RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

4th Annual National Conference

September 21–23, 2023

Give It a Trial

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Disclosures

- Danielle Gatti-Palumbo, PharmD:
  - There are no financial relationships to disclose
- Monica Richey, MSN:
  - Advisory Board: GSK, AstraZeneca

Case 1

- 22-year-old-female presents complaining of
  - Polyarthritis for 3 months
  - Chest pain
  - Weight loss, fatigue
  - Symptoms started after the birth of her 1st child
  - Hx of 2 miscarriages
    - 1st trimester
    - 2nd trimester
  - Pre-eclampsia on her last pregnancy
  - Had been seen at the ER 3 times and sent home on Tylenol

Physical Examination/Plan

- Multiple joints with synovitis and loss of ROM:
  - Bilateral shoulders
  - Right wrist
  - Left ankle
  - Bilateral knee effusion
  - Mild muscle weakness – related to pain
- +1 pitting peripheral edema
- Erythematous rash over bilateral arms – non-pruritic
- Plan
  - Full Labs
  - Prednisone 20 mg

Laboratory Studies

	01/06/2023	01/13/2023	03/14/2023	04/05/2023
Hg	7.8	7.9	9.3	8.4
PLt	440	503	628	463
ESR	120	111	80	34
CRP	18	10	<3	<3
Creatinine	0.76		0.80	0.64
DsDNA	84	Negative	Negative	negative
CCP	>250			
RNP	1.2			
Smith	Negative			
SSA/SSB	Negative			
ANA	1:320 - homogenous			
C3	35		63	71
C4	4		7	7

Laboratory Studies

	01/06/2023	01/13/2023	03/29/2023	
Coombs – CLDAT C3	positive			
Coombs CLDAT IGG	positive			
Iron	11		15	
Haptoglobin	335			
P/C ratio	4.3	6.1	3	
Mycophenolic Acid	< 0.6			

Clinical Course – January

- Started on prednisone 60 mg
- Referral to nephrology for possible biopsy
- 2 weeks later
  - Hospitalized for anasarca
  - Solumedrol 1000 mg X 2
  - Started on mycophenolate
  - Had kidney biopsy while hospitalized
  - Torsemide 20 mg daily
  - Started on eliquis

Pathology

Lupus nephritis, diffuse proliferative and membranous, ISN/RPS class IV (A) + V

- Small cellular crescents are present in about 15% of viable glomeruli
- Endocapillary proliferative changes are seen in all glomeruli
- The membranous component is segmental and involving about 50% of capillary walls
- NIH activity index is 14/24

Summary of chronic changes:
- Global glomerulosclerosis (6% of glomeruli)
- Tubular atrophy and interstitial fibrosis (10% of the sampled cortex)
- No significant arterial and arteriolar sclerosis
- NIH chronicity index is 2/12

Comment:
The preliminary findings were communicated via email to Dr. Hong on 1/25/2023 at 11AM.

The biopsy reveals an active immune complex-mediated renal disease in this patient with SLE. Chronic changes are mild. The overall pattern of injury is best summarized under the ISN/RPS class IV-A + V - diffuse proliferative and membranous lupus nephritis.

Immunofluorescence

The sample contains 8 glomeruli. Glomeruli with global sclerosis are not seen. There is finely granular reactivity for IgG (4+), IgA (4+), IgM (4+), C3 (3+) and C1q (4+) both along the capillaries and in the mesangium. Fibrin deposits are present segmentally in some glomeruli, representing inflammation. Tubular basement membranes show focal fine granular deposition of IgG (2+) and C1q (2+). The interstitium reveals scattered fibrin deposits. Arterioles reveal focal reactivity for C3. There is no difference in reactivity between kappa and lambda light chains in the glomeruli or in the background of the tissue.

3. Electron Microscopy:
The sample submitted for electron microscopy examination contains 6 glomeruli; 2 glomeruli are examined ultrastructurally. The glomerular visceral epithelial cells reveal moderate effacement of their foot processes. The glomerular basement membranes are of normal thickness and texture. Capillary loops reveal the presence of subepithelial and subendothelial electron-dense deposits. Endocapillary lumens contain increased numbers of cells. The endothelial cells show focal swelling. Tubuloreticular inclusions are not seen within the cytoplasm of glomerular endothelial cells. The mesangium reveals increased cells and matrix with frequent electron-dense deposits. Focal tubular basement membrane deposits are also noted.

