EULAR 2026

Systemischer Lupus erythematodes

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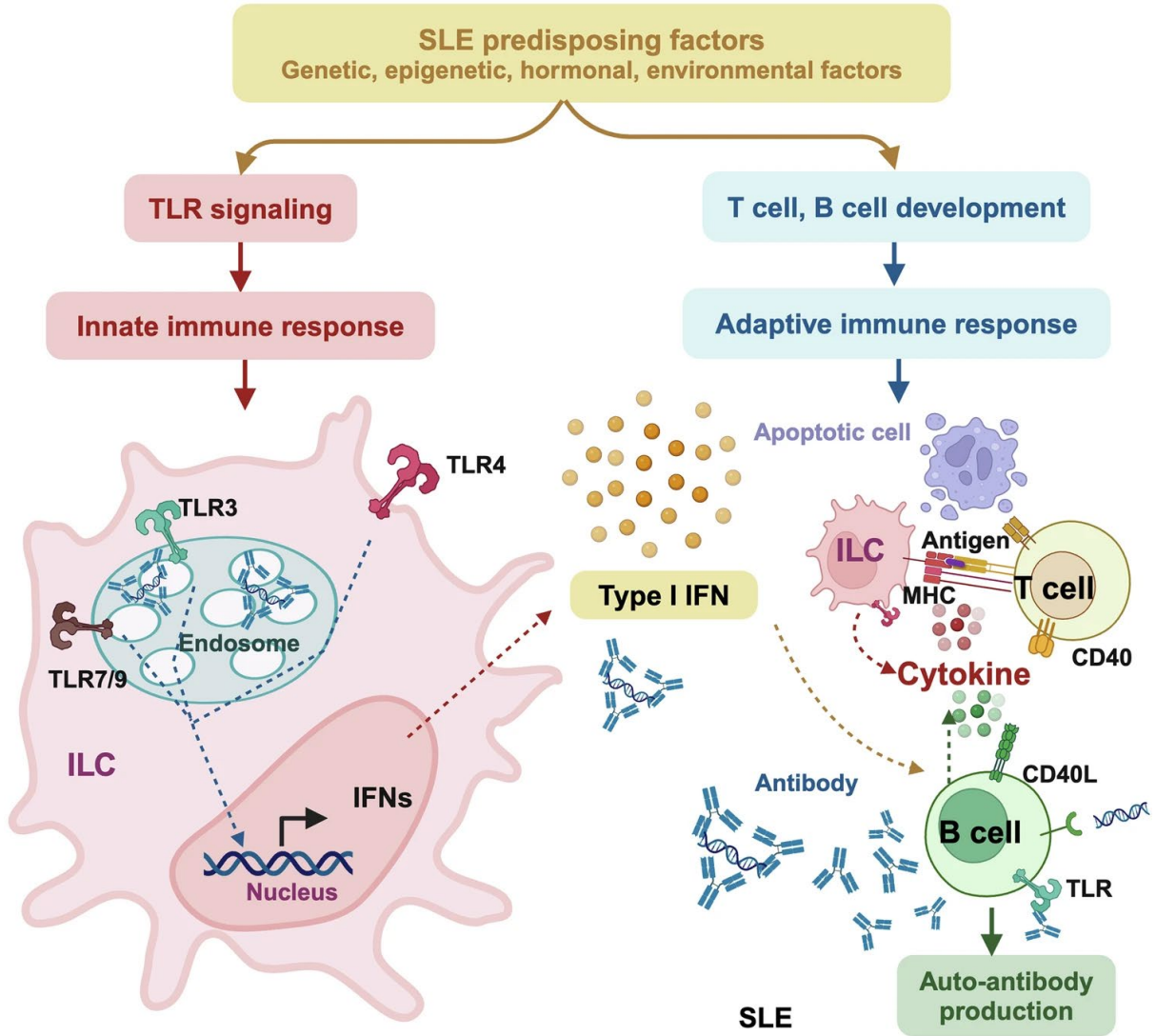
Rheumatologie · Universitätsspital Basel

3.–6. Juni 2026

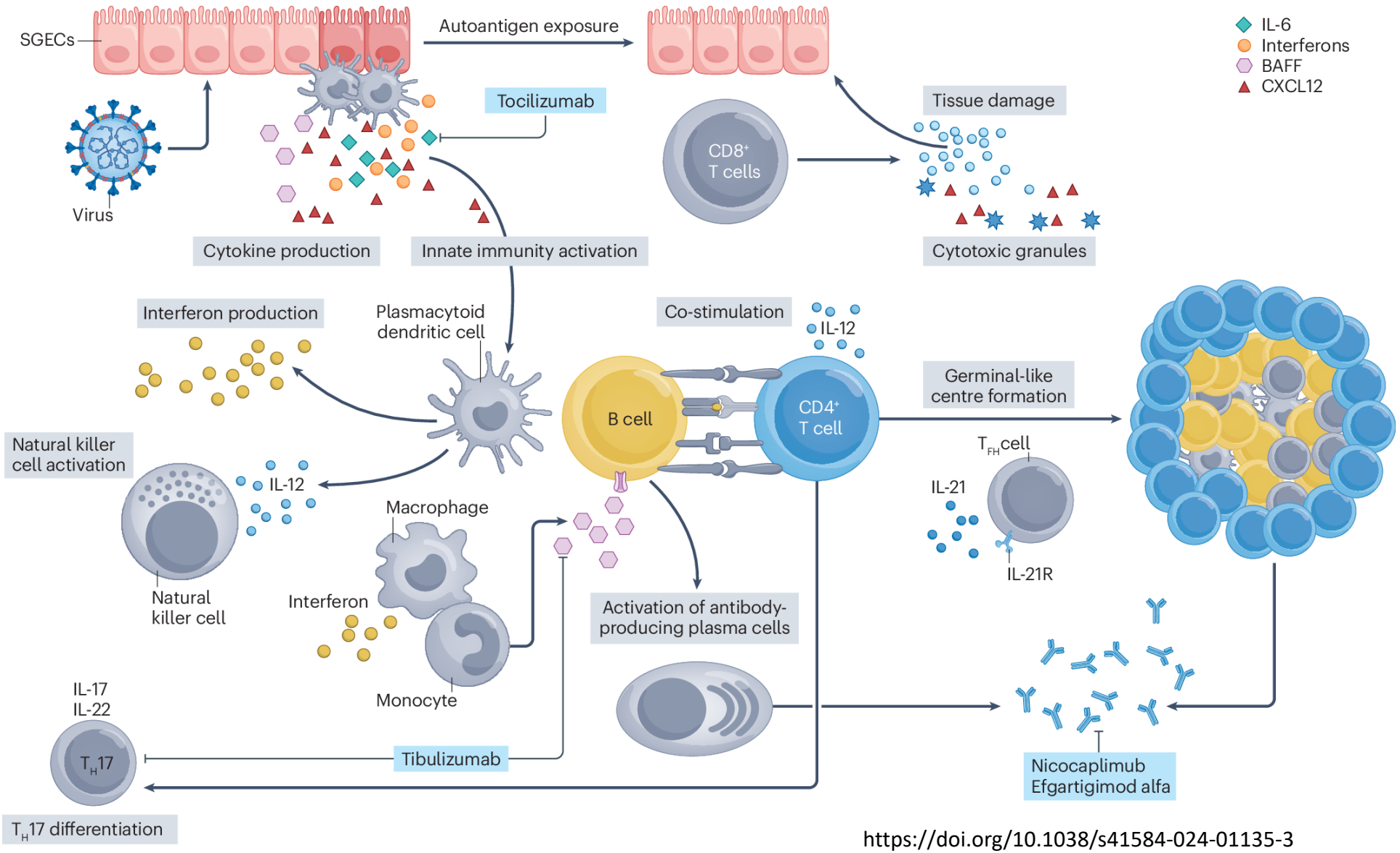
Ribonukleinsäure



JAK STAT pathway

doi.org/10.1038/s41392-025-02168-0

Sjögren



https://doi.org/10.1038/s41584-024-01135-3

SJÖGREN'S DISEASE

Mitochondrial dsRNA Accumulation via Defective m⁶A Regulation Drives the IFN Signature in Sjögren's Disease

Salivary gland epithelial cells (SGECs) from SjD patients & controls · METTL3 inhibition + REXO2 knockdown · RNA-seq, IF, qPCR, ELISA

Why do Sjögren's epithelial cells chronically produce IFN without any virus?

MECHANISM - 4 steps

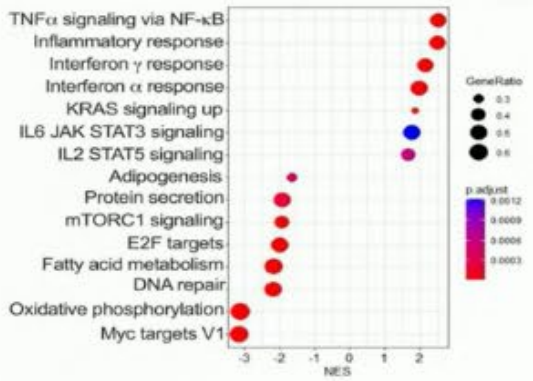
① METTL3 ↓	*m⁶A writer deficient in SjD epithelial cells*
② REXO2 ↓	*Mitochondrial exonuclease not expressed → RNA surveillance fails*
③ mt-dsRNA accumulates	*Endogenous mitochondrial dsRNA builds up intracellularly*
④ IFN-I + IFN-II	*Type I and II interferon transcriptional program activated*

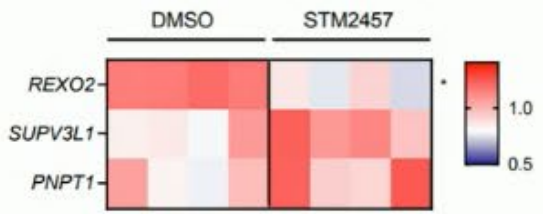
✓ **IN VIVO** *REXO2 protein reduced in EpCAM⁺ salivary gland epithelial cells of SjD patients vs controls (immunofluorescence, minor salivary gland biopsies)*

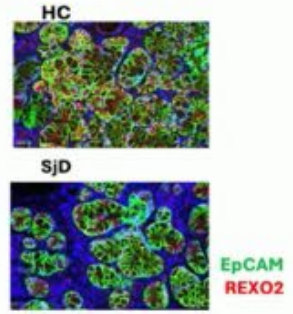
WHY IT MATTERS

The IFN signature in Sjögren's has no clear cause. This study shows the culprit could be endogenous: mitochondrial dsRNA leaking from poorly regulated epithelial cells. REXO2 emerges as a targetable checkpoint, restoring it could silence IFN at the source.

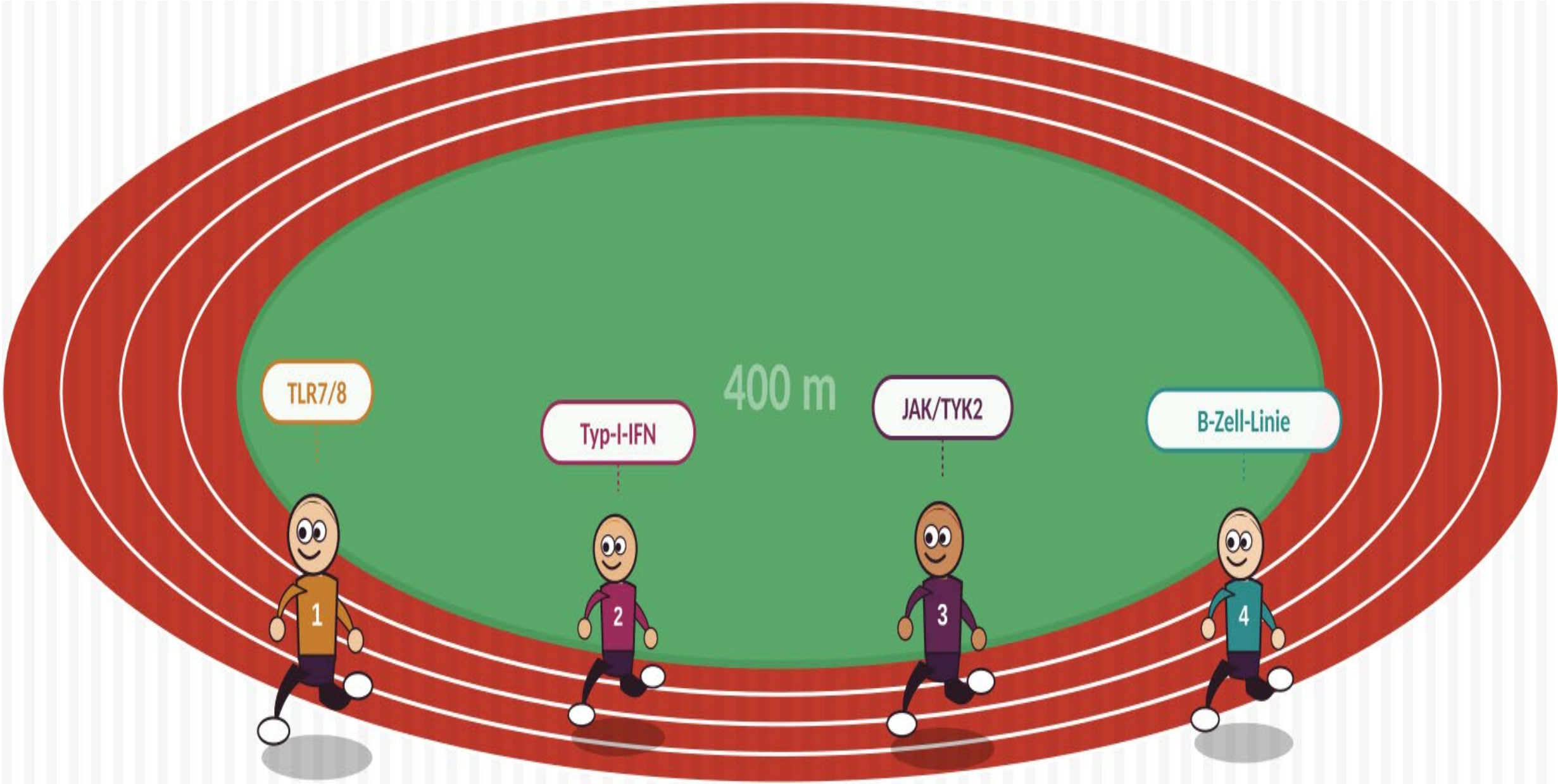
Poly(I:C)+STM2457vs.Poly(I:C)







Arco-Hierves A. et al. · Univ. Paris-Saclay / INSERM / Hôpital Bicêtre


TLR7/8
Typ-I-IFN
400 m
JAK/TYK2
B-Zell-Linie
1
2
3
4

TREAT-TO-TARGET IN SLE

LLDAS und DORIS-Remission

LLDAS

Lupus Low Disease Activity State · Franklyn et al. 2016

SLEDAI-2K ≤ 4

ohne Aktivität in Niere, ZNS, Vaskulitis, Fieber oder hämolytischer Anämie

Keine neue Aktivität

kein neues SLEDAI-Merkmal seit letzter Visite

PGA ≤ 1 (0–3)

ärztliche Gesamteinschätzung

Prednison ≤ 7,5 mg/d

aktuelle Tagesdosis oder Äquivalent

Stabile Immunsuppression

gut tolerierte Erhaltungsdosen

DORIS-Remission

Definitions Of Remission In SLE · 2021

cSLEDAI = 0

klinischer SLEDAI ohne anti-dsDNA/Komplement, vollständig null

PGA < 0,5 (0–3)

praktisch keine ärztlich beurteilte Aktivität

Prednison ≤ 5 mg/d

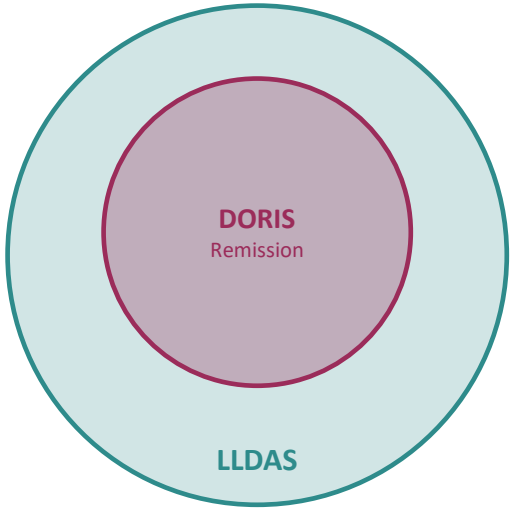
niedrigere Schwelle als LLDAS

Stabile Erhaltungstherapie

Antimalarika, Immunsuppressiva, Biologika erlaubt

On- vs. off-Therapie

Remission-off-therapy: nur Antimalarika erlaubt

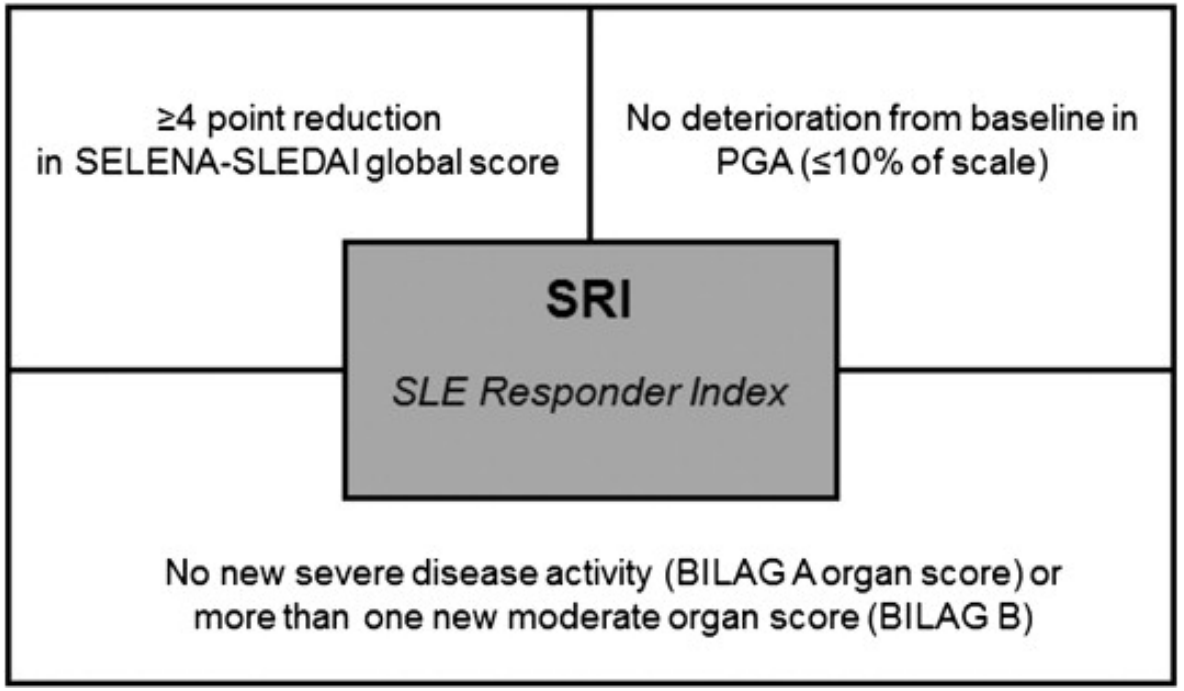


DORIS ist strenger definiert und liegt innerhalb von LLDAS

Klinische Relevanz: Beide Targets sind in rezenten Studien (Nipocalimab/JASMINE-SLE, Anifrolumab, Deucravacitinib) als Endpunkte etabliert und mit weniger Schüben sowie geringerer Organschaden-Akkumulation assoziiert.

