

# ASLAN A<sup>4</sup> Series: Aspects of Atopic Dermatitis and ASLAN004 with Dr April Armstrong

20 January 2022

NASDAQ: ASLN



# Aspects of Atopic Dermatitis and ASLAN004

- Company introduction and ASLAN004 Dr Carl Firth
- A closer look: Key factors affecting responses in Atopic Dermatitis clinical trials Dr April Armstrong
- ASLAN004 Phase 2b trial design Dr Karen Veverka
- Fireside Chat Dr Armstrong & Dr Veverka
- Q&A
- Close



# Introduction

Dr Carl Firth  
CEO





# Legal disclaimer

This presentation contains forward-looking statements. These statements are based on the current beliefs and expectations of the management of ASLAN Pharmaceuticals Limited (the “Company”). These forward-looking statements may include, but are not limited to, statements regarding the Company’s business strategy, the Company’s plans to develop and commercialize its product candidates, the safety and efficacy of the Company’s product candidates, including their potential to be best-in-class, the Company’s plans and expected timing with respect to clinical trials, clinical trial enrollment and clinical trial results for its product candidates, the Company’s plans and expected timing with respect to regulatory filings and approvals, the size and growth potential of the markets for the Company’s product candidates, and the potential for ASLAN004 as a first-in-class treatment for atopic dermatitis. The Company’s estimates, projections and other forward-looking statements are based on management’s current assumptions and expectations of future events and trends, which affect or may affect the Company’s business, strategy, operations or financial performance, and inherently involve significant known and unknown risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation the risk factors described in the Company’s US Securities and Exchange Commission filings and reports (Commission File No. 001-38475), including the Company’s Form 20-F filed with the U.S. Securities and Exchange Commission (the “SEC”) on April 23, 2021.

This presentation discusses product candidates that are under clinical study and which have not yet been approved for marketing by the US Food and Drug Administration. No representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied. Caution should be exercised when comparing data across trials of different products and product candidates. Differences existing between trial designs and patient populations and characteristics. The results across such trials may not have interpretative value on our existing or future results.

All statements other than statements of historical fact are forward-looking statements. The words “believe,” “view,” “may,” “might,” “could,” “will,” “aim,” “estimate,” “continue,” “anticipate,” “intend,” “expect,” “plan,” or the negative of those terms, and similar expressions that convey uncertainty of future events or outcomes are intended to identify estimates, projections and other forward-looking statements. Estimates, projections and other forward-looking statements speak only as of the date they were made, and, except to the extent required by law, the Company undertakes no obligation to update or review any estimate, projection or forward-looking statement.



# ASLAN Pharmaceuticals

- Clinical-stage, immunology-focused biopharma developing **innovative therapies to treat inflammatory disease**
- ASLAN004, also known as *eblasakimab*, is a potential **first-in-class antibody targeting the IL-13 receptor that has the potential to improve upon current biologics** used to treat allergic disease
  - There are few safe and effective treatments for moderate-to-severe atopic dermatitis (AD), expected to be a \$24B market by 2029<sup>1</sup>. Despite dupilumab advancing the standard of care, physicians / patients still seek additional options.
  - Topline data from recently completed multiple ascending dose study conclusively establishes proof of concept for ASLAN004 in AD, and supports a potentially differentiated safety and efficacy profile
  - Preparations for Phase 2b underway, evaluating 2-weekly and 4-weekly regimens. FPI expected Jan 2022
- ASLAN003 is a second generation **DHODH inhibitor with the potential to be best-in-class** for autoimmune disease
  - Stronger *in vitro* potency and lower potential for hepatotoxicity compared to other DHODH inhibitors
  - Expecting to initiate phase 2 in IBD in 1H 2022. Planning future studies in autoimmune skin diseases
- **Strong cash position (\$100M<sup>2</sup>) with runway to late 2023**

