Systemic Lupus Erythematosus

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Exagen Diagnostics
GlaxoSmithKline

1) **What is going on with all of these positive phase III SLE clinical trials?**
    - LN
        - Voclosporin
        - Belimumab (nephritis)
    - SLE
        - Anifrolumab (lesson in understanding disease activity measures)

~~**2) Glucocorticoids in SLE: Is it time to stop using them?**~~

News

December 17, 2020

Lupus Foundation of America Sees Big Win with FDA Approval of Benlysta® for Lupus Nephritis

The U.S. Food and Drug Administration (FDA) has approved Benlysta® to treat lupus nephritis (lupus-related kidney disease) in adults. The approval is for both the intravenous and subcutaneous formulations. The decision makes Benlysta the first lupus therapy authorized to treat this potentially life-threatening complication of the disease. Up to 60 percent of people with lupus will develop lupus nephritis.

Benlysta is a human monoclonal antibody sold by GSK. The FDA first approved Benlysta for lupus in 2011. However, at that time, Benlysta had not been studied for use in individuals with severe lupus nephritis.

Last year, GSK announced **positive results from a two-year clinical trial** involving several hundred people with active lupus nephritis treated with Benlysta. This is the most extensive controlled phase 3 study in active lupus nephritis, demonstrating that Benlysta could make a clinically meaningful improvement.

https://www.lupus.org/news/fda-approval-of-benlysta-for-lupus-nephritis
Accession date: 7 Feb 2021

Lupus Foundation of America Congratulates Aurinia Pharmaceuticals on FDA Approval of Lupkynis™ (voclosporin) to Treat Lupus Nephritis

Help Us Solve The Cruel Mystery

LUPUS FOUNDATION OF AMERICA

First FDA-approved oral treatment for lupus nephritis represents a significant milestone for people living with lupus-related kidney disease, a leading cause of disability and mortality in lupus

NEWS PROVIDED BY
Lupus Foundation of America →
Jan 22, 2021, 21:12 ET

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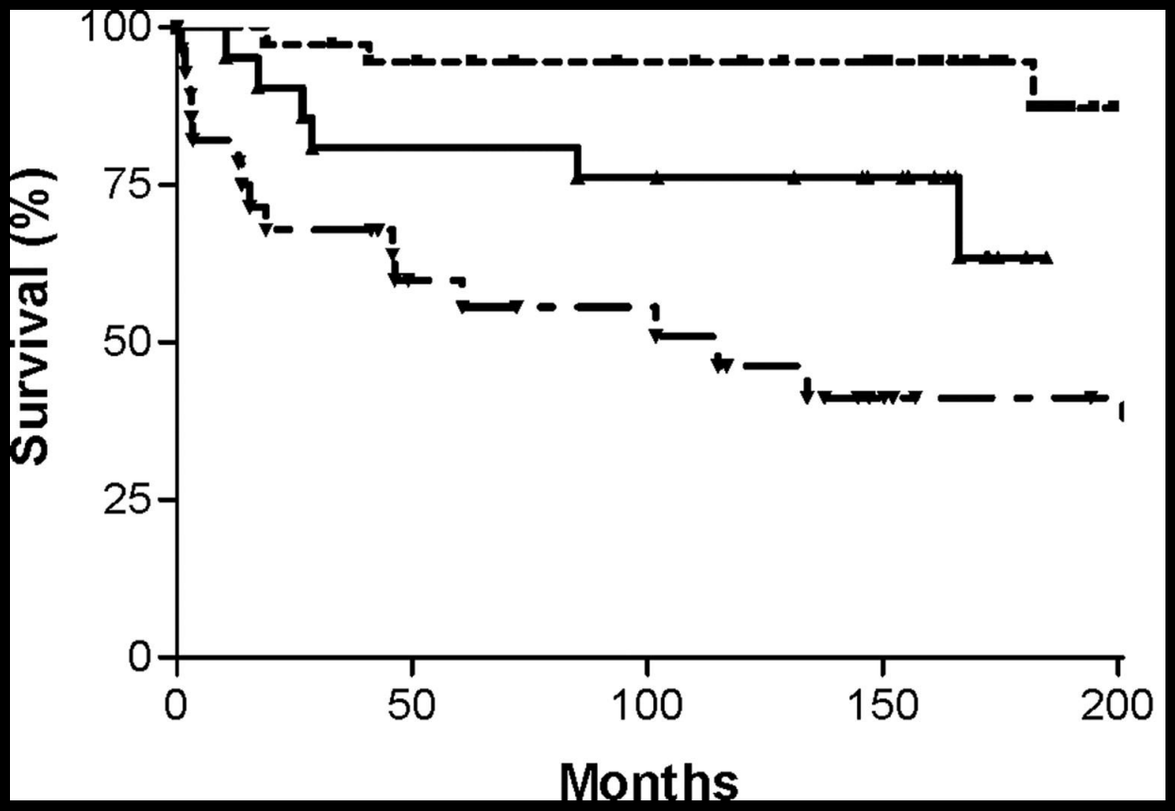
WASHINGTON, Jan. 22, 2021 /PRNewswire/ -- For the second time in less than two months, the U.S. Food and Drug Administration (FDA) has approved a new medication to treat adults with lupus nephritis (lupus-related kidney disease) in combination with a background immunosuppressive therapy regimen. Today, Aurinia Pharmaceuticals announced they received authorization from the FDA to market Lupkynis™ (voclosporin), a first-ever oral therapy for lupus nephritis that blocks a protein in the immune system called calcineurin. The company previously had reported positive data from a late-stage clinical study that demonstrated Lupkynis was superior to standard of care for treating lupus nephritis.

https://www.prnewswire.com/news-releases/lupus-foundation-of-america-congratulates-aurinia-pharmaceuticals-on-fda-approval-of-lupkynis-voclosporin-to-treat-lupus-nephritis-301213505.html
Accession date: 7 Feb 2021

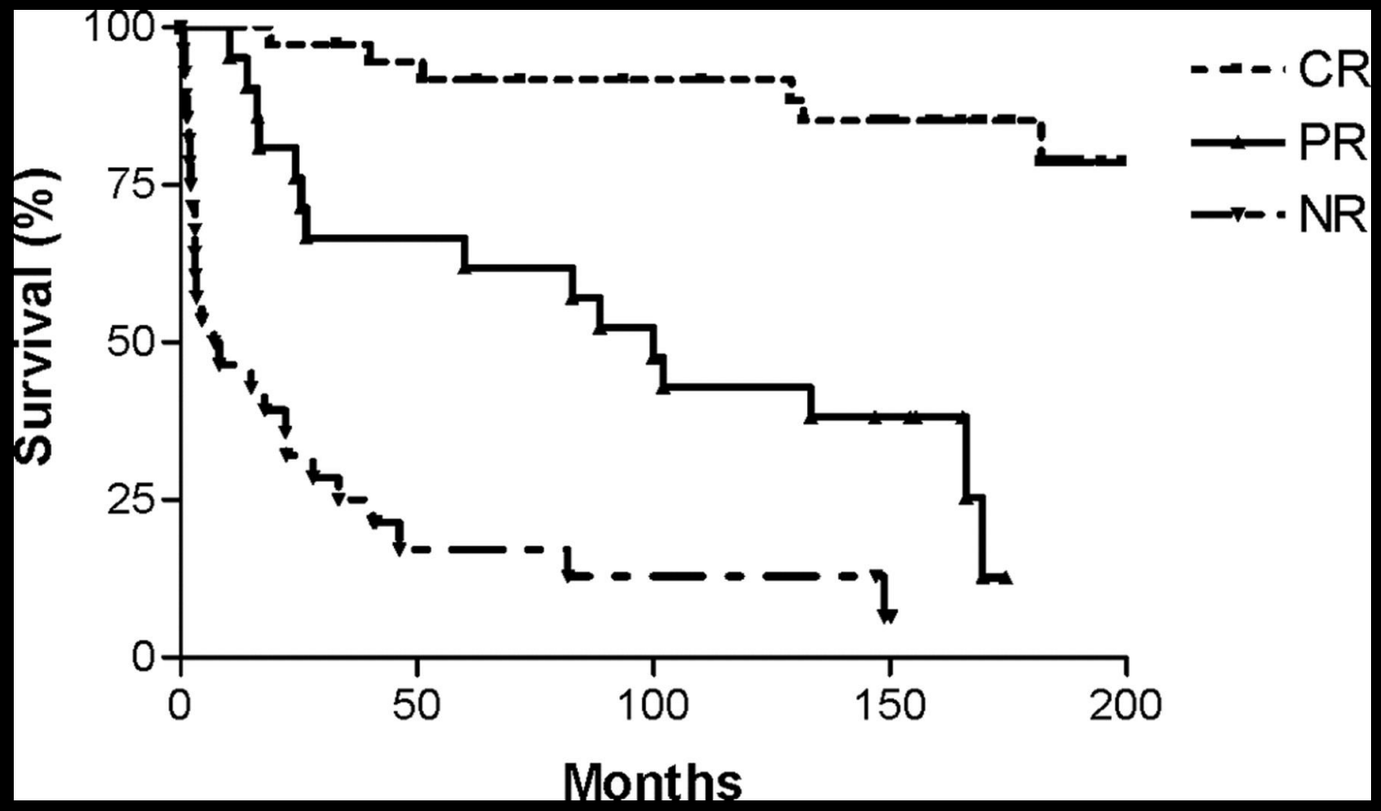
Outcomes matter: Complete response key in LN

Even partial response confers substantially worse outcomes

Patient survival



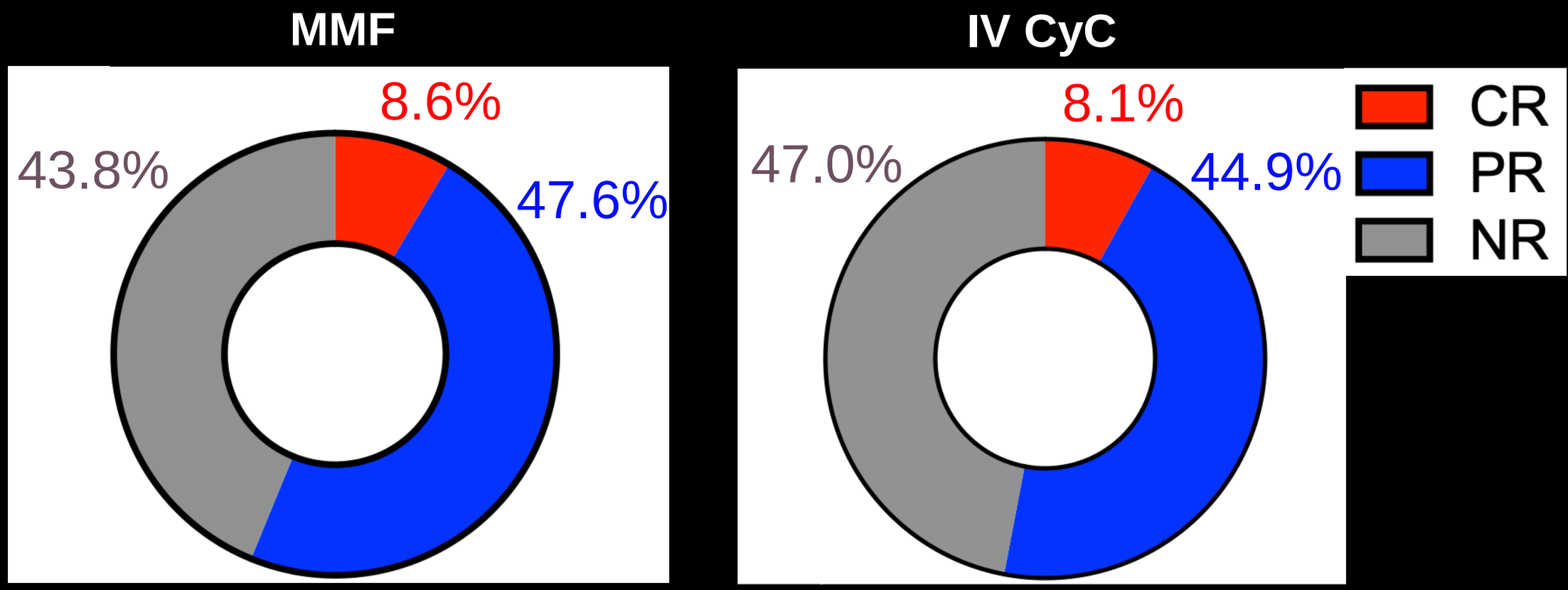
ESRD



Chen *et al.*, *Clin J Am Soc Nephrol*, **3**:46 (2008)

