These handouts are designed to complement the expert presentations. We strongly encourage you to view the full sessions before drawing conclusions based solely on the handout content.

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Therapies on the Horizon- II

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Disclosures

Consultant:

BMS, Novartis, Otsuka/Visterra, Amgen, Kiniksa, iCell, TearSolutions, Johnson&Johnson, Artiva, Aurinia, Veloxis

Owner:

Quench Therapeutics

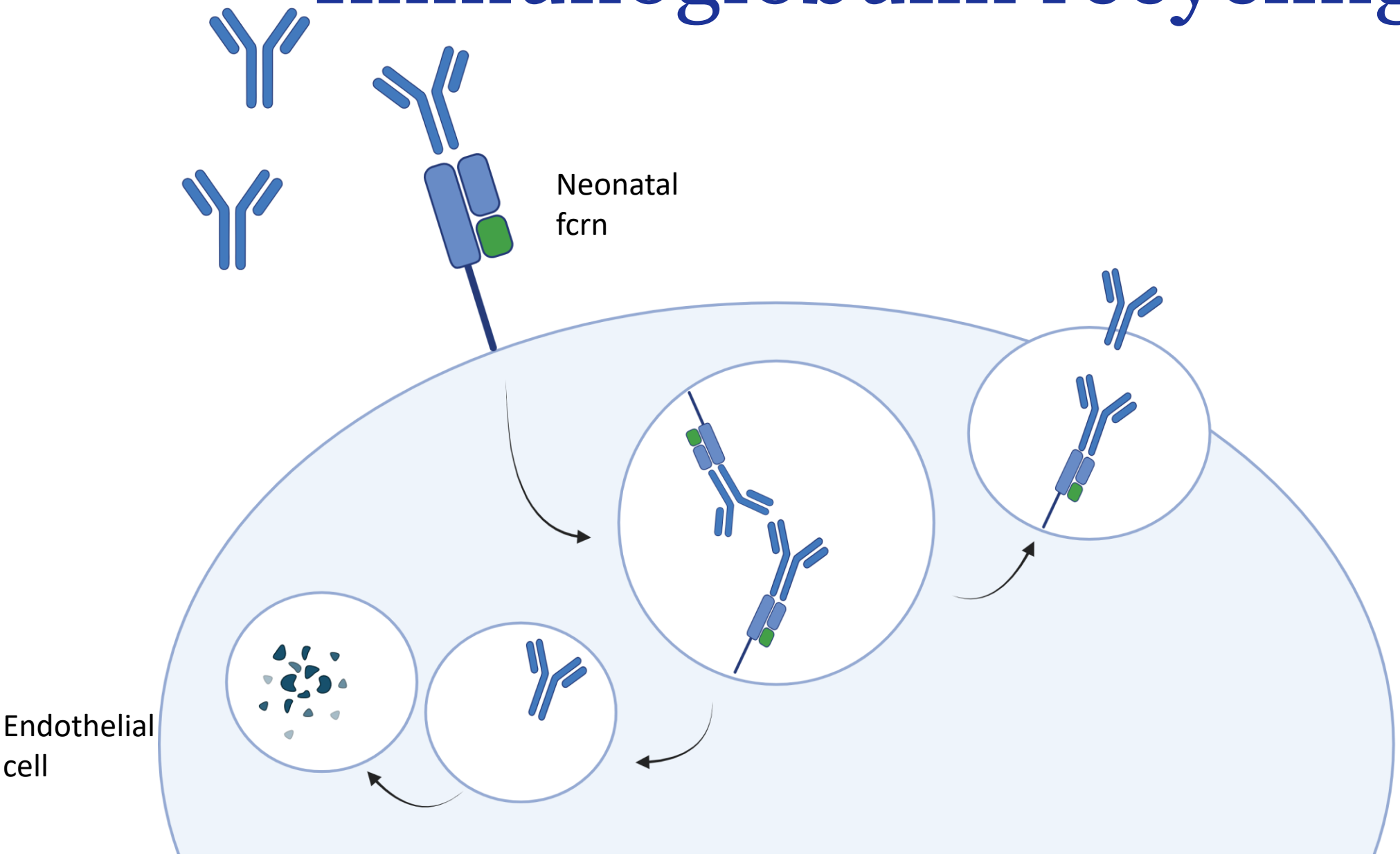
Outline

1. Nipocalimab
2. ARGX-113 efgartigimod
3. AMG 329- Formerly HZN-1116
4. Sibeprenlimab
5. RSLV-113

Caveats

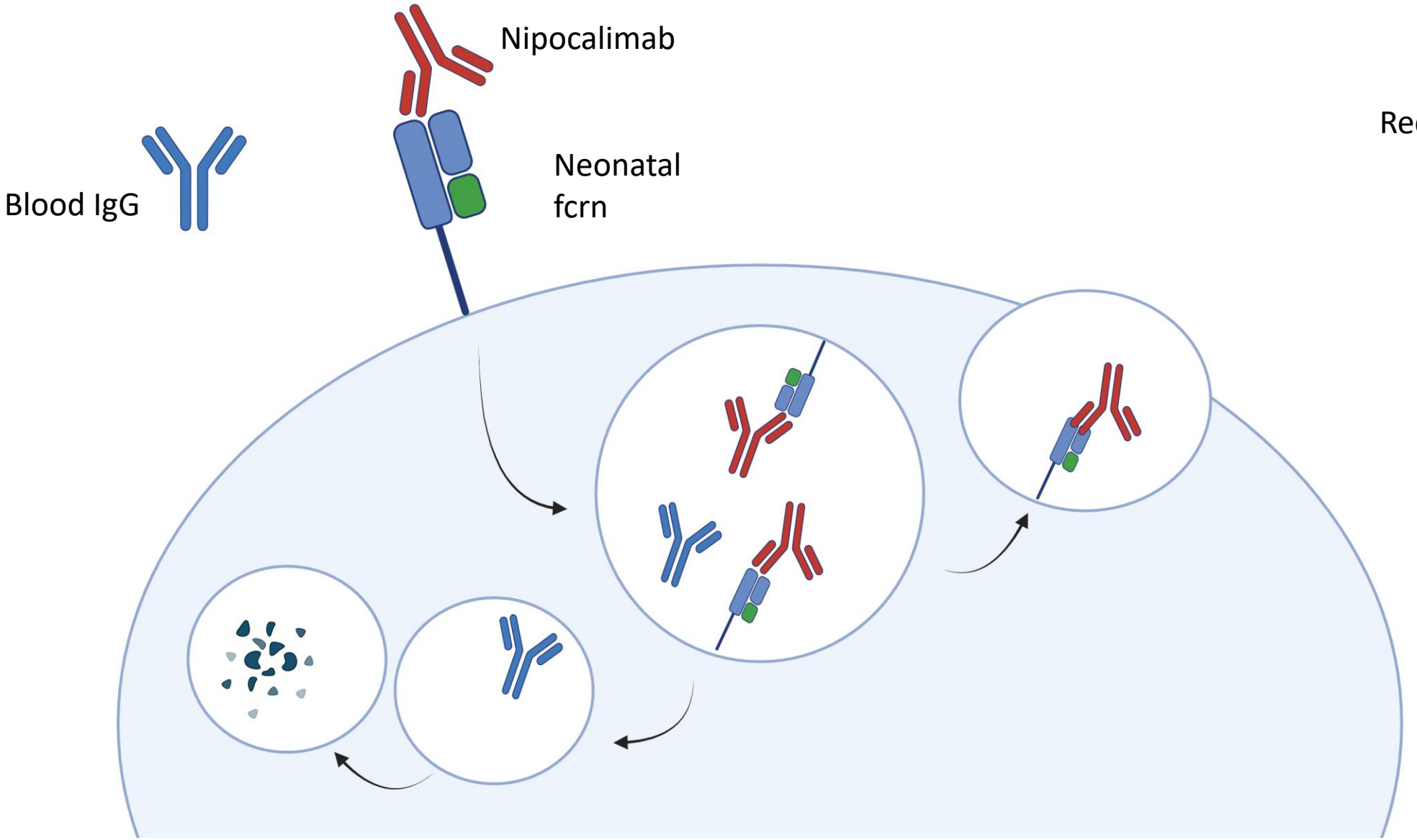
- SjD is heterogeneous →requires nuanced therapy for this nuanced disease
- Application based on phase 2 inc/exclusion; however, phase 3 usually more broad
- This is a rapidly evolving landscape

Immunoglobulin recycling



Nipocalimab

Nipocalimab-Mechanism



Reduces blood IgG

Nipocalimab-Phase 2 Study

Dahlias Study Structure

- 1:1:1 IV every 2 weeks until week 22
  - 5 mg/kg
  - 15 mg/kg
  - Placebo
- Change from baseline disease activity (clinESSDAI) @ week 24

Dahlias inclusion

- At least moderate disease activity
- Anti-SSA antibody positive

Nipocalimab-Phase 2 Results

Dahlias results

- N=163 enrolled
- The highest dose of 15 mg/kg showed significant improvement over placebo in disease activity improvement

Adverse reactions

- Serious adverse event
  - Nipo 15 mg/kg: 7.4%
  - Nipo 5 mg/kg: 7.5%
  - Placebo: 5.4%

2025 ACR Abstract LBA0010

Sjögren's FOUNDATION

Nipocalimab-Phase 3 Daffodil

Study structure

- Nipocalimab subcutaneously or placebo until week 48 on std of care
- Week 48 can enter open label until week 143 (cross over placebo arm)

Inclusion

- Criteria for SjD
- Anti-SSA antibody positive
- Disease activity moderate/severe

J&J. Nipocalimab in Moderate to Severe Sjogren's Disease (DAFFODIL) (NCT06741969). ClinicalTrials.gov.