Clinical Course – February

- Hospitalized 3 weeks later for anasarca
  - Had not been taking medications as prescribed
  - Mycophenolate increased to 3gm – switched to liquid
  - Hydroxychloroquine started
  - Still on prednisone 60 mg daily
  - Started on furosemide
- Severe lethargy
  - Headaches X 3 days
  - Muscle weakness
  - Taking both furosemide and torsemide

Laboratory Studies

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Iron	11		15	
Haptoglobin	335			
P/C ratio	4.3	6.1	3	
Mycophenolic Acid	< 0.6			

Clinical Course – March 2023

- Ongoing proteinuria
- DsDNA is negative
- Complements are low
- Ongoing Anemia
- Unsure if patient is taking medications

Laboratory Studies

	01/06/2023	01/13/2023	03/14/2023	04/05/2023
Hg	7.8	7.9	9.3	8.4
PLt	440	503	628	463
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Iron	11		15	
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Clinical Course 04/2023

- Could not say what medication she was taking
- Ongoing high-level proteinuria
- Anemia is ongoing and iron levels are still very low
- Cyclophosphamide discuss
- Referral for screening for Crovalimab study

Laboratory Studies

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Iron	11		15	
Haptoglobin	335			
P/C ratio	4.3	6.1	3	
Mycophenolic Acid	< 0.6			

Clinical Case 2

- 63-year-old female PMH of hypothyroid, knee osteoarthritis, HTN
- Presenting with
  - Erythematous rash over face, chest, back
  - Mucositis – severe
  - Muscle weakness – unable to ambulate
  - Hair loss – severe almost bald
  - Weight loss over 30 lbs
- Started on prednisone 60 mg
- Patient returns 1 week later with worsening symptoms – has been unable to swallow medication
- Urgent referral to the ER

	07/2021	10/2021	02/2022	05/2022	09/2022	12/2022	03/2023	
WBC	3.02							
Hg	12.2							
Creatinine	0.72							
Proteinuria	0	0	0	0	0	0	0.4	
AST	261							
ALT	214							
CPK	176							
myoglobin	98							
Aldolase	10							
DsDNA	318	330	33	27	97	353	1000	
Smith	8	8	8	8	8	8	8	
RNP	8	8	3.1	5.1			8	
SSA/SSB	negative	negative			8	8	8	
C3	49	47	83	91	71	36	30	
C4	8	3	11	16	11	1	4	

Hospital Course 1

- Skin biopsy – consistent with photosensitivity rash of SLE
- MRI of bilateral quadriceps
- SLE with Dermatomyositis
- Received IVIG 2KgXkg with significant improvement
- Started on HCQ
- IV solumedrol 30 mg QD switched to prednisone 30 mg daily
- Needed malignancy screening

Ambulatory Follow Up

08/2021

- IVIG denied by insurance
- Ongoing muscle weakness
- Questionable compliance
- Dizziness and headaches
- Confused about all her medication
- Started on mycophenolate liquid

10/2021

- Prednisone 10 mg only – self d/c
- Severe hypothyroidism
- Daily headaches with mental confusion
- Never pick-up medication from the pharmacy

	07/2021	10/2021	11/2021	02/2022	05/2022	09/2022	12/2022	03/2023	
WBC	3.02								
TSH	4.95	5.34			7.37	5.67	9.23	10.60	
Creatinine	0.72								
Proteinuria	0	0		0	0	0	0	0.4	
AST	261		700					204	
ALT	214		300					87	
CPK	176		74						
myoglobin	98								
Aldolase	10								
DsDNA	318	330		33	27	97	353	1000	
Smith	8	8		8	8	8	8	8	
RNP	8	8		3.1	5.1			8	
SSA/SSB	negative	negative				8	8	8	
C3	49	47		83	91	71	36	30	
C4	8	3		11	16	11	1	4	

2nd Hospitalization 11/2021

- Altered mental status – possible neuropsychiatric lupus
- MRI with advanced cerebral atrophy
- Elevated AST/ALT 700/300
- Solumedrol 500 mg X 3 days – d/c on Medrol 40 mg
- Started on mycophenolate 500 mg BID -tablets

Ambulatory Follow-Up 12/2021

- Mycophenolate again switched to liquid
- Order for belimumab sent for approval
- Patient reports taking some pills but not others, does now know which ones
- Current regimen
  - HCQ 400 mg
  - Mycophenolate 15 mg daily
  - Levothyroxine 88 mcg daily
  - Amlodipine 5 mg daily
  - Aspirin 81 mg daily
  - HCTZ 25 mg daily
  - Prednisone 20 mg TID
  - Eszopiclone 3 mg daily
  - Cetirizine 10 mg daily

