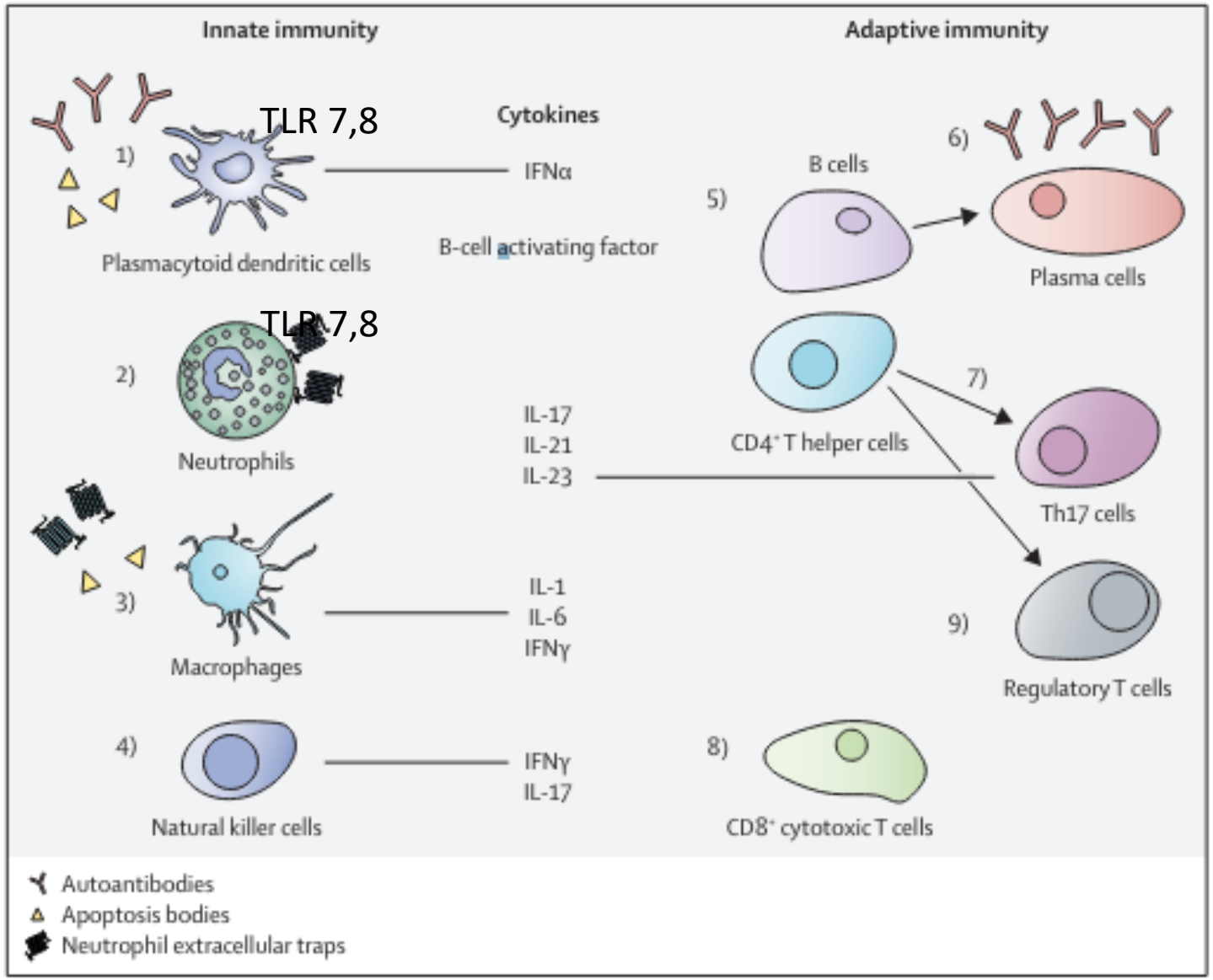
# Lupus/Sjögren Syndrom EULAR 2025

Thomas Daikeler

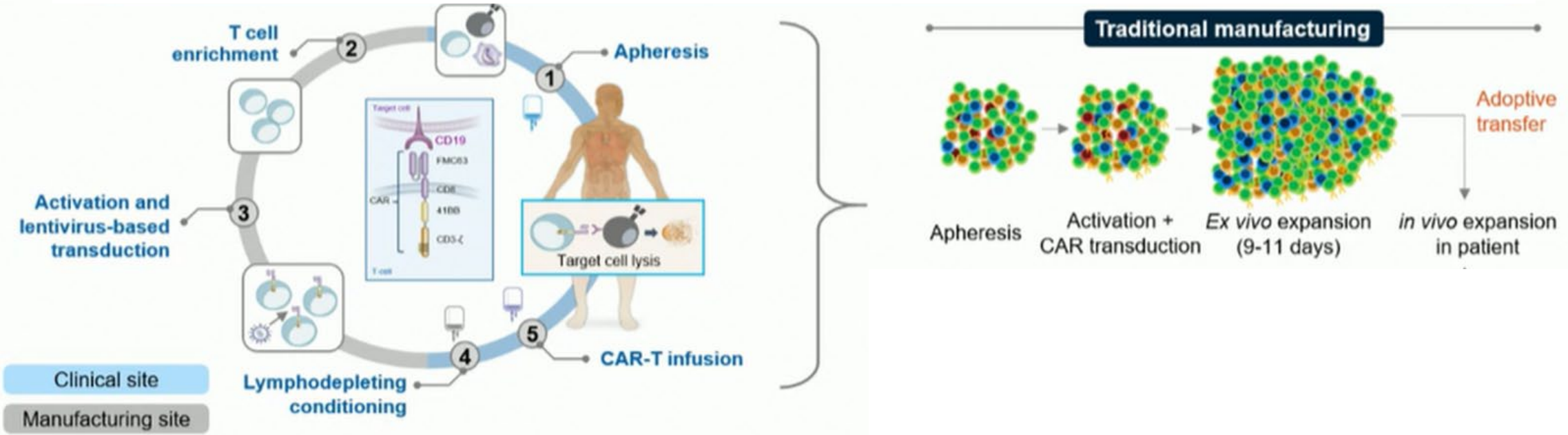
Rheumatologie

USB

SLE-Pathophysiologie



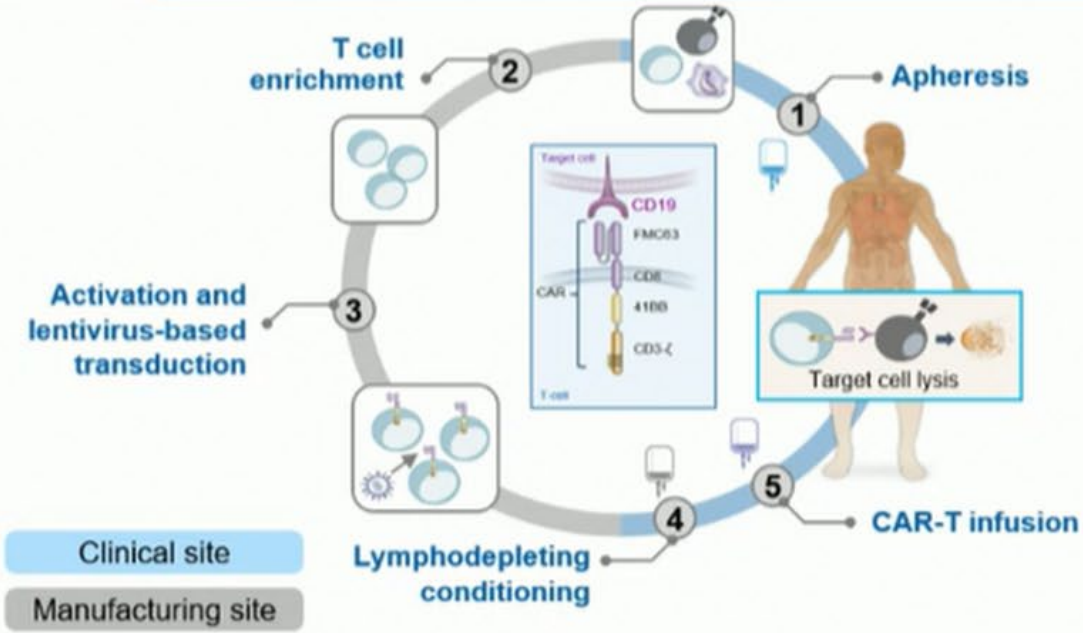

https://doi.org/10.1016/S0140-6736(24)00398-2

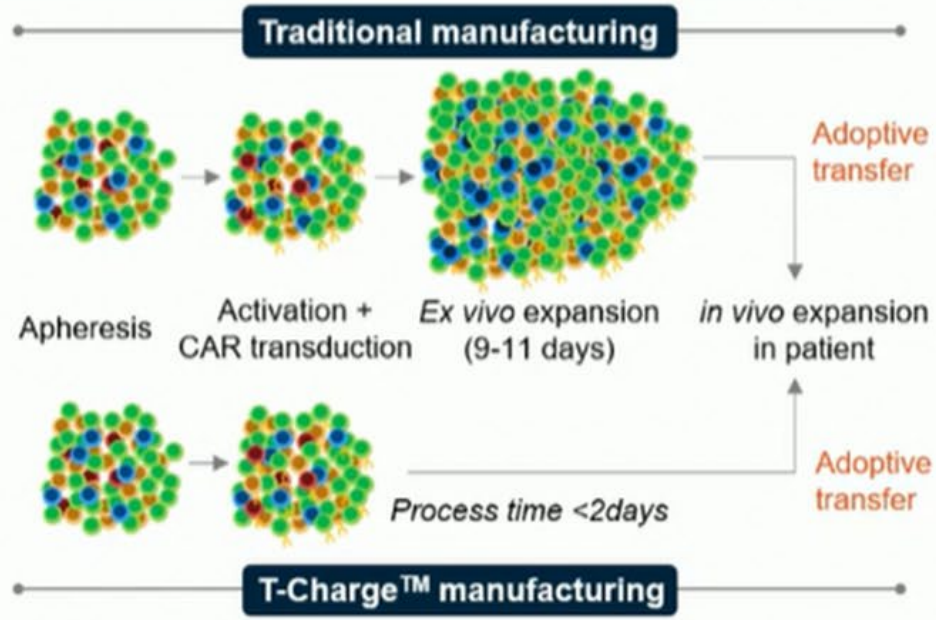



CAR-T, chimeric antigen receptor T-cell

**1.** Dickinson MJ et al. *Cancer Discov*. 2023;13:1982-1997. **2.** Flinn IW et al. *Blood*. 2021;138:740; **3.** Bu D, et al. ASH 2021. Poster 2770; **4.** Engels B, et al. ASH. 2021. **5.** Bao L et al. *Zool Res*. 2022;43:150-165. **6.** Schett G et al. *Ann Rheum Dis*. 2024;doi:10.1136/ard-2024-225727.

# Principle of CAR-T cell manufacturing : Traditional vs. T-Charge™ [1-6]




CAR-T, chimeric antigen receptor T-cell

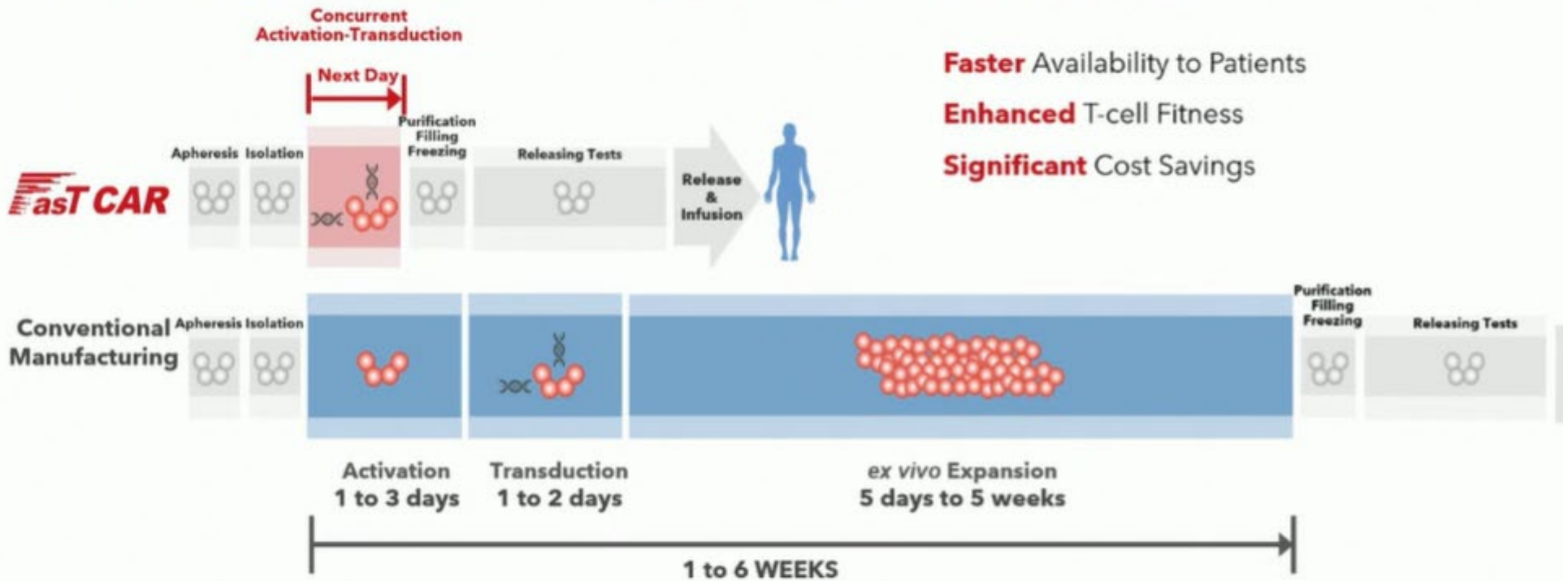
**1.** Dickinson MJ et al. *Cancer Discov*. 2023;13:1982-1997. **2.** Flinn IW et al. *Blood*. 2021;138:740; **3.** Bu D, et al. ASH 2021. Poster 2770; **4.** Engels B, et al. ASH. 2021. **5.** Bao L et al. *Zool Res*. 2022;43:150-165. **6.** Schett G et al. *Ann Rheum Dis*. 2024;doi:10.1136/ard-2024-225727.

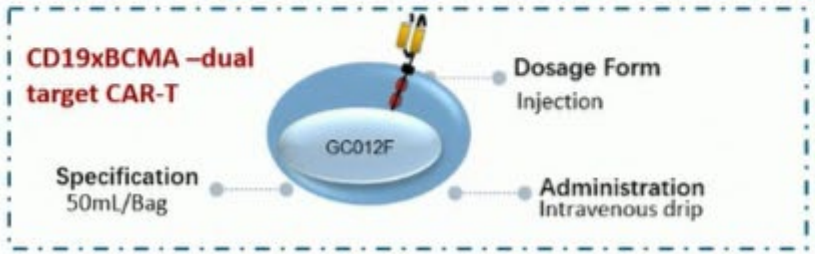
op0074

# *Introduction*

## GC012F, a CD19xBCMA dual targeting CAR-T manufactured by the FasT CAR platform

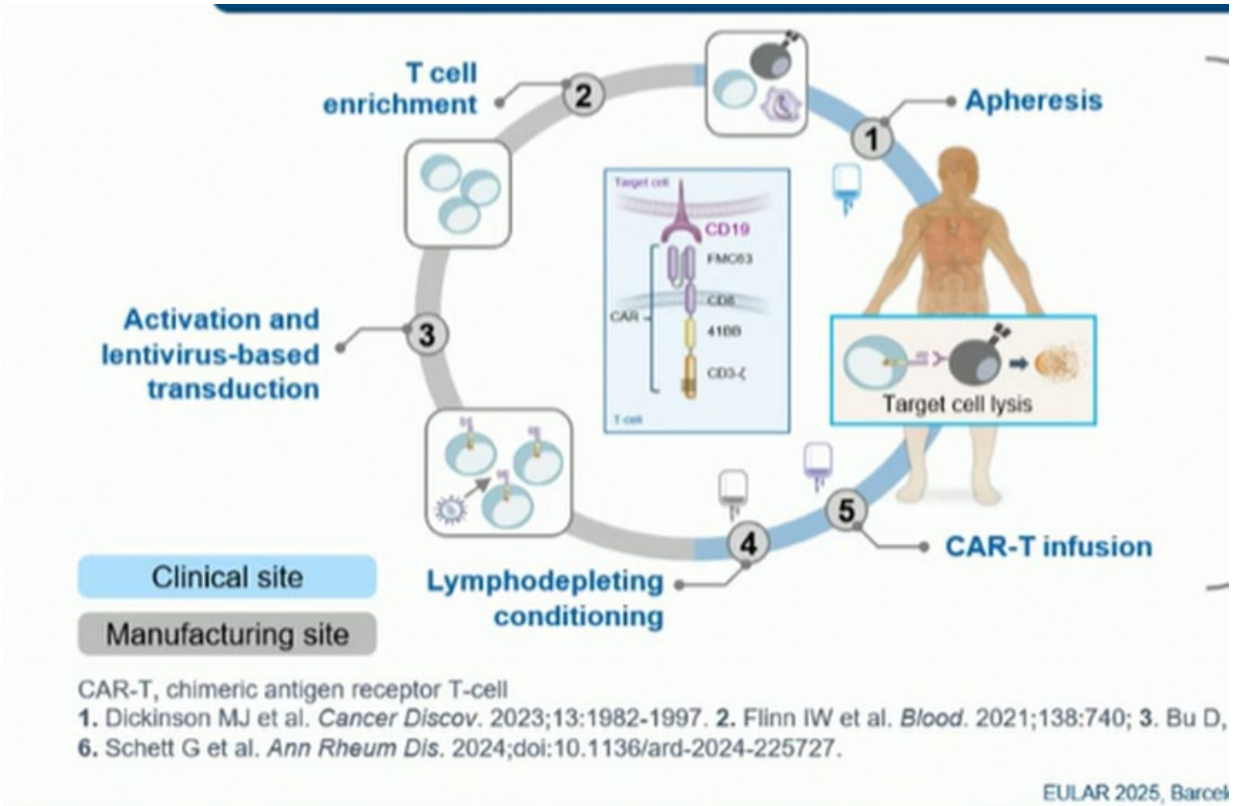
FasT CAR Platform Significantly Shortens CART Manufacturing Time and Improves T Cell Fitness



