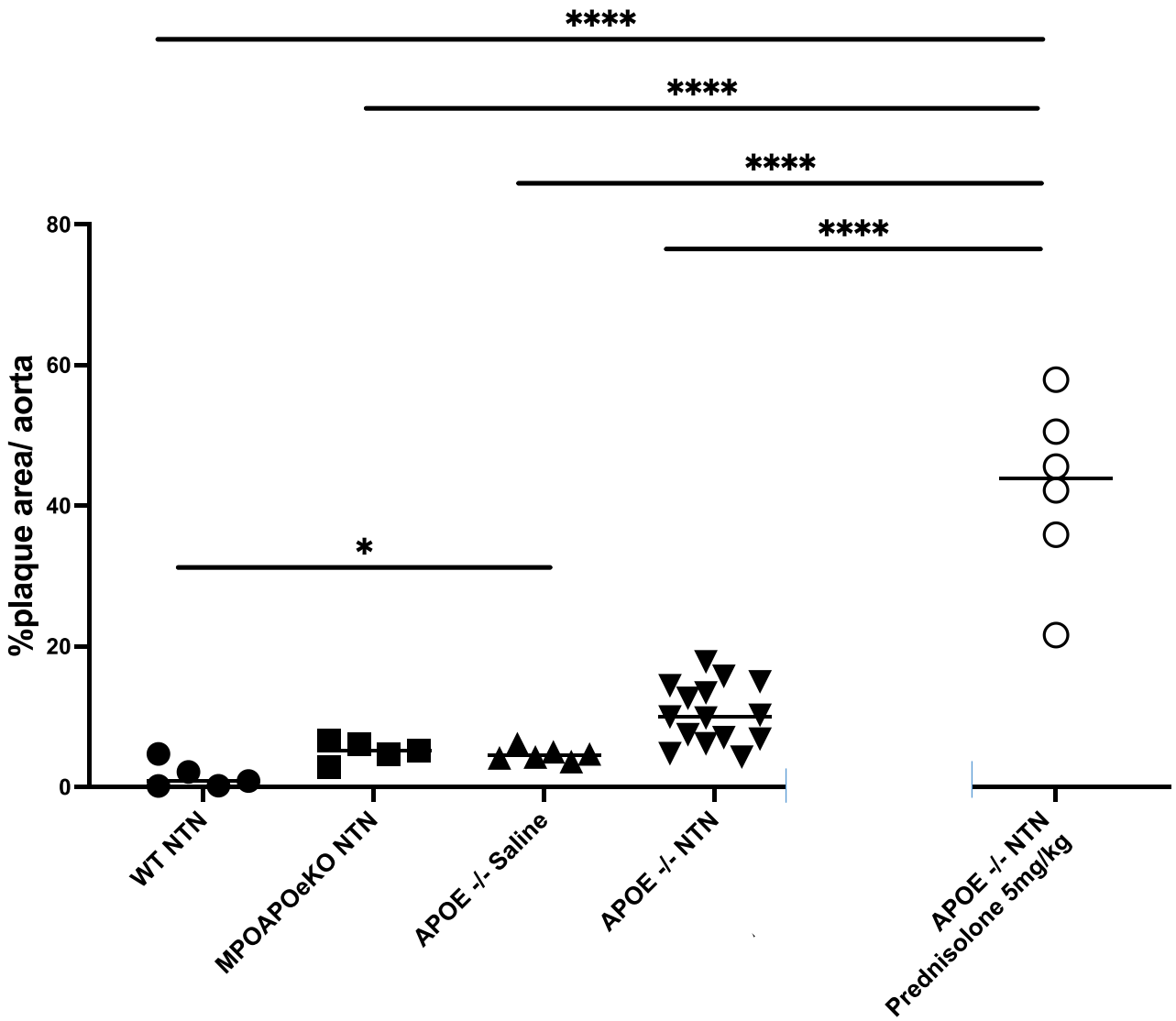
APOE-/- NTN



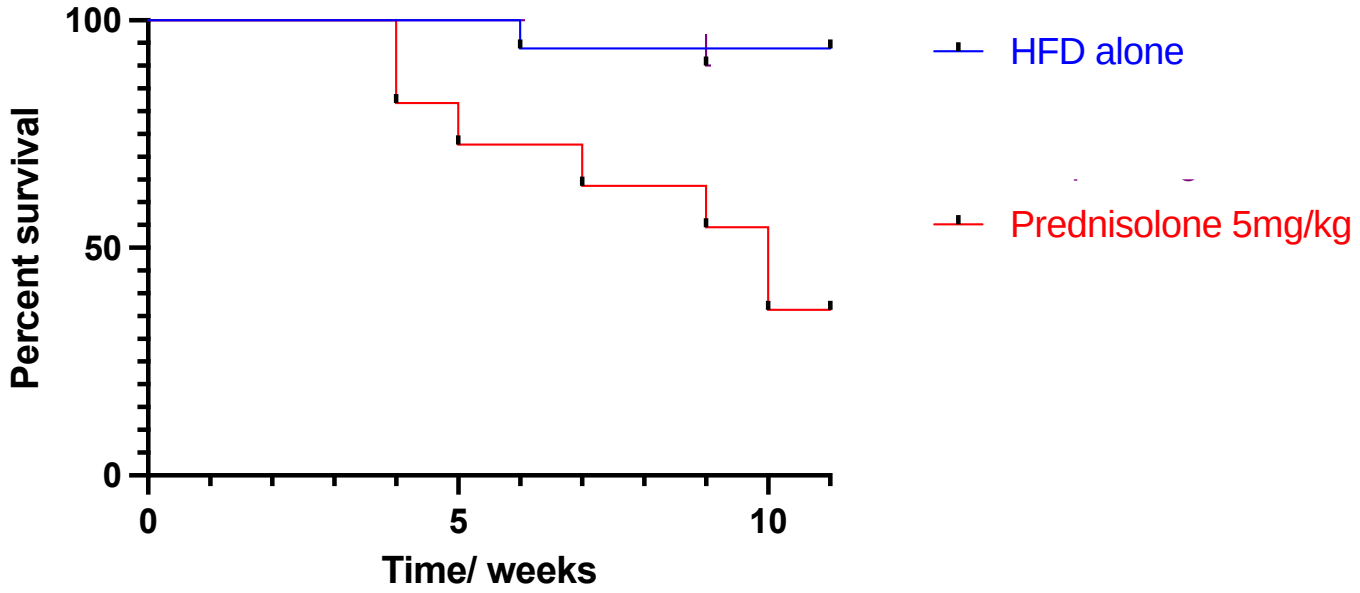
APOE-/- NTN + Prednisolone

In atheroma-susceptible mice, nephritis increases degree of atheroma and this is augmented by steroids

Impact of steroids on atheroma



Effect of prednisolone on survival



No differences in LDL or blood glucose levels between groups

Implications for therapy of GN

- Reducing steroids could reduce accelerated cardiovascular disease
- Other novel steroid sparing agents could alter side effect profiles