	07/2021	10/2021	11/2021	02/2022	05/2022	09/2022	12/2022	03/2023	
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SSA/SSB	negative	negative				8	8	8	
C3	49	47		83	91	71	36	30	
C4	8	3		11	16	11	1	4	

Ambulatory F/u 02/2022

02/2022

- Stable disease
  - Normal DsDNA
  - Resolving hypocomplementemia
  - Covid 19 infection – fully recovered

12/2022

- DsDNA trending up
- Lower complements
- Mild symptoms
- Dysphagia – severe
- No mucositis
- Depomedrol injection 80 mg

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myoglobin	98								
Aldolase	10								
DsDNA	318	330		33	27	97	353	1000	
Smith	8	8		8	8	8	8	8	
RNP	8	8		3.1	5.1			8	
SSA/SSB	negative	negative				8	8	8	
C3	49	47		83	91	71	36	30	
C4	8	3		11	16	11	1	4	

3rd Hospitalization

- Altered mental status
- Dysphagia severe with failure to thrive
- Again not taking medications
- Husband tried to commit suicide
- Switched to myfortic

	07/2021	10/2021	11/2021	02/2022	05/2022	09/2022	12/2022	03/2023	
WBC	3.02								
TSH	4.95	5.34			7.37	5.67	9.23	10.60	
Creatinine	0.72								
Proteinuria	0	0		0	0	0	0	0.4	
AST	261		700					204	
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CPK	176		74					159	
myoglobin	98								
Aldolase	10								
DsDNA	318	330		33	27	97	353	1000	
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SSA/SSB	negative	negative				8	8	8	
C3	49	47		83	91	71	36	30	
C4	8	3		11	16	11	1	4	

Ambulatory F/U

02/2023

- Better since discharge
- Confused about medication
- Myfortic was never dispensed
- Moving to Connecticut to live with her daughter

03/2023

- Complete disaster
- Referral to Obinutuzumab

Where Are We With Treatment Options?

SLE

Category		Targets/Agent
Interferons		• Type 1: Anifrolumab • pDC: Litifilimab, Daxdilimab
B Cell-Directed Therapies	Cellular	• BTK • CD20: Rituximab • BAFF receptor: Ianalumab • CD19:Obexelimab
	Extracellular	• BAFF/APRIL/ TACI: Atacicept, Telitacicept
Plasma Cell-Directed Therapies		• CD38:Zetomipzomib, Mezagitamab, Daratumumab • BCMA:Bispecific anti-CD3/BCMA mAb, CAR-T (CD19)
T Cells and T – B Cell Interactions		• CD40 Ligand:Dapirolizumab
Cytokine Target		• IL2 Restoration • JAK/STAT signaling (Jakinibs): Deucravacitinib, Upadacitinib + elsubrutinib (BTKi) : ABBV-599HD

Adapted from; *Novel Treatments for Systemic Lupus and Lupus Nephritis.* Richard Furie, MD. May 2023.

Lupus Nephritis

Category	Agent
Small Molecule Calcineurin Inhibitor	Voclosporin
B Cell-Directed Therapies: Extracellular Targets	Belimumab
B Cell-Directed Therapies: Cellular Targets	Obinutuzumab
Chimeric Antigen Receptor T-Cells (CAR-T)	KYV-101
Interferon Type 1	Anifrolumab
Anti-CD6	Itolizumab

Adapted from; *Novel Treatments for Systemic Lupus and Lupus Nephritis.* Richard Furie, MD. May 2023.

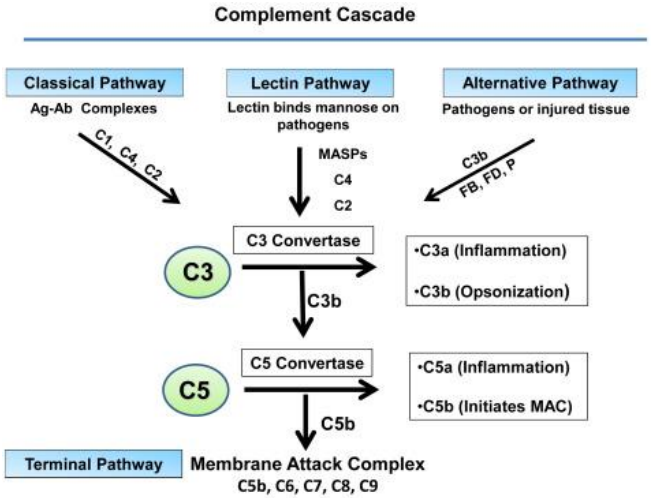
What Options Do We Have?