Outcomes matter: Complete response key in LN

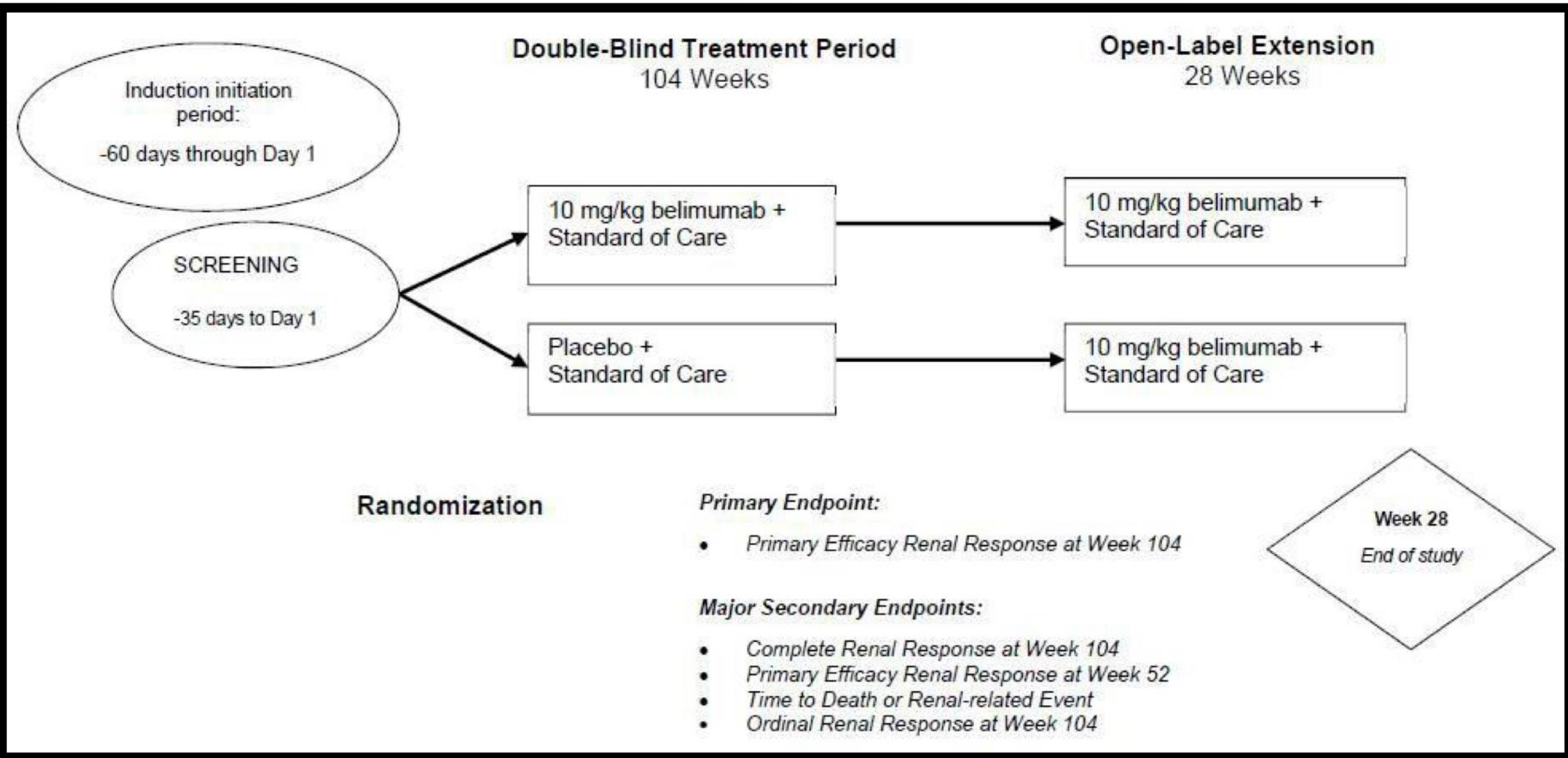
Problem is with standard of care, CR very difficult to attain



Appel *et al.*, *J Am Soc Nephrol*, **20**:1103 (2009)

BLISS-LN: Study design

New primary outcome (PERR) used, changed mid-trial from CRR



- 104 wk ph3, multicenter, placebo-controlled, double-blinded study
- Proliferative (58%, III or IV), membranous (16%, V), or mixed (26%) with uPCR ≥ 1
  - 446 subjects
  - 50% Asian, 33% White, 14% Black
- SOC: MMF (≤ 3 gms/day) or IV CyC (EuroLupus = 500 mg IV q2wks x 6) (provider discretion)
- Glucocorticoids must be tapered to PDN 10 mg/day by week 24

Furie *et al.*, *NEJM*, **383**:1117 (2020)

BLISS-LN: Outcome measures

New primary outcome (primary efficacy renal response, PERR) used, changed mid-trial (2017, 5 yrs after trial initiation) from ordinal renal response (ORR)

ORR

CRR	PRR	NRR
• uPCR<0.5 • Normal calculated GFR (CrCl) • Inactive urinary sediment	• uPCR ≤ 50% • CrCl ≤ 10% below pre-flare value or normal eGFR • RBCs/hpf ≥ 50% reduction or < 5 RBC/hpf with no RBC casts	• Does not meet CRR or PRR criteria

Eliminate PRR
Omitted sediment
GFR now estimated
Loosen proteinuria threshold

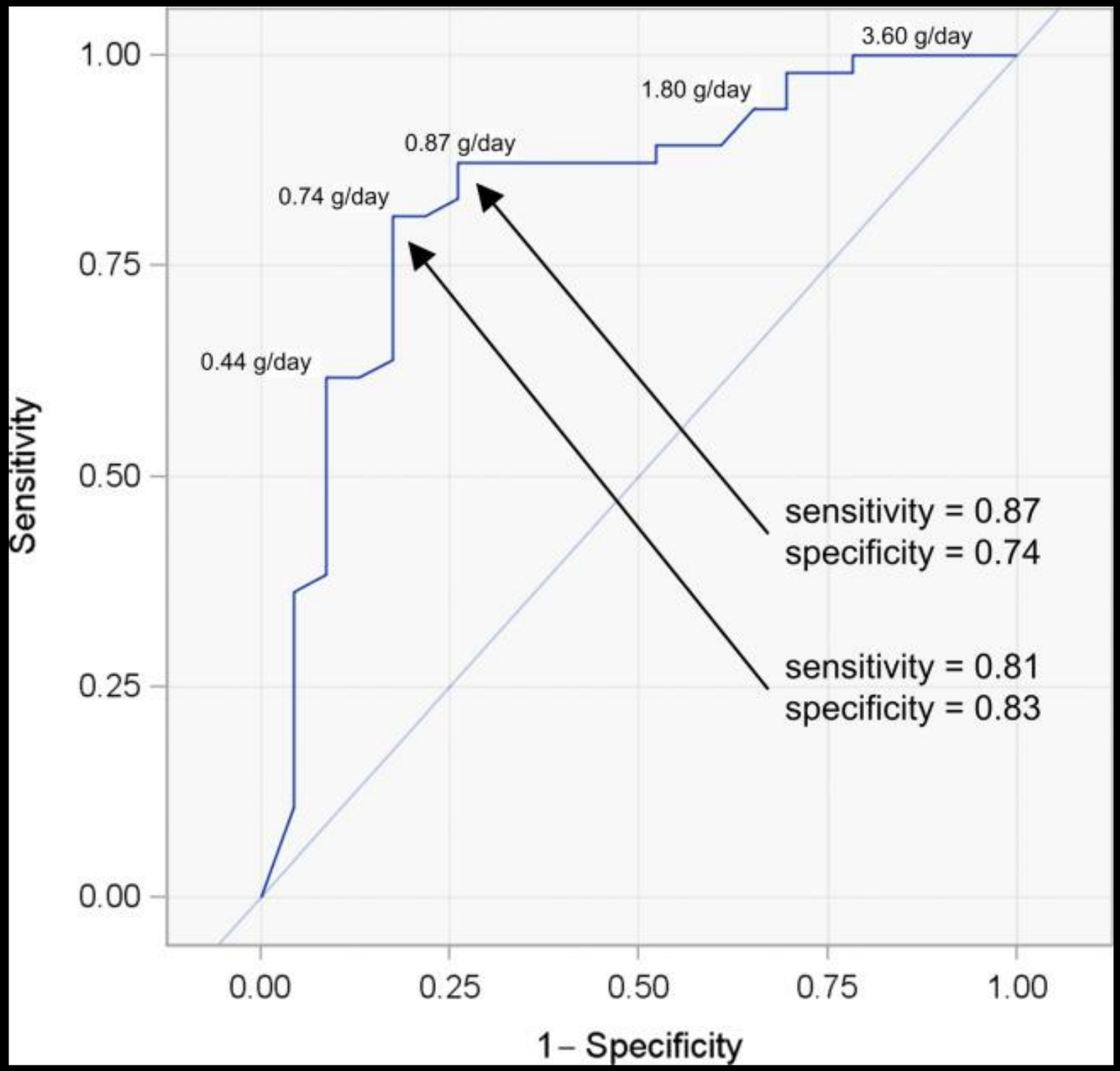
PERR

- uPCR ≤ 0.7
- eGFR ≤ 20% below pre-flare value or ≥ 60 mL/min/1.73m^2
- Not a treatment failure
- Must be consistent between weeks 100 and 104

Furie *et al.*, *NEJM*, **383**:1117 (2020)

BLISS-LN: Outcome measures

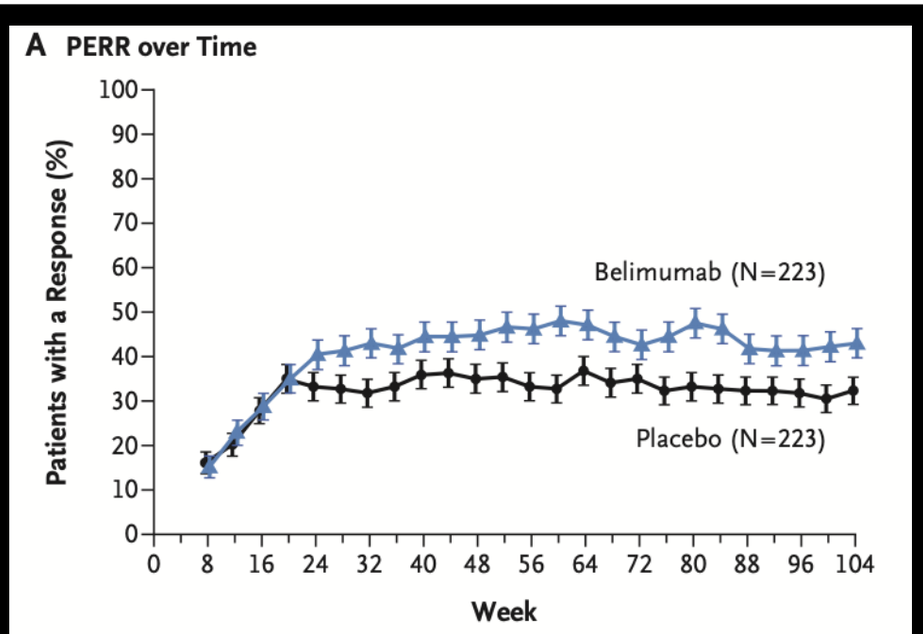
uPCR<0.8 at 12 mths single best predictor of good long-term renal function



Dell'era *et al.*, *Arthritis Rheumatol*, **67**:1305 (2015)

BLISS-LN: Results

BLM arm with 34% increase PERR compared to control arm

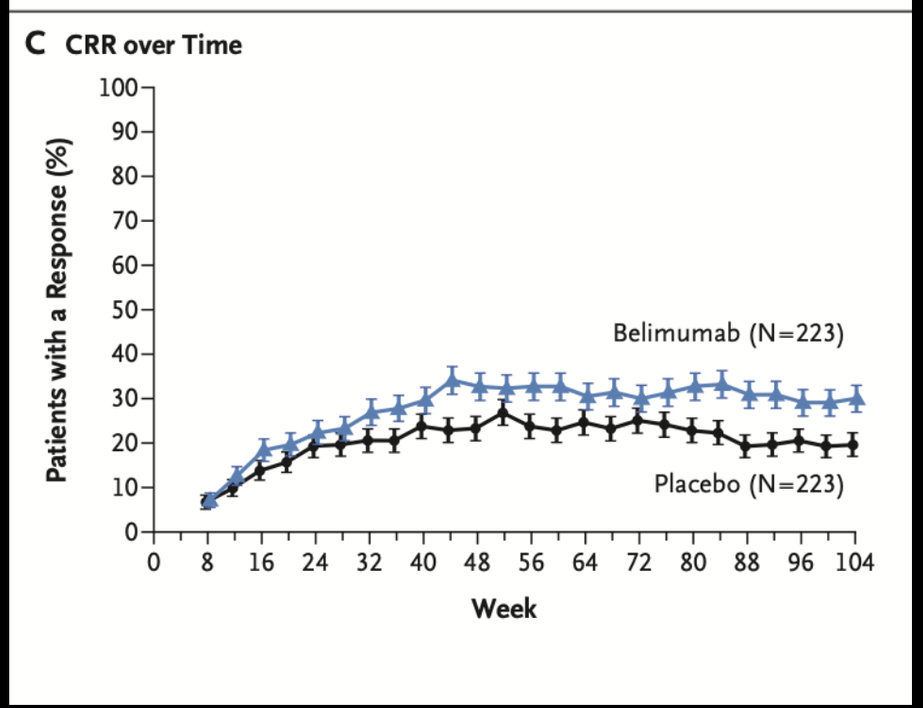


43%
32%

OR 1.6 (95% CI: 1.0-2.3)

