GLADEL LATIN AMERICA
SCIENCE & EDUCATION

PANLAR 2025
27 CONGRESO PANAMERICANO DE REUMATOLOGÍA
PAN-AMERICAN CONGRESS OF RHEUMATOLOGY
CONGRESSO PANAMERICANO DE REUMATOLOGIA

1051

SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS OF INITIAL TREATMENTS FOR LUPUS NEPHRITIS

Ariel Izcovich[1], Fernando Tortosa[2], Agustín Bengolea[3], Moira Magdalena Pissinis[3], Martín Ragusa[4], Mariano Fielli[3], Camila Agnoletti[3], Rosana Quintana[5], Ana Malvar[6], Marina Scolnik[7], Eloisa Bonfá[8], Eduardo F. Borba[9], Odirlei Andre Monticielo[10], Edgard Torres[11], Loreto Massardo[12], José A. Gómez-Puerta[13], Carlos Toro[14], Jorge A. Esquivel-Valerio[15], Hilda Fragoso Loyo[16], Juan Manuel Mejia-Vilet[17], Graciela S. Alarcón[18], Manuel Ugarte Gil[19 20], Bernardo A. Pons-Estel[5], Guillermo Pons-Estel[5] on behalf of the Grupo Latino Americano de Estudio del Lupus (GLADEL)

OBJECTIVES

This study aims to evaluate the comparative efficacy and safety of various initial treatments for lupus nephritis (LN) through a systematic review and network meta-analysis (NMA).

METHODS

We conducted a comprehensive literature search across multiple databases from inception to February 2025 to identify randomized controlled trials (RCTs) comparing initial treatments for lupus nephritis. We performed a frequentist random-effects NMA using the restricted maximum likelihood (REML) method to estimate heterogeneity. We used the GRADE approach to assess the certainty of evidence.

