Stratégies thérapeutiques des néphropathies lupiques

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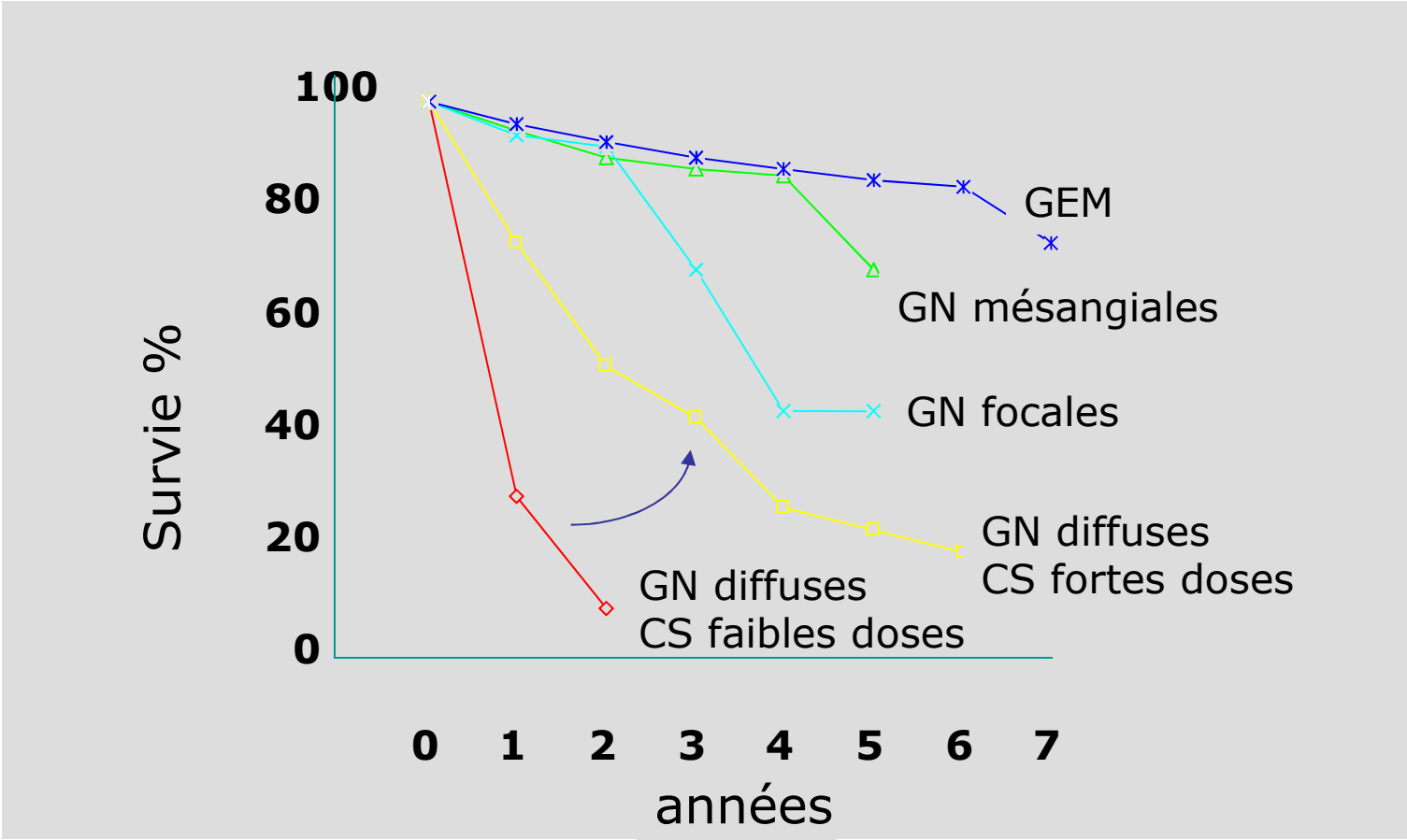
DHU FIRE

Histoire naturelle: Pronostic global

Pollak VE et al. Am. J. Kidney Dis. 2, suppl. 1:70, 1972



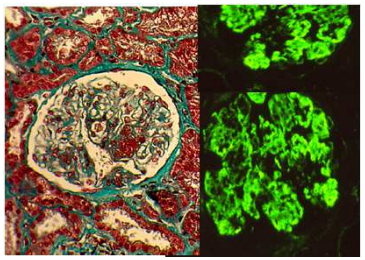
Traitement des GN prolifératives

Classes IIIA+/-C+/-V

Classes IVA+/-C+/-V

PAS LES CLASSES IIIC+/-V

PAS LES CLASSES IVC+/-V



Diagnostic

P/C<0,5g/g
DFG stable ou
Normalisé
=
Remission

\+

Prévention des rechutes

M0 M3 M6 M12

Induction

Entretien

Référence
=
stéroides + CYC
IV

Immunosuppresseur
+
Faible dose de stéroïdes

TRAITEMENT d'INDUCTION

=

traitement de la poussée

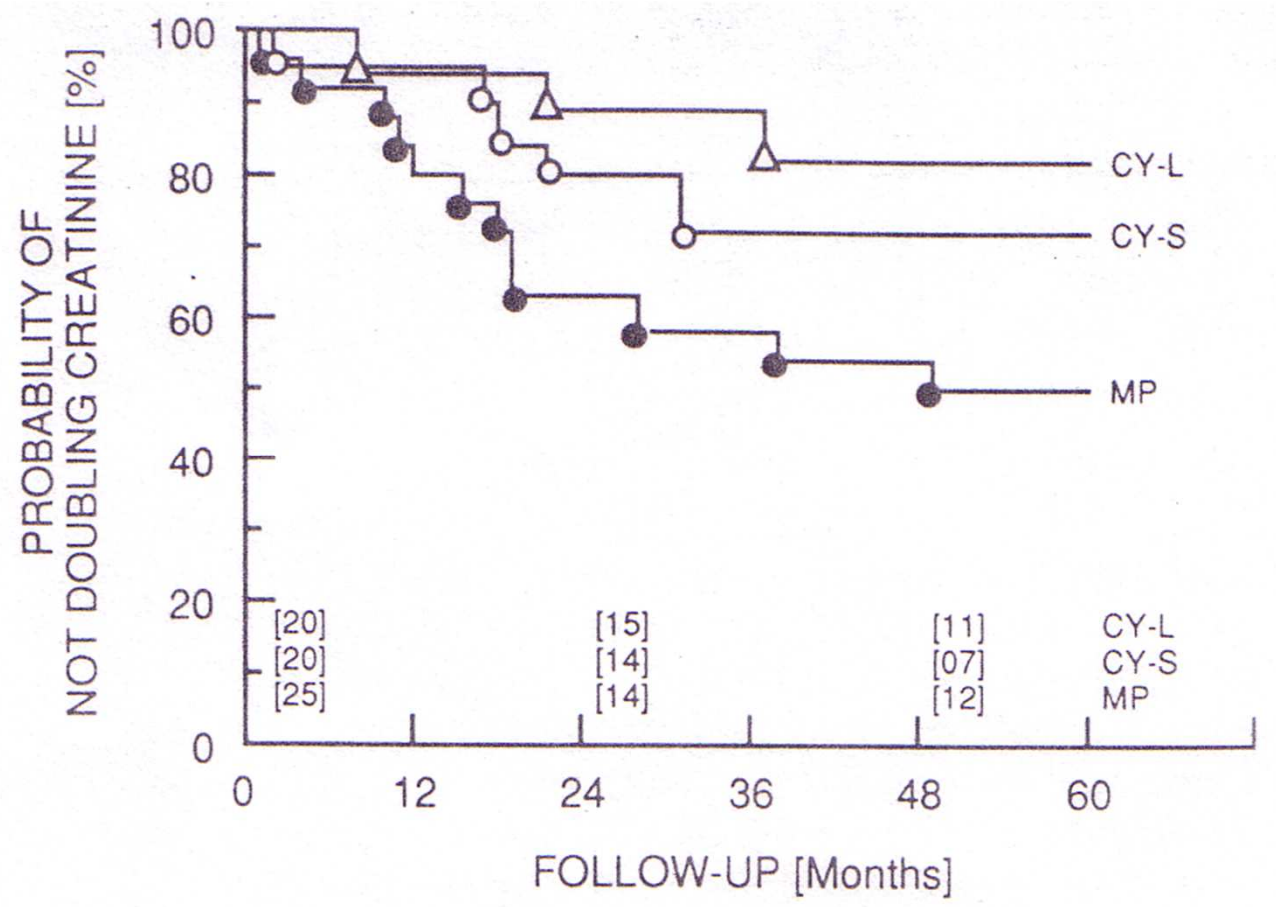
Donadio *NEJM* 1978
Austin *NEJM* 1986
Boumpas Lancet 1992

