Shining Light on Hidradenitis Suppurativa (HS): Research Results and Moving Forward

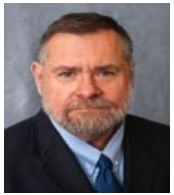
Brought to you by
Community-Engaged Research Core,
The Rockefeller University Center for Clinical Translational Science
Laboratory of Investigative Dermatology, The Rockefeller University
Clinical Directors Network

This program is supported in part by the National Center for Advancing Translational Sciences, National Institutes of Health, through Rockefeller University, Grant # UL1 TR001866

THE ROCKEFELLER UNIVERSITY HOSPITAL
CENTER FOR CLINICAL AND TRANSLATIONAL SCIENCE

Speakers:

Michelle A Lowes, MBBS, PhD
Visiting Associate Attending Physician
The Rockefeller University
Director, HS Foundation



James G Krueger, MD, PhD
D. Martin Carter Professor in Clinical Investigation
Senior Attending Physician
Laboratory Head, Investigative Dermatology
Principal Investigator, Center for Clinical and Translational Science
The Rockefeller University

John W Frew, MBBS, MMed, MS, FACD
Lecturer, University of New South Wales
Department of Dermatology
Liverpool Hospital, Australia

Yael Renert-Yuval, MD, MS
Instructor in Clinical Investigation
Laboratory for Investigative Dermatology
The Rockefeller University

Athena M Gierbolini
Patient Advocate
Community Lead and Director, Hope for HS
Director, HS Foundation

What is hidradenitis suppurativa (HS)?

Dr. Michelle Lowes
The Rockefeller University
Director, Hidradenitis Suppurativa Foundation

HS Foundation

Relationships

- Consultant for clinical trials: Abbvie, InflaRx, Janssen, and Viela Bio, and consulted for Almirall, BSN medical, Incyte, Janssen, Kymera, Phoenicis, and XBiotech.

- Director, Hidradenitis Suppurativa Foundation (HSF)

Question 1: For HS patients and family members

In **one word**, what
symptom or sign indicates
that a treatment for HS is working?

Question 2: Other attendees and stakeholders

In **one word**, what
symptom or sign indicates
that a treatment for HS is working?

How to make a diagnosis of HS?

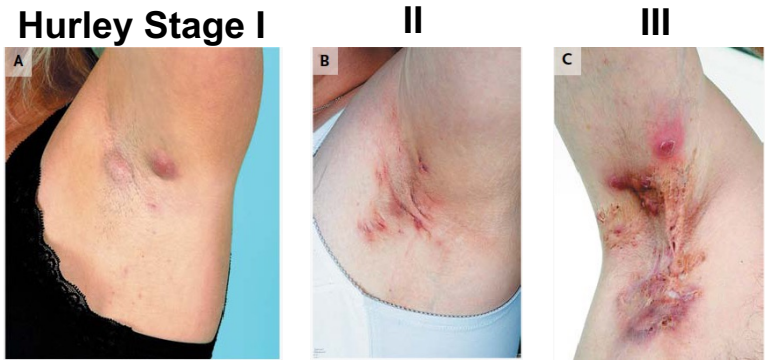
HS is a clinical diagnosis

Typical lesions:	Abscess, nodules, tunnels
Typical places:	Armpit, under breasts, groin
Recurrent:	Over 6 months

~1% of the population have HS

What is HS?

Signs



Symptoms

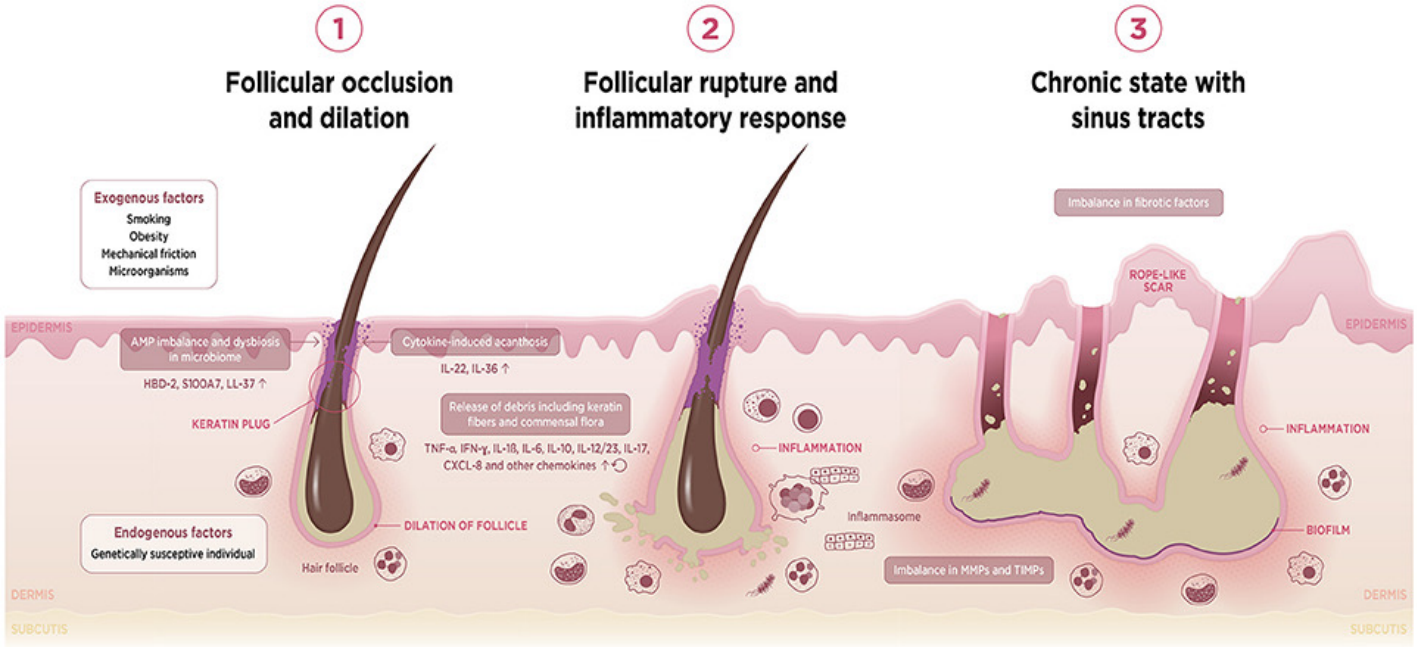
Pain

Drainage
Odor
Itch

Impact on QOL

Jemec, NEJM, 2012

How do HS lesions develop?