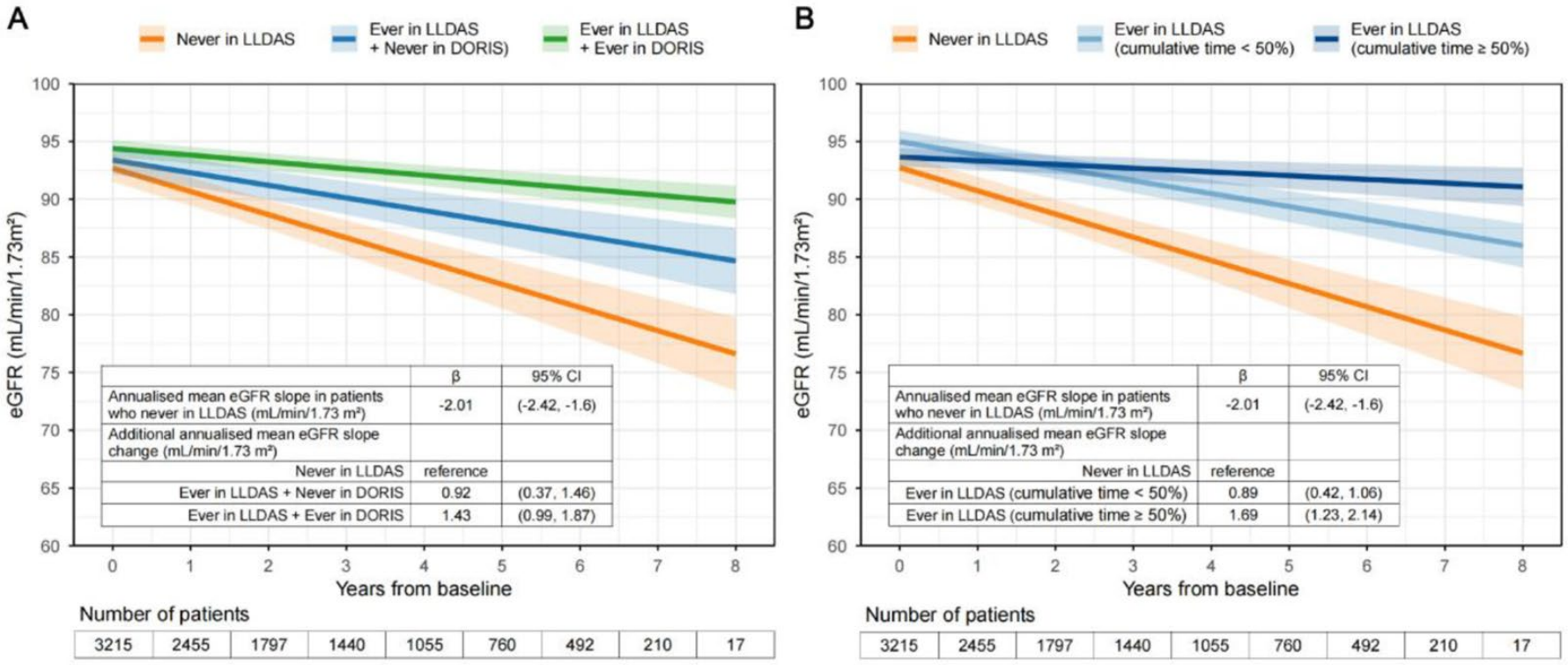
SLE Responder Index 4 (SRI-4)

Kombinierter Endpunkt aus drei Komponenten – SRI-4 gilt nur als erreicht, wenn alle drei Kriterien gleichzeitig erfüllt sind



LONGITUDINAL ANALYSIS OF KIDNEY FUNCTION DECLINE IN SYSTEMIC LUPUS ERYTHEMATOSUS: CORRELATION WITH LOW DISEASE ACTIVITY AND PATIENT CHARACTERISTICS **OP0338**

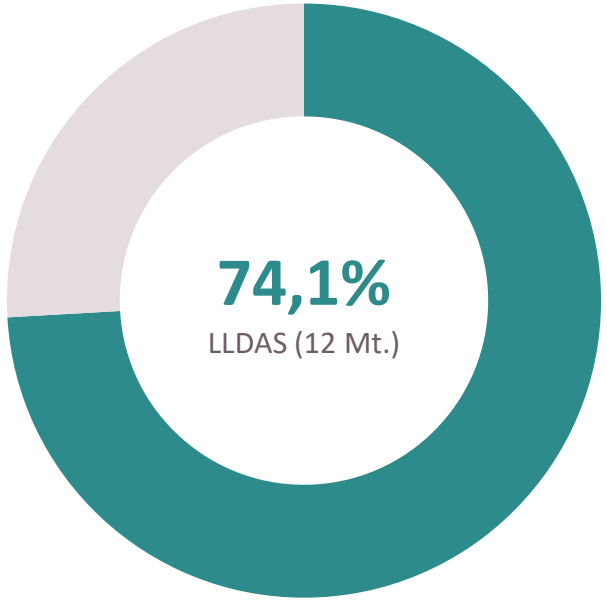
-Asia Pacific Lupus Collaboration (APLC)
-3215 patients (median disease duration: 8 years median age: 39.0 years, female 91.8%, Asian 88.1%,

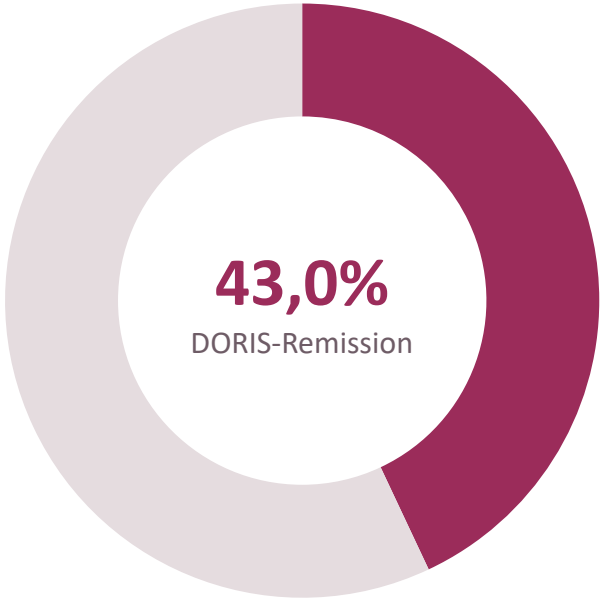


Sex, Asian ethnicity, age at baseline, SLE duration at baseline, GDP per capita, diabetes (time-varying, from absent to present), baseline renal involvement, baseline eGFR categories, and treatment target attainment during observation period were considered in multivariable mixed-linear model for eGFR slope.

Anifrolumab in der Versorgungsrealität

OP0342 / OP0219 ASTER · multinationale, observationelle Post-Launch-Studie · bis 12 Monate Anifrolumab + Standardtherapie · n=135



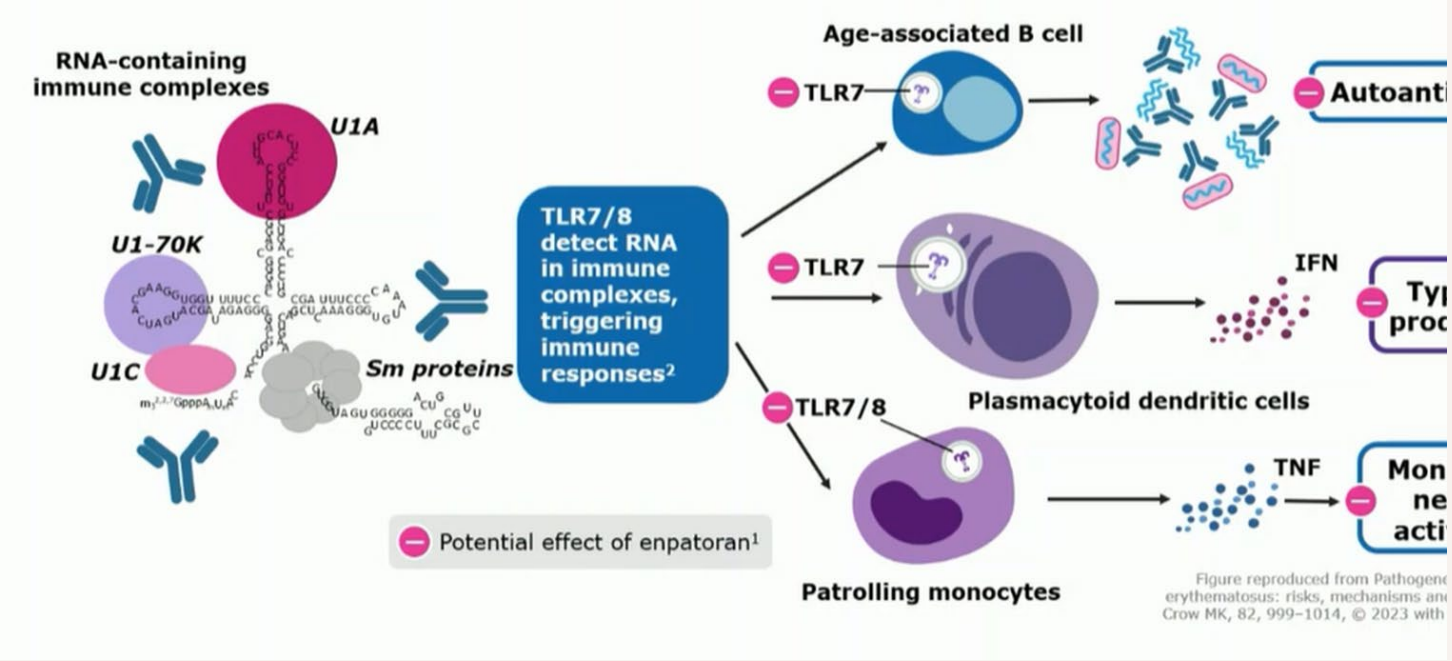


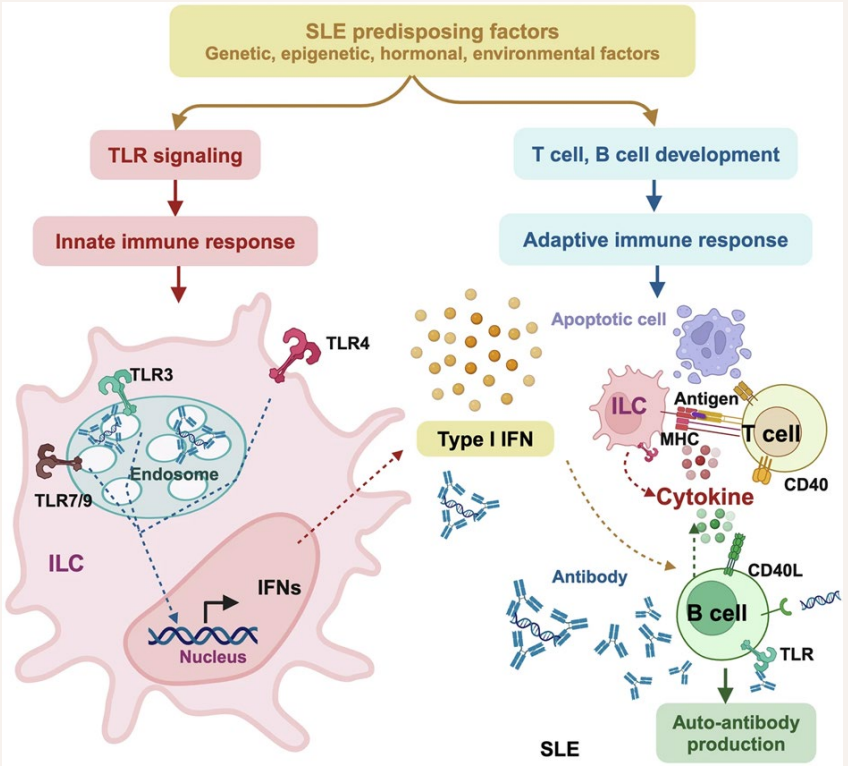
Was die Daten zeigen

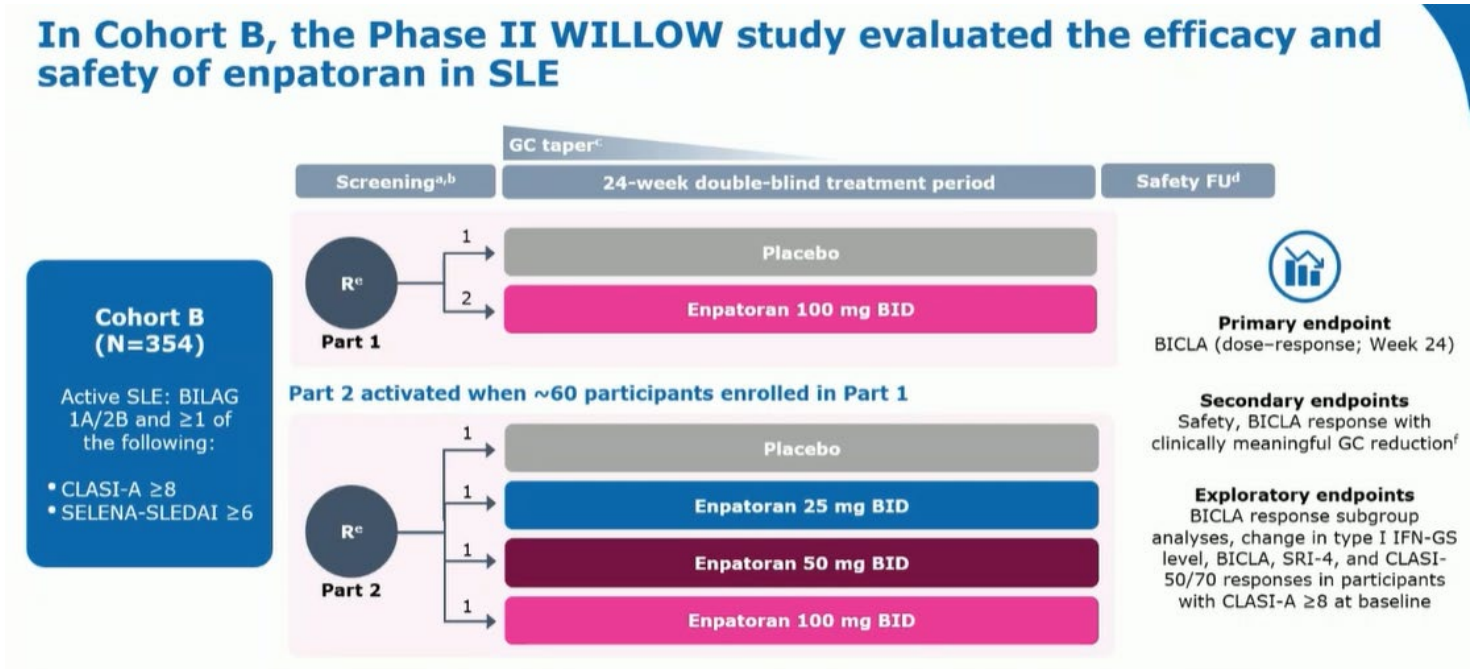
- n=135 mit ≥12 Monaten Verlauf
- Multiorgan-Ansprechen: kutan, muskuloskelettal, serologisch
- Klinisch relevante Glukokortikoid-Reduktion
- Bestätigt Studienwirksamkeit im Alltag

Konsequenz für die Praxis: Real-World-Daten stützen den frühen, zielgerichteten Einsatz von Anifrolumab bei moderatem bis schwerem SLE – mit erreichbaren Remissions-/LLDAS-Zielen und Steroidspareffekt.

TLR7/8 Antagonismus Enpatoran



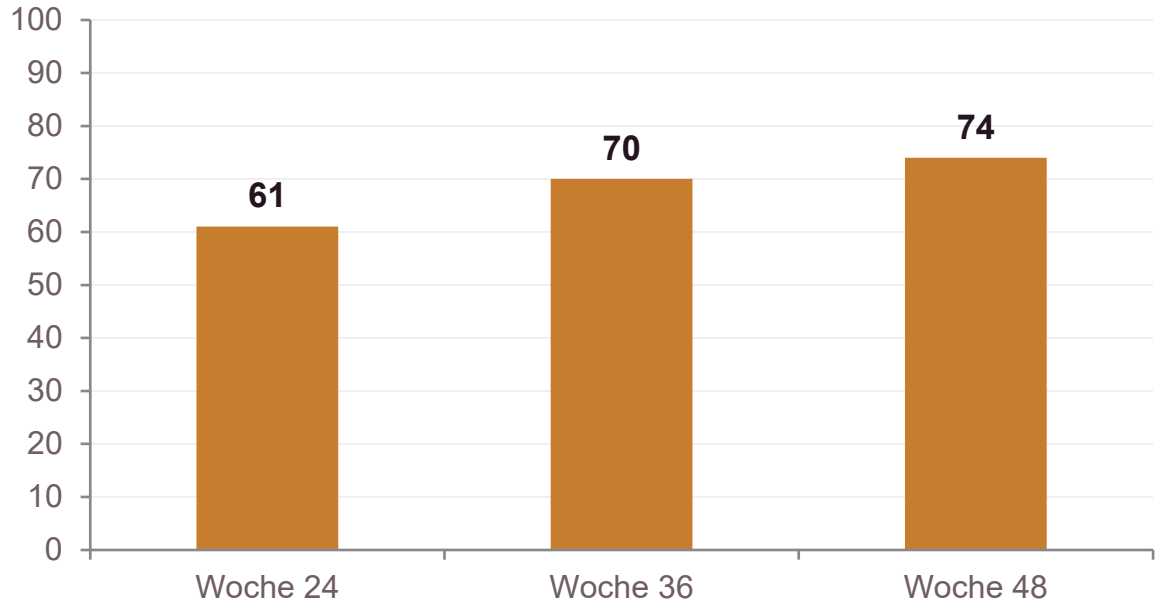




- BICLA response
  - Placebo 39%
  - Enpatoran 2x25mg 58%
  - Enpatoran 2x50mg 47%
  - Enpatoran 2x100mg 50%
- Reduktion von Prednison >=10mg zu <= 5mg
  - Placebo 31%
  - Enpatoran 2x25mg 59%
  - Enpatoran 2x50mg 56%
  - Enpatoran 2x100mg 48%

Enpatoran – kutanes Ansprechen

OP0337 WILLOW Phase-II-Langzeitverlängerung (LTE) · n=379 · kutaner und/oder systemischer Lupus · 48 Wochen



CLASI-70-Ansprechen über die Zeit (%, illustrativer Bereich aus LTE-Daten)

Wirkstoff

Oraler, selektiver, reversibler dualer Inhibitor von TLR7 und TLR8 – first-in-class oraler Ansatz oberhalb der Typ-I-Interferon-Achse.