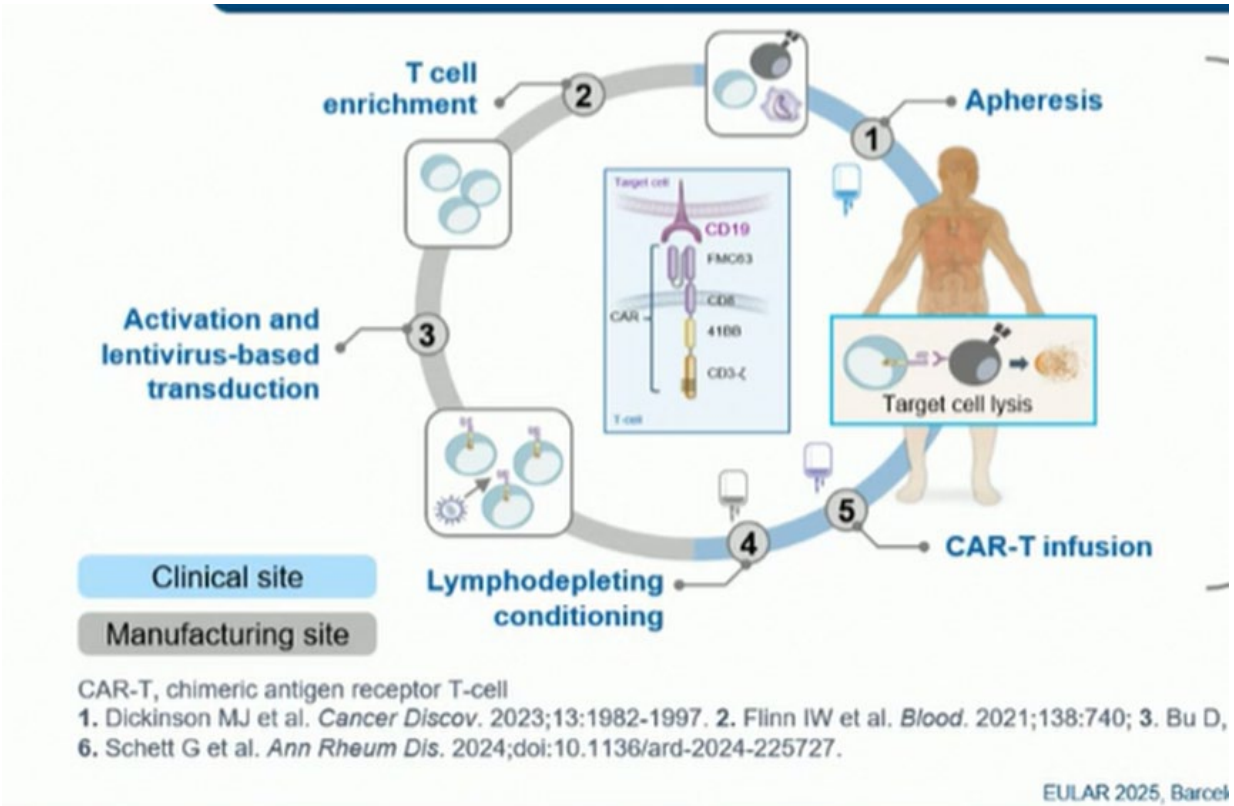

**Preclinical Studies suggest:**

- ✓ High transduction efficiency and high CAR-positive rate
- ✓ Specific killing of CD19+ and BCMA+ cells in vitro
- ✓ Specific elimination of CD19+ and BCMA+ cells in mouse models in vivo
- ✓ Favorable safety profile in preclinical studies




CAR-T, chimeric antigen receptor T-cell

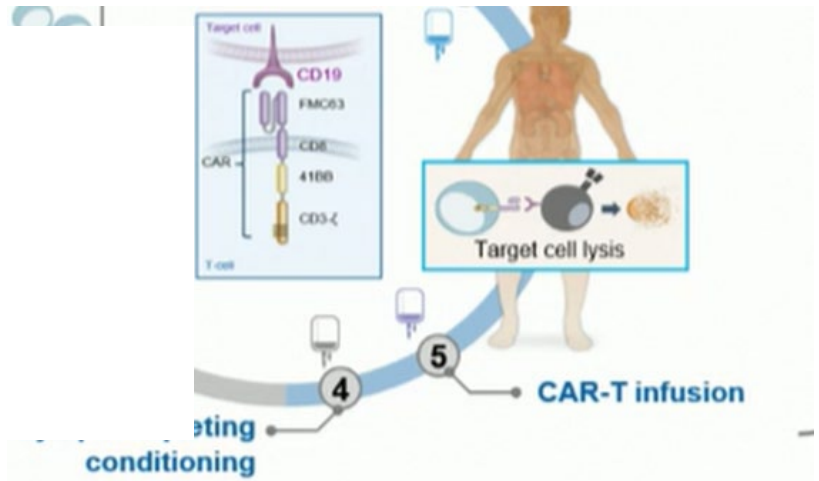
**1.** Dickinson MJ et al. *Cancer Discov*. 2023;13:1982-1997. **2.** Flinn IW et al. *Blood*. 2021;138:740; **3.** Bu D, **6.** Schett G et al. *Ann Rheum Dis*. 2024;doi:10.1136/ard-2024-225727.




CAR-T, chimeric antigen receptor T-cell

**1.** Dickinson MJ et al. *Cancer Discov*. 2023;13:1982-1997. **2.** Flinn IW et al. *Blood*. 2021;138:740; **3.** Bu D, **6.** Schett G et al. *Ann Rheum Dis*. 2024;doi:10.1136/ard-2024-225727.






tor T-cell

*iscov*. 2023;13:1982-1997. **2.** Flinn IW et al. *Blood*. 2021;138:740; **3.** Bu D
*is*. 2024;doi:10.1136/ard-2024-225727.

LB0009


# Allogenic CD19 CAR NK Cell Therapy in Relapse or Refractory Systemic Lupus Erythematosus

Ruina Kong, Ph.D
Changhai Hospital

06-14-2025

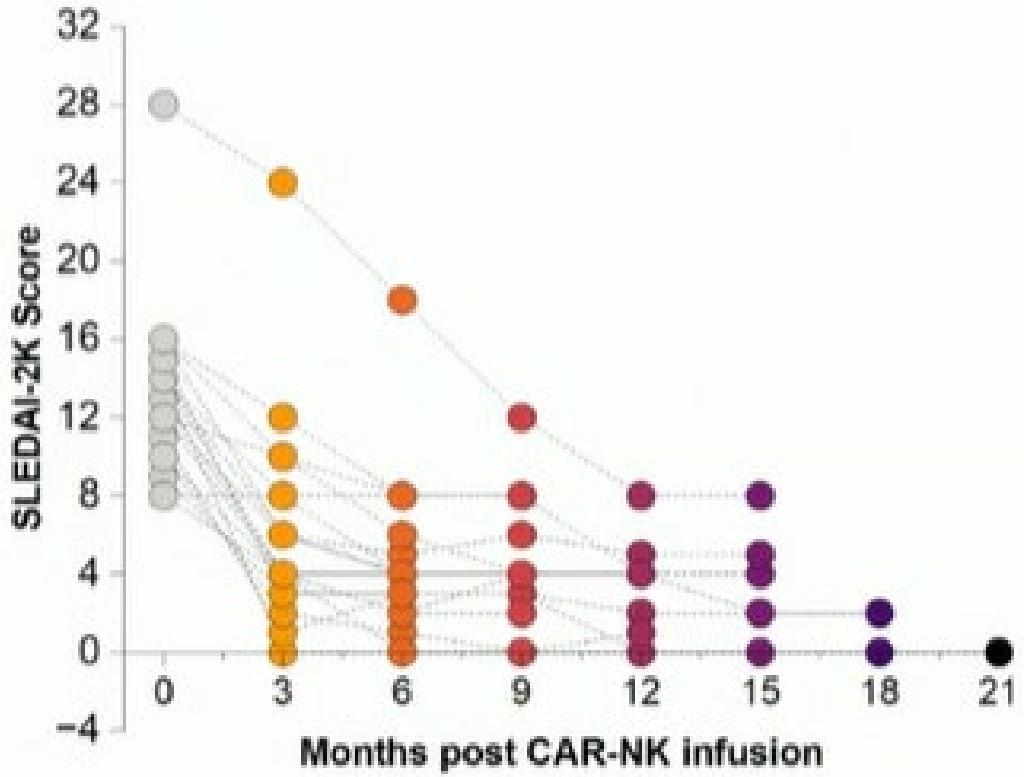
**23 Female** and **4 Male** Patients with Relapsed and Refractory SLE

- SLEDAI-2K ≧8, The Median SLEDAI-2K:**12** (Range 8-28 )
- Age: Median **37** Years old (Range 18-48 )
- The Median Disease Duration: ***8.2 years*** (1 to 19)
- Anti-dsDNA (positive:>10 IU/mL): ***Positive, 16***; Negative, 11
- Complements: **Abnormal,25**: Normal 2
- **Organ involvement**
  - ✓ Mucocutaneous and Joints: 13
  - ✓ Kidney: 16 (4 patient Proteinuria> 3.5g)
  - ✓ Blood system: 8
  - ✓ Vasculitis: 2
- **Prior Disease-SpecificTherapy**
  - ✓ Steroids, HCQ, Mycophenolate Mofetil, Cyclophosphamide, Tacrolimus
  - ✓ B cell-target medications, e.g., Rituximab、Belimumab、Telitacicept: 19

# Safety

- 2/27 CRS  >=1
- No ICAN
- No Infection
- No hypogamma

# Improvement of SLEDAI-2K



# OP0032


Better Cells For Better Therapies™
Treatment of Refractory SLE with Off-the-Shelf iPSC-derived Anti-CD19 CAR T-cell Therapy
EULAR European Congress of Rheumatology
June 11, 2025
Vaneet K Sandhu, MD, MS
Fate Therapeutics, Inc.

# A Unique Platform for the True Delivery of Off-the-Shelf Cellular Therapies

*Mass Produced, Multiplexed-engineered Cell Products for On-demand Patient Treatment*

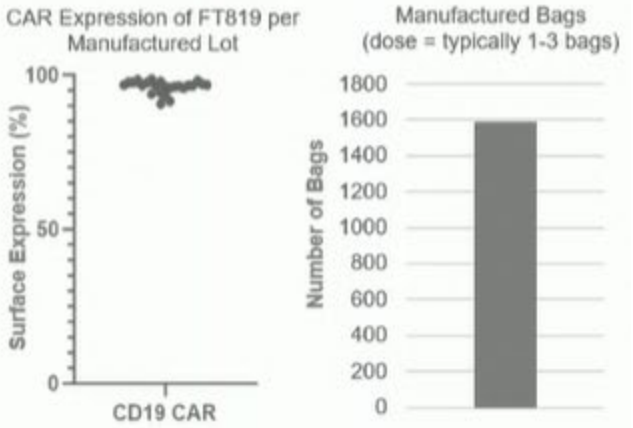

## Platform Advantages

- ✓ Defined Clonal MCB: Single-cell derived, complete and uniform for genetic edits, selected for genomic integrity & potency
- ✓ Engineered MCB as the Starting Material: Highly-scalable, uniform final product, one-time genetic engineering, high-quality cellular products, and eliminates the need for repeated donor search
- ✓ Modular Innovation: Rapid, efficient development through multiplexed engineering

## iPSC-derived Cell Therapy Products

- ➢ Reliable, Scalable Drug Product: Uniform, consistent and well-characterized with >5-year stability in storage; ~50,000-dose GMP-scale manufacturing capability at current GMP site
- ➢ Cost-Effective & Consistent: Low COGs (~$3,000 per dose), inventory-based cost management, and no donor variability
- ➢ Patient-Centered Therapy: Off-the-shelf, antibody-like treatment with repeat dose capability and combinability ease, reduced toxicity, and administration with reduced hospitalization requirements in community setting

*Uniform and Consistent Inventory of Thousands of Doses Generated per Routine Manufacture Starting with a MCB Vial*



# FT819: Off-the-Shelf anti-CD19 CAR T-Cell Product Candidate

*Safe and effective targeting of CD19+ B cells with broad patient accessibility in autoimmune*

## True Off-the-Shelf CAR T cell Drug Product

**CAR19**

State-of-the-art CAR motif and expression control

**TCR null**

Complete TCR knock-out to prevent GvHD in allogeneic settings


**Uniform Product**

Clonally engineered iPSC-derived CD8αβ T cell

Derived from a defined clonal MCB incorporating unique functional elements to balance safety and efficacy:

- **1XX CAR19**: Novel CAR with CD28 costimulatory and modified CD3ζ signaling domains for optimal safety and activity
- **TRAC-targeted CAR**: CAR inserted in the T-cell receptor alpha constant (TRAC) locus to reproduce endogenous TCR expression for regulated and optimal function
- **TCR Null**: Complete bi-allelic disruption of TRAC ablates TCR expression and eliminates the possibility of GvHD
- **On-Demand Delivery**: Routinely manufactured at large scale from an engineered MCB that uniquely ensures a uniform, off-the-shelf drug product for broad patient access

Memorial Sloan Kettering Cancer Center

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

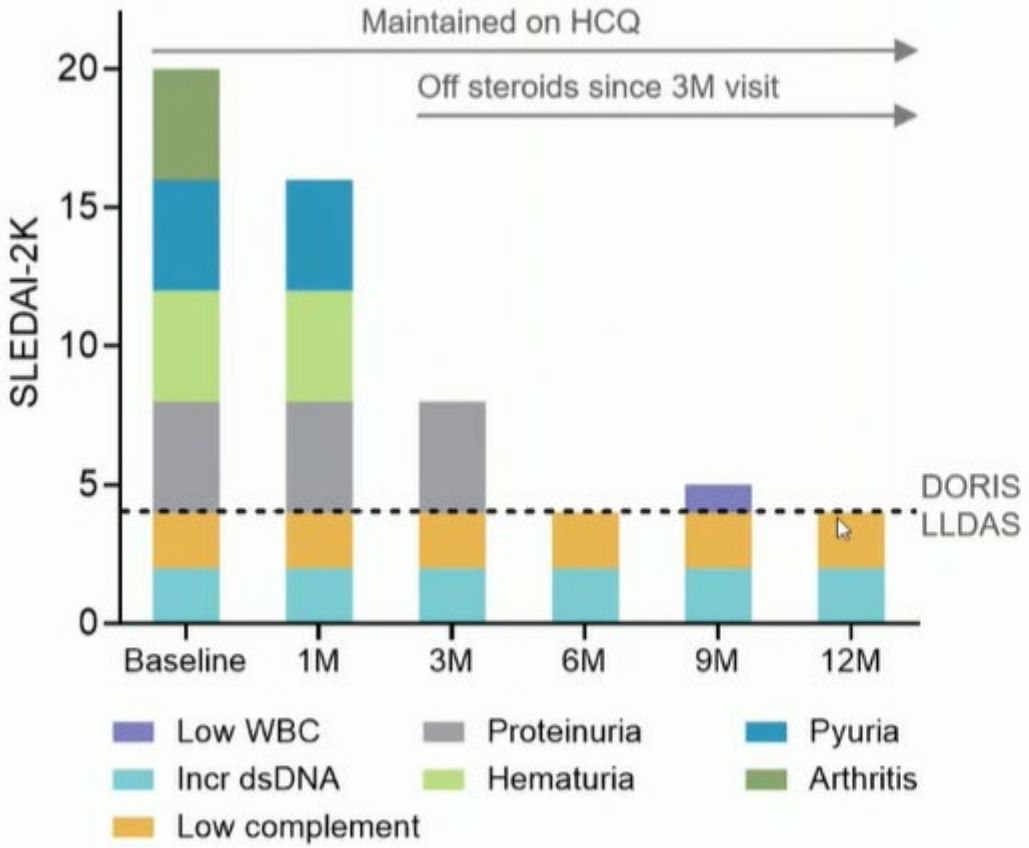
nature biomedical engineering ARTICLES

**Generation of T-cell-receptor-negative CD8αβ-positive CAR T cells from T-cell-derived induced pluripotent stem cells**

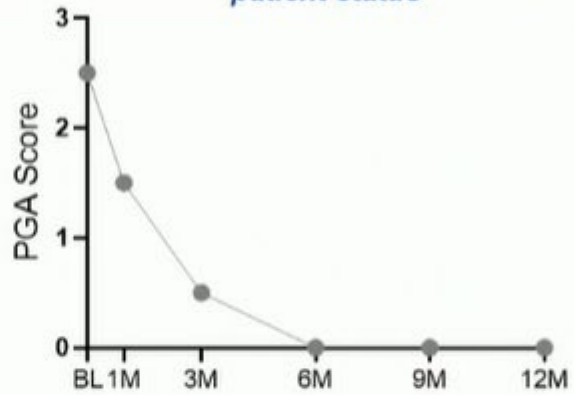
Sjoukje J. C. van der Stegen, Pieter L. Lindenbergh, Roseanna M. Petrovic, Hongyao Xie, Mame P. Diop, Vera Alexeeva, Yuzhe Shi, Jorge Mansilla-Soto, Mohamad Hamieh, Justin Eyquem, Annalisa Cabriolu, Xiuyan Wang, Ramzey Abujarour, Tom Lee, Raedun Clarke, Bahram Valamehr, Maria Themeli, Isabelle Riviere and Michel Sadelain