PERR

- uPCR ≤ 0.7
- eGFR ≤ 20% below pre-flare value or ≥ 60 mL/min/1.73m^2
- Not a treatment failure



30%
20%

OR 1.7 (95% CI: 1.1-2.7)

CRR

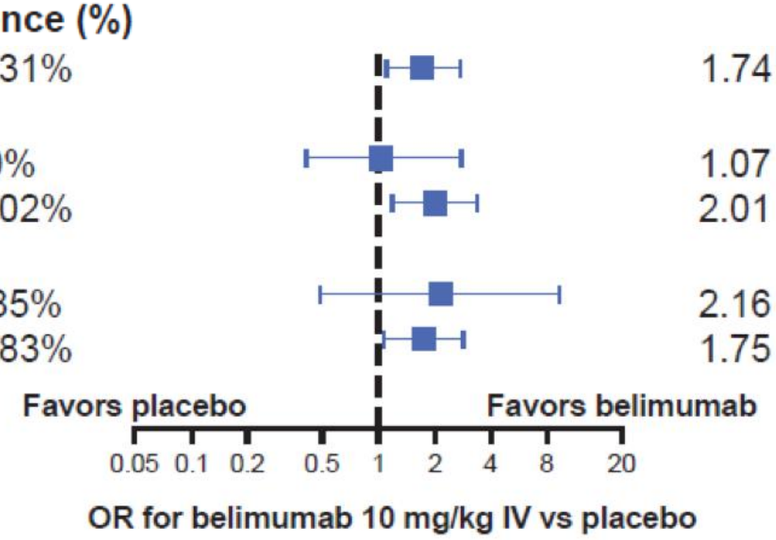
- uPCR ≤ 0.5
- CrCl ≤ 10% below pre-flare value or ≥ 90 mL/min/1.73m^2
- Not a treatment failure

Furie *et al.*, *NEJM*, **383**:1117 (2020)

BLISS-LN: Results

CRR most associated with concomitant MMF use

		Response rate (%)		Treatment difference (%)		
CRR	**Overall**	44/223 (19.7%)	67/223 (30%)	10.31%	1.74 (1.11, 2.74)	0.02
	Induction					
	Cyclophosphamide	11/59 (18.6%)	11/59 (18.6%)	0%	1.07 (0.41, 2.78)	
	Mycophenolate mofetil	33/164 (20.1%)	56/164 (34.1%)	14.02%	2.01 (1.19, 3.38)	
	Race					
	Black	4/32 (12.5%)	6/31(19.4%)	6.85%	2.16 (0.49, 9.43)	
	Non-black	40/191 (20.9%)	61/192 (31.8%)	10.83%	1.75 (1.08, 2.83)	



Furie *et al.*, *NEJM*, **383**:1117 (2020)

BLISS-LN: Adverse events

Similar to SLE trials, adverse events similar between BLM and controls

Table 3. Adverse Events, Adverse Events of Special Interest, and Suicidality in the Safety Population.*

Event	Belimumab (N = 224)	Placebo (N = 224)
	no. of patients (%)	
All adverse events†	214 (96)	211 (94)
All treatment-related adverse events†	123 (55)	119 (53)
Upper respiratory tract infection	26 (12)	24 (11)
Urinary tract infection	15 (7)	13 (6)
Herpes zoster	13 (6)	10 (4)
Bronchitis	11 (5)	10 (4)
Nasopharyngitis	8 (4)	8 (4)
Headache	9 (4)	5 (2)
Nausea	8 (4)	5 (2)
Rash	6 (3)	5 (2)
All serious adverse events†	58 (26)	67 (30)
All treatment-related serious adverse events†	23 (10)	25 (11)
Most common treatment-related serious adverse events, according to system organ class, occurring in ≥1% of patients in either group		
Infections and infestations	15 (7)	18 (8)
Respiratory, thoracic, and mediastinal disorders	5 (2)	1 (<1)
Blood and lymphatic system disorders	3 (1)	2 (1)
Nervous system disorders	0	3 (1)
Most common treatment-related serious adverse events occurring in ≥1% of patients in either group		
Pneumonia	3 (1)	4 (2)
Herpes zoster	3 (1)	2 (1)

BLISS-LN: Adverse events

Similar to SLE trials, adverse events similar between BLM and controls

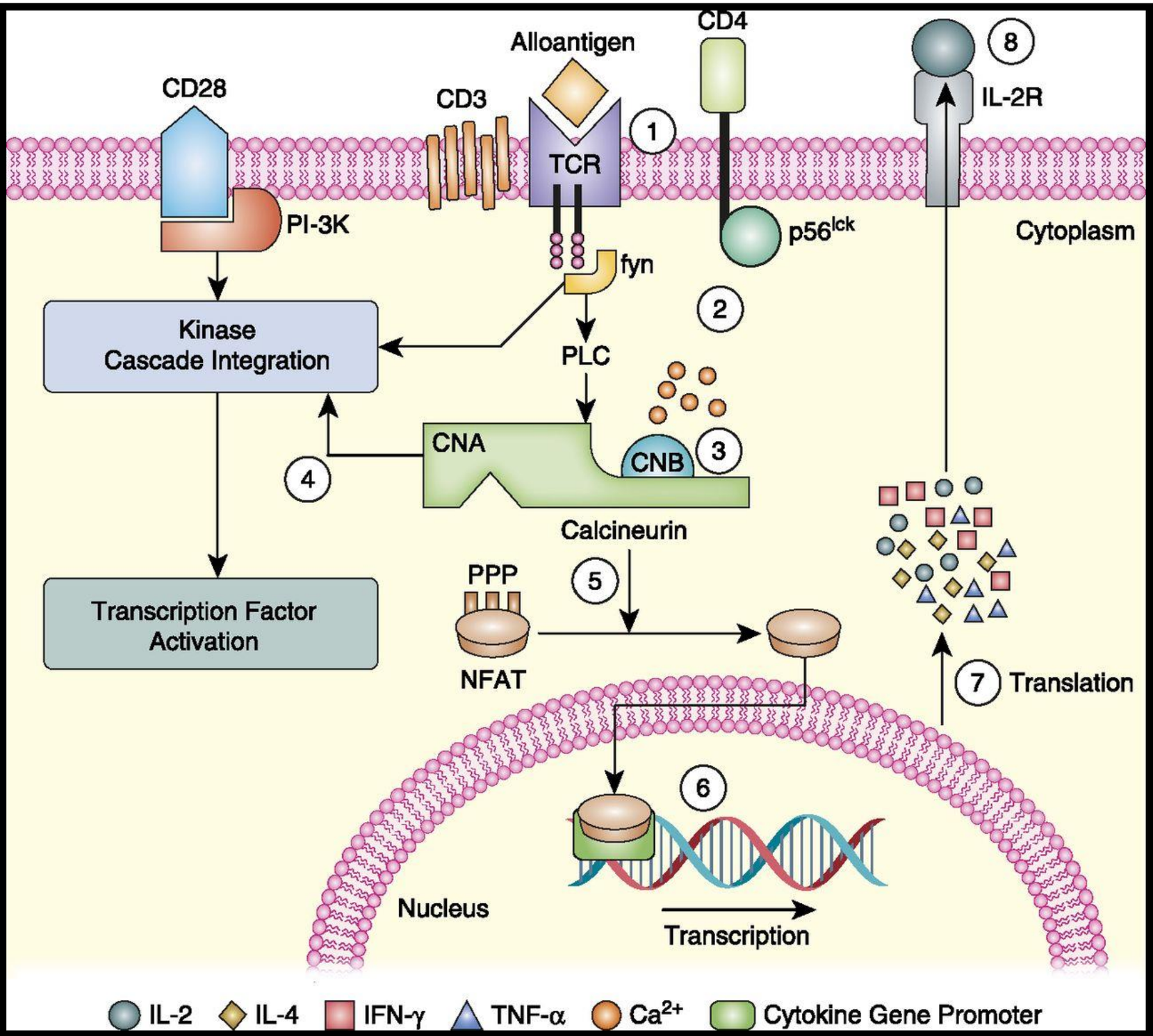
Adverse events resulting in discontinuation of trial drug	29 (13)	29 (13)
Adverse events of special interest‡		
Cancer		
Excluding nonmelanoma skin cancer§	2 (1)	0
Including nonmelanoma skin cancer§	3 (1)	0
Postinfusion reactions¶	26 (12)	29 (13)
All infections of special interest, including opportunistic infections, herpes zoster, tuberculosis, and sepsis	30 (13)	34 (15)
Serious infections	9 (4)	7 (3)
Depression, suicide, or self-injury	11 (5)	16 (7)
C-SSRS suicidal ideation or behavior during trial intervention	7 (3)	12 (5)
Death	6 (3)	5 (2)
Fatal serious adverse events that began during trial intervention	4 (2)	3 (1)
Fatal serious adverse events that did not begin during trial intervention	2 (1)	2 (1)

BLM for LN: Final thoughts

- Appears to be an effective (for specific populations) add-on therapy to MMF without any concerning safety signal at the population-level
- Dosing different that SLE:
  - IV: 10 mg/kg at 2 wk intervals x 3 doses, then q4wks
  - SC: 400 mg weekly x 4 doses, then 200 mg weekly
- Lack of effect in CyC group: Racial differences? Bias in CyC usage?
- Despite length of trial, likely too short to evaluate for renal damage (I'm sure it'll be coming though)
- Cost considerations: 42% of SLE patients have issues with treatment costs (Lupus and Allied Diseases Association LFoA, and the Lupus Research Alliance,. Lupus: Patient Voices. http://lupuspfdd.org/LupusPatientVoicesFINAL.pdf. Published 2018. Updated September 25, 2017)

Voclosporin: new calcineurin inhibitor (CNI)

CNIs bind intracellular cyclophilins, which bind and inhibit calcineurin and subsequent NFAT activation in T cells

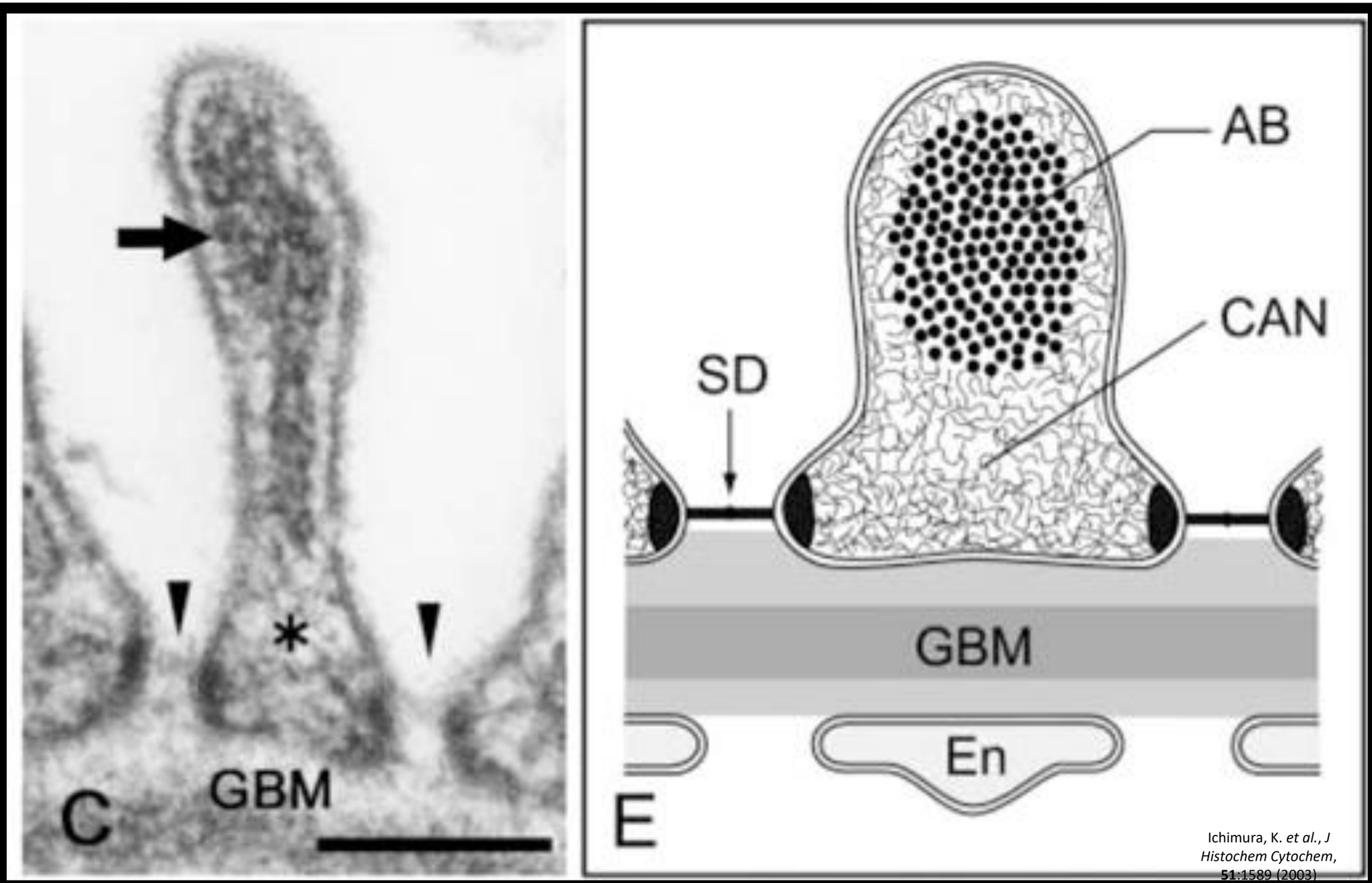


- Reduces cytokine production
  - IL-2
  - IL-4
  - TNF-α
  - IFN-γ
- Reduces T cell proliferation
- Reduces surface CD40L (implications in B cell activation during germinal center reactions)