Nipocalimab-phase 3 Daffodil

Primary outcome

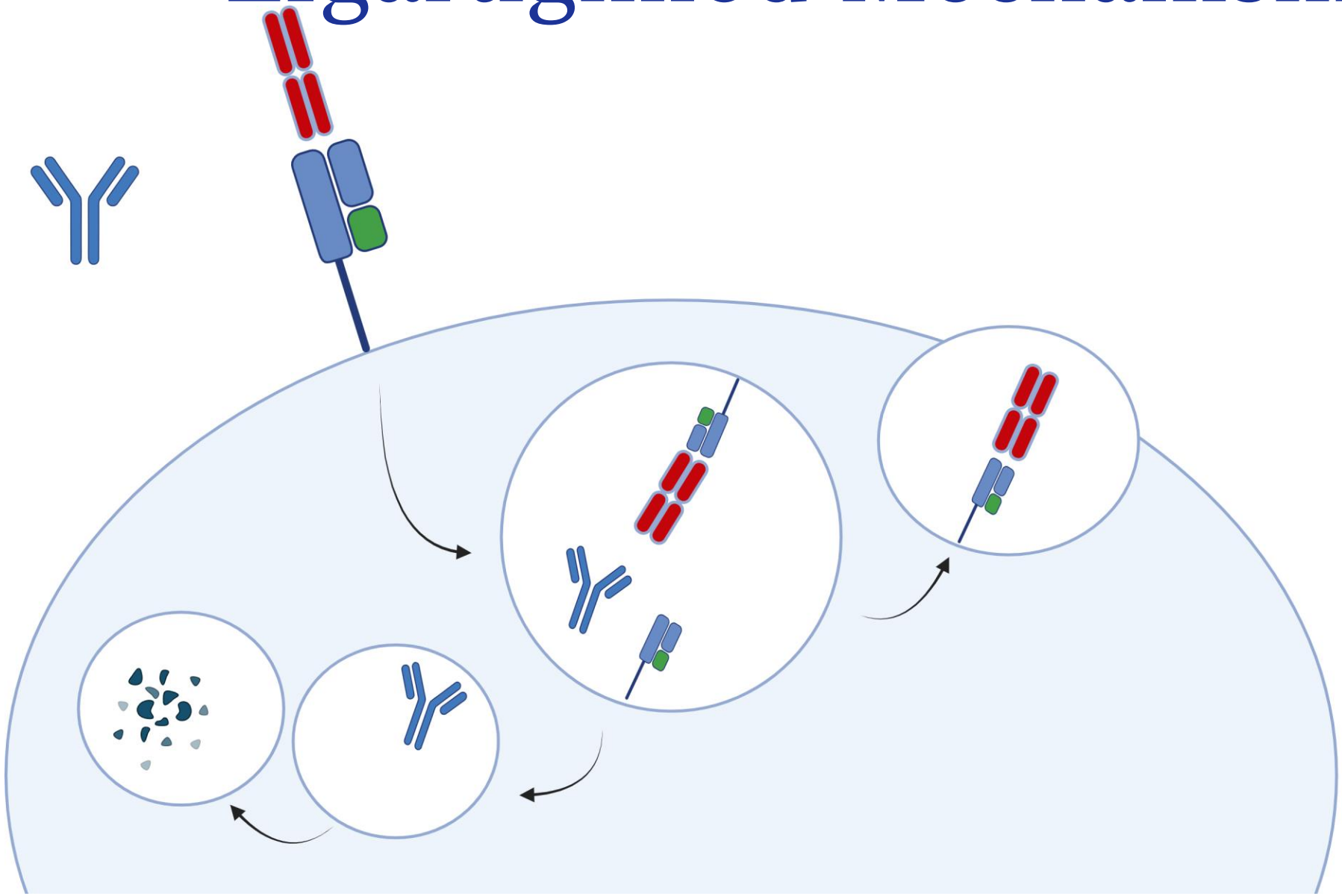
- Change from baseline in disease activity (clinESSDAI) at week 48

Nipocalimab- who might be suited to it?

- Anti-SSA antibody positive
- Evidence of B cell activity/IgG activity
  - High immunoglobulin g levels
  - Positive rheumatoid factor
  - Positive cryoglobulins
  - Low complement (C3, C4)

Efgartigimod

Efgartigimod-Mechanism



Efgartigimod-Phase 2 Study

Study Structure

- 2:1 IV efgartigimod or placebo until week 24
- Proportion of responders (CRESS) @ week 24

Inclusion criteria

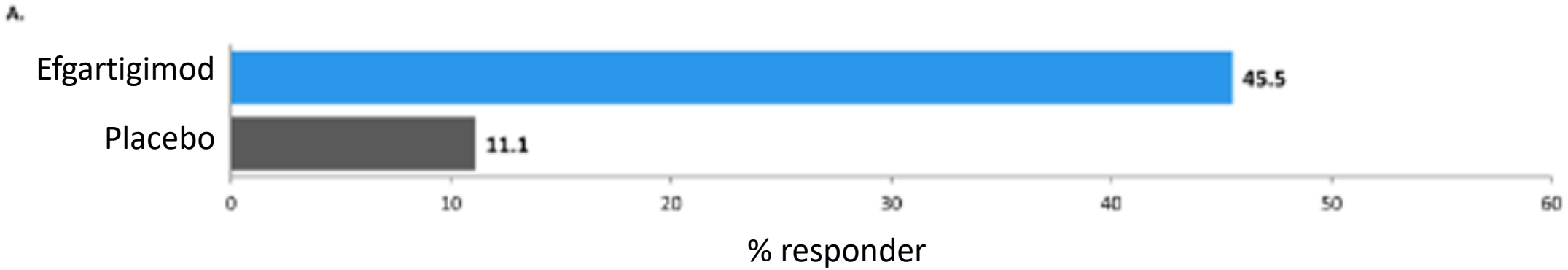
- SjD by criteria
- Time from dx of ≤7 yrs
- Anti-SSA/Ro positive
- Residual salivary flow
- ≥ moderate systemic disease activity

Argenx presents new efgartigimod data at EULAR 2025 highlighting positive phase 2 proof-of-concept results in myositis and Sjogren's disease [news release]. Argenx. 2025 Jun 11.

