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

Ariel Izcovich, Fernando Tortosa, Agustin Bengolea,Moira Magdalena Pissinis, Martín Ragusa, Mariano Fielli, Camila Agnoletti, Rosana Quintana, Ana Malvar, Marina Scolnik, Eloisa Bonfá, Eduardo F. Borba, Odirlei Andre Monticielo , Edgard Torres, Loreto Massardo, José A. Gómez-Puerta, Carlos Toro, Jorge A. Esquivel-Valerio, Hilda Fragoso Loyo , Juan Manuel Mejia-Vilet, Graciela S. Alarcón, Manuel Ugarte Gil, Bernardo A. Pons-Estel, Guillermo Pons-Estel on behalf of the Grupo Latino Americano De Estudio del Lupus (GLADEL) .*

GLADEL LATIN AMERICA

LUPUS 21-24 MAY 2025 TORONTO

ID 261
*Presenting Author

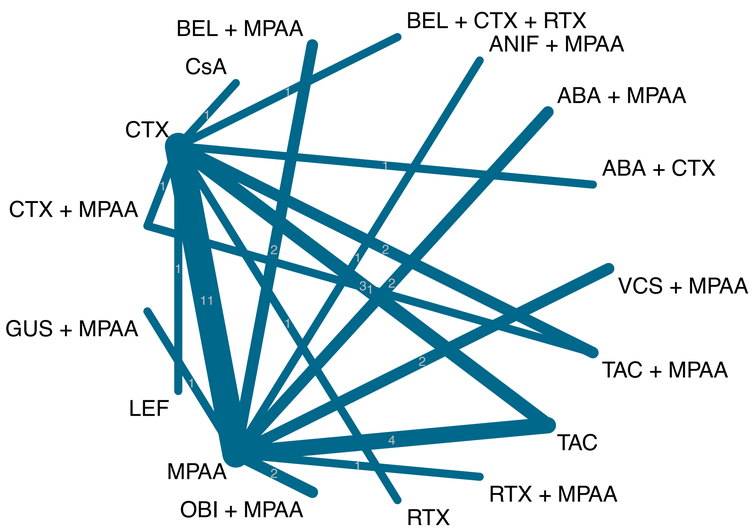
Background

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

Methods

A comprehensive literature search was conducted across MEDLINE, EMBASE, Cochrane Library, and LILACS from inception to June 2024 in order to identify randomized controlled trials (RCTs) comparing initial treatments for lupus nephritis. Two reviewers independently performed data extraction and assessed the risk of bias. A frequentist random-effects network meta-analysis was conducted using the restricted maximum likelihood (REML) method to estimate heterogeneity. The certainty of evidence was evaluated using the GRADE approach.

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

Results

We included 38 RCTs encompassing 5,146 participants and 11 interventions. Mycophenolate mofetil was selected as the common comparator. The network meta-analysis revealed that voclosporin combined with Mycophenolate mofetil (RR 1.9 95% CI 1.47 to 2.47, RD 281.4, 95% CI 146.3 to 465.4; high certainty) and belimumab combined with Mycophenolate mofetil (RR 1.47, 95% CI 1.23 to 1.74, RD 145, 95% CI 72.7 to 230.9; high certainty) increased complete renal response compared to Mycophenolate mofetil alone. Tacrolimus combined with Mycophenolate mofetil (RR 1.24 95% CI 1.05 to 1.46, RD 113.7, 95% CI 25.2 to 217.7; low certainty) and Obinutuzumab combined with Mycophenolate mofetil (RR 1.57 95% CI 1.05 to 2.34, RD 270.4, 95% CI 22.7 to 640.5; low certainty) also showed potential benefits but with low certainty evidence. Cyclophosphamide was possibly associated with a small decrease in complete renal response compared to Mycophenolate mofetil (RR 0.90, 95% CI 0.77 to 1.04; low certainty). However, the effects of the assessed interventions on mortality and renal replacement therapy outcomes were highly uncertain.

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

Conclusion

Combination therapies, particularly voclosporin or belimumab with Mycophenolate mofetil, may provide enhanced outcomes for lupus nephritis initial treatment. Given the complexity of lupus nephritis, clinicians should weigh these findings alongside considerations such as drug availability, cost, and individual patient preferences to guide treatment decisions.