Azzi *et al.*, *J Immunol*, **191**:5785 (2013)

Voclosporin: new calcineurin inhibitor (CNI)

CNIs may also exert direct effects on the podocyte actin cytoskeleton, which reinforces normal foot process morphology



Ichimura, K. *et al.*, *J Histochem Cytochem*, **51**:1589 (2003)

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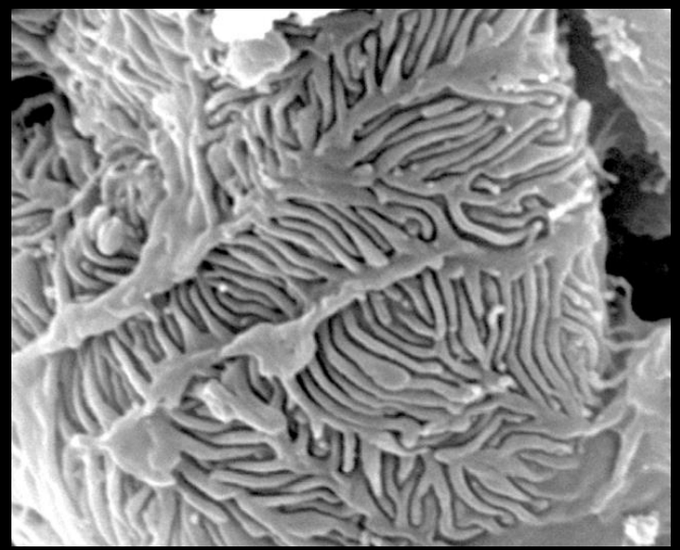
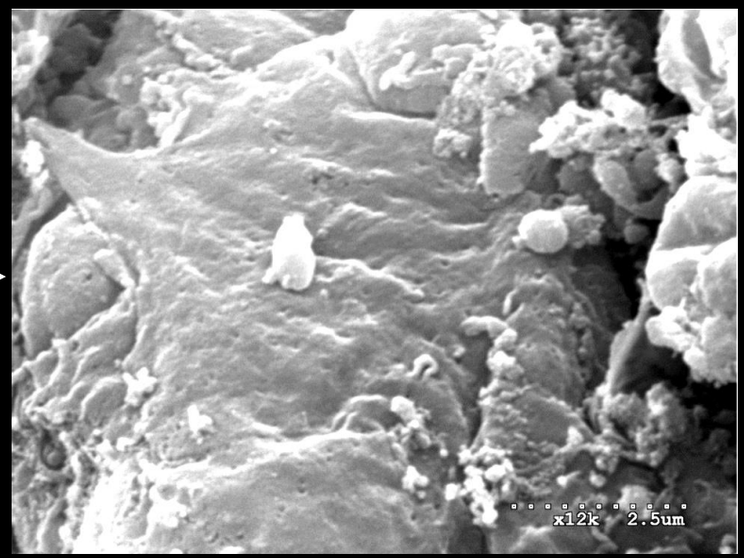


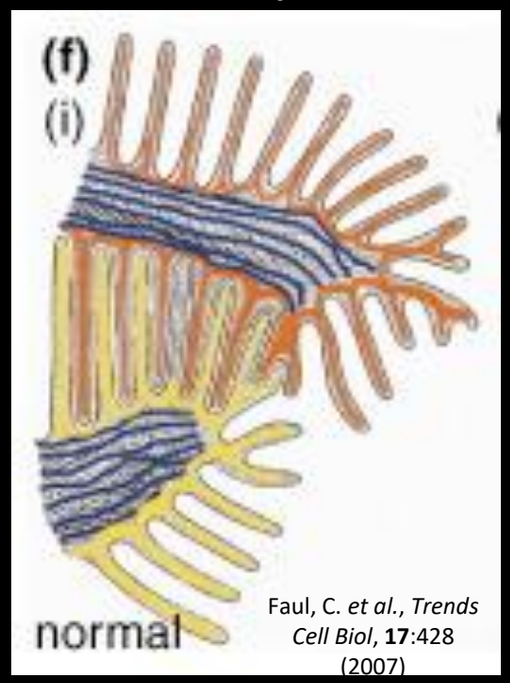
Normal foot processes

Podocyte injury

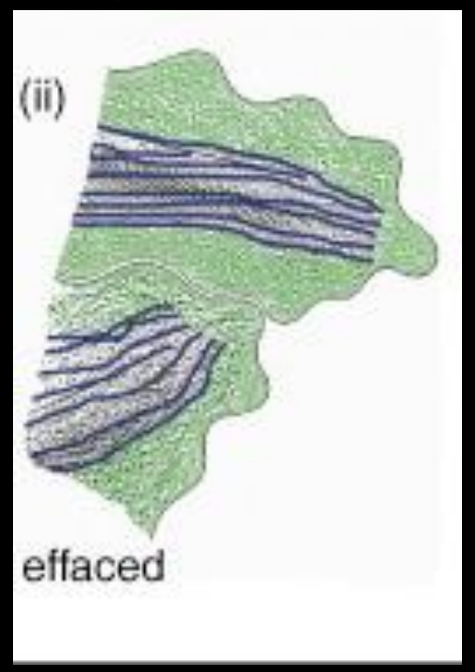
Voclosporin



Foot process effacement



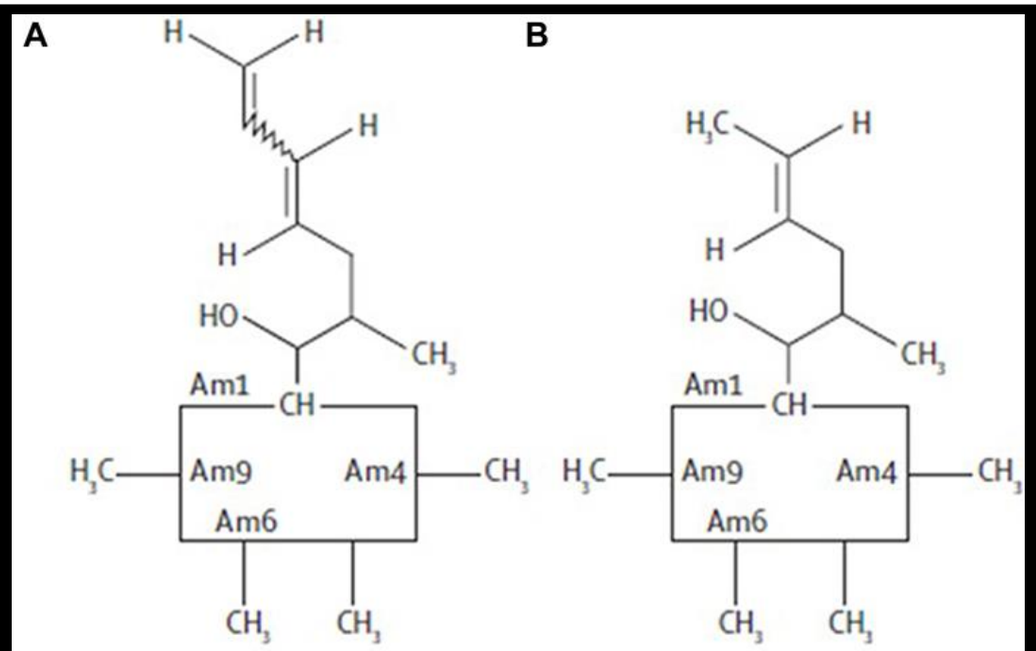
Faul, C. *et al.*, *Trends Cell Biol*, **17**:428 (2007)



Faul *et al.*, *Trends Cell Biol*, **17**:428 (2007)

Voclosporin: new calcineurin inhibitor

Simple addition of methyl group to aa 1 of cyclosporin confers several-fold reduction in EC_{50}, also no need for drug level monitoring



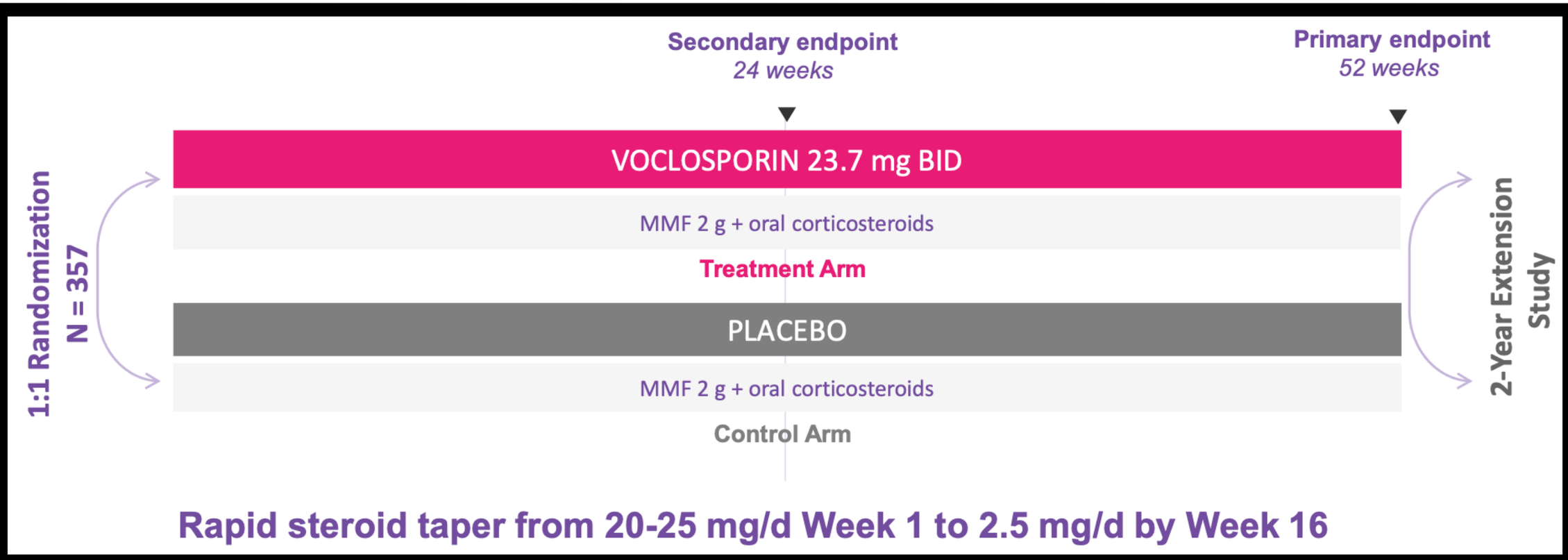
Voclosporin Cyclosporin

Immune function	EC_{50} (ng/ml)		*P*
	Cyclosporine	ISA 247 Voclosporin	
[^{3}H]-TdR incorporation assay	766.03 ± 257.81	202.79 ± 59.44	0.043
PCNA expression on S/G_2M cells	494.96 ± 49.48	240.57 ± 73.04	0.043
IL-2 production in CD3$^+$ cells	537.29 ± 107.06	135.32 ± 30.43	0.043
IFN-γ production in CD3$^+$ cells	680.83 ± 198.50	177.11 ± 58.93	0.043
TNF-α production in CD3$^+$ cells	541.81 ± 117.82	138.56 ± 27.48	0.043
CD71 expression on CD3$^+$ cells	568.55 ± 228.10	169.75 ± 57.12	0.043
CD25 expression on CD3$^+$ cells	431.93 ± 132.91	137.66 ± 38.11	0.043
CD11a expression on CD3$^+$ cells	583.80 ± 86.10	266.58 ± 105.81	0.068
CD95 expression on CD3$^+$ cells	422.36 ± 67.88	190.98 ± 98.78	0.043
CD154 expression on CD3$^+$ cells	638.34 ± 201.56	248.15 ± 84.82	0.043