✓ *Fludarabine-free lympho-conditioning* ✓ *On-demand CAR T-cell delivery with no apheresis* ✓ *No DLT, CRS, GvHD or ICANS* ✓ *Reduced hospitalization*

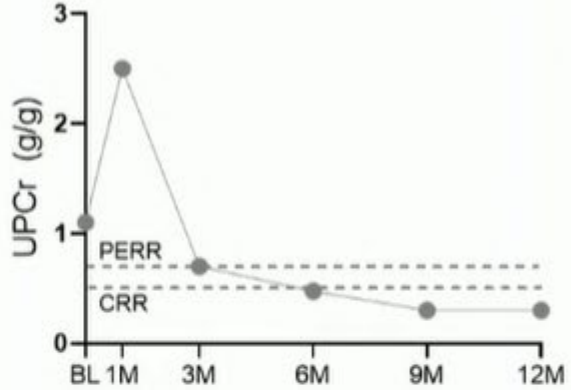
## *Remission in SLE without use of steroids*



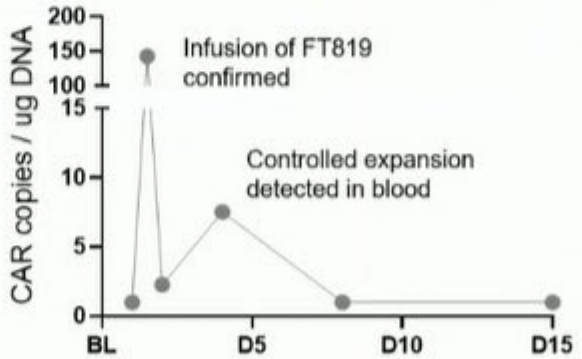

## *Sustained improvement in overall patient status*



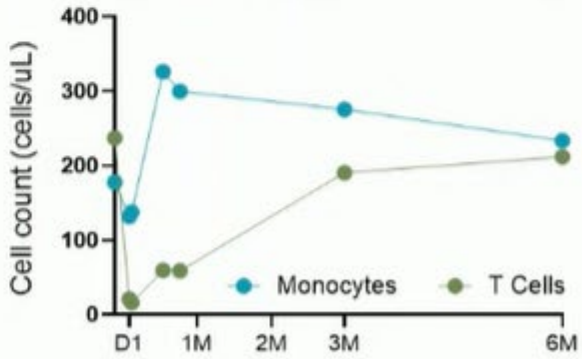

## *Durable renal response*




## *FT819 designed to show a balance of efficacy and safety*




## *Less intensive conditioning facilitates recovery of patient's immune cells*

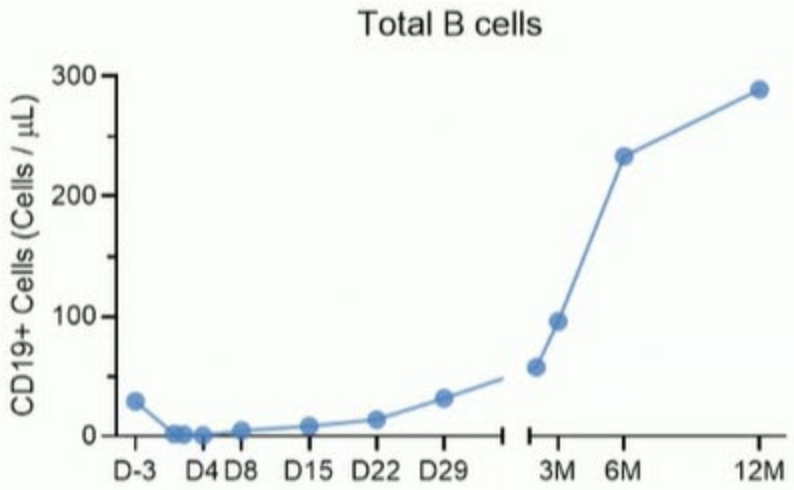



***PERR**: Primary Efficacy Renal Response* ***CRR**: Complete Renal Response* ***DORIS**: Definition Of Remission In SLE* ***LLDAS**: Low Lupus Disease Activity State* ***SLEDAI**: SLE Disease Activity Index* ***PGA**: Physician Global Assessment*

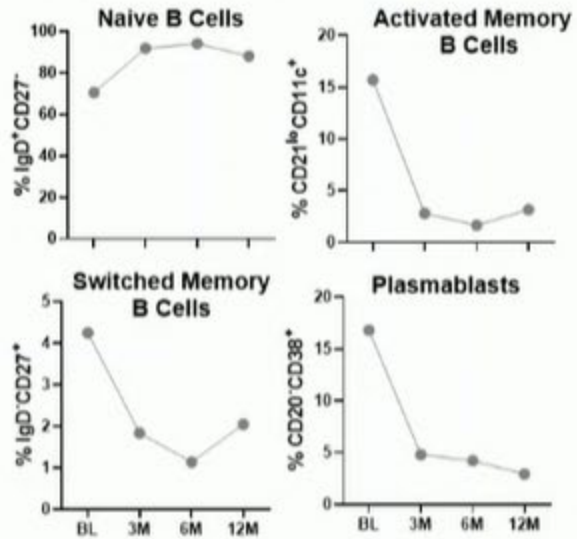
Fate

Data cutoff 15 May 2025; Graphs show measurements across study timepoints. BL = baseline, Dur=Month

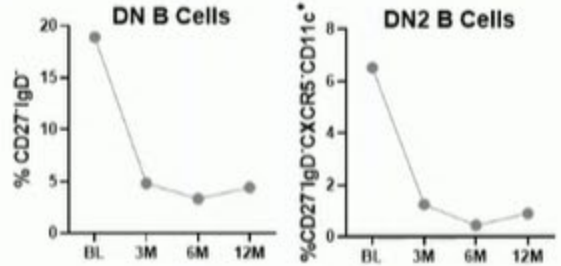
***Effective B cell depletion and repopulation to normal levels****



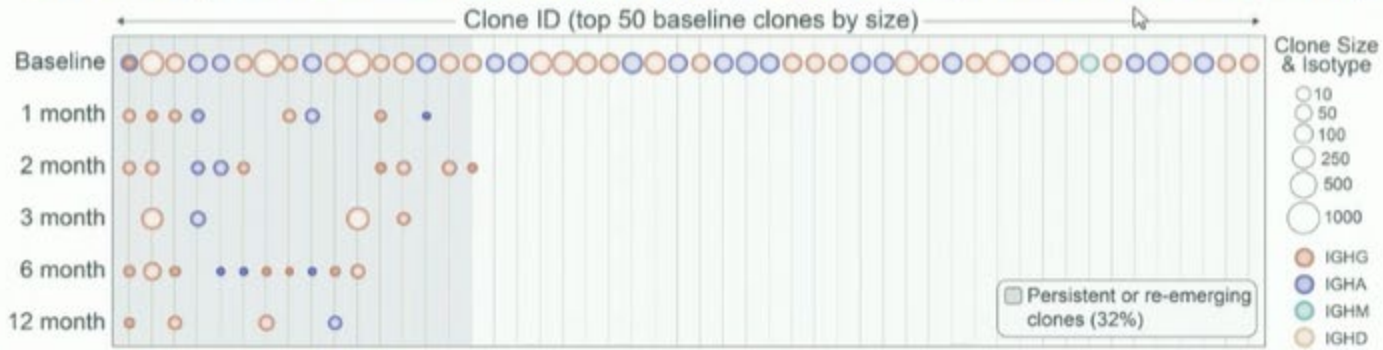

***Reconstituting B cells appear to be predominantly naïve with a limited switched memory phenotype***

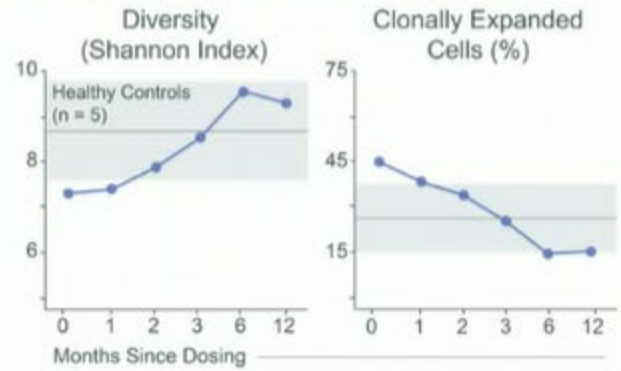



***Low pathogenic DN B cell subset in the reconstituting B cells, suggesting immune reset***



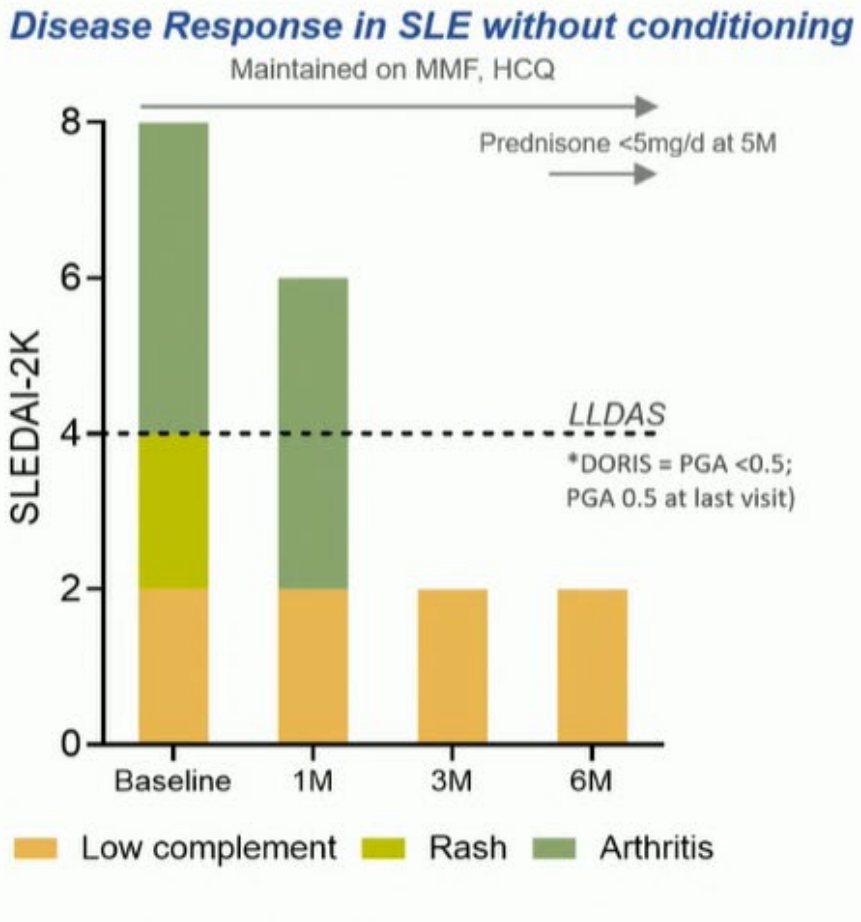

***Persistent depletion of dominant clones and reshaping of the B cell compartment toward a more diverse, less expanded repertoire after treatment with FT819***

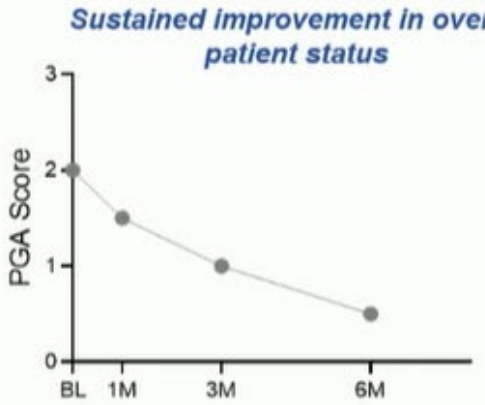


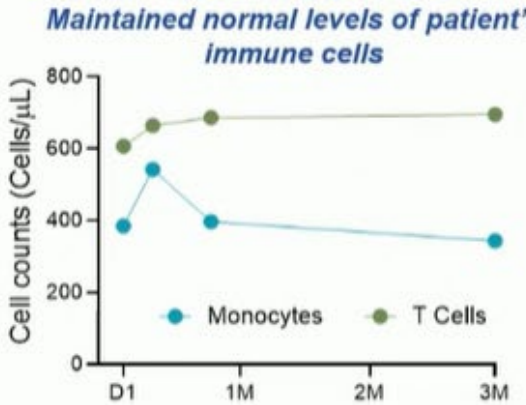



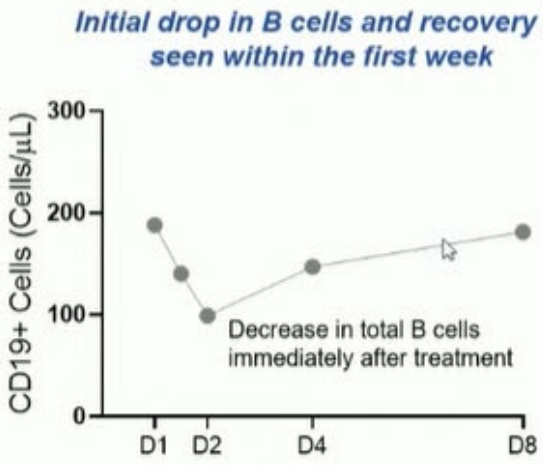
# Without conditioning

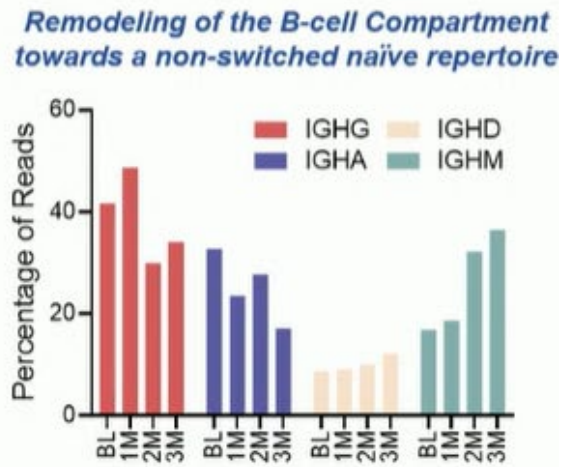
✓ No lympho-conditioning (Regimen B) ✓ On-demand CAR T cell delivery with no apheresis ✓ No DLT, CRS, GvHD or ICANS ✓ Reduced hospitalization



