Nephrology and Transplantation Department
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B cell Inhibition in Glomerular Disease

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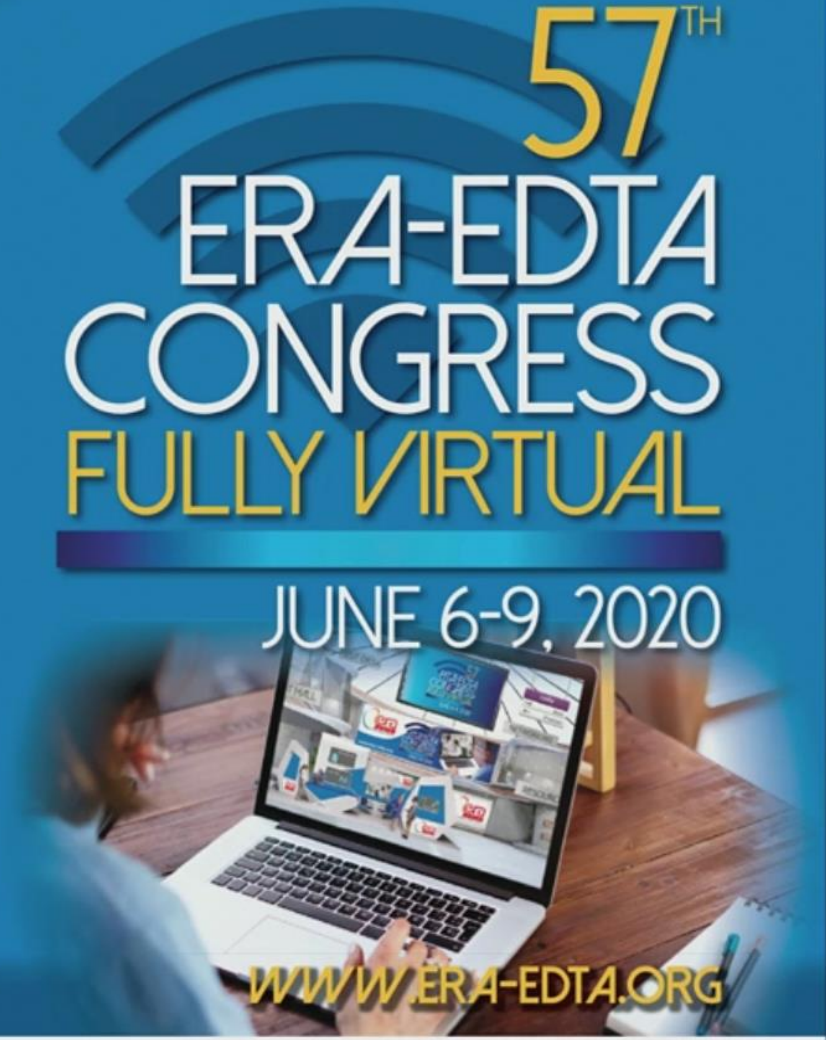
Day 4th, 1399

LEADING EUROPEAN NEPHROLOGY

B cell inhibition in glomerular diseases

David Jayne, Cambridge, UK

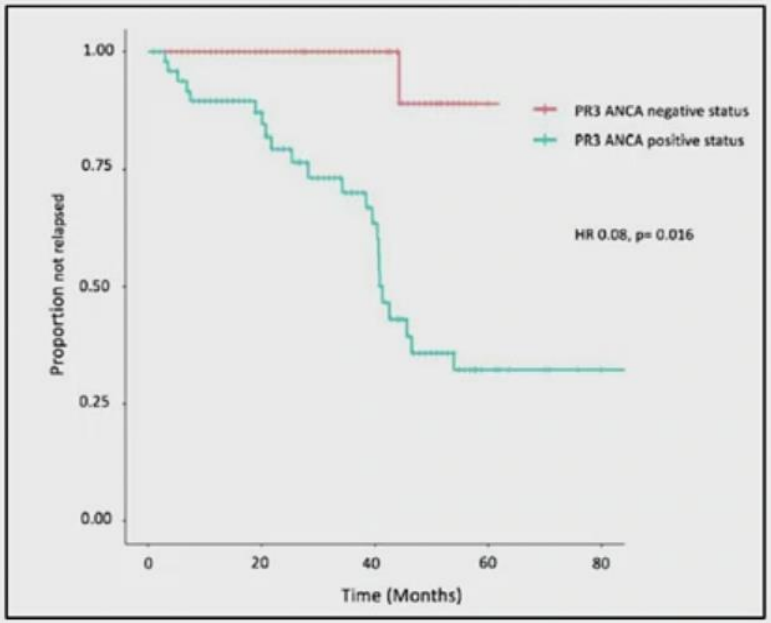


UNIVERSITY OF CAMBRIDGE

- Introduction to B cell therapy
- B cell therapy in secondary glomerulonephritis
  - Vasculitis & lupus nephritis
- B cell therapy in primary glomerulonephritis

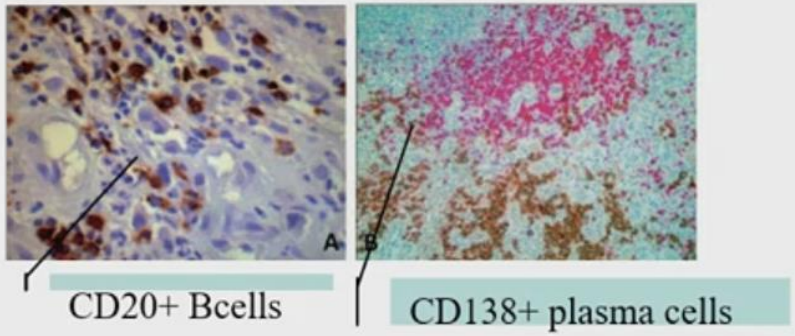
Mechanisms for B cell targeting

Reductions in autoantibody levels

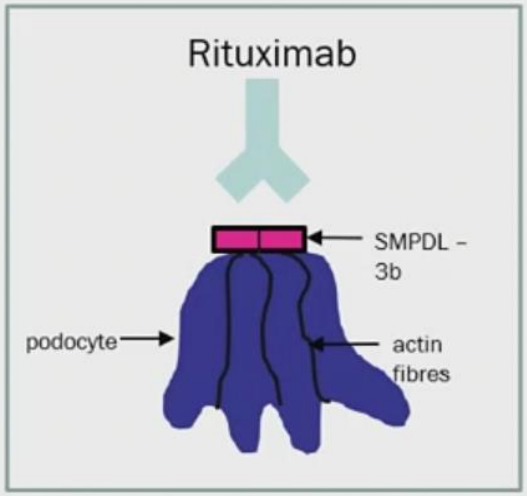


ANCA change after rituximab associates with clinical response

B cells at sites of GPA inflammation



Rituximab binding to podocytes



McClure M et al, *J Clin Immunol* 2019 Zhao et al. *Rheumatology* 2012 Fornoni et al. *Sci Transl Med* 2011

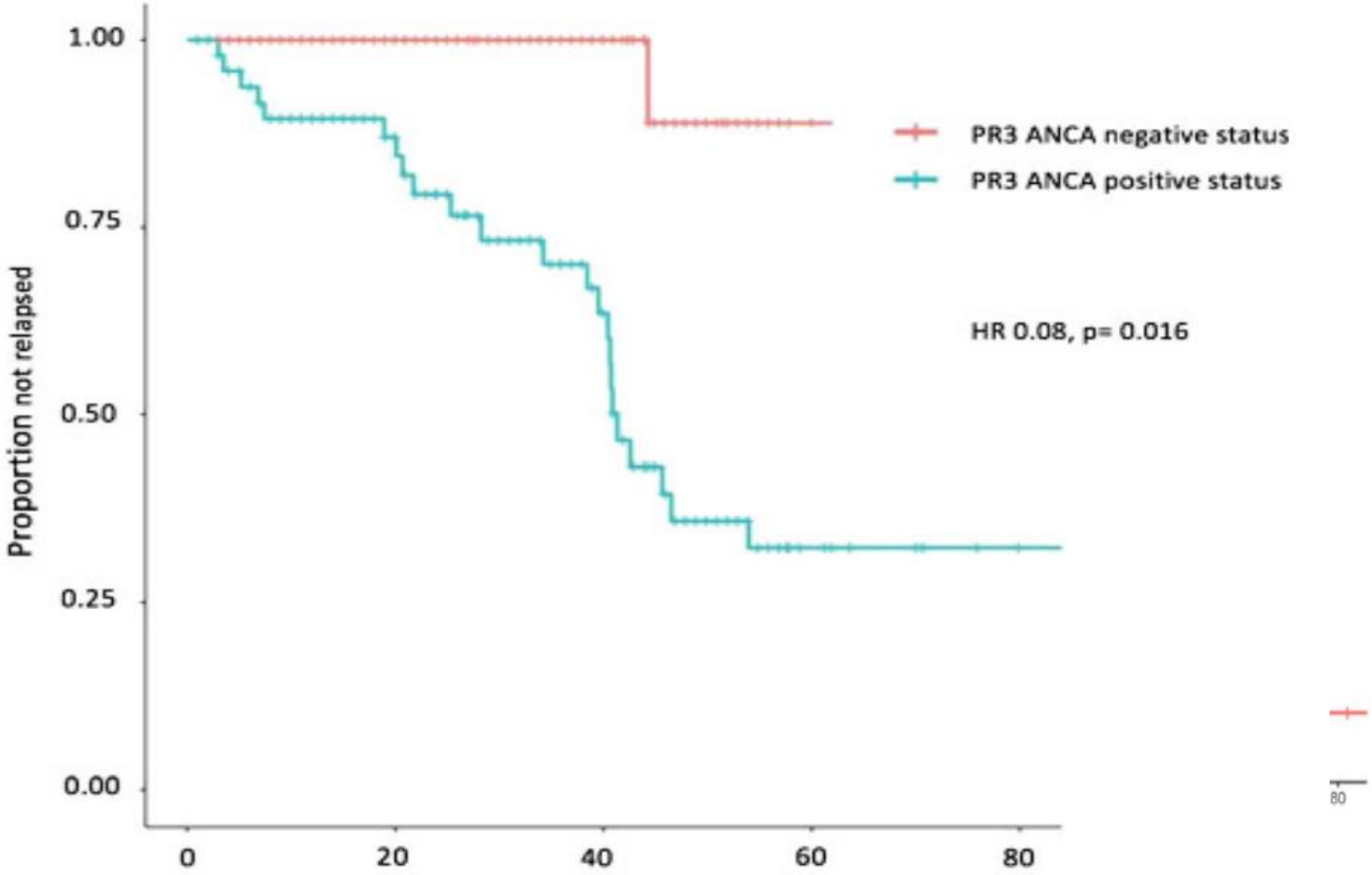
ORIGINAL ARTICLE

Evaluation of PR3-ANCA Status After Rituximab for ANCA-Associated Vasculitis

Mark E. McClure, MRCP, James Wason, PhD,†‡ Seerapani Gopaluni, MCRP,* Joanna Tieu, FRACP,* Rona M. Smith, MRCP, MD,* David R. Jayne, FMedSci,* and Rachel B. Jones, FRCP, MD**

Patients and Methods:

