What’s New in SLE?

ΣΤΑΜΑΤΗΣ-ΝΙΚΟΣ ΛΙΟΣΗΣ
Καθηγητής
Πανεπιστήμιο Πατρών & ΠΓΝΠ

What's New (στη Θεραπεία του) SLE?

ΣΤΑΜΑΤΗΣ-ΝΙΚΟΣ ΛΙΟΣΗΣ
Καθηγητής
Πανεπιστήμιο Πατρών & ΠΓΝΠ

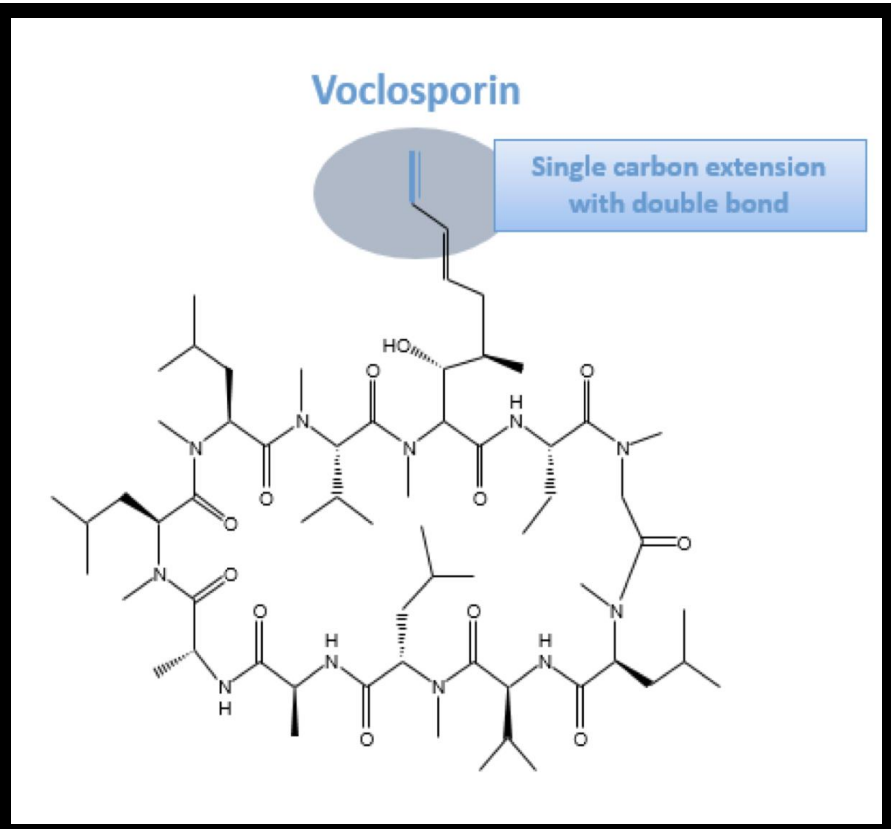
Σύγκρουση Συμφερόντων

- Για κανένα από τα προϊόντα τα οποία αναφέρονται στην ομιλία μου
- Δεν προβλέπεται τιμητική αμοιβή μου από τον χορηγό

AURORA PHASE 3 STUDY DEMONSTRATES VOCLOSPORIN STATISTICAL SUPERIORITY OVER STANDARD OF CARE IN LUPUS NEPHRITIS (LN)

C. Arriens[1,2], S. Polyakova[3], I. Adzerikho[4], S. Randhawa[5], N. Solomons[5]

[1]Oklahoma Medical Research Foundation, Oklahoma City, United States of America
[2]University of Oklahoma Health Sciences Center, Oklahoma City, United States of America
[3]LLC Medical Center, Kemerovo, Russian Federation
[4]Minsk Regional Clinical Hospital, Minsk, Belarus
[5]Aurinia Pharmaceuticals, Victoria, Canada