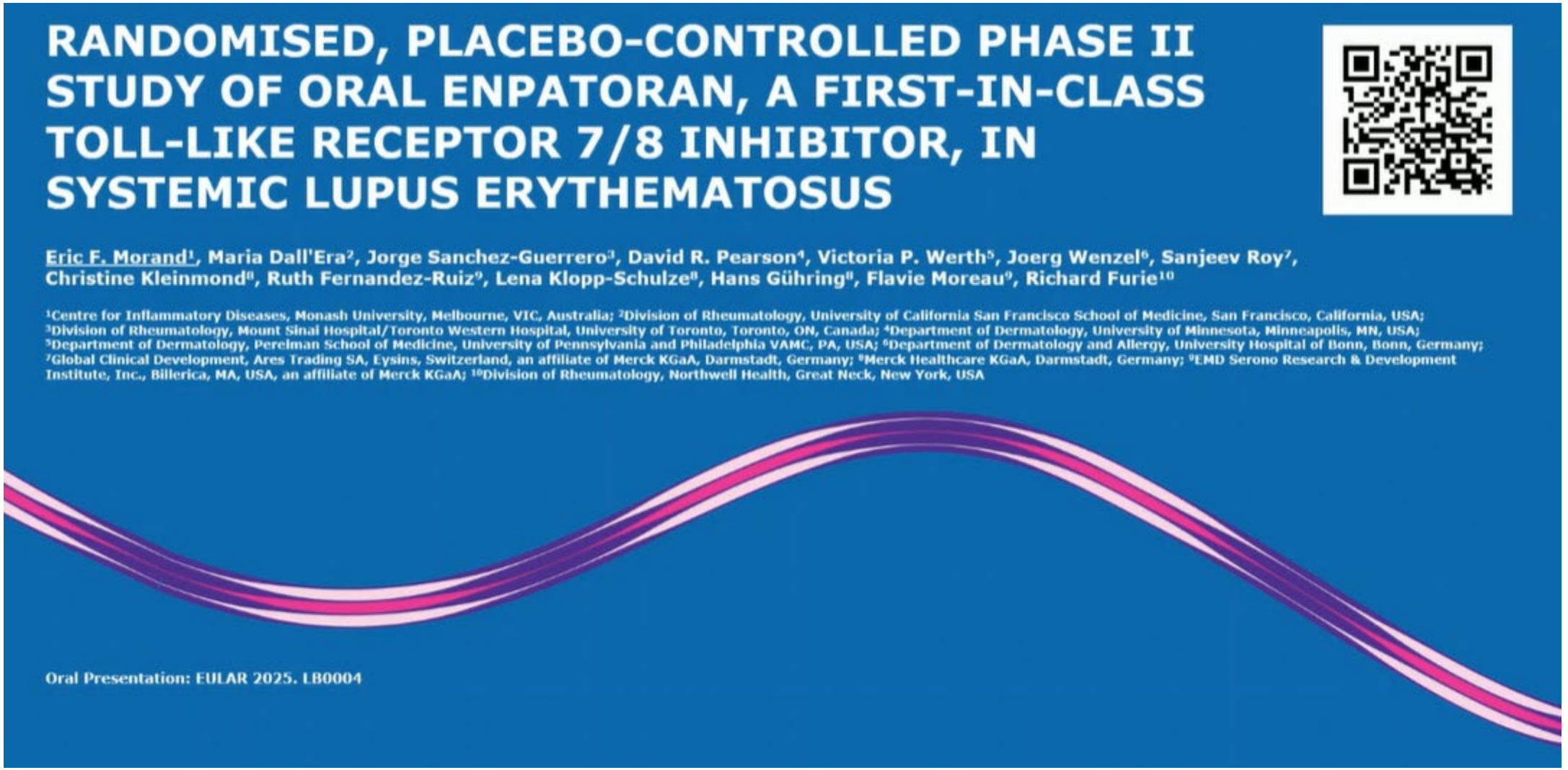



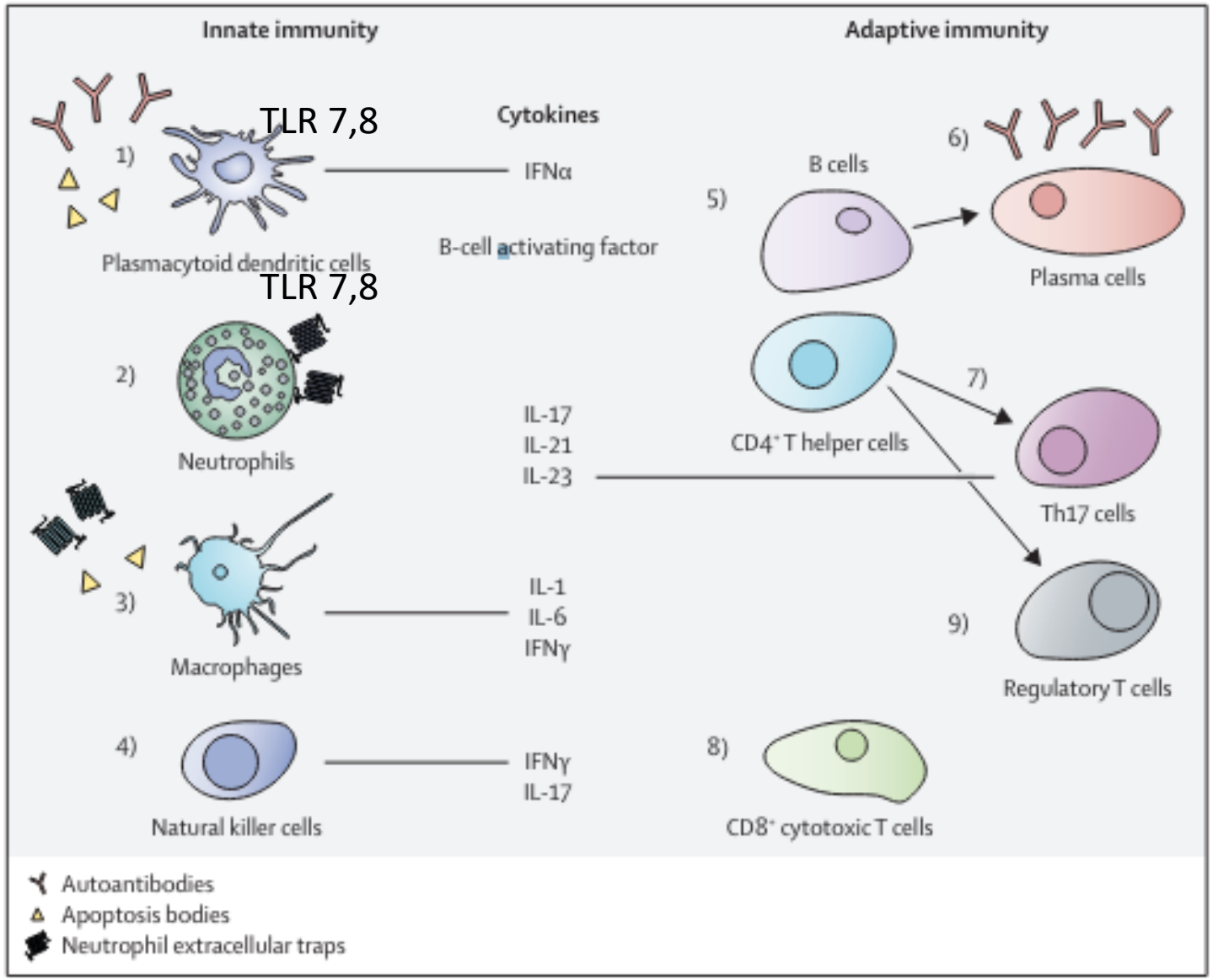



# LB0004


RANDOMISED, PLACEBO-CONTROLLED PHASE II STUDY OF ORAL ENPATORAN, A FIRST-IN-CLASS TOLL-LIKE RECEPTOR 7/8 INHIBITOR, IN SYSTEMIC LUPUS ERYTHEMATOSUS
Eric F. Morand[1], Maria Dall'Era[2], Jorge Sanchez-Guerrero[3], David R. Pearson[4], Victoria P. Werth[5], Joerg Wenzel[6], Sanjeev Roy[7], Christine Kleinmond[8], Ruth Fernandez-Ruiz[9], Lena Klopp-Schulze[8], Hans Gühring[8], Flavie Moreau[9], Richard Furie[10]
[1]Centre for Inflammatory Diseases, Monash University, Melbourne, VIC, Australia; [2]Division of Rheumatology, University of California San Francisco School of Medicine, San Francisco, California, USA; [3]Division of Rheumatology, Mount Sinai Hospital/Toronto Western Hospital, University of Toronto, Toronto, ON, Canada; [4]Department of Dermatology, University of Minnesota, Minneapolis, MN, USA; [5]Department of Dermatology, Perelman School of Medicine, University of Pennsylvania and Philadelphia VAMC, PA, USA; [6]Department of Dermatology and Allergy, University Hospital of Bonn, Bonn, Germany; [7]Global Clinical Development, Ares Trading SA, Eysins, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany; [8]Merck Healthcare KGaA, Darmstadt, Germany; [9]EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA; [10]Division of Rheumatology, Northwell Health, Great Neck, New York, USA
Oral Presentation: EULAR 2025. LB0004

SLE-Krankheitsmechanismen




https://doi.org/10.1016/S0140-6736(24)00398-2

# TLR7 is required for the formation of pathogenic 'atypical B cells,' or ABCs, DN2 or CD11c+ B cells[1]

**$CD19^{hi}$ CD27– IgD– $CD21^{lo}$ $CXCR5^{lo}$ $CD11c^{+}$ $FcRL5^{+1,2}$**

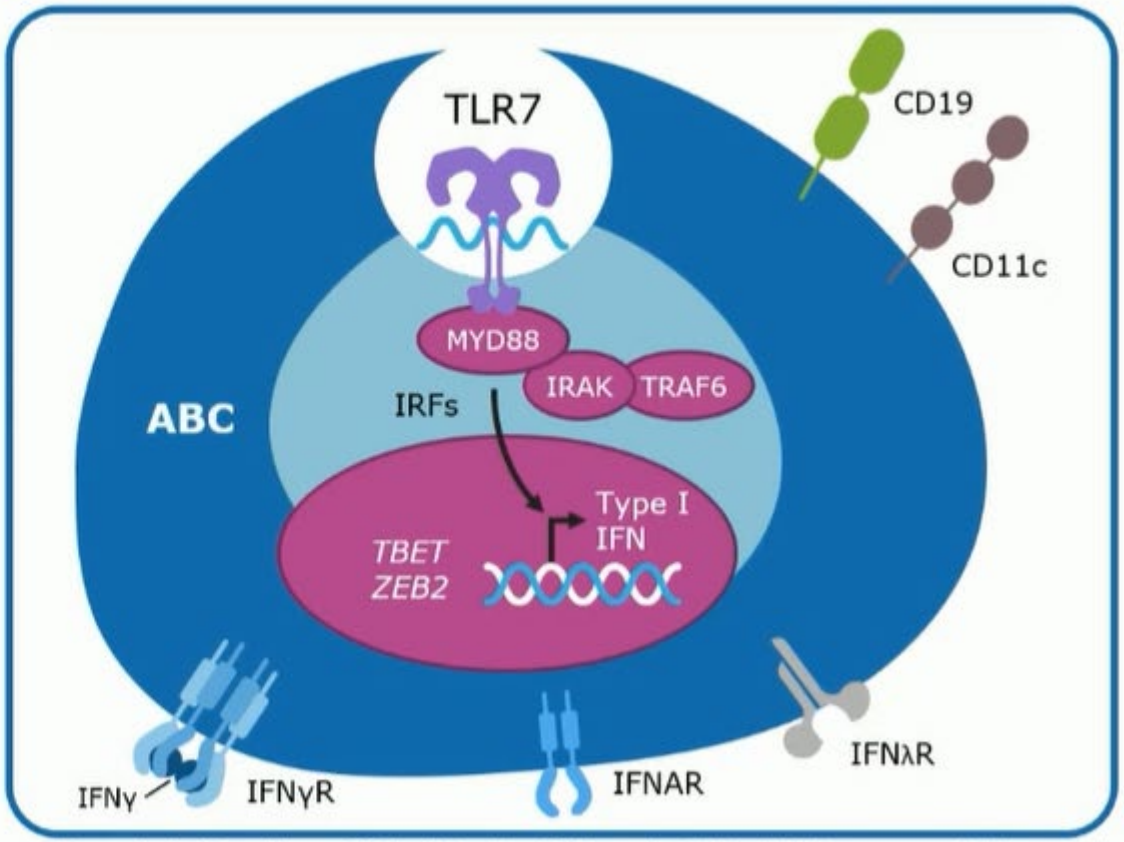



Figure adapted from Vinuesa CG et al, Genetics of SLE: mechanistic insights from monogenic disease and disease-associated variants, Nat Rev Nephrol, 19:558–72, 2023, Springer Nature

# Enpatoran is a highly selective, potent and reversible dual inhibitor of TLR7 and TLR8[1]

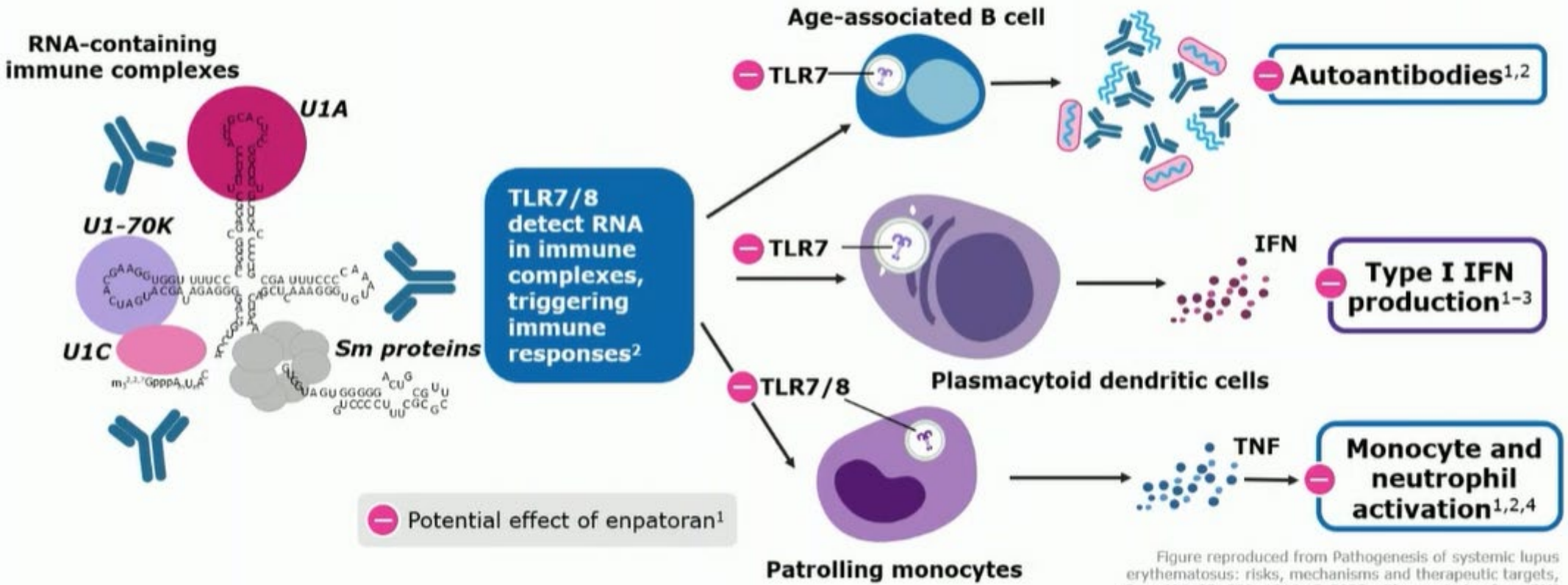


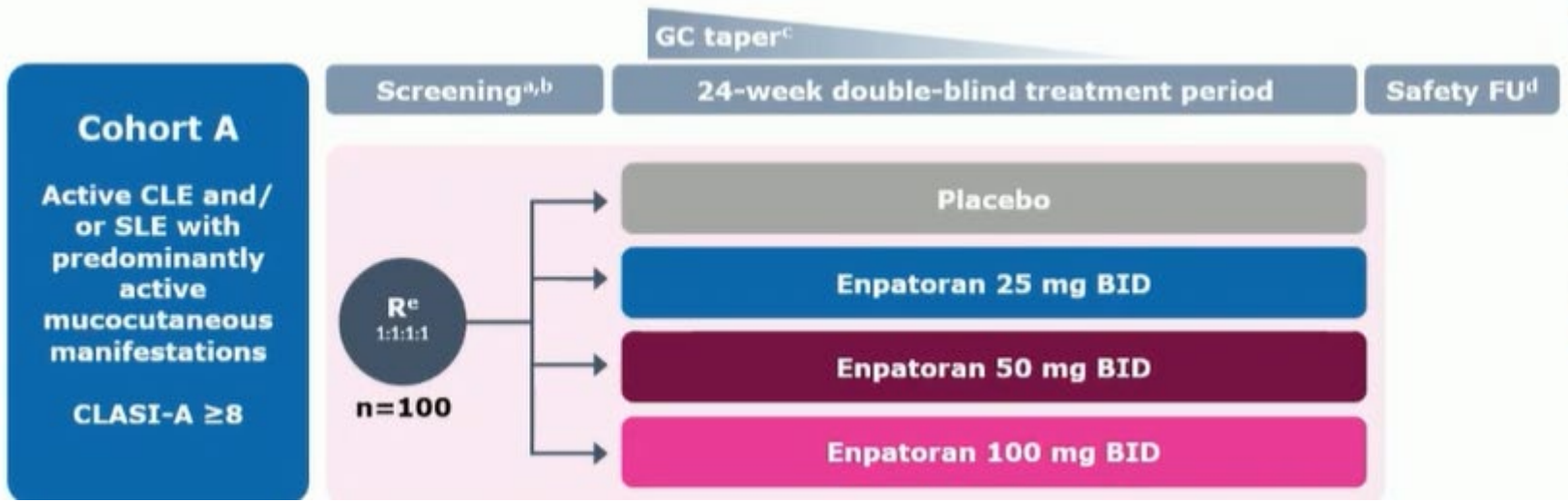

Figure reproduced from Pathogenesis of systemic lupus erythematosus: risks, mechanisms and therapeutic targets, Crow MK, 82, 999–1014, © 2023 with permission from BMJ Publishing Group Ltd