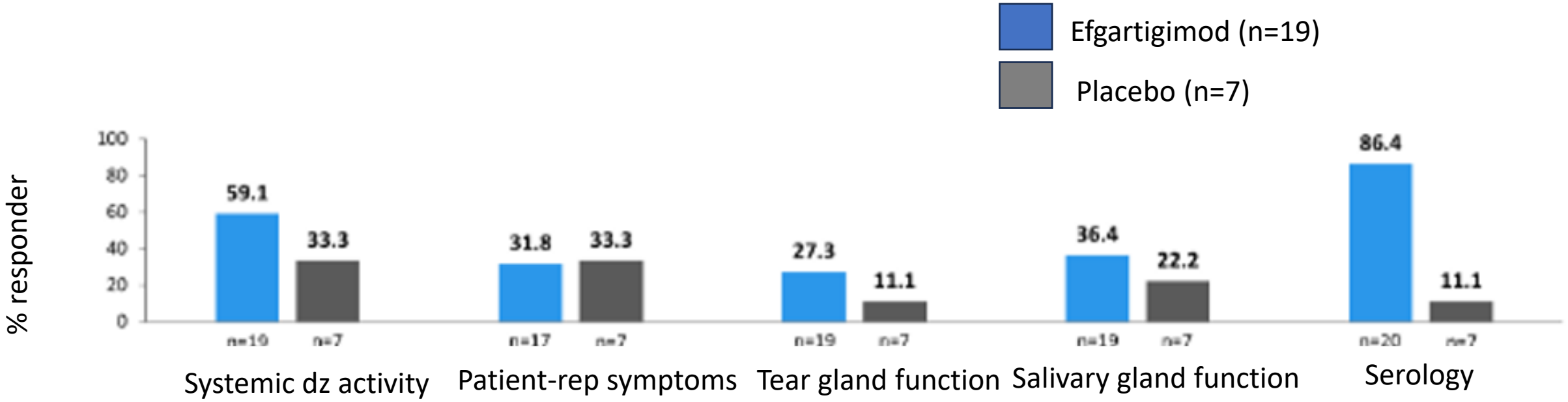
Efgartigimod-Phase 2 Results

Results

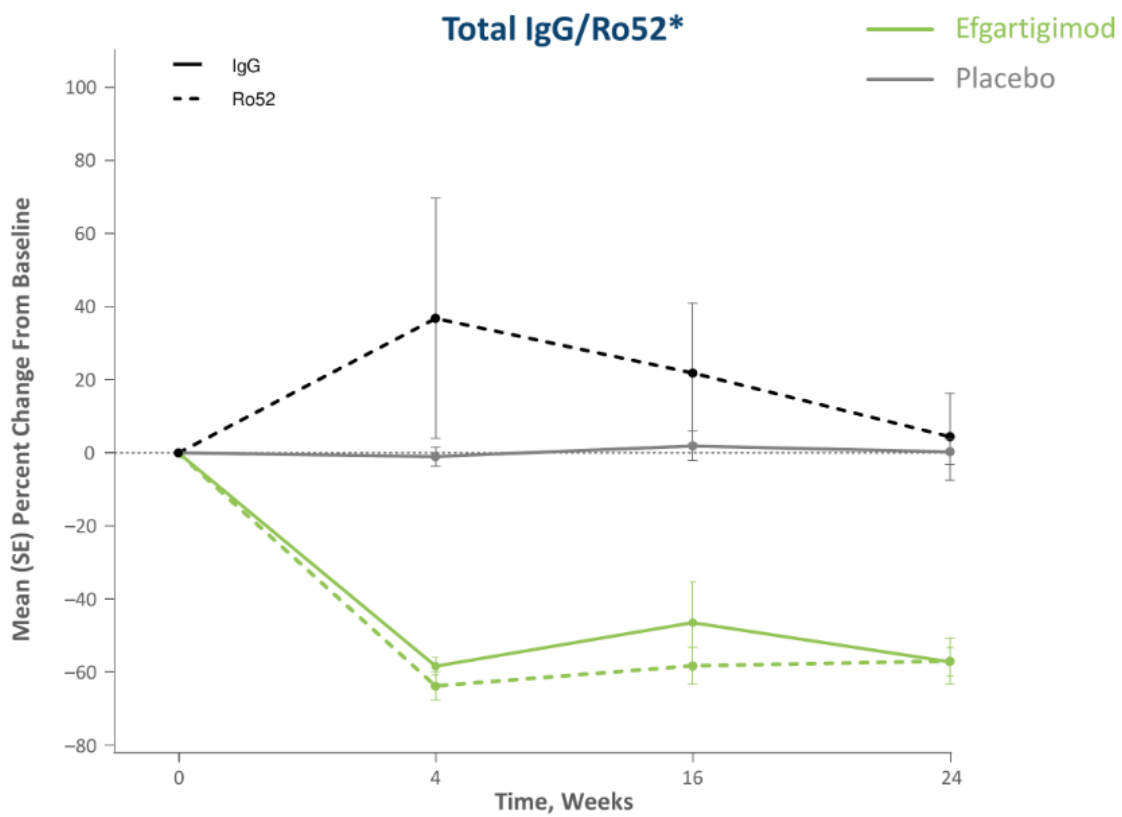
- N=34 enrolled
- 45.5% of efgartigimod achieved improved on the CRESS composite vs. 11.1% among placebo