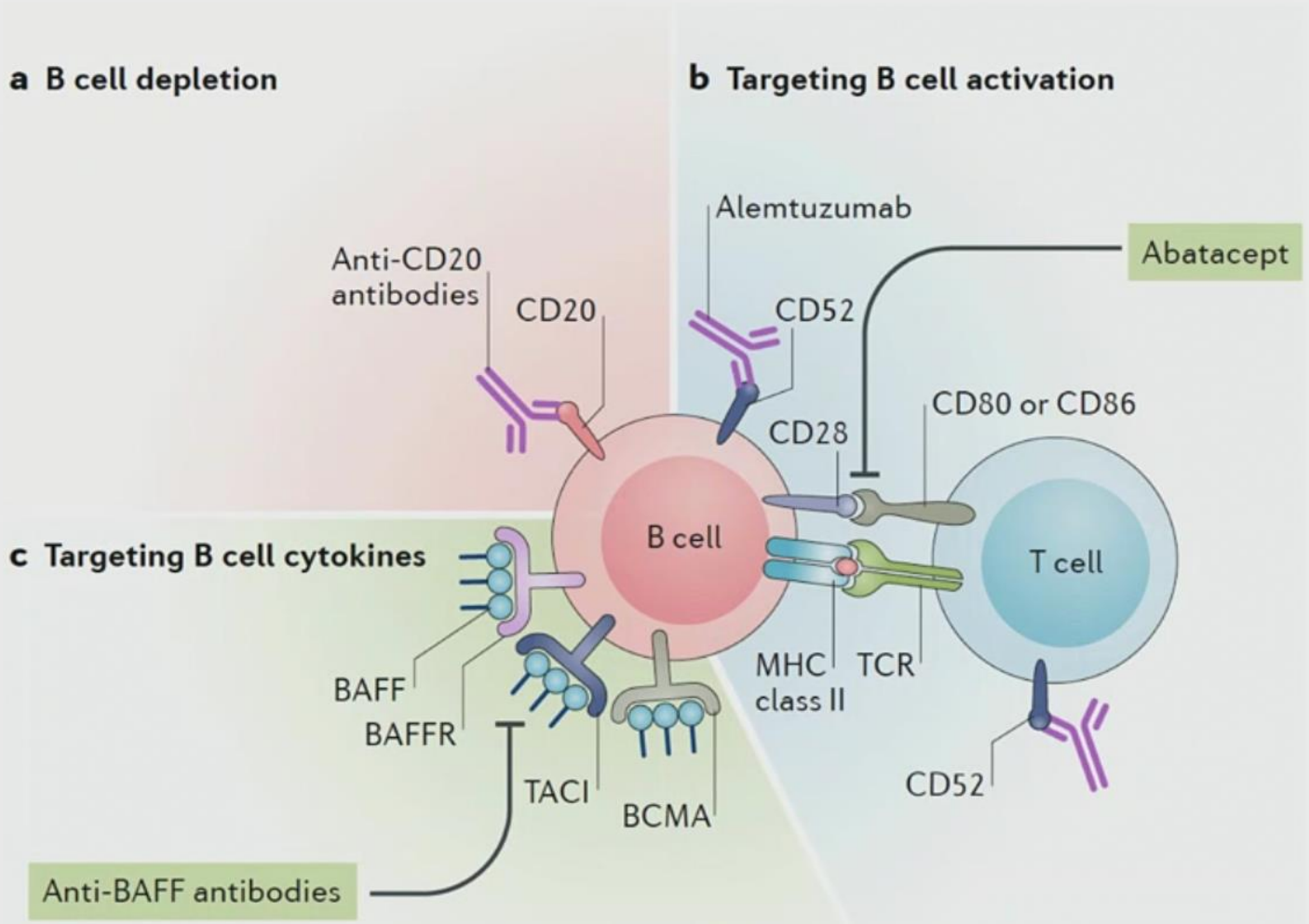
All patients with active vasculitis and positive proteinase 3 (PR3)–ANCA starting a 2-year treatment course of rituximab for induction . Practice consists of 6 g of rituximab given over 2 years, concomitant corticosteroids (0.5–1.0 mg/kg) with rapid taper over 3 months, and cessation of oral maintenance immunosuppressive agents at time of first rituximab dose.



Among the 53 patients who achieved remission during follow-up, 24 (45%) relapsed with a median time to relapse of 36 months from remission. Both PR3-ANCA–negative status and 50% reduction in PR3-ANCA from baseline were significantly associated with a longer time to relapse.

Conclusions: Achieving and maintaining PR3-ANCA negativity after rituximab was associated with longer-lasting remission

Methods of targeting B cells



McClure & Jayne, *Nature Rev Nephrology* 2018

B cell depleting agents (anti-CD20s)

Table 1 Type I and type II antibodies

Type I	Type II
Rituximab, ofatumumab	Obinutuzumab
Strong CDC	Weak CDC
Weak direct cell death	Strong direct cell death
Moderate ADCC	Strong ADCC
Moderate ADCP	Strong ADCP

Note: Data from Cartron,[7] Goede et al[8] and Klein et al.[59]

Abbreviations: ADCC, antibody-dependent cell-mediated cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; CDC, complement-dependent cytotoxicity.

- Introduction to B cell therapy
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  - Vasculitis & lupus nephritis
- B cell therapy in primary glomerulonephritis

Rituximab for ANCA vasculitis with low GFR

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 15, 2010 VOL. 363 NO. 3

Rituximab versus Cyclophosphamide in ANCA-Associated Renal Vasculitis

Compared rituximab with cyclophosphamide as induction therapy in ANCA-associated vasculitis.

44 patients with newly diagnosed ANCA-associated vasculitis and renal involvement

IV Methyl 1 gr + Pred 1mg/kg taper to 5 mg in 6 months

1- Rituximab 375mg/m^2 per week for 4 weeks +two intravenous cyclophosphamide pulses (33 patients, the rituximab group)

2- Intravenous cyclophosphamide for 3 to 6 months followed by azathioprine (11 patients, the control group).

Primary end points were sustained remission rates at 12 months and severe adverse events.

The median age was 68 years, and the glomerular filtration rate (GFR) was 18 ml per minute per 1.73 m2

A rituximab-based regimen was not superior to standard intravenous cyclophosphamide for severe ANCA-associated vasculitis. Sustained-remission rates were high in both groups, and the rituximab-based regimen was not associated with reductions in early severe adverse events.

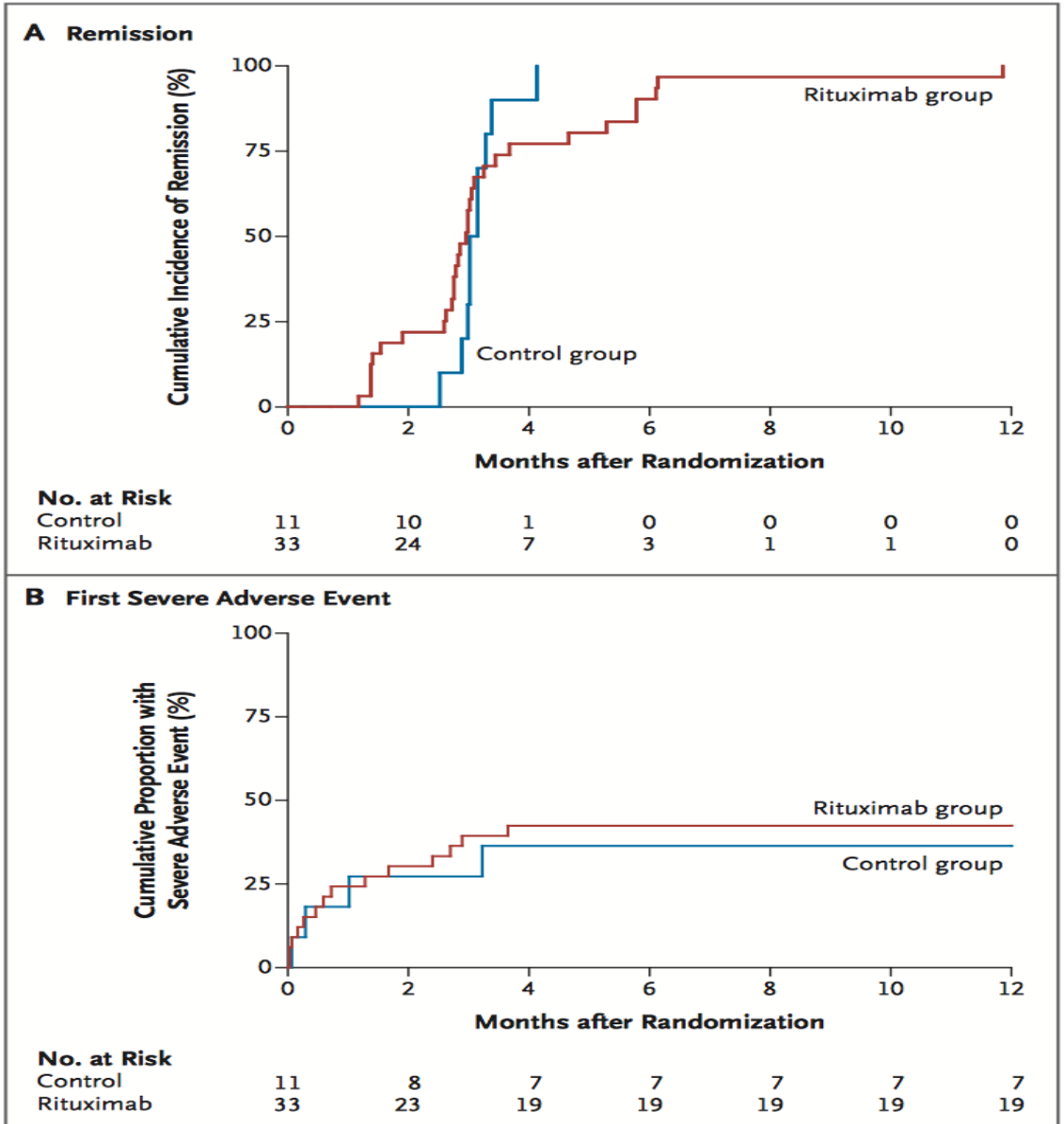
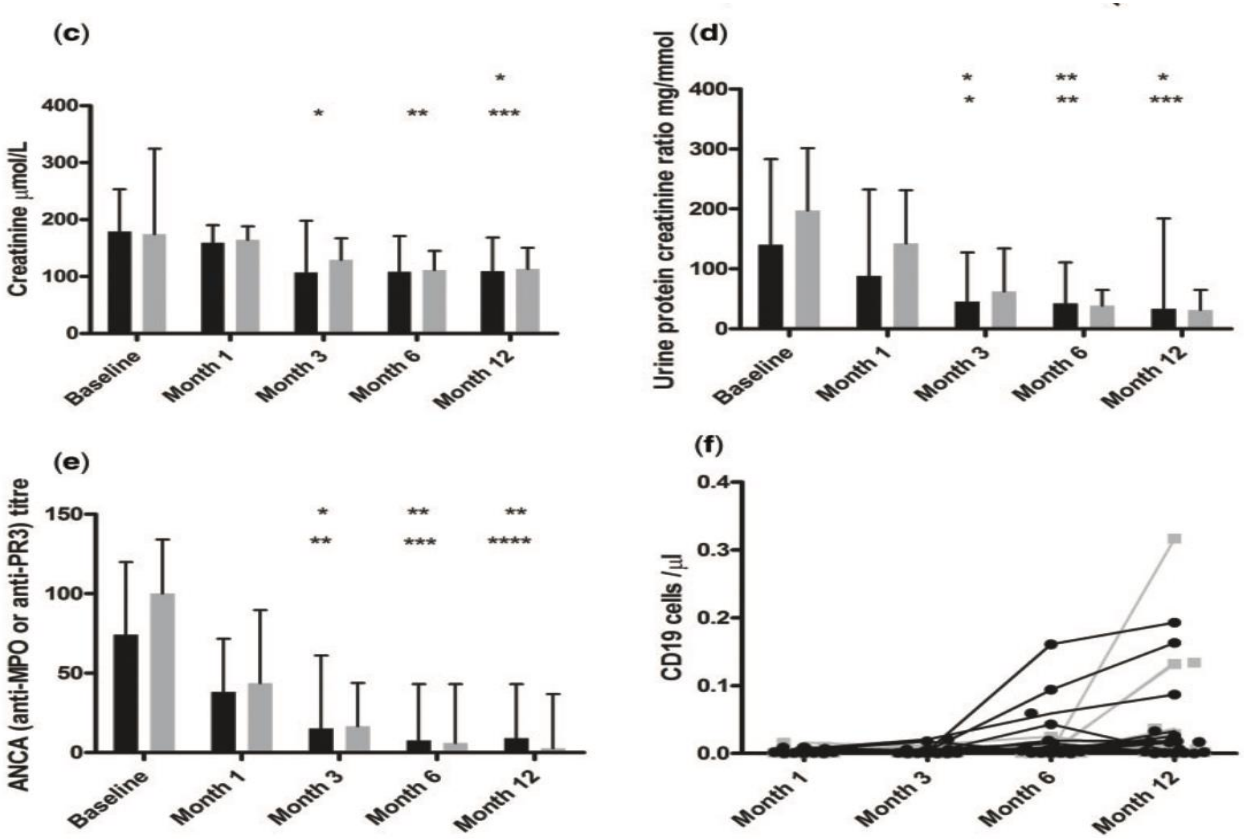


Figure 2. Cumulative Incidence of Remission and Cumulative Proportion of Patients with a Severe Adverse Event.