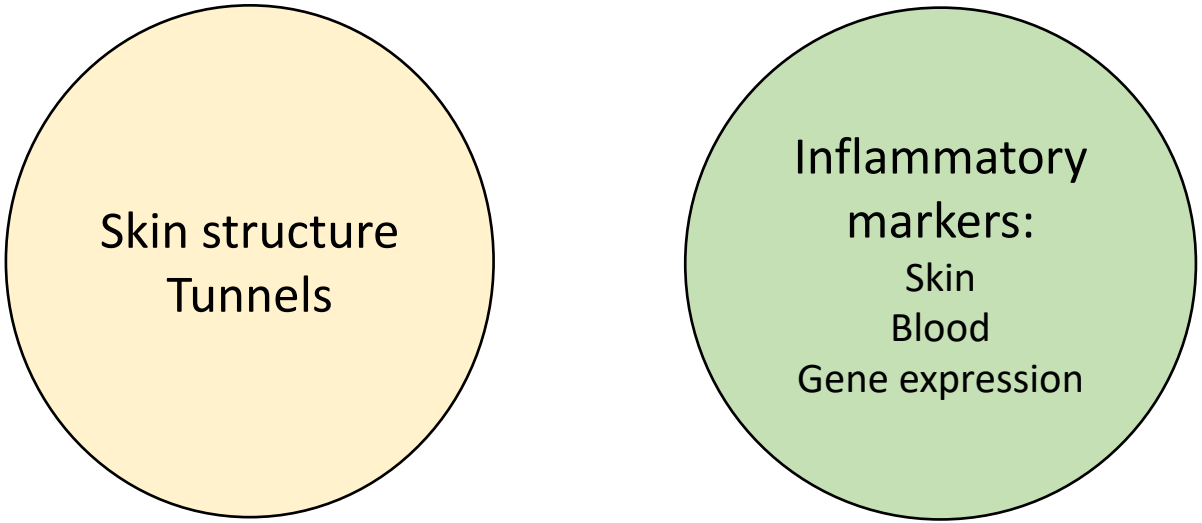


Vossen et al, Frontiers in Immunology, 2018

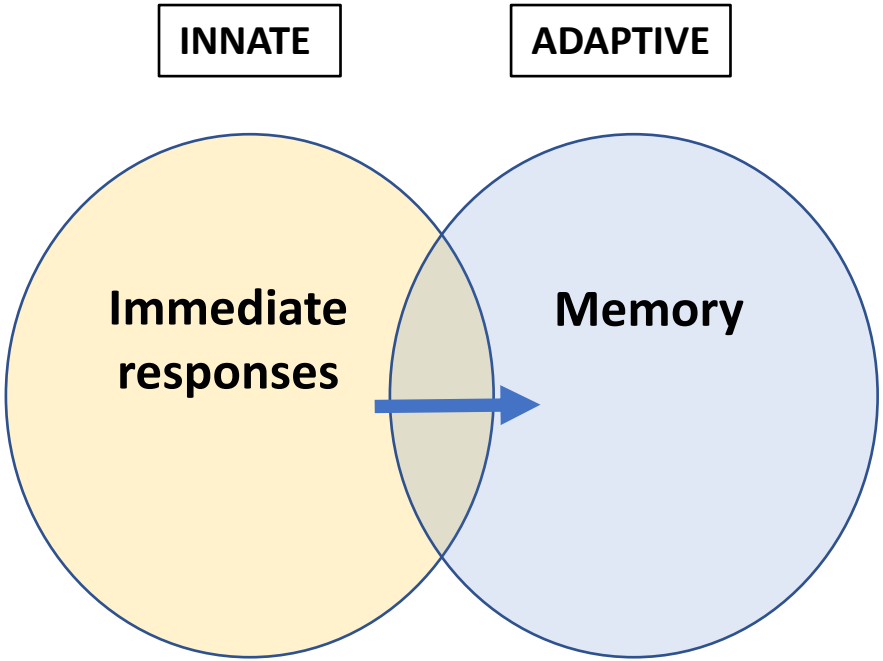
Frew et al, JAMA Derm, 2021

Evaluating the skin

HISTOPATHOLOGY (BIOPSY SLIDES)	LABORATORY

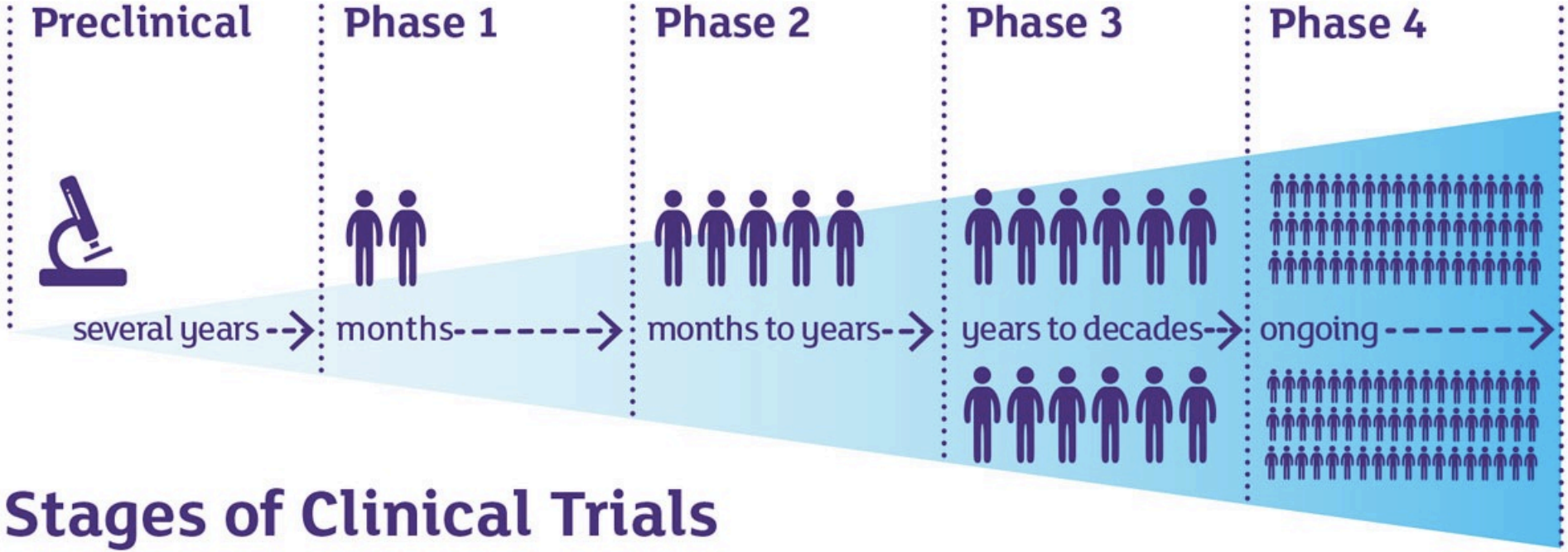


The Immune System



Diseases: **Auto-inflammatory** **Auto-immune**

Clinical Trials in HS



https://www.cancer.nsw.gov.au/

Measuring clinical outcomes in HS: HISTORIC

CLINICIAN REPORTED (ClinRO)

Physical Signs
Global

PATIENT REPORTED (PRO)

Pain
Quality of Life
Symptoms
Global
Flare

CHORD
Consortium for Harmonizing Outcomes Research in Dermatology

Thank you!

lowesm@rockefeller.edu
lowesm8@gmail.com

https://www.shsa2021.org/

HS Patients and family members

Word cloud generated from the responses to:
"What symptom or sign indicates that a treatment for HS is working?"

Other attendees and stakeholders

Word cloud generated from the responses to:
“What symptom or sign indicates that a treatment for HS is working?”

Athena M. Gierbolini

Patient Advocate

Community Lead and Director, Hope for HS

Director, HS Foundation

The Translational Approach to Chronic Skin Disease

Jim Krueger, MD PhD

The Rockefeller University

New York, NY

jgk@rockefeller.edu

My perspective

- Human skin is the body's barrier to the outside world of microbes (bacteria, viruses, fungi, worms, bugs, and other nasty substances)