Traitement de référence

=

stéroïdes + CYC IV

Référence = CYC IV + Stéroïdes



Prednisone PO et

CY-L
Bolus/mois – 6mois
et /3mois – 2 ans

CY-S
Bolus/mois – 6mois

MP
Bolus/mois – 6mois

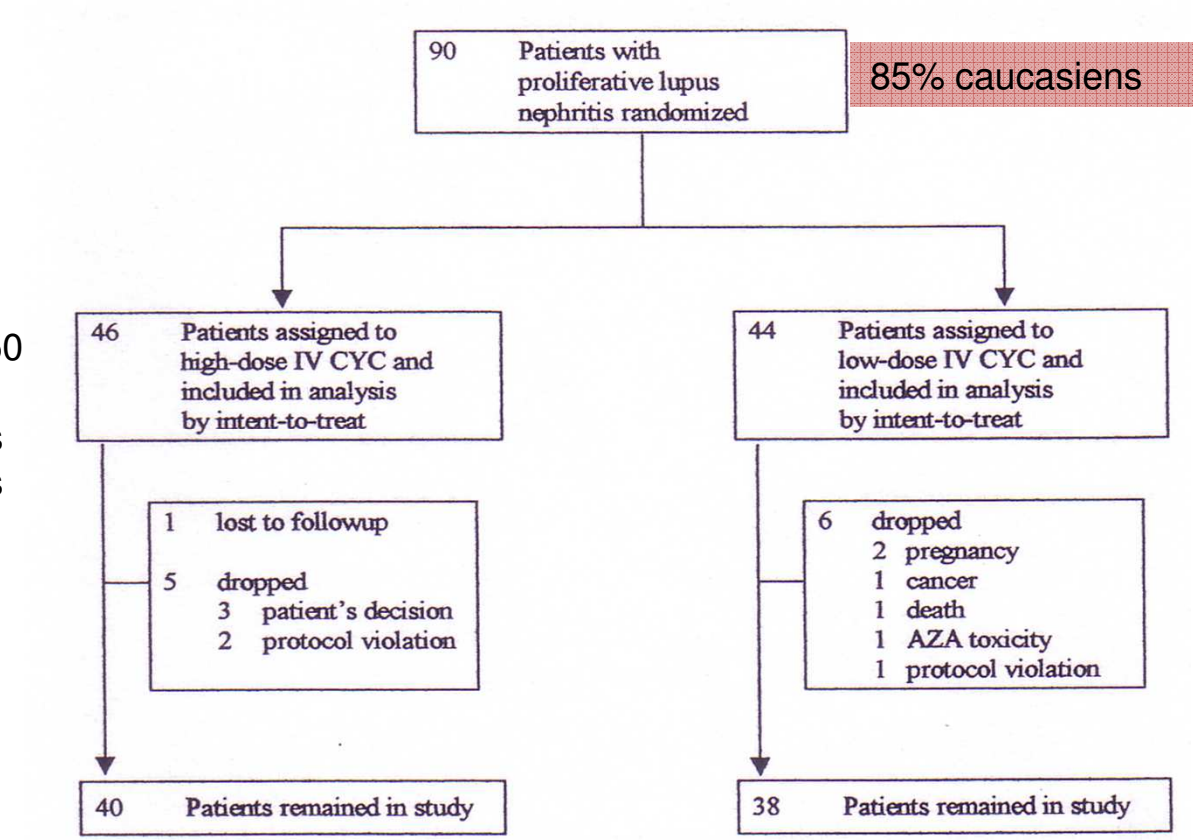
Boumpas *Lancet* 1992; 340:741

Affinement 1

réduction du CYC pendant l'induction

EUROLUPUS

CYC = 500 mg – 750 mg/m^2
CYC/mois – 6mois
CYC/3mois 6 mois
=
8.5 g

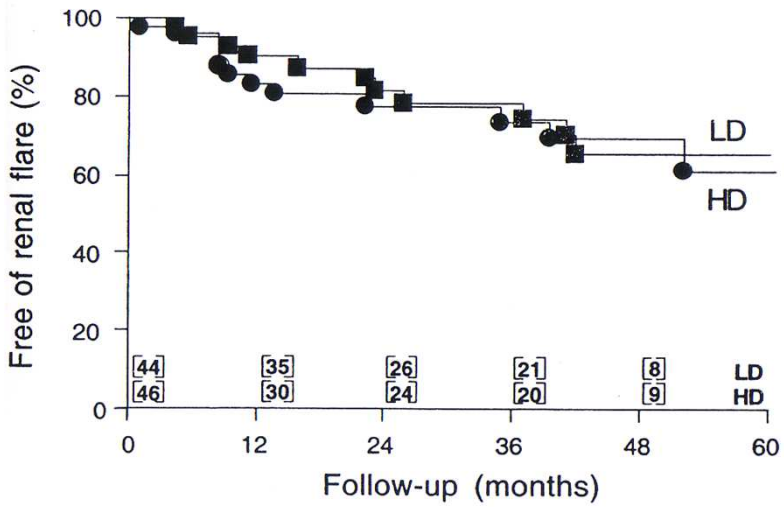


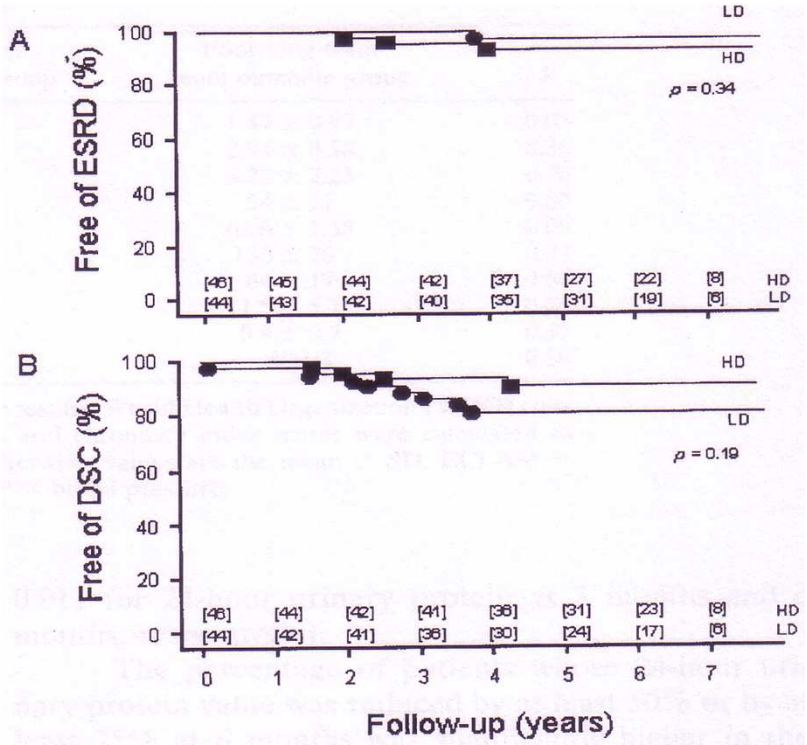
500 mg CYC/2s
3mois
= 3 g

Entretien = AZA – 2 ans

Houssiau FA *Arth Rheum* 2002; 46 : 2121 et 2004; 12: 3934

EUROLUPUS

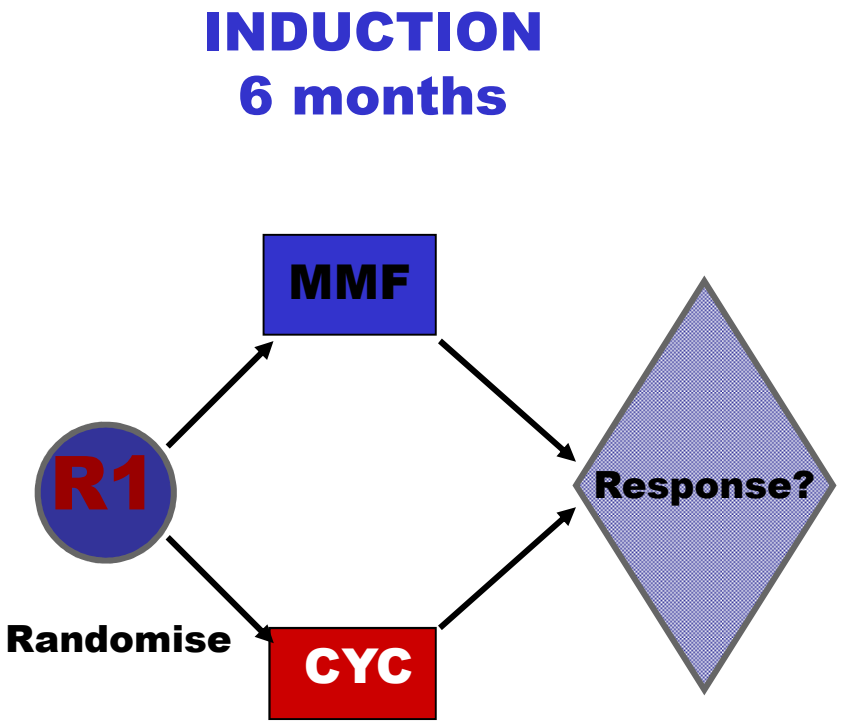

Free of renal flare (%)
100
80
60
40
20
0
LD
HD
[44]
[46]
[35]
[30]
[26]
[24]
[21]
[20]
[8]
[9]
LD
HD
0
12
24
36
48
60
Follow-up (months)


A
Free of ESRD (%)
LD
HD
p = 0.34
[46] [45] [44] [42] [37] [27] [22] [8] HD
[44] [43] [42] [40] [35] [31] [19] [6] LD
B
Free of DSC (%)
HD
LD
p = 0.19
[46] [44] [42] [41] [36] [31] [23] [8] HD
[44] [42] [41] [36] [30] [24] [17] [6] LD
0 1 2 3 4 5 6 7
Follow-up (years)

Affinement 2?

Suppression du CYC pendant l'induction MMF?

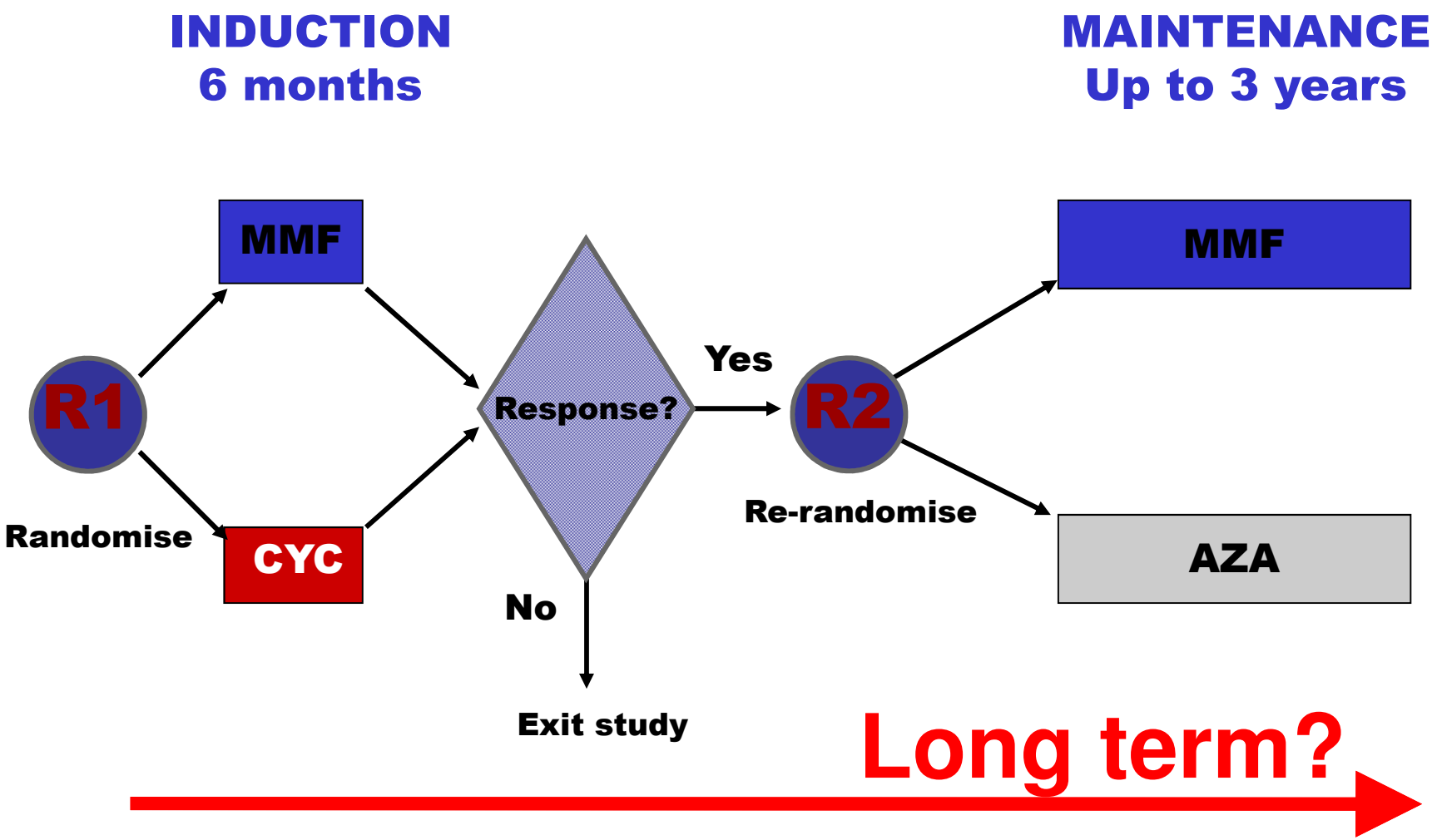
Aspreva Lupus Management Study



370 patients	MMF	CYC
Réponse	56.2%	53%
Arrêt pour intolérance	24	13
Arrêt pour infection	12	4
Décès	9	5

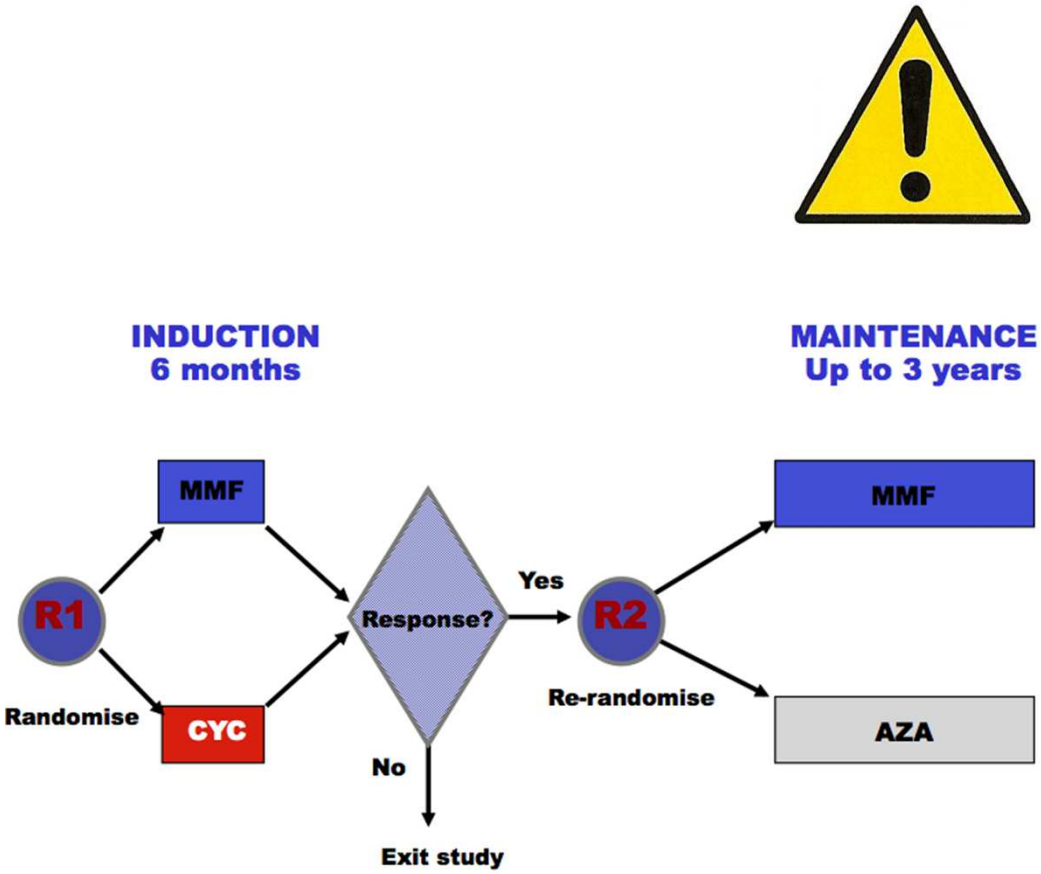
Appel G JASN 2009, 20: 1103-

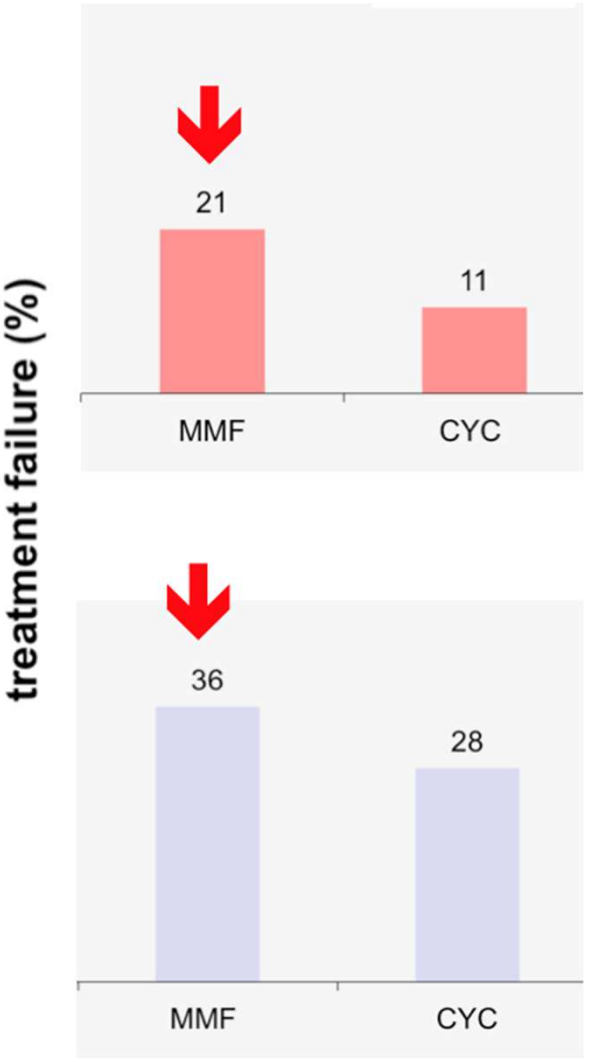
Aspreva Lupus Management Study



ALMS II = 227 patients

induits par CYC ou MMF re-randomisés AZA vs MMF en entretien





Jayne/ Appel ASN2010
Rovin cJASN 2013

Tentative d’affinement 3

+ Rituximab
en induction
??

