THE ROAD TO REMISSION IN PLAQUE PSORIASIS

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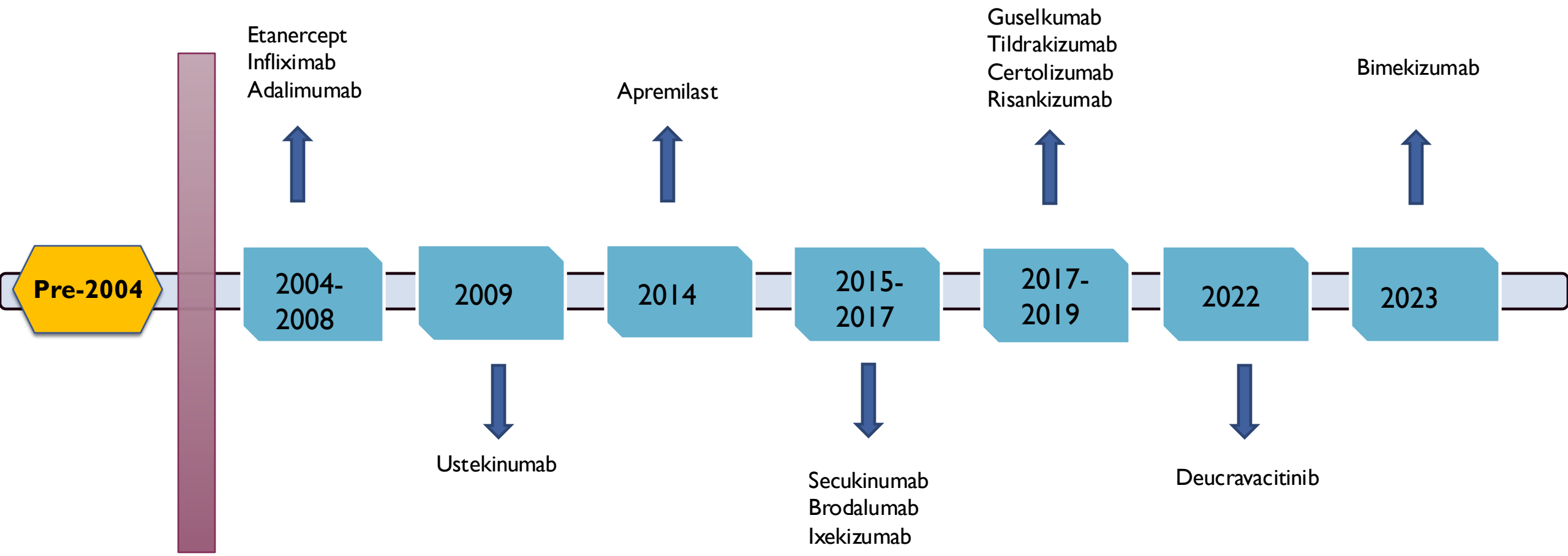
THERAPIES FOR PLAQUE PSORIASIS



WHY PSORIASIS COMES BACK…EVEN AFTER CLEARANCE

Once therapy is discontinued, psoriasis tends to recur at the same sites

→

Leaves behind "molecular scar"

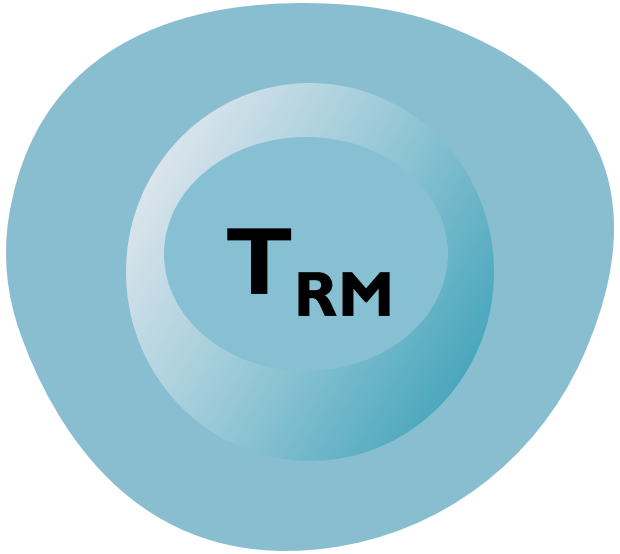
→

Strategy: target tissue resident memory T-cells

Suárez-Fariñas M et al. J Invest Dermatol. 2011 Feb;131(2):391-400; Iversen L et al. J Eur Acad Dermatol Venereol. 2018 Nov;32(11):1930-1939

WHAT IS THE ROLE OF THE TISSUE RESIDENT MEMORY CELLS?

Normal Function:
Develop in a pathogen specific manner in response to infections



Re-activation:
Amplify the immune response by quickly recruiting effector T cells

Long Lived:
Responsible for tissue protection from re-infection with original pathogen

Blauvelt A. J Psoriasis Psoriatic Arthritis. 2022 Oct;7(4):157-159

CONCEPT 1: HIT PSORIASIS EARLY!

THE WINDOW OF OPPORTUNITY

Hypothesis:
Early stages of psoriasis → limited memory T cells have invaded the skin