- As such the skin is a complex tissue that has many protective immune functions—some are "natural" (innate immunity) and some are "learned with exposure" (acquired immunity)

Alternative Inflammatory States

- Homeostasis (normal appearing skin)– Immune cells and molecules are present, but kept in check by the "immune police" (negative regulators or immune checkpoints).
- Inflammation that is transient and then resolves (often fighting an infection)
- Inflammation that persists over time (often seen in skin diseases like psoriasis, eczema, and hidradenitis)

Protective vs. Pathogenic Immunity

Protective pathways can cause skin disease when activated persistently.
Causes can be unresolved infections, auto-inflammation, or auto-immunity.

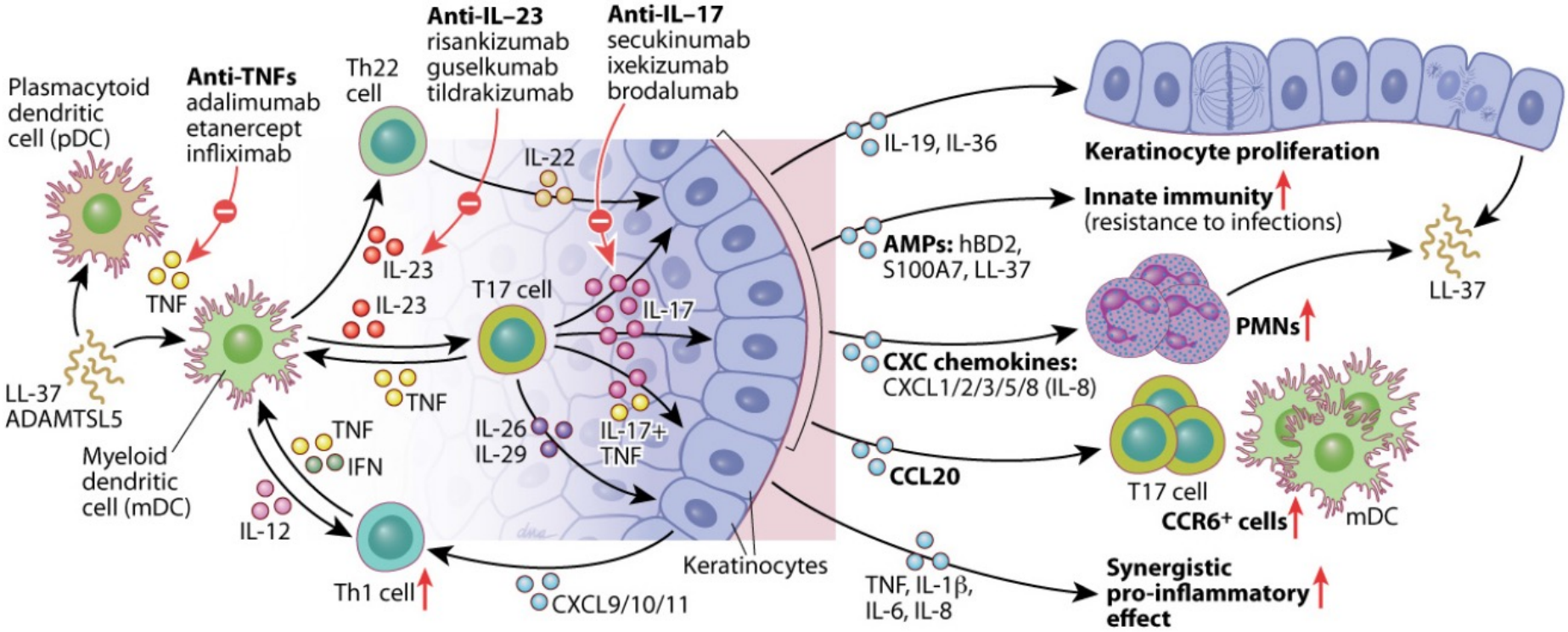
Translational Science Approach

- Starts with the recognition that there is a skin disease with high need for better treatment
- Involves a partnership between patients with a disease and physician-scientists
- A component is “Bedside to Bench” research where possible disease mechanisms are discovered and studied in affected skin tissues or blood
- Another component is “Bench to Bedside” research where new possible therapies are tested and studied in clinical trials of patients with a specific skin disease