# Cohort A of the Phase II WILLOW study evaluated the efficacy and safety of enpatoran in active CLE or SLE with predominantly active mucocutaneous manifestations

**Phase II randomized double-blind placebo-controlled dose-finding parallel adaptive study in adults with CLE and/or SLE receiving standard of care**

## Primary objective

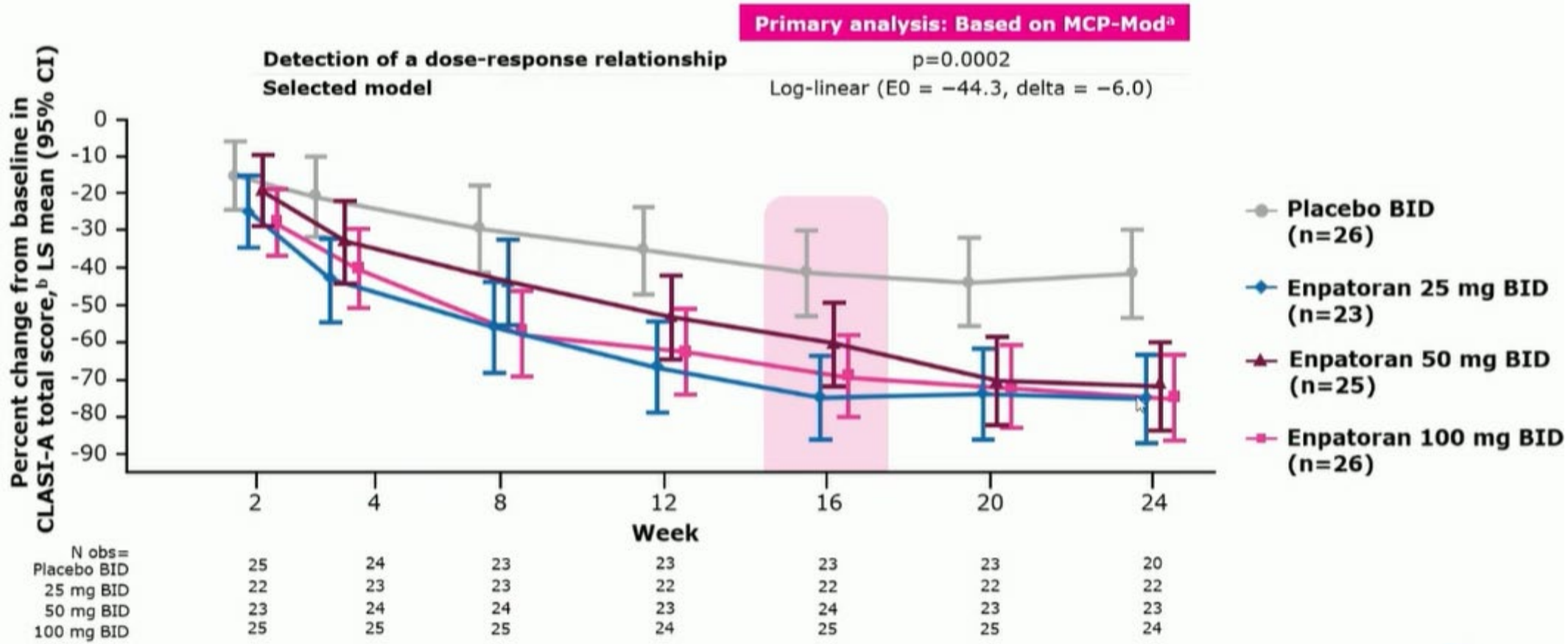
To evaluate the dose–response relationship of enpatoran in reducing disease activity based on CLASI-A



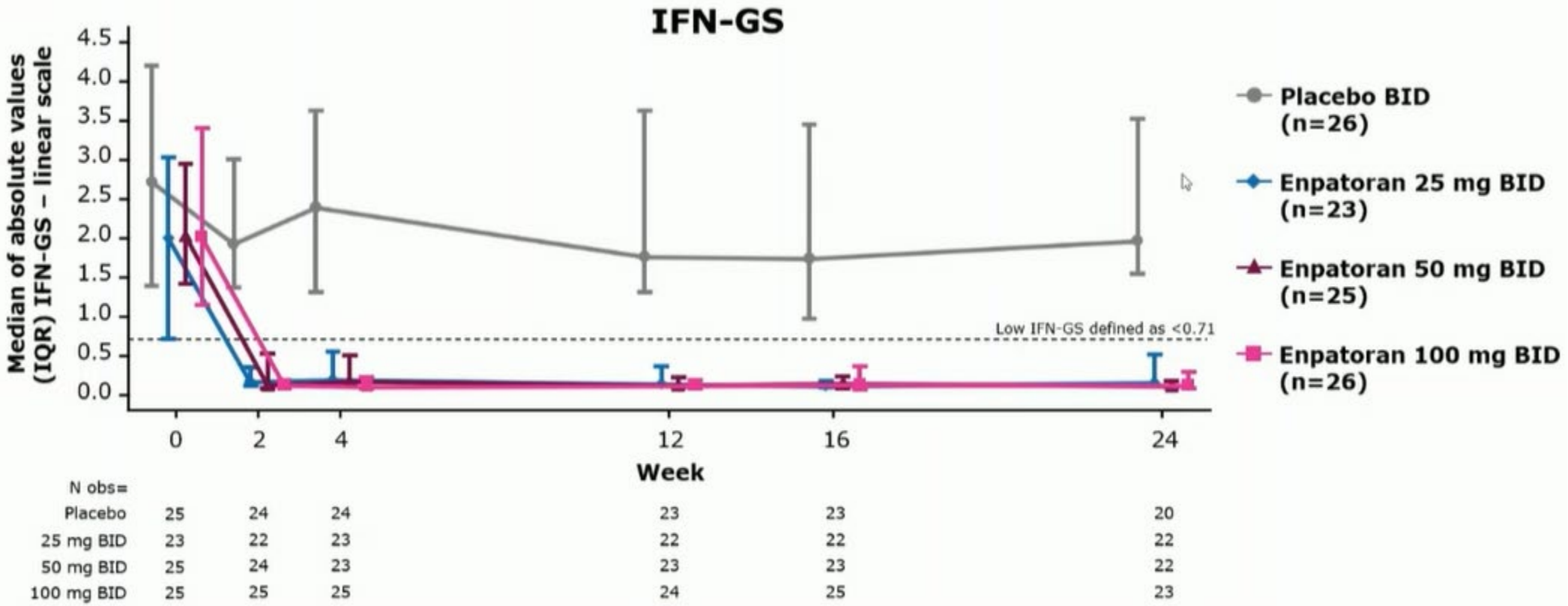

## Endpoints

| | |
|---|---|
| **Primary endpoint** | **Percentage change from baseline in CLASI-A at Week 16** |
| **Secondary endpoints** | • Clinically meaningful reduction in GC dose<br>• TEAEs, SAEs and AESIs |
| **Exploratory endpoints** | • Percentage change from baseline in CLASI-A<br>• CLASI-50 and CLASI-70 response[f]<br>• Change in IFN-GS score |

# There was a significant dose response for enpatoran in reducing CLASI-A from baseline to Week 16



# Enpatoran reduced IFN-GS scores as early as Week 2




| N obs= | | | | | | |
|---|---|---|---|---|---|---|
| Placebo | 25 | 24 | 24 | 23 | 23 | 20 |
| 25 mg BID | 23 | 22 | 23 | 22 | 22 | 22 |
| 50 mg BID | 25 | 24 | 23 | 23 | 23 | 22 |
| 100 mg BID | 25 | 25 | 25 | 24 | 25 | 23 |

Compared with placebo, **IFN-GS scores were reduced for all enpatoran doses by Week 2**, which was maintained to Week 24

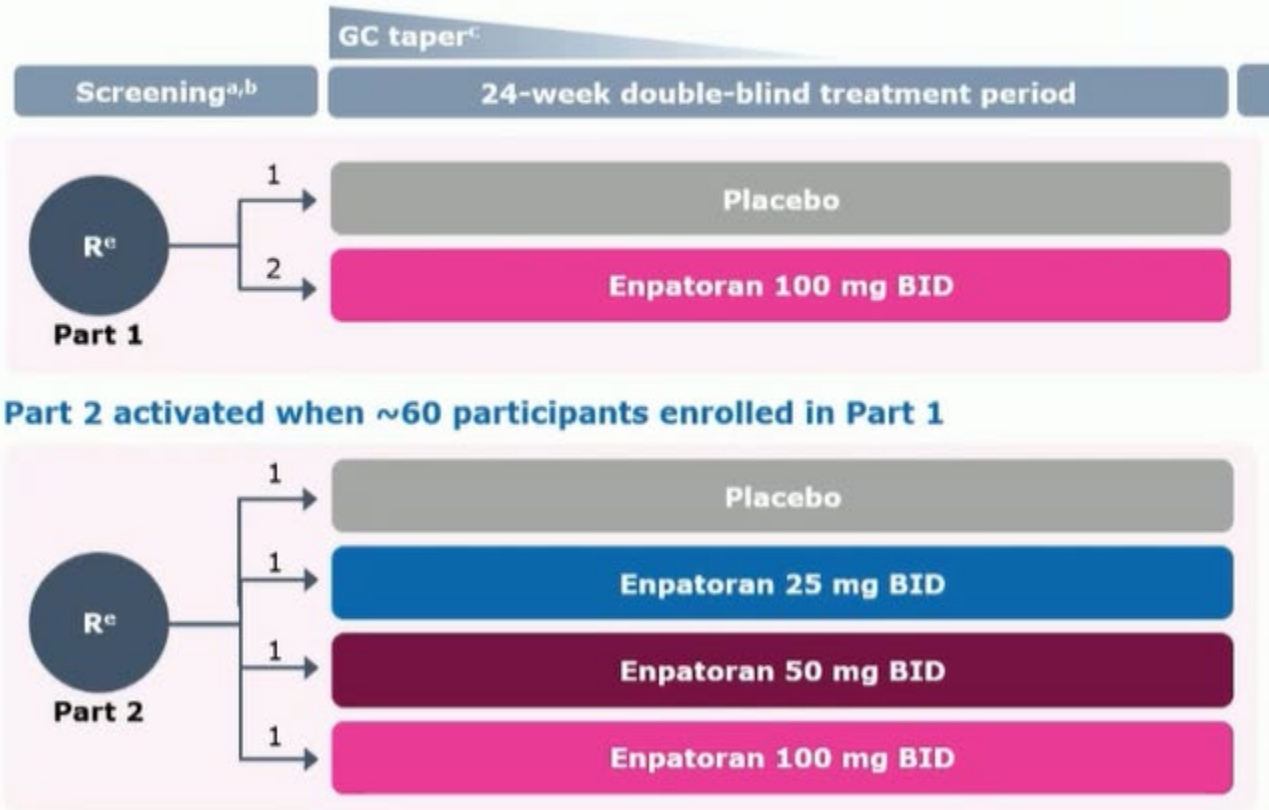
IFN-GS, interferon gene signature; Nobs, number of observations

# In Cohort B, the Phase II WILLOW study evaluated the efficacy and safety of enpatoran in SLE

**Cohort B (N=354)**

Active SLE: BILAG 1A/2B and ≥1 of the following:

- CLASI-A ≥8
- SELENA-SLEDAI ≥6




**Primary endpoint**
BICLA (dose–response; Week 24)

**Secondary endpoints**
Safety, BICLA response with clinically meaningful GC reduction[f]

**Exploratory endpoints**
BICLA response subgroup analyses, change in type I IFN-GS level, BICLA, SRI-4, and CLASI-50/70 responses in participants with CLASI-A ≥8 at baseline

# Einschluss Kriterien

- Moderate Aktivität
- SELENA SLEDAI >5
- Stabile IS
- Steroide > 2 Wochen vor Einschluss

# Results

- 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%

# Results

- 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%

Response höher in Patienten
mit Prednison >10mg oder mit INF S high

# Side effects

- No signal
- Herpes Zoster nicht häufiger als bei Placebo

OP0199

11–14 JUNE

# Defining Safe Hydroxychloroquine (HCQ) Blood Levels: Enhancing Lupus Management Through Precision Monitoring

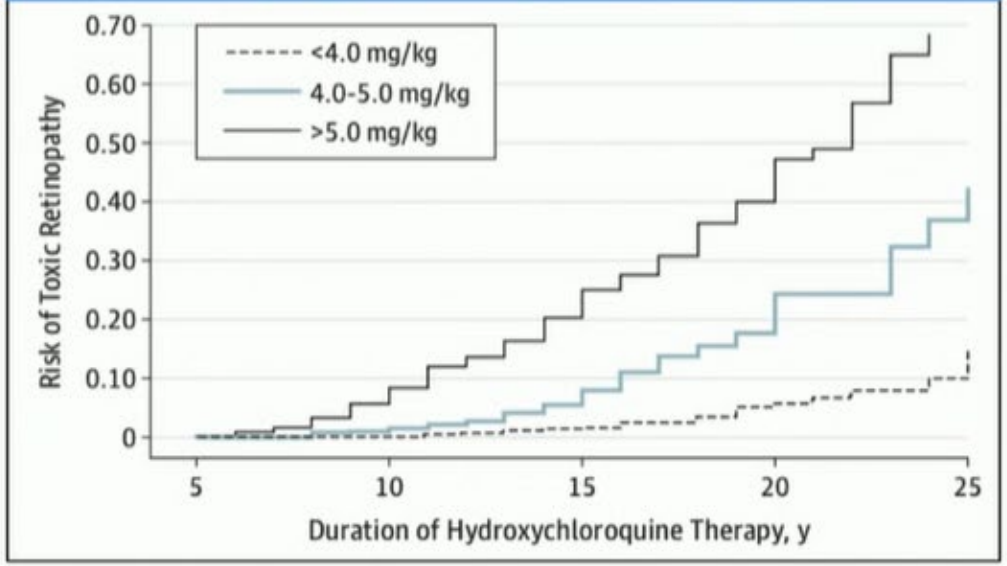
**Shivani Garg MD PhD**
Assistant Professor of Medicine, Rheumatology Division
Medical Director of Lupus and Lupus Nephritis Clinics
University of Wisconsin, School of Medicine and Public Health, Madison, WI

**Authors:** **Shivani Garg**, Ada Clarke, Charlie Dentz, Yann Nguyen, **Nathalie Costedoat-Chalumeau**
Correspondence: sgarg@medicine.wisc.edu; Nathalie.Costedoat@aphp.fr

# HCQ is the cornerstone of lupus treatment, but the optimal dose is unclear

- HCQ prolongs SLE disease-free and damage-free survival
- Optimal HCQ dosing is unclear

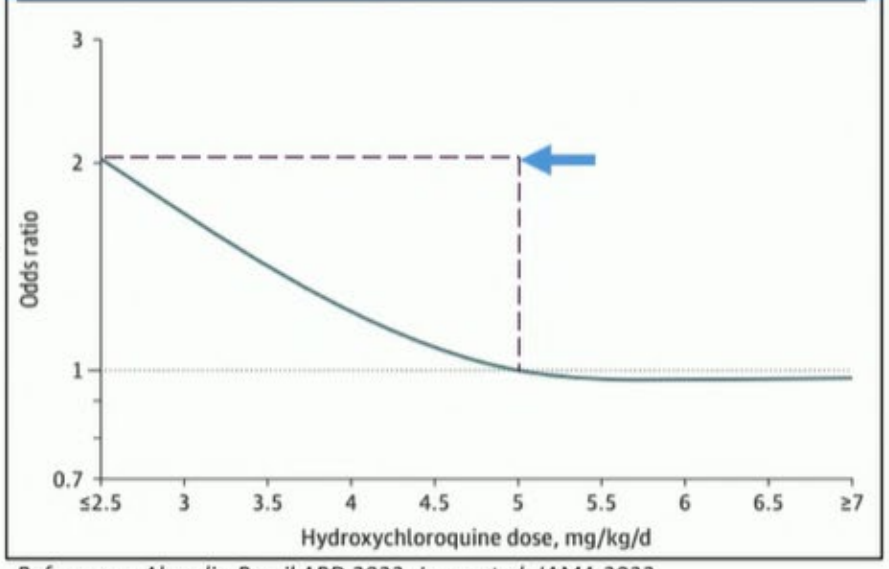
## Dose >5mg/kg/d: 2x Higher Retinopathy Risk