Li *et al.*, *Clin Pharmacol*, **12**:83 (2020)
Bîrsan *et al.*, *Transpl Int*, **17**:767 (2005)

AURORA: Study design

More aggressive steroid taper than BLISS-LN study



- 52 wk ph3, multicenter, placebo-controlled, double-blinded study
- Proliferative (60.8%, III or IV), membranous (14.3%, V), or mixed (24.9%) with uPCR ≥ 1.5 (proliferative) or 2 (membranous)
  - 357 subjects
  - 30% Asian, 36% White, 9.5% Black; 32% Hispanic
- SOC: MMF (≤ 2 gms/day)
- Glucocorticoids must be tapered to PDN 2.5 mg/day by week 16

Arriens *et al.*, EULAR E-Congress, 2020 (OP0277)

AURORA: Outcome measures

Primary outcome

CRR (Voclosporin)

- uPCR ≤ 0.5
- eGFR ≤ 20% below pre-flare value or ≥ 60 mL/min/1.73m^2
- Sustained (wks 44-52), low-dose (PDN ≤ 10 mg/day)
- No rescue medications

ORR: CRR (BLM)

- uPCR<0.5
- Normal calculated GFR (CrCl)
- Inactive urinary sediment

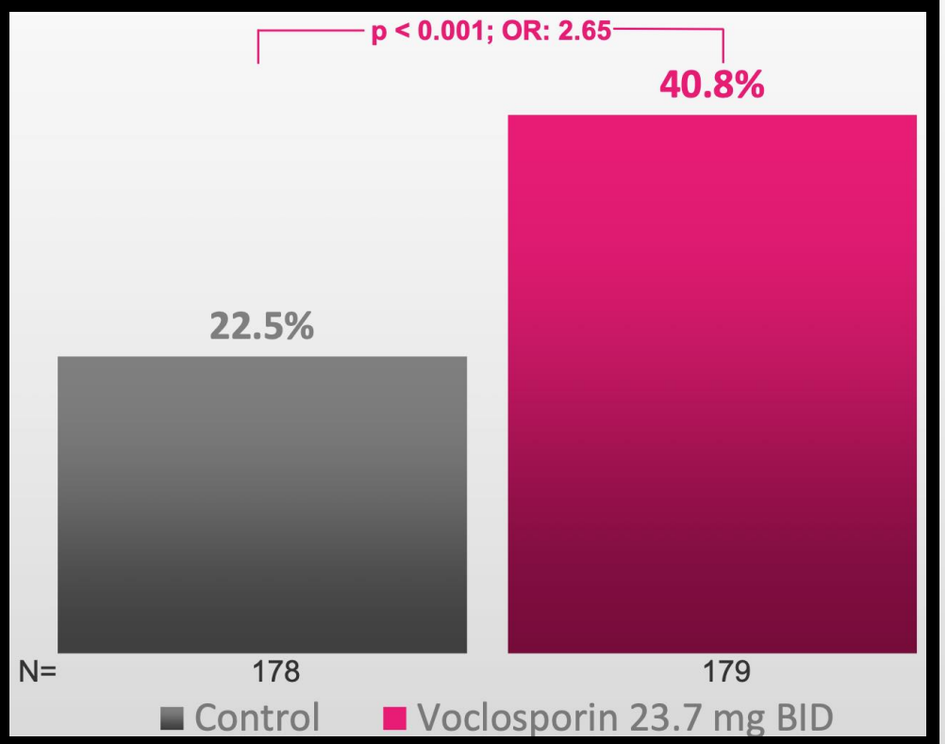
PERR (BLM)

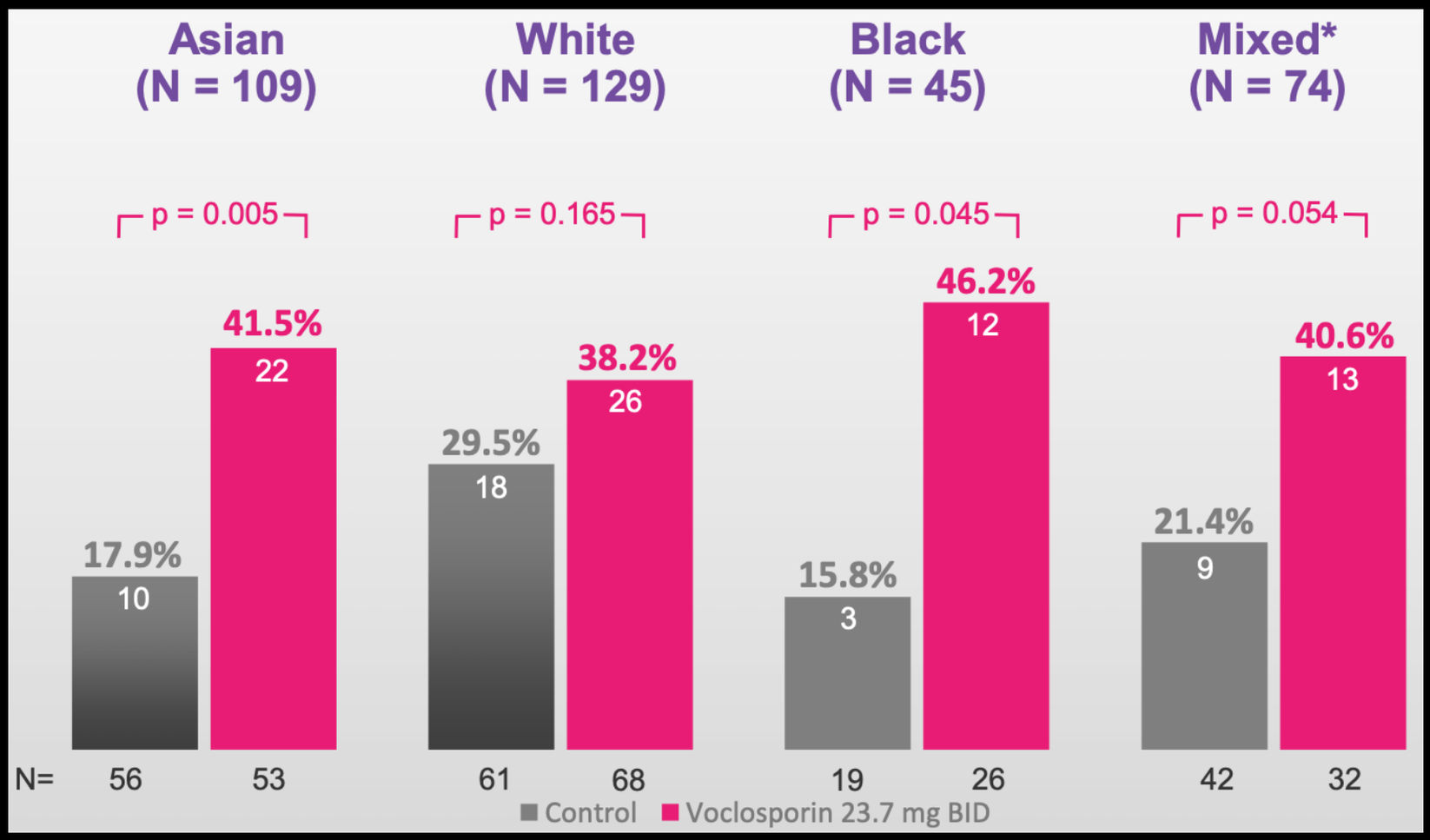
- uPCR ≤ 0.7
- eGFR ≤ 20% below pre-flare value or ≥ 60 mL/min/1.73m^2
- Not a treatment failure
- Must be consistent between weeks 100 and 104

Arriens *et al.*, EULAR E-Congress, 2020 (OP0277)
Furie *et al.*, *NEJM*, **383**:1117 (2020)

AURORA: Outcome measures

Primary endpoint driven by proteinuria reduction in Asians, Blacks, and Mixed races





Arriens *et al.*, EULAR E-Congress, 2020 (OP0277)

AURORA: Outcome measures

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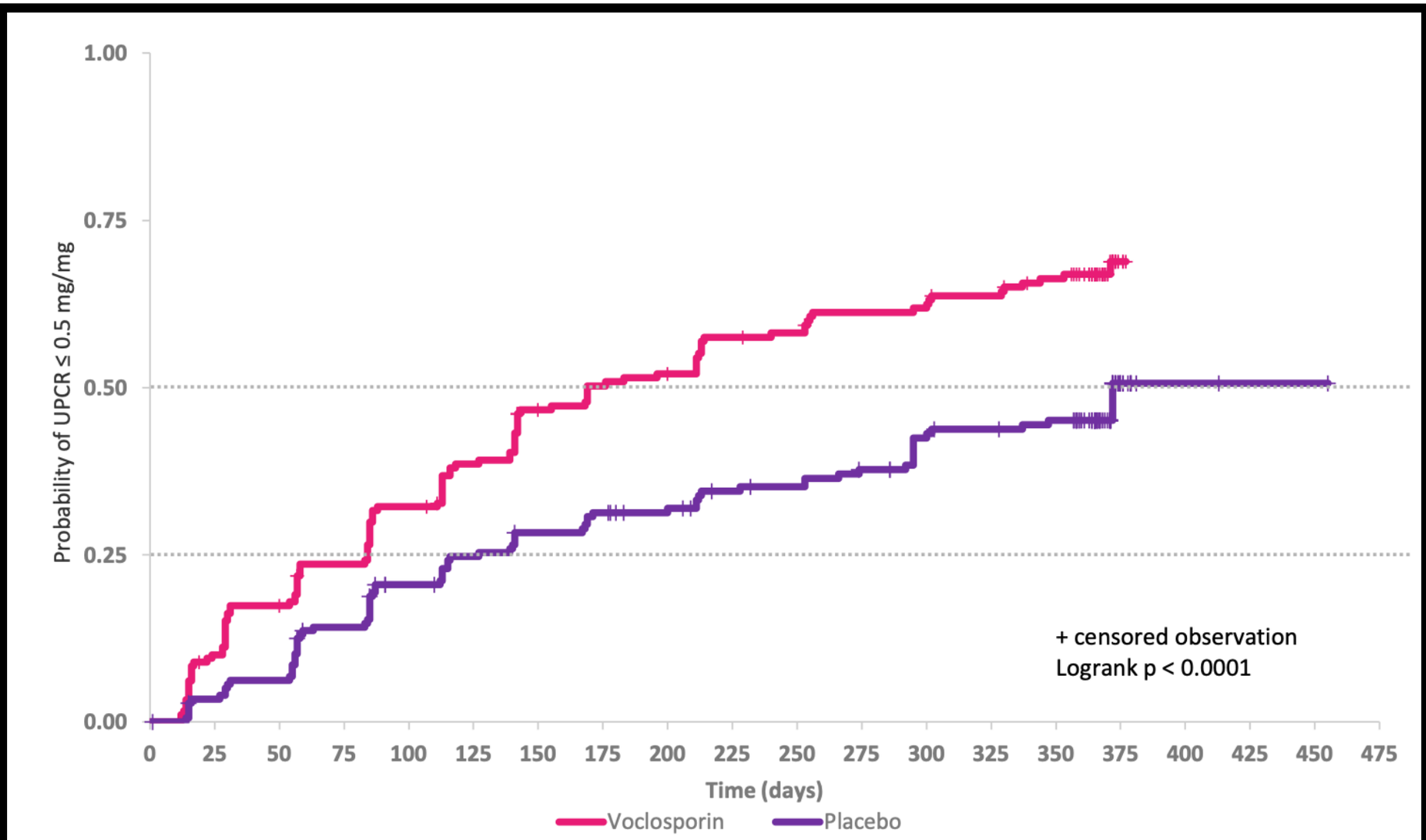


Measure	Result (Days)	p-value
Median Time (50%) to UPCR ≤ 0.5 mg/mg	Voclosporin:169 Control: 372	< 0.001
Median Time (25%) to UPCR ≤ 0.5 mg/mg	Voclosporin: 84 Control: 127	< 0.001

Arriens *et al.*, EULAR E-Congress, 2020 (OP0277)

AURORA: Outcome measures

Increased vascular tone drives the majority of adverse events (reduced eGFR and HTN)

Table 1: Adverse Reactions in ≥3% of Patients Treated with LUPKYNIS 23.7 mg Twice a Day and ≥2% Higher than Placebo in Studies 1 and 2

Adverse Reaction	LUPKYNIS 23.7 mg twice a day (n=267)	Placebo (n=266)
Glomerular filtration rate decreased*	26%	9%
Hypertension	19%	9%
Diarrhea	19%	13%
Headache	15%	8%
Anemia	12%	6%
Cough	11%	2%
Urinary tract infection	10%	6%
Abdominal pain upper	7%	2%
Dyspepsia	6%	3%
Alopecia	6%	3%
Renal Impairment*	6%	3%
Abdominal pain	5%	2%
Mouth ulceration	4%	1%
Fatigue	4%	1%
Tremor	3%	1%
Acute kidney injury*	3%	1%
Decreased appetite	3%	1%