Panel A shows the time to remission. Remission time was the time at which a Birmingham Vasculitis Activity Score of 0 was first recorded. Data for patients who died were censored at the time of death. Panel B shows the time to the first severe adverse event.

doi:10.1093/rheumatology/key288

A novel glucocorticoid-free maintenance regimen for anti-neutrophil cytoplasm antibody–associated vasculitis



(**A**) Median and IQR of the BVAS at baseline and follow-up. (**B**) Changes in CRP with treatment. Red line indicates the upper limit of the normal range. (**C**, **D**) Serum creatinine and proteinuria (uPCR). (**E**) Changes in ANCA titre with treatment. (**F**) Changes in CD19 counts in individual patients (black line group 1, grey line group 2). *$P < 0.05$, **$P < 0.01$ and *** $P < 0.001$. IQR: interquartile range.

Gopaluni et al. Trials (2017) 18:112
DOI 10.1186/s13063-017-1857-z

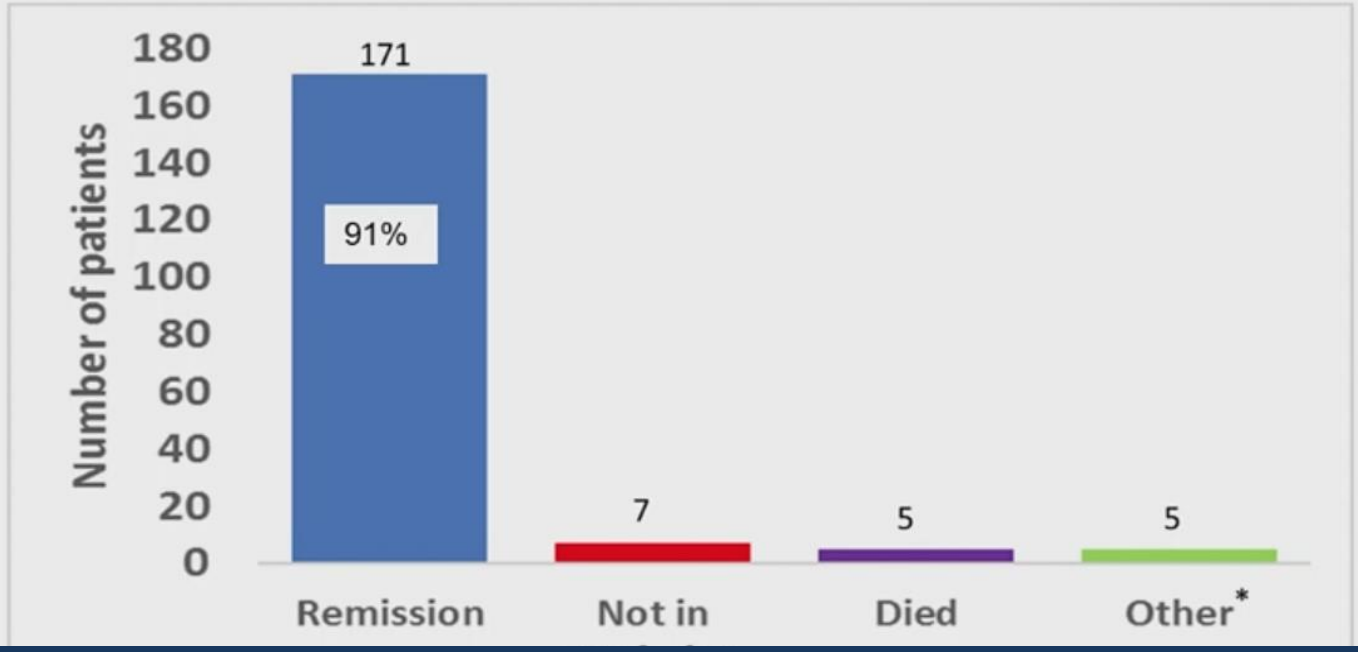
Trials

STUDY PROTOCOL Open Access

Rituximab versus azathioprine as therapy for maintenance of remission for anti-neutrophil cytoplasm antibody-associated vasculitis (RITAZAREM): study protocol for a randomized controlled trial

Seerapani Gopaluni[1†], Rona M. Smith[1,4*†], Michelle Lewin[1], Carol A. McAlear[2], Kim Mynard[1], Rachel B. Jones[1], Ulrich Specks[3], Peter A. Merkel[2], David R. W. Jayne[1] and on behalf of the RITAZAREM Investigators

Rituximab – effectiveness in relapsing GPA/MPA



Conclusion:

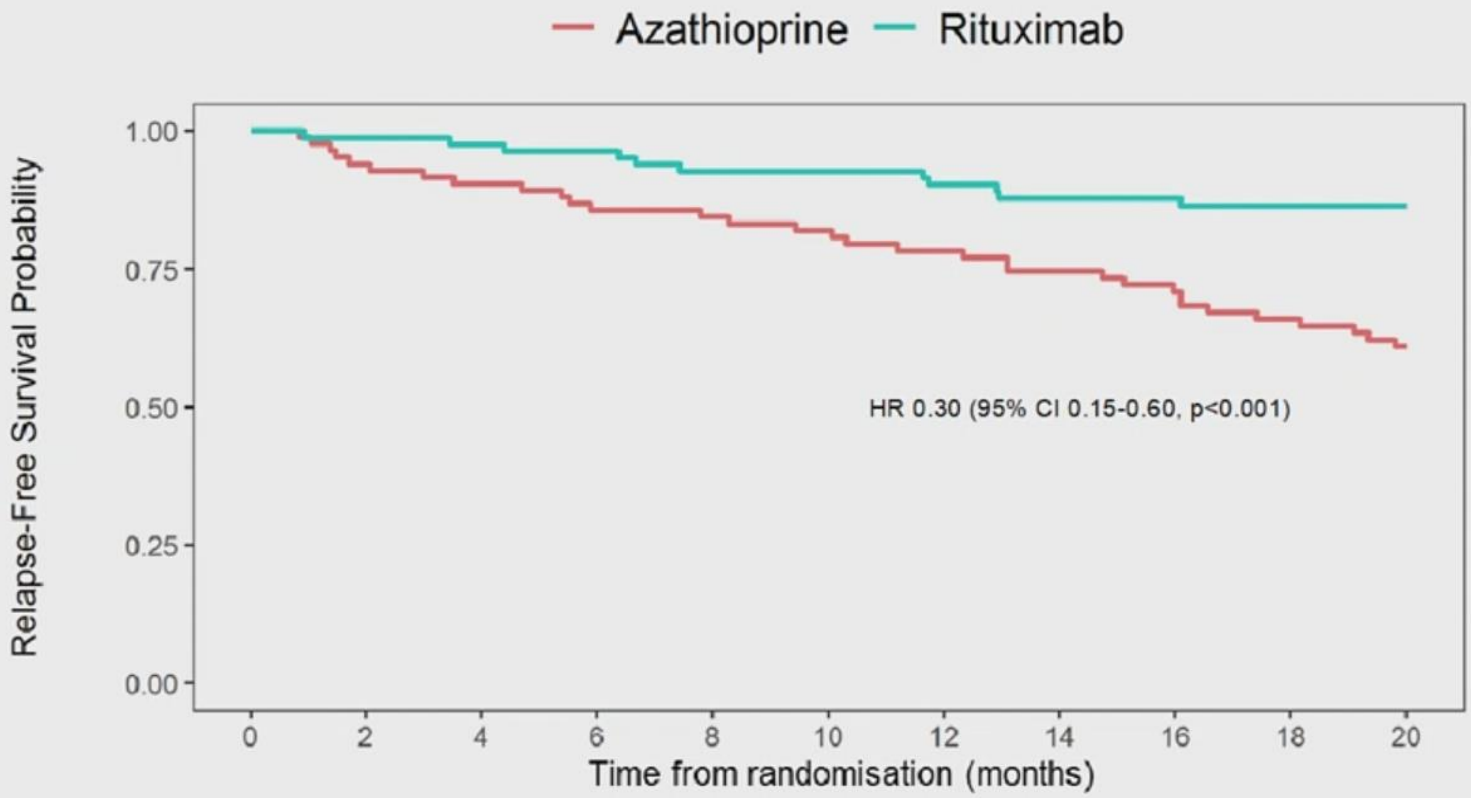
Data from the first phase of RITAZAREM, the largest reported cohort of patients with relapsing AAV, demonstrates that rituximab, in conjunction with glucocorticoids, is highly effective at re-inducing remission in patients with AAV who have relapsed, with an acceptable safety profile.

RITAZAREM

Smith R et al, *Am Coll Rheum (abstract)* 2017

Riruximab vs. azathioprine

RITAZAREM



Conclusion: In the RITAZAREM trial, following induction of remission with rituximab, rituximab was superior to azathioprine for preventing disease relapse in patients with AAV with a prior history of relapse. There were no new major safety signals for use of these medications in this population

Relapse after rituximab: B cells and ANCA

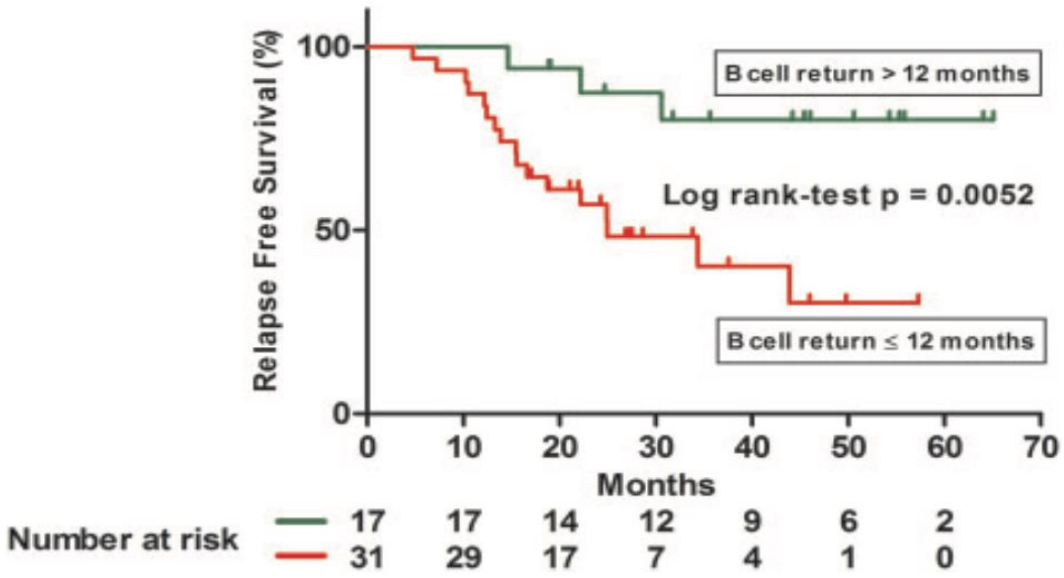
RHEUMATOLOGY

Rheumatology 2015;54:1153–1160
doi:10.1093/rheumatology/keu452
Advance Access publication 3 December 2014

Original article

Long-term follow-up of patients who received repeat-dose rituximab as maintenance therapy for ANCA-associated vasculitis

FIG. 4 Relapse-free survival stratified by B cell return within or after 12 months of the last rituximab dose



32% B cells < 0.02×10^9/L at relapse

48% ANCA negative at relapse

- 9/11 converting from ANCA negative to positive relapsed

Conclusion. This study supports the efficacy and safety of a fixed-interval RTX maintenance regimen in relapsing/refractory AAV. Relapses after discontinuation of maintenance therapy did occur, but at a lower rate than after a single RTX induction course. **PR3-associated disease, the switch from ANCA negative to positive and the return of B cells within 12 months of the last RTX administration were risk factors for further relapse.**

Rituximab - What do I do ?