Befund

Anhaltendes, hohes kutanes Ansprechen über 48 Wochen LTE; günstiges Sicherheitsprofil ohne neue Signale. Erste orale 48-Wochen-Langzeitdaten bei Lupus.

Konsequenz für die Praxis: Potenziell erste orale Option für therapierefraktären kutanen Lupus – Phase-III-Entwicklung beobachten.

Enpatoran – Wirkung auf die Lupusarthritis

POS0071 Post-hoc-Analyse · WILLOW Cohort B (Phase II) · moderater bis schwerer SLE mit aktiven kutanen Manifestationen

≥50%

der Gelenke gebessert: höherer Anteil mit ≥50%-Reduktion an druckschmerzhaften und geschwollenen Gelenken (28-Joint-Count) unter allen Enpatoran-Dosen vs. Placebo in Woche 24

BILAG

Verschiebung von schwerer (Score A) zu milder Arthritis (Score C) – muskuloskelettale Domäne verbessert

Einordnung: Derselbe TLR7/8-Mechanismus, der die Haut bessert, wirkt auch auf die Gelenke – konsistent mit der gemeinsamen upstream-Pathophysiologie. Die systemische Trennung von Placebo war bei Patienten mit aktiven kutanen Manifestationen am deutlichsten.

Konsequenz für die Praxis: Enpatoran adressiert mit einem oralen Wirkstoff zwei der häufigsten SLE-Manifestationen – Haut und Gelenke – zugleich.

LB0007 · EULAR 2026

Nipocalimab in SLE

First-in-class efficacy and safety demonstrating proof of concept for FcRn blockade — Phase 2 JASMINE-SLE study

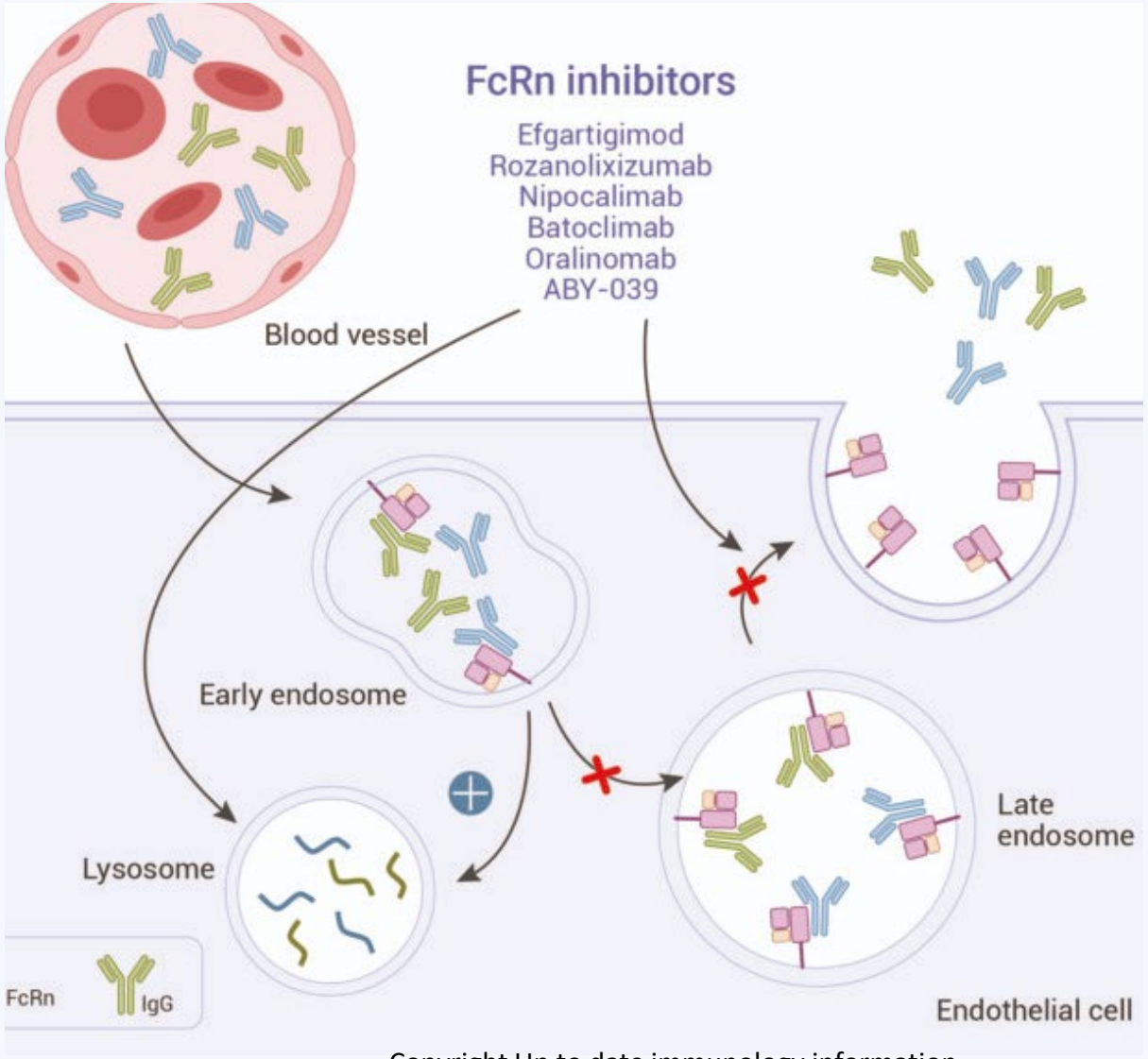
Presenter: Richard A. Furie et al.

Sponsor: Johnson & Johnson

Congress: EULAR 2026, London, 3–6 June 2026 | Late-Breaking Abstract Session

ClinicalTrials.gov: NCT04882878

Mechanism & Study Design



Copyright Up to date immunology information

JASMINE-SLE — Phase 2b (NCT04882878)

Population	228 Adults with moderate-to-severe SLE
Design	Randomised, placebo-controlled
Arms	Nipocalimab 15 mg/kg vs. placebo + background therapy
Primary EP	SRI-4 response at Week 24
Key secondary	SRI-4 & LLDAS at Week 52
Special pop.	Autoantibody-positive subgroup (~80% of SLE)

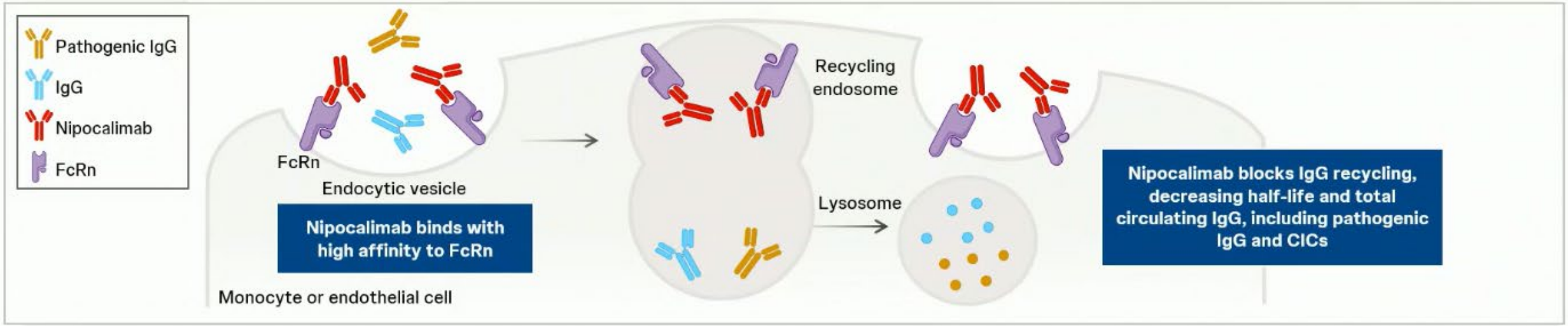
Nipocalimab: FcRn Blocker Decreases Serum IgG, Including Pathogenic IgG and CICs

FcRn:

- A recycling or transcytosis receptor → maintains IgG levels in circulation[1-3]
- Expressed in multiple cell types, including monocytes and endothelial cells[1-3]

Nipocalimab:

- A high-affinity, fully human, IgG1 FcRn blocker → selectively blocks IgG recycling[4]
- Decreases serum IgG, including pathogenic IgG and CICs while preserving immune cell functions[4-6]
- Approved for gMG in the US, Brazil, Japan, Europe, and China[7]



Phase 2 JASMINE-SLE Study Design

Key eligibility criteria

- Adults with active SLE (SLICC 2012) for ≥6 months
- Received standard of care (antimalarials, oral GCs, and protocol-permitted immunomodulators)
- Positive for ANA, anti-dsDNA, and/or anti-Smith
- 1 BILAG A and/or 2 BILAG B scores
- SLEDAI-2K score ≥6

Primary endpoint[a]

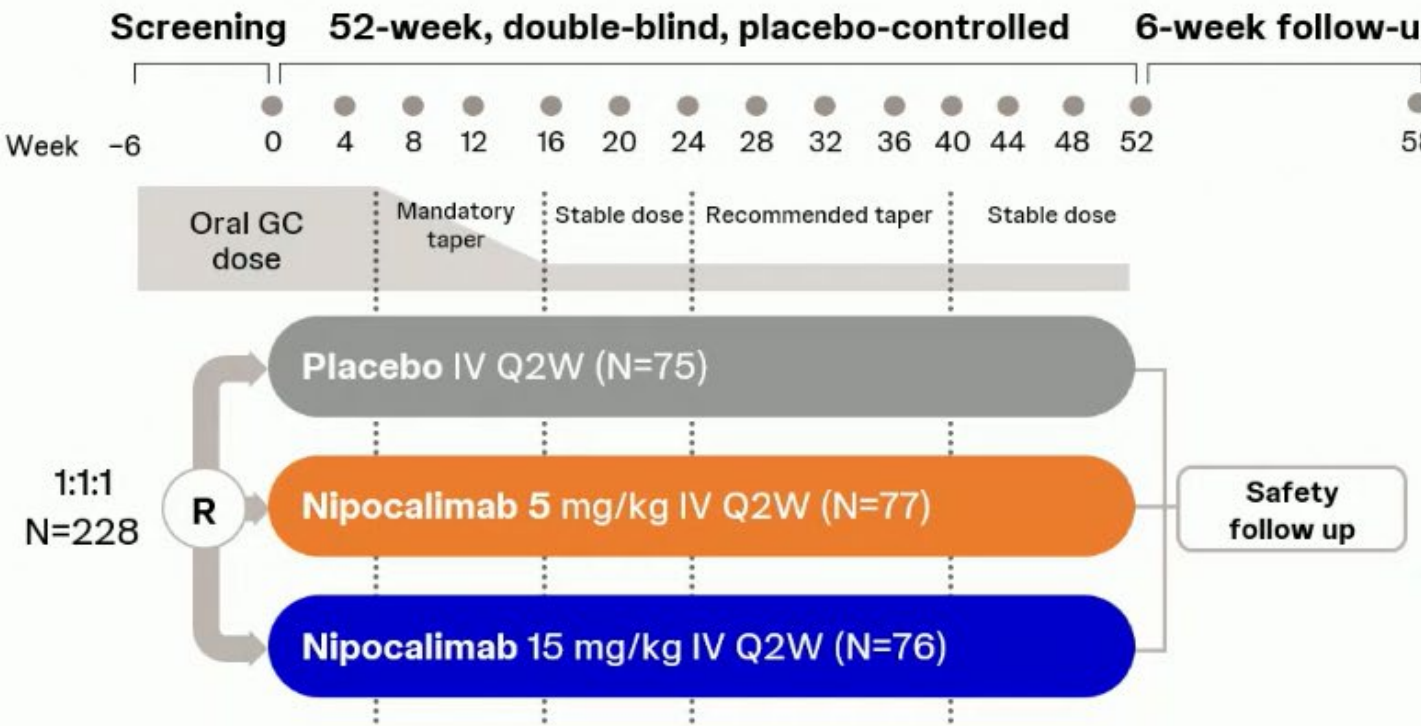
- % participants achieving SRI-4 composite response at Week 24

Key secondary/exploratory endpoints[b]

- % participants achieving SRI-4 composite response at Week 52
- % participants achieving LLDAS response at Week 52

Oral GC taper

- **Mandatory taper:** Weeks 6 to 16 to a target of 7.5 mg/day and maintained through Week 24[c]
- **Recommended taper:** Weeks 24 to 40 to a target of 7.5 mg/day and maintained through Week 52



[a]Only the primary endpoint was controlled for multiplicity, with a prespecified 2-sided alpha level of 0.10. [b]All other efficacy analyses were not adjusted for multiplicity, with nominal *P* values reported. [c]Participants on ≥10 mg/day oral GCs were required to taper; tapering could be paused/increased for disease worsening or safety concerns. FAS included all randomized participants who received ≥1 dose of any study intervention (for safety

Demographic and Baseline Characteristics

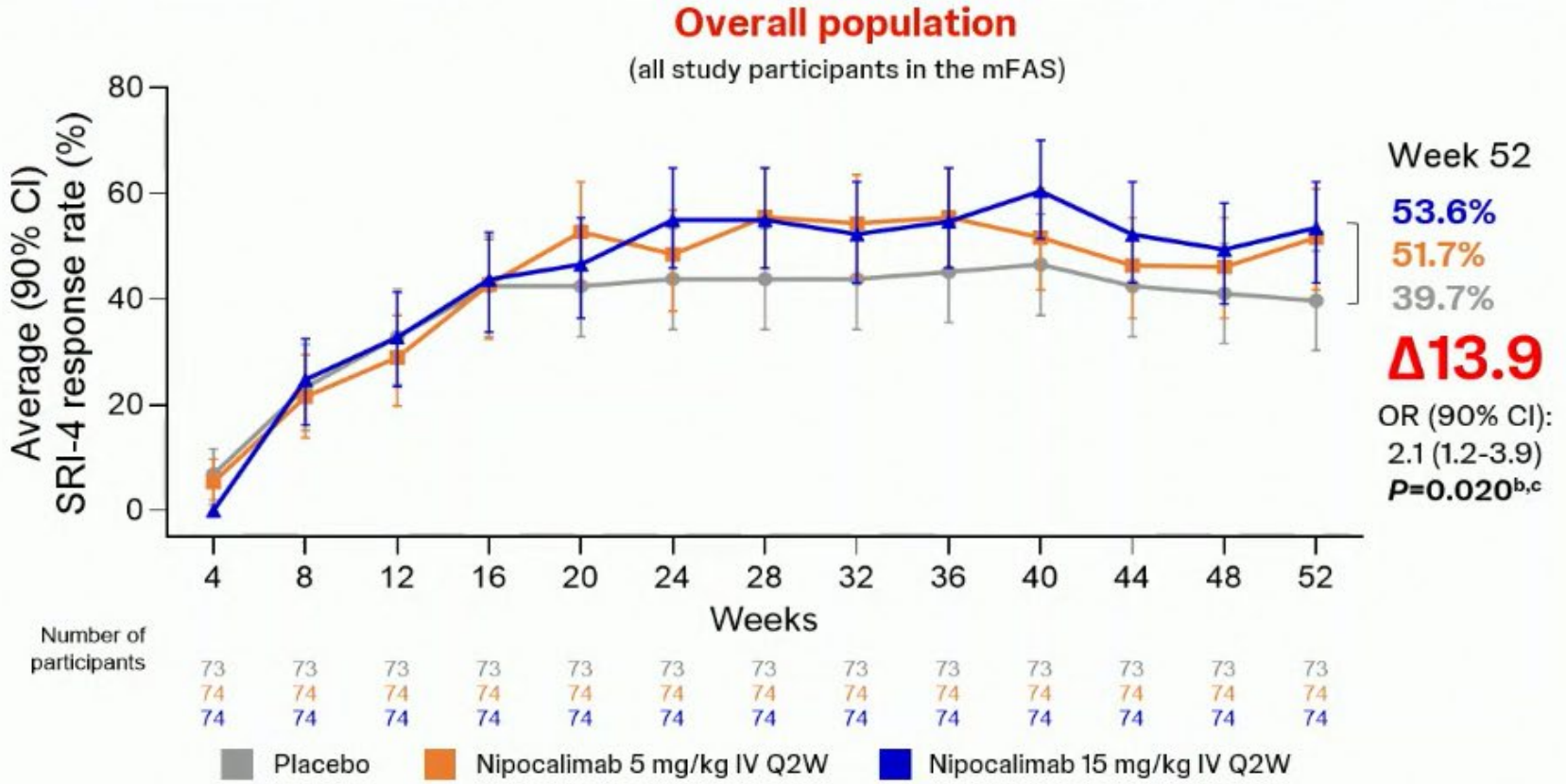
Demographic and baseline clinical characteristics were comparable across treatment groups