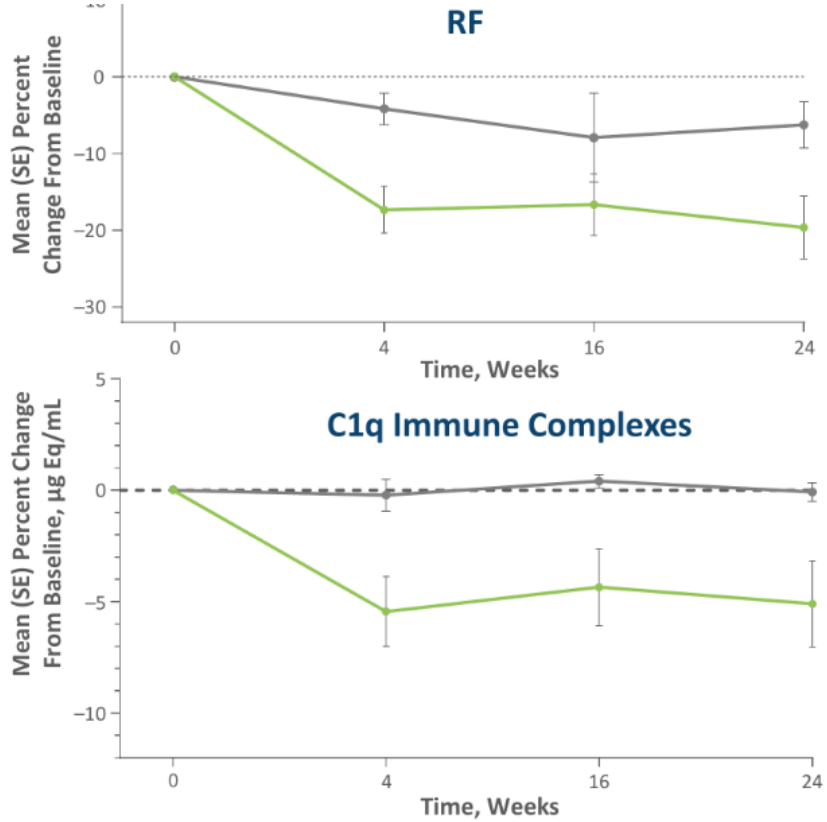


Efgartigimod-Phase 2 Results



Efgartigimod-Phase 2 Results





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

Efgartigimod-Phase 3 Design

Inclusion-UNITY

- Criteria for SjD
- Anti-SSA antibody positive
- Disease activity moderate/severe
- Residual salivary flow

Exclusion-UNITY

- Active fibromyalgia
- Associated SjD

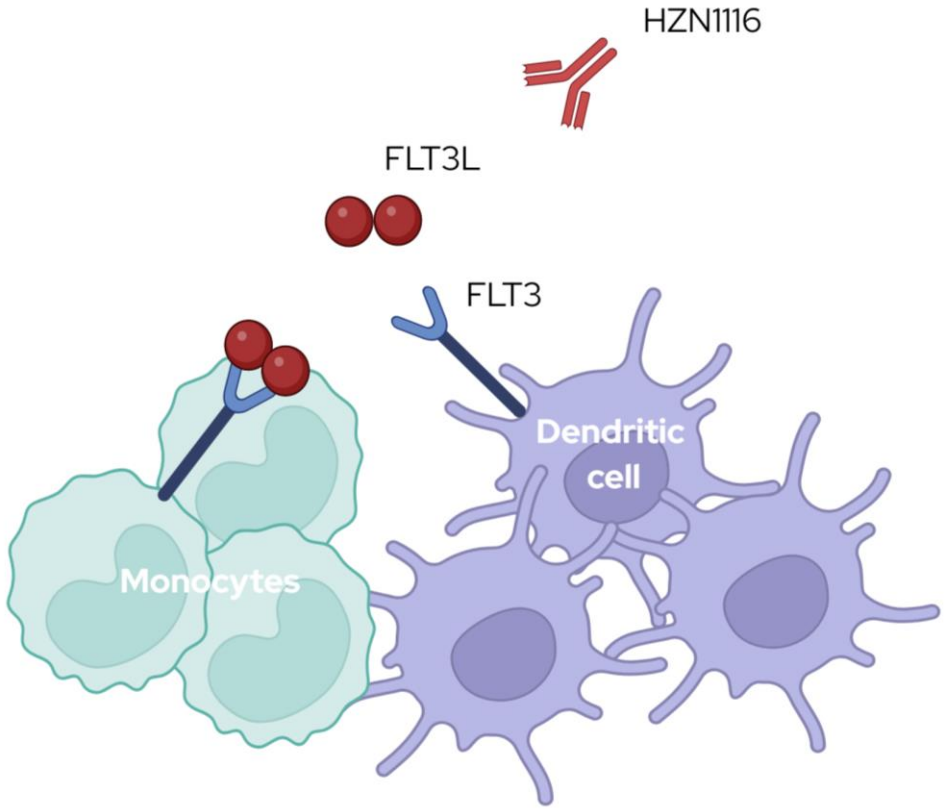
Argenx. A study of the efficacy and safety of efgartigimod in patients with primary Sjögren's syndrome (NCT06684847). ClinicalTrials.gov. 2025 Jun 13.

Efgartigimod- who might be suited to it?

- Anti-SSA antibody positive
- Evidence of B cell activity/IgG activity
  - High immunoglobulin g levels
  - Positive rheumatoid factor
  - Positive cryoglobulins
  - Low complement (C3, C4)

AMG 329- Formerly HZN1116

AMG 329-Mechanism tyrosine kinase 3 receptor ligand (FLT3L) inhibitor



AMG 329-Phase 2 Study

Study Structure 1

- HZN-1116 (2 doses) or placebo sc
- Change from baseline disease activity at week 48

Inclusion criteria-1

- SjD by criteria
- Anti-SSA/Ro or RF positive
- Residual gland fcn
- ≥ moderate systemic disease activity

A Phase 2 Study to Investigate Efficacy and Safety of HZN-1116 in Participants with Sjogren's Syndrome (NCT06312020). ClinicalTrials.gov.