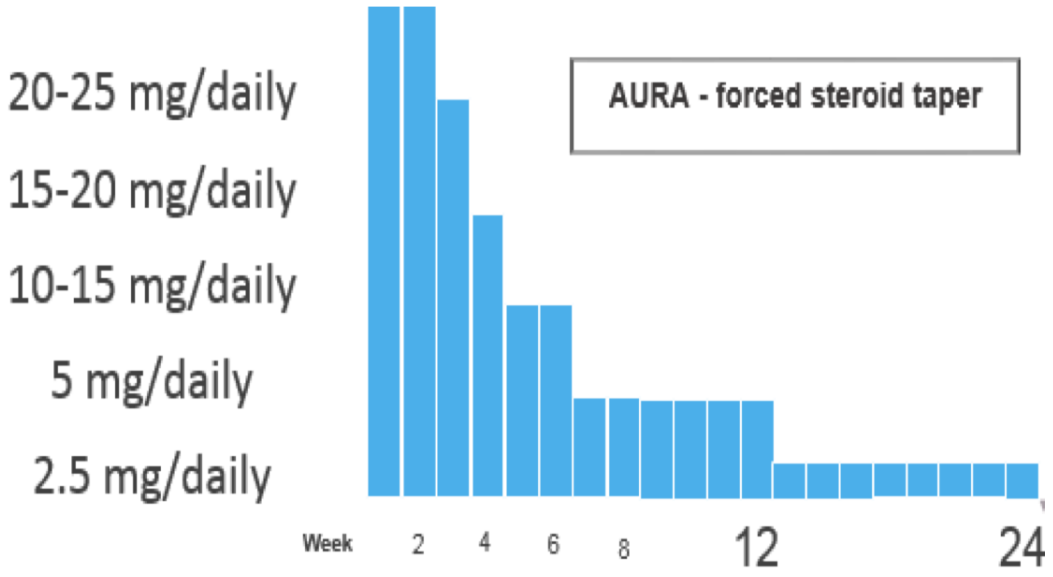
357 pts, 52 wk
RR VCS: 40.8%
RR Control: 22.5%