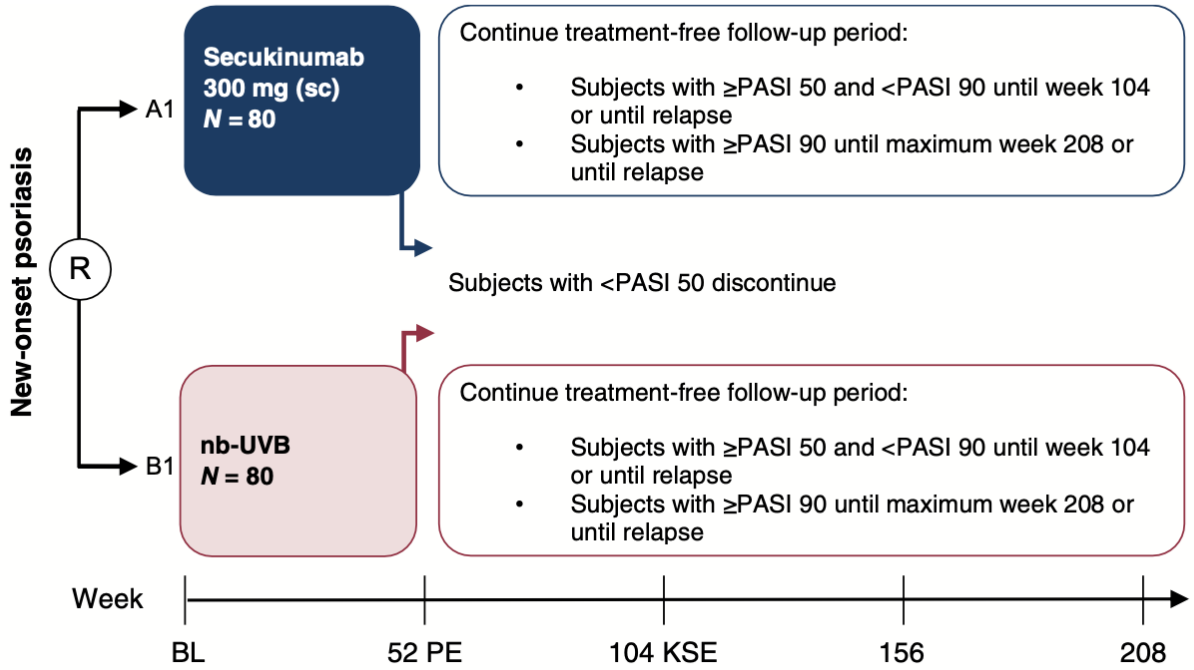
Hope:
Treat psoriasis early with biologics → potential disease modification

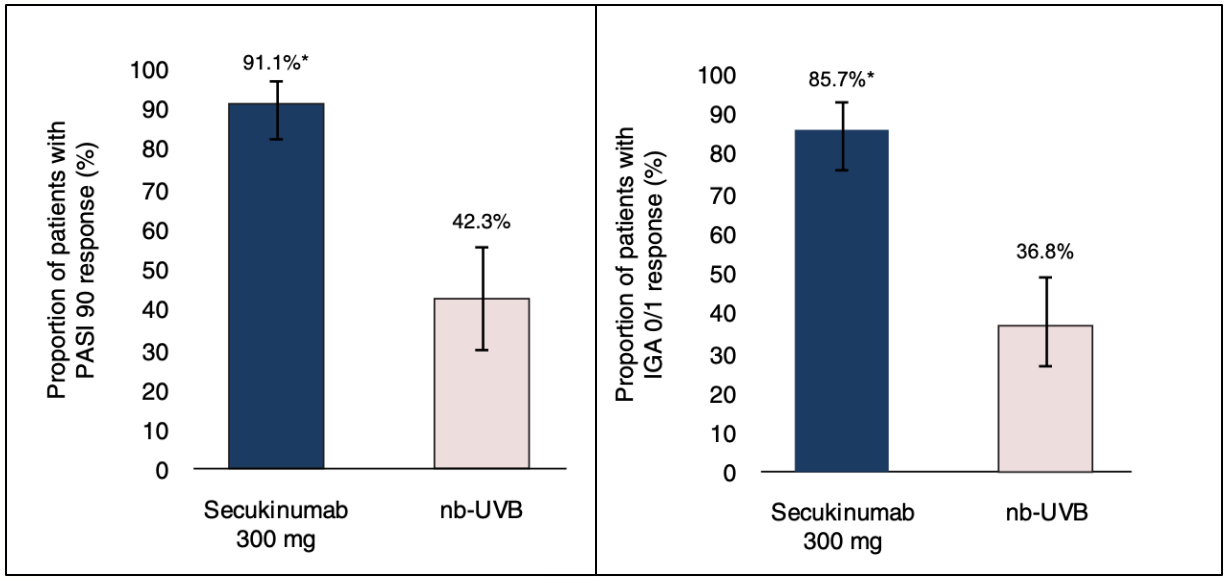
Practical Problem:
Systemic agents including biologics are considered second-line

Iversen L et al. J Eur Acad Dermatol Venereol. 2018 Nov;32(11):1930-1939

SECUKINUMAB FOR THE TREATMENT OF NEW ONSET PSORIASIS

STEPIn Study:





New-onset psoriasis defined as <12 months

SEC is superior to nb-UVB at 52wks

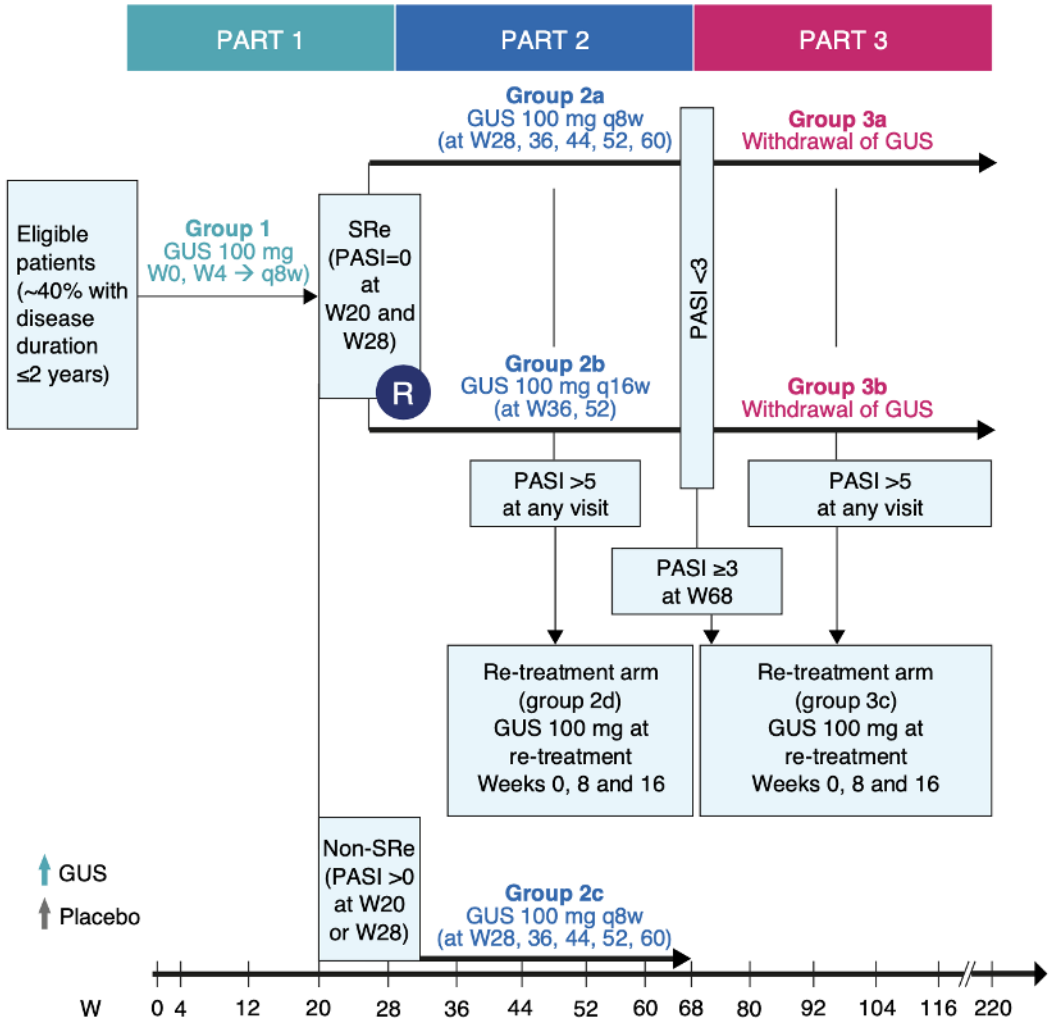
Iversen L, et al. J Eur Acad Dermatol Venereol. 2023 May;37(5):1004-1016