Baseline characteristics[a]	Placebo (N=73)	Nipocalimab 5 mg/kg IV Q2W (N=74)	Nipocalimab 15 mg/kg IV Q2W (N=74)	Total (N=221)
Demographics				
Age, years, mean (SD)	45.5 (11.3)	40.9 (11.9)	44.0 (11.9)	43.4 (11.8)
Female, n (%)	69 (94.5)	70 (94.6)	70 (94.6)	209 (94.6)
White, n (%)	50 (68.5)	50 (67.6)	44 (59.5)	144 (65.2)
Disease characteristics, mean (SD)				
SLE duration, years	9.3 (8.0)	8.1 (6.0)	10.8 (9.6)	9.4 (8.0)
SLEDAI-2K score (0-105)	**10.4 (3.0)**	**10.0 (3.2)**	**9.8 (2.5)**	**10.1 (2.9)**
PGA score (0-3)	2.0 (0.3)	1.9 (0.3)	2.0 (0.3)	2.0 (0.3)
BILAG, n (%)				
≥1 BILAG A	41 (56.2)	40 (54.1)	50 (67.6)	131 (59.3)
≥2 BILAG B	31 (42.5)	32 (43.2)	24 (32.4)	87 (39.4)
≥1 BILAG A or ≥2 BILAG B	72 (98.6)	71 (95.9)	72 (97.3)	215 (97.3)
CLASI activity score (0-70)	7.1 (4.5)	8.2 (7.2)	7.6 (6.7)	7.6 (6.2)
Number of active joints (0-62)[b]	8.0 (4.6)	8.6 (4.5)	10.1 (7.1)	8.9 (5.6)
Total IgG, g/L	14.2 (4.8)	15.2 (6.8)	14.4 (5.4)	14.6 (5.7)
Anti-dsDNA (positive ≥75), IU/mL	**167.0 (467.2)**	**155.7 (354.1)**	**225.5 (663.2)**	**182.8 (509.8)**
C3 (0.9-1.8), g/L	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)
CIC,[c] µg Eq/mL	11.4 (7.9)	12.7 (9.2)	11.9 (8.1)	12.0 (8.4)
Concomitant medications, n (%)				
Antimalarials	62 (84.9)	61 (82.4)	64 (86.5)	187 (84.6)
Oral GCs	**46 (63.0)**	**59 (79.7)**	**52 (70.3)**	**157 (71.0)**
Immunomodulators	**38 (52.1)**	**33 (44.6)**	**35 (47.3)**	**106 (48.0)**

[a]Based on the mFAS. Sample sizes for each parameter reflect nonmissing values. [b]Active joints are joints that are painful (as reported by participants) and tender and swollen (on physical exam as determined by the joint assessor). [c]Based on the mFAS with available baseline CIC values (placebo n=72, nipocalimab 5 mg/kg n=71, nipocalimab 15 mg/kg n=72).
BILAG=British Isles Lupus Assessment Group Scale, **C3**=complement component 3, **CIC**=circulating immune complex, **CLASI**=Cutaneous Lupus Erythematosus Disease Area and Severity Index, **dsDNA**=double-stranded deoxyribonucleic acid, **Eq**=equivalent, **GC**=glucocorticoid, **IgG**=immunoglobulin G, **IV**=intravenous, **mFAS**=modified full analysis set, **PGA**=Physician's Global Assessment of Disease Activity, **Q2W**=every 2 weeks, **SD**=standard deviation, **SLE**=systemic lupus erythematous, **SLEDAI-2K**=Systemic Lupus Erythematosus Disease Activity Index 2000.

Primary endpoint: SRI-4 at Week 24, maintained through Week 52

Primary endpoint: SRI-4 composite response at Week 24 was met for nipocalimab 15 mg/kg versus placebo (53.5% vs 46.7% *P*=0.081[a]) but not for nipocalimab 5 mg/kg versus placebo



Oral GC taper

- Among participants eligible for oral GC taper, a higher proportion of participants treated with 15 mg/kg nipocalimab achieved sustained oral GC taper and achieved SRI-4 composite response with sustained taper at Week 24

[a]Only the primary endpoint was controlled for multiplicity, with a prespecified 2-sided alpha level of 0.10 across doses, appropriate for a phase 2, proof-of-concept study. **FAS** included all randomized participants who received ≥1 dose of any study intervention (for safety analyses and primary endpoint analysis). **mFAS** included all randomized participants who received ≥1 dose of any study intervention, excluding 7 participants from one study site due to noncompliance with Good Clinical Practice identified between Week 24 and Week 52, for Week 52 efficacy analyses. [b]Analysis based on average response rates with imputed data. [c]The *P* value was nominal.

aAb=autoantibody, **CI**=confidence interval, **FAS**=full analysis set, **GC**=glucocorticoid, **IV**=intravenous, **mFAS**=modified full analysis set, **OR**=odds ratio, **Q2W**=every 2 weeks, **SRI-4**=Systemic Lupus Erythematosus Responder Index.

Predefined Biomarker-Based Populations

Efficacy was evaluated in 3 predefined biomarker-based populations based on nipocalimab's MOA

aAb-positive (79%)

- Positive for ≥1:
  - Anti-dsDNA
  - Anti-Smith
  - ANA with anti-RNP, anti-Ro, or historical anti-dsDNA
- Positive for a range of additional autoantibodies based on extended profiling

aAb-high (15%)

- Identified using machine learning through unsupervised clustering of baseline aAb levels
- Consisted of patients with (all present):
  - Increased CICs
  - High IFN signature
  - Low C3

IFN-high (66%)

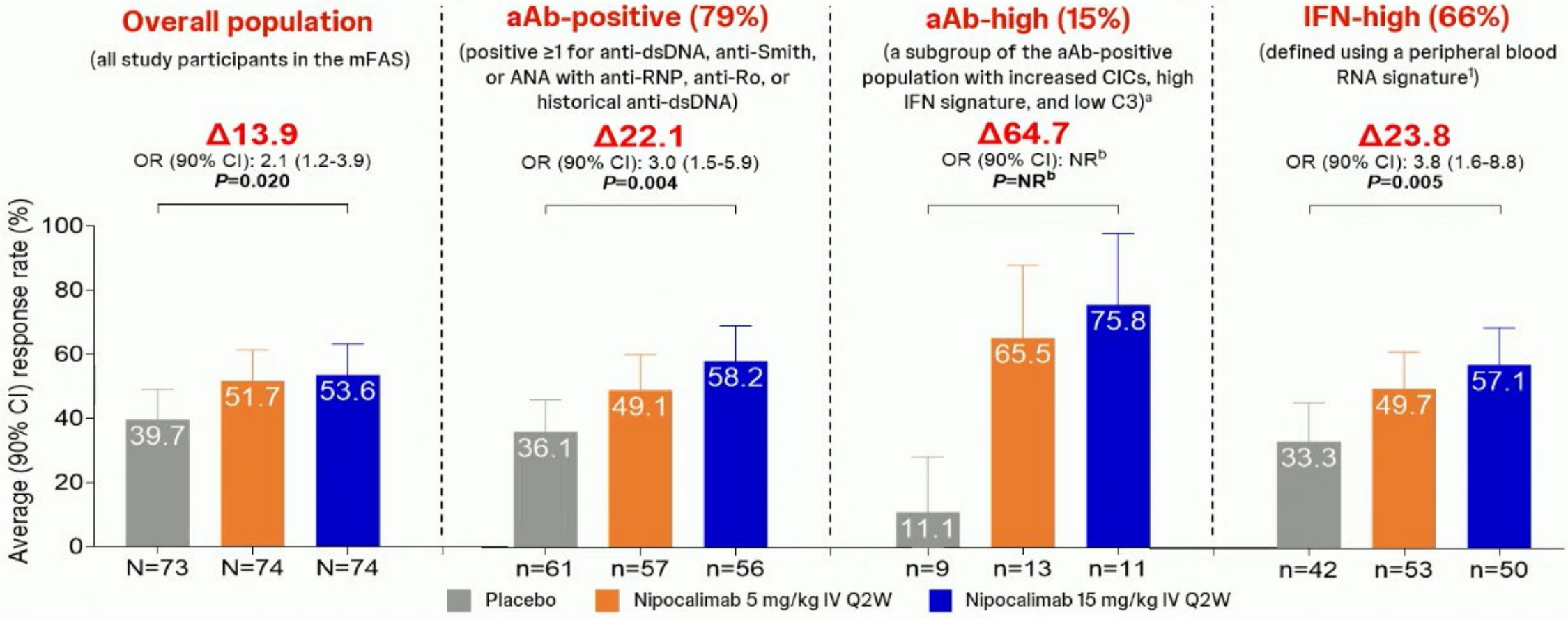
- Defined using a peripheral blood RNA signature[1]

aAb=autoantibody, **ANA**=antinuclear antibody, **C3**=complement component 3, **CIC**=circulating immune complex, **dsDNA**=double-stranded deoxyribonucleic acid, **IFN**=interferon, **MOA**=mechanism of action, **RNP**=ribonucleoprotein, **SLE**=systemic lupus erythematous.

1. Cesaroni M, et al. Type i interferon signatures and methods of use. WO2020084591A1. Issued October 25, 2019.

SRI-4 Composite Response at Week 52

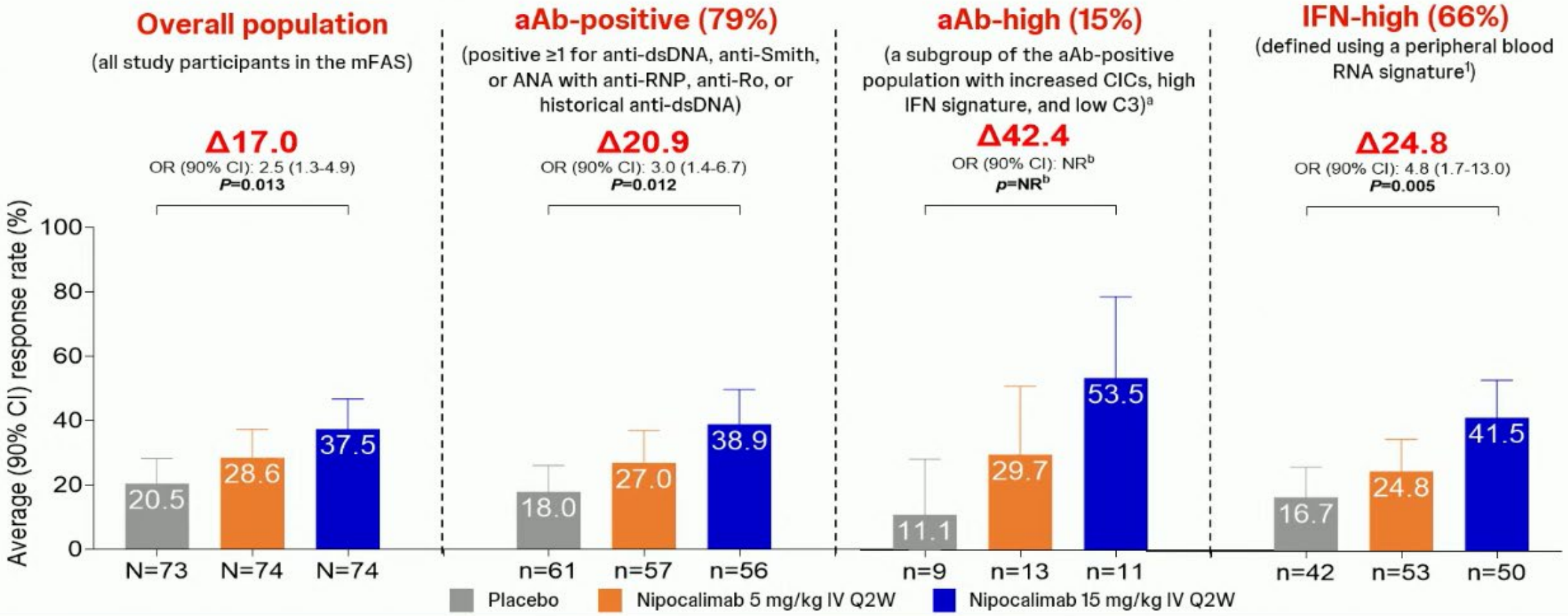
Nipocalimab improved Week 52 SRI-4 composite response rates compared with placebo, with greater response rates in predefined biomarker-based populations



Analyses based on the mFAS with imputed data. All *P* values reported here are nominal. [a]Identified through unsupervised consensus clustering based on semiquantitative baseline aAb intensities.
[b]Due to small sample sizes and large variability, the OR and *P* value are NR.
aAb=autoantibody, **ANA**=antinuclear antibody, **C3**=complement component 3, **CI**=confidence interval, **CIC**=circulating immune complex, **dsDNA**=double-stranded deoxyribonucleic acid, **IFN** =interferon, **IV**=intravenous, **mFAS**=modified full analysis set, **NR**=not reported, **OR**=odds ratio, **Q2W**=every 2 weeks, **RNP**=ribonucleoprotein, **SRI-4**=Systemic Lupus Erythematosus Responder Index.
1. Cesaroni M, et al. Type i interferon signatures and methods of use. WO2020084591A1. Issued October 25, 2019.

LLDAS Response at Week 52

Nipocalimab improved Week 52 LLDAS response rates compared with placebo, with greater response rates in predefined biomarker-based populations



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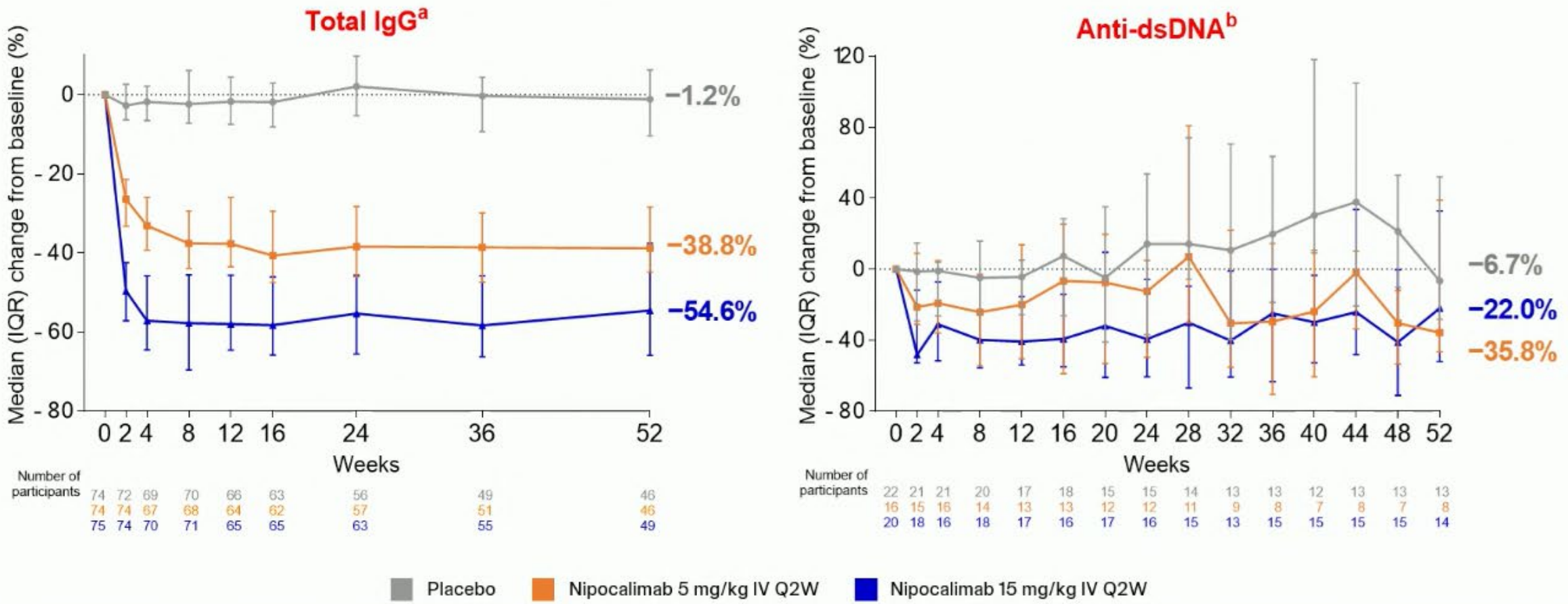
1. Cesaroni M, et al. Type i interferon signatures and methods of use. WO2020084591A1. Issued October 25, 2019.