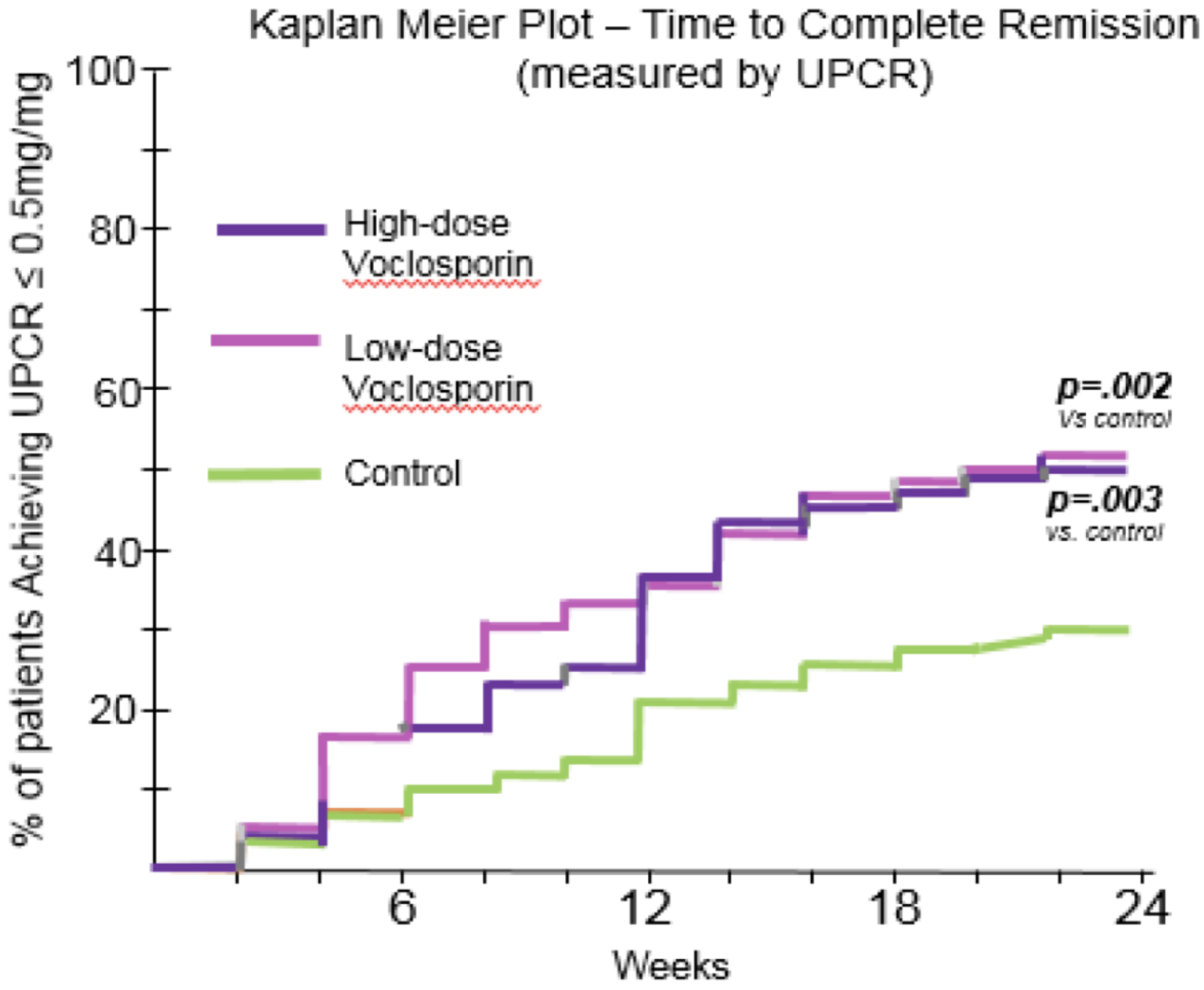
Καλά ανεκτή Tx
No safety signals

eGFR, BP, lipids, Glu

AURA - LN

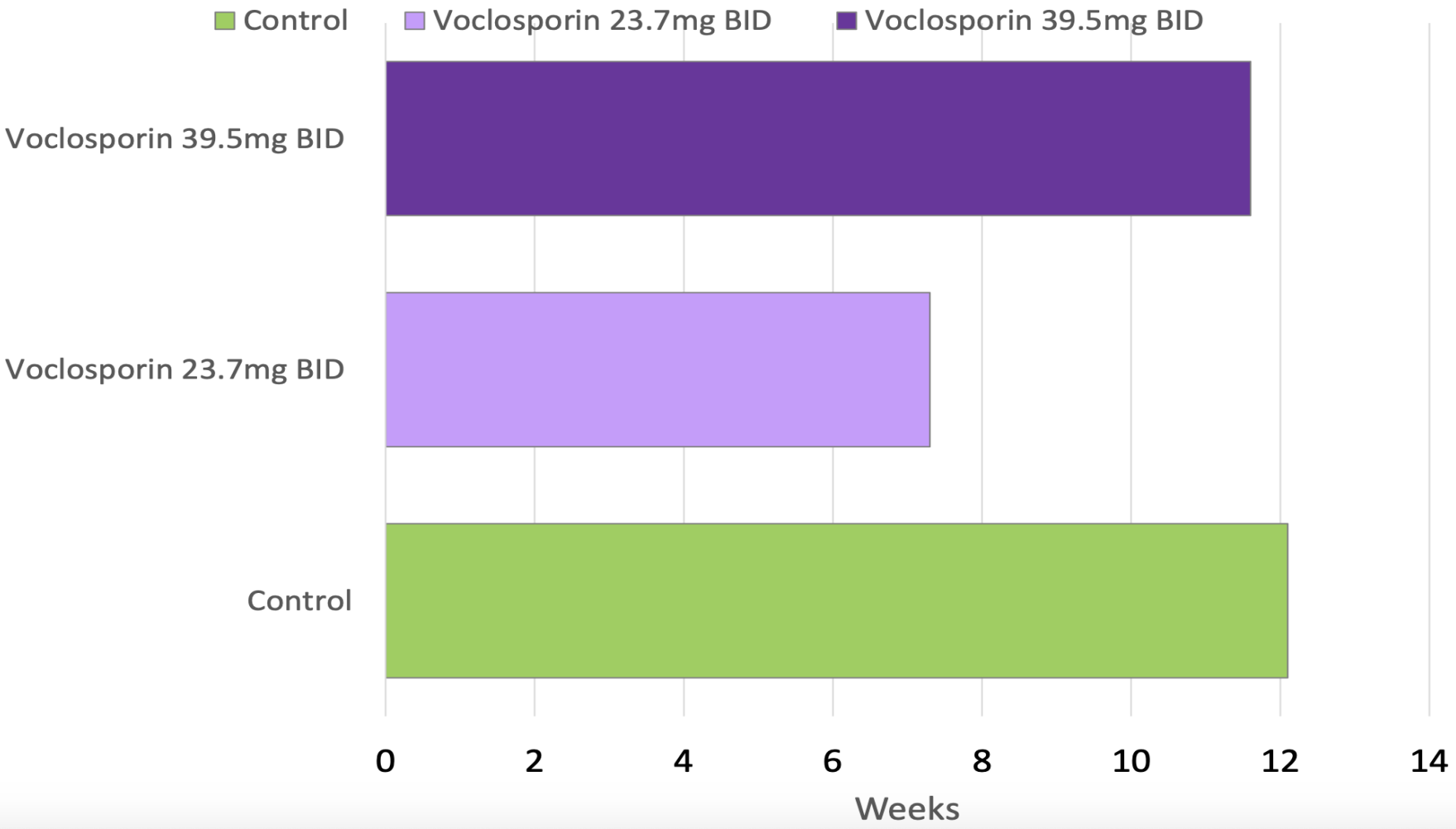
Patients entered CR rapidly despite forced prednisone taper