144 pts
class IIIA and IVA
Prot/UCreat >1

standard treatment
MMF + prednisone

+

N=72 **rituximab 1g**
J1, 15, 168, 182

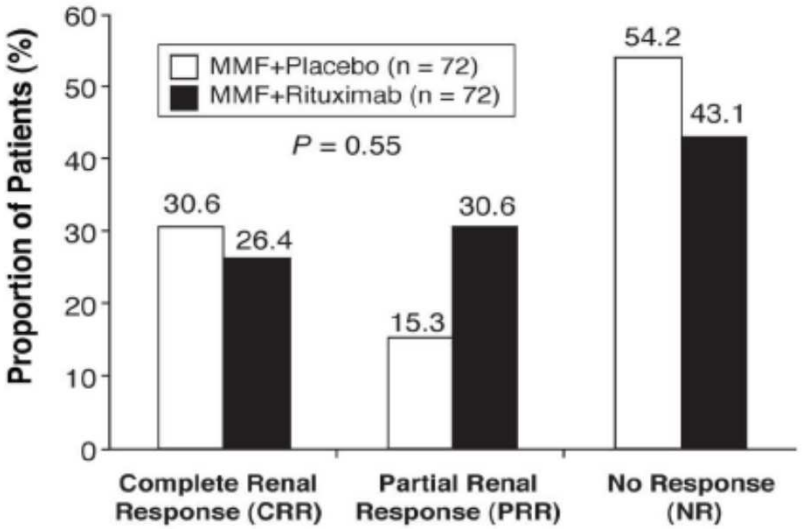
placebo **N=72**

1 year
% complete or partial remission?

Rovin Arthritis & Rheum 2012

March 2009

- LUNAR trial did not meet its primary endpoint
- safety data did not reveal any new or unexpected safety signals in patients receiving Rituxan.

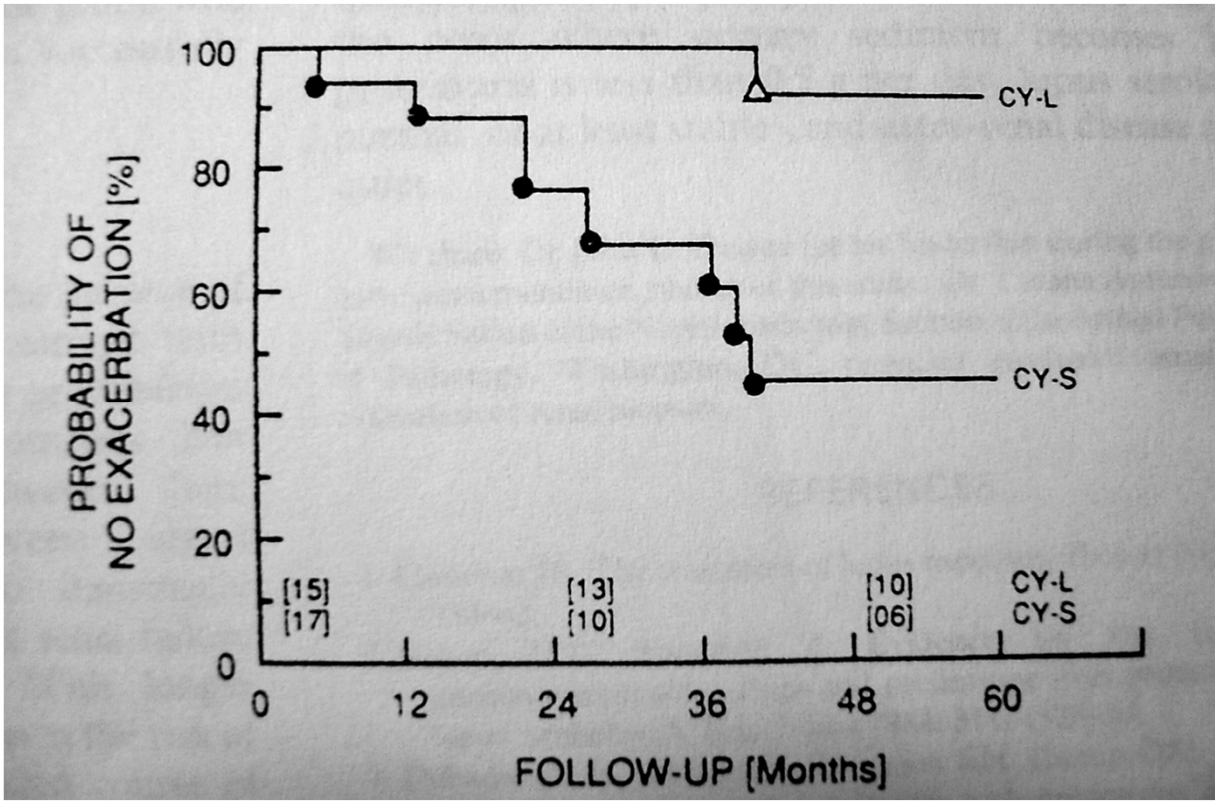


Rovin Arthritis & Rheum 2012

TRAITEMENT d’ENTRETIEN

1ère démonstration de l'intérêt d'un traitement d'entretien

Réduction risque de rechute avec CY-L



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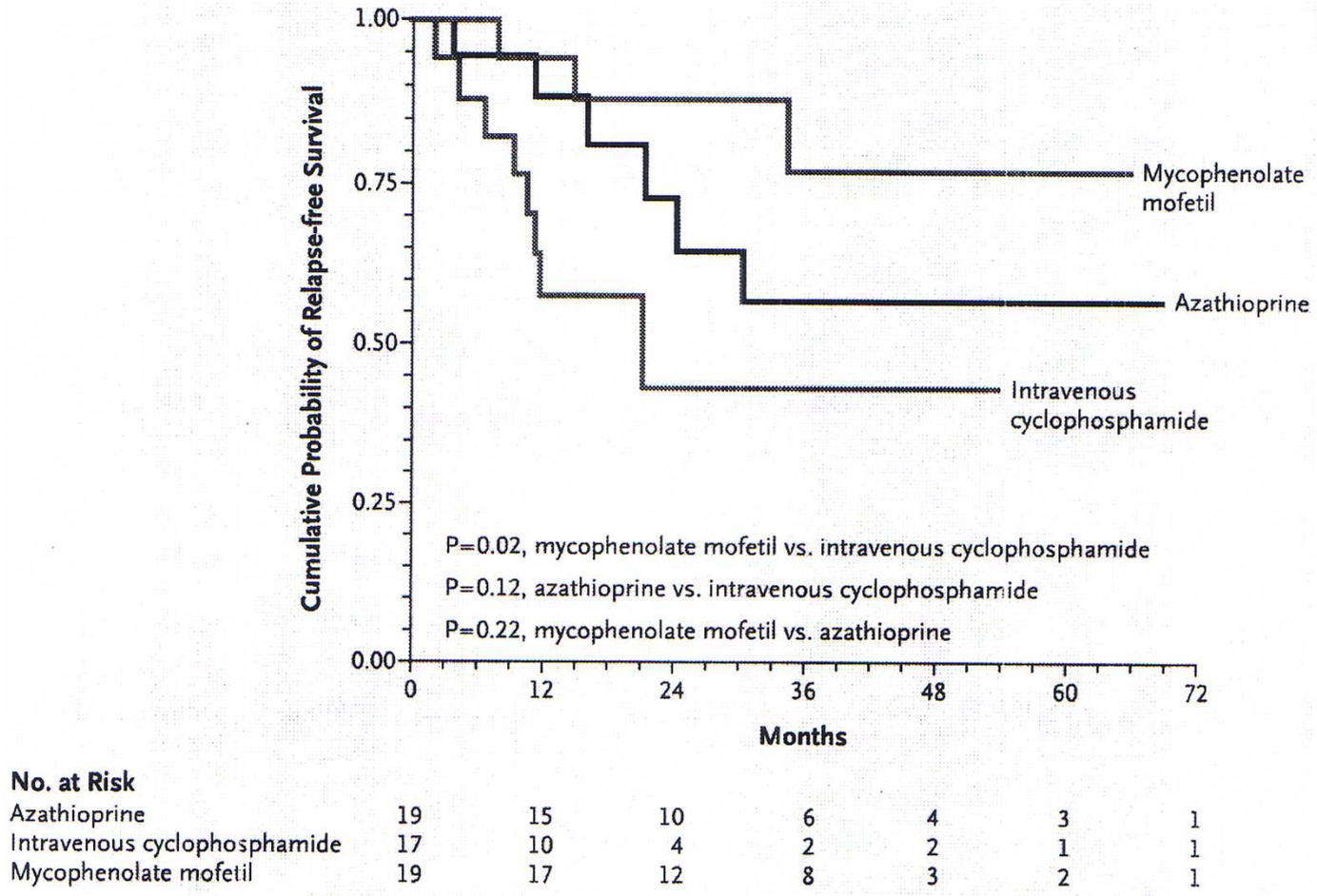
CY-S
Bolus/mois – 6mois

Boumpas *Lancet* 1992; 340:741

Affinement

Suppression du CYC en entretien

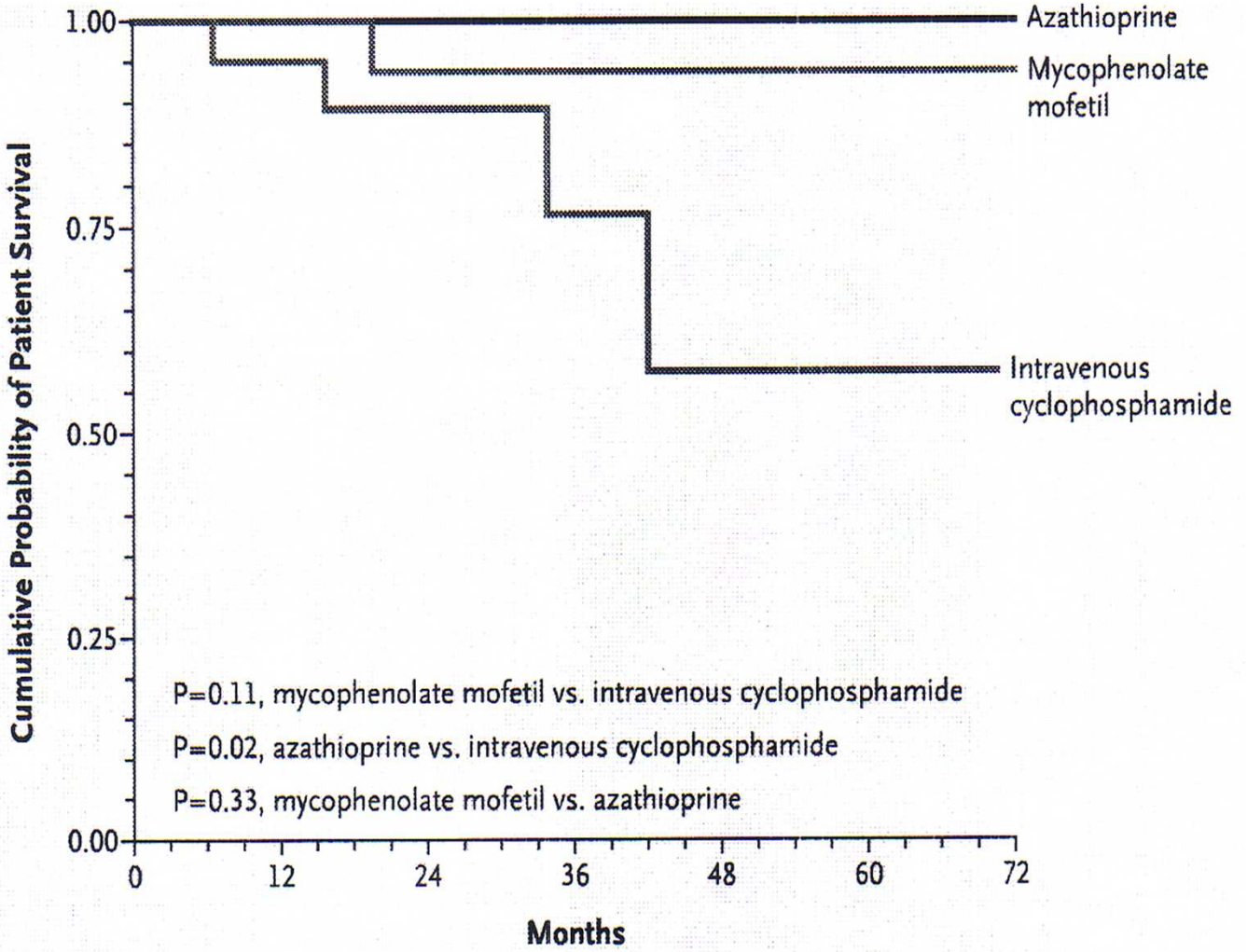
Entretien



No. at Risk

Azathioprine	19	15	10	6	4	3	1
Intravenous cyclophosphamide	17	10	4	2	2	1	1
Mycophenolate mofetil	19	17	12	8	3	2	1