Best example of this approach: Psoriasis vulgaris

- Psoriasis is a disease that affects 25 million people across North America and Europe
- 25 years ago had a small number of effective treatments that were available for short-term treatment (due to toxicity)
- Since, 2003 there has been FDA approval of 11 new drugs that treat psoriasis extremely well (good control in 90% of patients; no disease in ~50% of patients)

Basis for success in psoriasis: Disease maps of underlying immune pathways that can be targeted with specific inhibitors



Hawkes JE, Chan TC, Krueger JG. JACI (2017).

High Efficacy of IL-17 antagonists in Phase 3 Studies in Psoriasis

- Secukinumab (anti-IL-17A) superior to ustekinumab in CLEAR study, 87% PASI75 in JUNCTURE study
- Ixekizumab (anti-IL-17A) superior to etanercept in UNCOVER study, 90% PASI75 in best performing dosing group
- Brodalumab (anti-IL-17 Receptor, A subunit) superior to ustekinumab in AMAGINE-3 study, 86% PASI75 in AMAGINE-2 Study, best performing dose group
- Bimekizumab (anti-IL-17A & anti-IL-17F) >90% PASI 75 and 60% PASI100 (clear skin) in BE-ABLE 1 study.

Does the translational approach work in other skin diseases?

- Atopic eczema or atopic dermatitis– a disease even more common than psoriasis and also difficult to treat
- About a dozen years ago, creation of disease-associated immune maps started by Emma Guttman and collaborators at Rockefeller University, then continued at Mt. Sinai Medical Center.
- 4 years ago FDA approved first modern drug to treat AD and many “Bench to Bedside” clinical trials are recently completed on in progress (including some at Rockefeller University). This disease is about 10 years behind psoriasis, but it is catching up fast for new and improved treatments.

What about Hidradenitis suppuritiva (HS)?

- Now recognized as one of the most important skin diseases lacking treatments that will benefit most patients with this disease
- The Rockefeller Investigative Dermatology Group began studies in HS about 3 years ago with Translational Science approaches of “Bench to Bedside” and “Bedside to Bench”– Dr. John Frew will tell you about some advances in HS later this evening.
- We have developed new disease models based on this research that will stimulate testing of new drugs.
- We welcome your partnership with us in trying to understand, treat and maybe one day cure this important skin disease

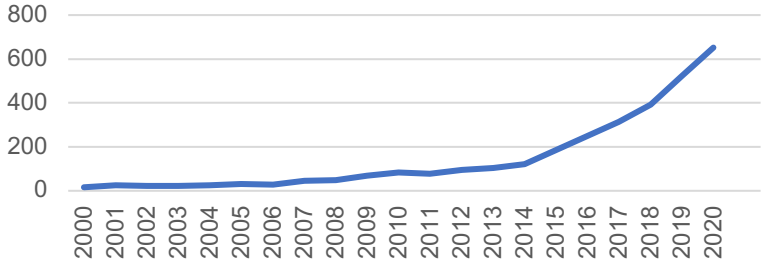
Studies in Hidradenitis Suppurativa: Feedback of Results

Dr John W Frew MBBS MMed MS FACD
University of New South Wales, Sydney, Australia

What's Coming down the Pipeline for HS

Yael Renert-Yuval, MD
Instructor in Clinical Investigations
Laboratory for Investigative Dermatology
The Rockefeller University

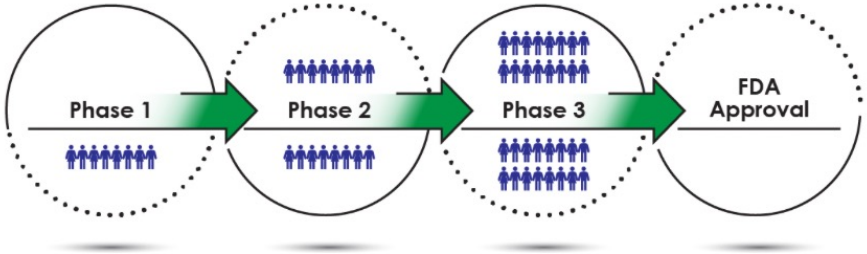
PubMed Publications Including “Hidradenitis Suppurativa”



- Increasing awareness and diagnosis of HS
- Increasing recognition of the great unmet therapeutic need in HS