Potential therapies

* In trials

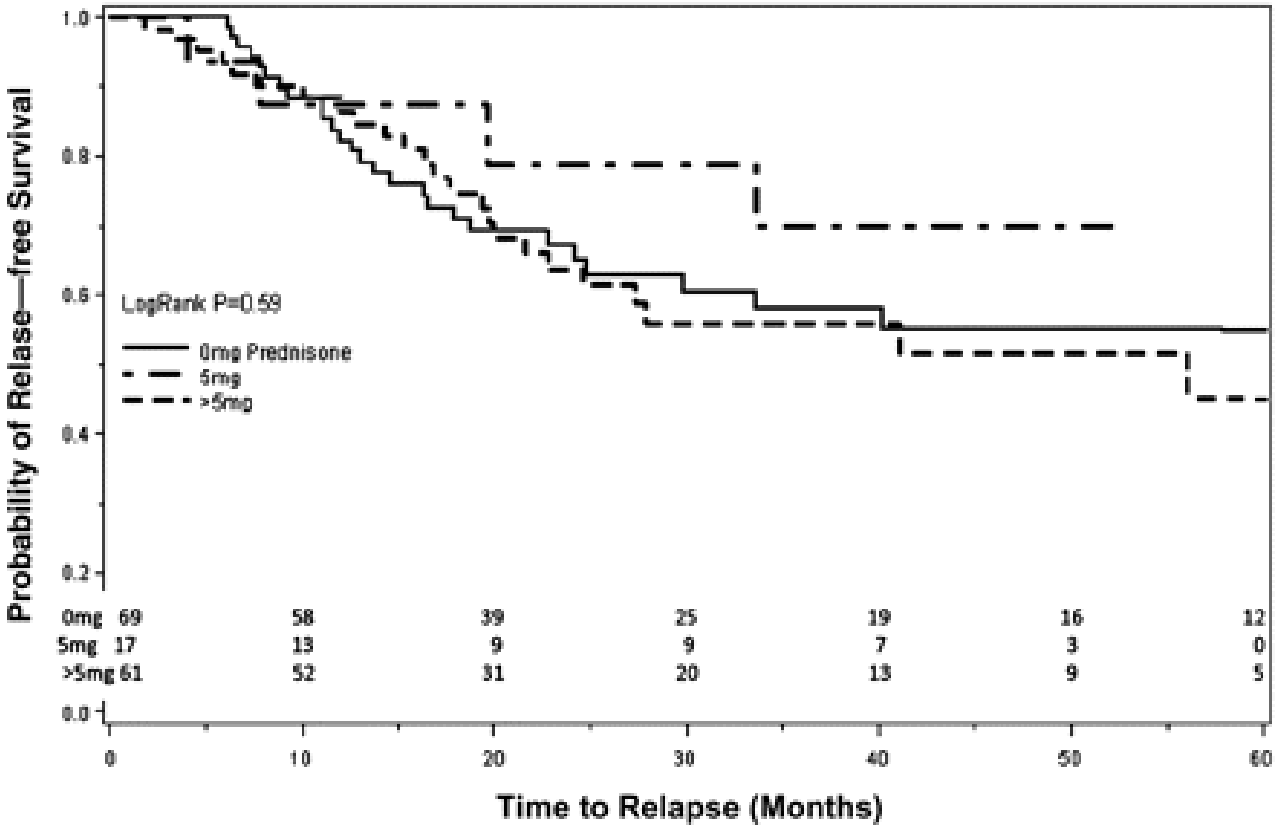
Condition	Steroids	With	Alternatives
MCN/FSGS	Yes , 1mg/Kg		CNI, RTX*, CYC
Membranous*	Yes	CYC	RTX, CNI, Obinutuzimab*, Complement blockade*
SLE	Yes	MMF, CYC	CNI, RTX, B cell blockade, IFN-blockade, anti-BAFF; steroid free
AAV	Yes	CYC, RTX	MMF, MTX, Avacopan, CYC-RTX steroid low
IgAN*	Yes		Complement blockade*, local steroids, BAFF-APRIL inhibitors
GBM	Yes	CYC, PEX	RTX, IDES*
Immune Complex GN/C3GN	Yes	MMF	Eculizumab

Duration of therapy

- Use of maintenance therapy almost universal in SLE, AAV, and many other GNs
- Despite this, relapse occurs, at historical rates of 50% @ 5 years for AAV
- Data on how long we should continue for is unclear
- Not without risks; In AAV patients:
  - 5 fold increase in invasive pneumococcal infection
  - Increased mortality compared to age matched population
  - Poor response to vaccination, marker of all cause mortality in AAV

Harm of steroids

- McGregor et al 2013- glucocorticoids beyond 6 months do not prevent relapse but increase adverse events



No so fast…..

A note of caution …..

The Effect of Cyclophosphamide on Leukocyte Kinetics and Susceptibility to Infection in Patients With Wegener's Granulomatosis

David C. Dale, Anthony S. Fauci, and Sheldon M. Wolff

In eight patients with Wegener's granulomatosis effective cyclophosphamide therapy significantly reduced blood neutrophil, monocyte, and lymphocyte counts; lymphocyte counts were most severely reduced. The turnover rate for DF^{32}P-labeled neutrophils were decreased from elevated to normal levels with treatment. Cutaneous inflammatory responses were normal before and during therapy. In five patients, cyclophosphamide eventually had to be discontinued because of progressive severe leukopenia. Infectious complications of therapy have not been observed.