AURA - LN

Median Time to Complete Remission in those patients achieving CR



New Drug Application & Fast-track review (FDA): Ιανουάριος 2021

Obinutuzumab: anti-hCD20 mAb

SUN-374

B-CELL DEPLETION AND RESPONSE IN A RANDOMIZED, CONTROLLED TRIAL OF OBINUTUZUMAB FOR PROLIFERATIVE LUPUS NEPHRITIS

Rovin, B*[1], Furie, R[2], Aroca, G[3], Garg, JP[4], Alvarez, A[5], Fragoso-Loyo, H[6], Zuta Santillan, E[7], Brunetta, P[4], Schindler, T[8], Looney, CMD[4], Hassan, I[9], Cascino, MD[4], Malvar, A[10]

Gazyvaro

	Obinutuzumab sustained depletion (N=32)	Obinutuzumab detectable B-cells (N=20)	Placebo group (N=62)
CRR	50%**	35%*	18%
Modified CRR	72%**	50%	37%
ORR	66%***	45%*	29%

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

* P < 0.2 vs. placebo group
** P < 0.05 vs. placebo group
*** P < 0.001 vs. placebo group

CRR = complete renal response, which required UPCR <0.5 with serum creatinine ≤ the upper limit of normal and not increased >15% from baseline with <10 RBCs/HPF and no RBC casts.

Modified CRR = UPCR < 0.5 with normal serum creatinine.

ORR = overall renal response, which required either CRR or partial renal response: ≥50% reduction in UPCR from baseline to <1 (<3 if baseline UPCR ≥3) with serum creatinine not increased >15% from baseline and ≤50% increase in urinary RBCs (or <10 RBCs/HPF).