EARLY INTERVENTION WITH GUSELKUMAB FOR PSORIASIS

GUIDE Study:

- **Part 1: Identify super-responders**
  - Achieved PASI 0 at wk 20 and wk 28
- **Part 2: Disease control with extended dosing intervals for super-responders**
- **Part 3: Super responders are withdrawn from GUS**
  - SRe was defined as PASI <3

Short disease duration was defined as ≤2 yrs

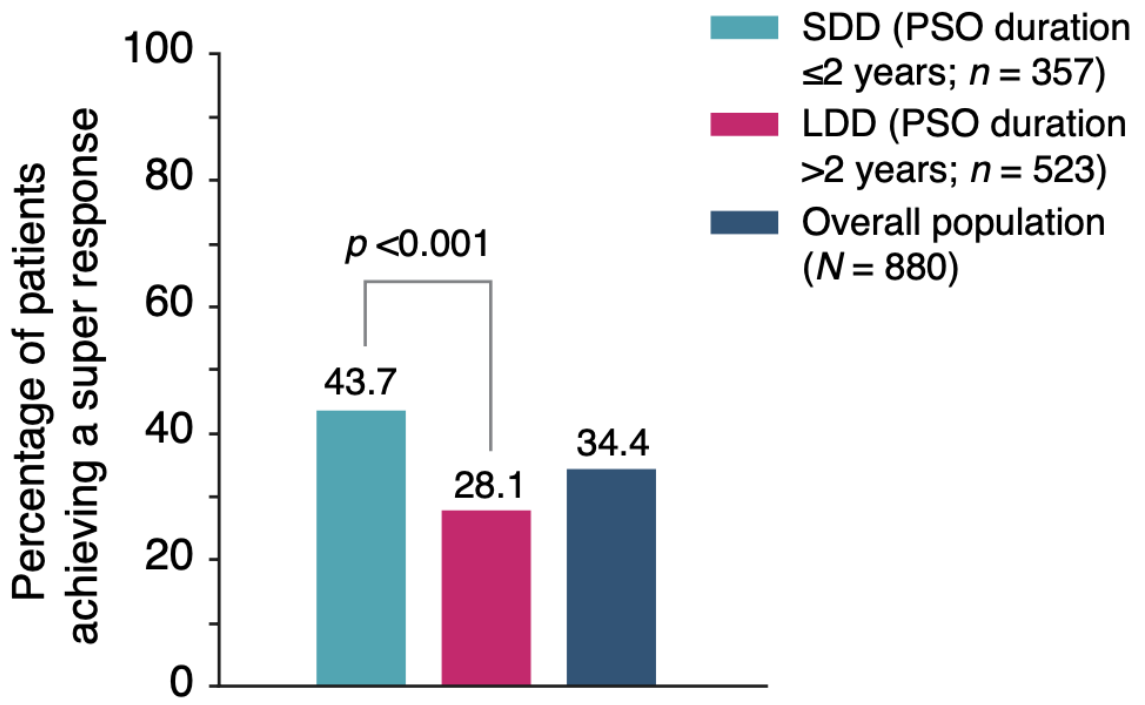


Javaid K et al.J Eur Acad Dermatol Venereol. 2024 Apr;38(4):e302-e303

SHORT DISEASE DURATION CAN PREDICT SUPER RESPONSE

- Patients who had disease for ≤2yrs (short disease duration) had a higher likelihood of being a super-responder to standard GUS therapy