AMG 329-Phase 2 Study

Study Structure 2

- HZN-1116 (4 doses) or placebo sc
- Change from baseline symptoms at week 24

Inclusion criteria-2

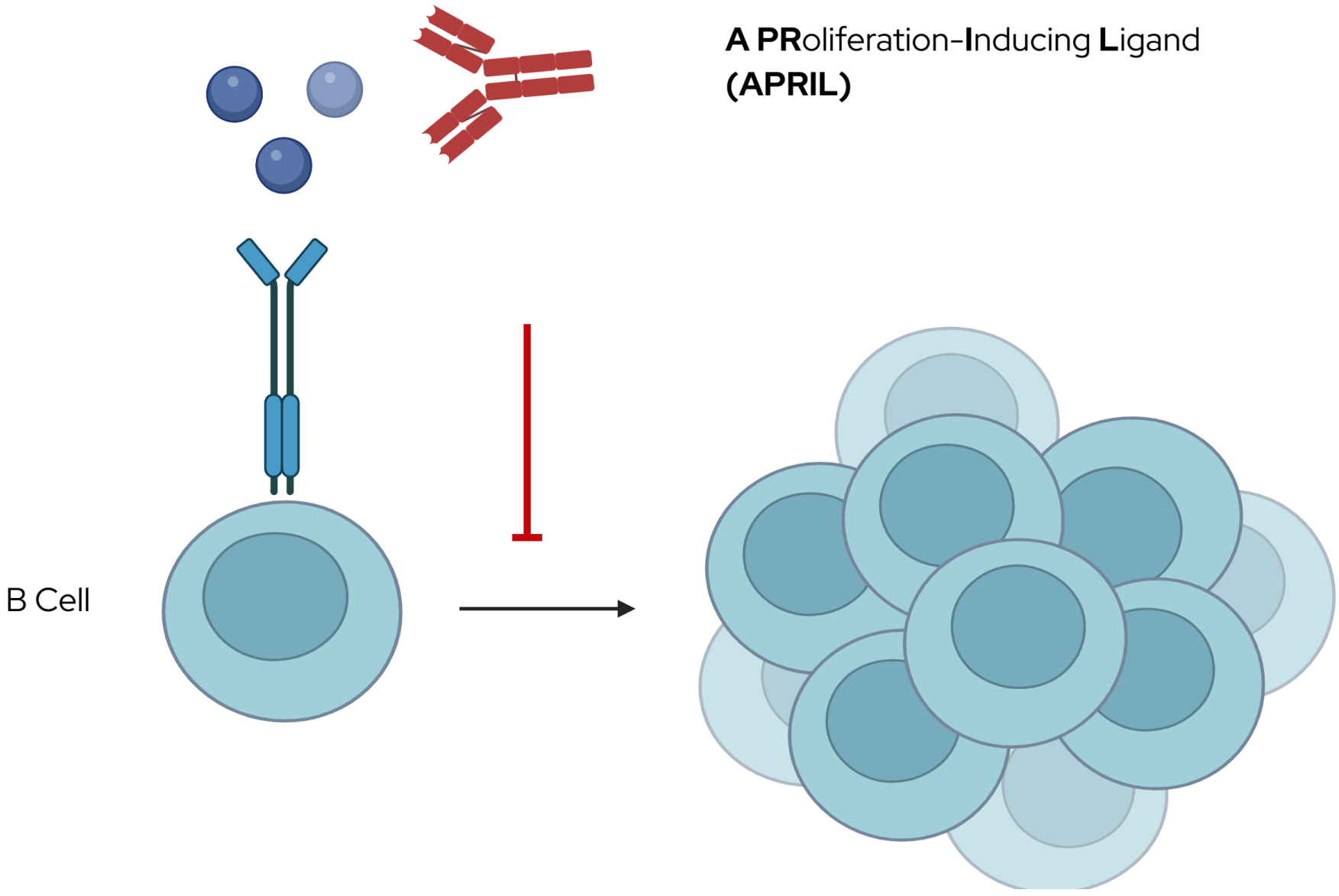
- SjD by criteria
- Anti-SSA/Ro or RF positive
- Residual gland fcn
- Low systemic disease activity
- Moderate-high symptom burden

AMG 329- who might be suited to it?

- Anti-SSA/RF positive
- High disease activity (organ involvement) OR high symptom burden
- Not for those with history of major viral infection

Sibeprenlimab

Sibeprenlimab



Sibeprenlimab-Phase 2 Study

Study Structure

- Subcutaneous every 4 wks
  - 400 mg sibeprenlimab
  - Placebo
- Change from baseline disease activity @ week 28

Inclusion

- SjD
- Moderate/high disease activity
- Salivary gland function
- IgG > 900 mg/dL
- Anti SSA antibody positive

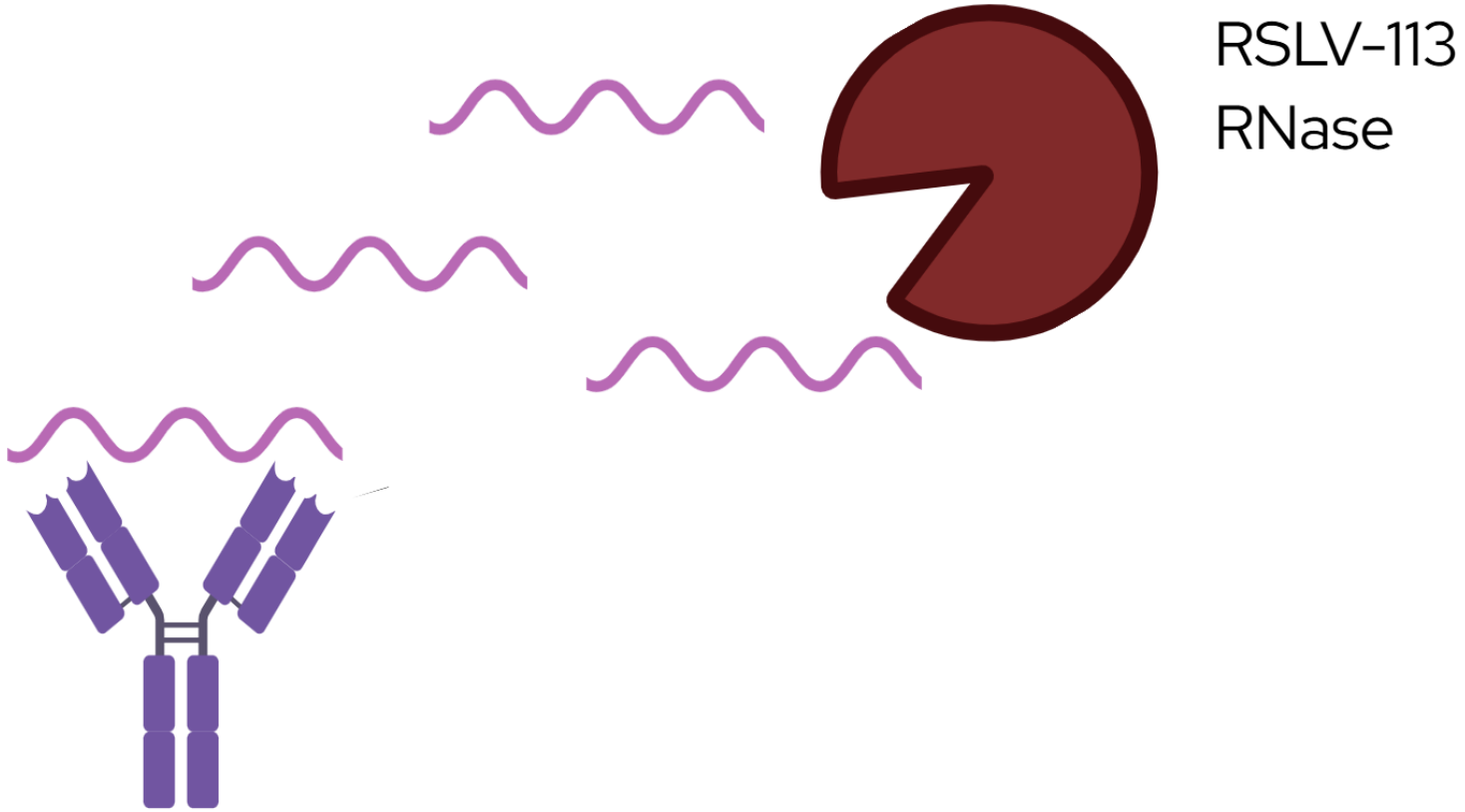
Otsuka. A trial to evaluate the efficacy and safety of sibeprenlimab administered subcutaneously in participants with Sjogren's (EnVISage) (NCT06928142). ClinicalTrials.gov.