- Decreased eGFR occurs early (within 3 mths: 71%) and largely reversible (78% improvement with dose modification)
  - 6 of 70 subjects with reduced eGFR after 3 mths of voclosporin discontinuation
  - Dosing adjustments required for those with eGFR < 60 mL/min/1.73 m^2
- Monitoring requirements
  - eGFR: every 2 weeks for 1st month, monthly afterwards
  - BP: every 2 weeks for 1st month, as clinically indicated afterwards

Lupkynis (voclosporin) [package insert]. Victoria, Canada, Aurinia Pharmaceuticals; 2021

Voclosporin for LN: Final thoughts

- Appears to be another effective add-on therapy to MMF with some largely reversible safety signals at the population-level
- Pill burden may be a challenge for LN patients:
  - Full dose: 3 tabs PO BID
  - Think about this: patients already on HCQ (1 tab BID), MMF (4-6 tabs BID), ACEi/ARB, etc. This translates to 15-20+ tabs daily!!
- No idea about damage reduction, yet

Cost considerations for BLM and voclosporin for LN

- BLM: $9,811 1st month, $3,560 monthly thereafter
- Voclosporin: $7,686.10 monthly (wow…also includes presumed 22.5% discount)
- ICER (Institute for Clinical and Economic Review) considers a threshold of < $150,000/QALYs to be “high care value”

Treatment	Drug Cost	Total Cost	QALYs	Life Years	evLYGs
Belimumab	$ 93,465	$929,962	11.666	17.861	11.740
Standard Care-Belimumab	-	$886,343	11.180	17.478	11.180
Increment	-	$43,620	0.49	0.38	0.56
Incremental Cost-Effectiveness Ratios	-	-	$89,663	$113,847	$77,835

QALY: quality-adjusted life year, evLYG: equal value life years gained

Treatment	Drug Cost	Total Cost	QALYs	Life Years	evLYGs
Voclosporin	$215,296	$928,486	12.640	18.408	12.770
Standard Care-Voclosporin	-	$784,416	11.674	17.581	11.674
Increment	-	$144,070	0.97	0.83	1.10
Incremental Cost-Effectiveness Ratios	-	-	$149,260	$174,250	$131,528

Tice *et al.*, https://icer.org/wp-content/uploads/2020/11/ICER_Lupus-Nephritis_Final-Evidence-Report_041621.pdf (2021)

TULIP trials

Treatment of Uncontrolled Lupus via the Interferon Pathway

Type I interferon inhibitor anifrolumab in active systemic lupus erythematosus (TULIP-1): a randomised, controlled, phase 3 trial

*Richard A Furie, Eric F Morand, Ian N Bruce, Susan Manzi, Kenneth C Kalunian, Edward M Vital, Theresa Lawrence Ford, Ramesh Gupta, Falk Hiepe, Mittermayer Santiago, Philip Z Brohawn, Anna Berglind, Raj Tummala, on behalf of the TULIP-1 study investigators**

Failed to achieve primary outcome

Trial of Anifrolumab in Active Systemic Lupus Erythematosus

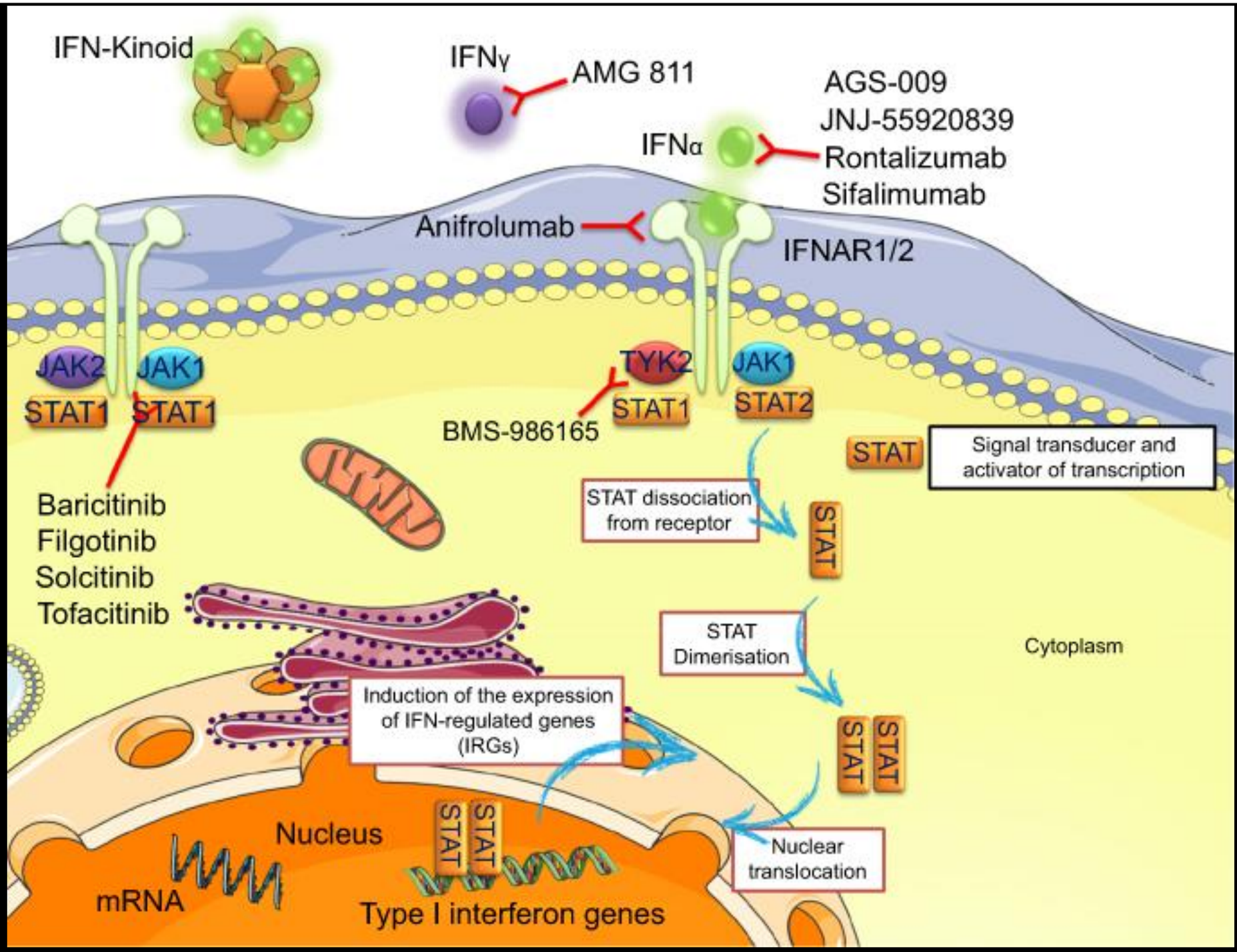
E.F. Morand, R. Furie, Y. Tanaka, I.N. Bruce, A.D. Askanase, C. Richez, S.-C. Bae, P.Z. Brohawn, L. Pineda, A. Berglind, and R. Tummala, for the TULIP-2 Trial Investigators*

Succeeded in achieving primary outcome

Why?

Anifrolumab

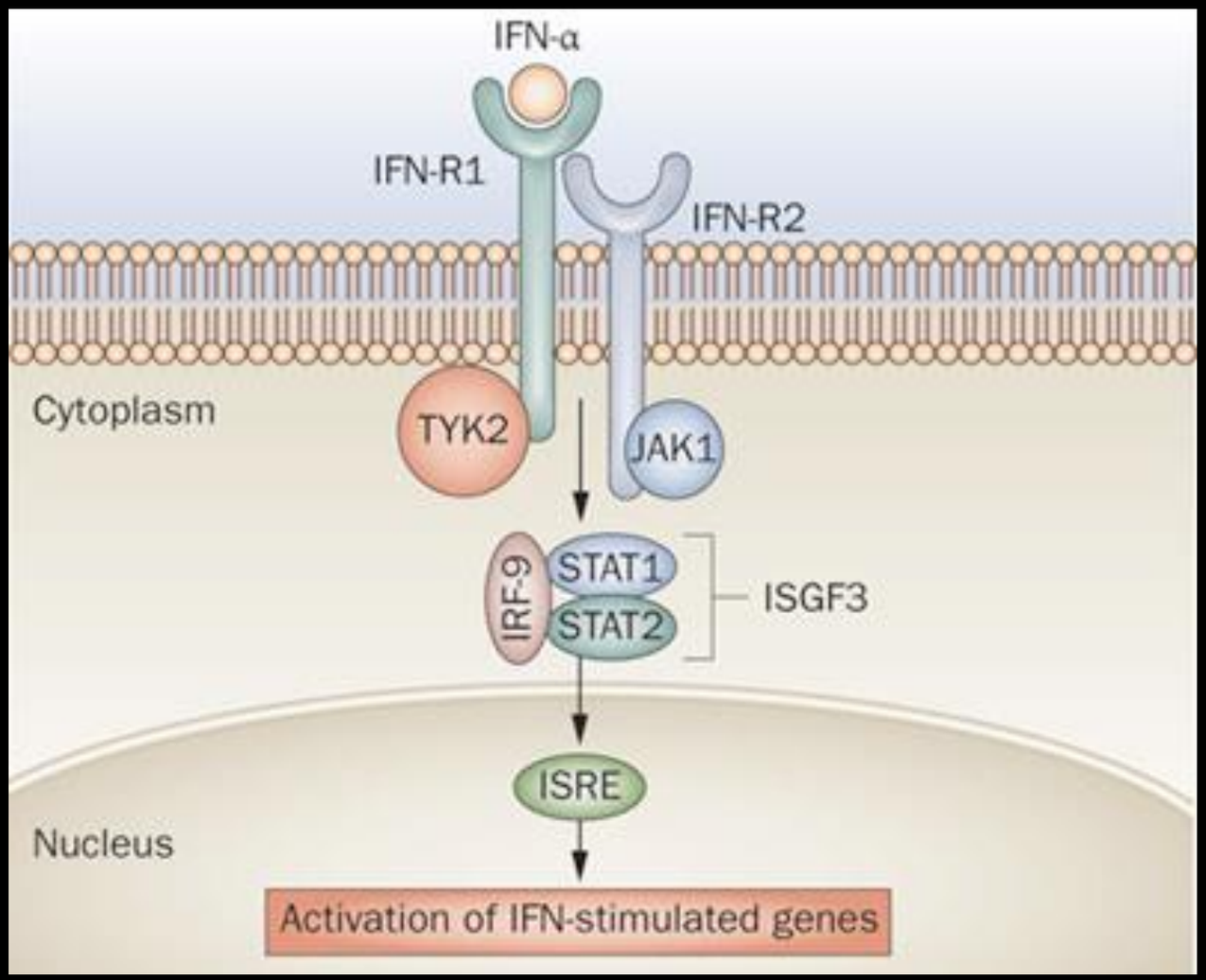
Fully human, effector-null, $IgG_1\kappa$ monoclonal antibody binding to type I IFN receptor subunit 1 (IFNAR1)



Felten *et al*., *Drug Des Dev Ther*, **13**:1535 (2019)

What are type 1 interferons?

Type 1 interferons are a large class of proteins known to induce antiviral effects



Many different types of type I interferons
(α, β, ε, κ, ω)

Type 1 interferon activates the transcription of genes with antiviral effects

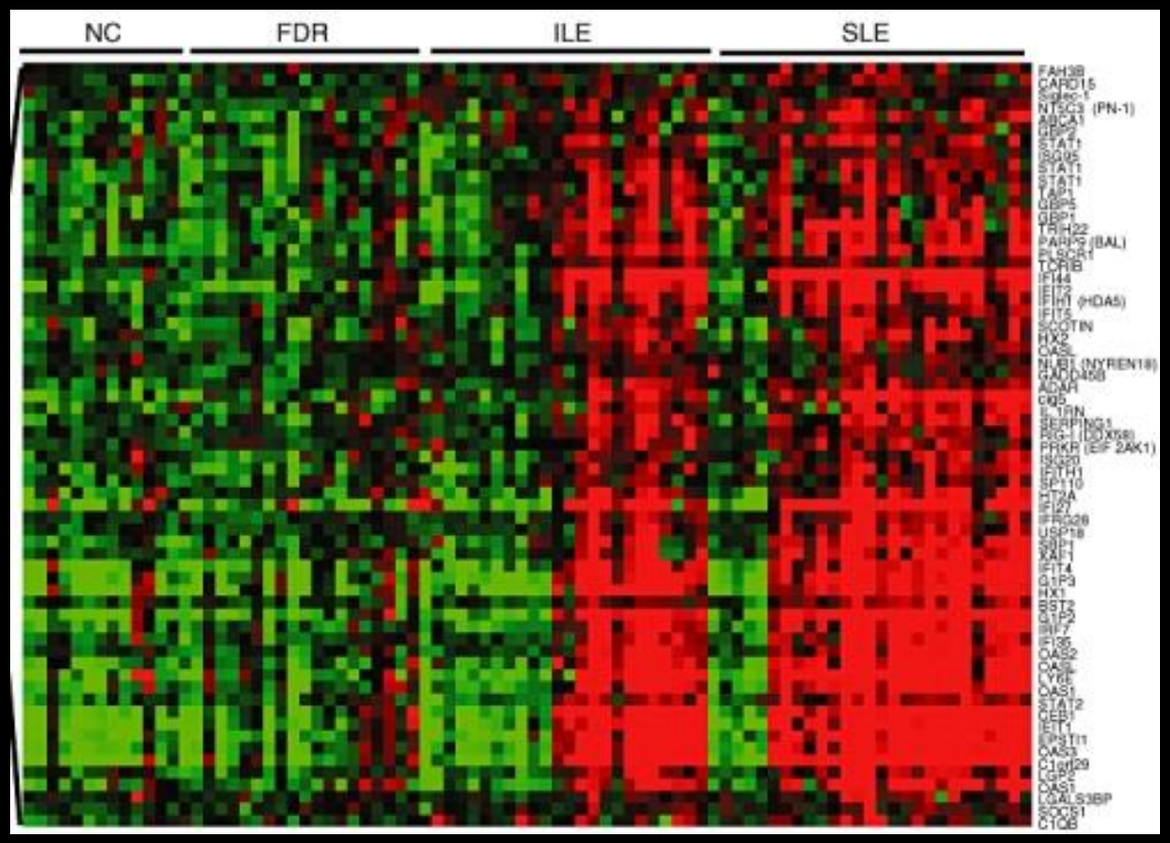
Source: plasmacytoid dendritic cells (induced by viral proteins)

Aghemo, A., *et al.*, *Nat Rev Gastro Hep.*, **7**:495 (2010)

Why target IFN-α in SLE?