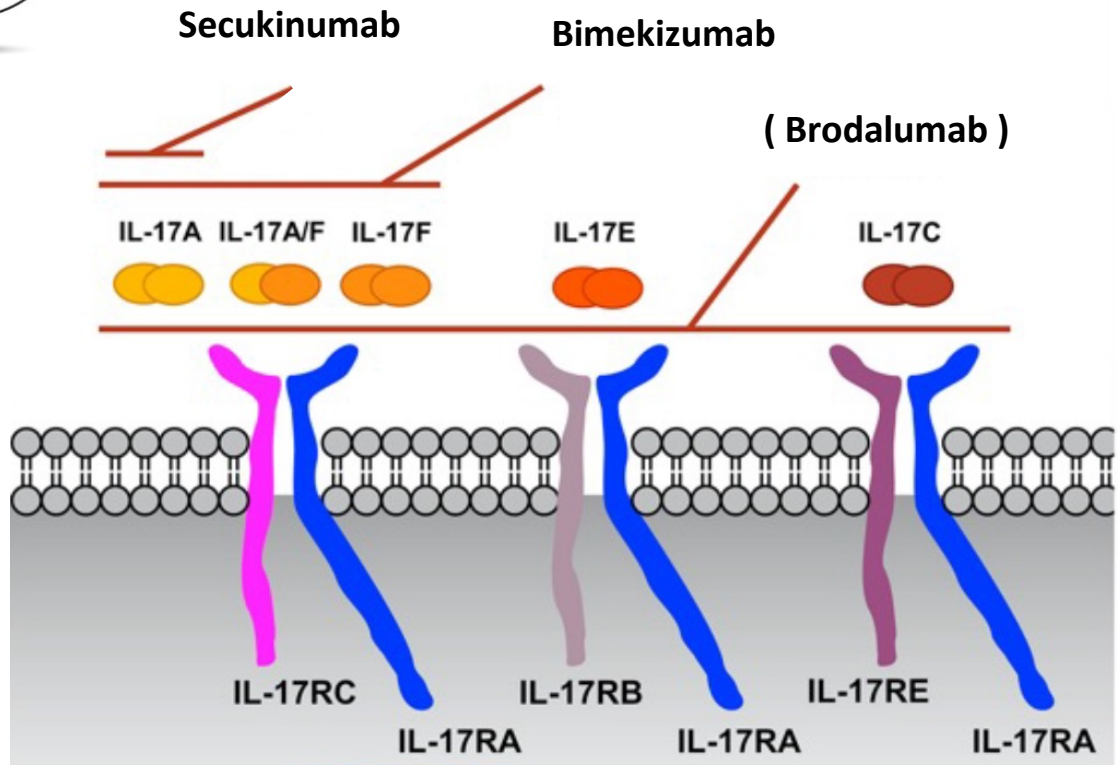
- Growing interest from the scientific community and pharma

- More research focusing on HS and greater funding for the development of better HS therapeutics!



Two drugs in phase III for HS:

- Secukinumab
- Bimekizumab



https://www.cell.com/immunity/comments/S1074-7613(15)00504-X

Secukinumab

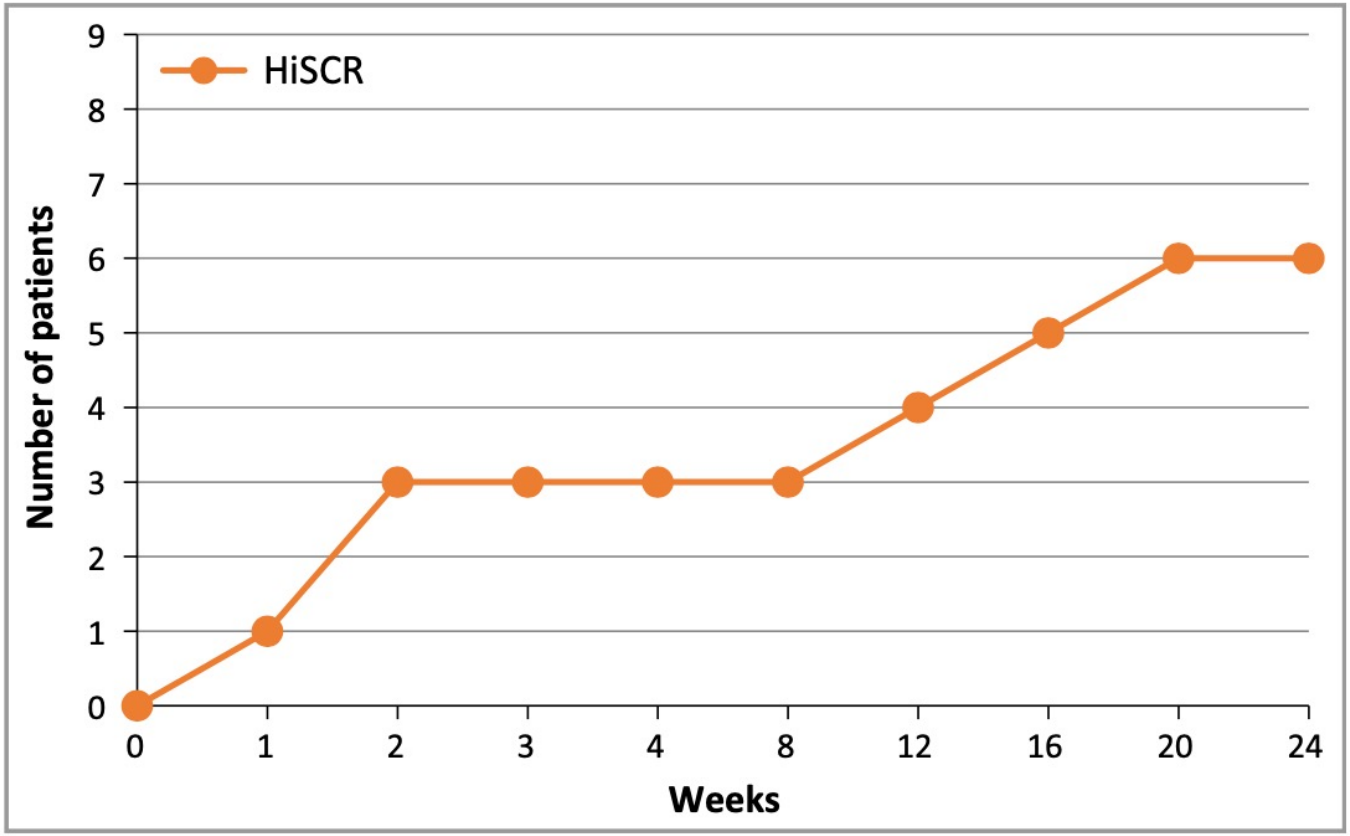
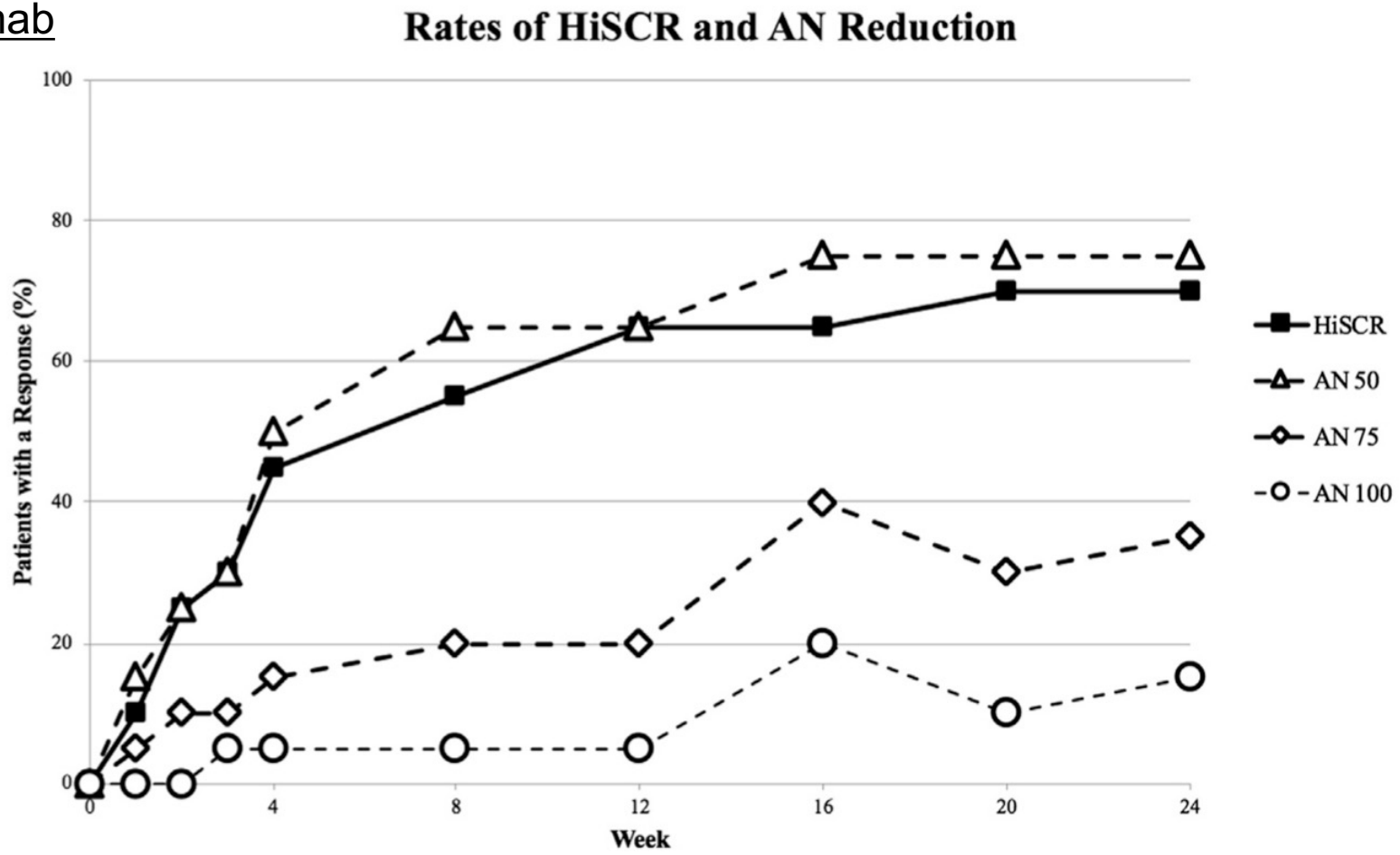