Sibeprenlimab- who might be suited to it?

- Anti-SSA antibody positive
- Evidence of B cell activity/IgG activity
  - High immunoglobulin g levels
  - Positive rheumatoid factor
  - Positive cryoglobulins
  - Low complement (C3, C4)

RSLV-132

RSLV-132-Mechanism



RSLV-132-Phase 2 Study RESOLVE

Study Structure

- 3:1 IV every week x2, then every 2 weeks x 12 weeks
  - 10 mg/kg
  - Placebo
- IFN inducible gene expression

Resolve inclusion

- SjD
- Positive anti-SSA antibody
- IFN signature

Posada et al. Arthritis & Rheumatology. 2020

RSLV-132-Phase 2 Results

Resolve results

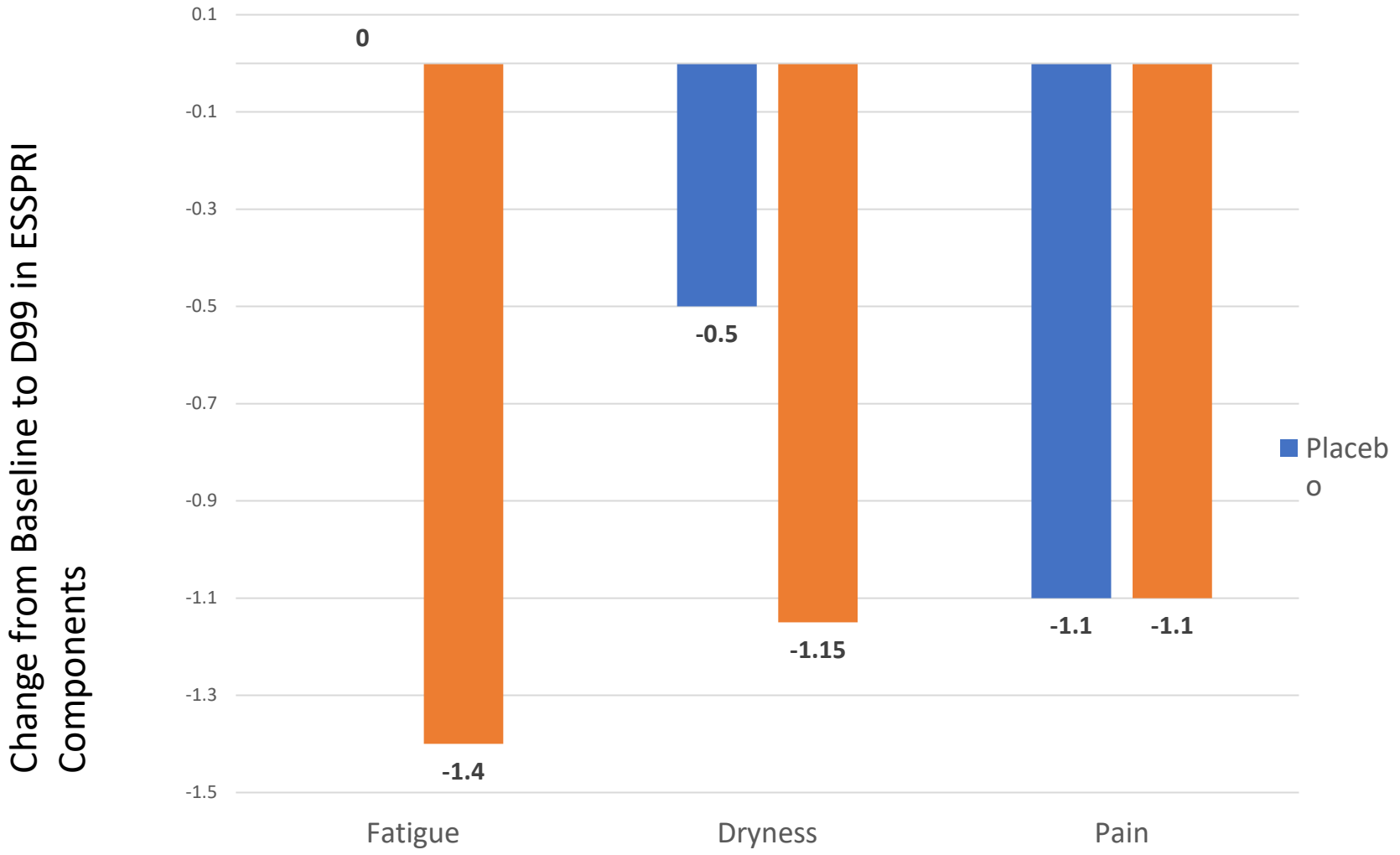
- N=30 enrolled
- **increased** IFN-inducible genes in the RSLV-132–treated patients vs. placebo
- Fatigue improved