FDA: Breakthrough therapy

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

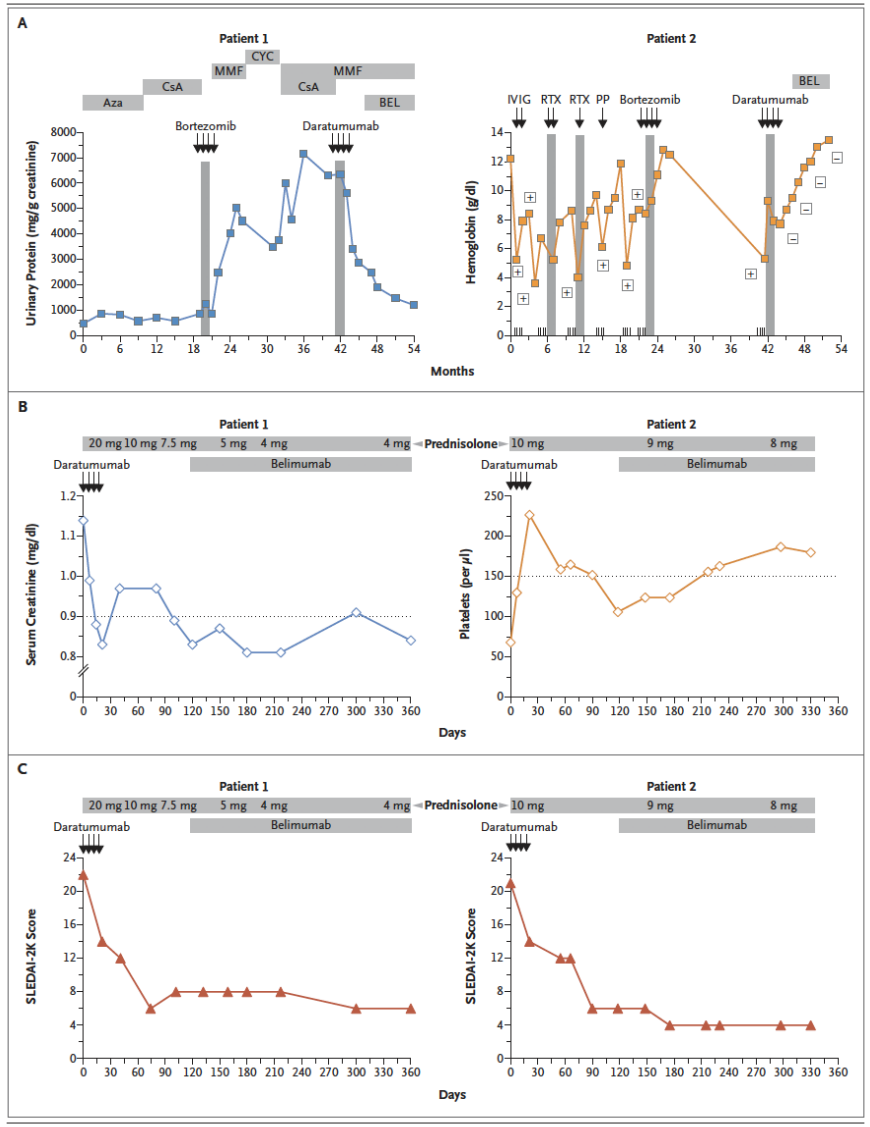
Targeting CD38 with Daratumumab in Refractory Systemic Lupus Erythematosus