Wegener's granulomatosis is characterized by necrotizing granulomatosis vasculitis of the upper and lower respiratory tracts and the kidneys (1, 2). On the basis of histopathologic studies, this disease has been considered to be of autoimmune origin. Recent reports indicate that a variety of cytotoxic, immunosuppressive drugs are beneficial in treating this disorder (3–7) and that favorable clinical responses and several measures of immunosuppression can be correlated (8). All of these drugs also suppress granulocyte formation, but the contribution of this effect to the outcome of therapy is not known. On the other hand, it is well known that by suppressing granulocytopoiesis this form of therapy imposes on the patient the potential risk of an enhanced susceptibility to infections. The level of the blood granulocyte count, or the total blood leukocyte count, is therefore commonly used to determine the tolerable extent to which the therapy can be pursued.

In assessing use of immunosuppressive therapy for this disorder several important questions thus arise: Is marked marrow suppression necessary for a favorable clinical response? Does this therapy alter granulocyte turnover and function as well as immunologic responsiveness? Can effective therapy be achieved without undue risk of infectious complications?

In attempting to answer these questions we have studied the effects of cyclophosphamide on the blood leukocyte counts, bone marrow neutrophil reserves, neutrophil kinetics, and acute inflammatory responses of a group of patients with Wegener's granulomatosis. We have also carefully observed these patients for any infectious complications during therapy.

From the Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20014

DAVID C. DALE, MD: Senior Investigator; ANTHONY S. FAUCI, MD: Senior Investigator; SHELDON M. WOLFF, MD: Clinical Director.

Reprint requests should be addressed to: Dr. David C. Dale, Building 10, Room 11B13, National Institutes of Health, Bethesda, MD 20014.

Submitted for publication April 9, 1973; accepted June 22, 1973.

MATERIALS AND METHODS

Patients

The study group was composed of 8 patients, 6 of whom had the classical features of upper and lower respiratory involvement with renal disease. The other 2 patients (JT and AS) had the localized form of the disease which involved

What drug and dose would you use

- A 25 year old woman, weight 90Kg, with first presentation of minimal change disease and nephrotic syndrome ?

1. 1mg/Kg prednisolone tapering over 4 months
2. 0.5 mg/Kg prednisolone tapering over 6-8 months
3. Tacrolimus 2mg bd for 6-12 months
4. Rituximab 1 g x2
5. Methylprednisolone x3 followed by Tacrolimus

What drug and dose would you use

- A 60 year old woman, with lupus nephritis class IV/V, Creatinine 90mcmol/, UPCR 300, arthralgias, rash and mouth ulcers?

1. Methylprednisolone 500 mg x3 followed by 1mg/Kg prednisolone with MMF/cyclo
2. 1mg/Kg prednisolone with MMF/cyclo
3. Prednisolone 1 mg /Kg, Tacrolimus 2mg bd and MMF
4. Rituximab 1 g x2, and MMF

What drug and dose would you use

- A 75 year old woman, with ANCA associated vasculitis, MPO-ANCA, Creatinine 501 mcmol/l, rash and arthralgias, and osteoporosis.

1. Methylprednisolone 500 mg x3 followed by prednisolone with cyclo/RTX
2. prednisolone with cyclo/RTX
3. prednisolone with MMF
4. Rituximab 1 g x2 and Cyclo with 2 weeks of pred
5. PEX, MP, Pred and cyclo/RTX
6. PEX, Pred and cyclo/RTX

Conclusions

- Steroid dosing not properly considered in GN
- Accounts for significant toxicity
- May itself contribute to atheromatous disease
- Can be avoided using novel protocols or novel agents which need to be tested in randomised trials
- Time to rethink our use of steroids

Take Home messages

- Think about the dose of steroid and duration that you are prescribing
- Do they need pulsed methylprednisolone and if they do can you reduce the oral steroid
- They are not benign drugs
- Many can do without them
- Enrol patients in steroid avoiding trials and consider steroid avoiding strategies

Next Webinars

ERA/ERKNet Advanced Webinars on Rare Kidney Disorders

Date: **30 Nov 2021**

Speaker: **Giacomo Quattrocchio**

Topic: **IgG4 related diseases**

ESPN/ERKNet Educational Webinars on Pediatric Nephrology & Rare Kidney Diseases

Date: **07 Dec 2021**

Speaker: **Joseph Flynn**

Topic: **Hypertension**

ERA/ERKNet Advanced Webinars on Rare Kidney Disorders

Date: **21 Dec 2021**

Speaker: **Francesco Trepiccione**

Topic: **Monogenic forms of hypertension**

Subscribe the ERKNet and IPNA Newsletter and don‘t miss Webinars!