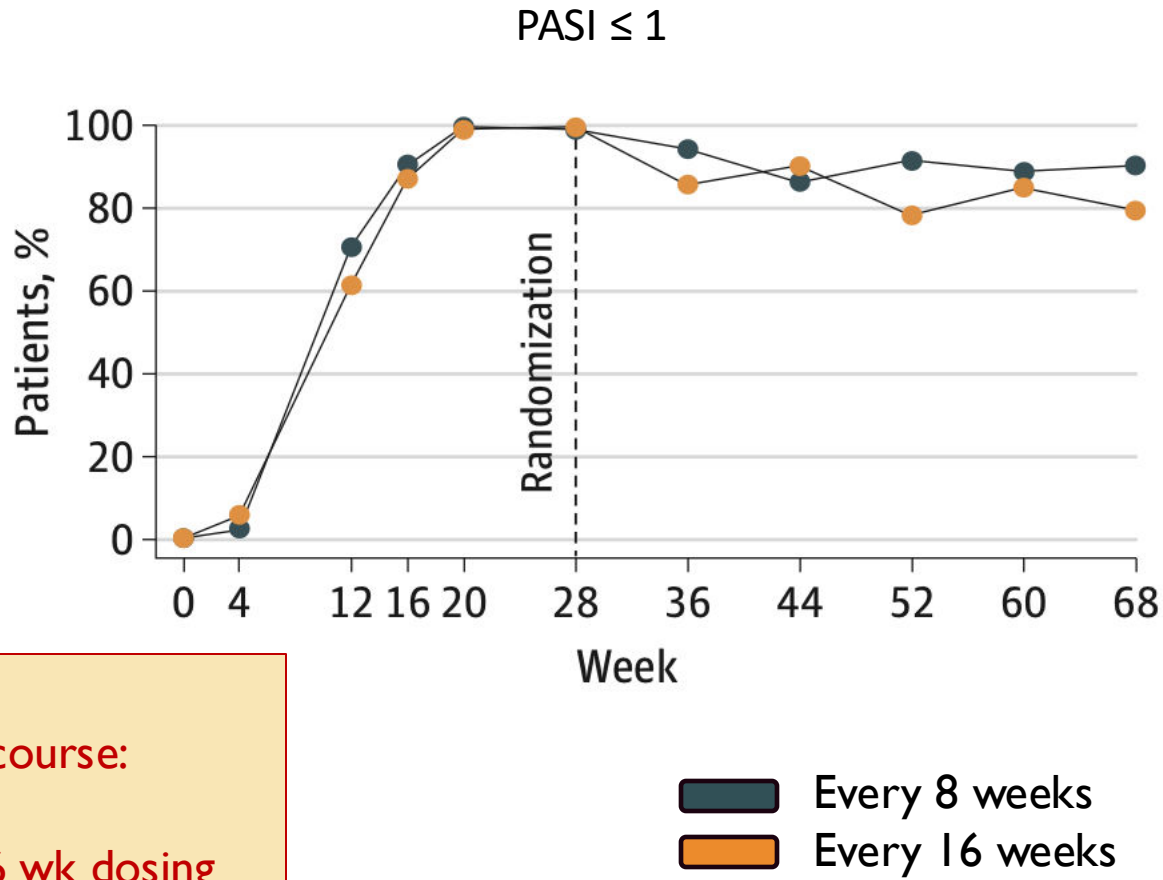
Super Response: PASI 0 at wk 20 and wk 24



Javaid K et al.J Eur Acad Dermatol Venereol. 2024 Apr;38(4):e302-e303

SUPER RESPONDERS ARE MORE LIKELY TO MAINTAIN DISEASE CONTROL WITH LESS FREQUENT DOSING

- A high rate of PASI ≤ 1 response was maintained over time in super responders, regardless of the dosing interval



Take Home Points:

- Those who are treated early in their psoriasis disease course:
  - More likely to achieve complete skin clearance
  - More likely to be able to down-titrate to every 16 wk dosing

Eyerich K et al. JAMA Dermatol. 2024 Sep 1;160(9):953-963.

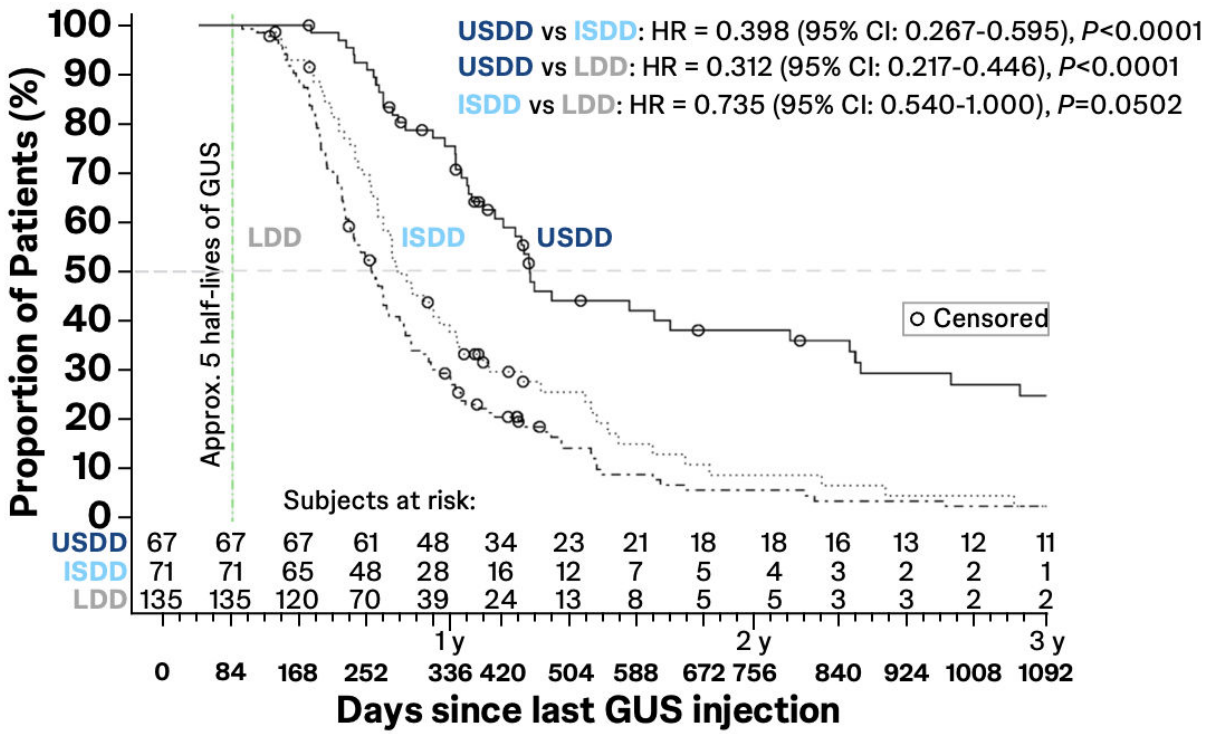
SUPER RESPONDERS TREATED EARLY IN THEIR DISEASE COURSE

- At wk 68, those with a PASI <3 were withdrawn from GUS
- They were retreated if they had loss of response defined as PASI>5