Biomarkers Through Week 52

Nipocalimab reduced total IgG and anti-dsDNA across the treatment period

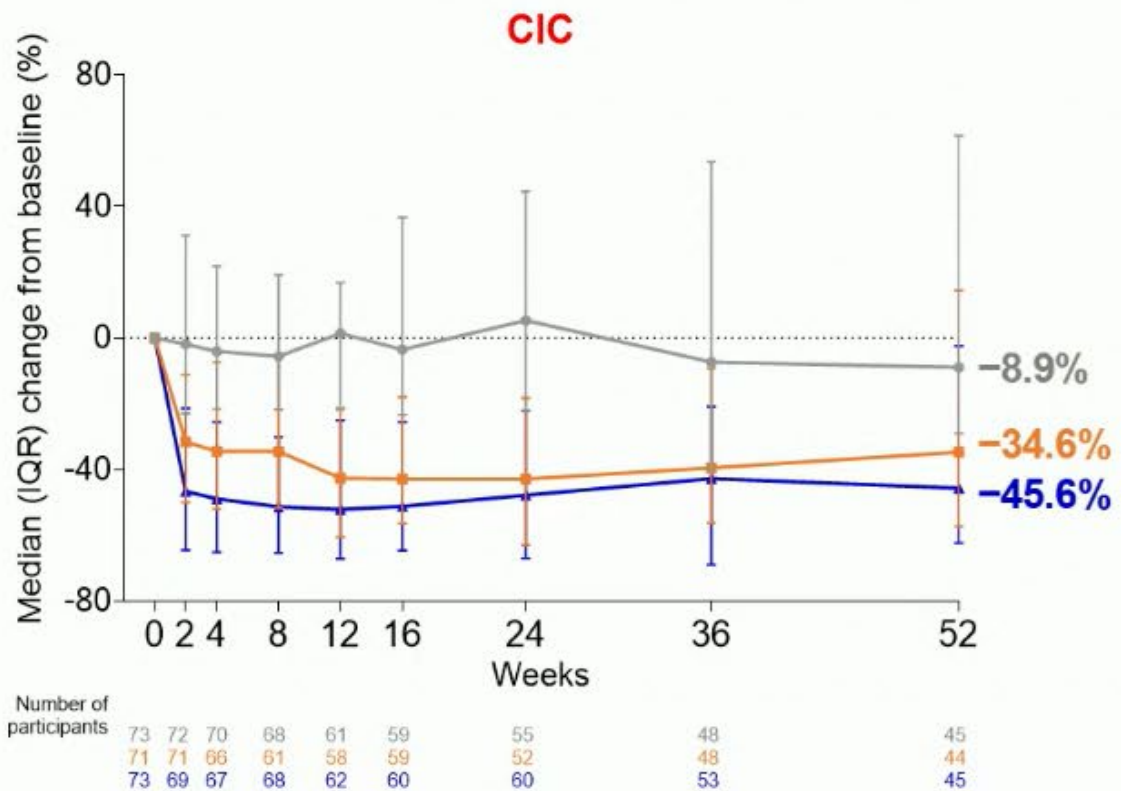


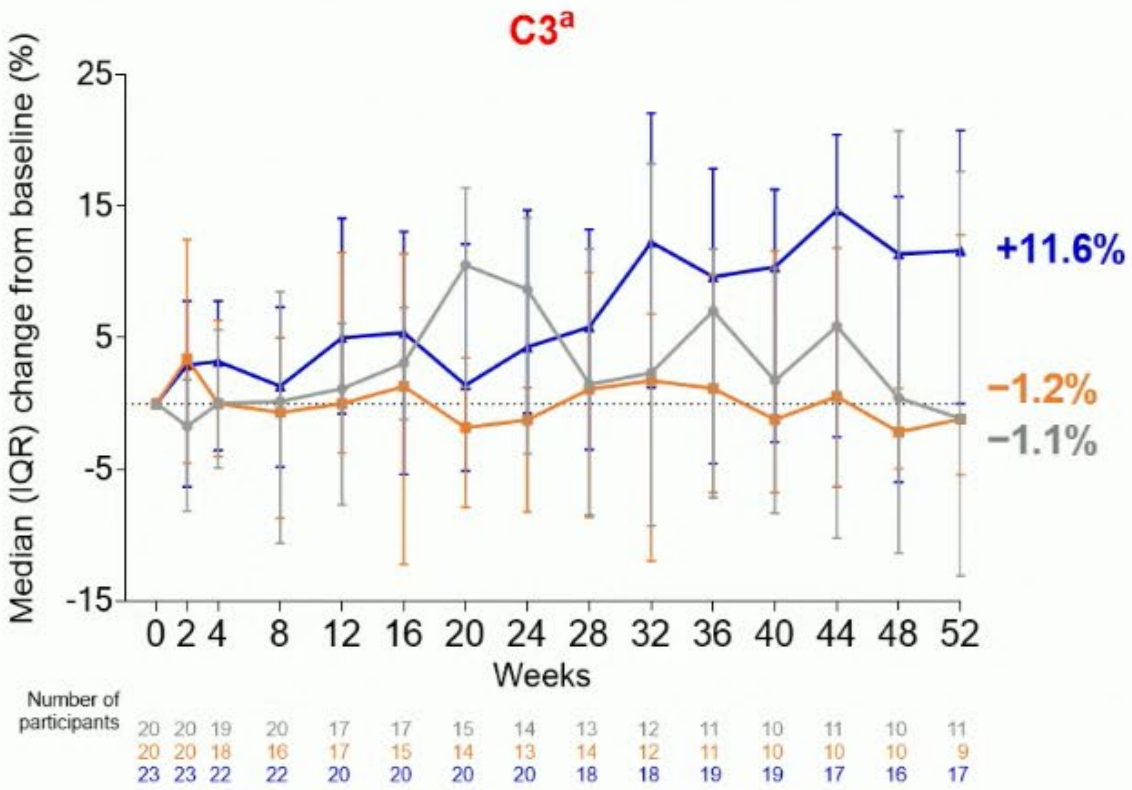
Based on the FAS with ≥1 valid postdose blood sample drawn for pharmacodynamic analysis. If a participant missed a planned dose of study intervention at any visit, their data was excluded from all subsequent visits after the first occurrence of a missed dose. [a]20 (27%) participants in the nipocalimab 5 mg/kg group and 47 (63%) in the nipocalimab 15 mg/kg group had minimum IgG <LLN (6 g/L). [b]In anti-dsDNA–positive participants at baseline.

dsDNA=double-stranded deoxyribonucleic acid, **FAS**=full analysis set, **IgG**=immunoglobulin G, **IQR**=interquartile range, **IV**=intravenous, **LLN**=lower limit of normal, **Q2W**=every 2 weeks.

Biomarkers Through Week 52

Nipocalimab reduced CIC and increased C3 levels across the treatment period





Placebo | Nipocalimab 5 mg/kg IV Q2W | Nipocalimab 15 mg/kg IV Q2W

Based on the FAS with ≥1 valid postdose blood sample drawn for pharmacodynamic analysis. If a participant missed a planned dose of study intervention at any visit, their data was excluded from all subsequent visits after the first occurrence of a missed dose. [a]In participants with low baseline C3.

C3=complement component 3, **CIC**=circulating immune complexes, **FAS**=full analysis set, **IgG**=immunoglobulin G, **IQR**=interquartile range, **IV**=intravenous, **Q2W**=every 2 weeks.

Safety Through Week 58

Nipocalimab was well tolerated, with no new safety signals observed

Participants with ≥1 AE,[a] n (%)	Placebo (N=75)	Nipocalimab 5 mg/kg IV Q2W (N=77)	Nipocalimab 15 mg/kg IV Q2W (N=76)	Combined nipocalimab (N=153)
AEs	57 (76.0)	69 (89.6)	63 (82.9)	132 (86.3)
Serious AEs	6 (8.0)	6 (7.8)	10 (13.2)	16 (10.5)
AEs leading to death	0	1 (1.3)	1 (1.3)	2 (1.3)
Infections and infestations	42 (56.0)	45 (58.4)	46 (60.5)	91 (59.5)
Serious infections and infestations	3 (4.0)	4 (5.2)	3 (3.9)	7 (4.6)
Opportunistic infections	0	0	1 (1.3)	1 (0.7)
Infusion reactions	6 (8.0)	10 (13.0)	5 (6.6)	15 (9.8)
Hypersensitivity reactions[b]	9 (12.0)	10 (13.0)	14 (18.4)	24 (15.7)
MACE[c]	1 (1.3)	1 (1.3)	1 (1.3)	2 (1.3)

- Rates of AEs were not dose dependent
- Through Week 58, nadir IgG <3 g/L was observed in 0%, 2.7%, and 22.7% of participants treated with placebo, nipocalimab 5 mg/kg, and nipocalimab 15 mg/kg, respectively. None of the participants with IgG <3 g/L developed serious AEs; 1 participant in the nipocalimab 15 mg/kg IV Q2W group discontinued due to protocol-specified IgG stopping criteria
- No severe hypoalbuminemia (<20 g/L) was observed
- Two deaths were reported in participants from each nipocalimab treatment group due to septic shock. Both events were assessed by the investigator as unrelated to the study intervention

[a]Based on the FAS. [b]Defined by the Standardized Medical Dictionary for Regulatory Activities (MedDRA) Queries. [c]Cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke.
AE=adverse event, **FAS**=full analysis set, **IgG**=immunoglobulin G, **IV**=intravenous, **MACE**=major adverse cardiovascular events, **Q2W**=every 2 weeks.

Key Takeaways

JASMINE-SLE, the first study of an FcRn blocker in SLE, demonstrated that:

- ✓ Nipocalimab 15 mg/kg IV Q2W treatment led to significant improvement over placebo in SRI-4 composite response at Week 24 and improved SRI-4 composite and LLDAS responses at Week 52
- ✓ Nipocalimab 15 mg/kg treatment led to sustained oral GC reduction
- ✓ Greater treatment effects were observed in populations of aAb-positive, aAb-high, and IFN-high participants
- ✓ Nipocalimab was well tolerated among participants

These results establish proof of concept for FcRn blockade with nipocalimab in SLE and support the evaluation of nipocalimab in an ongoing phase 3 trial (GARDENIA; NCT07438496)

aAb=autoantibody, **FcRn**=neonatal crystallizable fragment receptor, **GC**=glucocorticoid, **IFN**=interferon, **IV**=intravenous, **LLDAS**=Lupus Low Disease Activity State, **Q2W**=every 2 weeks, **SLE**=systemic lupus erythematous, **SRI-4**=Systemic Lupus Erythematosus Responder Index.

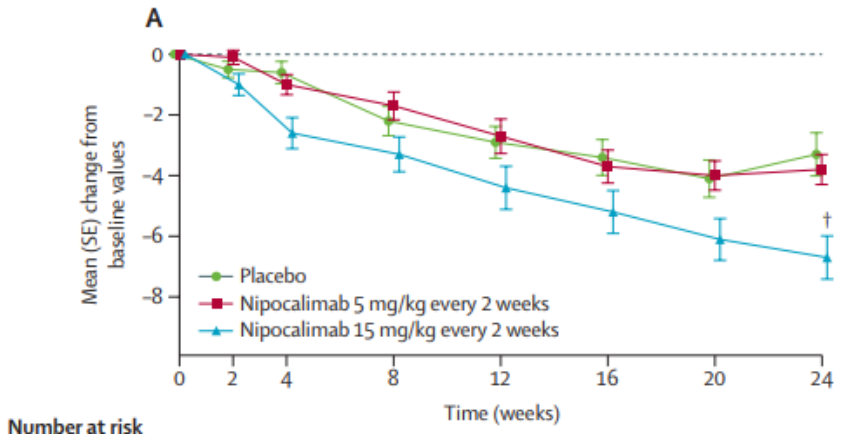
Nipocalimab in anderen Indikationen

Nipocalimab received FDA approval in May 2025 for the treatment of generalized myasthenia gravis

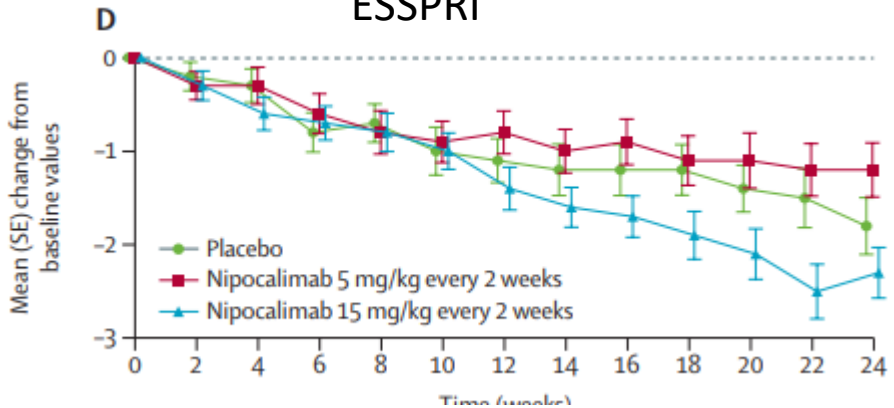
Phase 2 data in Sjögren's disease (DAHLIAS):

The DAHLIAS trial 163 patients with moderate-to-severe Sjögren's disease, --r -- randomized to nipocalimab 5 mg/kg, 15 mg/kg, or placebo every 2 weeks

ClinESSDAI



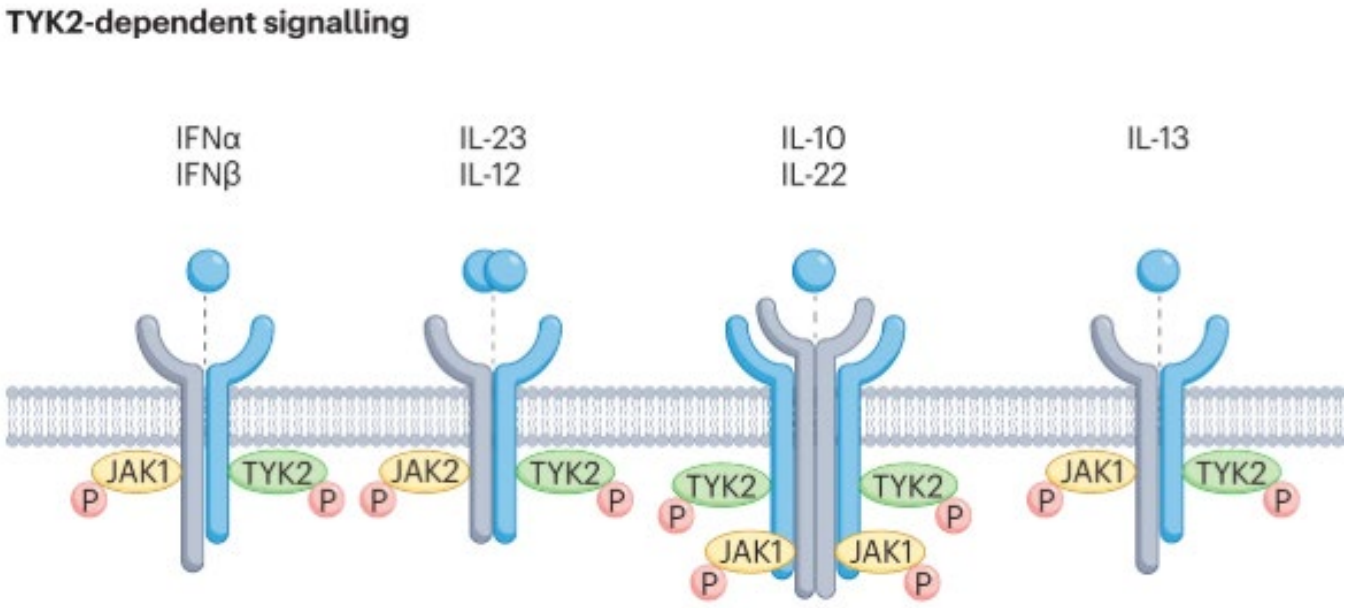
ESSPRI



doi: 10.1016/S0140-6736(25)01430-8

https://doi.org/10.1016/S0140-6736(25)01430-8

TYK2 ist eine Janus-Kinase, die intrazellulär die Signale von Typ-I-Interferon, IL-12 und IL-23 weiterleitet. Sie sitzt downstream der Rezeptoren und aktiviert die STAT-Transkriptionsfaktoren.



https://doi.org/10.1038/s41584-024-01093

Deucravacitinib in Systemic Lupus Erythematosus

Deucravacitinib
- Oral, selective, allosteric tyrosine kinase 2 (TYK2) inhibitor
- Unique mechanism of action distinct from Janus kinase (JAK) 1/2/3 inhibitors

PAISLEY Trial
- Phase 2, randomized, double-blind, multicenter, placebo-controlled
- Evaluated efficacy and safety of deucravacitinib in adult patients with active SLE on standard therapy
- Primary endpoint: SRI(4) at week 32

363 patients with active SLE	**Placebo** N=90	**Deucravacitinib** 3 mg Twice Daily N=91	**Deucravacitinib** 6 mg Twice Daily N=93	**Deucravacitinib** 12 mg Once Daily N=89
Primary endpoint SLE Responder Index 4 [SRI(4)] at week 32	**34.4%**	**58.2%**	**49.5%**	**44.9%**

Difference (placebo and 3 mg twice daily): 23.8%; 95% CI, 8.5 to 37.7; *P*<0.001

Difference (placebo and 6 mg twice daily): 15.0%; 95% CI, -0.0 to 29.2; *P*=0.02

Patients who received deucravacitinib were more likely to achieve an SRI(4) response at week 32 than those who received placebo

All secondary endpoints were achieved or meaningfully improved at week 48, including SRI(4), BICLA, LLDAS, CLASI-50, and change in joint counts

- **Well tolerated**
- **Safety consistent with trials in psoriasis**

Eric Morand, Marilyn Pike, Joan T. Merrill, Ronald van Vollenhoven, Victoria P. Werth, Coburn Hobar, Nikolay Delev, Vaishali Shah, Brian Sharkey, Thomas Wegman, Ian Catlett, Subhashis Banerjee, Shalabh Singhal - Deucravacitinib, a Tyrosine Kinase 2 Inhibitor, in Systemic Lupus Erythematosus: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial, *Arthritis Rheumatol*, 2022

Arthritis & Rheumatology ACR American College of Rheumatology

https://doi.org/10.1002/art.42391

LONG-TERM DISEASE CONTROL IN SLE USING LLDAS AND DORIS CRITERIA: INTEGRATED POST HOC ANALYSES FROM THE PAISLEY SLE AND LTE TRIALS POS0695 (2026)

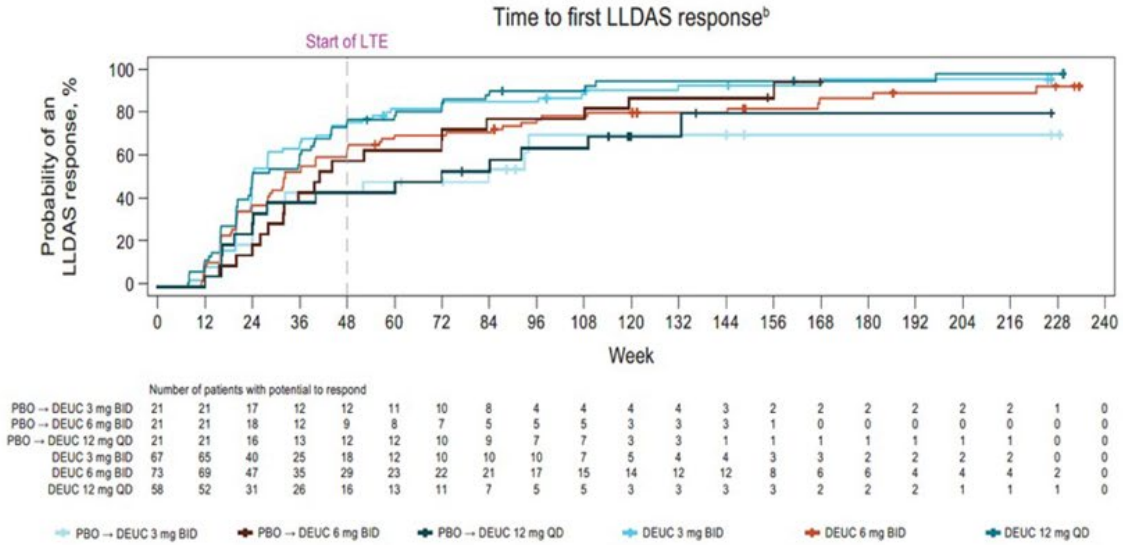
Deucravacitinib demonstrated superior efficacy vs placebo in patients in the phase 2 PAISLEY SLE trial

post hoc analyses of LLDAS response, DORIS remission, and flares using integrated analyses from the PAISLEY SLE and PAISLEY long-term extension trials.