Option 1

Crovalimab

Crovalimab – Lupus Nephritis

- Eculizumab has shown beneficial outcomes in LN, especially those complicated with thrombotic microangiopathy (TMA)
- C5 convertase, cleaves C5 to its proinflammatory effector subunits, C5a and C5b
- Blocking the formation of C5b inhibits the subsequent formation of terminal complex C5b-9 or MAC
- Crovalimab is a humanized anti-C5 sequential monoclonal antibody recycling technology (SMART) antibody
- Recycling antibodies allow antibodies to bind to target antigen multiple times and to act longer in the body
- Significant improvement in glomerulonephritis and increased survival



Wang Y, et al. Proc Natl Acad Sci U S A. 1996 Aug 6;93(16):8563-8.; Nester CM & Thomas CP. *Hematology Am Soc Hematol Educ Progra*. 2012;2012:617-25; Sciascia S et al. *Rheumatol Int*. 2017 Aug;37(8):1249-1255.; Chugai News Releases: Chugai Pharmaceutical CO., LTD. Aug 10,2022. chugai-pharm.co.jp; Fukuzawa, T., et al. *Sci Rep* **7**, 1080 (2017).; John P. Atkinson & C. Yung Yu. Chapter 12: Systemic Lupus Erythematosus. *Basic, Applied and Clinical Aspects.* 2016, Pages 81-112.

Crovalimab – Lupus Nephritis – Trial CA43761

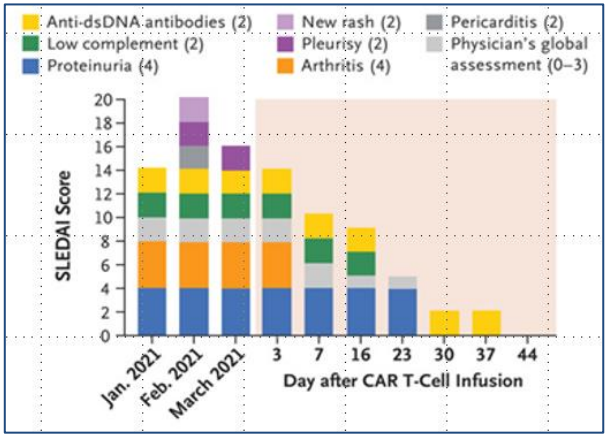
- A Phase I, multicenter, single-arm study to evaluate the pharmacokinetics, pharmacodynamics, and safety of Crovalimab in patients with lupus nephritis (GENETECH)
- Objective: To evaluate the PK, safety, PD, immune response, and safety of Crovalimab in active LN
- 48 week study with weight based Crovalimab first dose IV, followed by SQ for subsequent doses
- Participants will have to get vaccinated against Neisseria meningitidis (meningococcal), Haemophilus influenzae type B, and Streptococcus pneumoniae at or before screening
- Side effects: Neisseria meningitidis Infection, infection, allergic reactions, infusion related reactions

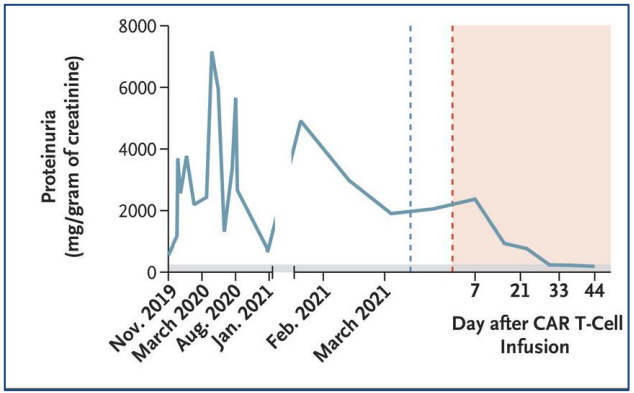
Option 2

CAR-T

CD19-Targeted CAR T Cells in Refractory Systemic Lupus Erythematosus

- Chimeric antigen receptor (CAR)–modified T cells that have been genetically engineered to recognize CD19 and other B-cell surface antigens
- 20-year-old woman with severe/refractory SLE/LN (class IIIA), nephrotic syndrome, pericarditis, pleurisy, rash, arthritis, and a history of Libman–Sacks endocarditis
- HCQ, high-dose GC, CYC, MMF, and tacrolimus, as well as the B-cell–targeting therapies belimumab and rituximab, did not control symptoms, deplete B cells, or abrogate autoimmunity
- Rapid remission of refractory SLE, rapid disappearance of dsDNA autoantibodies, low C3 and C4 levels normalized, decreased proteinuria, SLEDAI