Subgroup

- Fertility protection
- The young
- Severe disease:
  - Combine with short course cyclophosphamide
- Difficult scenarios
  - ITU
  - Severe infection
  - Malignancy

Regimen

- 1g x 2 (375mg/m^2 /week x 4)
  - No oral immunosuppressive
  - Stop steroid by 4-6 months
- Monitor IgG levels
- Do not measure B cells
- Use maintenance rituximab

RHEUMATOLOGY

Rheumatology 2020;59:e24–e32
doi:10.1093/rheumatology/kez640

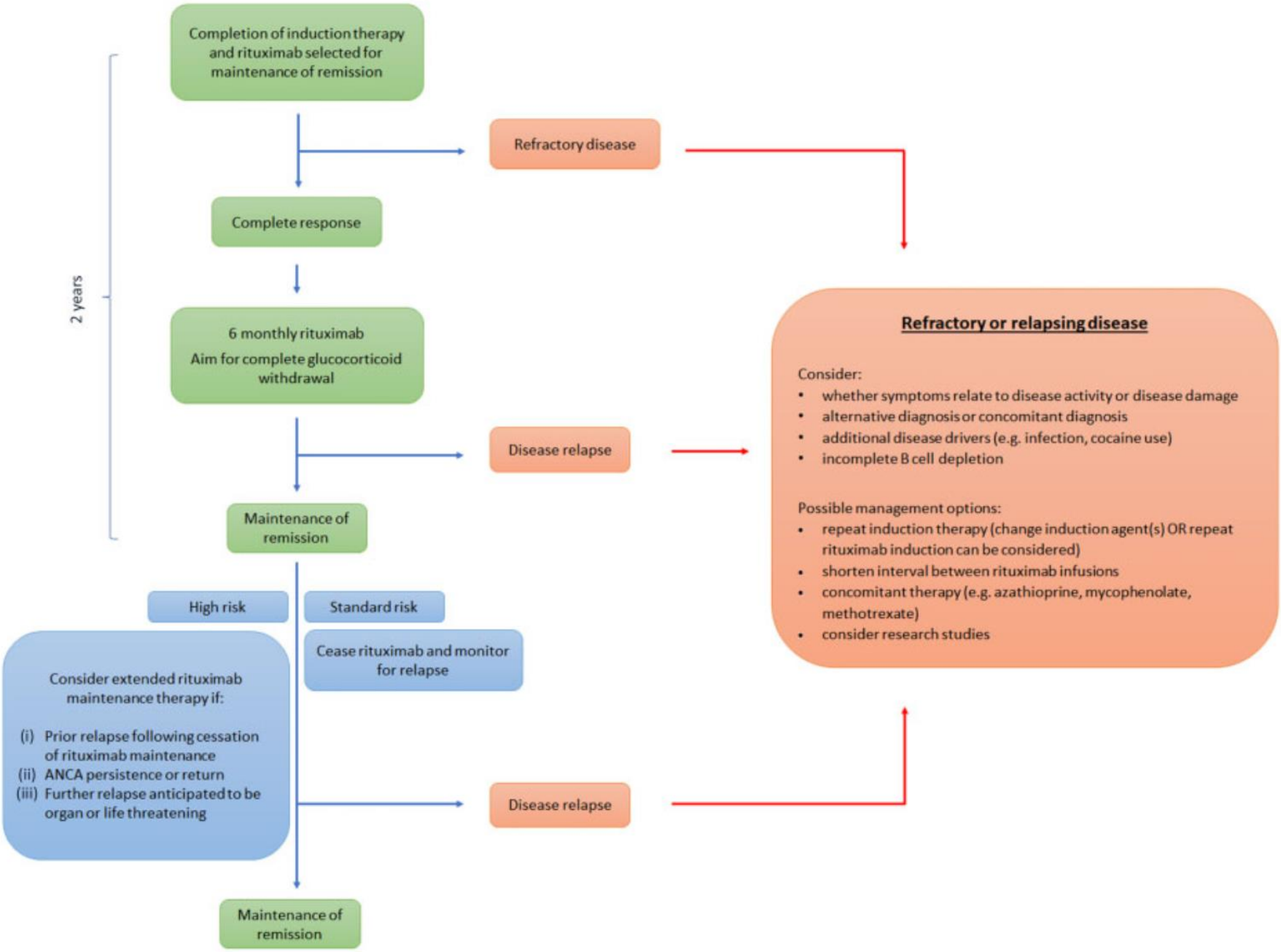
Guideline

British Society for Rheumatology

Rituximab for maintenance of remission in ANCA-associated vasculitis: expert consensus guidelines

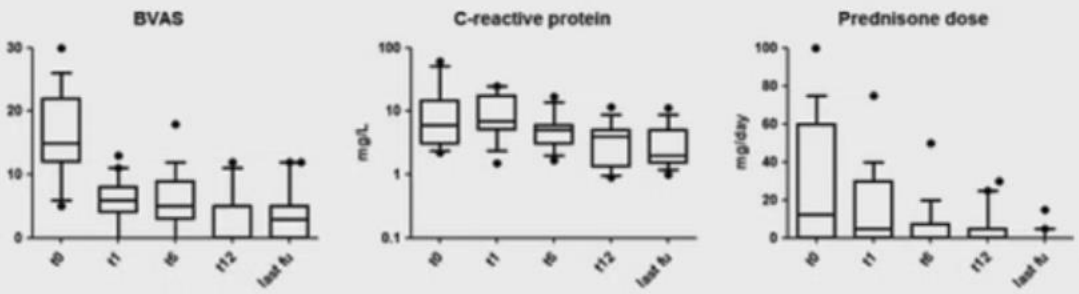
Joanna Tieu[1,2], Rona Smith[1], Neil Basu[3], Paul Brogan[4,5], David D'Cruz[6], Neeraj Dhaun[7,8], Oliver Flossmann[9], Lorraine Harper[10], Rachel B. Jones[1,11], Peter C. Lanyon[12,13], Raashid A. Luqmani[14], Stephen P. McAdoo[15], Chetan Mukhtyar[16,17], Fiona A. Pearce[18,19], Charles D. Pusey[15], Joanna C. Robson[20,21], Alan D. Salama[22,23], Lucy Smyth[24], Richard A. Watts[25,26], Lisa C. Willcocks[11] and David R. W. Jayne[1,27]

Fig. 1 A guide to treatment decisions



Rituximab for other vasculitides

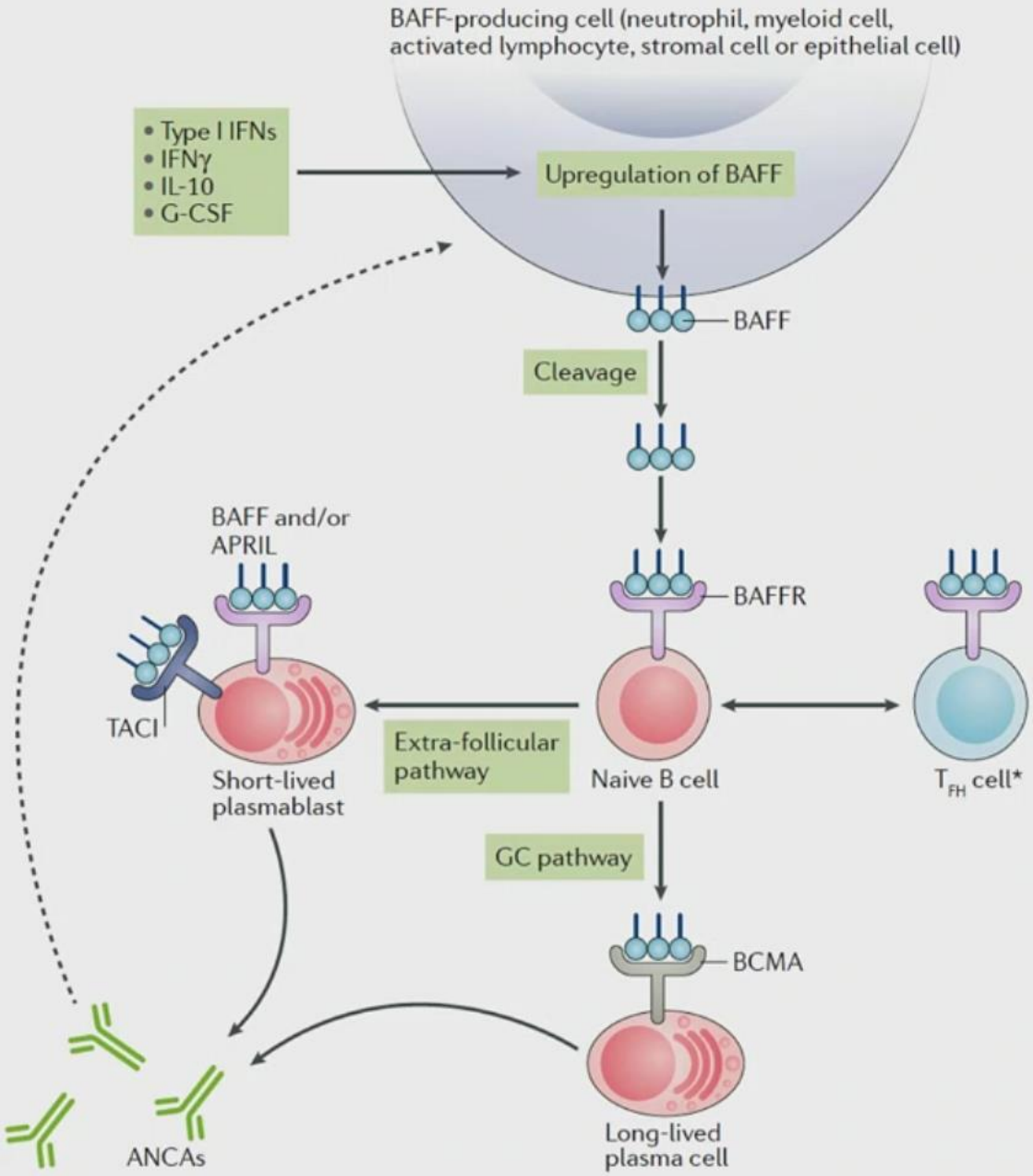
- IgA Vasculitis (HSP)



- Cryglobulinemia

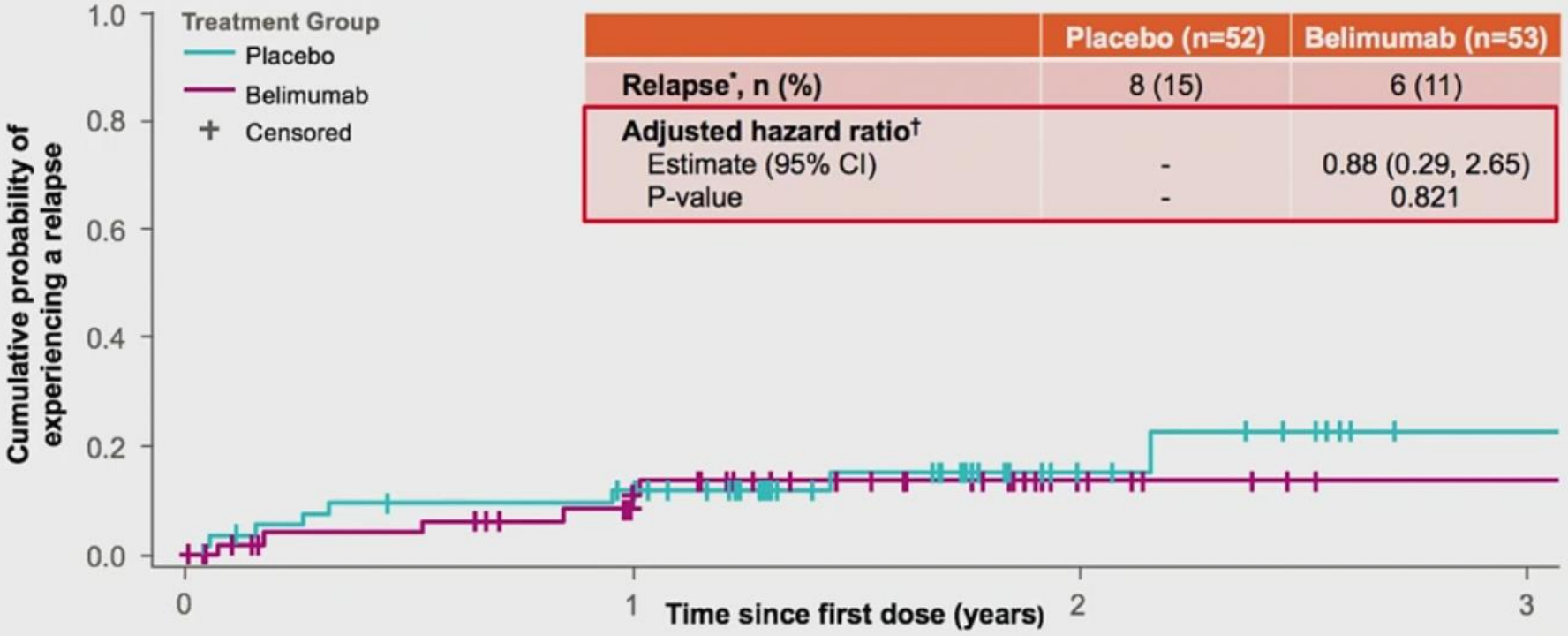
- Anti-GBM
  - anecdotes

Maritati F et al, *Arthritis Rheumatol* 2018. Galli M et al, *Autoimmunity Reviews* 2019



McClure & Jayne, *Nature Rev Nephrology* 2018

Belimumab to prevent relapse in ANCA vasculitis
The BREVAS trial



	Placebo (n=52)	Belimumab (n=53)
Relapse*, n (%)	8 (15)	6 (11)
Adjusted hazard ratio†		
Estimate (95% CI)	-	0.88 (0.29, 2.65)
P-value	-	0.821

Conclusion. Belimumab plus azathioprine and glucocorticoids for the maintenance of remission in AAV did not reduce the risk of relapse

Jayne D et al, *Arthritis Rheumatol* 2018

LUPUS NEPHRITIS

Lupus nephritis

Recommendation

2019 Update of the Joint European League Against Rheumatism and European Renal Association–European Dialysis and Transplant Association (EULAR/ERA–EDTA) recommendations for the management of lupus nephritis

4.14 For active non-responding/refractory disease, treatment may be switched to one of the alternative initial therapies mentioned above, or RTX (1000 mg on days 0 and 14) may be given.