Contreras *NEJMed* 2004; 350: 971

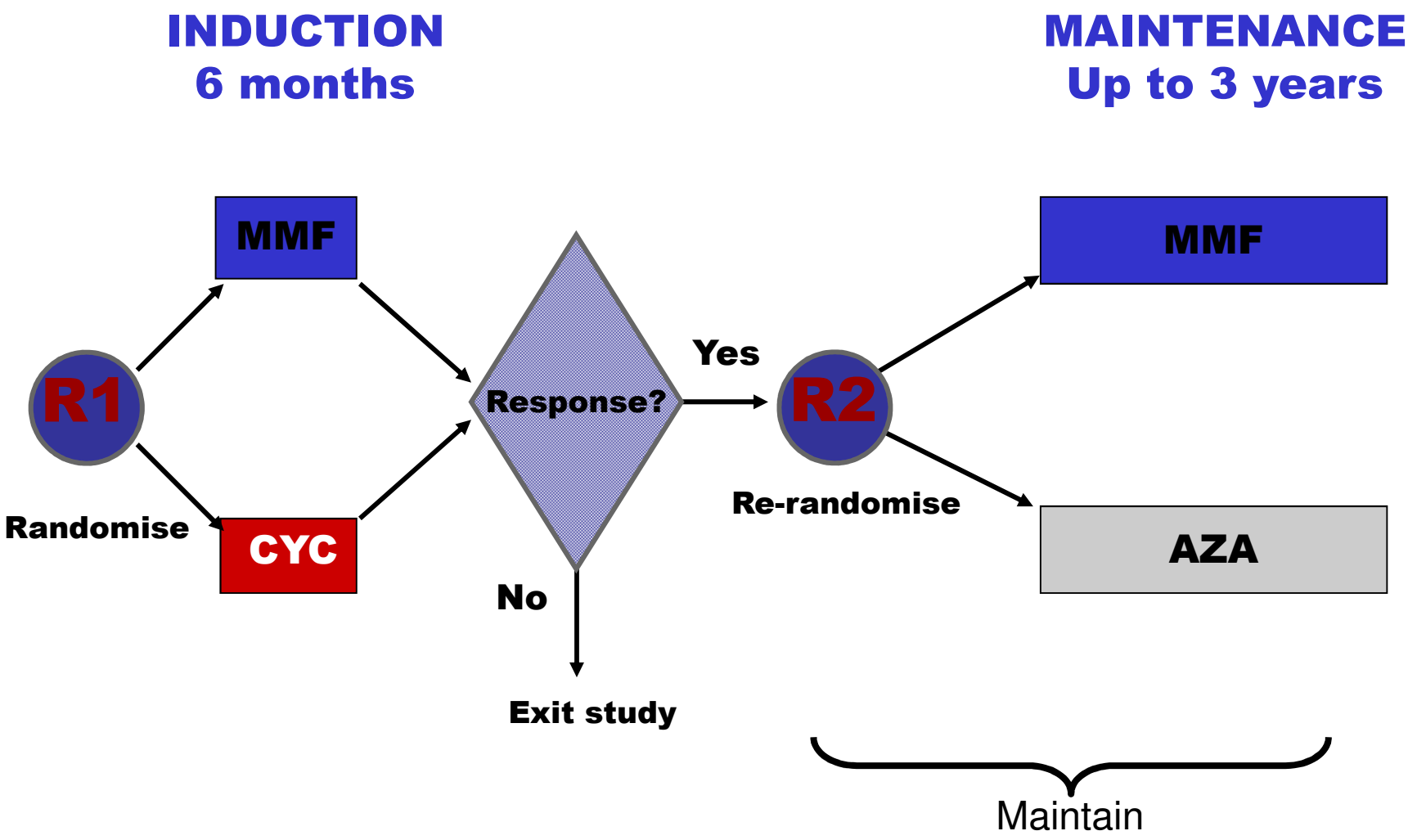


No. at Risk

Azathioprine	19	19	15	10	9	4	2
Intravenous cyclophosphamide	20	19	12	6	3	2	1
Mycophenolate mofetil	20	20	14	11	6	2	2

Contreras NEJMed 2004; 350: 971

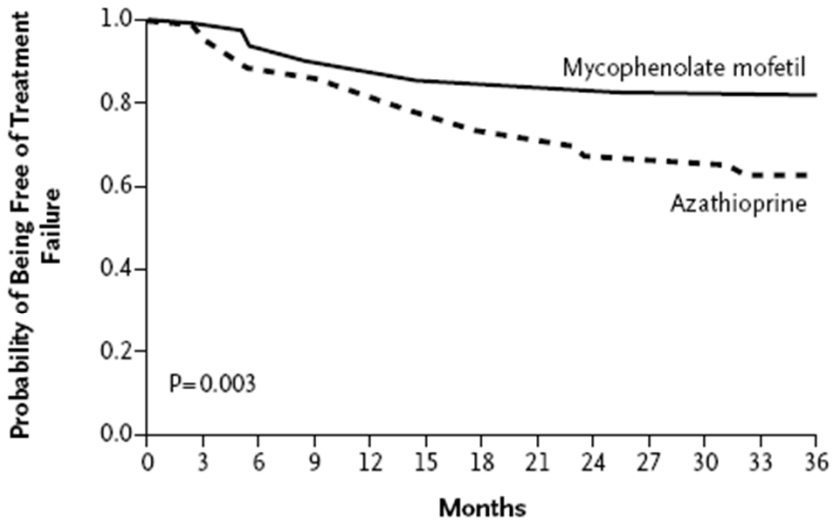
Aspreva Lupus Management Study



Mycophenolate versus Azathioprine as Maintenance Therapy for Lupus Nephritis

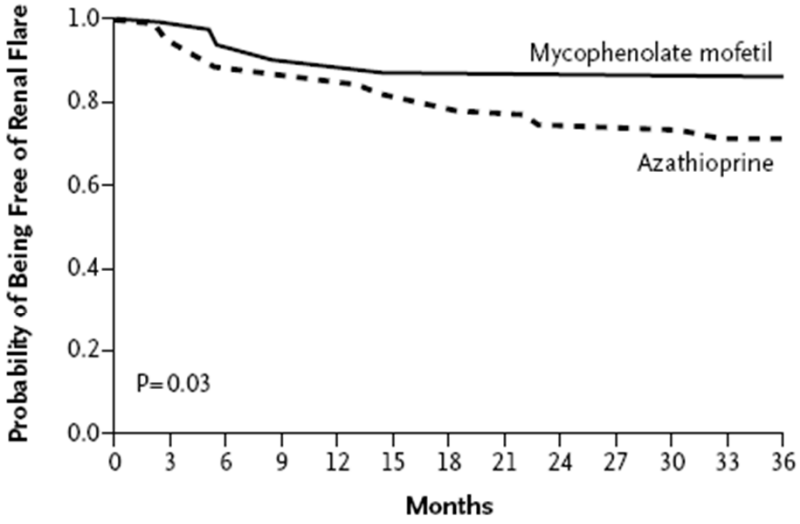
Mary Anne Dooley, M.D., M.P.H., David Jayne, M.D., Ellen M. Ginzler, M.D., M.P.H., David Isenberg, M.D., Nancy J. Olsen, M.D., David Wofsy, M.D., Frank Eitner, M.D., Gerald B. Appel, M.D., Gabriel Contreras, M.D., M.P.H., Laura Lisk, B.Sc., and Neil Solomons, M.D., for the ALMS Group*

A



No. at Risk												
Mycophenolate mofetil	116	109	101	92	88	87	82	79	78	75	74	72
Azathioprine	111	101	88	81	77	70	64	61	58	56	52	51

B



No. at Risk												
Mycophenolate mofetil	116	109	102	92	89	88	82	80	78	75	74	73
Azathioprine	111	101	89	82	77	71	65	62	60	58	56	54

En résumé

	Induction	Entretien	Ne pas oublier
1ère ligne	« Eurolupus »	MMF > Aza (Durée? ⬇ Essai WIN-lupus) GROUPE COOPÉRATIF LUPUS RÉNAL	ACE Hydroxychloroquine Prophylaxie antiinfectieuse
En cas de sévérité	« NIH » ?		
Si CYC non souhaité	MMF as ALMS		
2e ligne	Switch from CYC to MMF or MMF to CYC		
3e ligne	Rituximab		

PERSPECTIVES

CJASN ePress. Published on August 8, 2018 as doi: 10.2215/CJN.01070118

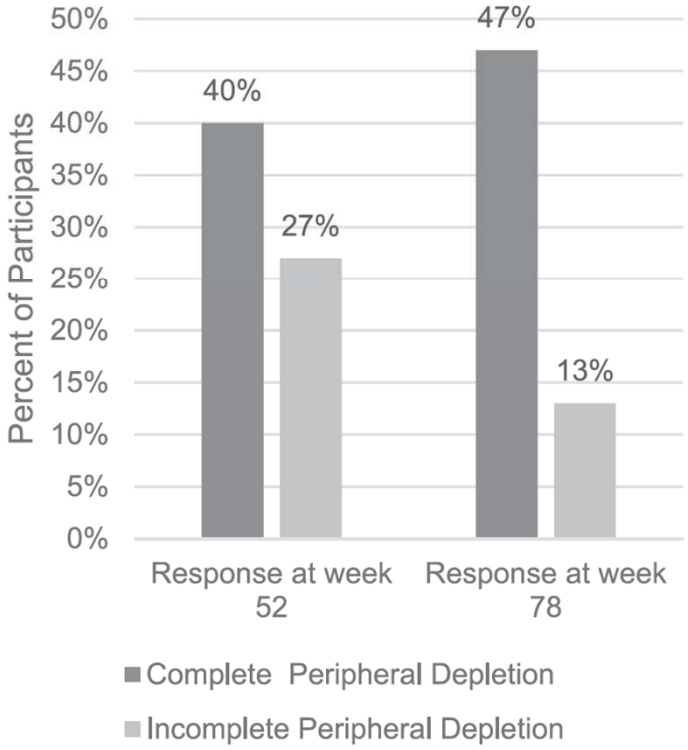
Article

Peripheral Blood B Cell Depletion after Rituximab and Complete Response in Lupus Nephritis

Liliana Michelle Gomez Mendez,[1] Matthew D. Cascino,[2] Jay Garg,[2] Tamiko R. Katsumoto,[2] Paul Brakeman,[1] Maria Dall'Era,[1] Richard John Looney,[3] Brad Rovin,[4] Leonard Dragone,[2] and Paul Brunetta[2]

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

LUNAR, the Lupus Nephritis Assessment with Rituximab study.



RITUXILUP

EXTENDED REPORT

Prospective observational single-centre cohort study to evaluate the effectiveness of treating lupus nephritis with rituximab and mycophenolate mofetil but no oral steroids

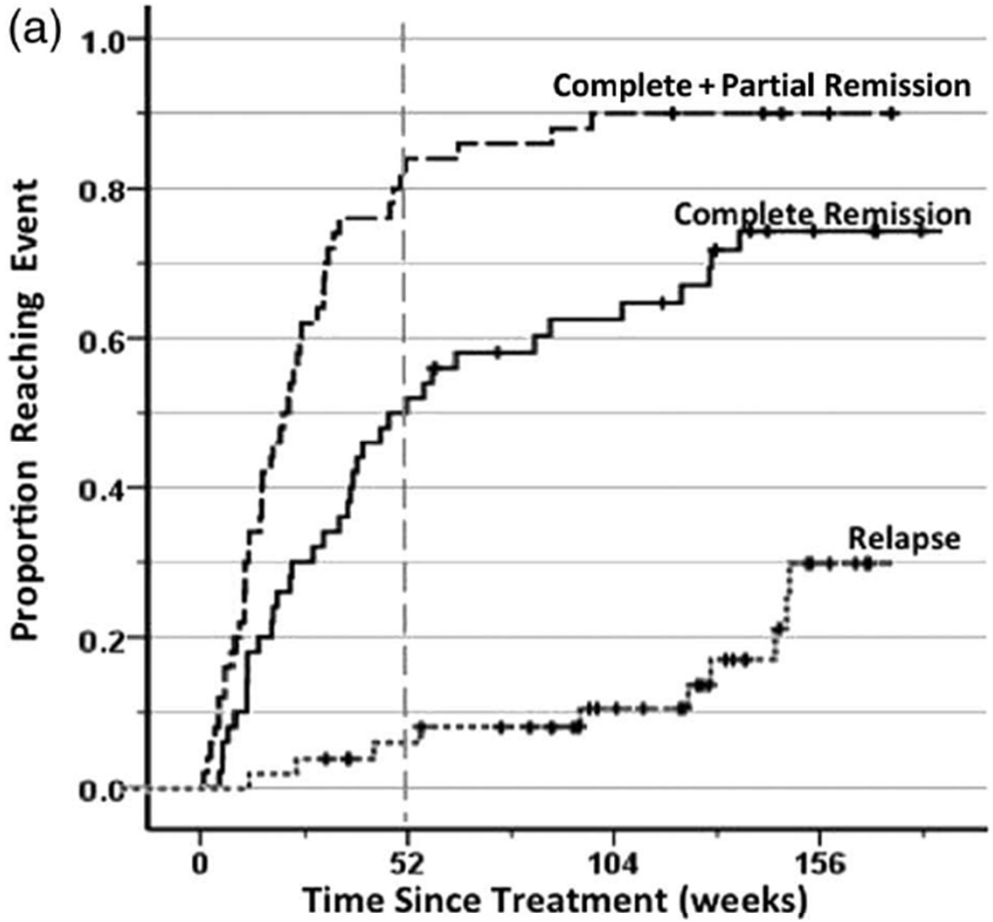
Marie B Condon,[1] Damien Ashby,[1] Ruth J Pepper,[1] H Terence Cook,[1,2] Jeremy B Levy,[1] Megan Griffith,[1] Tom D Cairns,[1] Liz Lightstone[1,2,3]

50 consecutive patients enrolled

Condon, Ann Rheum Dis 2013

RITUXILUP regimen for new episodes of LN in patients not on oral steroids

- Rituximab 1g + MP 500mg IV – d0 and d14
- Maintenance MMF – start at 500mg bd and titrate to trough levels 1.4-2.4mg/l
- NO oral steroid



- 24 week data:

Rituxilup	ALMS	
	MMF	CyP
31/50 (62%) in CR or PR	104/185 56.2%	98/185 53%
CR 16/50 (32%)	8.5%	8.5%