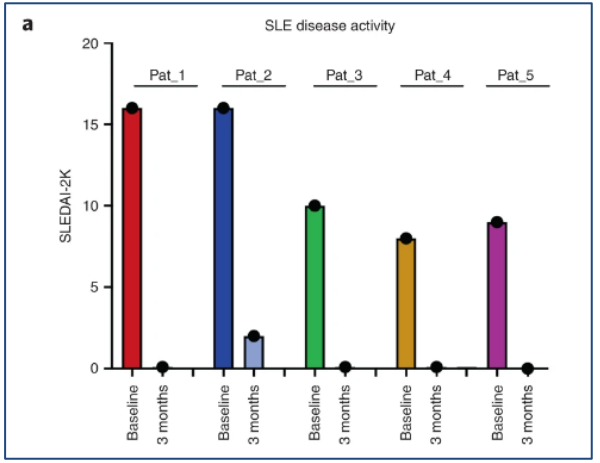


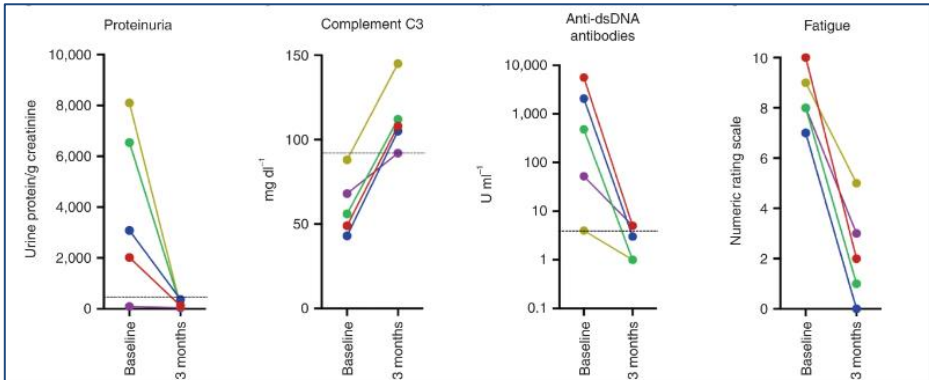


D Mougiakakos et al. *N Engl J Med.* 2021;385:567-569.

Anti-CD19 CAR T Cell Therapy for Refractory Systemic Lupus Erythematosus

- 5 SLE pts with median (age 22, disease duration 4 years and active disease SLEDAI (range): 16 (8)), refractory to several immunosuppressives, enrolled in a compassionate-use CAR T cell program
- Autologous T cells from SLE pts were transduced with a lentiviral anti-CD19 CAR vector, expanded and reinfused into the pts after lymphodepletion with fludarabine and CYC
- Deep depletion of B cells, improvement of clinical symptoms and normalization of laboratory parameters including seroconversion of Anti-dsDNA
- Remission of SLE via DORIS criteria in all 5 pts and the median (range) SLEDAI 0 (2) after 3 months
- Drug-free remission was maintained during longer follow-up after CAR T cell administration and even after the reappearance of B cells





Mackensen, A. et al. *Nat Med.* **28**, 2124–2132 (2022).

Kyverna – KYV-101 Lupus Nephritis

- A Phase 1, Open-Label, Multicenter Study of KYV-101, an Autologous Fully-Human Anti-CD19 Chimeric Antigen Receptor T-Cell (CD19 CAR T) Therapy, in Subjects With Refractory Lupus Nephritis
- KYV-101 is an autologous version of a novel fully human clinical-stage anti-CD19 CAR T that depletes pathogenic B cells
- Since CD19 CAR-T cells target and lyse B cells in both circulation and tissues, a more complete depletion of autoreactive B cells is expected with KYV-101, resulting in better disease control and clinical remission than the current immunotherapies.
  - **Primary Outcome:** Incidence of adverse events (AEs) and laboratory abnormalities, frequency of dose limiting toxicities
  - **Secondary Outcome:** PK, PD, biomarkers (anti-dsDNA, C3, C4), renal response rates (CRR)

Park S et al. POS0007 KYV-101, *Annals of the Rheumatic Diseases.* 2023;**82:**208-209;
ClinicalTrials.gov: NCT05938725; Kyverna Press Release; June 29,2023.