Patients completing the 48-week PAISLEY SLE parent trial while on study drug (deucravacitinib 3 mg twice daily [BID], 6 mg BID, or 12 mg once daily [QD]) or placebo were given the opportunity to enroll in the **3-year PAISLEY LTE trial.**

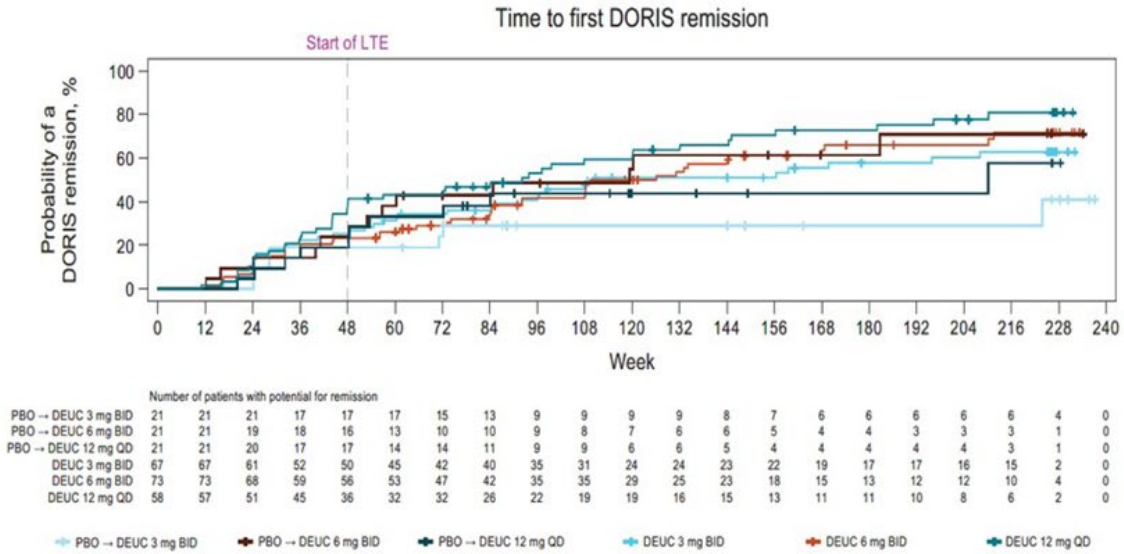
Figure 1. Time to first LLDAS response and DORIS remission (as observed and using the treatment failure rule)[a]

A.



	Median time to first LLDAS response (95% CI[c]), weeks
PBO → DEUC 3 mg BID	83.9 (24.1-NR)
PBO → DEUC 6 mg BID	41.1 (28.1-72.1)
PBO → DEUC 12 mg QD	72.0 (24.1-132.6)
DEUC 3 mg BID	24.3 (23.9-31.9)
DEUC 6 mg BID	32.4 (28.0-48.1)
DEUC 12 mg QD	24.2 (20.4-39.0)

B.

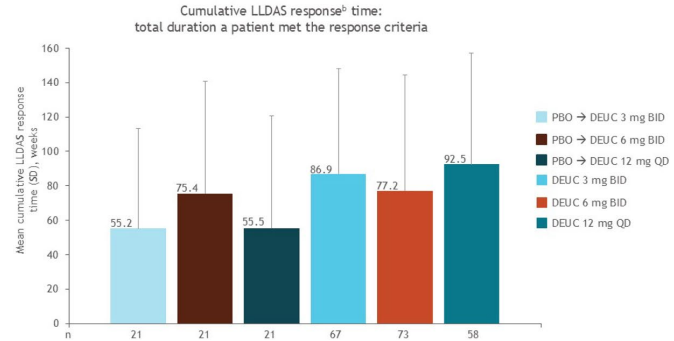


	Median time to first DORIS remission (95% CI[c]), weeks
PBO → DEUC 3 mg BID	NR (72.1-NR)
PBO → DEUC 6 mg BID	119.4 (48.1-NR)
PBO → DEUC 12 mg QD	210.1 (48.4-NR)
DEUC 3 mg BID	110.0 (84.3-208.0)
DEUC 6 mg BID	126.1 (84.6-168.0)
DEUC 12 mg QD	92.1 (48.0-120.3)

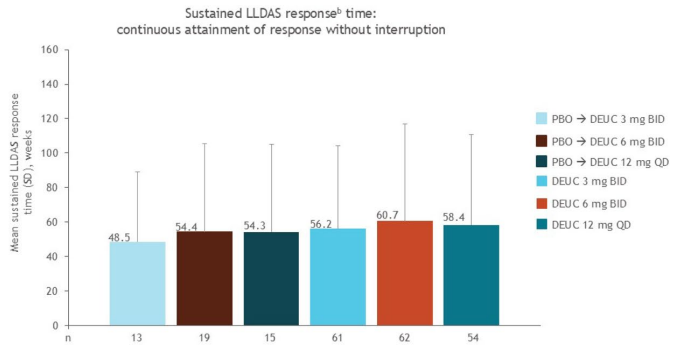
[a]TFR data align with the as-observed data because no patient had an LLDAS response or DORIS remission status of "Responder" at the visit when treatment was discontinued due to lack of efficacy;
[b]LLDAS responses were evaluated using the 2019 definition; [c]Calculated using log-log transformation.
BID, twice daily; CI, confidence interval; DEUC, deucravacitinib; DORIS, Definitions of Remission in Systemic Lupus Erythematosus; LLDAS, Lupus Low Disease Activity State; NR, not reached; PBO, placebo; QD, once daily; TFR, treatment failure rule.

Figure 2. Time in LLDAS response or DORIS remission.[a] A. Cumulative time in LLDAS response. B. Sustained time in LLDAS response. C. Cumulative time in DORIS remission.

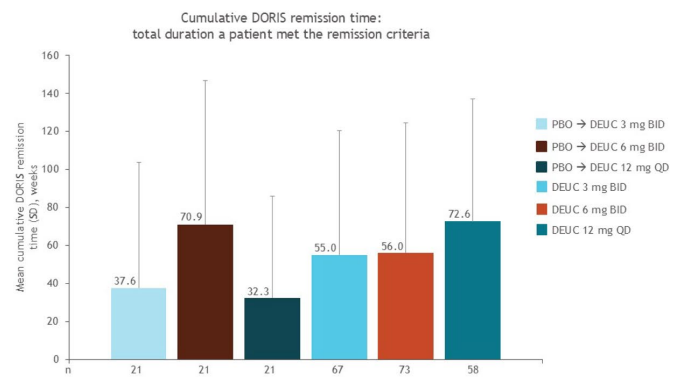
A.



B.



C.



[a]Calculated using the AUC approach; missing data for patients, up to the last available visit, were imputed using the last observation carried forward approach for the first missing visit, and subsequent missing visits were imputed as a nonresponse; 95% CIs were obtained using the Clopper-Pearson method; [b]LLDAS responses were evaluated using the 2019 definition.
AUC, area under the curve; BID, twice daily; CI, confidence interval; DEUC, deucravacitinib; DORIS, Definitions of Remission in Systemic Lupus Erythematosus; LLDAS, Lupus Low Disease Activity State; PBO, placebo, QD, once daily; SD, standard deviation.

Deucravacitinib – oraler TYK2-Inhibitor

POS0695 Integrierte Post-hoc-Analyse · PAISLEY SLE + Langzeitverlängerung · bis >4 Jahre kontinuierliche Exposition

Schneller

LLDAS- & DORIS-Ansprechen rascher erreicht unter kontinuierlicher Therapie

Länger

Anhaltende Remission über die Zeit – auch bei späterem Wechsel von Placebo

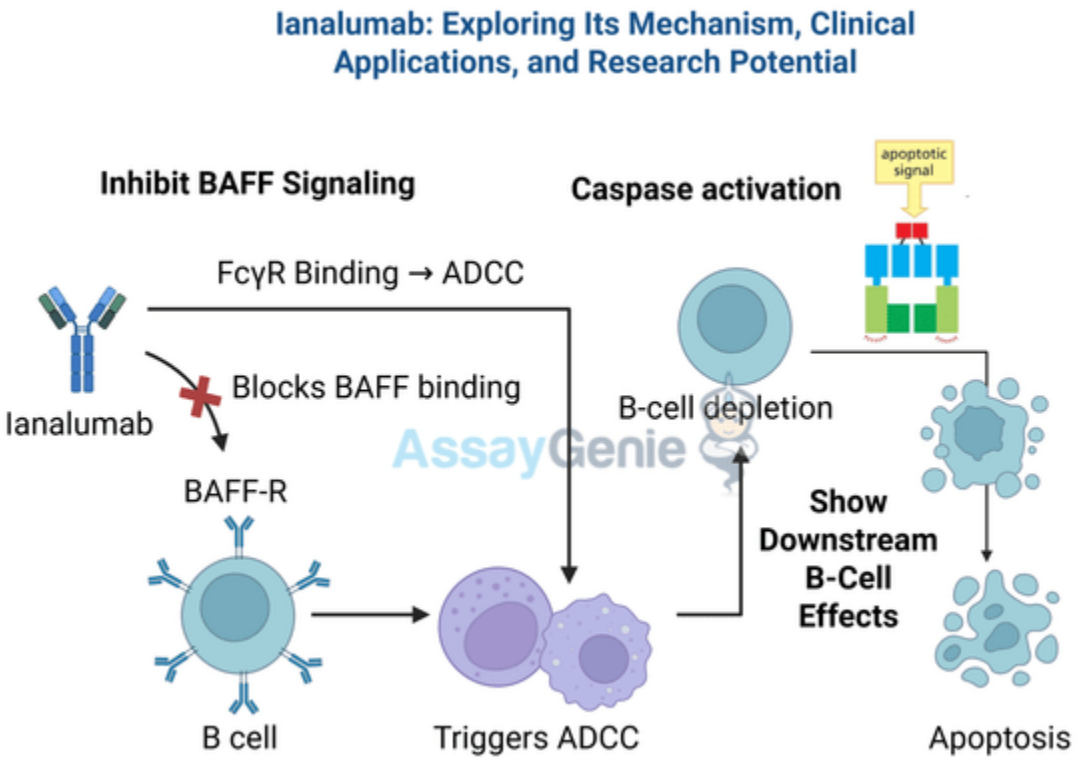
Stabiler

Längeres Flare-freies Intervall bei kontinuierlicher Behandlung

Einordnung
Bislang längste Datenreihe zu einem TYK2-Inhibitor bei SLE. Derselbe orale downstream-Mechanismus liegt auch GLPG3667 zugrunde. Bestätigende Phase-III-Studien (POETYK SLE) laufen.

Konsequenz für die Praxis: Vielversprechende künftige orale Option; aktuell Post-hoc-Evidenz – endgültige Bewertung nach Phase III.

Ianalumab-Anti Baff Ak



Die Sjögren Studien NEPTUNUS-1 und NEPTUNUS-2 (mit über 700 Teilnehmern) konnte Ianalumab signifikante Verbesserungen der Krankheitsaktivität erzielen und damit die primären und sekundären Studienziele erfolgreich erreichen

SJÖGREN'S DISEASE | 2 TRANSLATIONAL STUDIES

Sjögren's Disease as a Tractable Immune Ecosystem

Context

SjD is characterised by the infiltration of immune cells in exocrine glands, notably in the salivary glands (SG), as focal dense aggregates of B and T cells around ducts known as foci

IANALUMAB · Anti-BAFF-R · B Cell Depletion

Does anti-BAFF-R clear B cells from blood AND salivary gland?

BLOOD **CD19+ B cells ↓99% in blood**

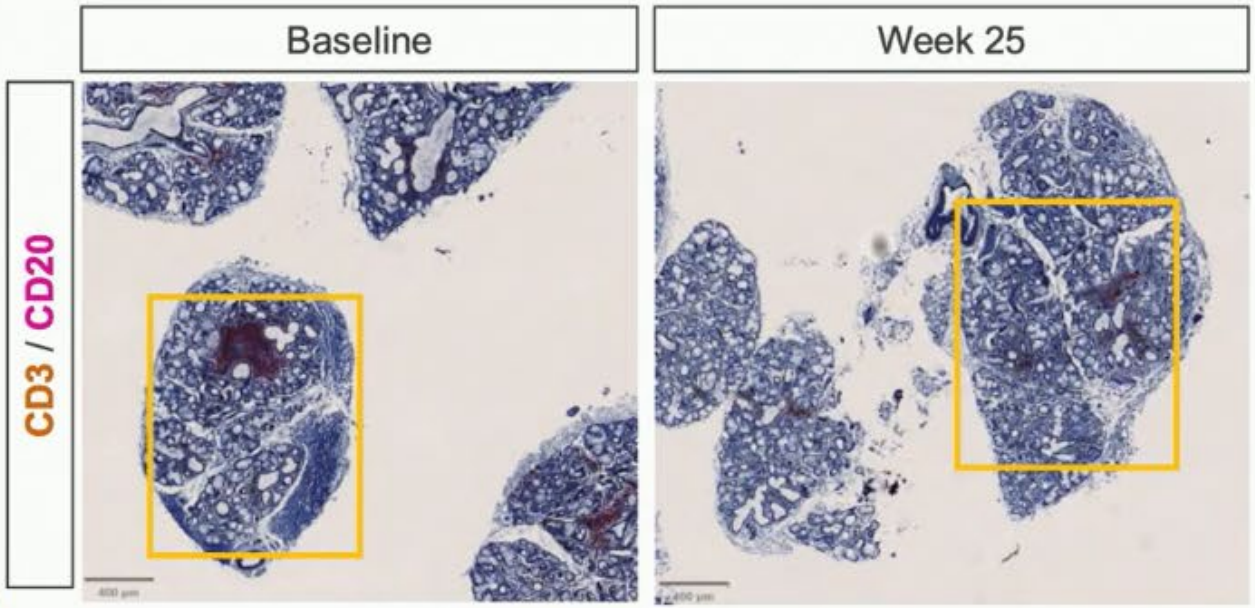
All subsets depleted · BCL2↓ CXCR4↓ NF-kB↓
Cytoskeleton ↑ · B cell development genes ↑

TISSUE **SG B cells ↓84% · B/B+T ↓41%**

CXCR5+CD20+ naïve B cells ↓ (TLS-homing)
Foci B+T inflammatory infiltrate ↓ W25

CLINIC **SG B cells ↔ Schirmer r=−0.52**

CD19+ ↔ salivary flow r=−0.45 p<0.05
ESSDAI + ESSPRI improved at Week 25



Monthly treatment with ianalumab 300 mg over 24 weeks modified B cell phenotype and improved dryness-related outcomes at a clinical level.

Divi Cornec et al. · CHU Brest · OP0163

Obinutuzumab Induces Histological Remission and Deep Kidney Parenchymal B-Cell Depletion in Patients With Lupus Nephritis: Exploratory Analyses of the Phase III REGENCY Trial

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Presented at the EULAR 2026 Congress;

3-6 June, 2026; London, UK

Background

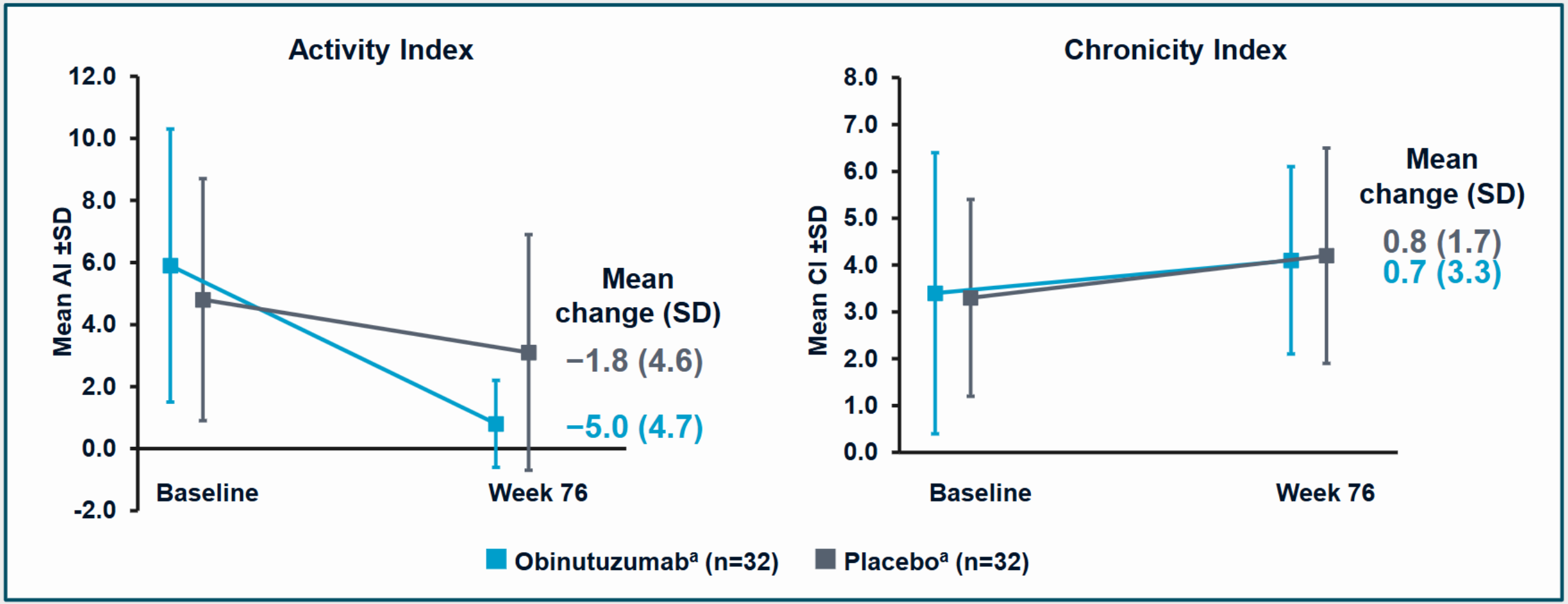
- Obinutuzumab is a recombinant, humanized, glycoengineered type II anti-CD20 IgG1 monoclonal antibody that leads to greater B-cell depletion compared with type I anti-CD20 antibodies[1]
- The REGENCY trial (NCT04221477)[2] randomized adults with active lupus nephritis to placebo[a] or obinutuzumab[a]
  - At Week 76, significantly more obinutuzumab[a]-treated patients vs placebo[a]-treated patients achieved clinical complete renal response (CRR; 46.4% vs 33.1% [adjusted difference, 13.4%; 95% confidence interval [CI], 2.0% to 24.8%; *P*=0.0232]),[2] which led to the approval of obinutuzumab[a] for the treatment of lupus nephritis in the US and EU[3,4]
- All enrolled patients had a kidney biopsy performed in the 6 months prior to, or during screening, with an optional post-Week 76 kidney biopsy
- We postulated that obinutuzumab[a] treatment would lead to deep tissue-level B-cell depletion, resulting in more histologic remissions than placebo[a]