Fig 1. Number of patients achieving a Hidradenitis Suppurativa Clinical Response (HiSCR) during secukinumab treatment using the last-observation-carried-forward.

Prussick L, et al. Open-label, investigator-initiated, single-site exploratory trial evaluating secukinumab, an anti-interleukin-17A monoclonal antibody, for patients with moderate-to-severe hidradenitis suppurativa
Br J Dermatol. 2019 Sep;181(3):609-611. doi: 10.1111/bjd.17822.

Secukinumab

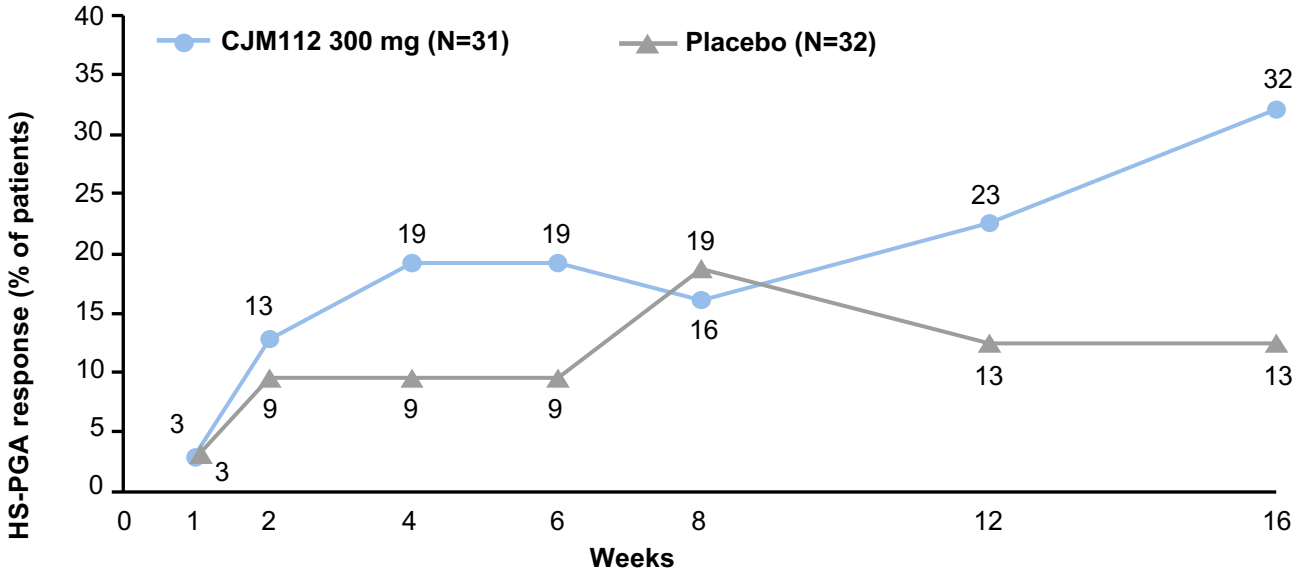
N=20



Casseres RG, et al. Secukinumab in the treatment of moderate to severe hidradenitis suppurativa: Results of an open-label trial. J Am Acad Dermatol. 2020 Jun;82(6):1524-1526.