Take Home Points:

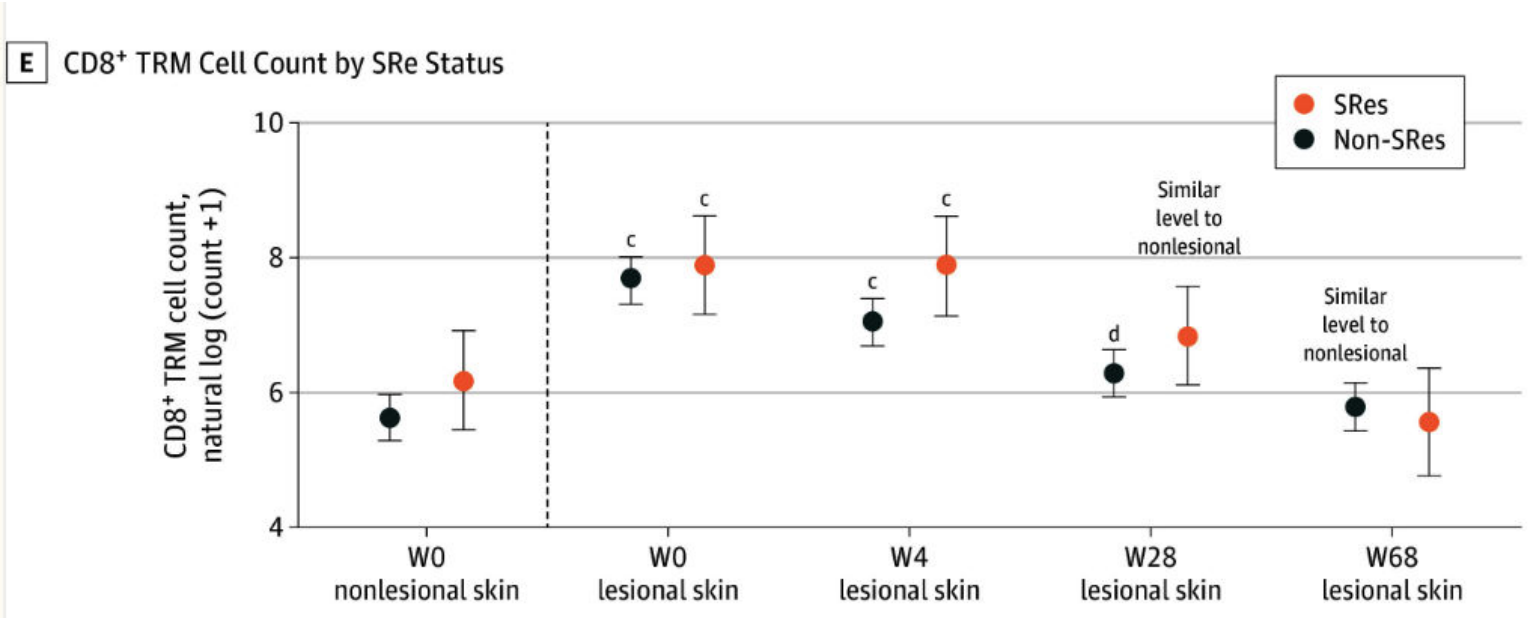
- Those who are treated early in their psoriasis disease course (<15months disease duration) have slower recurrence of psoriasis than those with longer disease duration

Proportion of patients who remain treatment-free by disease duration (USDD <15 months, ISDD 15-34 months, or LDD >24 months.



Schakel et al. EADV 2025

SUPER RESPONDERS SHOW FASTER NORMALIZATION OF MEMORY T CELL COUNTS TO NON-LESIONAL SKIN LEVELS



- A reduction of resident memory T cell counts in lesional skin, to nonlesional skin levels, was seen at wk 28 in super responders but not till wk 68 in non-super responders
- IL-23 has a key role in differentiation, expansion and survival of TRM.

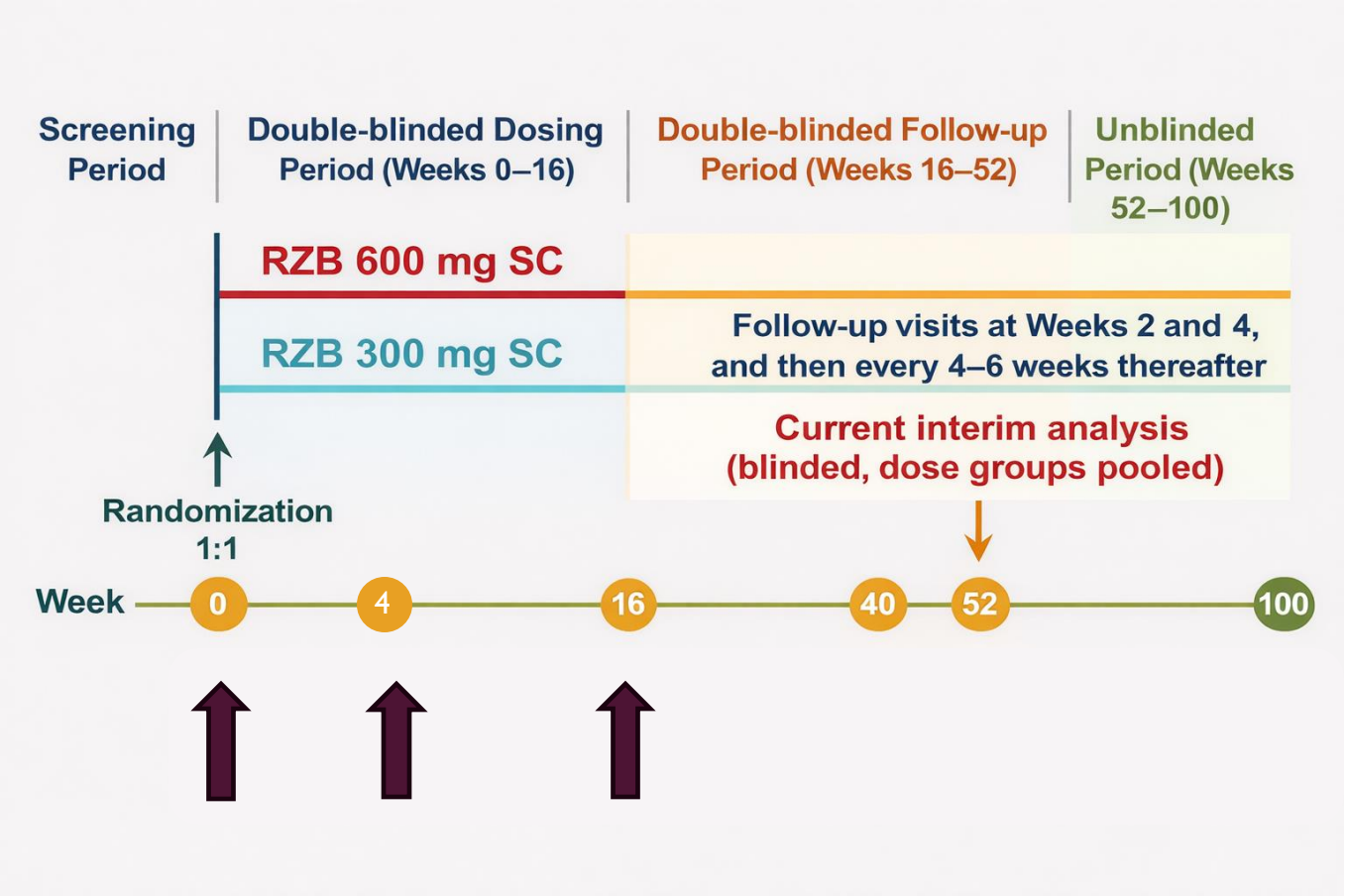
Eyerich K et al. JAMA Dermatol. 2024 Sep 1;160(9):953-963.