Type 1 interferons (i.e. IFN-α) associates with lupus disease activity and flares

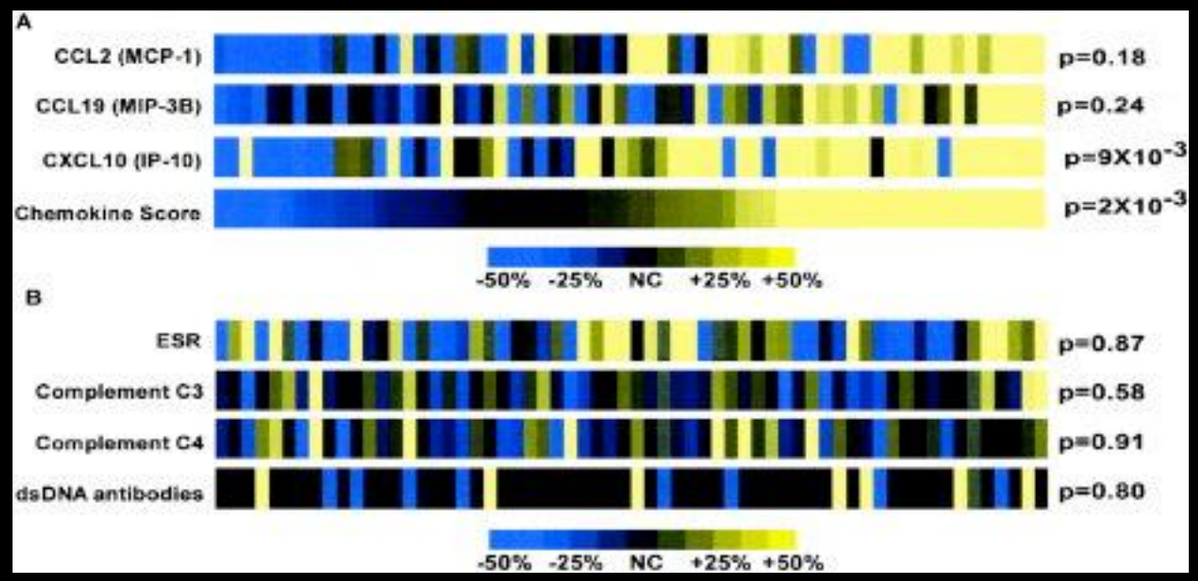
Many (80-90%) of SLE patients have elevated expression of ~100 type 1 interferon-regulated genes



Li Q.Z., *et al.*, *Clin. Exp. Immunol.*, **3**:281 (2010)

Interferon signature

Type 1 interferon response correlated closely with SLE disease activity



Bauer JW, *et al.*, *Arthritis Rheum.*, **60**:3098 (2009)

- Lupus-associated genetic variations have been shown to directly increase IFN-α levels or response to IFN-α signaling (IRF5, IRF7)
- Patients treated with IFN-α (Hep C) have developed lupus or lupus-like syndrome

TULIP-1 and TULIP-2: Essentially identical trials

Only major difference: primary outcome measures used

TULIP-1	TULIP-2
Randomized, double-blinded, placebo-controlled, parallel-group phase III	
Inclusion criteria complicated: non-neurologic, non-renal, serologically and clinically active disease on treatment	
Three arms: placebo, 150 mg, 300 mg	Two arms: placebo, 300 mg
123 sites/18 countries (460 pts)	119 sites/16 countries (362 pts)
Primary outcome: SRI-4	Primary outcome: Originally SRI-4, changed to BICLA mid-trial

SRI-4 versus BICLA

SRI-4: SLEDAI for improvement, BILAG for worsening

BICLA: BILAG for improvement, SLEDAI for worsening

SRI-4

- 4-point improvement in SLEDAI
- No worsening in BILAG (one B in any organ domain tolerated)
- No worsening in PGA (<0.3 point increase tolerated)

BICLA

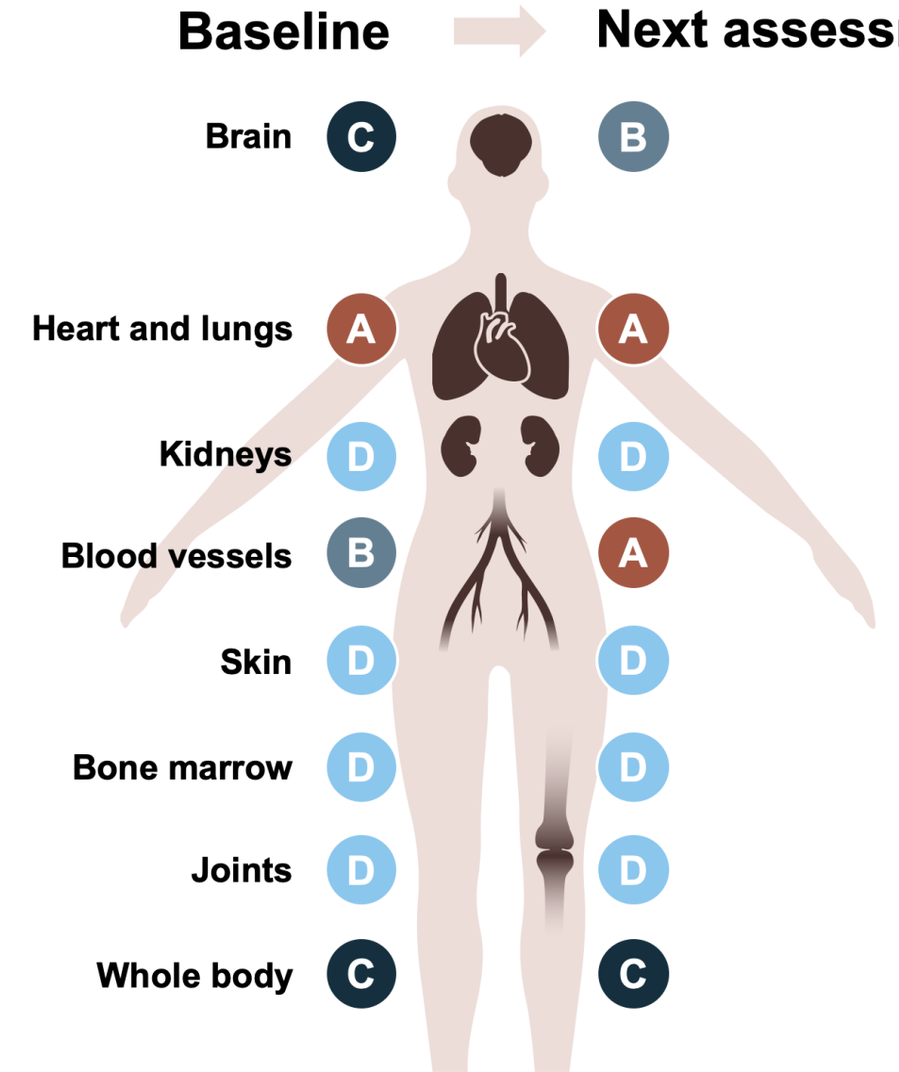
- Reduction of all BILAG A and B
- No worsening of other BILAG domains
- No worsening in SLEDAI
- No worsening in PGA (<0.3 point increase tolerated)

BILAG

British Isles Lupus Activity Group

Each organ domain assigned a category of A through E

A	Requires prednisone >20 mg/day or immunosuppressive
B	Requires antimalarials, NSAID or prednisone <20 mg/day
C	Mild, stable disease
D	Domain previously affected, currently inactive
E	Domain never involved



SLEDAI

Systemic Lupus Erythematosus Disease Activity Index

SLE Disease Activity Index (SLEDAI) assesses 24 manifestations of SLE

Each given a score weighted 1, 2, 4, or 8

Manifestations are either present or absent (i.e., improvement or worsening not measured)

Maximum score of 105, few score higher than 45

- Low score = less active SLE
- High score = more active SLE

Weight	Check if Present	Descriptor
8	☐	Seizure
8	☐	Psychosis
8	☐	Organic brain syndrome
8	☐	Visual disturbance
8	☐	Cranial nerve disorder
8	☐	Lupus headache
8	☐	CVA
8	☐	Vasculitis
4	☐	Arthritis
4	☐	Myositis
4	☐	Urinary casts
4	☐	Hematuria
4	☐	Proteinuria
4	☐	Pyuria
2	☐	Rash
2	☐	Alopecia
2	☐	Mucosal ulcers
2	☐	Pleurisy
2	☐	Pericarditis
2	☐	Low complement
2	☐	Increased DNA binding
1	☐	Fever
1	☐	Thrombocytopenia
1	☐	Leukopenia