Objective

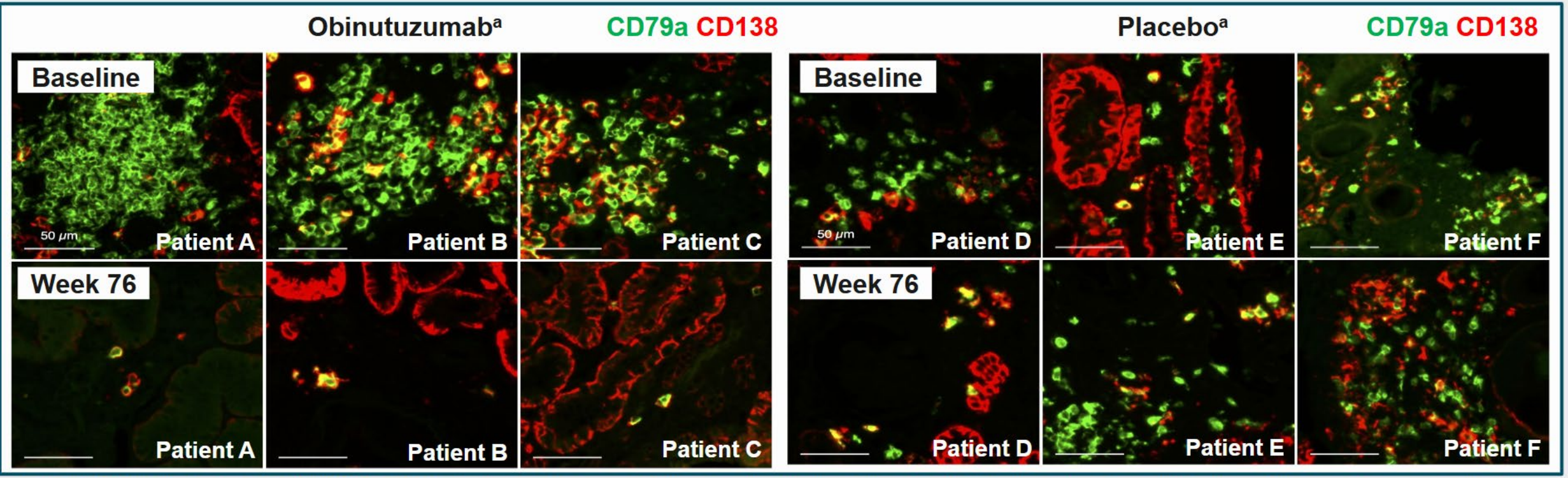
To evaluate the effect of obinutuzumab[a] vs placebo[a] on tissue-level changes in kidney inflammation between baseline and post-Week 76 paired biopsies from the REGENCY trial by assessing:

- Histologic remission
- Depletion of B cells and antibody-secreting cells

The Mean Change in AI was Greater With Obinutuzumab vs Placebo Treatment at Week 76



Obinutuzumab-Induced Kidney Tissue Depletion of B Cells and Plasma Cells in the REGENCY Trial

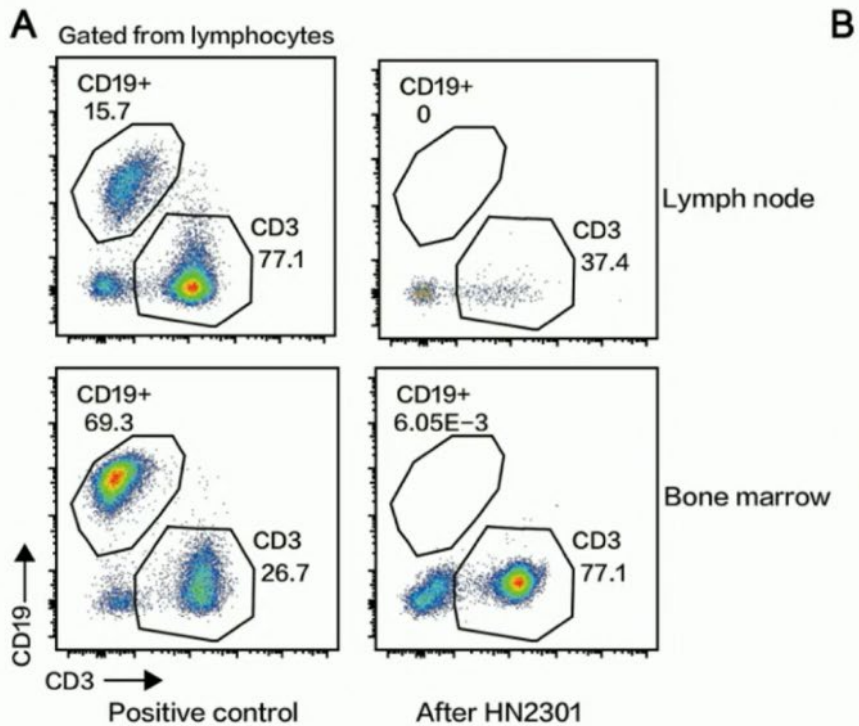


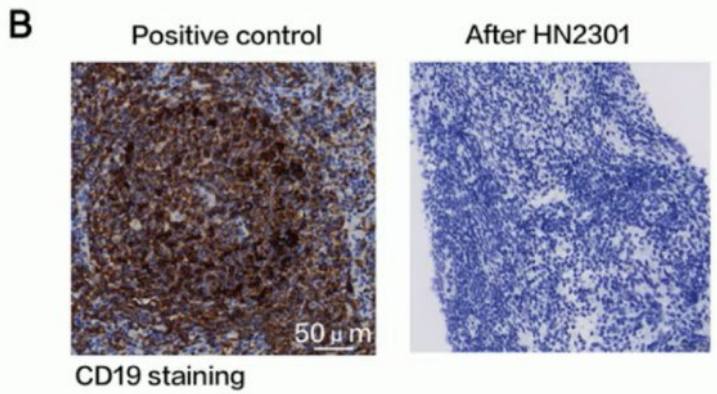
CD79a+/CD138− B cells and CD138+/CD79a+/Ki67− plasma cells were quantified on formalin-fixed, paraffin-embedded tissue sections by multiplex immunofluorescence microscopy and digital whole-slide image analysis

This is the first demonstration of kidney tissue-level B-cell depletion with obinutuzumab or any anti-CD20 agent in any glomerular disease

B cells are CD79a+ (green) and CD138−. Antibody-secreting cells are CD79a+ (green) and CD138+ (red), the large majority of which are plasma cells and Ki-67− (not shown). Renal tubular epithelium cells are CD138+ (red) and CD79a−. B cell-rich areas from study patients with the highest baseline B-cell counts from obinutuzumab[a] or placebo[a] groups at baseline and Week 76+. MMF, mycophenolate mofetil; ST, standard therapy.
[a]Plus ST consisting of MMF plus glucocorticoids.

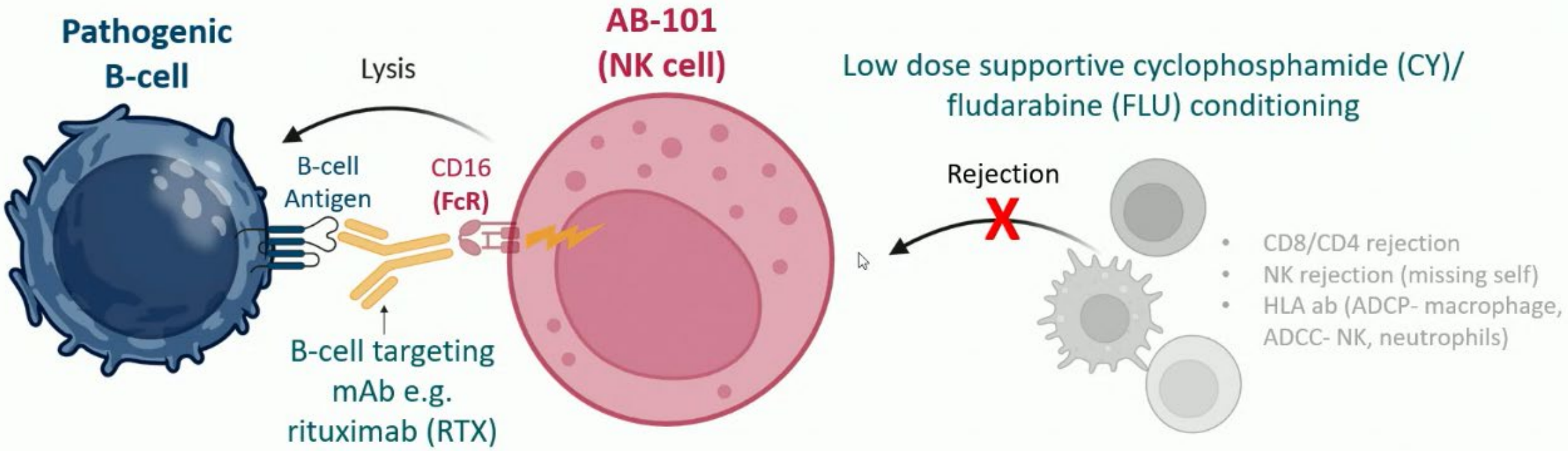
Q. WANG, POS0078: IN VIVO CD19 CAR T-CELL THERAPY INDUCES TISSUE B-CELL DEPLETION IN SYSTEMIC LUPUS ERYTHEMATOSUS





In vivo CAR T (HN2301) therapy induces deep tissue B-cell depletion in systemic lupus erythematosus.
(A) Representative images showing B-cell distribution in lymph node (upper panels) and bone marrow (lower panels) from a lupus-positive control patient and a patient after HN2301 treatment.
(B) Immunohistochemical staining of CD19 in lymph node sections from a lupus-positive control patient and a patient after HN2301 treatment.

AB-101 + Rituximab (RTX) in Rheumatological Diseases

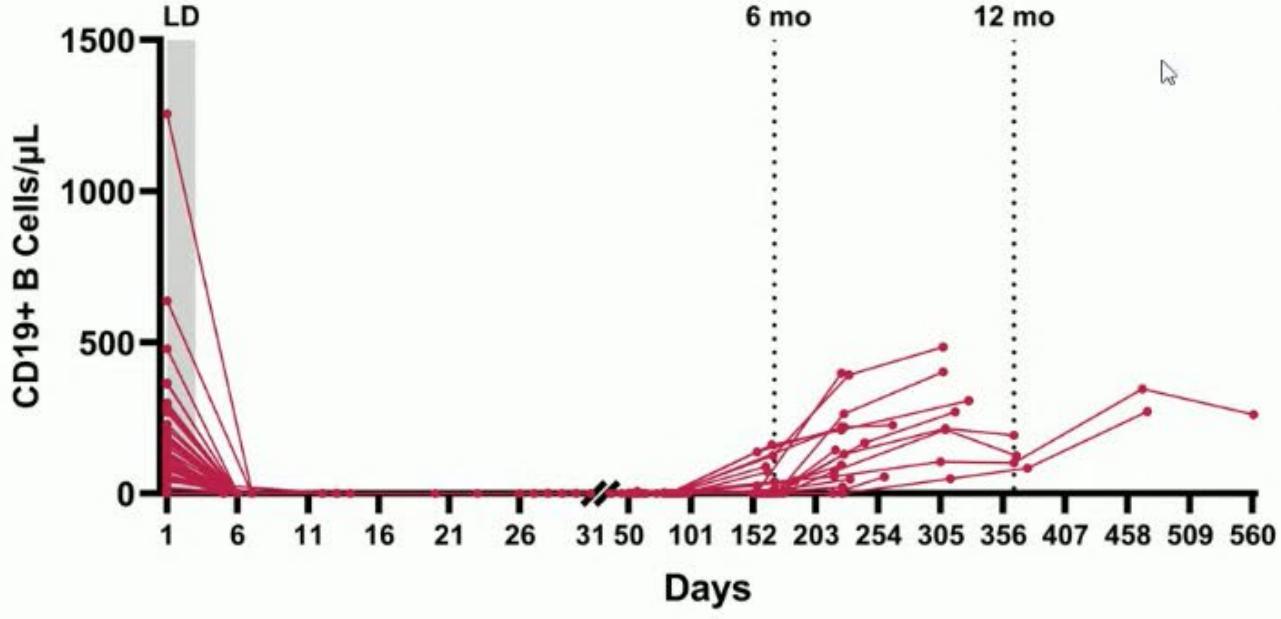


- Allogeneic, **non-genetically modified NK cells** from cord blood selected for **high affinity CD16 variant**
- Cryopreserved, **off-the-shelf**, investigational therapy
- **Outpatient-administered** with most patients treated in non-academic, community sites

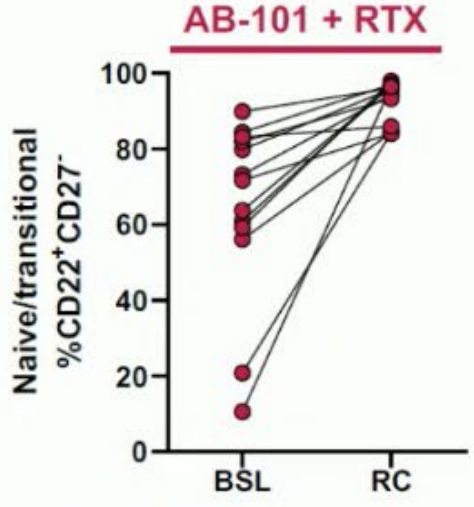
Complete B-Cell Depletion with AB-101 + RTX Across Autoimmune Diseases

Demonstrates Resetting of the Immune System

Uniform and consistent B-cell depletion
seen by D13 in all patients with autoimmune diseases (N=51)



B-cell reconstitution with increase in naïve/transitional B cells (N=13)



BSL: Baseline, RC: Reconstitution.

- B-cell reconstitution after AB-101 + RTX demonstrated an increase in naïve B cells
- Studies with RTX showed correlation between higher proportion of naïve/transitional cells with a good response in RA patients[1,2]

Left panel: Phase 2a basket trial, Phase 1/1b trial in SLE/LN, investigator-initiated basket trial; Right panel: Reflects patients who have seen B-cell reconstitution since treatment from AB-101 + RTX treated patients. (n=13);
[1]Dass et al 2008; [2]Adlowitz et al 2015; RTX: rituximab

Phase 2a Basket Study in Refractory Rheumatological Diseases

Indications: Rheumatoid Arthritis (RA); Sjogren Disease (SjD); Systemic Sclerosis (SSc); Idiopathic Inflammatory Myopathies (IIM)

Dosing (All IV):

- **Cyclophosphamide** (1000 mg/m^2 x 1) + **Fludarabine** (30 mg/m^2 x 3)
- **RTX:** 1000 mg x 2, 2 weeks apart
- **AB-101:** 1 billion or 4 billion cells x 3, weekly

Primary objective: Safety and tolerability

Secondary objectives: Preliminary efficacy

Key Inclusion Criteria

RA (2010 ACR/EULAR criteria)

- **ACPA/RF positive**
- **hs-CRP ≥3 mg/L**
- **≥6/66 Swollen Joints and 6/68 Tender Joints**
- **DAS28-ESR >3.2**
- **Inadequate response to ≥1 bDMARD (bDMARD-IR)**

SjD (2016 ACR/EULAR criteria)

- **Total ClinESSDAI ≥ 6**
- **Extra-glandular involvement**
- **Refractory to standard of care**

SSc (2013 ACR/EULAR criteria)

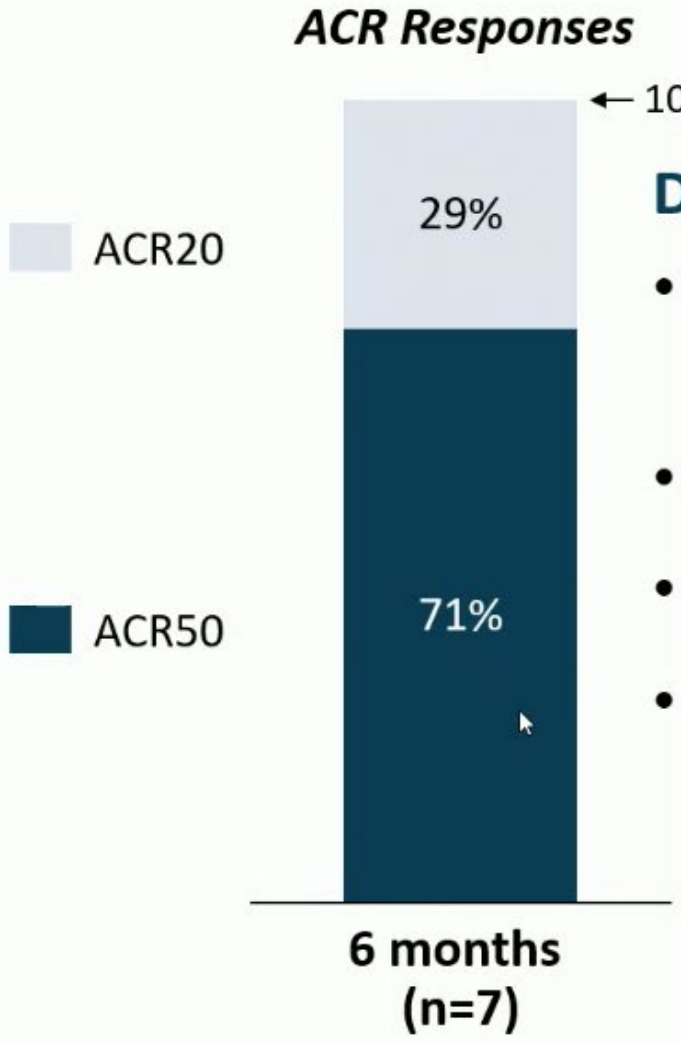
- **Modified Rodnan Score (mRSS) >10**
- **Refractory to immunosuppressive agents**

Initial dataset includes subjects in study with 3+ months follow-up as of 03 Apr 2026