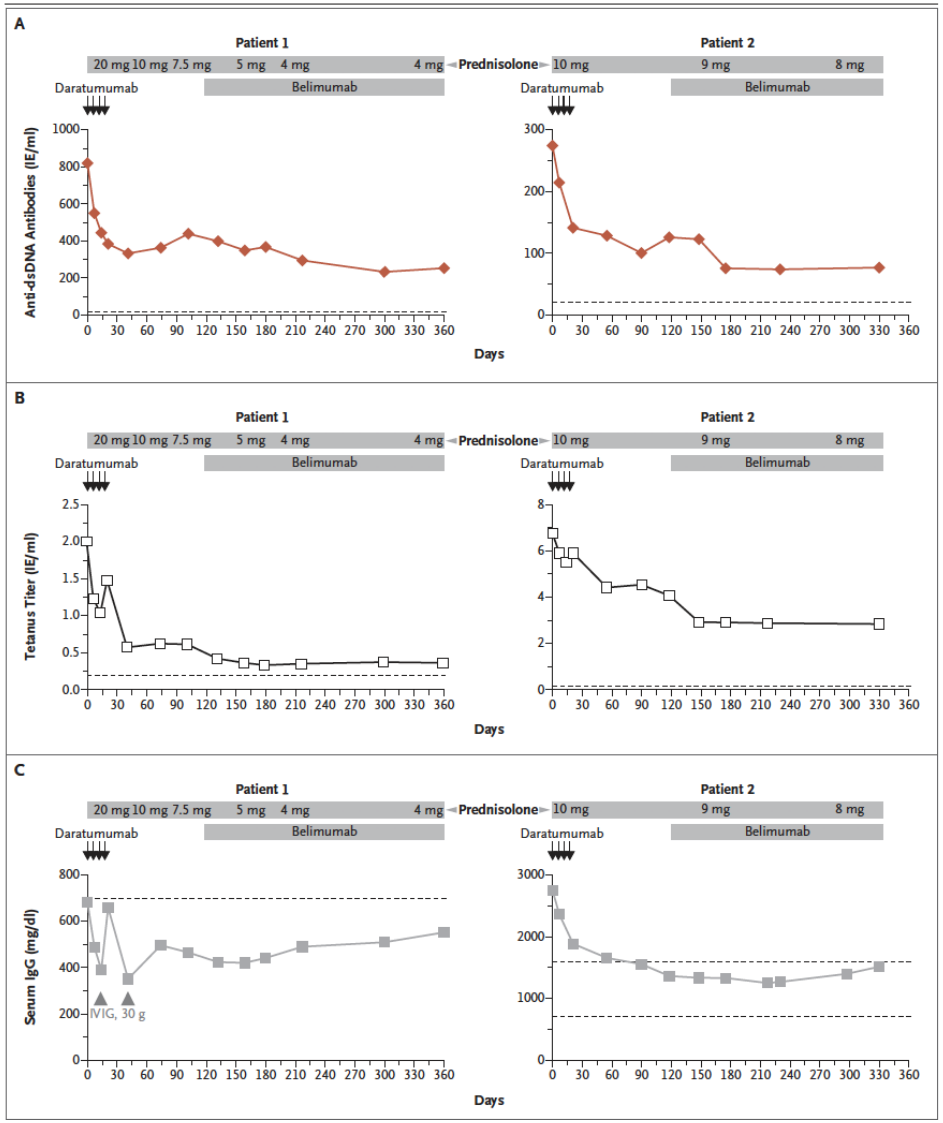
Lennard Ostendorf, M.D., Marie Burns, M.Sc., Pawel Durek, Ph.D., Gitta Anne Heinz, Ph.D., Frederik Heinrich, Ph.D., Panagiotis Garantziotis, M.D., Philipp Enghard, M.D., Ulrich Richter, M.D., Robert Biesen, M.D., Udo Schneider, M.D., Fabian Knebel, M.D., Gerd Burmester, M.D., Andreas Radbruch, Ph.D., Henrik E. Mei, Ph.D., Mir-Farzin Mashreghi, Ph.D., Falk Hiepe, M.D., and Tobias Alexander, M.D.

Daratumumab in SLE

n = 2 (δύο, two, deux, due, zwei,….)

DARZALEX


A
Patient 1
Patient 2
Aza
CsA
CYC
MMF
CsA
MMF
BEL
Bortezomib
Daratumumab
IVIG
RTX
RTX
PP
Bortezomib
Daratumumab
BEL
Urinary Protein (mg/g creatinine)
Hemoglobin (g/dl)
Months
B
Patient 1
Patient 2
20 mg 10 mg 7.5 mg
5 mg
4 mg
4 mg
Prednisolone
10 mg
9 mg
8 mg
Daratumumab
Belimumab
Serum Creatinine (mg/dl)
Platelets (per μl)
Days
C
Patient 1
Patient 2
SLEDAI-2K Score
Days


A
Patient 1
Patient 2
20 mg 10 mg 7.5 mg
5 mg
4 mg
4 mg
Prednisolone
10 mg
9 mg
8 mg
Daratumumab
Belimumab
Anti-dsDNA Antibodies (IE/ml)
Days
B
Tetanus Titer (IE/ml)
Days
C
Serum IgG (mg/dl)
IVIG, 30 g
Days

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Two-Year, Randomized, Controlled Trial of Belimumab in Lupus Nephritis