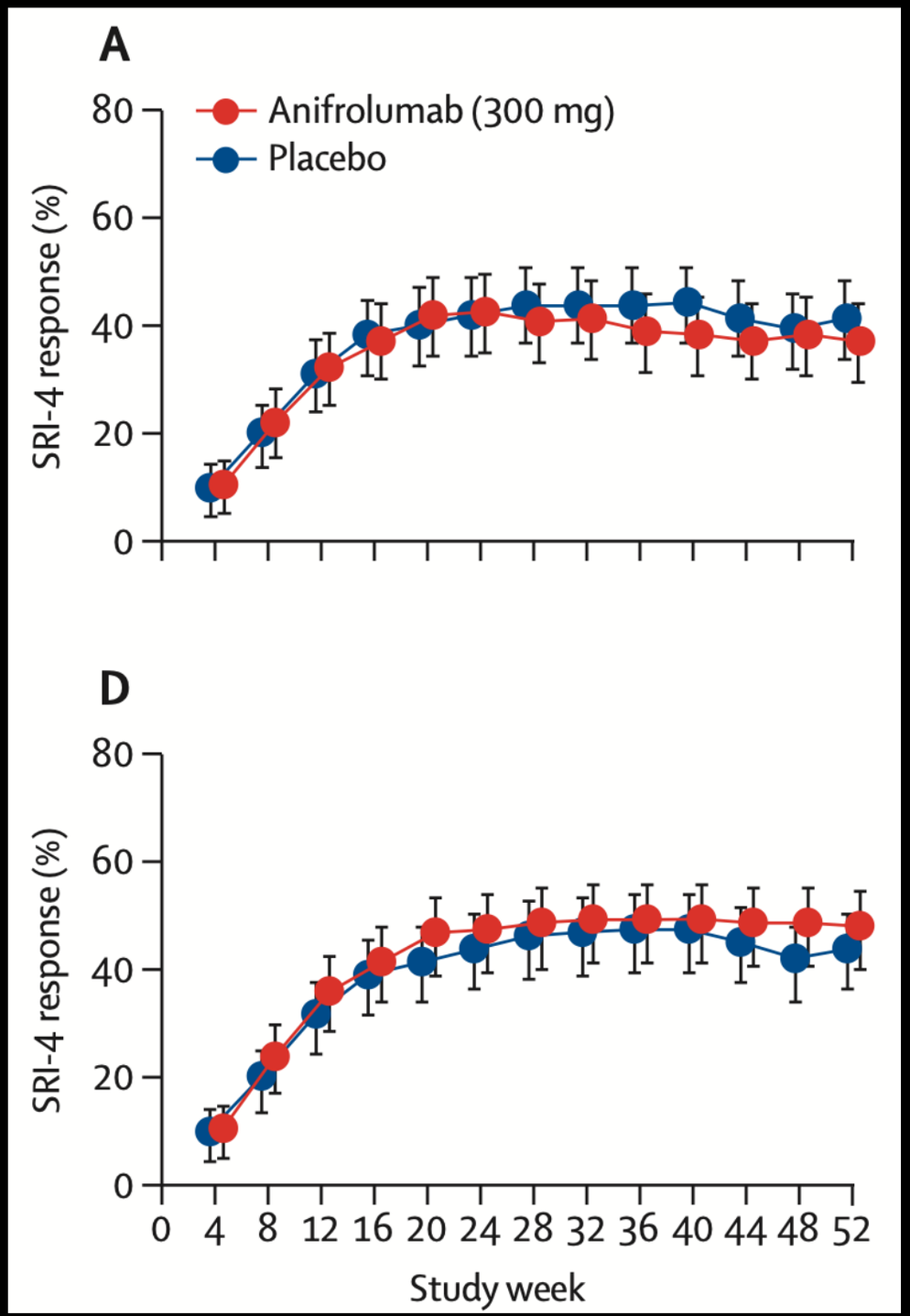
PGA

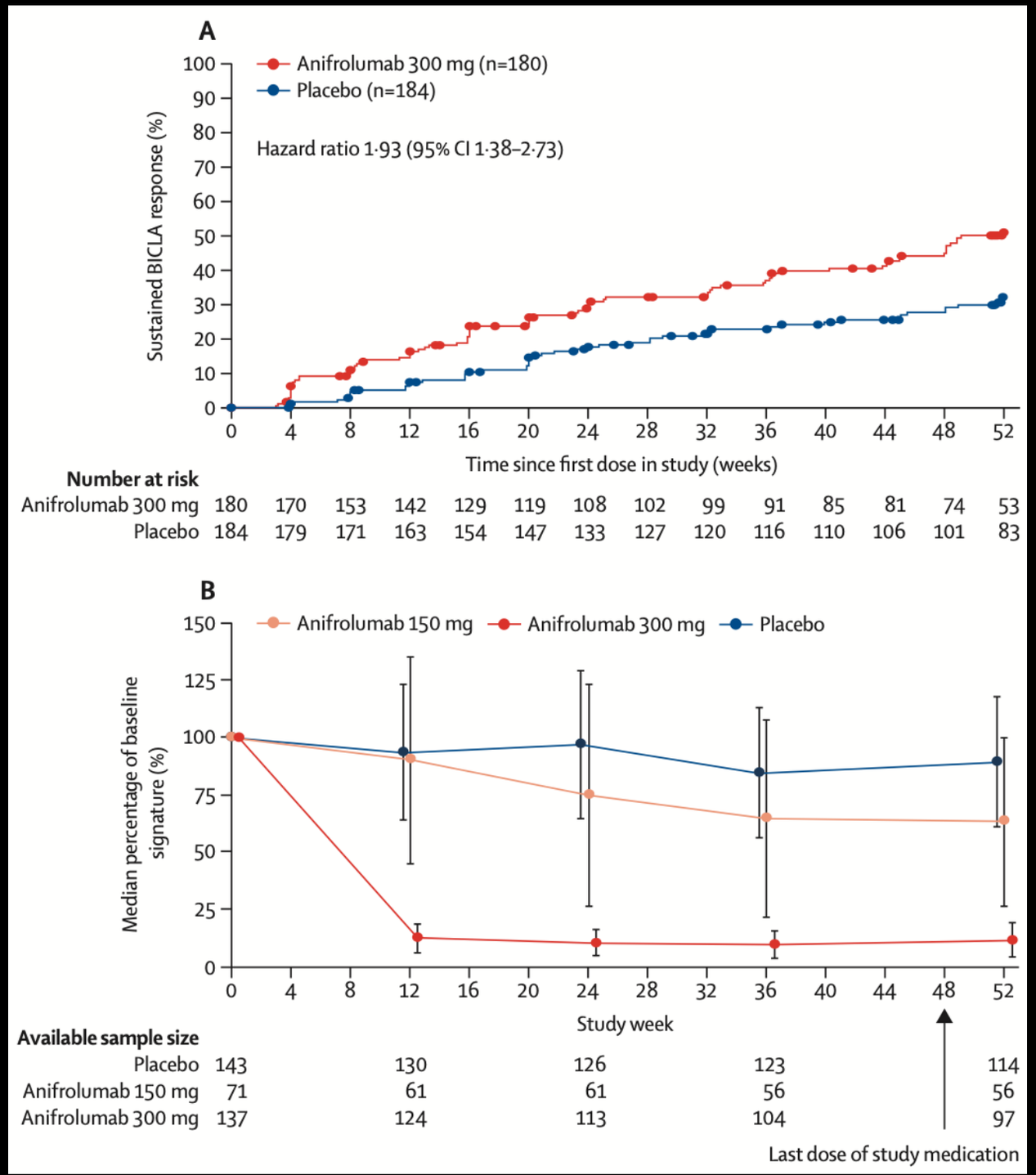
Physician’s Global Assessment

- Assesses the patient’s overall condition
- A 10-cm visual analog scale ranging from 0 to 3 (higher score = more severe disease activity)

TULIP-1 results

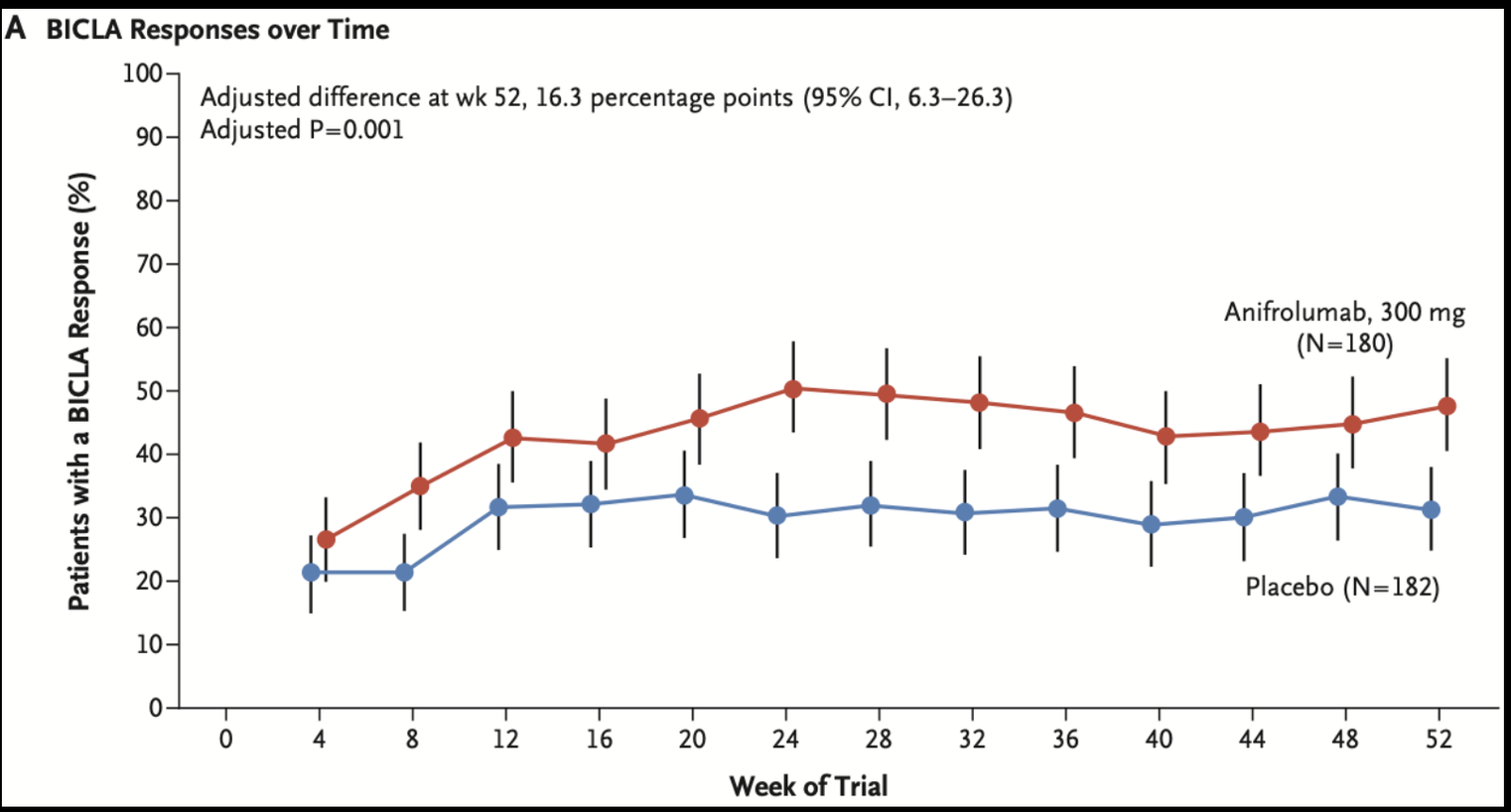
SRI-4 did not meet statistical significance, but BICLA did



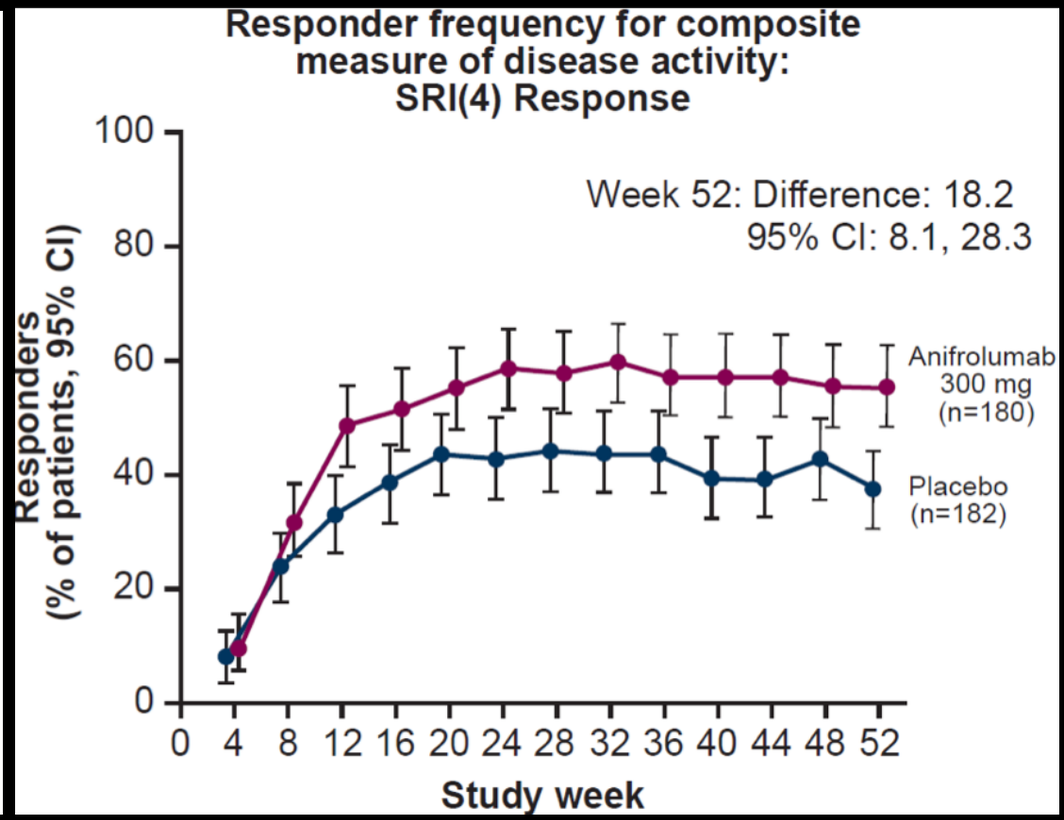


TULIP-2 results

Both BILCA and SRI-4 met statistical significance



NNT = 6



NNT = 6

SRI-4 versus BICLA

SRI-4: SLEDAI for improvement, BILAG for worsening
BICLA: BILAG for improvement, SLEDAI for worsening

SRI-4

- 4-point improvement in SLEDAI
- No worsening in BILAG (one B in any organ domain tolerated)
- No worsening in PGA (<0.3 increase tolerated)

To demonstrate improvement SRI-4, need complete resolution of the affected domain

BICLA

- Reduction of all BILAG A and B
- No worsening of other BILAG domains
- No worsening in SLEDAI
- No worsening in PGA (<0.3 point increase tolerated)

To demonstrate improvement BICLA, only need partial resolution of the affected domain

TULIP-2 results

Infections main concern with anifrolumab

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)

Take home points from TULIP studies

- Anifrolumab will likely obtain FDA-approval Q4 2020
- Difficult to say what to do with holding anifrolumab during viral infections
  - Did someone say COVID-19? IFN responses essential for better COVID-19 outcomes
- Nuances in outcome measures will define whether a future SLE investigation drug will demonstrate effectiveness