Fanourakis A et al, *Ann Rheum Dis* 2020

In pure class V LN, no high-quality evidence has emerged over the last 7 years.

MMF/MPA is recommended as first-choice at the same doses as in class III/IV disease.

CY and CNI (especially TAC), the latter as monotherapy or combined with MMF, are alternative options.

Similar to class III/IV LN, rituximab (RTX) is reserved for non-responders in class V LN.

American College of Rheumatology
Empowering Rheumatology Professionals

Arthritis & Rheumatology
Vol. 71, No. 10, October 2019, pp 1670–1680
DOI 10.1002/art.40932

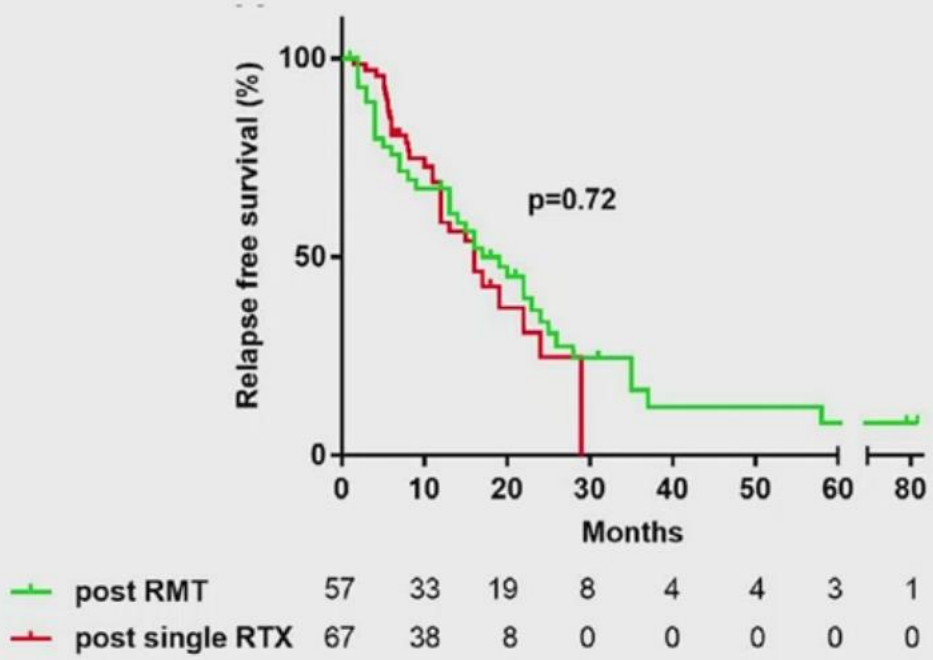
Rituximab as Maintenance Treatment for Systemic Lupus Erythematosus: A Multicenter Observational Study of 147 Patients

Matthias A. Cassia,[1] Federico Alberici,[1] Rachel B. Jones,[2] Rona M. Smith,[2] Giovanni Casazza,[3] Maria L. Urban,[4] Giacomo Emmi,[4] Gabriella Moroni,[5] Renato A. Sinico,[6] Piergiorgio Messa,[7] Frances Hall,[8] Augusto Vaglio,[4] Maurizio Gallieni,[9] and David R. Jayne[2]

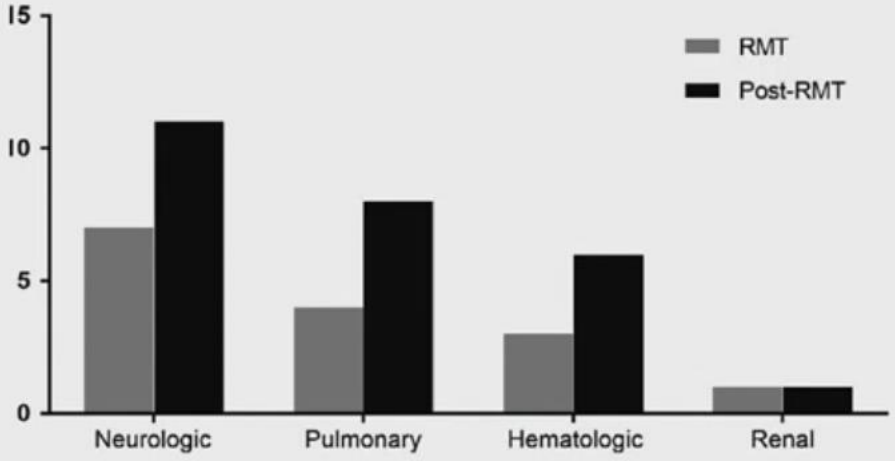
147 patients with SLE who were receiving RTX as induction therapy in 4 centers were included. Patients who received a single course of RTX and those who received RTX maintenance treatment (RMT) were followed up after treatment

Rituximab as a second line lupus therapy

High relapse rate after withdrawal



Better control of renal manifestations



Cassia M et al, *Arthritis Rheumatol* 2019

Mendez L et al, *Clin J Am Soc Nephrol* 2018

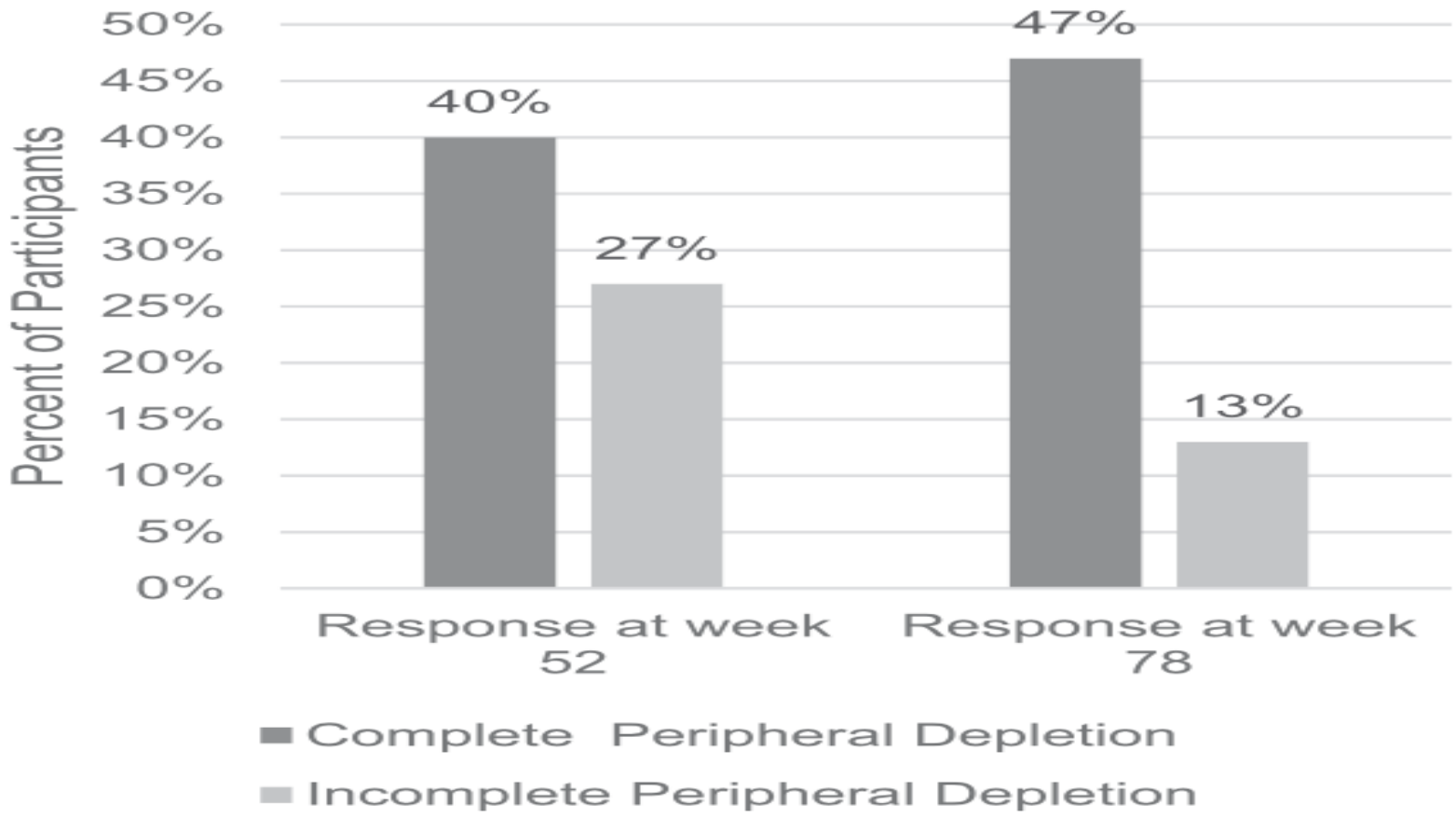


Figure 1. | A larger percentage of participants from the LUNAR trial who achieved complete peripheral depletion (n = 53) achieved complete response at week 52 and at week 78, compared to participants who did not achieve peripheral depletion (n = 15).

Table 1. Number of patients from the LUNAR trial treated with rituximab that achieved the three different definitions of B cell depletion at week 52 and 78 and maximum time to depletion in days

Definition of B Cell Depletion	Patients Who Achieved Depletion by Week 52, *n* (% of Total)	Patients Who Achieved Depletion by Week 78, *n* (% of Total)	Maximum Time to Achievement of Depletion in Days
CD19<20 cells/μl	68 (100)	68 (100)	86
CD19<5 cells/μl	68 (100)	68 (100)	182
CD19=0 cells/μl	53 (78)	53 (78)	365

Conclusions: There was substantial variability in peripheral blood B cell depletion in patients with lupus nephritis treated with rituximab from the LUNAR trial. Achievement of complete peripheral depletion, as well as the rapidity and duration of complete peripheral depletion, were associated with complete response at week 78.

Characteristics	Complete Response, *N* (%)	Unadjusted Odds Ratio (95% CI)	*P* Value
Complete peripheral depletion		5.8 (1.2 to 28)	0.03
Achieved (*n*=53)	25 (47)		
Never achieved (*n*=15)	2 (13)		
Duration of complete peripheral depletion		4.1 (1.5 to 11)	0.008
≥71 d (*n*=34)	19 (70)		
<71 d (*n*=34)	8 (30)		
Each incremental delay of 30 d to complete peripheral depletion	53 (78)	0.89 (0.81 to 0.98)	0.02

95% CI, 95% confidence interval.