ORIGINAL RESEARCH

Annals of Internal Medicine

Multitarget Therapy for Induction Treatment of Lupus Nephritis

A Randomized Trial

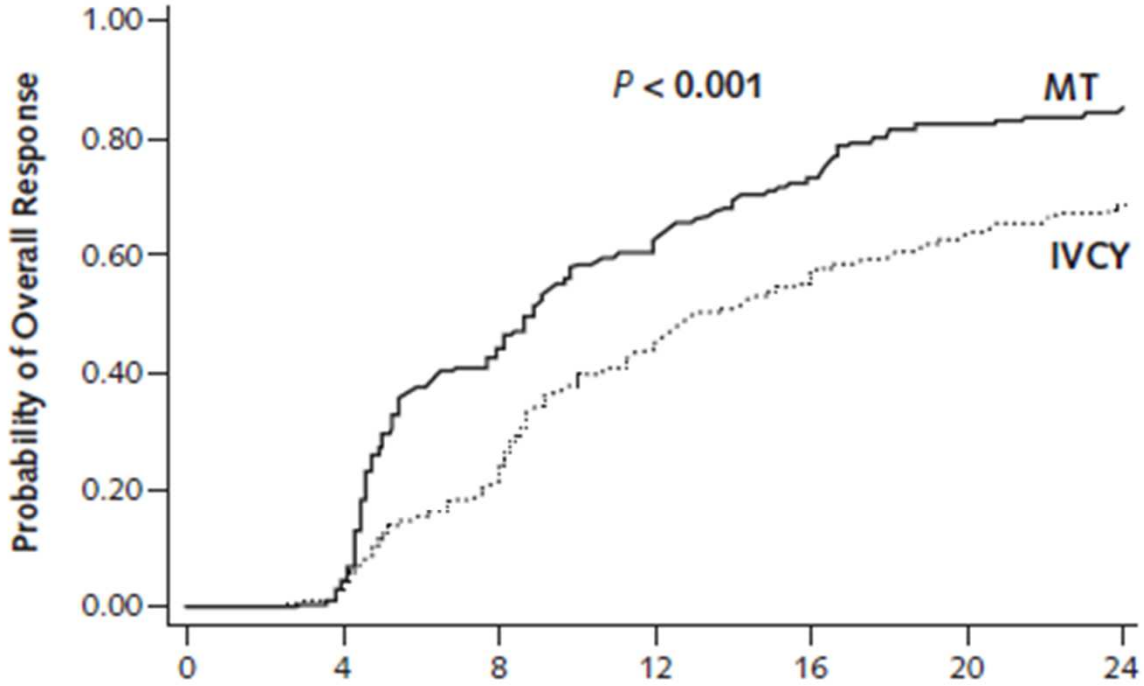
Zhihong Liu, MD; Haitao Zhang, MD; Zhangsuo Liu, MD; Changying Xing, PhD; Ping Fu, MD; Zhaohui Ni, MD; Jianghua Chen, MD; Hongli Lin, MD; Fuyou Liu, MD; Yongcheng He, MD; Yani He, MD; Lining Miao, MD; Nan Chen, MD; Ying Li, MD; Yong Gu, MD; Wei Shi, MD; Weixin Hu, MD; Zhengzhao Liu, MD; Hao Bao, MD; Caihong Zeng, PhD; and Minlin Zhou, MD

Tac 2mg twice daily
MMF 500 twice daily
High dose steroids

« NIH-short »

Characteristic	Multitarget (*n* = 181)	Intravenous Cyclophosphamide (*n* = 181)
Women, *n* (%)	168 (92.8)	161 (89.0)
Age at enrollment, *y*	30.3 (23.3, 38.6)	33.6 (24.2, 41.5)
Duration of LN, *mo*	2 (1, 12)	3 (1, 13)
First onset of LN, *n (%)*	102 (56.4)	87 (48.1)
Pathologic classification, *n* (%)†		
Class III	10 (5.5)	9 (5.0)
Class IV	74 (40.9)	76 (42.0)
Class V	32 (17.7)	37 (20.4)
Class III+V	19 (10.5)	7 (3.9)
Class IV+V	46 (25.4)	52 (28.7)

Ann Intern Med. 2015;162:18-26.



Patients at risk, *n*							
MT	181	175	98	67	45	29	20
IVCY	181	176	132	91	71	58	45

MT = multitarget; IVCY = intravenous cyclophosphamide.

Ann Intern Med. 2015;162:18-26.

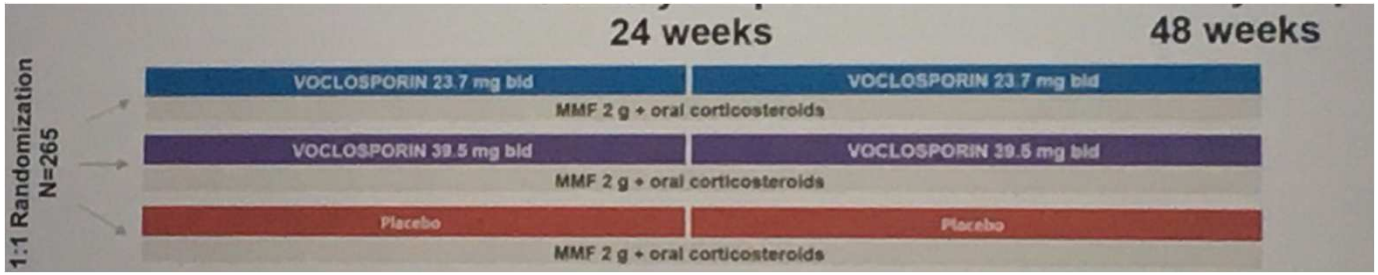
Effet curateur ou antiprotéinurique?
Ailleurs qu'en Asie? Après 6 mois?

Calcineurin inhibitor use in Lupus nephritis : an old friend returns

Samir Pariikh et al.

ASN 2018, San Diego, 23-28 octobre 2018

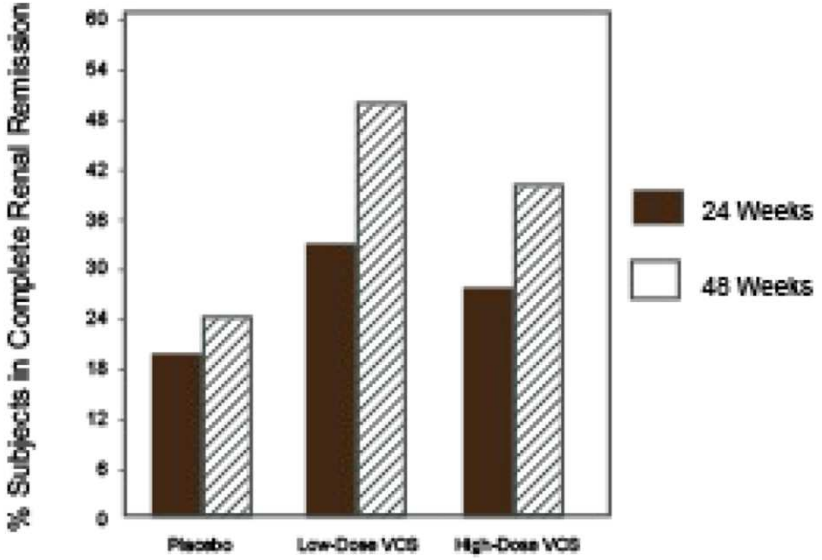
Rovin et al, Kidney Int 2018



CR in AURA is a **composite end-point** which includes *efficacy, safety and low-dose steroids*

- UPCR ≤ 0.5mg/mg (confirmed)
- eGFR >60ml/min or within 20% of baseline
- Steroids ≤ 10mg/day
- No use of rescue medication(s)

Study was powered to show a difference in either arm vs. control arm, not between doses



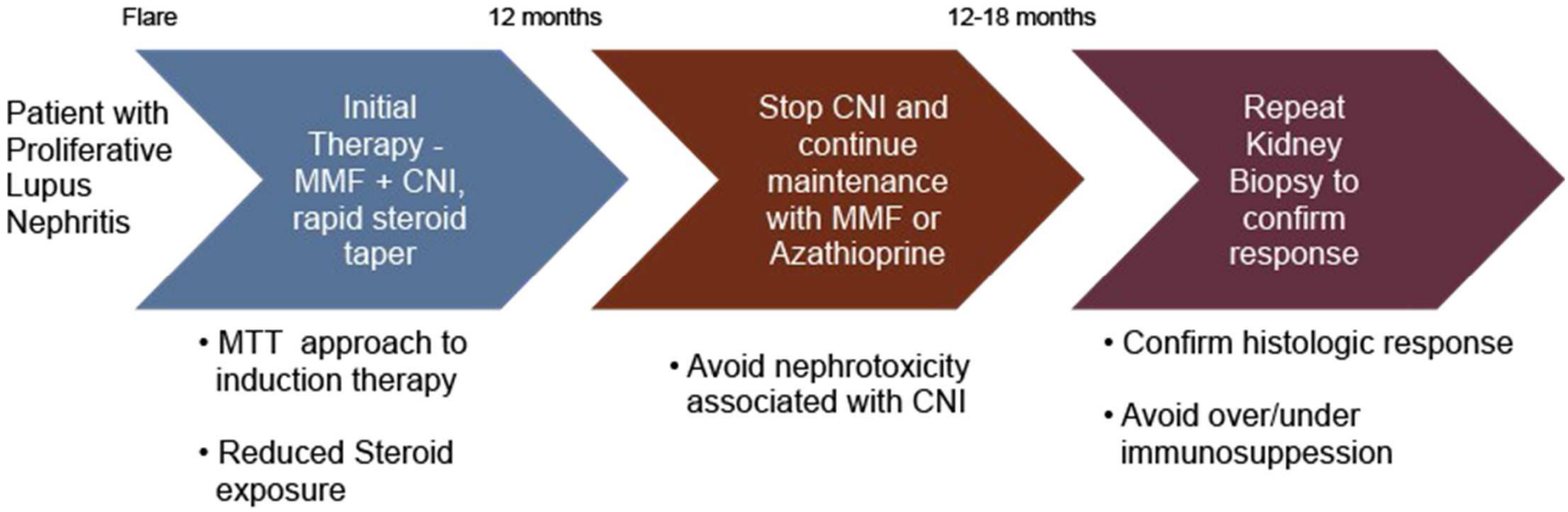
*p=0.046, **p<0.001, +p=0.20, ++p=0.026 versus placebo

Primary End Point

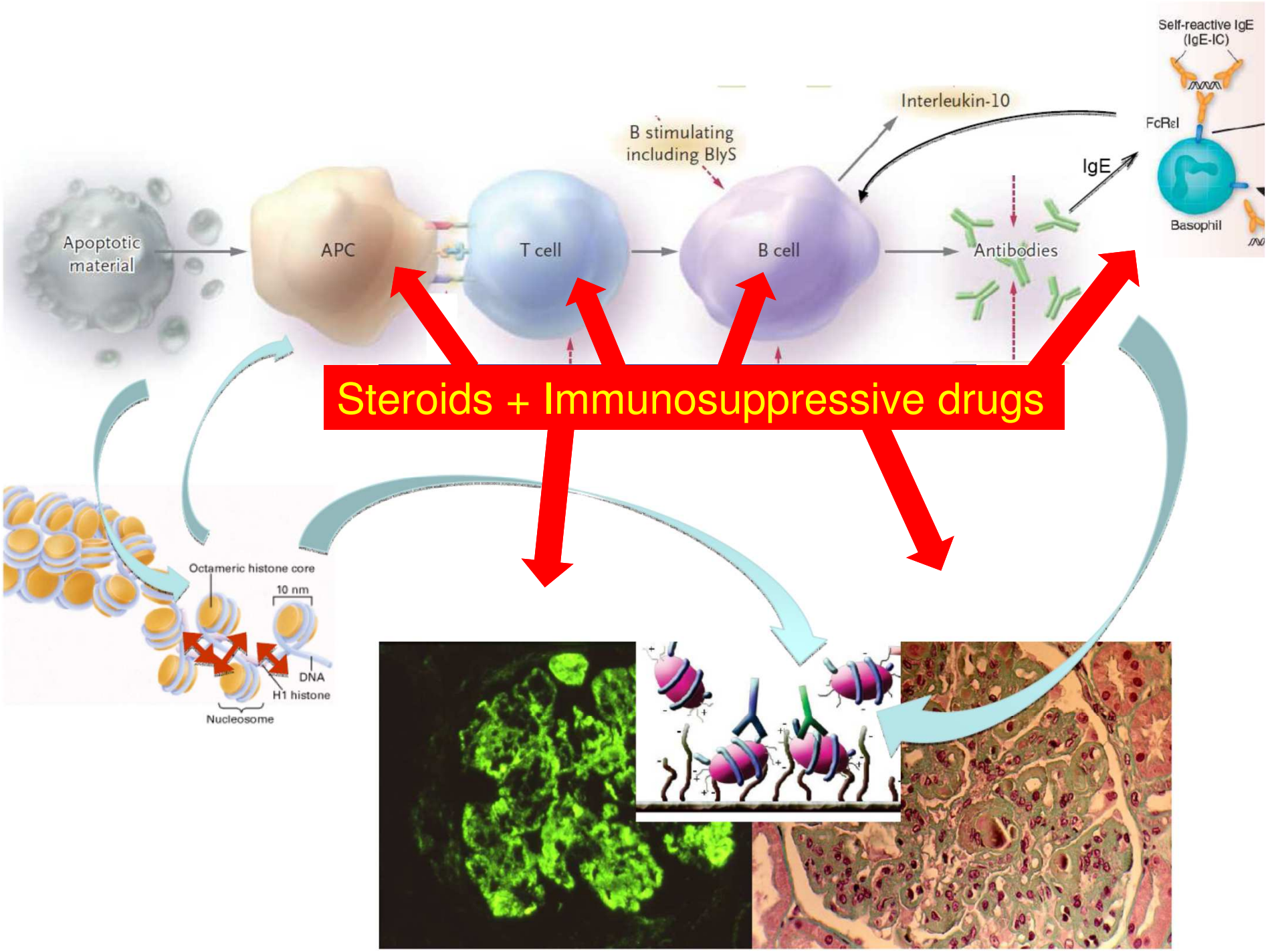
Calcineurin inhibitor use in Lupus nephritis : an old friend returns