*References: Marmor et al. 2016; Jorge 2024*

**vs.**

## Dose ≤5mg/kg/d: 2-6x ↑ SLE Flares



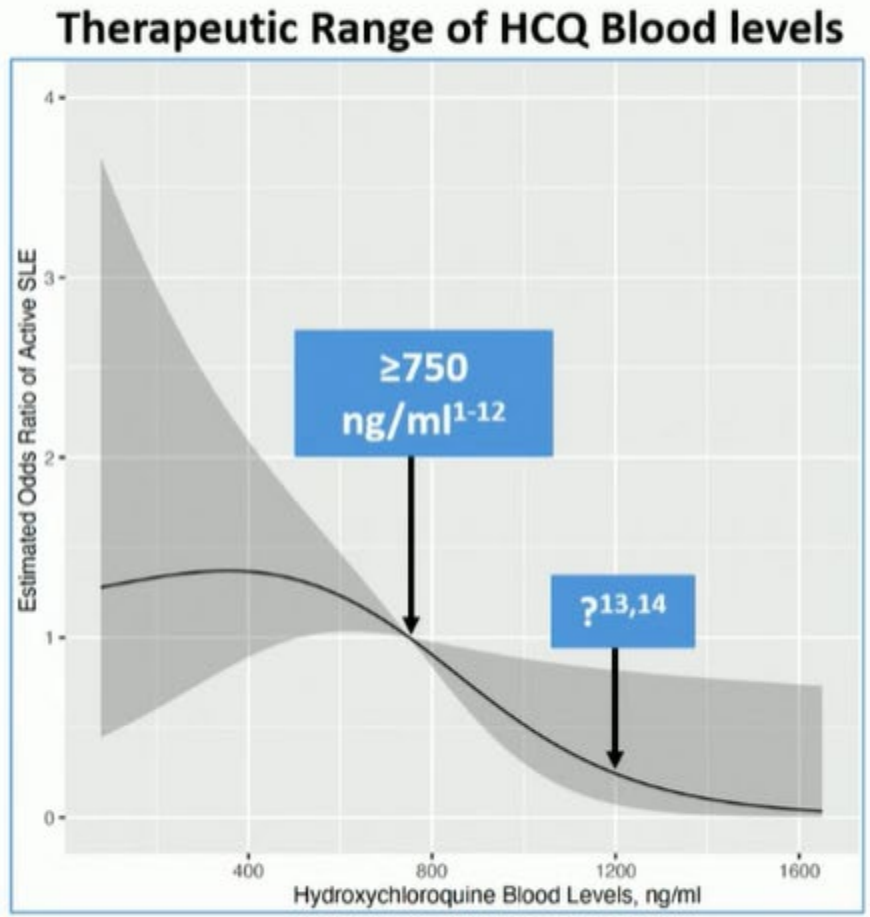

*References: Almedia-Brasil ARD 2022; Jorge et al. JAMA 2022*

**Conundrum: A need to guide optimal HCQ use to balance safety vs. efficacy**

# HQC

- Wird hepatisch metabolisisert und überwiegend renal ausgeschieden
- Hohe Verteilung im Gewebe = lange HWZ
- Interaktionen mit anderen Medikamenten die über cytochrome P450 metabolisisert werden z.B. Cyclosporin

# What is an Effective Reference Range for Targeted HCQ Level Monitoring?




**Gap 1**: Upper threshold for HCQ blood level monitoring linked with toxicity w/o additional clinical benefits

Population:
N = 1240 patients from US & France; 110 excluded with levels <200ng/mL

HCQ Levels:
Measured HCQ levels in whole blood using LC-MS/MS on study visit day ($T_0$)

Outcomes:
i) Active SLE (SLEDAI ≥6) ($T_0$)
ii) HCQ eye/heart toxicity ($T_t$)

Analyses for toxicity & ceiling effect on active SLE:
i) ROC analysis
ii) Mixed regression

**Table. Baseline Patient Characteristics (n=1240)**

| Variables | |
|---|---|
| Age in years (mean±SD) | 40±14 |
| Sex | |
| Female, n(%) | 1137 (92%) |
| Male, n(%) | 103 (8%) |
| eGFR at LN diagnosis in ml/min/1.73m$^2$ (mean±SD) | 98±32 |
| HCQ dose ≤5mg/kg/day, n(%) | 520 (42%) |
| HCQ dose >5mg/kg/day, n(%) | 720 (58%) |
| Cumulative HCQ dose in g (mean±SD) | 2381±1028 |
| HCQ blood levels in ng/ml (mean±SD) | 947±419 |
| SLEDAI (mean±SD) | 3.8±4.6 |
| HCQ Toxicity (cardiac or retinal) | 4.4% |

*Abbreviations: eGFR=glomerular filtration rate; HCQ=Hydroxychloroquine; SLEDAI=SLE Disease Activity Index.*

# Results 1: Upper Threshold for HCQ Levels: Adjusted Odds of HCQ Toxicity

**Table. Multivariable logistic regression analysis showing factors associated with systemic toxicity with HCQ use using data from 2 diverse cohorts (n=1240)**

| **Variables** | Adjusted OR (95% CIs) | p-value |
|---|---|---|
| Age per 10 years increase | 1.01 (0.98-1.03) | 0.65 |
| Female | 0.86 (0.33-2.97) | 0.79 |
| Weight based HCQ dose, >5mg/kg/d | 1.42 (0.61-3.60) | 0.44 |
| **Cumulative HCQ dose per 100g increase** | **1.02 (1.01-1.03)** | **0.011** |
| eGFR per 10 ml/min/1.73m$^2$ increase | 1.11 (1.01-1.20) | 0.058$^+$ |
| **HCQ blood levels >1150 ng/ml** | **2.15 (1.21-3.80)** | **0.0086** |

**>1150 ng/mL associated with 2.2x Higher HCQ toxicity (even after including on retinopathy)**

# Results 1: Upper Threshold: Adjusted Odds of Active SLE

**Table. Multivariable logistic regression analysis showing factors associated with clinical response (active SLE defined as SLEDAI ≥6) with HCQ use using data from 2 diverse cohorts (n=1240)**

| Variables | Adjusted OR (95% CIs) | p-value |
|---|---|---|
| **Age per 10 years increase** | 0.98 (0.97-0.99) | <0.0001 |
| Female | 1.36 (0.84-2.28) | 0.22 |
| **Weight-based HCQ dose, >5mg/kg/d** | 0.47 (0.34-0.67) | <0.0001 |
| eGFR per 10 units decrease | 0.99 (0.98-1.1) | 0.27 |
| **Cumulative HCQ dose in 100 g increase** | 0.99 (0.98-1.00) | 0.0021 |
| ***HCQ levels 750-1150 ng/ml*** | ***Reference category*** | |
| **HCQ levels <750 ng/ml** | **1.36 (1.07-1.72)** | **0.0126** |
| **HCQ levels >1150 ng/ml** | 0.95 (0.72-1.24) | 0.69 |

**>1150 ng/mL not associated with any further reduction in odds of active SLE (supratherapeutic)**

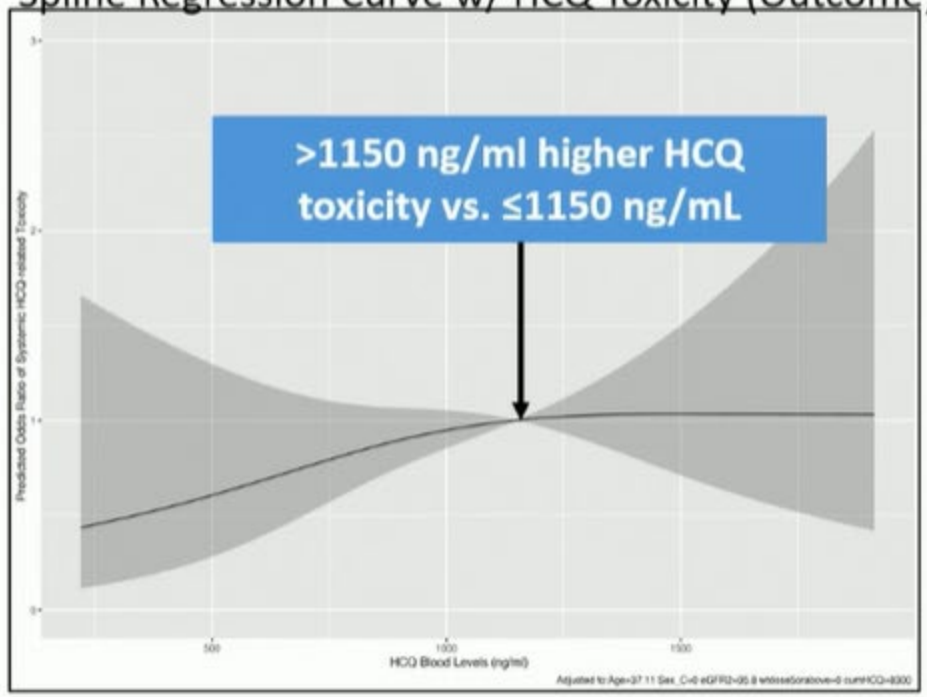
**Conclusion 1: Upper Threshold for HCQ Blood Level Monitoring is >1150 ng/mL (confirming prior studies[1-2])**

1. Petri et al. 2020; 2. Gora 2024

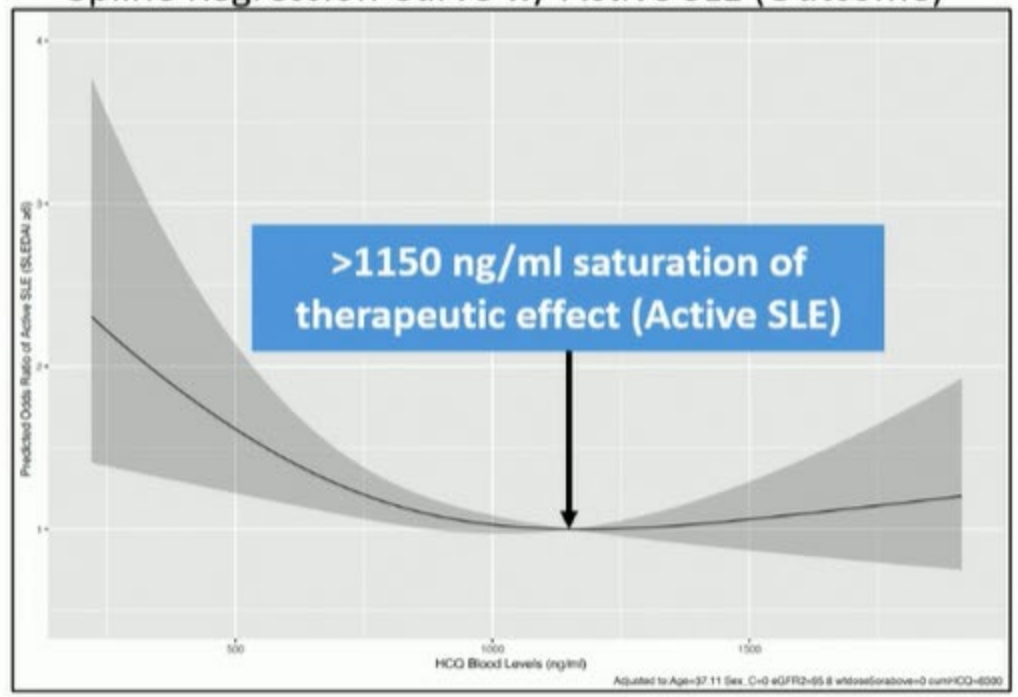
# Results 1: Upper Threshold for HCQ Levels: ROC & Spline Regression

- Optimal Cut-off (ROC): 1150 ng/mL NPV 96%; ceiling thereafter
- Adjusted spline regression:

Spline Regression Curve w/ HCQ Toxicity (Outcome)




Spline Regression Curve w/ Active SLE (Outcome)



# Comparing the Impact of GLP-1 Agonists and SGLT-2 Inhibitors on Outcomes in Lupus Nephritis: A Retrospective Cohort Study

Kinga Grzybowski[1], Rafal Ali[2], Hanieh Akbari[1], Irene Tan[2]

*[1]Jefferson Einstein Montgomery Hospital, Internal Medicine, East Norriton, United States of America,*

*[2]Jefferson Einstein Philadelphia Hospital, Rheumatology, Philadelphia, United States of America*

# Objectives

- We designed an observational, retrospective cohort study that aimed to evaluate the effect of GLP-1 (glucagon-like peptide-1) agonists compared to SGLT2 (sodium- glucose cotransporter-2) inhibitors on the outcomes in patients with Lupus Nephritis using the TrinetX database which included electronic healthcare records from >142 global collaborative healthcare organizations.

# Methods

- Our study utilized patients 18 years or older with a diagnosis of LN (Lupus Nephritis) using the International Classification of Diseases, Tenth Revision (ICD-10) codes.
- Two different cohorts were created: the first cohort consisted of patient with LN who were on SGLT2 inhibitors, and the second cohort consisted of patients with LN who were on GLP-1 agonists.
- The index event in our study was defined as the initial diagnosis of LN, later followed by three years of treatment with either SGLT-2 inhibitors or GLP-1 agonists.
- Propensity matching was used for the age at index, gender, race/ethnicity, comorbidities (hypertension, obesity, diabetes, tobacco use), and other medications (DMARDS, steroids, biologics, statins, aspirin).

694 Patienten

Table 1: Baseline Characteristics of Both Cohorts Before and After Propensity Matching

| Characteristics | SGLT-2 | GLP-1 | p-value | SGLT-2 | GLP-1 | p-value |
|---|---|---|---|---|---|---|
| **Demographics** | | | | | | |
| Age at Index; mean ± SD | 51.9 ± 16 | 48.2 ± 12.8 | <0.0001 | 50.3 ± 15.8 | 49.6 ± 15.8 | 0.3863 |
| Females | 75.9% | 85.5% | <0.0001 | 81.7% | 82.4% | 0.7265 |
| Males | 22.5% | 11.2% | <0.0001 | 16.4% | 15.1% | 0.5075 |
| Whites | 30.8% | 37.0% | 0.0014 | 35.3% | 35.1% | 0.9552 |
| Hispanic/Latino | 12.7% | 17.0% | 0.0026 | 15.3% | 17.0% | 0.3813 |
| Asians | 13.0% | 3.6% | <0.0001 | 5.0% | 5.0% | 1.0000 |
| Other Races | 6.3% | 7.5% | 0.2421 | 7.8% | 7.6% | 0.9198 |
| **Diagnoses** | | | | | | |
| Hypertension | 85.0% | 81.0% | 0.0069 | 82.4% | 82.9% | 0.8317 |
| Obesity | 33.9% | 70.2% | <0.0001 | 57.9% | 56.9% | 0.7040 |
| Diabetes | 37.2% | 50.0% | <0.0001 | 46.4% | 43.8% | 0.3316 |
| Tobacco Use | 5.1% | 3.6% | 0.0745 | 4.2% | 4.6% | 0.6944 |
| **Medications** | | | | | | |
| Prednisone | 61.7% | 63.8% | 0.2952 | 65.3% | 64.3% | 0.6941 |
| HCQ | 65.4% | 56.0% | <0.001 | 59.8% | 58.5% | 0.6231 |
| Azathioprine | 12.9% | 12.7% | 0.8823 | 11.8% | 12.0% | 0.9339 |
| Belimumab | 11.2% | 11.1% | 0.9519 | 10.7% | 11.8% | 0.4966 |
| Rituximab | 6.3% | 5.8% | 0.5945 | 6.8% | 5.9% | 0.5087 |

**Table 1: Complications and Outcomes in Patients with LN on SGLT2 inhibitors versus GLP-1 agonists**

| Outcomes[a,b] | LN on SGLT2 | LN on GLP-1 | RR (95% CI) | P-value |
|---|---|---|---|---|
| Dialysis (n,%) | 36 (5.8%) | 36 (6.26%) | 0.926 (0.592-1.449) | 0.7362 |
| ESRD (n,%) | 37 (6.38%) | 31 (5.91%) | 1.08 (0.68-1.715) | 0.7431 |
| CKD (n,%) | 75 (43.35%) | 73 (28.4%) | 1.526 (1.179-1.976) | 0.0014 |
| Renal Transplant (n,%) | <10 (1.59%) | 12 (2.1%) | 0.759 (0.331-1.744) | 0.5146 |
| Mortality (n,%) | 48 (6.96%) | 24 (3.48%) | 2 (1.239-3.227) | 0.0037 |
| Acute MI (n,%) | 37 (6.3%) | 18 (2.8%) | 2.248 (1.294-3.904) | 0.0030 |
| Stroke (n,%) | 21 (3.541%) | 13 (2.0%) | 1.754 (0.886-3.472) | 0.1018 |
| Heart Failure (n,%) | 39 (10%) | 40 (7.1%) | 1.421 (0.932-2.166) | 0.1013 |

Abbreviations: Acute MI: Acute Myocardial Infarction, CKD: Chronic Kidney Disease, ESRD: End-Stage Renal Disease, GLP-1: glucagon-like peptide-1agonists, LN: Lupus Nephritis, RR: Relative Risk, SGLT 2: sodium-glucose cotransporter-2 inhibitors, 95% CI: 95% Confidence Interval

[a] Propensity matched cohorts based on baseline demographics, comorbidities, and medication use.
[b] All patients with outcomes that occurred prior to the time window were excluded from our cohorts.

# Conclusion

- The findings suggest that patients with Lupus Nephritis taking GLP-1 receptor agonists have a reduced risk of mortality, acute myocardial infarctions, and a decreased rate of progression of CKD compared with patients taking SGLT-2 inhibitors.
- Further research should be conducted with larger groups, and with longer follow up time to confirm and possibly explain any potential explanations or contributing factors.