Obinutuzumab

Type 2 anti-CD20, NOBILITY trial

A Study to Evaluate the Safety and Efficacy of Obinutuzumab Compared With Placebo in Participants With Lupus Nephritis (LN)

ClinicalTrials.gov Identifier: NCT02550652

Recruitment Status : Active, not recruiting

Study Description Go to

Brief Summary:

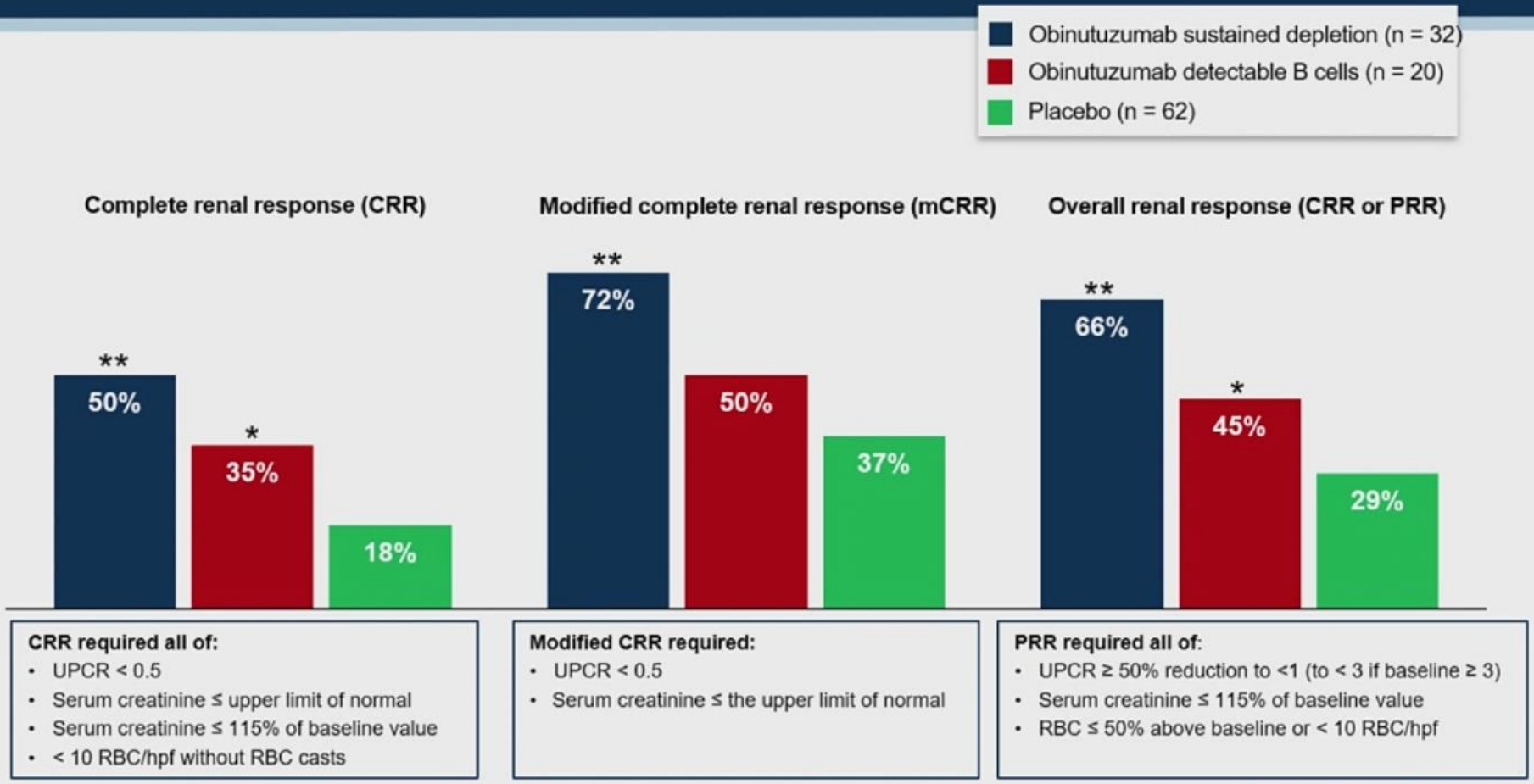
This Phase II study will compare the efficacy and safety of obinutuzumab plus mycophenolate mofetil (MMF)/mycophenolic acid (MPA) with placebo plus MMF/MPA in participants with proliferative LN.

Condition or disease	Intervention/treatment	Phase
Lupus Nephritis	Drug: Mycophenolate Mofetil/Mycophenolic Acid Drug: Obinutuzumab Other: Placebo Drug: Methylprednisolone Drug: Prednisone	Phase 2

Study Design Go to

Study Type :	Interventional (Clinical Trial)
Actual Enrollment :	126 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Double (Participant, Investigator)
Primary Purpose:	Treatment
Official Title:	A Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study to Evaluate the Safety and Efficacy of Obinutuzumab in Patients With ISN/RPS 2003 Class III or IV Lupus Nephritis
Actual Study Start Date :	November 13, 2015
Actual Primary Completion Date :	January 15, 2019
Estimated Study Completion Date :	December 23, 2020

Renal Responses at Week 76 by B-Cell Depletion Status



* $P < 0.2$ vs placebo group. ** $P < 0.05$ vs placebo group.

Eleven patients in the obinutuzumab group with insufficient data to determine depletion status are excluded.

PRR, partial renal response

Belimumab (Benlysta), BLISS LN

Lupus nephritis
Class III/IV
+ MMF or CYC / prednisone
N = 448
2 years

Conclusion: In this large 2-year LN study, compared with ST alone, BEL plus ST improved renal outcomes, overall SLE disease activity, and biomarker levels, while reducing steroid use, with a favorable safety profile.

Table 2. Other efficacy endpoints

Endpoint, n (%)	PBO (n=223)	BEL 10 mg/kg IV (n=223)	OR/HR (95% CI) vs PBO	p-value
Time to first severe SFI flare*	70 (31.4)†	42 (18.8)†	HR 0.6 (0.4, 0.8)	0.004
SLEDAI-S2K‡ score <4 at Wk 104	41 (18.4)	62 (27.8)	OR 1.8 (1.1, 2.8)	0.016
Prednisone dose ≤7.5 mg/day at Wk 104§	66 (29.6)	91 (40.8)	OR 1.7 (1.1, 2.5)	0.014
Prednisone dose ≤5 mg/day at Wk 104§	62 (27.8)	82 (36.8)	OR 1.5 (1.0, 2.3)	0.044

*Defined as (event date − treatment start date) + 1; †number/proportion of pts reporting the event; ‡SLEDAI-S2K defined as SELENA-SLEDAI with proteinuria scoring as per SLEDAI-2000 rules; §pts required to taper steroids to ≤10 mg/day by Wk 24

BEL, belimumab; CI, confidence interval; HR, hazard ratio; IV, intravenous; OR, odds ratio; PBO, placebo; pts, patients; SELENA-SLEDAI, Safety of Estrogens in Lupus National Assessment-SLE Disease Activity Index; SFI, SELENA-SLEDAI Flare Index; SLE, Systemic Lupus Erythematosus

Furie R et al, *Ann Rheum Dis* 2020 (abstract)

- Introduction to B cell therapy
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Rituximab in membranous nephropathy

GEMRITUX Study

Rituximab for Severe Membranous Nephropathy: A 6-Month Trial with Extended Follow-Up

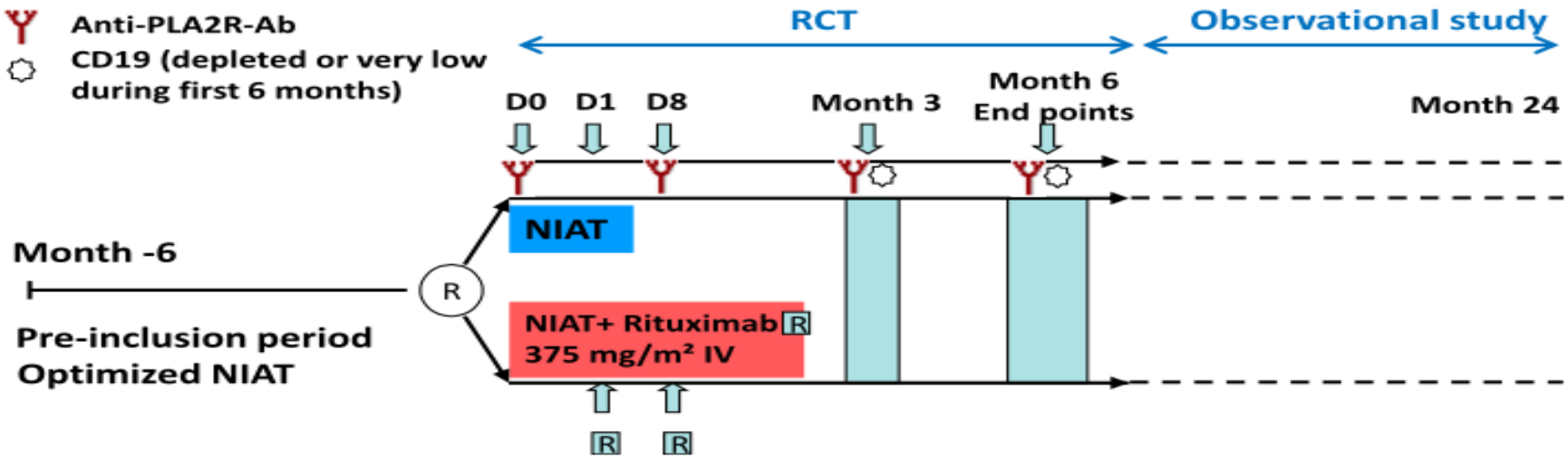
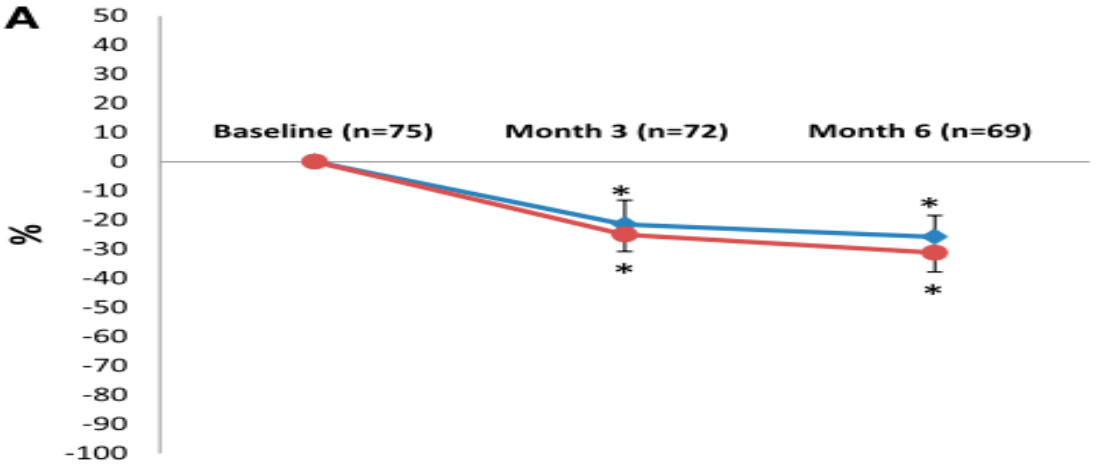
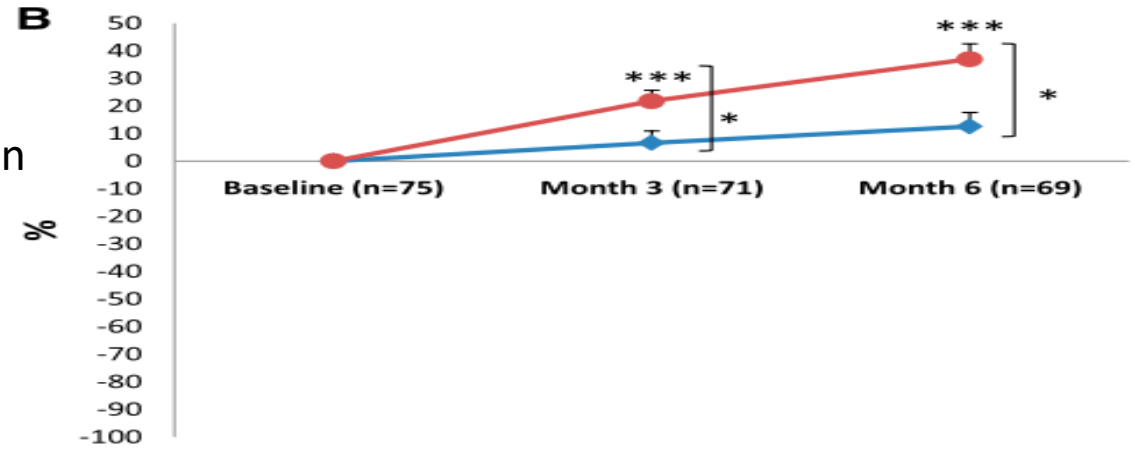