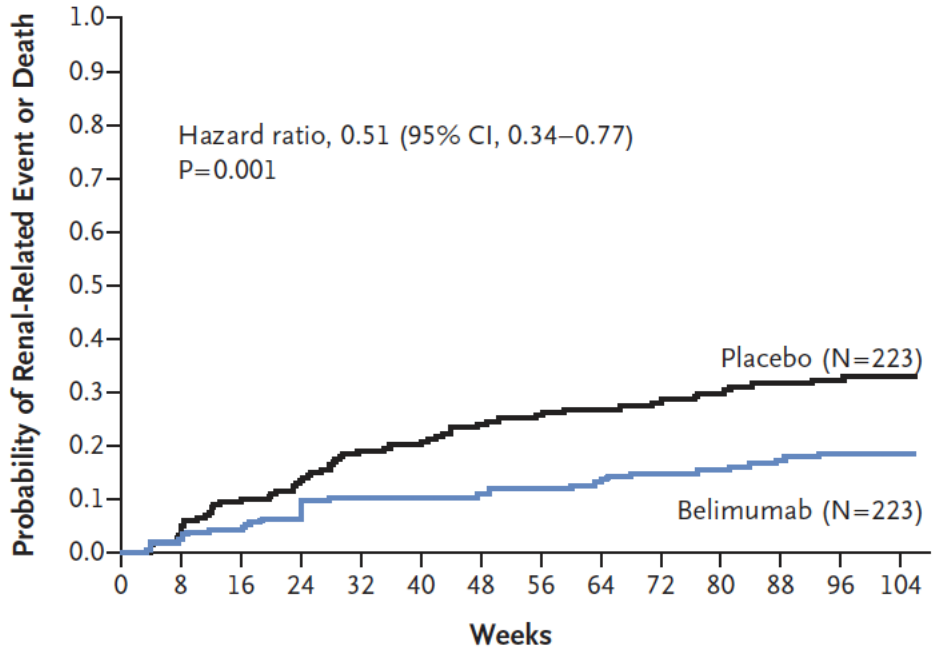
Richard Furie, M.D., Brad H. Rovin, M.D., Frédéric Houssiau, M.D., Ph.D., Ana Malvar, M.D., Y.K. Onno Teng, M.D., Ph.D., Gabriel Contreras, M.D., M.P.H., Zahir Amoura, M.D., Xueqing Yu, M.D., Chi-Chiu Mok, M.D., Mittermayer B. Santiago, M.D., Amit Saxena, M.D., Yulia Green, M.D., Beulah Ji, M.D., Christi Kleoudis, M.P.H., Susan W. Burriss, M.S., Carly Barnett, M.P.H., and David A. Roth, M.D.

BLISS-LN

Table 2. Primary and Major Secondary Efficacy End Points in the Modified Intention-to-Treat Population.

End Point	Belimumab (N = 223)	Placebo (N = 223)	Difference	Odds Ratio or Hazard Ratio (95% CI)*	P Value
	number (percent)		*percentage points*		
Primary end point: primary efficacy renal response at wk 104†	96 (43)	72 (32)	11	1.6 (1.0 to 2.3)	0.03
Major secondary end points					
Complete renal response at wk 104‡	67 (30)	44 (20)	10	1.7 (1.1 to 2.7)	0.02
Primary efficacy renal response at wk 52§	104 (47)	79 (35)	11	1.6 (1.1 to 2.4)	0.02
Time to renal-related event or death¶	NA	NA	NA	0.5 (0.3 to 0.8)	0.001
Ordinal renal response without urinary sediment at wk 104‖					
Complete renal response	67 (30)	44 (20)	10	NA	0.01
Partial renal response**	39 (18)	38 (17)	<1	NA	
No response	117 (52)	141 (63)	−11	NA	

A



No. at Risk

Placebo	203	185	175	154	147	137	129	126	120	116	112	110	78
Belimumab	209	192	186	167	162	159	157	151	142	139	133	130	102

B

Event	Belimumab (N=223)	Placebo (N=223)
	no.	
Any event	35	63
Death from any cause	1	2
Progression to ESKD	0	1
Doubling of creatinine level from baseline	1	1
Increased proteinuria, impaired kidney function, or both	17	39
Treatment failure related to kidney event	16	20

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Anifrolumab in Active Systemic Lupus Erythematosus

E.F. Morand, R. Furie, Y. Tanaka, I.N. Bruce, A.D. Askanase, C. Richez, S.-C. Bae, P.Z. Brohawn, L. Pineda, A. Berglind, and R. Tummala, for the TULIP-2 Trial Investigators*

This article was published on December 18, 2019, at NEJM.org.