Option 3

Obinutuzumab

Obinutuzumab

- FDA approved for Chronic Lymphocytic Leukemia (CLL) and Follicular lymphoma
- The CD20 antigen is expressed on the surface of pre B- and mature B-lymphocytes
- Glycoengineered Humanized Type II anti-CD20 antibody that binds to CD20, activates CDC, antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP), resulting in cell death
- Glycoengineering increases binding affinity for FcγRIII resulting in improved cellular cytotoxicity in in-vitro ADCC and ADCP-based assays
- Greater B-cell depletion, B-cell cytotoxicity and activation of natural killer cells than RTX

Sehn. 2012; Pievani et al. 2011; Herter. *Mol Cancer Ther.* 2013; Mossner. *Blood.* 2010; Reddy. *Rheumatology (Oxford).* 2017; Goede. *N Engl J Med.* 2014; Marcus. *N Engl J Med*. 2017; Furie R et al. *Ann Rheum Dis.* 2022, Lexicomp.

Nobility

Phase 2 NOBILITY study design

104-week double-blind period

1:1

- **Obinutuzumab 1000 mg + MMF (n = 63)**
- All patients received MMF, 1000-3000 mg IV methylprednisolone, and a prednisone taper*
- **Placebo + MMF (n = 62)**

OBI or PBO infusions: 0, 2

Week 104

Key inclusion criteria:	Key exclusion criteria:	Primary endpoint:
• ISN/RPS Class III or IV LN within six months; concomitant class V permitted • UPCR ≥1 on 24-hour collection	• Rapidly progressive glomerulonephritis • eGFR <30 mL/min/1.73 m^2 • >50% of glomeruli with sclerosis	• Complete renal response (CRR) at week 52 **Key secondary endpoints:** • Overall renal response (CRR or PRR) • Change in levels of dsDNA, C3, C4 **Prespecified alpha level = 0.2**

* MMF target dose 2-2.5g, oral prednisone 0.5 mg/kg/day tapered to 7.5 mg/day by Week 12 and held until Week 52.
MMF = mycophenolate mofetil.

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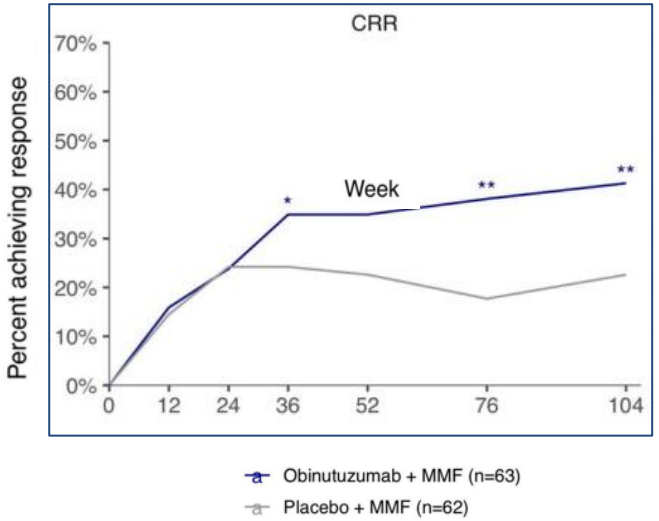


Furie R et al. *Ann Rheum Dis*. 2022.

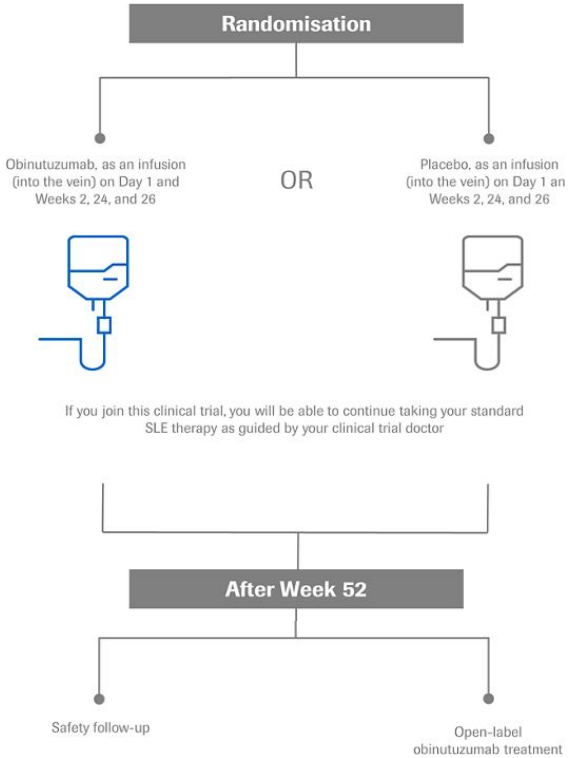
A Study to Evaluate the Efficacy and Safety of Obinutuzumab in Patients With ISN/RPS 2003 Class III or IV Lupus Nephritis (REGENCY) NCT04221477