Figure 3. Study design. After a pre-inclusion period of 6 months during which NIAT was optimized, patients were assigned either to NIAT plus Rituximab (375 mg/m^2, two infusions at days 1 and 8) or to NIAT alone. Serum for anti-PLA2R-Ab determination was sampled at days 0 and 8, months 3 and 6, CD19 counts were determined at months 3 and 6; end points were assessed at month 6. The RCT was followed by an observational study during which follow-up was extended up to 24 months. IV, intravenous; R, rituximab.

proteinuria



serum albumin



anti–PLA2R-Ab levels

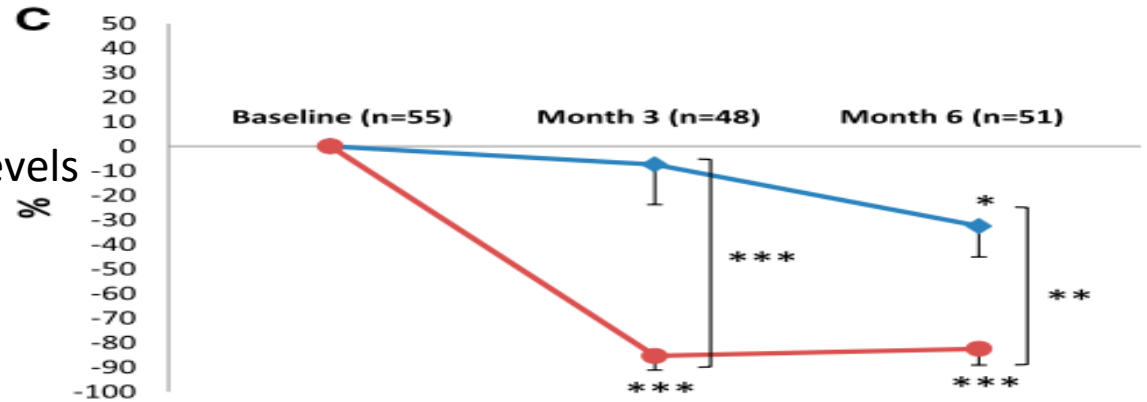


Table 3. Results of efficacy analysis at last follow-up

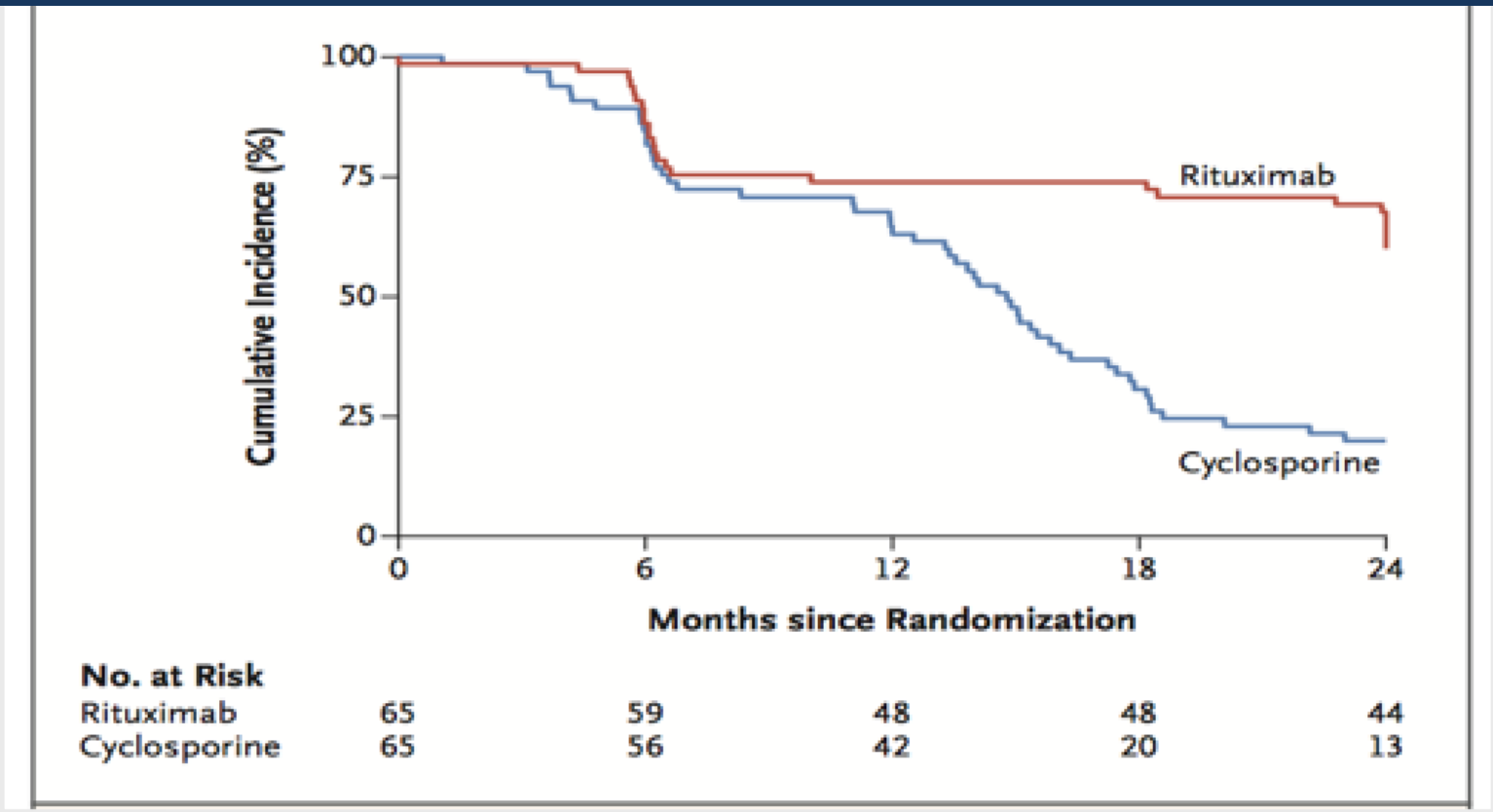
End Point	NIAT-Rituximab Group, *n*=37	NIAT Group, *n*=38	*P* Value
Remission, complete and partial[a]	24 (64.9; 49.5 to 80.2)	13 (34.2; 19.1 to 49.3)	<0.01
Protein-to-creatinine ratio, mg/g	2194.8 (1309.8–5310.0)	4701.1 (2027.8–8265.3)	0.02
Serum albumin, g/L	32 (26–35)	27 (20–30)	0.03
Serum creatinine, μmol/L	101 (87–135)	97.2 (78.5–133.5)	0.50
eGFR, ml/min per 1.73 m^2	61.1 (48.7–83.4)	73.1 (50.4–90.5)	0.48

Data are shown as *n* (%; 95% CI) or median (IQR). Data were recorded before any potential modification of treatment assigned at randomization (modification of initial immunosuppressive treatment in the NIAT-rituximab group or addition of any immunosuppressive treatment in the NIAT group).
[a]Complete and partial remissions were defined according to 2012 KDIGO criteria on the basis of proteinuria.

Positive effect of rituximab on proteinuria remission occurred after 6 months. These data suggest that PLA2R-Ab levels are early markers of rituximab effect and that addition of rituximab to NIAT does not affect safety.

Rituximab in membranous nephropathy

Rituximab was noninferior to cyclosporine in inducing complete or partial remission of proteinuria at 12 months and was superior in maintaining proteinuria remission up to 24 months



Fervenza F et al, *New Engl J Med* 2020

Rituximab in membranous nephropathy

- STARMEN trial
  - Tacrolimus. Followed by rituximab, versus
  - Cyclophosphamide/corticosteroid

ClinicalTrials.gov Identifier: NCT01955187

Recruitment Status : Completed
First Posted : October 7, 2013
Last Update Posted : January 18, 2020

The STARMEN trial indicates that alternating treatment with corticosteroids and cyclophosphamide is superior to sequential treatment with tacrolimus and rituximab in primary membranous nephropathy.

86 adult patients

Biopsy-proven Primary Membranous Nephropathy

eGFR ≥45 ml/min/1.73m²
Proteinuria >4 g/24h
Serum albumin ≤3.5 g/dl

N=43
- Methylprednisolone at months 1, 3 and 5
- Cyclophosphamide at months 2, 4 and 6

6 months observational period

At 24 months

N=43
- Oral tacrolimus (full-dose for 6 months and tapering for another 3 months)
- Rituximab 1g at month 6

	PRIMARY ENDPOINT Complete/Partial Remission	SECONDARY ENDPOINT Complete Remission
Corticosteroid-Cyclophosphamide	83.7%	60%
Tacrolimus-Rituximab	58.1%	26%

- **Immunological response** significantly faster in Corticosteroid-Cyclophosphamide group.
- **Relapses**: 2.7% in Corticosteroid-Cyclophosphamide group, 12% in Tacrolimus-Rituximab group.
- **No differences in serious adverse events**.

CONCLUSION: Treatment with Corticosteroid-Cyclophosphamide induced significantly more remissions of nephrotic syndrome than treatment with Tacrolimus-Rituximab.

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Fernández-Juárez et al, 2020

Table 3. Evolution of anti-PLA2R and percentage of immunological response according to treatment group*.

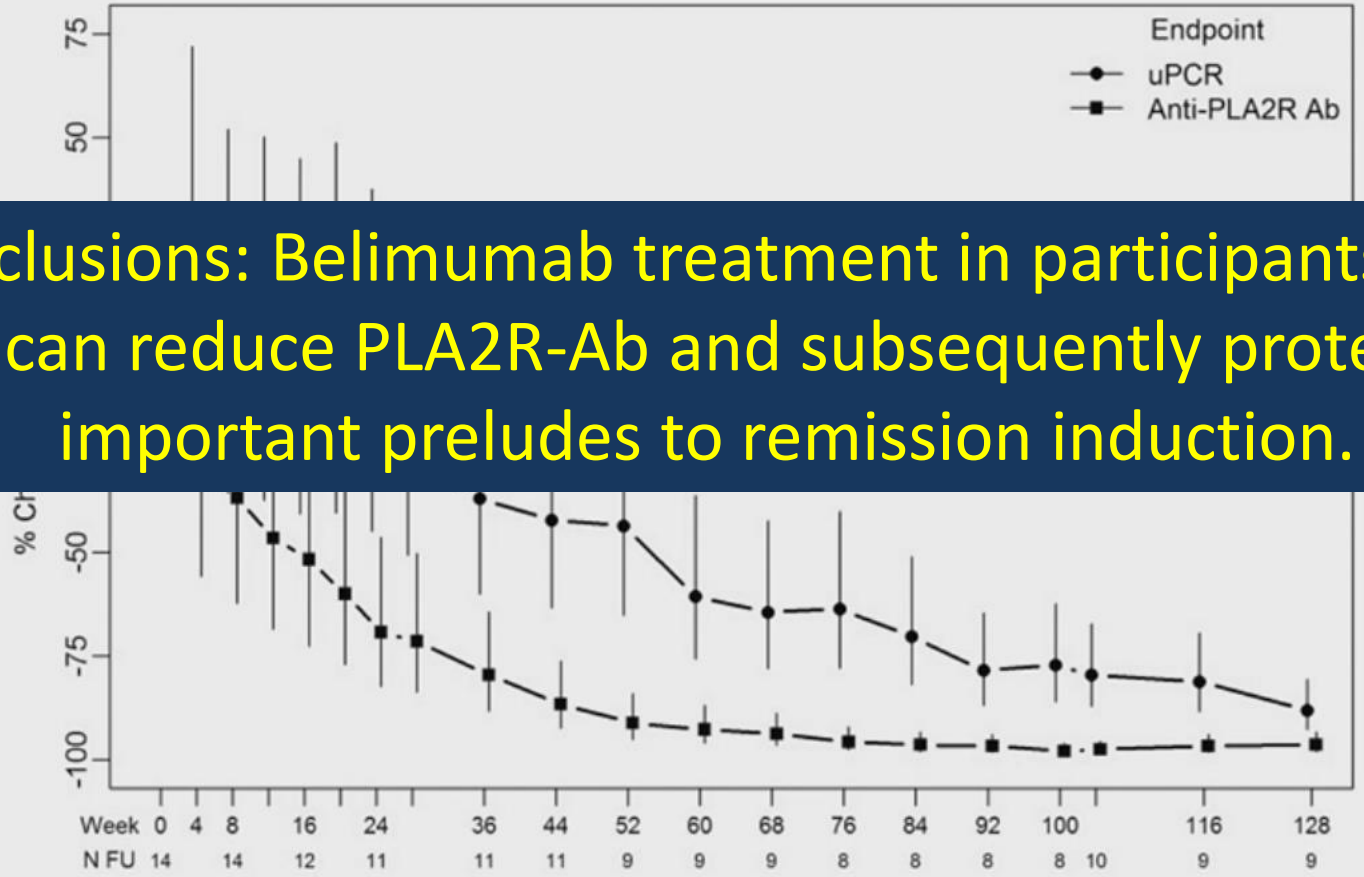
Time from Randomization	Anti-PLA$_2$R antibodies (RU/mL)				Immunological Response		
	All patients *Median (IQR)*	Corticosteroid-Cyclophosphamide *median (IQR)*	Tacrolimus-Rituximab *median (IQR)*	P Value	Corticosteroid-Cyclophosphamide *(%)*	Tacrolimus-Rituximab *(%)*	P Value
Baseline	80 (44–149)	59 (37–150)	113 (61–151)	0.1			
3 mo	2.3 (1.3–65)	1.4 (0.7–14)	33 (2.6–76)	0.003	77	45	0.03
6 mo	1.4 (0.7–7.4)	1.4 (0–1.7)	2.6 (1.4–30)	0.02	92	70	0.04
12 mo	1.6 (0–8.1)	1.5 (0–5)	2.1 (0–15)	0.5	88	79	0.31
18 mo	1.5 (0–2)	1.3 (0–2.3)	1.6 (0–15)	0.3	88	83	0.88
24 mo	1.6 (1.3–5.1)	1.4 (0.9–3.2)	1.9 (1.7–14)	0.06	88	83	0.91