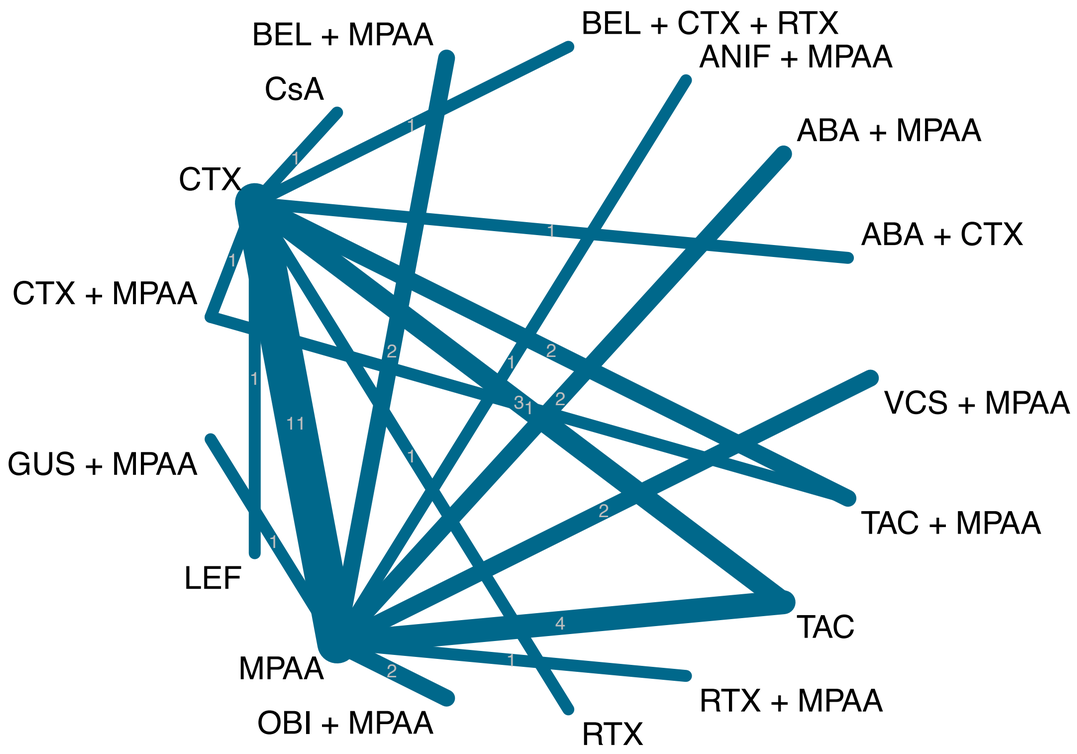
RESULTS

We included 40 RCTs encompassing 5450 patients and 12 interventions. Mycophenolic acid analogs (MPAA) were selected as the common comparator. The network meta-analysis revealed that voclosporin (VCS) combined with MPAA (Risk difference [RD] 281.38 more per 1000, 95% CI 146.26 more to 456.42 more; high certainty), belimumab (BEL) combined with MPAA (RD 145.02 more per 1000, 95% CI 72.73 more to 230.92 more; high certainty) and obinutuzumab (OBI) combined with MPAA (RD 134.23 more per 1000, 95% CI 30.37 more to 269.68 more; moderate certainty) increased complete renal response compared to MPAA alone. Tacrolimus combined with MPAA (RD 113.69 more per 1000, 95% CI 25.23 more to 217.7 more; low certainty) also showed potential benefits but with low certainty evidence.

CONCLUSION

Combination therapies, particularly VCS, BEL or OBI with MPAA, provide enhanced outcomes for LN initial treatment. Given the complexity of LN, clinicians should weigh these findings alongside considerations such as drug availability, cost, and individual patient preferences to guide treatment decisions.

Complete renal response network plot



MPAA = mycophenolic acid analogues
VCS = voclosporin
BEL = belimumab
TAC = tacrolimus
RTX = rituximab
OBI = obinutuzumab
ABA = abatacept
CTX = cyclophosphamide
ANIF = anifrolumab
CsA = cyclosporin
LEF = leflunomide
GUS = guselkumab

Summary of findings table of the effects of the assessed interventions at one year follow up

NODES	MORTALITY	RENAL REPLACEMENT THERAPY	COMPLETE RENAL RESPONSE	OVERALL RENAL RESPONSE	SEVERE ADVERSE EVENTS	INFECTIONS	SEVERE INFECTIONS
Risk with reference: MPAA at 1 year	28 per 1000	7 per 1000	311 per 1000	478 per 1000	187 per 1000	507 per 1000	92 per 1000
Minimal important difference	10 per 1000	23 per 1000	30 per 1000	53 per 1000	30 per 1000	43 per 1000	30 per 1000
VCS + MPAA	15.34 (-18.07 to 161.13)		281.38 (146.26 to 456.42)	167.83 (65.99 to 288.73)	33.49 (-28.69 to 120.08)	70.28 (-19.07 to 175.99)	6.01 (-32.58 to 69.66)
BEL + MPAA	5.6 (-17.59 to 80.5)	-4.67 (-6.9 to 49.97)	145.02 (72.73 to 230.92)	139.9 (17.61 to 292.36)	-25.12 (-66.93 to 31.25)	-59.65 (-223.04 to 197.76)	26.29 (-47.17 to 220.07)
OBI + MPAA	56.62 (-19.09 to 775.36)	-5.59 (-6.93 to 22.1)	134.23 (30.37 to 269.68)	117.36 (13.86 to 242.63)	66.79 (-7.68 to 172.19)	93.36 (15.17 to 183.26)	23.43 (-28.4 to 117.47)
TAC + MPAA			168.03 (44.98 to 333.61)	113.69 (25.23 to 217.7)	179.37 (-63.16 to 813)	358.92 (87.07 to 493)	255.33 (-33.77 to 1979.87)
RTX + MPAA	103.64 (-21.56 to 972)		-58.44 (-159.1 to 108.91)	80.42 (-65.54 to 278.04)	-41.48 (-91.14 to 33.9)	-58.95 (-171.52 to 91.39)	-22.79 (-56.82 to 44.15)
ABA + MPAA	-8.78 (-20.14 to 19.04)		21.78 (-53.1 to 118.39)	6.66 (-70.84 to 98.89)	25.78 (-25.66 to 93.63)	17.41 (-39.33 to 81.03)	31.91 (-58.4 to 364.9)
CTX	0.74 (-13.72 to 29.83)	1.79 (-6 to 69.91)	-32.18 (-70.68 to 12.49)	-20.76 (-62.49 to 25.16)	-39.16 (-97.72 to 57.82)	324.95 (179.95 to 493)	7.24 (-50.56 to 145.63)
TAC	-8.88 (-21.98 to 32.75)		30.37 (-36.46 to 113.46)	-0.46 (-70.81 to 82.05)	-15.61 (-96.56 to 137.8)	-123.07 (-361.2 to 493)	-15.4 (-62.47 to 106.69)
ABA + CTX	-18.13 (-27.62 to 228.72)		-10.05 (-131.13 to 192.54)	-18.68 (-137.16 to 140.98)	-42.3 (-117.32 to 113.49)		
ANIF + MPAA			-0.77 (-129.46 to 219.16)	14.34 (-181.54 to 339.64)	42.08 (-78.87 to 298.29)		-68.27 (-87.5 to 33.03)
BEL + CTX + RTX			17.61 (-77.94 to 152.34)	60.89 (-222.79 to 659.89)	-130.68 (-168.22 to -18.08)		-57.35 (-85.81 to 101.95)
CTX + MPAA	-0.63 (-26.38 to 433.78)		86.53 (-25.64 to 242.79)	-0.09 (-142.84 to 203.45)	13.26 (-144.45 to 755.5)	-202.25 (-389.79 to 285.32)	
CsA			-2.83 (-206.69 to 599.48)				
LEF	32.09 (-26.08 to 972)		-81.97 (-196.02 to 145.22)	108.66 (-82.38 to 391.96)		493 (166.91 to 493)	
RTX			525.47 (130.52 to 689)	-234.14 (-362.81 to 38.26)	-39.16 (-184.09 to 813)		
GUS + MPAA			19.44 (-233.29 to 689)		11.69 (-173.46 to 813)	139.43 (-262.15 to 1199.62)	