# OP0041

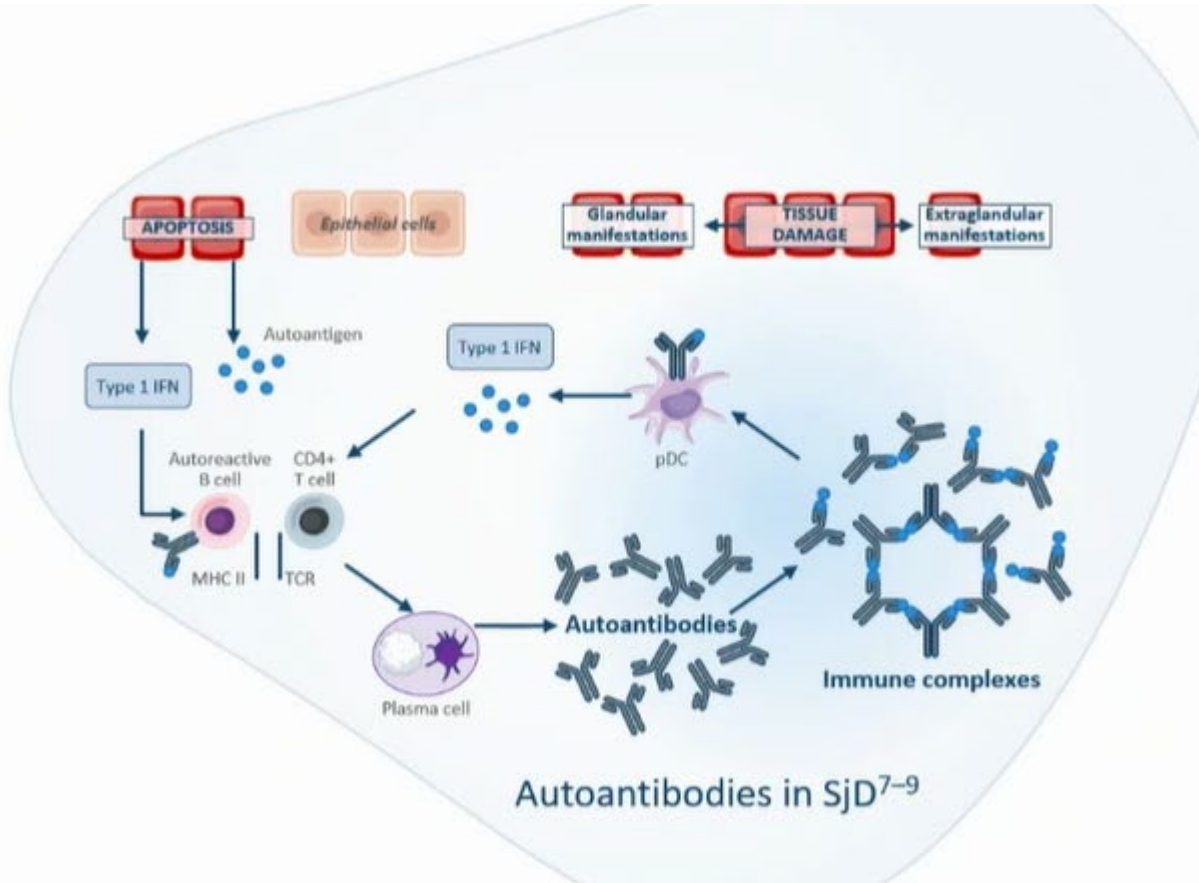
## Treatment of Primary Sjögren's Disease by Blocking FcRn

## Clinical and Translational Data From RHO, a Phase 2 Randomized, Placebo Controlled, Double-Blind, Proof-of-Concept Study With Efgartigimod

Isabelle Peene,[1] Gwenny M. Verstappen,[2] Joke Deprez,[1] Frans G.M. Kroese,[2] Suzanne Arends,[2] Andrew Kelly,[3] Lana Vandersarren,[3] Edward Bowen,[4] Julie Jacobs,[3] Paul Meyvisch,[3] Dirk Elewaut,[1*] Hendrika Bootsma[2*]

## There is an unmet need for effective treatments targeting the complex pathophysiology of SjD

- SjD is a **chronic** and **progressive, systemic, autoimmune disease**
- Characterized by **lymphocytic infiltration** and **immune-mediated dysfunction of exocrine glands**, with **possible extraglandular manifestations**[1–4]
- **IgG autoantibodies** targeting **Ro52, Ro60, and La antigens** contribute to **disease pathology**[5,6]

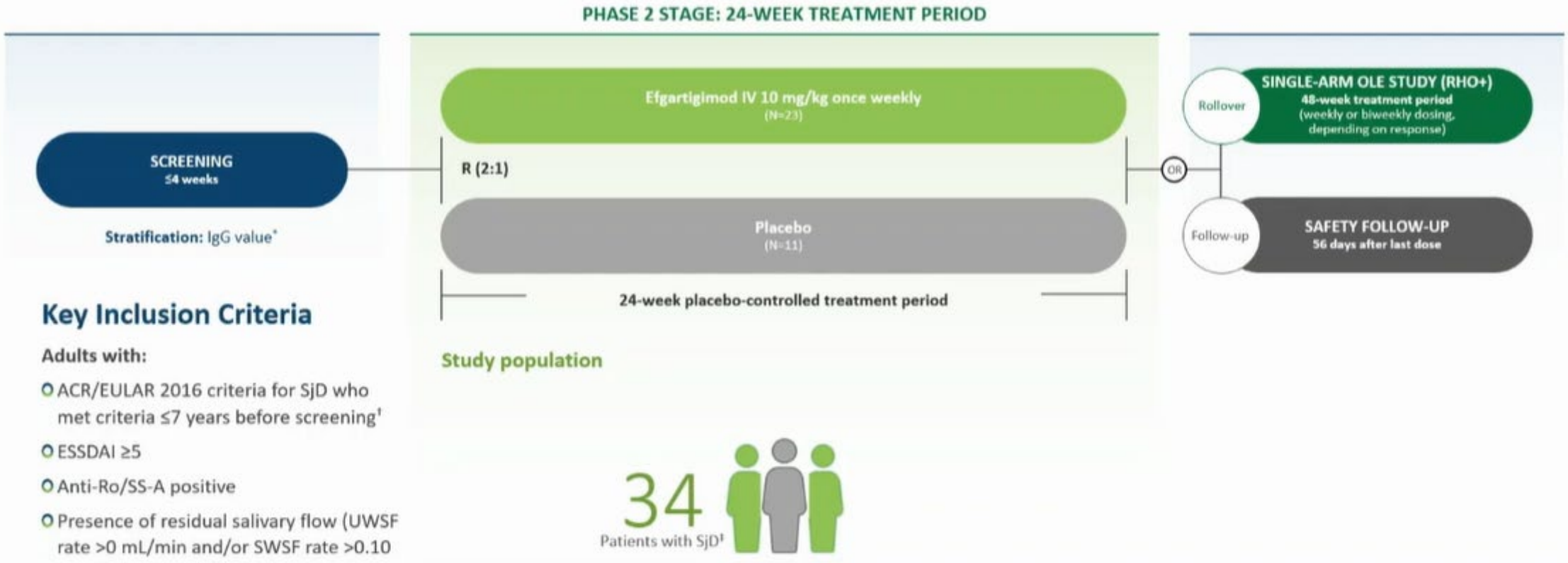


## Efgartigimod

- Human **IgG1** antibody **Fc fragment**
- Engineered for **increased affinity to FcRn**
- Uniquely composed of the **only part of the IgG antibody** that **normally binds FcRn**[1,2]
- **Selectively reduces IgG antibodies** and **pathogenic autoantibodies without**:[1,5–7]
  - Impacting antibody production (including other Ig antibodies) or other parts of the immune system
  - Decreasing albumin levels
  - Increasing LDL cholesterol levels


FcRn, neonatal Fc receptor; IgG, immunoglobulin G; LDL, low-density lipoprotein.

**1.** Ulrichts P, et al. *J Clin Invest*. 2018;128:4372–86. **2.** Vaccaro C, et al. *Nat Biotechnol*. 2005;23:1283–8. **3.** Roopenian DC, Akilesh S. *Nat Rev Immunol*. 2007;7:715–25. **4.** Ward ES, Ober RJ. *Trends Pharmacol Sci*. 2018;39:892–904. **5.** Howard JF,




## Key Inclusion Criteria

**Adults with:**

- ACR/EULAR 2016 criteria for SjD who met criteria ≤7 years before screening†
- ESSDAI ≥5
- Anti-Ro/SS-A positive
- Presence of residual salivary flow (UWSF rate >0 mL/min and/or SWSF rate >0.10 mL/min)

### Study population

34
Patients with SjD‡

*> 16.0 g/L or ≤ 16 g/L. †Patients with secondary Sjögren's syndrome overlap syndromes where another confirmed autoimmune rheumatic or systemic inflammatory condition (eg, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, inflammatory bowel disease) is the primary diagnosis were excluded. ‡3 patients did not meet eligibility criteria and were (i) discontinued within the first weeks after randomization, and (ii) removed from the efficacy analysis..

ACR, American College of Rheumatology; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; EULAR, European Alliance of Associations for Rheumatology; IgG, Immunoglobulin G; IV, Intravenous; OLE, open-label extension; R, randomization; SS-A, anti-Sjögren's syndrome–related antigen; SjD, Sjögren's disease; SWSF, stimulated whole salivary flow; UWSF, unstimulated whole salivary flow.

ClinicalTrials.gov Identifier: NCT05817669. https://clinicaltrials.gov/study/NCT05817669. Accessed April 2025.

**OBJECTIVE** *To evaluate the efficacy and safety of intravenous efgartigimod in adults with SjD*

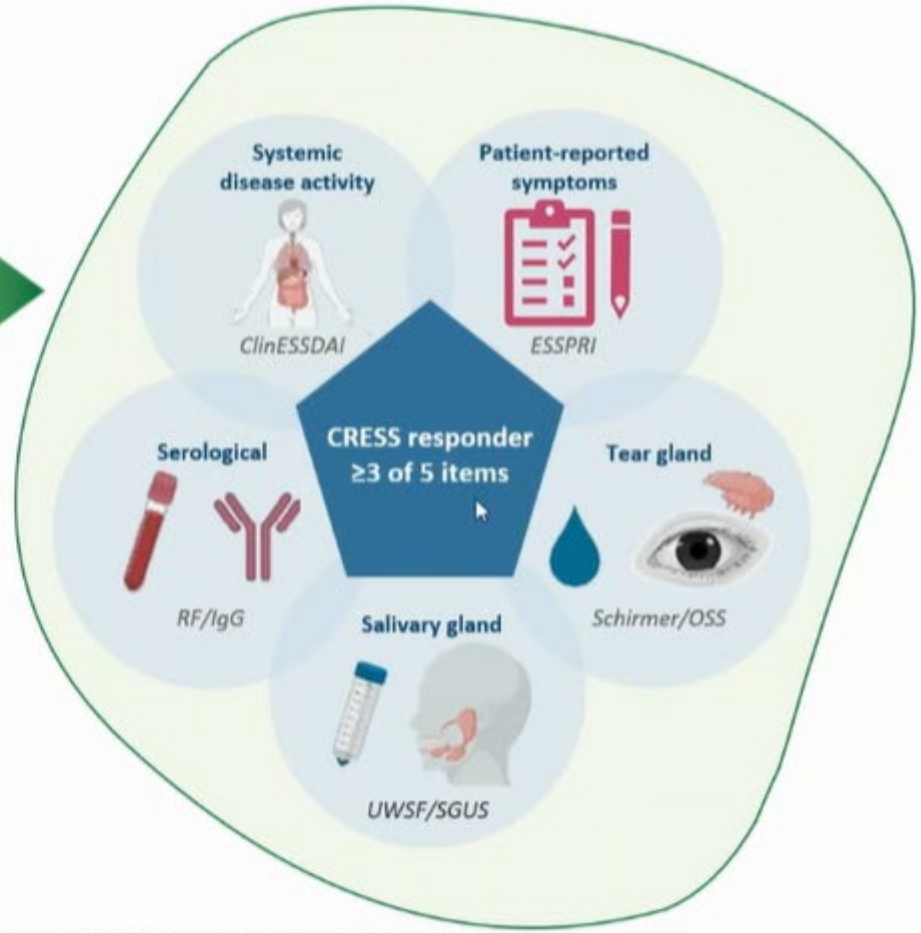
**Primary Endpoint** Proportion of responders to CRESS* (response on ≥3 out of 5 items) at Week 24

**Select Secondary Endpoints**

- Proportion of responders to cSTAR (score ≥5) at Week 24
- Effect on disease activity (ESSDAI, clinESSDAI, ESSPRI)
- Safety, evaluated by the incidence and severity of AEs

**Exploratory**

- Exploratory biomarkers to understand the effects of efgartigimod on disease pathology




*CRESS response thresholds: clinESSDAI (score of <5 points); ESSPRI (decrease of ≥1 point or ≥15% from baseline); tear gland function (increase of ≥5 mm from baseline in Schirmer's test or decrease of ≥2 points from baseline in OSS); UWSF/SGUS (increase of ≥25% in UWSF or decrease of ≥25% in the SGUS Hocevar score, or if UWSF was 0 mL/min at baseline, any increase from baseline); RF/IgG (RF decrease of ≥25% from baseline or IgG reduction of ≥10%).

AE, adverse event; clinESSDAI, Clinical EULAR Sjögren's Syndrome Disease Activity Index; CRESS, Composite of Relevant Endpoints for Sjögren's Syndrome; cSTAR, candidate Sjögren's Tool for Assessing Response; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, Sjögren's Syndrome Patient Reported Index; IgG, immunoglobulin G; OSS, ocular staining score; RF, rheumatoid factor; SGUS, salivary gland ultrasound; SjD, Sjögren's disease; UWSF, unstimulated whole salivary flow.

**OBJECTIVE** *To evaluate the efficacy and safety of intravenous efgartigimod in adults with SjD*

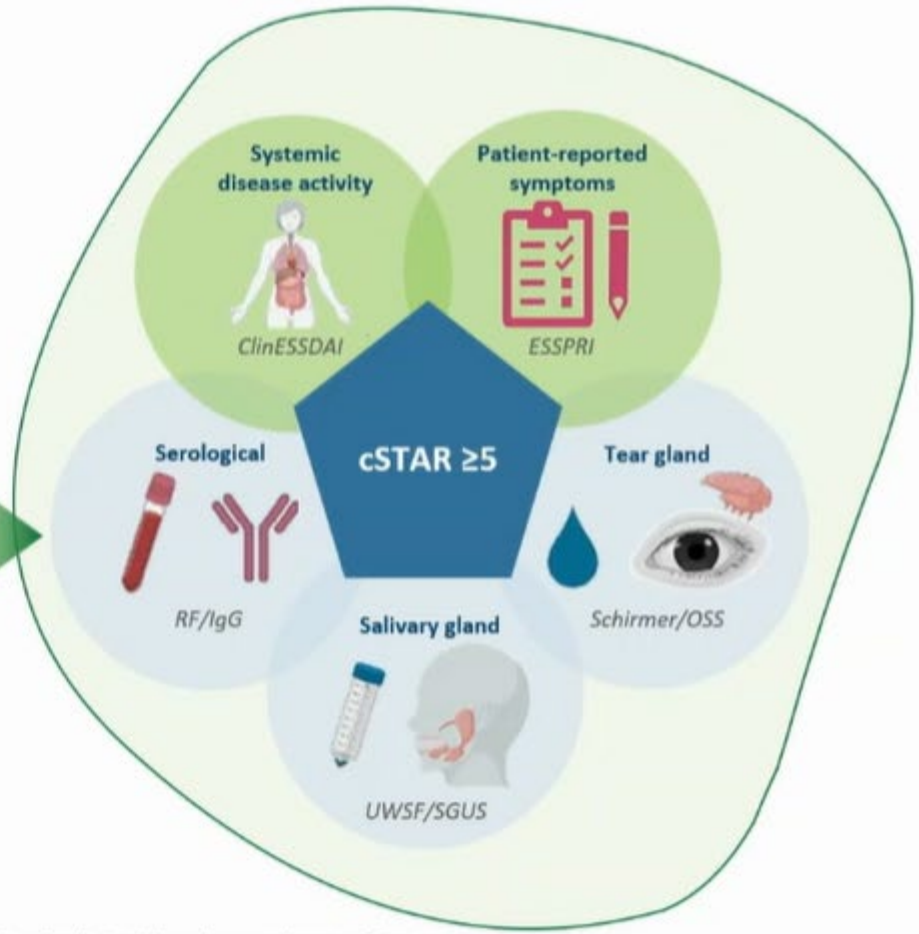
**Primary Endpoint** Proportion of responders to CRESS* (response on ≥3 out of 5 items) at Week 24

**Select Secondary Endpoints**

- Proportion of responders to cSTAR (score ≥5) at Week 24
- Effect on disease activity (ESSDAI, clinESSDAI, ESSPRI)
- Safety, evaluated by the incidence and severity of AEs

**Exploratory**

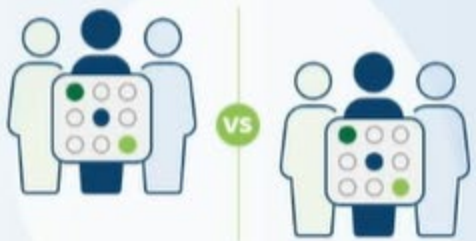
- Exploratory biomarkers to understand the effects of efgartigimod on disease pathology




*CRESS response thresholds: clinESSDAI (score of <5 points); ESSPRI (decrease of ≥1 point or ≥15% from baseline); tear gland function (increase of ≥5 mm from baseline in Schirmer's test or decrease of ≥2 points from baseline in OSS); UWSF/SGUS (increase of ≥25% in UWSF or decrease of ≥25% in the SGUS Hocevar score, or if UWSF was 0 mL/min at baseline, any increase from baseline); RF/IgG (RF decrease of ≥25% from baseline or IgG reduction of ≥10%).