CONCEPT 2: HIT PSORIASIS HARD!

HIGH INDUCTION DOSING OF RISANKIZUMAB FOR PSORIASIS

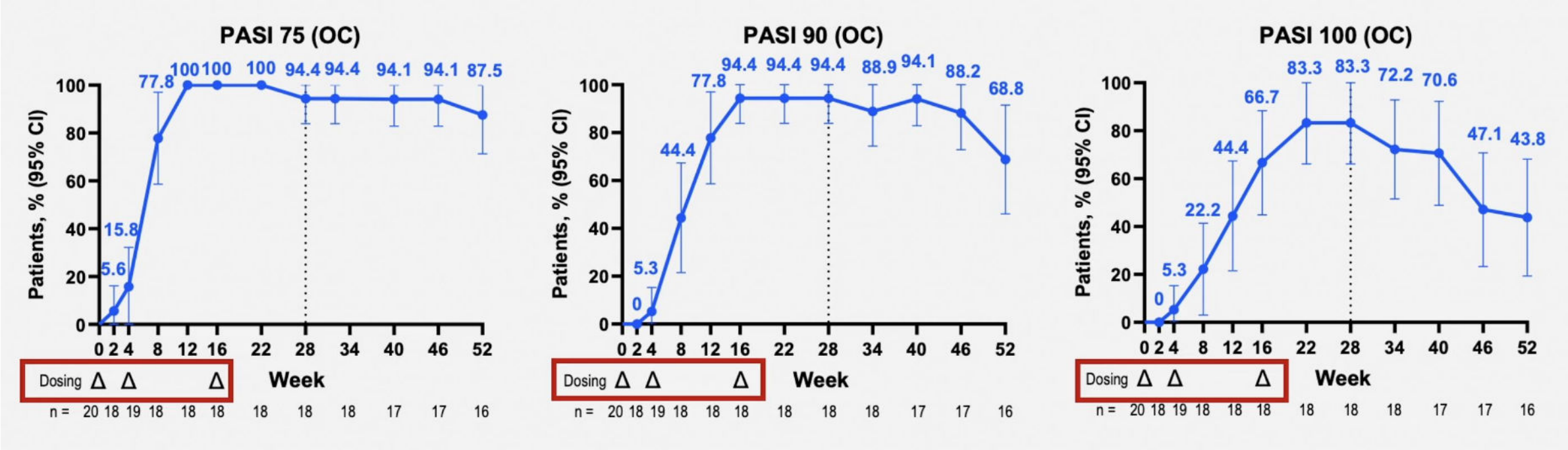
KNOCKOUT Study, Phase 2:

- Primary Endpoint: Change from baseline in TRM cell number
- Secondary endpoints:
  - ❖ PASI 100 at wk 28, 40, 52
  - ❖ Safety at wk 52