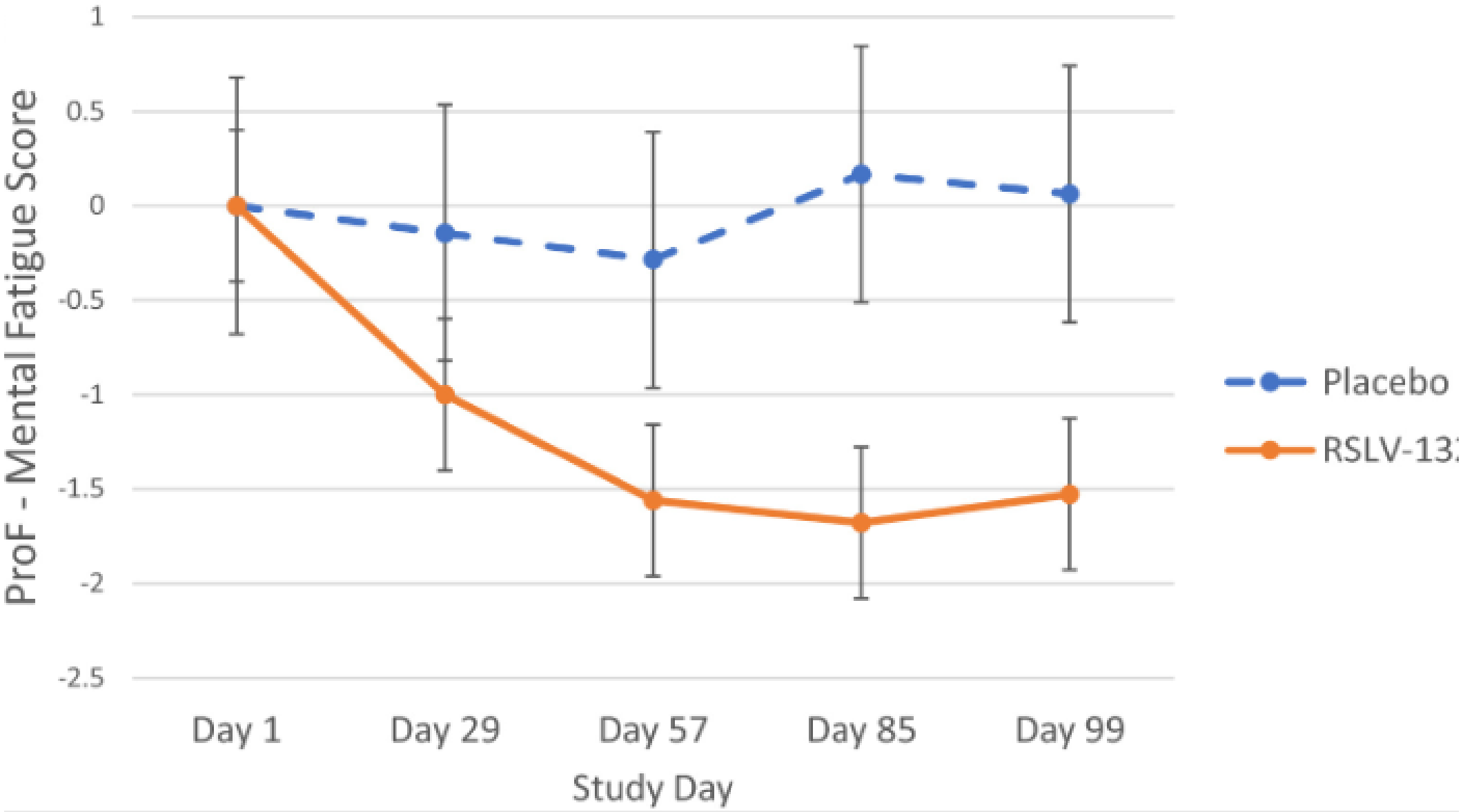
Adverse reactions

- No serious infections/infusion reactions

Posada et al. Arthritis & Rheumatology. 2020

RSLV-132-Phase 2 Results





Posada et al. Arthritis & Rheumatology. 2020

RSLV-132 Phase 2 expanded

Study structure

- RSLV-132 or a placebo 1:2 IV
- 13 times over 22 weeks
- Visit the clinic once every week for the first 2 weeks, then every 2 weeks x 22 weeks

Inclusion

- Criteria for SjD
- Dx within 10 years
- Anti-SSA antibody positive
- moderate/severe symptoms
- Residual gland function

Resolve Therapeutics. A study of RSLV-132 in females with Sjogren's disease (NCT06440525). ClinicalTrials.gov.

RSLV-132-Phase 2 expanded

Primary outcome

- Change from baseline in symptoms

RSLV-132- who might be suited to it?

- Anti-SSA antibody positive
- Fatigue, brain fog, dryness
- Interferon?

Conclusions

- An exciting time for SjD patients!
- Multiple drugs in pipeline with feasible mechanisms
- Yet to be seen who each drug fits best-likely some drugs will work better for specific patients than others