	Large beneficial effect	Moderate beneficial effect	Small beneficial effect	Trivial to no effect	Small harmful effect	Moderate harmful effect	Large harmful effect
High/Moderate certainty							
Low certainty							
Very low certainty							
No evidence							

MPAA = mycophenolic acid analogues
VCS = voclosporin
BEL = belimumab
TAC = tacrolimus
RTX = rituximab
OBI = obinutuzumab
ABA = abatacept;
CTX = cyclophosphamide
ANIF = anifrolumab
CsA = cyclosporin
LEF = leflunomide
GUS = guselkumab

1 *Facultad de Medicina, Universidad del Salvador. Buenos Aires, Argentina.*
2 *Universidad Nacional de Río Negro, Argentina*
3 *Servicio de Clínica Médica, Hospital Alemán, Buenos Aires, Argentina.*
4 *División Clínica Médica, Hospital Fernández, Buenos Aires, Argentina.*
5 *Centro Regional de Enfermedades Autoinmunes y Reumáticas, Grupo Oroño, Rosario, Argentina*
6 *Hospital Fernández, Buenos Aires, Argentina.*
7 *Seccion Reumatologia, Hospital Italiano de Buenos Aires, Argentina.*
8 *Faculdade de Medicina, Universidade de Sao Paulo, Brazil*
9 *Rheumatology Division, Hospital das Clinicas, Faculdade de Medicina da Universidade de Sao Paulo (HCFMUSP), Sao Paulo, SP, Brazil*
10 *Rheumatology Division, Department of Internal Medicine, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil.*
11 *Division of Rheumatology, Department of Medicine, Escola Paulista de Medicina, Universidade Federal de São Paulo (EPM/Unifesp).*
12 *Pontificia Universidad Católica de Chile: Santiago, Chile*
13 *Rheumatology Department, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain*
14 *Universidad Pontificia Bolivariana, Medellín, Colombia*
15 *Servicio de Reumatología del Hospital Universitario "Dr Jose Eleuterio González " de la Universidad Autónoma de Nuevo Leon. Monterrey, Nuevo León, México*
16 *Departamento de Inmunología y Reumatología. Instituto Nacional de Ciencias Médicas y Nutrición. Dr. Salvador Zubirán. Mexico City.*
17 *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico.*
18 *University of Alabama at Birmingham (UAB)*
19 *Grupo Peruano de Estudio de Enfermedades Autoinmunes Sistemicas, Universidad Científica del Sur, Lima, Peru*
20 *Rheumatology Department, Hospital Guillermo Almenara Irigoyen, EsSalud, Lima, Peru*