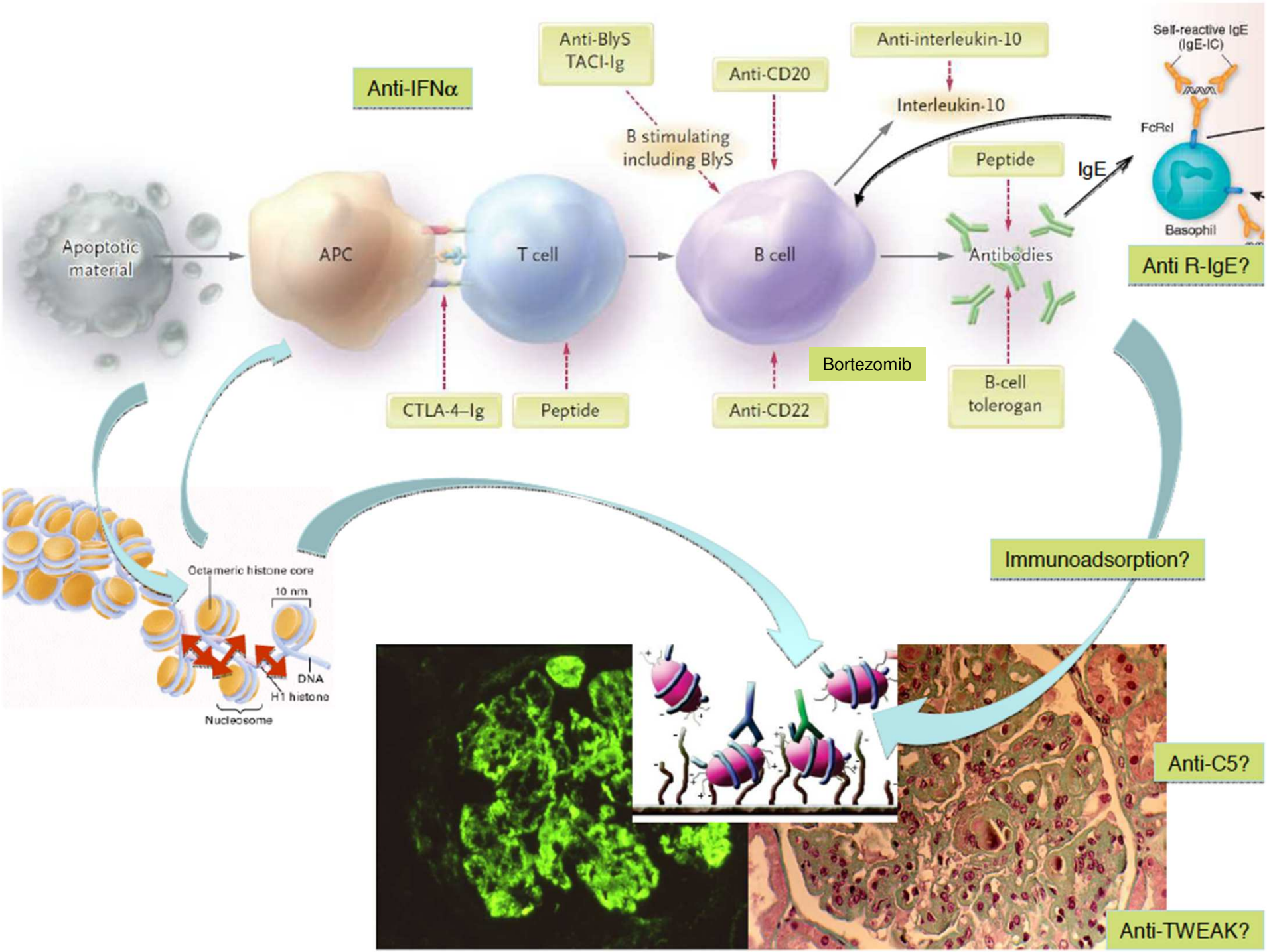
Samir Pariikh et al.

ASN 2018, San Diego, 23-28 octobre 2018



AUTRES PERSPECTIVES thérapeutiques


Self-reactive IgE
(IgE-IC)
FcRεI
Basophil
Interleukin-10
B stimulating
including BlyS
IgE
Apoptotic
material
APC
T cell
B cell
Antibodies
Steroids + Immunosuppressive drugs
Octameric histone core
10 nm
DNA
H1 histone
Nucleosome


Anti-IFNα
Anti-BlyS
TACI-Ig
Anti-CD20
Anti-interleukin-10
Interleukin-10
B stimulating
including BlyS
Peptide
IgE
Self-reactive IgE
(IgE-IC)
FcRcI
Basophil
Anti R-IgE?
Apoptotic
material
APC
T cell
B cell
Antibodies
Bortezomib
CTLA-4–Ig
Peptide
Anti-CD22
B-cell
tolerogan
Octameric histone core
10 nm
DNA
H1 histone
Nucleosome
Immunoadsorption?
Anti-C5?
Anti-TWEAK?

Drug	Trial Stage	Target	Phase/Status or Mechanism	Reference/ Clinical Trial Number
Completed Clinical Trials				
Abatacept – BMS	Completed clinical trials	CTLA4-B7 interaction	Phase 3 – Failed to meet end point	8
Abatacept – ACCESS	Completed clinical trials	CTLA4-B7 interaction	Phase 2 – Failed to meet end point	15
Anti-CD40L	Completed clinical trials	CD40-ligand	Phase 2 – Terminated	89
Anti-TWEAK	Completed clinical trials	TWEAK	Phase 2 – Terminated	NCT01499355
Bortezomib	Completed clinical trials	Plasma cells	Phase 4 – Terminated	85
Laquinamod	Completed clinical trials	Inflammation	Phase 2 – Encouraging	101
Rituximab	Completed clinical trials	CD20	Phase 3 – Failed to meet end point	10
Ocrelizumab	Completed clinical trials	CD20	Phase 3 – Failed to meet end point	88
Sirukumab	Completed clinical trials	IL-6	Phase 2 – Failed to meet end point	102
Tabalumab	Completed clinical trials	B lymphocyte stimulator	Phase 3 – Failed to meet end point	68
Active Clinical Trials				
Anifrolumab	Active clinical trials	IFN-α	Phase 2 – Recruiting	NCT02547922
Belimumab	Active clinical trials	B lymphocyte stimulator	Phase 3 – Recruitment closed	NCT01639339
Ixazomib	Active clinical trials	Plasma cells	Phase 1 – Recruiting	NCT02176486
Obinutuzumab	Active clinical trials	CD20	Phase 2 – Recruiting	NCT02550652
Rituximab	Active clinical trials	CD20/steroid reduced	Phase 3 – Recruiting	NCT01773616
Rituximab/Belimumab	Active clinical trials	CD20/B lymphocyte stimulator	Phase 2 – Recruiting	NCT02260934
Voclosporin	Active clinical trials	Calcineurin	Phase 2 – Recruitment closed	NCT02141672
Therapies for Consideration				
Eculizumab	Therapy for consideration	C5	Anti-inflammatory	98
Anti-C5aR (CCX168)	Therapy for consideration	C5a	Anti-inflammatory	103
Anti–IL-17	Therapy for consideration	IL-17	Anti-inflammatory	104

Samir V. Parikh and Brad H. Rovin J Am Soc Nephrol **27:** 2929–2939, 2016

ASN, October 27, 2018 / Abstract: SA-OR066
A Phase III Study of Abatacept on Standard of Care in Patients with Active Class III or IV Lupus Nephritis

24-month, randomized, Phase III, double-blind study with long-term extension. Patients (pts) were randomized to pbo or IV ABA every 4 wks on MMF + corticosteroids.

BMS-188667 30 mg/kg injection by intravenous on Days 1,15, 29, and 57, followed by a weight-tiered dose approximating 10mg/kg injection by intravenous every 4 weeks, Mycophenolate mofetil 1.5 g tablet by mouth and Prednisone up to 60 mg tablet by mouth Daily for 104 weeks

Primary endpoint: complete response (UPCR ≤0.5, preserved eGFR, no cellular casts, CS ≤10 mg/day) at Year (Yr) 1

Data up to Yr 3 of tx

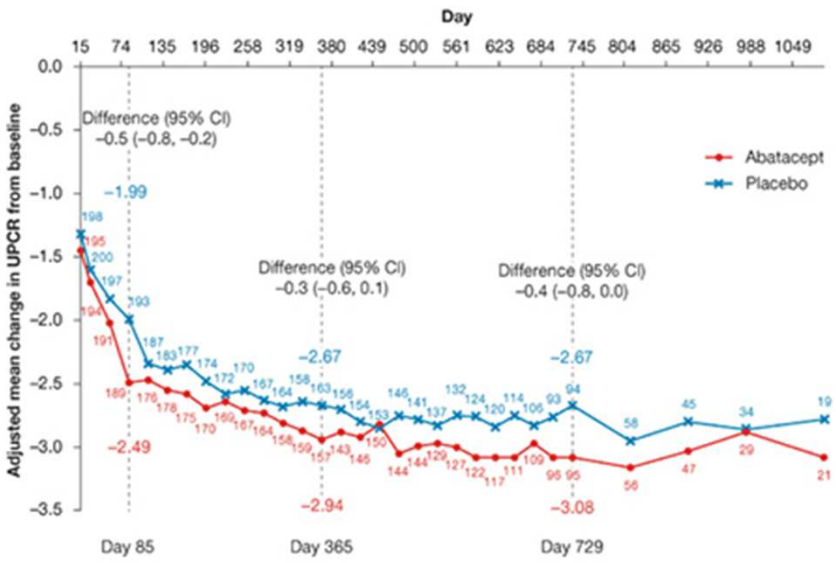
405 pts were randomized (ABA n=202; pbo n=203)

No differences between tx arms in CR rates at Yr 1 (ABA 35.1%, pbo 33.5%, p=0.73)

Sustained CR more frequent and earlier in ABA pts

CR rates higher and non-response rates lower in ABA arm in Yr 2 and 3

Figure: Adjusted Mean Change in UPCR Over Time (all Patients)



Adjusted mean change is estimated from longitudinal model repeated mixed model which includes stratification factors (race, ACEi/ARBs use) treatment group, time, time*treatment group interaction and baseline UPCR as continuous covariate

ACEi=angiotensin-converting enzyme inhibitor; ARBs=angiotensin receptor blockers; UPCR=urine protein-to-creatinine ratio

A prospective observational cohort study highlights kidney biopsy findings of lupus nephritis patients in remission who flare following withdrawal of maintenance therapy

Marcelo De Rosa[1], Francisco Azzato[1], Jorge E. Toblli[2], Graciela De Rosa[1], Federico Fuentes[1], Haikady N. Nagaraja[3], Ryan Nash[4] and Brad H. Rovin[5]

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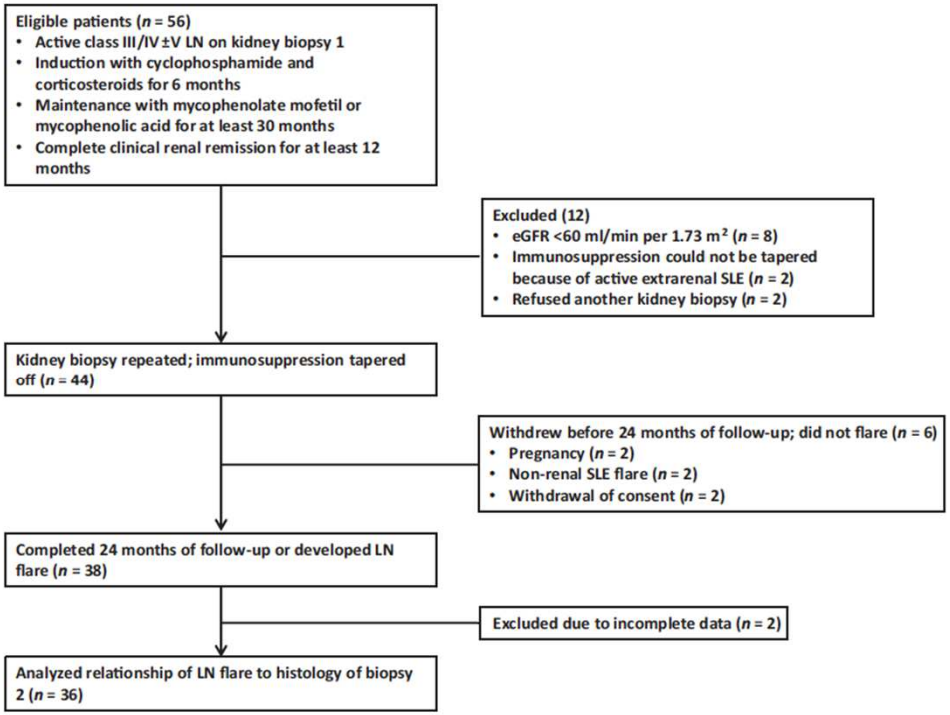
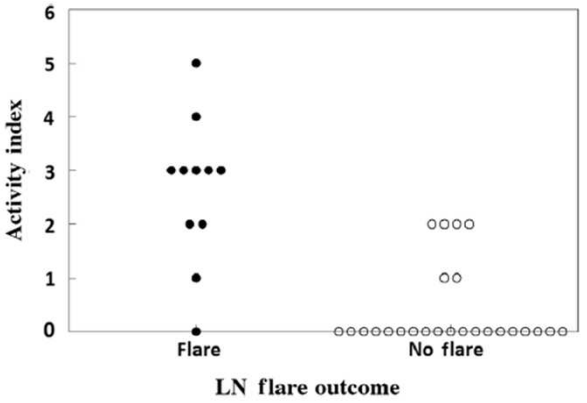


Table 2 | Clinical and histologic findings at biopsy 2

Variable	Entire cohort (*n* = 36)	Flare group (*n* = 11)	No-flare group (*n* = 25)	*P* value[a]
Duration of treatment (mo)	38 (36–54)	38 (36–48)	38 (36–54)	0.61
Time to remission (mo)	24 (12–40)	24 (16–36)	24 (12–40)	0.75
Duration of remission (mo)	12 (12–30)	12 (12–20)	13 (12–30)	0.43
Proteinuria (g/d)	0.11 (0.03–0.48)	0.16 (0.06–0.48)	0.07 (0.03–0.48)	0.06
SCr (mg/dl)[b]	0.70 (0.50–1.12)	0.66 (0.60–0.90)	0.70 (0.50–1.12)	0.70
eGFR (ml/min per 1.73 m²)	114 (81–135)	114 (95–127)	114 (81–135)	0.85
C3 (mg/dl)	112 (55–188)	100 (55–170)	116 (64–188)	0.19
C4 (mg/dl)	19 (3–51)	15 (3–28)	20 (6–51)	0.20
% low C3	13.9	27.3	8.0	0.15
% low C4	36.1	45.5	32.0	0.47
ΔC3[c]	1 (–36 to 77)	–7 (–30 to 26)	10 (–36 to 77)	0.07
ΔC4[c]	0 (–15 to 15)	–3 (–13 to 11)	0 (–15 to 15)	0.42
% anti-dsDNA–positive	22.2	36.3	16.0	0.21
Activity index	0 (0–5)	3 (0–5)	0 (0–2)	<0.0001
% endocapillary proliferation[d]	30.6	90.9	4	<0.0001
% subendothelial deposits[d]	38.9	90.9	16	<0.0001
% glomerular leukocytes[d]	25	45.5	16	0.075
Chronicity index	3 (0–5)	3 (0–4)	2 (0–5)	0.13



De Rosa KI 2018

Traitement des GN classes V pures

Classes V

Classes IIIC+V

Classes IVC+V

Qui traiter?