AE, adverse event; clinESSDAI, Clinical EULAR Sjögren's Syndrome Disease Activity Index; CRESS, Composite of Relevant Endpoints for Sjögren's Syndrome; cSTAR, candidate Sjögren's Tool for Assessing Response; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, Sjögren's Syndrome Patient Reported Index; IgG, immunoglobulin G; OSS, ocular staining score; RF, rheumatoid factor; SGUS, salivary gland ultrasound; SjD, Sjögren's disease; UWSF, unstimulated whole salivary flow.

- **34 patients were randomized** in the study; **3 did not meet eligibility criteria** and were removed from the efficacy analysis
- Participant demographics were **generally comparable** between treatment groups



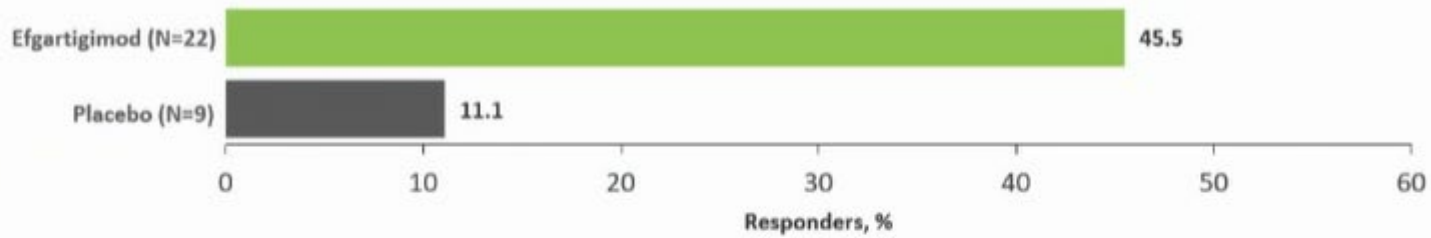

| | Efgartigimod (N=23) | Placebo (N=11) |
|---|---|---|
| **Age,** years, median (Q1, Q3) | 49 (39, 64) | 58 (45, 69) |
| **Sex,** female, n (%) | 22 (95.7) | 11 (100.0) |
| **Time since diagnosis,** years, median (Q1, Q3) | 3 (1, 6) | 6 (3, 7) |
| **Race,** n (%) | | |
| White | 22 (95.7) | 11 (100.0) |
| Unknown | 1 (4.3) | 0 |
| **ESSDAI total score,** median (Q1, Q3) | 12 (8, 15) | 17 (8, 19) |
| **clinESSDAI total score,** median (Q1, Q3) | 13 (9, 17) | 18 (9, 21) |
| **ESSPRI score,** median (Q1, Q3) | 6.7 (5.8, 7.7) | 5.0 (4.7, 6.3) |
| **Schirmer <5 mm/5 min in ≥1 eye,** n (%) | 18 (78.3) | 9 (81.8) |
| **UWSF,** mL/min, median (Q1, Q3) | 0.12 (0.05, 0.17) | 0.10 (0.07, 0.15) |
| **IgG,** g/L, median (Q1, Q3) | 17.32 (10.91, 22.20) | 17.75 (10.77, 18.76) |
| **RF,** IU/mL, median (Q1, Q3) | 51.0 (21.0, 89.0) | 59.0 (37.0, 176.0) |



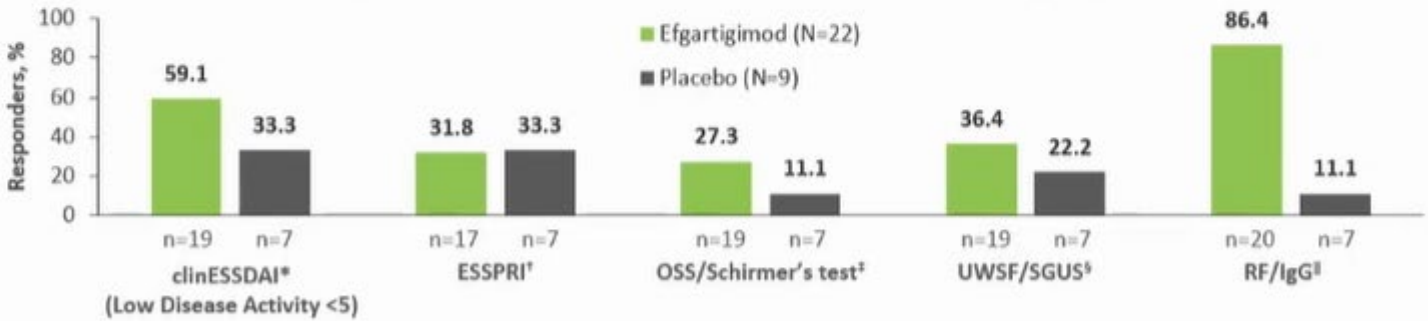
clinESSDAI, Clinical EULAR Sjögren's Syndrome Disease Activity Index; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, Sjögren's Syndrome Patient Reported Index; IgG, immunoglobulin G; IU, international units; Q, quartile; RF, rheumatoid factor; UWSF, unstimulated whole salivary flow.

- A **numerical difference of 34.4 percentage points** in the proportion of **responders to ≥3 of 5 CRESS items at Week 24 was observed** in this proof-of-concept study
- For 4 of the 5 individual CRESS items, the **proportion of responders was numerically higher with efgartigimod** versus placebo
- **50.0% of efgartigimod-treated participants responded on RF only** (≥25% reduction), compared with 0% in the placebo group

## Proportion of CRESS Responders (≥3 of 5 CRESS Items)



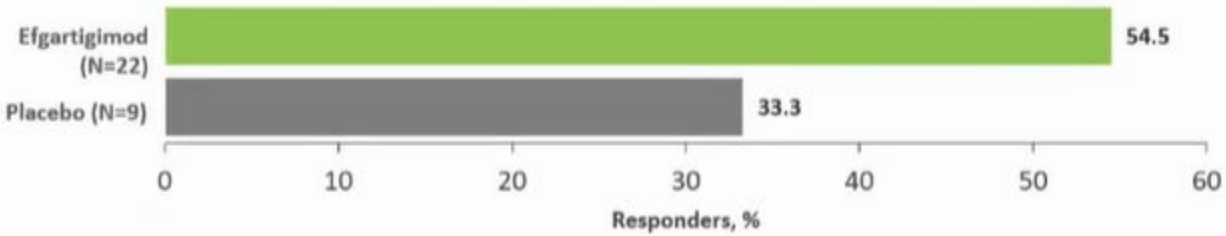

## Proportion of Responders to Individual CRESS Items at Week 24




*Total clinESSDAI score <5 points from baseline. †Total ESSPRI score decrease of ≥1 point or ≥15% from baseline. ‡Increase in Schirmer's test ≥5 mm or a decrease in OSS ≥2 points from baseline or stable. §Increase in UWSF ≥25%, or any increase if baseline is 0, or decrease in SGUS ≥25%. ‖Decrease in RF ≥25% or decrease in IgG ≥10%; 50.0% of participants in the efgartigimod group had a ≥25% decrease from baseline in RF compared with 0% in the placebo group.

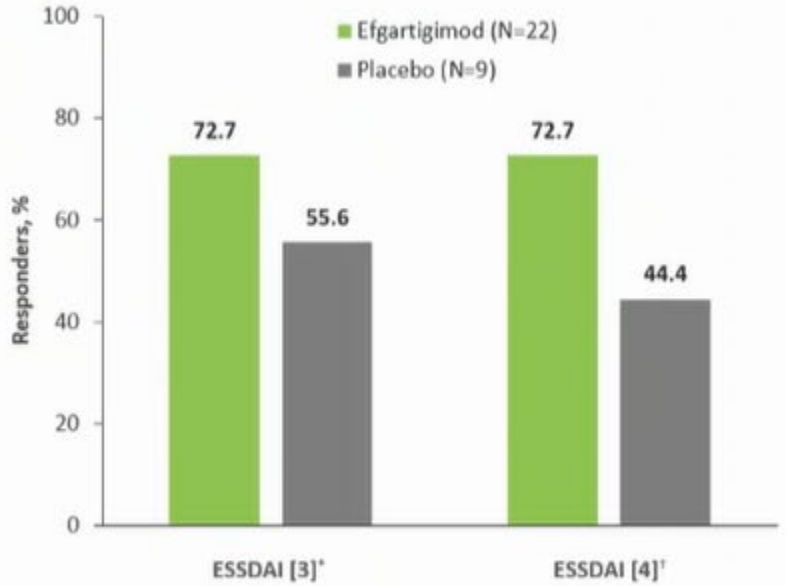
CRESS, Composite of Relevant Endpoints for Sjögren's Syndrome; clinESSDAI, Clinical EULAR Sjögren's Syndrome Disease Activity Index; ESSPRI, Sjögren's Syndrome Patient Reported Index; IgG, immunoglobulin G; OSS, ocular staining score; RF, rheumatoid factor; SGUS, salivary gland ultrasound; UWSF, unstimulated whole salivary flow.

## Proportion of cSTAR Responders (≥5 Score)




- Median (Q1, Q3) **change from baseline in the clinESSDAI total scores was –7.0 (–12.0, –3.0) in the efgartigimod group** and –4.0 (–17.0, –3.0) in the placebo group at Week 24

## Clinically Meaningful Changes in ESSDAI Response



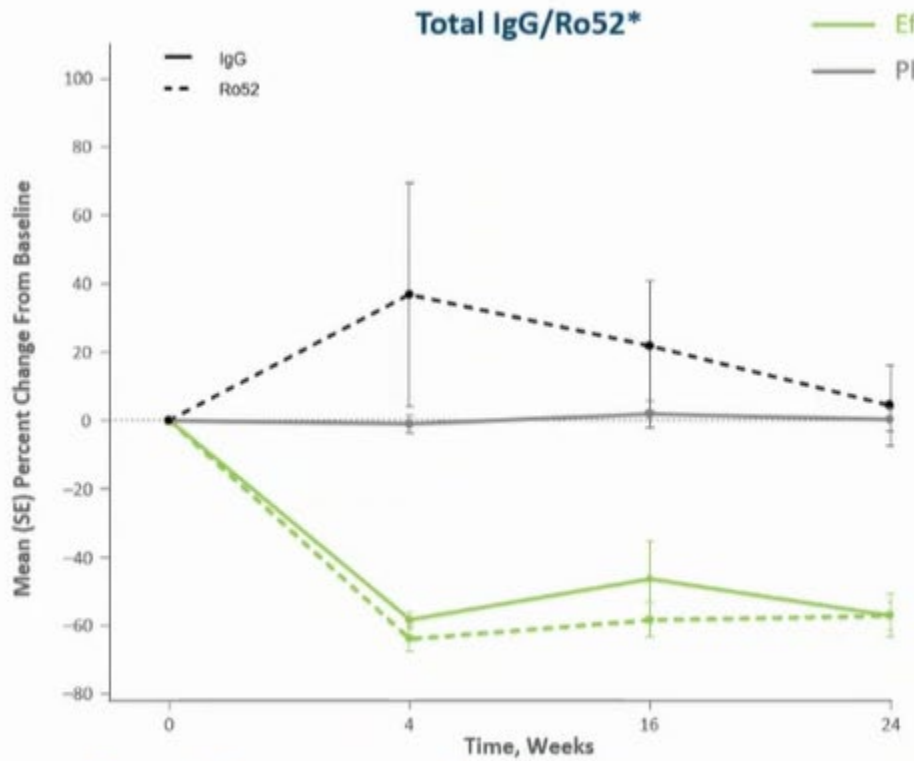

*Defined as improvement of ≥3 points in ESSDAI score at Week 24. †Defined as improvement of ≥4 points in ESSDAI score at Week 24.

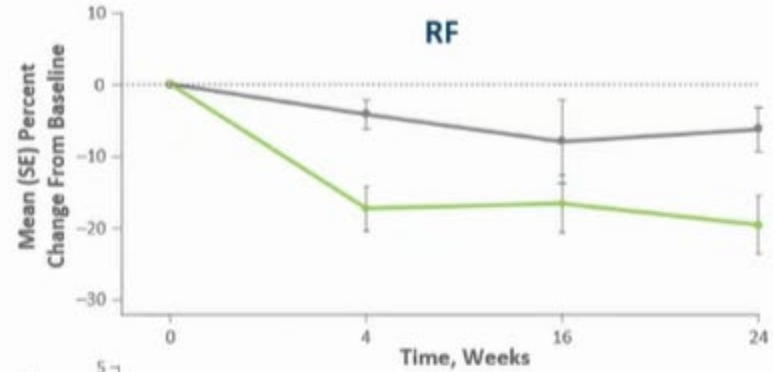
clinESSDAI, Clinical EULAR Sjögren's Syndrome Disease Activity Index; cSTAR, candidate Sjögren's Tool for Assessing Response; ESSDAI, EULAR Sjögren's Syndrome Disease Activity Index.

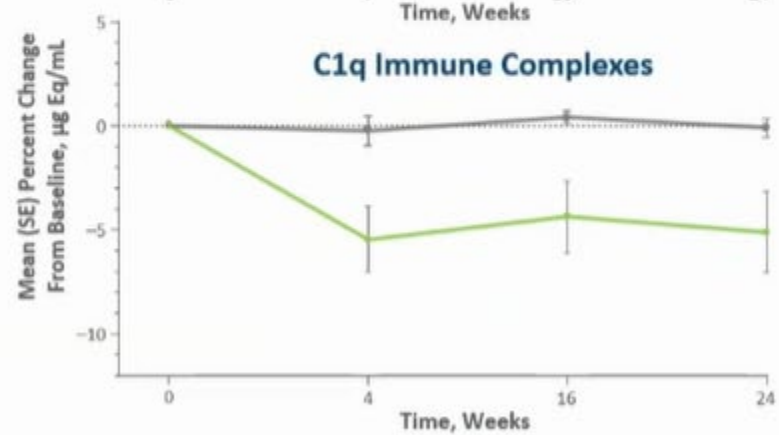
- **Efgartigimod well tolerated,** with **no grade ≥3 AEs reported** and a **low rate of discontinuation** due to AEs


| | Efgartigimod (N=23; PYFU=12.62)* | | Placebo (N=11; PYFU=5)† | |
|---|---|---|---|---|
| **Number of administrations,** median (Q1, Q3) | 22 (20, 24) | | 22 (2, 23) | |
| | **n (%)** | **m (ER)** | **n (%)** | **m (ER)** |
| **≥1 AE** | 20 (87.0) | 81 (6.4) | 7 (63.6) | 23 (4.6) |
| **≥1 SAE‡** | 1 (4.3) | 1 (0.1) | 0 | 0 |
| **≥1 Grade ≥3 AE** | 0 | 0 | 0 | 0 |
| **≥1 AE leading to study drug discontinuation** | 1 (4.3) | 1 (0.1) | 0 | 0 |
| **≥1 AESI (infection)§** | 15 (65.2) | 25 (2.0) | 5 (45.5) | 7 (1.4) |
| **≥1 injection- and infusion-related reaction** | 3 (13.0) | 5 (0.4) | 1 (9.1) | 1 (0.2) |
| **≥1 fatal AE** | 0 | 0 | 0 | 0 |
| **Most common AEs** (occurring in >10% of participants) | | | | |
| Headache | 4 (17.4) | 6 | 1 (9.1) | 1 |
| Nasopharyngitis | 4 (17.4) | 5 | 1 (9.1) | 1 |
| Influenza | 3 (13.0) | 3 | 0 | 0 |
| Upper respiratory tract infection | 3 (13.0) | 3 | 2 (18.2) | 2 |
| Urinary tract infection | 3 (13.0) | 3 | 1 (9.1) | 1 |

*18 participants from the efgartigimod arm completed study treatment. †7 participants from the placebo arm completed study treatment. ‡Grade 2 SAE of vasospasm, which the investigator and sponsor considered not related to efgartigimod.
§Efgartigimod treatment leads to reduced IgG levels; as low IgG levels are associated with increased infection risks, events in the MedDRA System Organ Class Infections and Infestations are considered adverse events of special interest in this study.
AE, adverse events; AESI, adverse events of special interest; ER, event rate (number of events/PYFU); m, number of events; MedDRA, Medical Dictionary for Regulatory Activities;
N, number of participants; PYFU, participant years of follow-up; SAE, serious adverse event.




- A **similar pattern of response** was observed for **anti-Ro60** and **anti-La** autoantibodies