RA: Refractory With High Disease Activity and Long Disease Duration

Parameter	Values (n=15)
Demographics	
Age (y)	53.9
Female, %	100%
Disease Duration (y)	**13.3**
Region	US only
Disease Activity	
CDAI	**50.7**
DAS28-ESR	**7.4**
Concomitant Medications	
csDMARDs	**0**
Glucocorticoid use, %; median dose	60%; 7.5 mg/day
*Prior Distinct Classes of b/tsDMARD Therapies**	
≥ 2 (TNFi, IL-6i, CTLA4-Ig, RTX, JAKi)	**73%** (20% RTX-IR)

RA: 71% ACR50 Response Observed in Patients Reaching 6 Months



Deep responses support target profile of ≥50% ACR50 at 6 months

- **DMARD-free during study:** All patients discontinued DMARDs prior to enrollment and remained DMARD-free
- **ACR50 higher than rituximab (27%)** in less refractory patients[1].
- **No patients have discontinued**
- **None have received an immunosuppressive agent**, including b/tsDMARDs

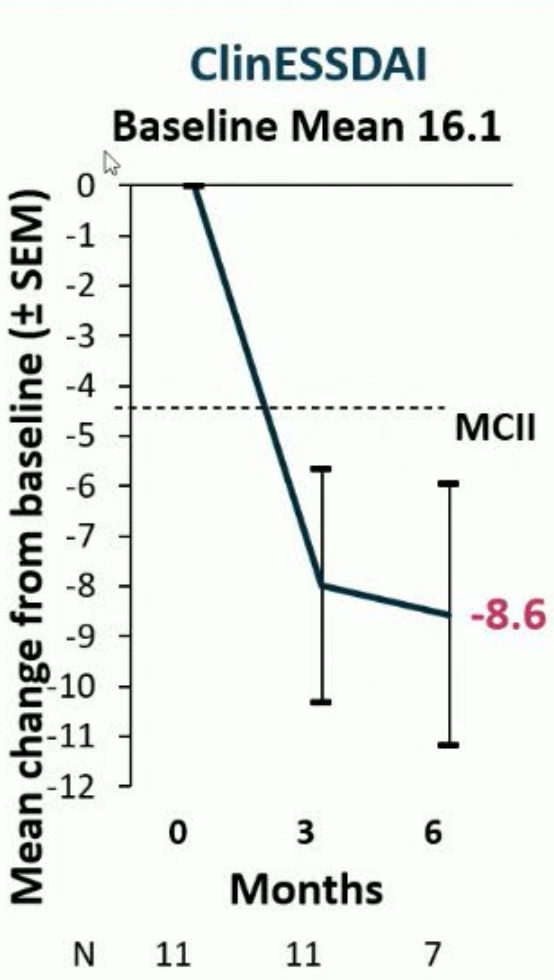
Month 6 = 22 wks; Last Visit Carried Forward for missing data

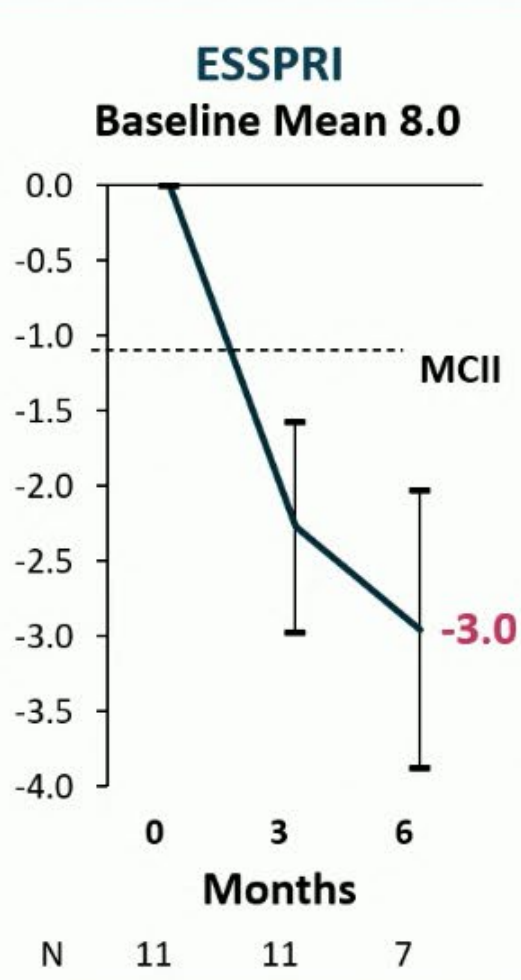
[1] Rituximab: REFLEX. (Cohen et al 2006) DAS28 of -1.9 and ACR50 of 27% at 6 months in TNF-IR RA patients

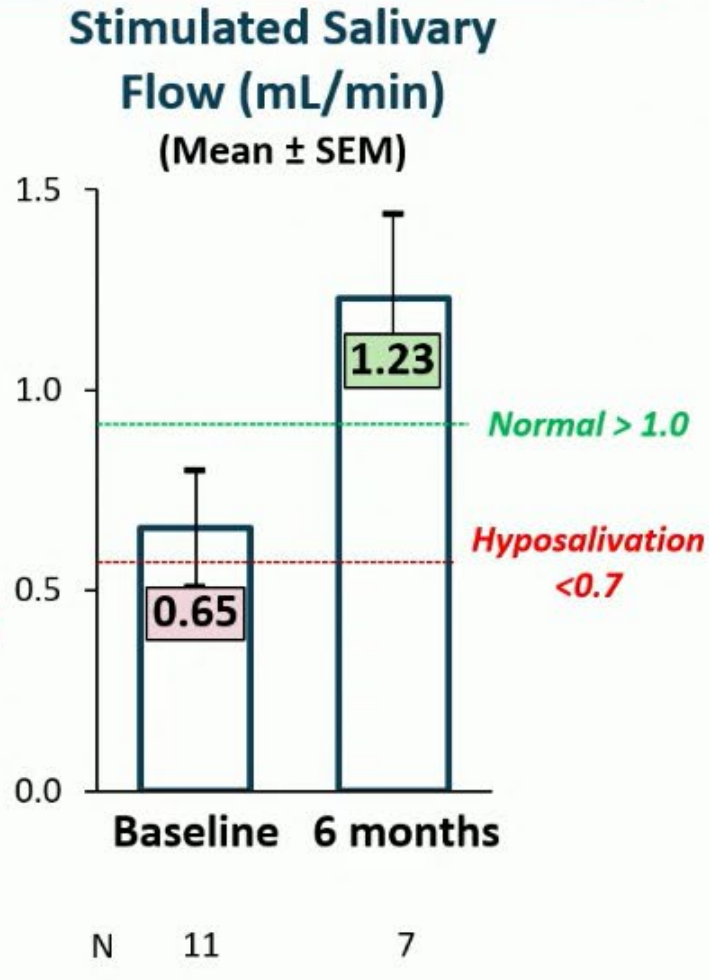
SjD: Robust Clinical Responses at 3 months that Deepened at 6 months

Baseline Characteristics (n=11)

- **Age (y),** mean: **53.6**
- **Sex:** 100% female
- **Disease duration** (y), mean: **12.2**
- **High baseline disease activity** (ClinESSDAI, ESSPRI, SSF*)
- **Refractory** to multiple prior immunomodulators
- **Prior RTX use (IR)**: **27%**







FACIT-F
Mean +13.0 @ 6 mo

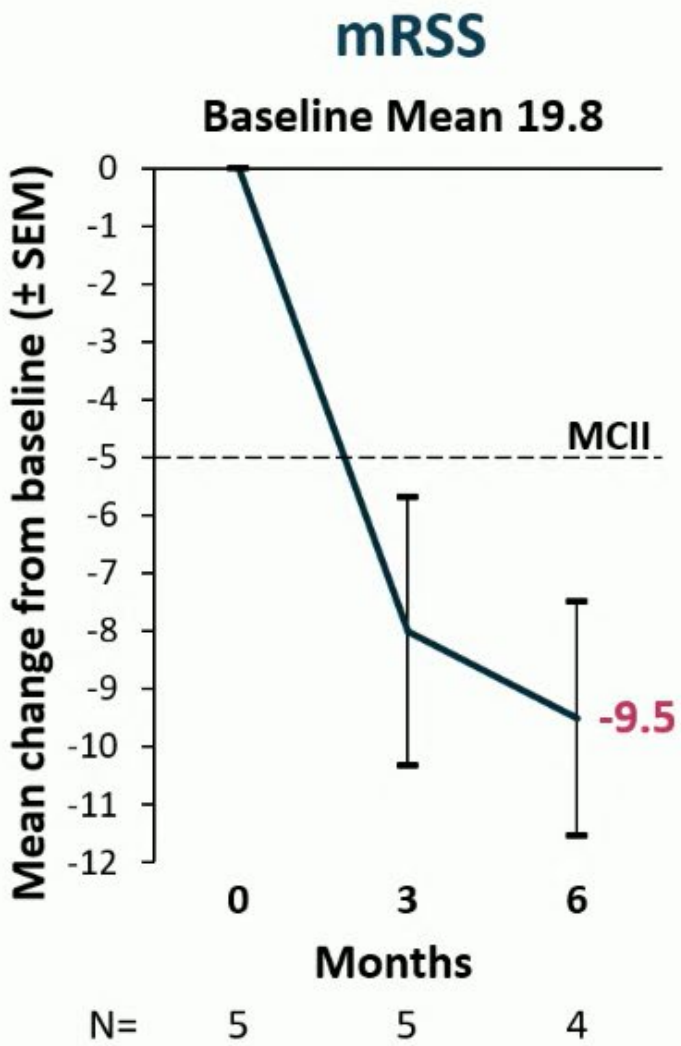
Stimulated salivary flow, mean intrapatient change was +0.76 mL/min at 6 months

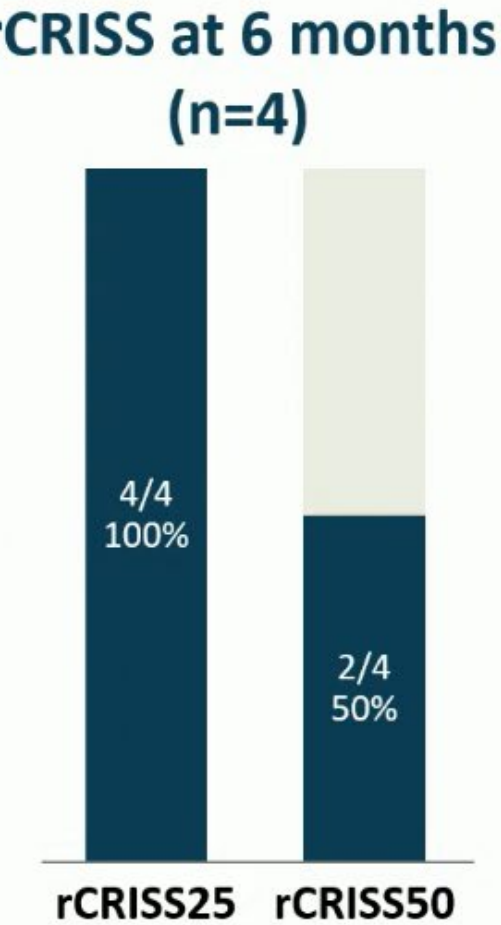
* *MCII: Minimal Clinically Important Improvement; Month 3 = 12 wks; Month 6 = 22 wks*
* *SSF: Stimulated Salivary Flow*

SSc: Robust Clinical Responses at 3 months that Deepened at 6 months

Baseline Characteristics (n=5)

- **Age** (y), mean: 54.2
- **Females:** 40%
- **Disease duration** (y), mean: **4.1**
- **Mod. Rodnan score (mRSS): high activity**
- **No concomitant immunosuppressives**
- **Prior immunosuppressives: 100%**
- **Prior RTX use (IR): 60%**



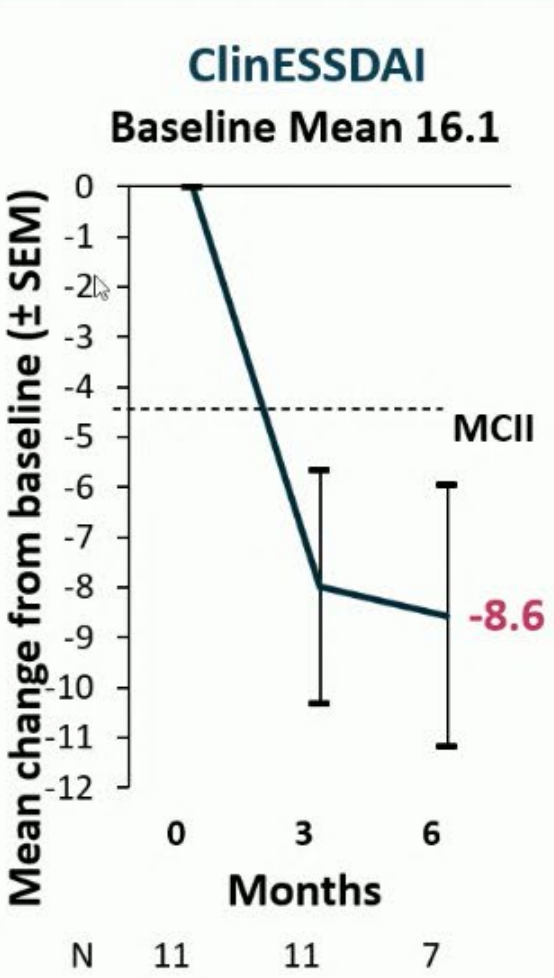


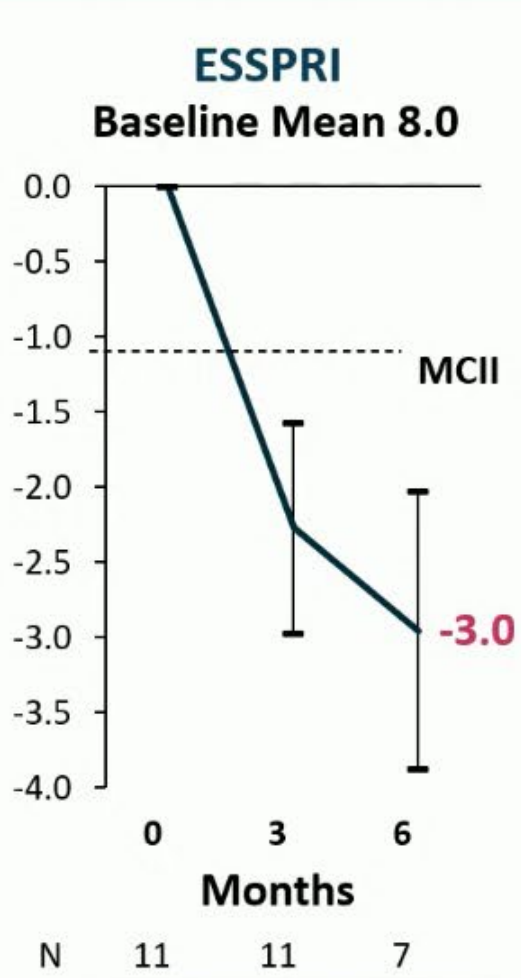
rCRISS25: ≥25% improvement in ≥2 of 5 domains (≥5% ppFVC, ≥ 25% in mRSS, HAQ-DI, PtGA, PhGA with no worsening in more than 1 domain)
rCRISS50: ≥50% improvement in ≥2 of 5 domains (≥5% ppFVC, ≥ 50% in mRSS, HAQ-DI, PtGA, PhGA with no worsening in more than 1 domain).
No significant SSc-related event.

SjD: Robust Clinical Responses at 3 months that Deepened at 6 months

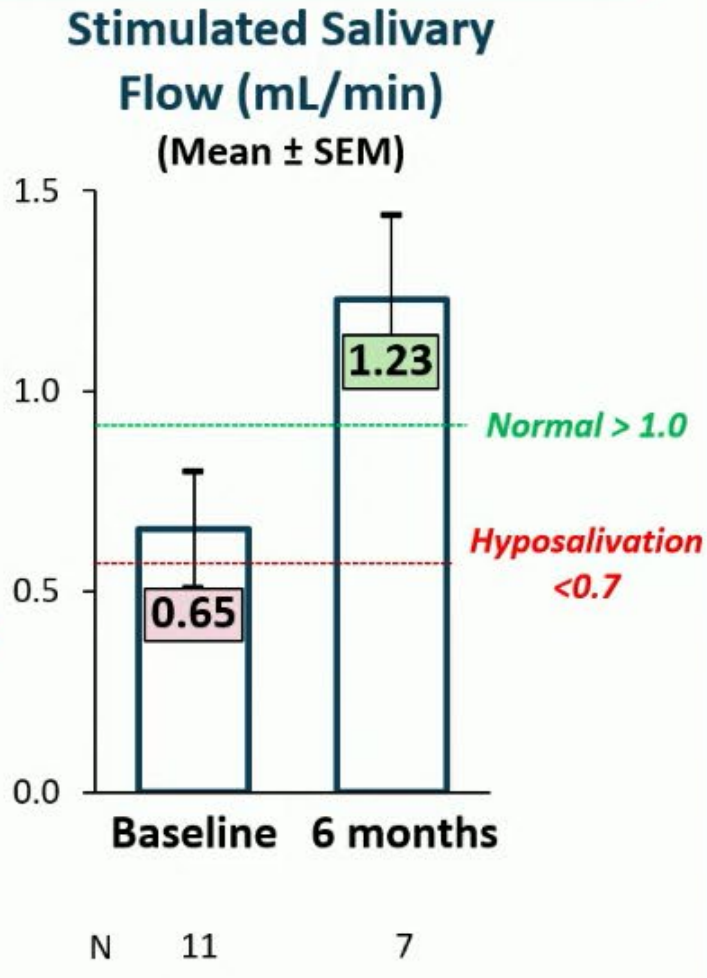
Baseline Characteristics (n=11)

- **Age (y),** mean: **53.6**
- **Sex:** 100% female
- **Disease duration** (y), mean: **12.2**
- **High baseline disease activity** (ClinESSDAI, ESSPRI, SSF*)
- **Refractory** to multiple prior immunomodulators
- **Prior RTX use (IR)**: **27%**





FACIT-F
Mean +13.0 @ 6 mo



Stimulated salivary flow, mean intrapatient change was +0.76 mL/min at 6 months

* *MCII: Minimal Clinically Important Improvement; Month 3 = 12 wks; Month 6 = 22 wks*
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