Secukinumab – Phase 2 Results

HS-PGA response rate

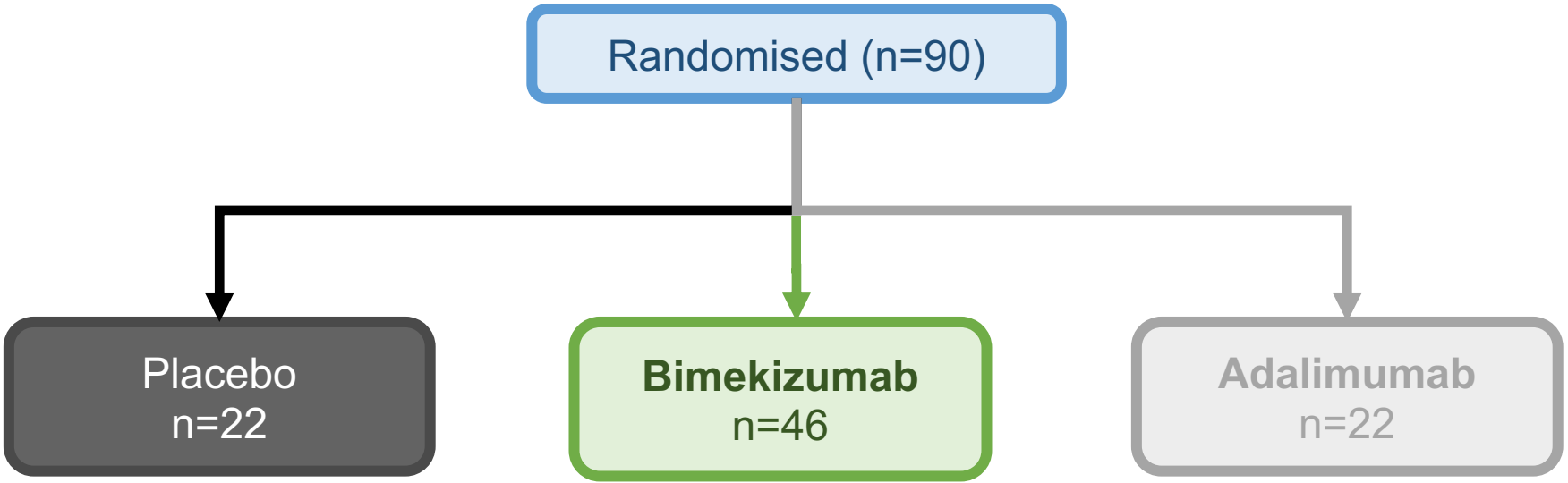


HS-PGA, Hidradenitis Suppurativa Physician Global Assessment
Kimball AB et al. *WCD.* 2019, (Poster 4999).

Bimekizumab

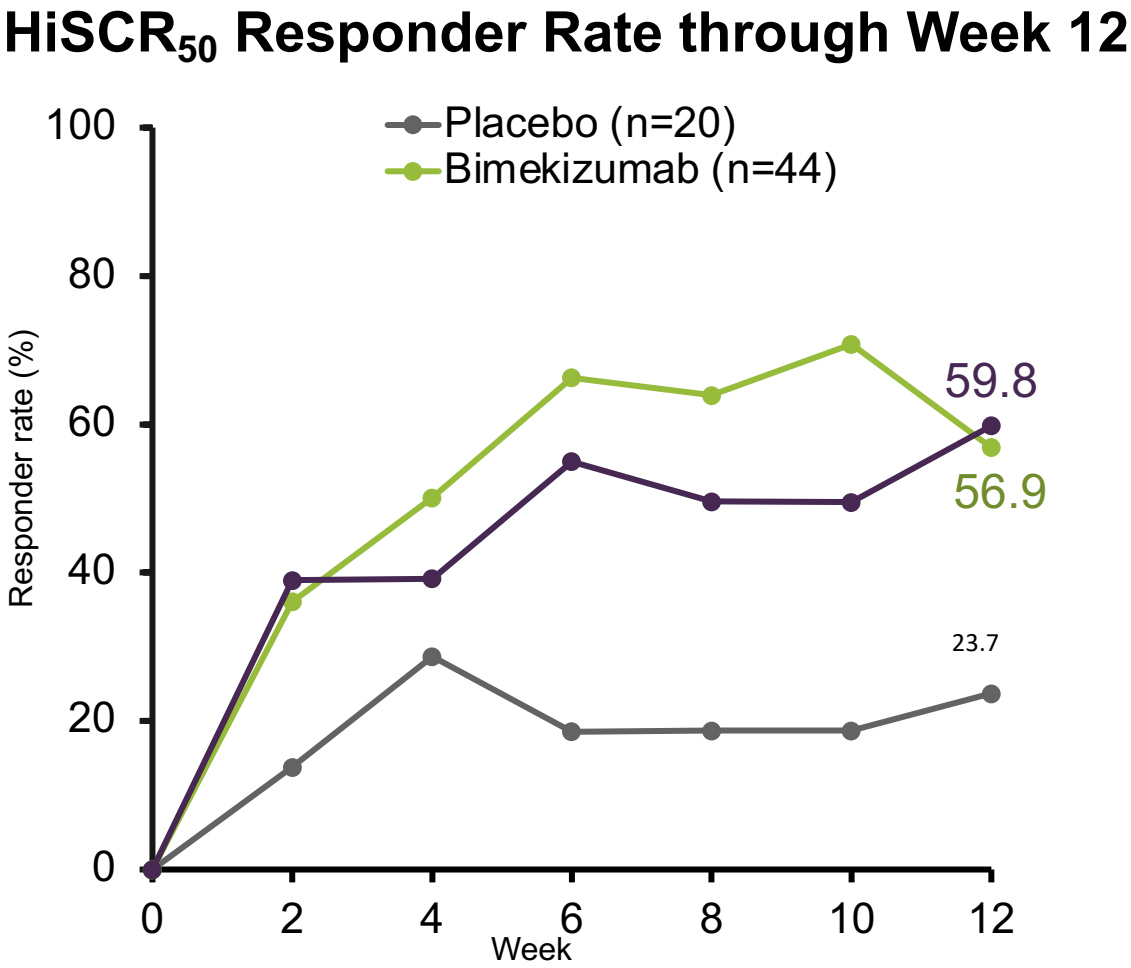
Efficacy and Safety of Bimekizumab, a Dual Interleukin (IL)-17A and IL-17F Inhibitor, for the Treatment of Moderate-to-Severe Hidradenitis Suppurativa (HS): a 12-Week, Randomised, Double-Blind, Placebo-Controlled, Phase 2 Study