DOI: 10.1056/NEJMoa1912196

TULIP 2

Table 2. Primary and Key Secondary Efficacy End Points.

End Point	Placebo (N = 182)*	Anifrolumab, 300 mg (N = 180)*	Difference (95% CI)*	Adjusted P Value†
	number/total number (percent)		*percentage points*	
Primary end point: BICLA response at wk 52‡	57/182 (31.5)	86/180 (47.8)	16.3 (6.3 to 26.3)	0.001
Key secondary end points				
BICLA response at wk 52 in patients with a high type I interferon gene signature	46/151 (30.7)	72/150 (48.0)	17.3 (6.5 to 28.2)	0.002
Glucocorticoid reduction to target dose, sustained from wk 40 to wk 52§	25/83 (30.2)	45/87 (51.5)	21.2 (6.8 to 35.7)	0.01
≥50% Reduction in CLASI activity from baseline to wk 12¶	10/40 (25.0)	24/49 (49.0)	24.0 (4.3 to 43.6)	0.04
≥50% Reduction in both swollen and tender joints from baseline to wk 52‖	34/90 (37.5)	30/71 (42.2)	4.7 (–10.6 to 20.0)	0.55**
Annualized flare rate through wk 52††	0.64	0.43	0.67 (0.48 to 0.94)‡‡	0.08**

Μια άλλη μελέτη Φάσης ΙΙΙ με το anifrolumab (TULIP 1) ΔΕΝ είχε δείξει αποτελεσματικότητα….????

Table 3. Adverse Events during the Intervention Period.*

Event	Placebo (N=182)	Anifrolumab, 300 mg (N=180)
	number (percent)	
Any adverse event	153 (84.1)	159 (88.3)
Serious adverse event	31 (17.0)	15 (8.3)
Death	0	1 (0.6)†
Adverse event leading to discontinuation of intervention	13 (7.1)	5 (2.8)
Adverse events of special interest‡	18 (9.9)	25 (13.9)
Herpes zoster	2 (1.1)	13 (7.2)
Nonopportunistic serious infections	10 (5.5)	5 (2.8)
Influenza	6 (3.3)	4 (2.2)
Tuberculosis	0	3 (1.7)
Major adverse cardiovascular event	0	1 (0.6)
Cancer	1 (0.5)	0
Serious adverse event occurring in ≥2 patients in the trial		
Pneumonia	7 (3.8)	3 (1.7)
Gastroenteritis, viral	0	2 (1.1)
Worsening of SLE§	6 (3.3)	1 (0.6)
Radius fracture	2 (1.1)	0
Adverse events with frequency of >5% in the anifrolumab group		
Upper respiratory tract infection	18 (9.9)	39 (21.7)
Nasopharyngitis	20 (11.0)	28 (15.6)
Infusion-related reaction	14 (7.7)	25 (13.9)
Bronchitis	7 (3.8)	22 (12.2)
Urinary tract infection	25 (13.7)	20 (11.1)
Herpes zoster	2 (1.1)	13 (7.2)
Sinusitis	9 (4.9)	12 (6.7)
Arthralgia	6 (3.3)	10 (5.6)
Back pain	3 (1.6)	10 (5.6)
Cough	6 (3.3)	10 (5.6)

TULIP 2

Ανεπιθύμητες ενέργειες:

Ερπητας ζωστήρας 7%
Βρογχίτιδα 12%

Συμπερασματικά

- Πολλά νέα φάρμακα σε φάση προχωρημένων κλινικών δοκιμών.
- Μερικά με εντυπωσιακά (ΟΧΙ ΠΡΩΪΜΑ) αποτελέσματα.
- Μάλλον πιο κοντά σε «καθημερινή» χρήση το Belimumab (LN).
- Εξακολουθούμε να ζούμε στον ***αστερισμό του lupus B cell***