- Syndrome néphrotique
- Insuffisance rénale chronique imputable à la GN Classe V
- Protéinurie > 2g/j persistante??

BUT du TRAITEMENT

- RC: DFG au moins stable, Protéinurie < 1g/j
- RP: DFG au moins stable, Protéinurie ≤ 50% et entre 1 et 3 g/j

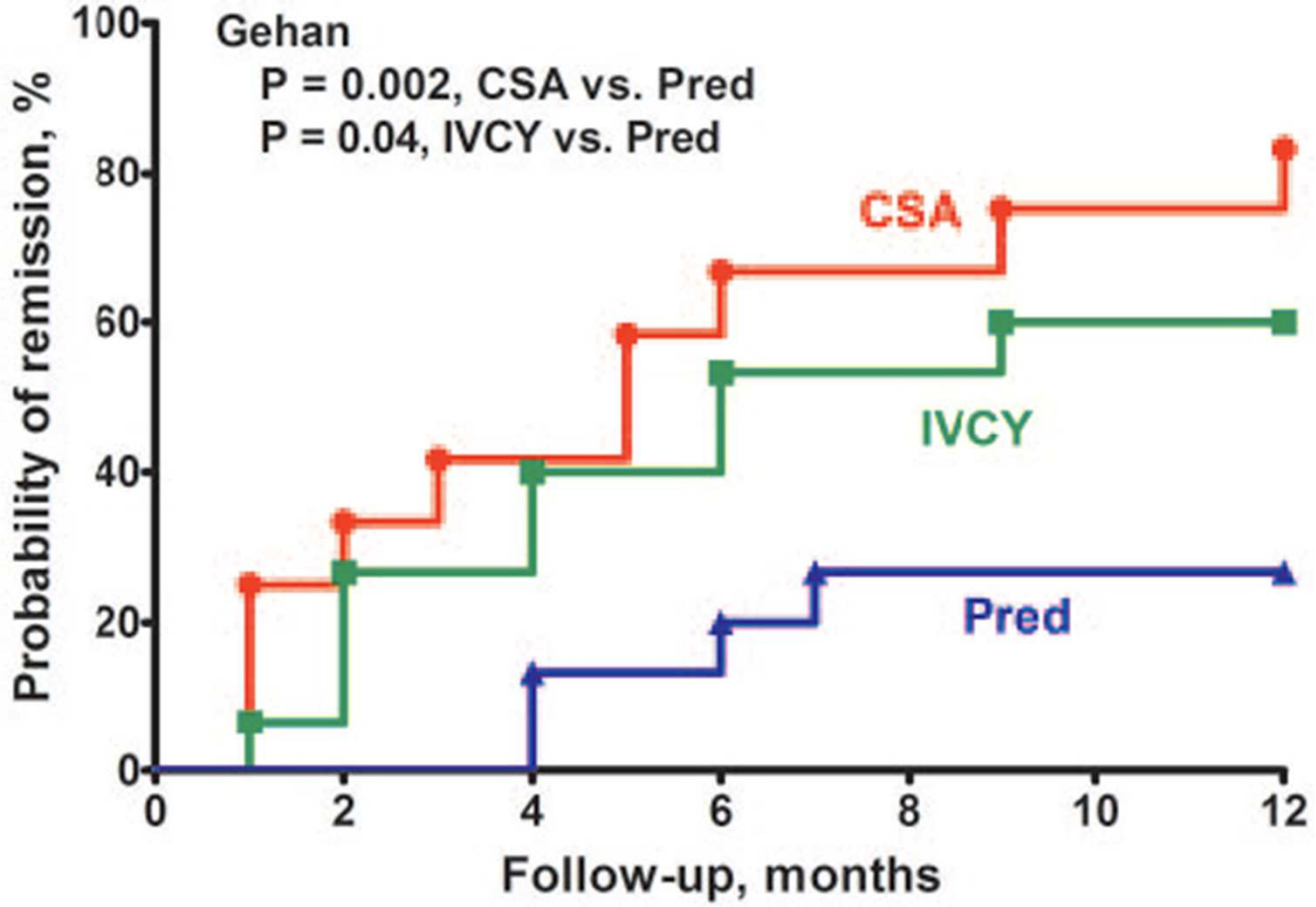
Une seule étude contrôlée

Randomized, Controlled Trial of Prednisone, Cyclophosphamide, and Cyclosporine in Lupus Membranous Nephropathy

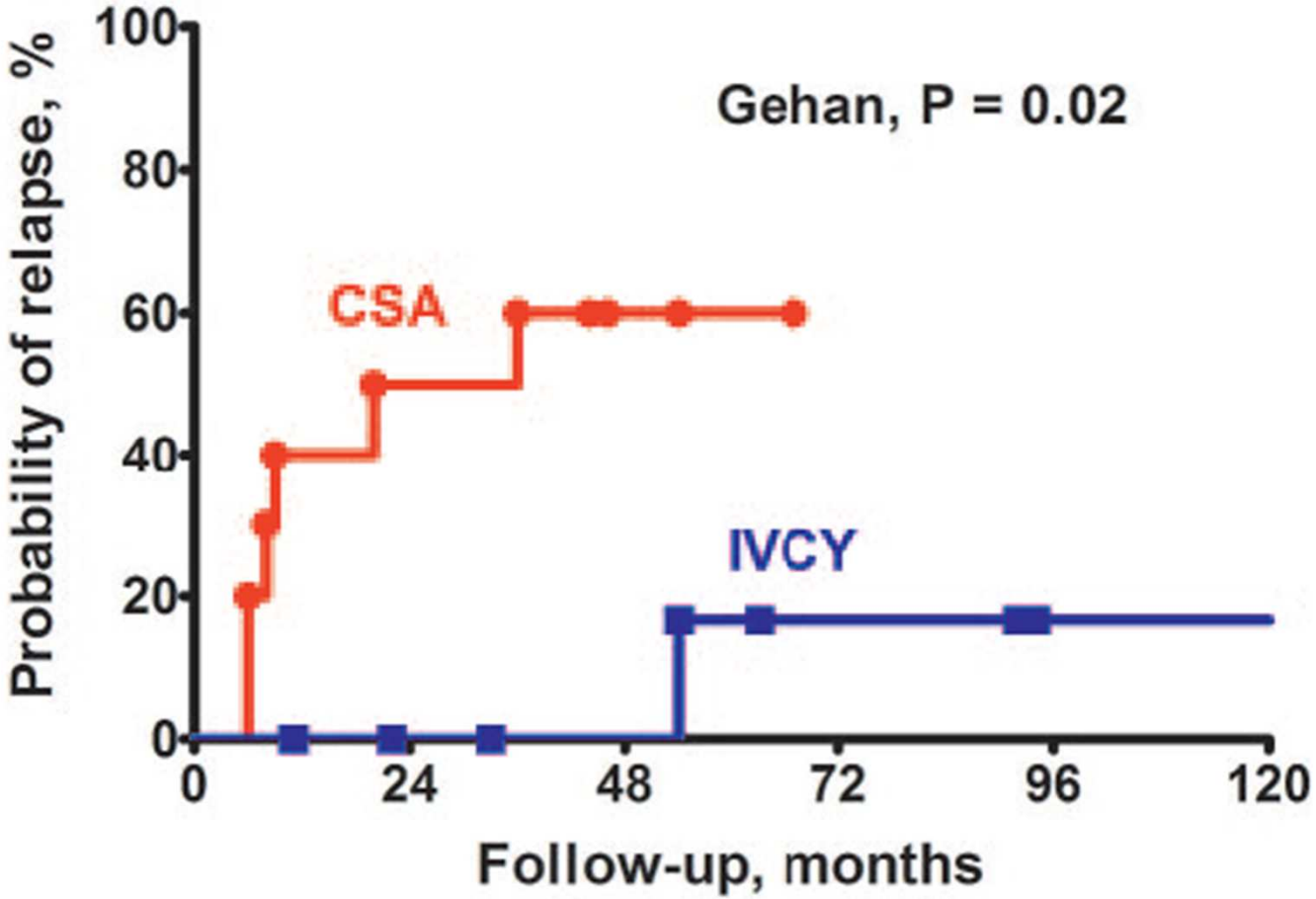
Howard A. Austin, III,* Gabor G. Illei,†‡ Michelle J. Braun,* and James E. Balow*

J Am Soc Nephrol 20: 901–911, 2009.

- 42 patients avec protéinurie 2.7-15.4g/j
- Randomisés entre trois bras
  - Prednisone 40mg/m^2/2j 8 semaines puis décroissance jusqu'à 10mg/m^2/2j
  - Prednisone (idem) + Ciclosporine (5mg/k/j)
  - Prednisone (idem) + CYC IV/ 2mois



Pas de dégradation fonction rénale avec CSA ou IVCY



+++ non répondeurs et rechuteurs après CSA rattrapés par IVCY

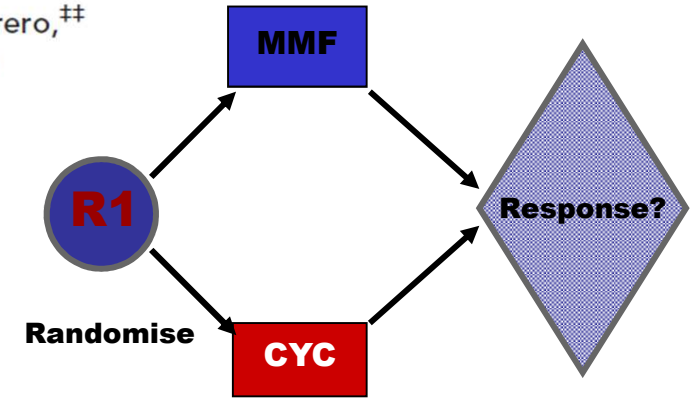
Mycophénolate mofétil?

Mycophenolate Mofetil *versus* Cyclophosphamide for Induction Treatment of Lupus Nephritis

INDUCTION
6 months

Gerald B. Appel,* Gabriel Contreras,† Mary Anne Dooley,‡ Ellen M. Ginzler,§ David Isenberg,‖ David Jayne,¶ Lei-Shi Li,** Eduardo Mysler,†† Jorge Sánchez-Guerrero,‡‡ Neil Solomons,§§ David Wofsy,‖‖ and the Aspreva Lupus Management Study Group

Appel, JASN 2009
&
Radhakrishnan Kidney Int 2010



Characteristic	MMF (*n* = 185)	IVC (*n* = 185)
Renal biopsy class (*n* [%])		
III/III + V	32 (17.3)	26 (14.1)
IV/IV + V	124 (67.0)	128 (69.2)
V only	29 (15.7)	31 (16.8)
Proteinuria	5 g/24h	5.8 g/24h
Patients with renal biopsy class V	16 (55.2)[d]	15 (48.4)[e]

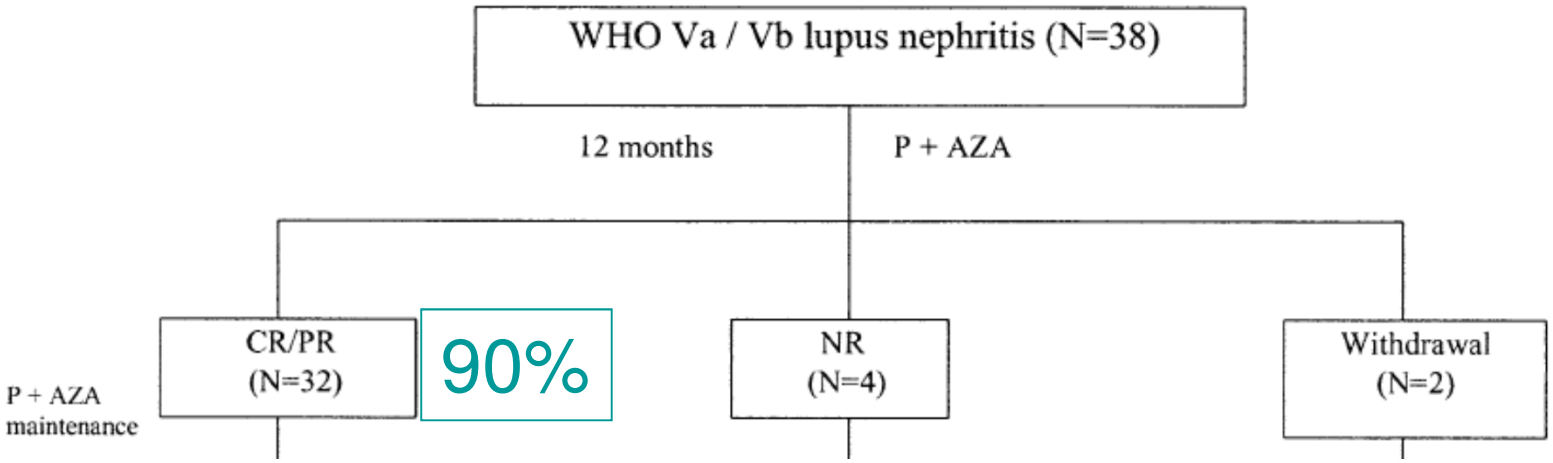
Stéroïdes + Azathioprine?