GB Jemec et al. Funded by UCB Pharma

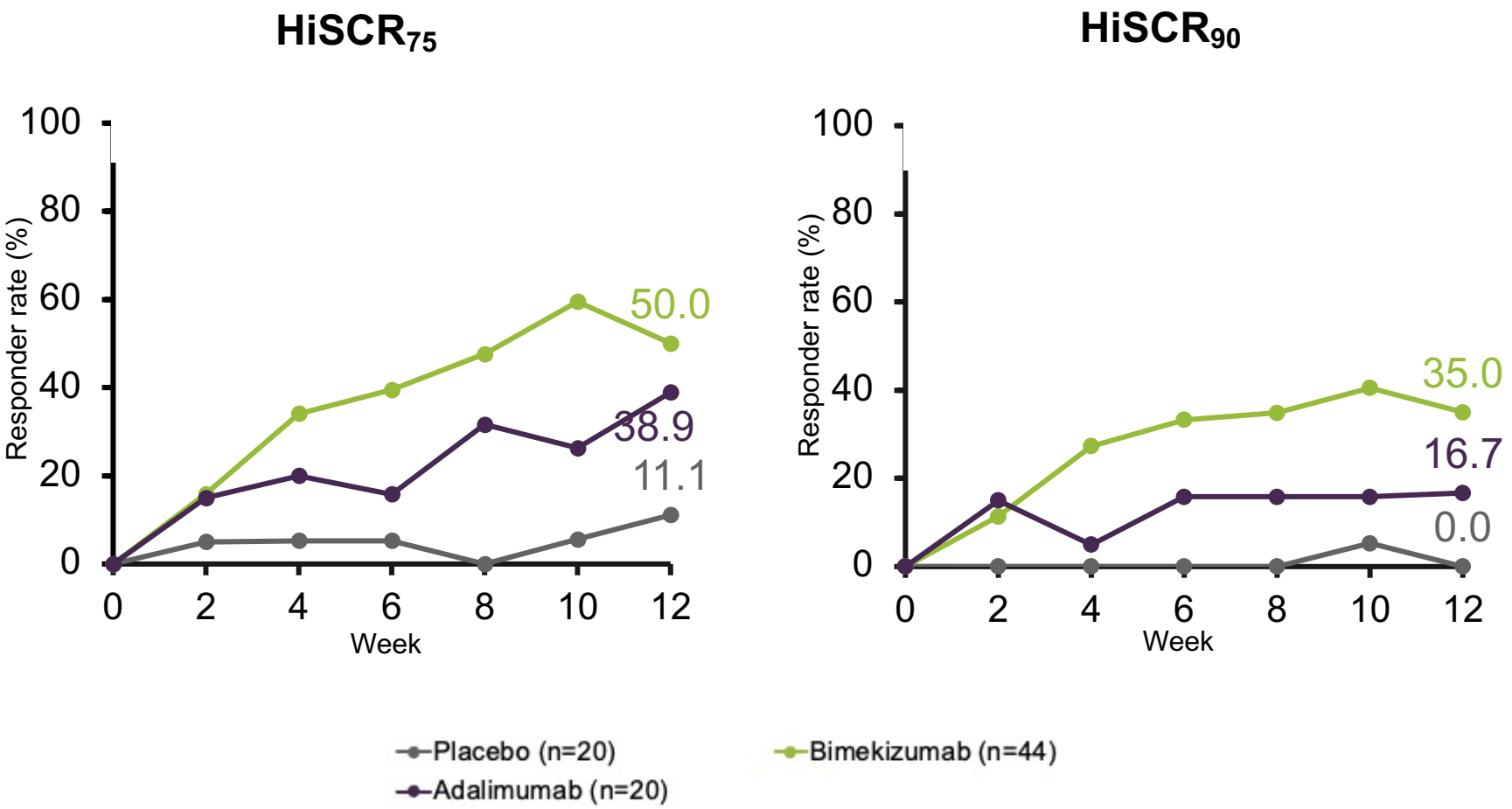


Full analysis set: N=88.

Bimekizumab – Phase 2 Results



Bimekizumab – Phase 2 Results



Potential therapeutic targets for HS….

IL-36

IL-1

IL-17

IL-12/23

IL-23

JAK/STAT

Complement

THANK YOU!

Contact at the Rockefeller University Hospital for HS clinical trials:

- Yael Renert-Yuval, MD

Yrenert@Rockefeller.edu

212-327-7581

- Kadija Fofana

RUCARES@rockefeller.edu

1-800-RUCARES

- https://rockefeller.trialstoday.org/ for a list of clinical studies enrolling at Rockefeller University

Q&A Session