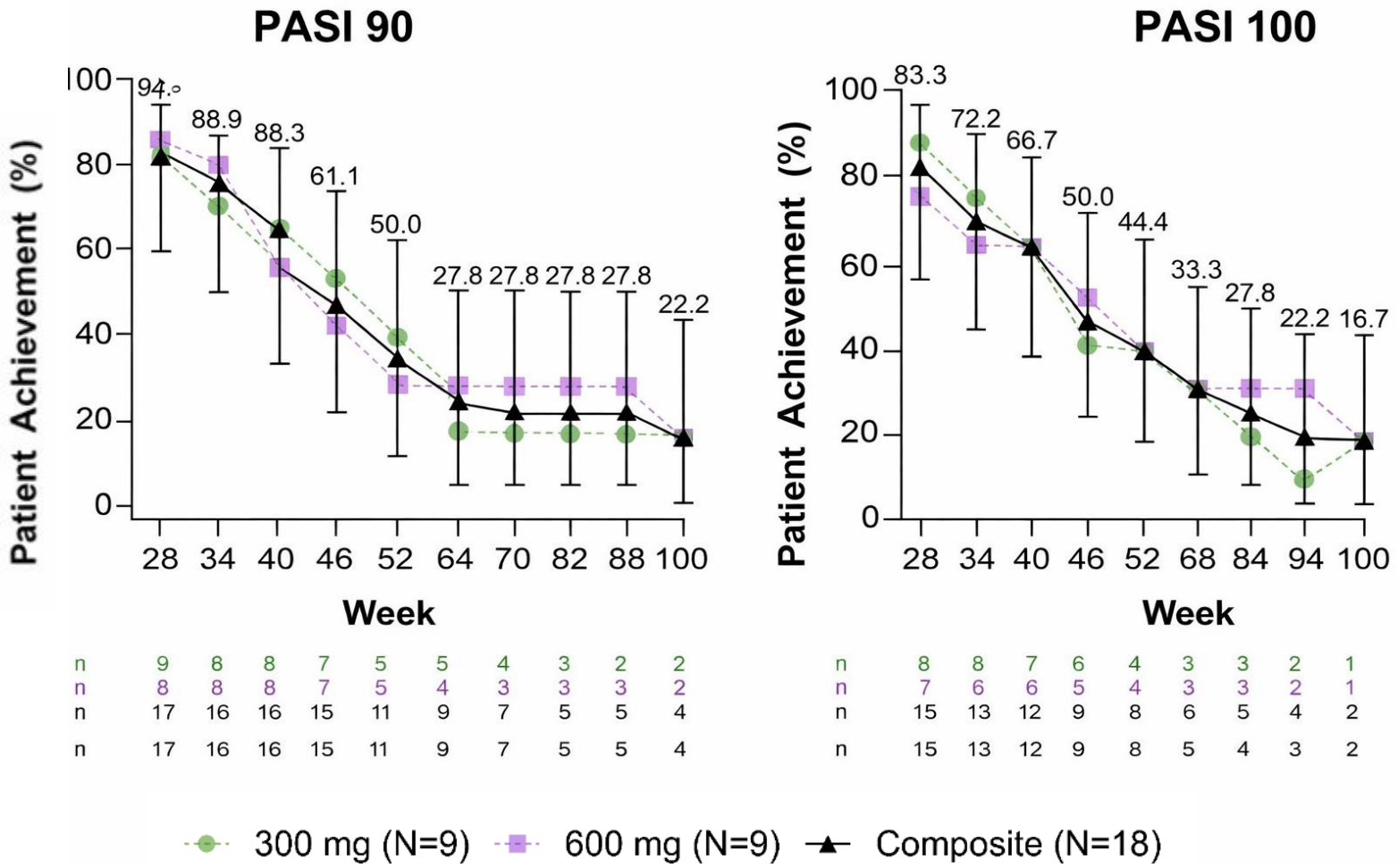
Blauvelt A et al, Nat Commun. 2025 Dec 11

HIGH LEVELS OF PASI 75/90/100 WITH INDUCTION DOSING OF RIS



Blauvelt A et al, Nat Commun. 2025 Dec 11

LONG TERM DURABILITY



Blauvelt A et al, Nat Commun. 2025 Dec 11

SAFETY OF HIGH DOSE RISANKIZUMAB

Treatment Emergent Adverse Events (TEAE) (Events/100PY)	300 mg (N=10)	600mg (N=10)
Any TEAE	11 (164.2)	11 (166.7)
Any serious TEAE	1 (14.9)	0
Any AE that was drug related	0	0
Any TEAE resulting in study drug discontinuation	0	0
Deaths	0	0

- No new safety signals with the higher dose
- Higher doses were well tolerated with safety that was consistent with the 150mg dose

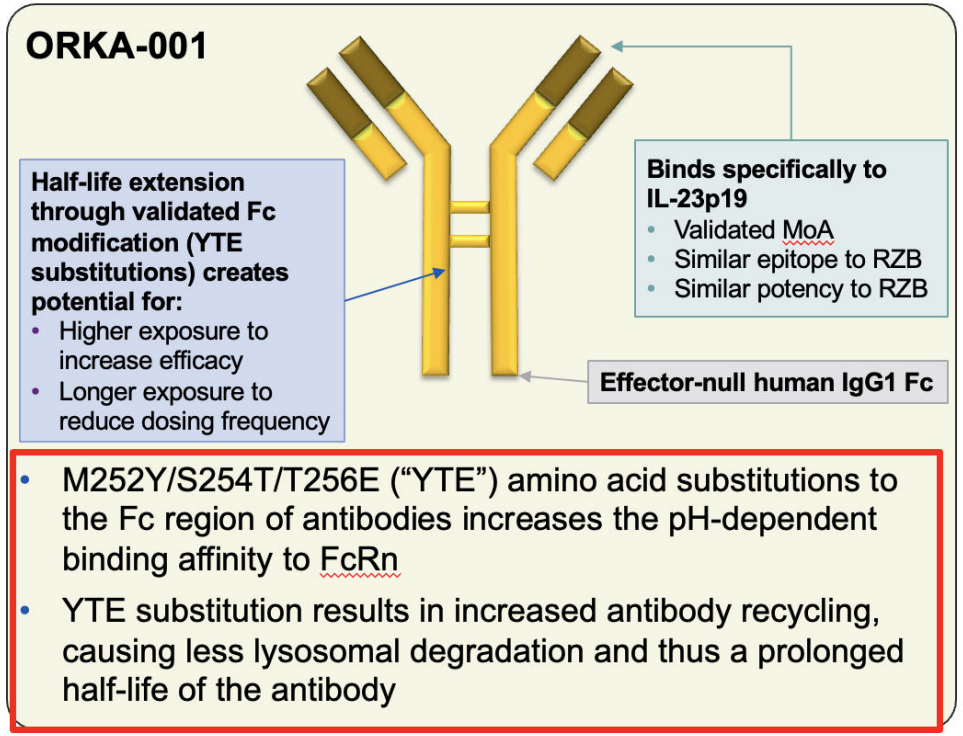
Blauvelt A et al, Nat Commun. 2025 Dec 11