Treatment of Pure Membranous Lupus Nephropathy With Prednisone and Azathioprine: An Open-Label Trial

Chi Chiu Mok, MD, MRCP, King Yee Ying, MB, MRCP, Chak Sing Lau, MD, FRCP, Cheuk Wan Yim, MB, MRCP, Woon Leung Ng, MB, MRCP, Woon Sing Wong, MB, FRCP, and Tak Cheung Au, MB, FRCP

American Journal of Kidney Diseases, Vol 43, No 2 (February), 2004: pp 269-276

Etude prospective non contrôlée ouverte
38 patients (58% néphrotiques)
Prednisone 0.8 mg/kg/j 6 semaines puis ↓
AZA 2 mg/kg/j



RITUXIMAB?

RITUXILUP

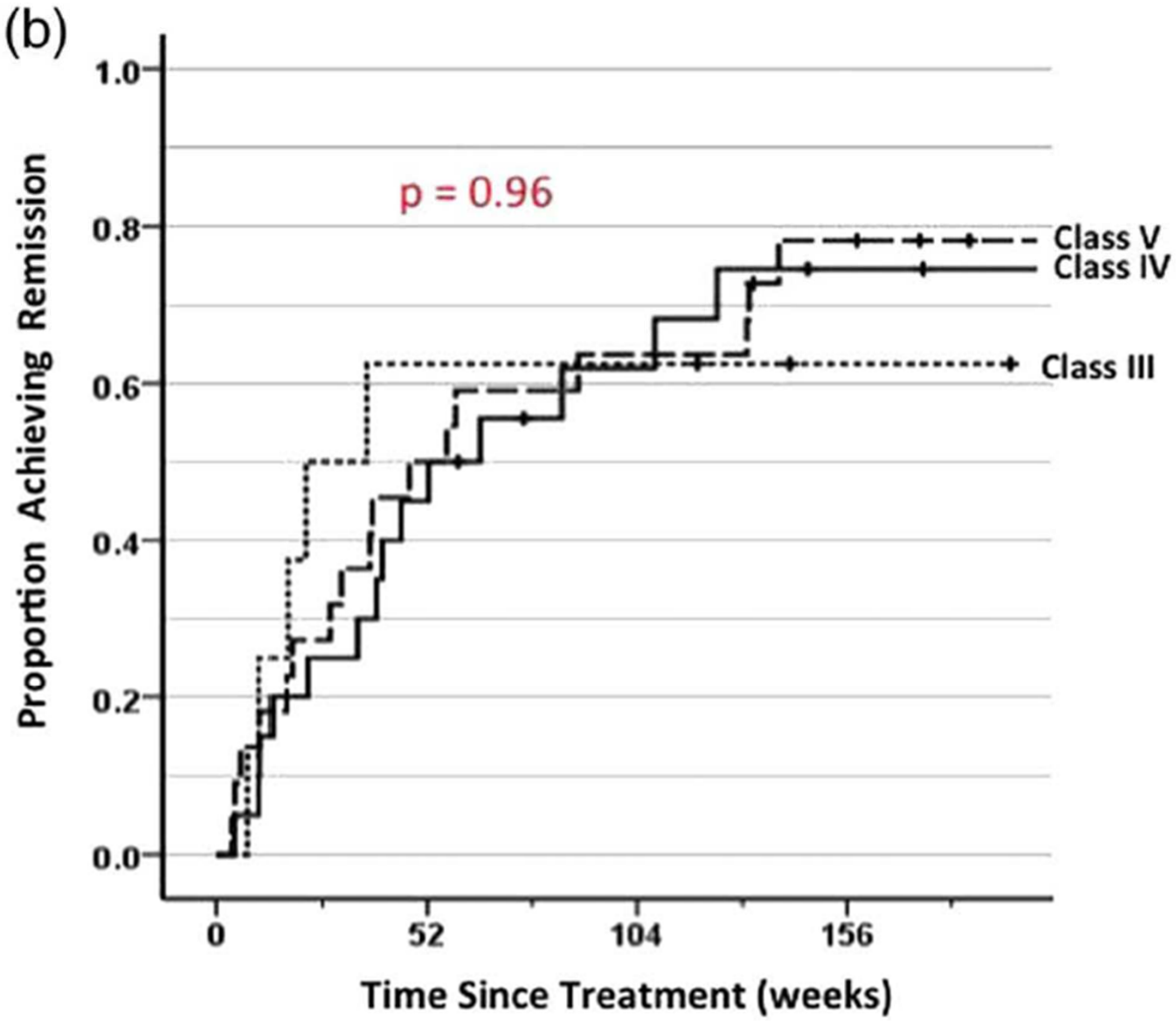
EXTENDED REPORT

Prospective observational single-centre cohort study to evaluate the effectiveness of treating lupus nephritis with rituximab and mycophenolate mofetil but no oral steroids

Marie B Condon,[1] Damien Ashby,[1] Ruth J Pepper,[1] H Terence Cook,[1,2] Jeremy B Levy,[1] Megan Griffith,[1] Tom D Cairns,[1] Liz Lightstone[1,2,3]

44% (22) had pure Class V LN

Condon et al, Ann Rheum Dis, 2012



Condon et al, Ann Rheum Dis, 2012

GROUPE COOPÉRATIF LUPUS RÉNAL

Observational Study

Medicine®

OPEN

Rituximab alone as induction therapy for membranous lupus nephritis

A multicenter retrospective study

Nathalie Chavarot, MD[a], David Verhelst, MD[b], Agathe Pardon, MD[c], Valérie Caudwell, MD[c], Lucile Mercadal, MD[d], Antoinette Sacchi, MD[e], Catherine Leonardi, MD[f], Véronique Le Guern, MD[g], Alexandre Karras, MD, PhD[h], Eric Daugas, MD, PhD[a,*], On behalf of the Groupe Coopératif sur le Lupus Rénal

Abstract

The optimal treatment for pure membranous lupus nephritis (MLN) remains undetermined. Rituximab constitutes a promising therapeutic option for lupus nephritis and is currently being evaluated for use in idiopathic membranous nephritis. We retrospectively analysed the efficacy and tolerance of rituximab as a monotherapy in the induction treatment of pure MLN.

We retrospectively investigated SLE patients with biopsy-proven pure class V lupus nephritis presenting with a protein-to-creatinine ratio of at least 2 g/g and treated with rituximab as monotherapy. A background low dose of corticosteroids (≤20 mg/day) was allowed, as was hydroxychloroquine; higher doses of steroids and/or immunosuppressive drugs fell under the exclusion criteria. Remission status was evaluated at baseline and 6, 12, and 24 months after rituximab.

The study included 15 patients (13 women, median age 37 years, 27% with extra-renal manifestations, median SLE duration 1.5 years). The median protein-to-creatinine ratio was 4.9 g/g, 80% of the patients had nephrotic-range proteinuria, the median serum albumin was 24 g/L, the median serum creatinine was 0.7 mg/dL, and the median eGFR was 122 mL/min/1.73 m^2. The median follow-up was 29 months (6–112 months). Treatment failure occurred in 2 patients. However, remission was recorded in the remaining 13 (87%, complete remission in 8 patients) with a median time to remission of 5 months. Median proteinuria decreased from 4.9 g/g to 0.16 g/g at month 12 and to 0.11 g/g at month 24. Median serum albumin increased to 36.5 g/L at month 24, and all patients had serum albumin levels greater than 30 g/L at month 12. Renal function remained stable in all patients. Relapse of proteinuria was recorded in 3 patients (at 12, 29, and 34 months). No patients experienced serious adverse events.

Rituximab as monotherapy may represent an effective treatment for pure MLN with an excellent tolerance profile.

Abbreviations: ACR = American College of Rheumatology, CKD = chronic kidney disease, CR = complete remission, ESRD = end-stage kidney disease, EULAR/ERA-EDTA = European Renal Association–European Dialysis and Transplant Association, HCQ = hydroxychloroquine, MLN = pure membranous lupus nephritis, NRs = nonresponders, PR = partial response, SLE = systemic lupus erythematosus, UPCR = urine protein to creatinine ratio.

Keywords: induction therapy, lupus nephritis, monotherapy, pure class V lupus nephritis, rituximab, systemic lupus erythematosus

1. Introduction

Lupus nephritis is a severe complication of systemic lupus erythaematosus (SLE). Lupus nephritis affects between 20% and 60% of patients[1,2] and is associated with a poor renal and cardiovascular prognosis. Progression to end-stage kidney disease (ESRD) occurs in 10% to 30% of patients despite treatment.[2]

Class V or pure membranous lupus nephritis (MLN) occurs in 7% to 20% of patients with lupus nephritis.[3,4] The prognosis of

Rituximab en monothérapie?

- Etude rétrospective multicentrique nationale
- GN lupique classe V pure
- Protéinurie ≥ 2 g/g
- induction par Rituximab

(une perfusion d'un gramme à J1 et J15 ou 4 perfusions hebdomadaires de 375mg/m^2)

- Pas de stéroïdes ou ≤20mg/j pour une autre indication que la V

- RC= Protéinurie <0.5g/g avec fonction rénale normale ou subnormale
- RP = réduction ≥50% de la protéinurie et <3g/g
- Echec = introduction autre immunosuppresseur et/ou d'augmentation des doses de stéroïdes dans les 12 mois

GROUPE COOPÉRATIF LUPUS RÉNAL

Chavarot et al. /GCLR, Medicine (Baltimore) 2017

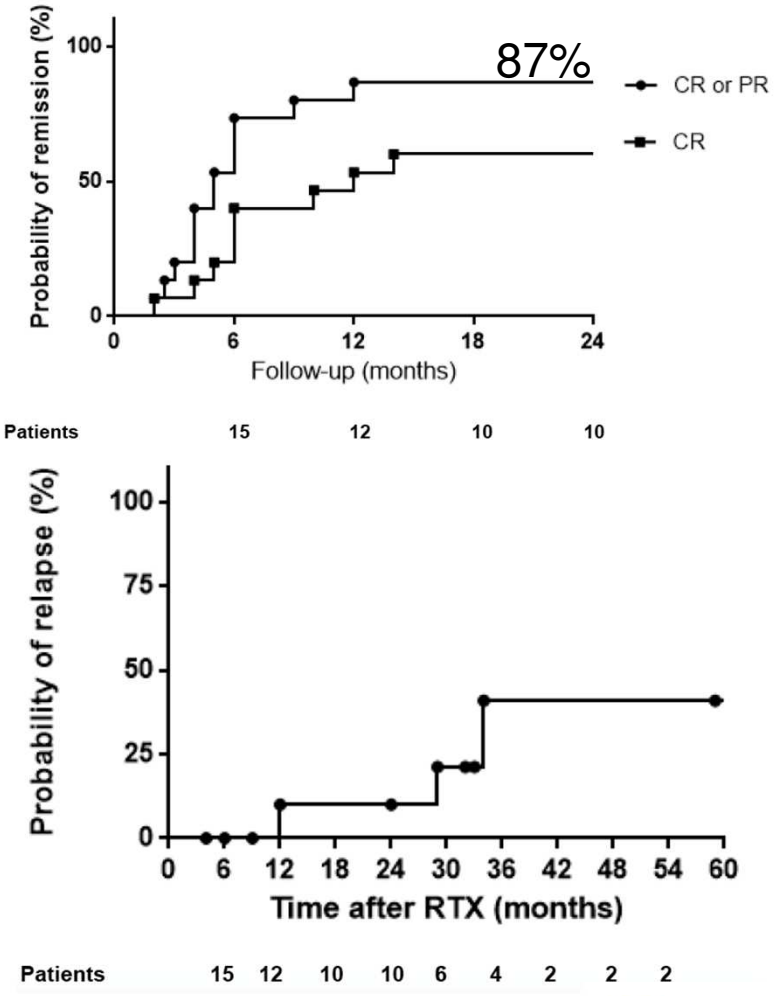
Rituximab en monothérapie?

GN classe V pure
Protéinurie ≥ 2g/g
Rituximab seul +/- stéroïdes ≤20mg/j

15 patients (13F/ 2H)

Protéinurie médiane = 4.9g/g
80% néphrotiques
DFG médian = 122 mL/min/1.73m^2

Suivi médian = 29 mois



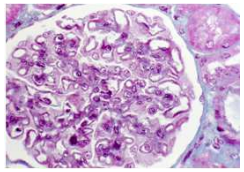
Chavarot et al. /GCLR, Medicine (Baltimore) 2017

GROUPE COOPÉRATIF LUPUS RÉNAL

En résumé

“Comment JE traite?”

GN Classe V pure en histologie
Protéinurie > 2g/g



Hydroxychloroquine
IEC/ARA2
PA<130/80 mmHg
LDL<2,6 mmol/L
Anticoagulation si alb < 20 g/L

+

1. **Rituximab seul** ou Stéroïdes + MMF
2. Rituxilup
3. Stéroïdes + AZA
4. Stéroïdes + CNI
5. Stéroïdes + CYC

Pas d'entretien

MERCI