- Evaluate the efficacy, safety, and PK of OBI vs. PBO in pts with Class III or IV LN when added on to SOC consisting of MMF and GC
  - **OBI:** IV infusion at a dose of 1000 mg at Baseline and Weeks 2, 24, 26, 50 (group 2: PBO), and 52 and subsequently from Week 80 and every 6 months thereafter, based on response
  - **MMF**: target dose of 2.0 - 2.5 g/day in divided doses through Week 80
  - **Prednisone** 0.5 mg/kg/day (maximum 60 mg/day) started on Day 2. Tapered to 5 mg/day beginning on Day 15, and continued until Week 80
  - **Placebo** matching OBI IV Infusions
  - **Pre Meds:** Methylprednisolone 80 mg IV, Acetaminophen 650-1000 mg, Diphenhydramine 50 mg
- **Primary Endpoint:** % with Complete Renal Response (CRR)
- **Secondary Endpoint:** % achieved a Proteinuric Response, CRR, ORR, AE, changes in biomarkers (Anti-dsDNA Titer, C3, SLEDAI-2K, Fatigue, onset of CRR, Drug antibodies, change in baseline B-cell count

ClinicalTrials.gov: NCT04221477.

A Study to Evaluate the Efficacy and Safety of Obinutuzumab in Participants With Systemic Lupus Erythematosus (ALLEGORY)

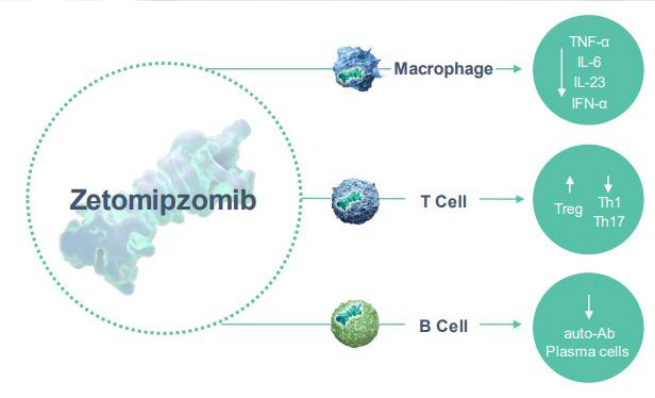
- Parallel-group, double-blind, PBO-controlled study will evaluate the efficacy and safety of OBI vs. PBO in pts with active, autoantibody-positive SLE who are treated with SOC
- OBI or PBO IV infusion on Day 1 and Weeks 2, 24 and 26
- **Primary Outcome:** % who Achieve Systemic Lupus Erythematosus Responder Index (SRI[4]) at Week 52
- **Secondary Outcome:** % who Achieve SRI at various scores and weeks including on low dose corticosteroids, Lupus Low Disease Activity State (LLDAS) at Week 52, Definition of Remission in SLE (DORIS) at Week 52, ADE, Fatigue, Bodily Pain assessment scale, Active Joint Count, Active Joint Count, Entering the Study on Prednisone >= 10 mg/day who Achieve Sustained Corticosteroid Control, Time to First BILAG Flare over 52 Weeks, anti-drug antibodies



ClinicalTrials.gov: NCT04963296.
For Patients by Roche: Allegory.

Option 4

Zetomipzomib



Muchamuel T et al. *Front Immunol*. 2023;14:1043680; Rovin, Brad, et al. Lupus nephirits-clinical: LO-017. *Lupus & KCR*. 2023.