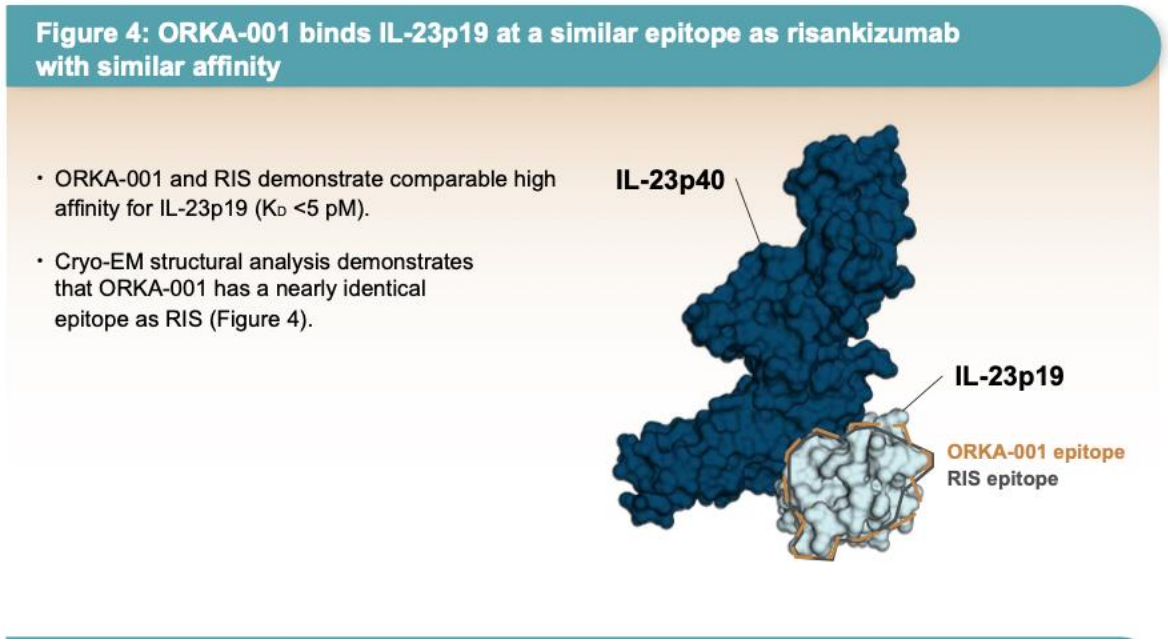
PUTTING IT ALL TOGETHER:
HIT EARLY AND HIT HARD?

THE NEXT FRONTIER

CURE!

ORK-001: EXTENDED HALF-LIFE MONOCLONAL ANTIBODY TARGETING IL-23





Kwan B, et al. EADV 2024, P3283.

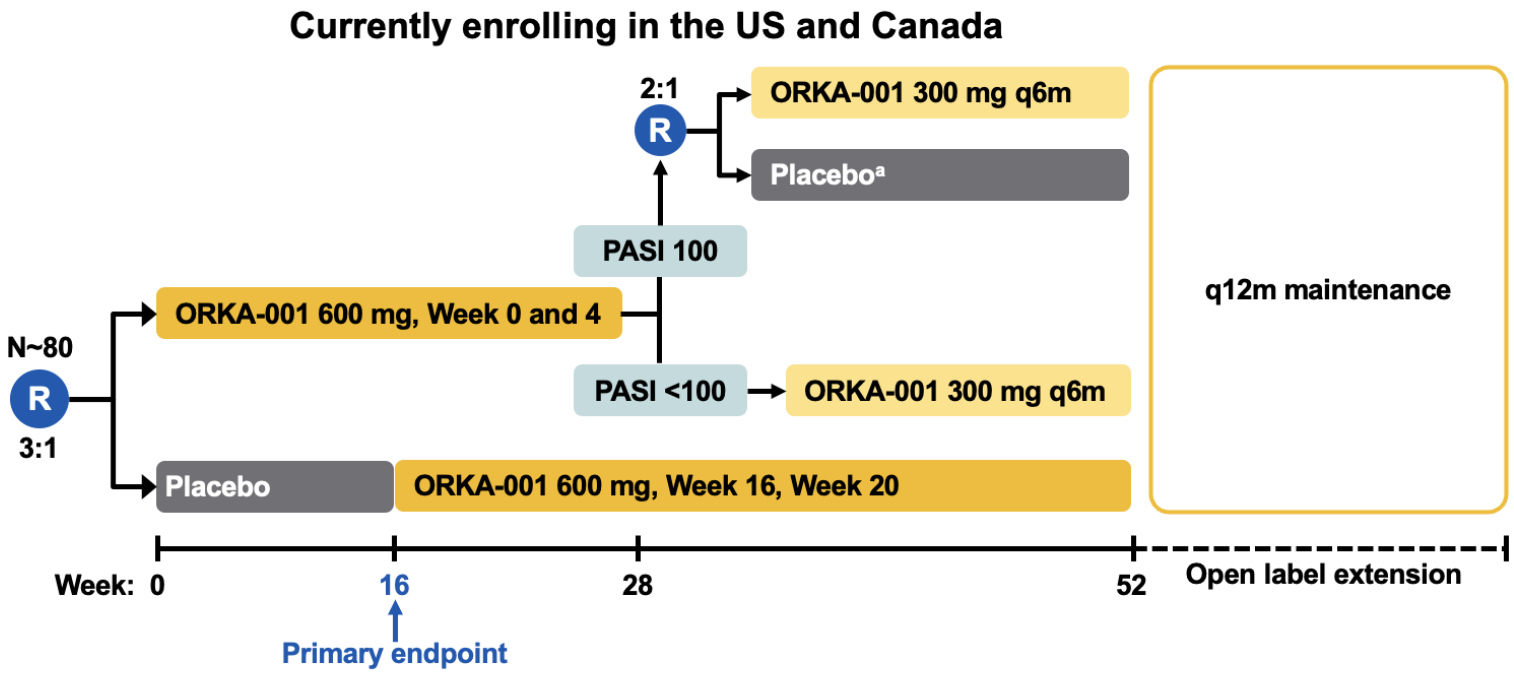
EVERLAST-A: PHASE 2A TRIAL OF ORKA-001IN ADULTS WITH MODERATE TO SEVERE PSORIASIS

Eligibility criteria

- Age ≥12 years
- Plaque psoriasis for ≥6 months
- PASI score ≥12; IGA ≥3; BSA ≥10%
- Candidate for systemic or phototherapy

Primary endpoint

- PASI 100 at Week 16



Krueger J, et al. EADV 2025

PUTTING IT ALL TOGETHER:
HIT EARLY AND HIT HARD?

Phase 3 studies of ORKA-001 will enroll a subset (10-20%) of short disease duration patients (psoriasis for less than 1 year) so we can finally answer this question

THANK YOU!

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