- Anti-PLA2R titers showed a significant decrease in both groups but the proportion of anti-PLA2R-positive patients who achieved immunological response (depletion of anti-PLA2R antibodies) was significantly higher at three and six months in the corticosteroid-cyclophosphamide group (77% and 92%, respectively), as compared to the tacrolimus-rituximab group (45% and 70%, respectively).
- Serious adverse events were similar in both groups.
- Thus, treatment with corticosteroid-cyclophosphamide induced remission in a significantly greater number of patients with primary membranous nephropathy than tacrolimus-rituximab.

Nephrol Dial Transplant (2019) 1–8
doi: 10.1093/ndt/gfz086

ndt
Nephrology Dialysis Transplantation

Effect of belimumab on proteinuria and anti-phospholipase A2 receptor autoantibody in primary membranous nephropathy



Conclusions: Belimumab treatment in participants with PMN can reduce PLA2R-Ab and subsequently proteinuria, important preludes to remission induction.

Barrett C et al, *Nephol Dial Transpl* 2020

Rituximab for FSGS/minimal change

	no	phenotype	Outcome
Munyentwani et al KI 2013	17	SD FR MCD	11/17 relapse free at median 27 months 9/11 discontinued all Immunosuppression
Guitard et al 2014 NDT	41	SD FR MCD	CR 25 PR 7 39 months 18 relapsed mean time 18 months 17/18 retreated rituximab 13/17 remission
Takei et al NDT 2013/ Iwabuchi et al Medicine (Baltimore) 2014	25	SD FR MCD	Only 4/25 relapsed within 12/12 Reduction in maintenance steroids

ISRCTN16948923 https://doi.org/10.1186/ISRCTN16948923

The use of rituximab in the treatment of nephrotic glomerulonephritis (TURING)

New Randomised Clinical Trial

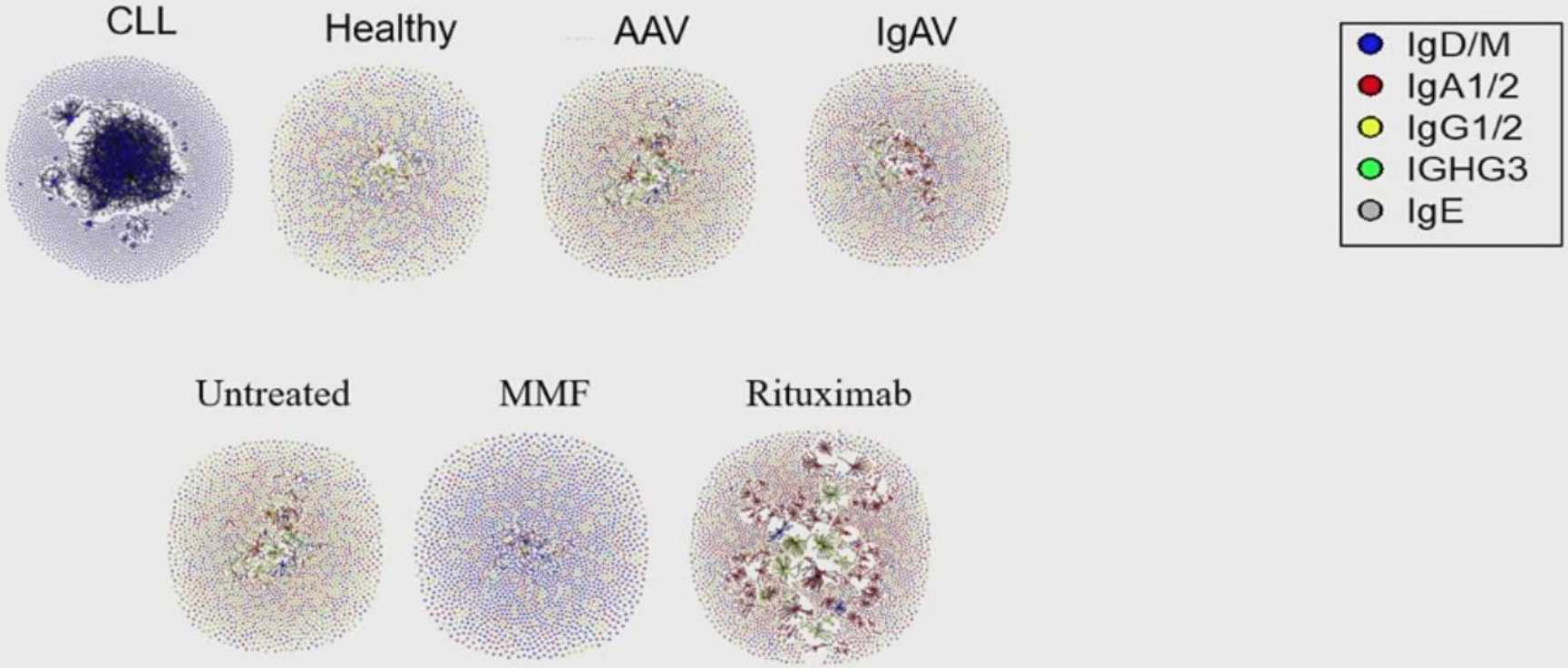
Complications of B cell depletion

LETTER

https://doi.org/10.1038/s41586-019-1595-3

Analysis of the B cell receptor repertoire in six immune–mediated diseases

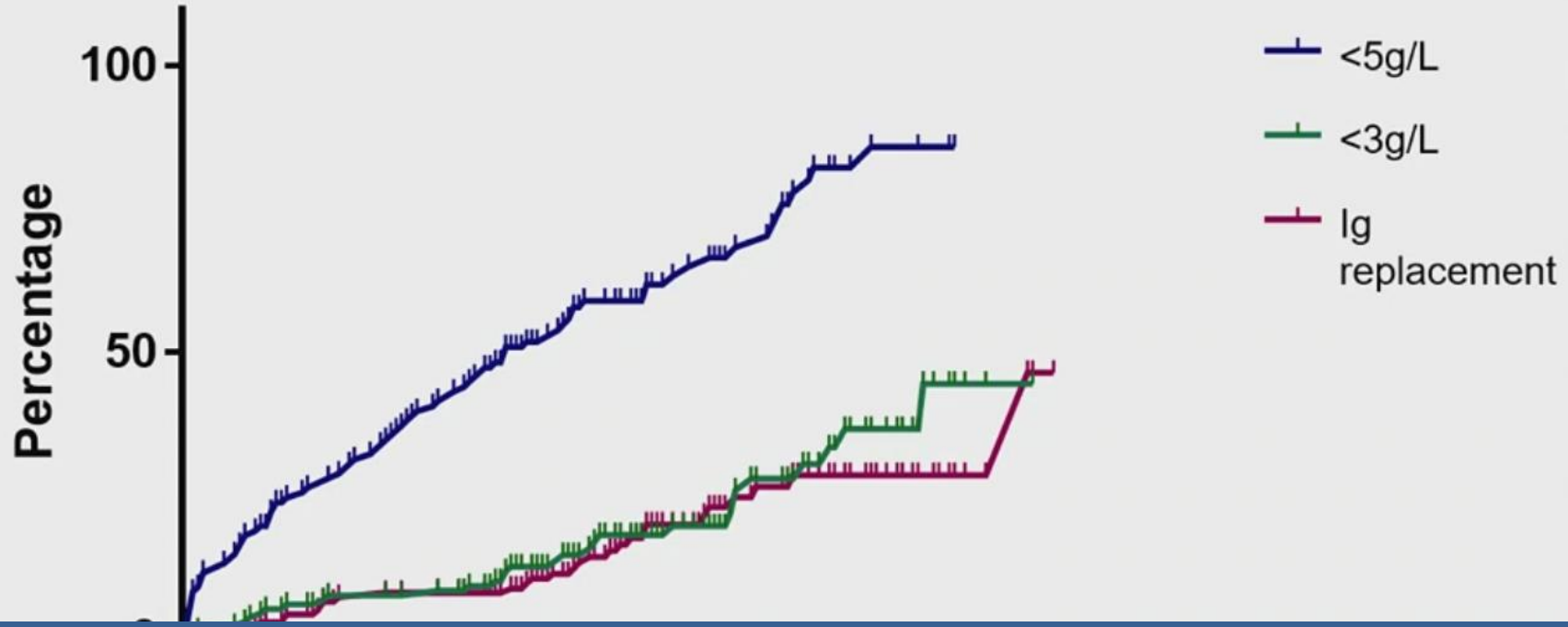
R. J. M. Bashford-Rogers[1,2*], L. Bergamaschi[1,3], E. F. McKinney[1,3], D. C. Pombal[1,3], F. Mescia[1,3], J. C. Lee[1,3], D. C. Thomas[1], S. M. Flint[1,5], P. Kellam[4], D. R. W. Jayne[1], P. A. Lyons[1,3] & K. G. C. Smith[1,3*]



Bashford-Rogers R et al. *Nature* 2019

Low immunoglobulins after rituximab

ANCA vasculitis142/260 (56%)



Conclusion:

Median time to IgG <5 g/L was 22.5 months and to IgG <3 g/L was 24.5 months .

RTX associated HG is progressively identified with longer term follow-up. Although annual infection rates were low, in patients with recurrent infection, use of IRT was associated with a reduction in infection burden.

Tieu et al, *(submitted)*

> Clin Rheumatol. 2020 Apr 4. doi: 10.1007/s10067-020-05042-2. Online ahead of print.

Evaluation of the Immune Response to Hepatitis B Vaccine in Patients on Biological Therapy: Results of the RIER Cohort Study

Table 2 Number of responders depending on the biological agent

From: Evaluation of the immune response to hepatitis B vaccine in patients on biological therapy: results of the RIER cohort study

Biological agent	Responders, *n* (%)	*p*
Etanercept, *n* = 58	53 (91.38)	***0.023***
Adalimumab, *n* = 55	47 (85.45)	0.405
Infliximab, *n* = 22	15 (68.18)	0.085
Golimumab, *n* = 17	17 (100.00)	***0.046***
Rituximab, *n* = 14	4 (28.57)	***< 0.001***
[illegible]	[illegible]	[illegible]
Certolizumab, *n* = 8	8 (100.00)	0.354
Abatacept, *n* = 3	2 (66.67)	0.454
Anakinra, *n* = 1	0 (0.00)	0.182

Summary

- B cell depletion is an established treatment in immune mediated renal disease
  - Rituximab
    - licensed for vasculitis, effective in maintenance
    - recommended second line in lupus nephritis
    - efficacy in primary glomerulonephritis
- Mechanism requires B cell depletion, other approaches - cytokine blockade
  - Obinutuzumab, a more effective deplete, potential role in lupus nephritis
  - Belimumab, Blys/BAFF inhibitor, efficacy in lupus nephritis over the long term
- B cell depletion has potential harms
  - Increased risk of infection
  - Development of immunodeficiency
  - Interference with vaccine responses

David Jayne

B cell inhibition in glomerular diseases

Thanks for Your Attention