Zetomipzomib KZR-616 – MISSION Phase 2 Trial

- Immunoproteasomes expressed in immune T cells and B cells with Increased expression on sites of inflammation (kidneys LN)
- Inhibition of immunoproteasomes, inhibits cytokine production and immune effector cell activity.
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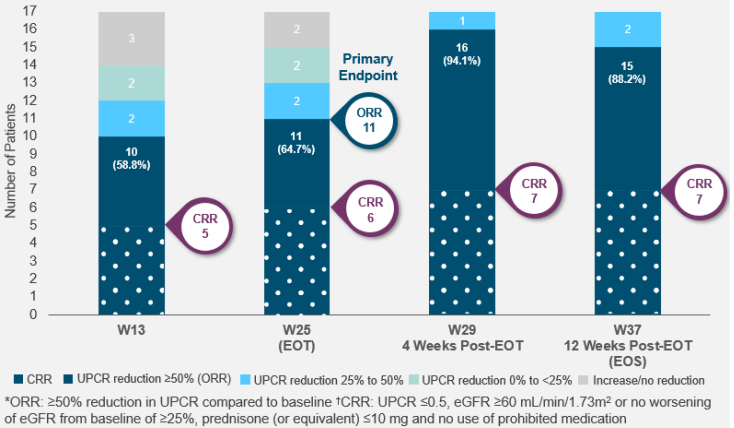
- A total of 17 people with active LN completed the 24-week Phase 2 trial
  - Four weeks post-treatment, nearly all (16) had a clinically meaningful reduction in proteinuria
  - Average daily corticosteroid dose req. decreased by 53%
  - **Overall renal responses (ORRs):** ≥50% reduction in UPCR from baseline
    - 58.8% Week 13, 64.7% *end of treatment (EOT), 94.1% Week 29, 88.2% Week 37*
  - **Complete renal responses:** UPCR of 0.5 or less
    - 29.4% Week 13, *35.3% at EOT*, *41.2% safety follow-up*
- Zetomipzomib once-weekly treatment demonstrated clinically meaningful renal responses in LN pts who had not responded to SOC therapy, with favorable safety and tolerability profile

Figure 2. **Zetomipzomib Treatment Demonstrated Clinically Meaningful Renal Response With Additional ORR*s and CRR†s Observed Through W37 (n=17)**



Saxena A et al. *ACR.* 2022, Lupus Foundation. June 28, 2022; Kezar Life Sciences. Press Release. November 14, 2022; Muchamuel T et al. *Front Immunol*. 2023;14:1043680; Rovin, Brad, et al. Lupus nephirits-clinical: LO-017. *Lupus & KCR.* 2023.

Zetomipzomib – KZR-616 PALIZADE

- A Phase 2b, Randomized, Controlled Double-blind, Multicenter Study Comparing the Efficacy and Safety of Zetomipzomib (KZR-616) 30 mg or 60 mg With Placebo in Patients With Active Lupus Nephritis
- To investigate zetomipzomib added to SOC in pts with active LN, is able to reduce disease activity over a treatment period of 52 weeks
- Background SOC with MMF and initial optional treatment with IV methylprednisolone, followed by a tapering course of oral corticosteroids
- Randomized in a 2:1 ratio to receive either zetomipzomib (30 mg or 60 mg) or PBO SQ once weekly for 52 weeks, followed by a 4-week safety follow-up period
- Efficacy will be assessed by measuring the level of proteinuria (as measured by urine protein to creatinine ratio [UPCR])
  - **Primary Outcome:** Proportion of patients achieving CRR (Baseline through Week 37) and safety, incidence of AE]
  - **Secondary Outcome:** Partial Renal Remission (PRR) [Baseline through Week 25, 37, and 53] and CRR (Baseline through Week 25 and Week 53)

Sec. Autoimmune and Autoinflammatory Disorders: Autoimmune Disorders. *Front. Immunol*. 10 March 2023.
A Study of Zetomipzomib (KZR-616) in Patients With Active Lupus Nephritis (PALIZADE): NCT03073525.

Option 5

Ianalumab

Ianalumab (VAY736) Lupus Nephritis **SIRIUS-LN-**

- To Evaluate the Safety, Efficacy and Tolerability of Ianalumab Versus Placebo, Combination With SoC Therapy, in Participants With Active Lupus Nephritis (SIRIUS-LN)
- A randomized, double-blind, parallel group, placebo controlled, multicenter phase 3 trial
- Ianalumab SQ every 4 weeks or every 12 weeks VS placebo, in combination with SoC, in adult participants with active LN
- **Primary Endpoint:**
  - Frequency and % of pts achieving stable CRR at Week 72
- **Secondary Endpoint:**
  - Time to first occurrence of stable urine protein-to-creatinine ratio (UPCR) <0.5 g/g or ≥50% reduction from baseline at Week 72, % achieving stable ORR, defined as achievement as either CRR or PRR at Week 48, Incidence of stable CRR while maintaining daily corticosteroid dose ≤5 mg/day at Week 72, Incidence of renal-related event or death, ADE, Change in BILAG score, Fatigue score, Ianalumab concentration in serum, Incidence and titer of anti-ianalumab antibodies in serum (ADA assay) over time at week 72

ClinicalTrials.gov: NCT05126277.