<sup>1</sup> Decision Resources Group, June 2021

<sup>2</sup> As of Q3 ending September 30, 2021

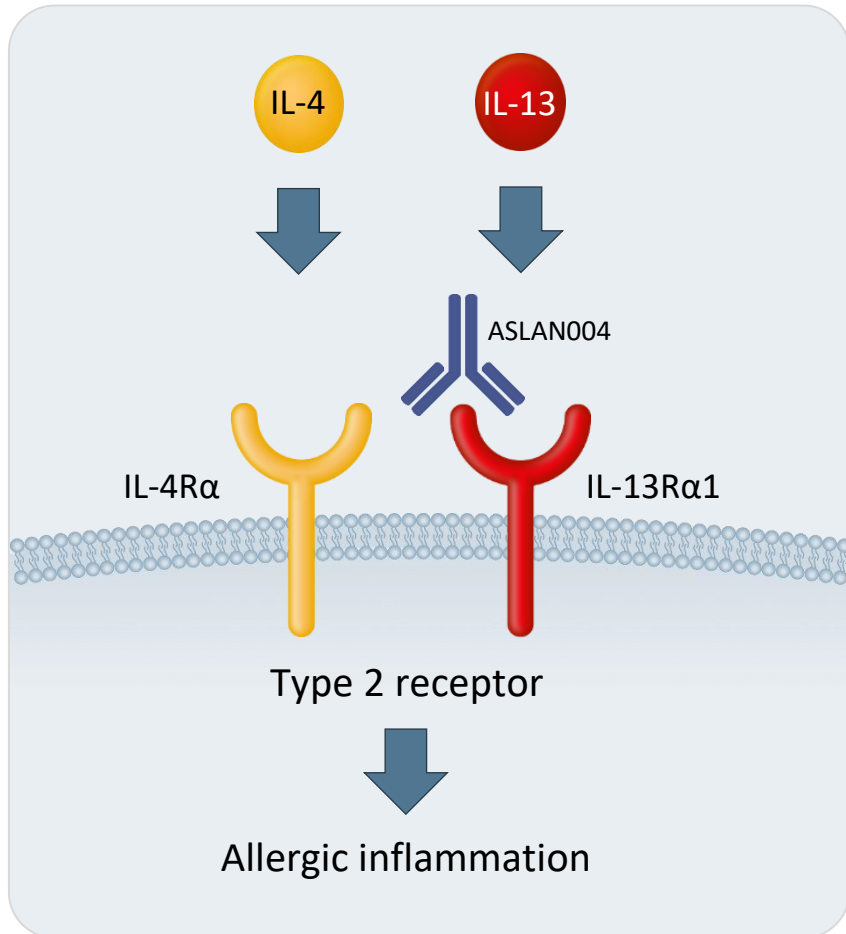


# Developing innovative therapies to treat inflammatory disease

Program	Target	Discovery	Preclinical	Phase 1	Phase 2	Anticipated milestones
ASLAN004	IL-13R $\alpha$ 1	Atopic dermatitis (AD)				• Initiate Phase 2b in Jan 2022
		Type-2 driven disease				
ASLAN003	DHODH	Inflammatory bowel disease				• Initiate Phase 2 in 1H 2022
		Autoimmune skin disease				



# ASLAN004 is the only monoclonal antibody in the clinic targeting IL-13R $\alpha$ 1



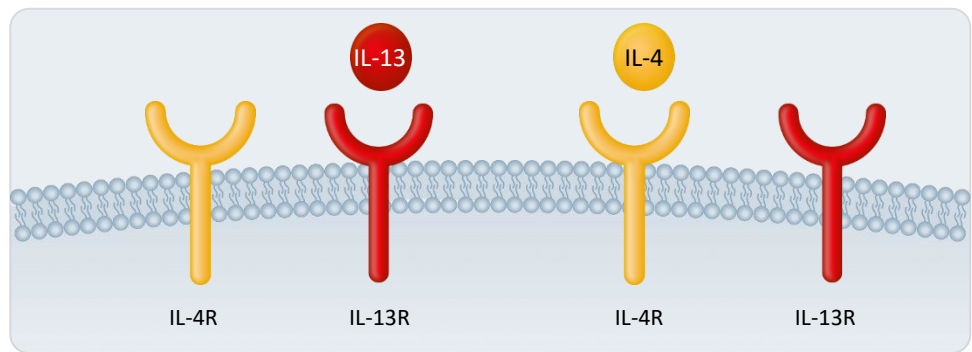
- IL-4 and IL-13 are central to triggering allergy and symptoms of atopic dermatitis
- ASLAN004 blocks the Type 2 receptor, preventing signaling through **both** IL-4 and IL-13

## Potential for improved efficacy, safety and dose regimen:

- Selectively targets the Type 2 receptor. Blocking the Type 1 receptor may lead to unwanted effects
- Stronger binding to receptor than *dupilumab* relative to its respective ligand



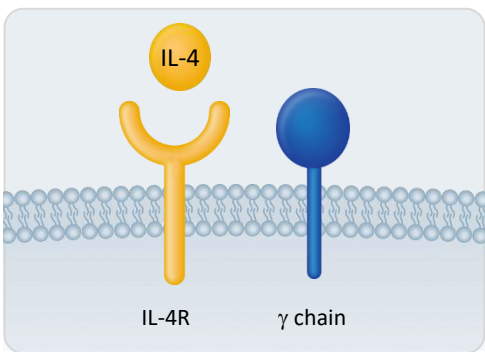
# ASLAN004 selectively blocks the Type 2 receptor



Type 2 receptor

Blocks IL-13 signalling

Blocks IL-4 signalling



Type 1 receptor

Blocks IL-4 signalling

ASLAN004

Specific and complete blockade of Type 2 receptor

*Lebrikizumab*

Partial blockade of Type 2 receptor signalling

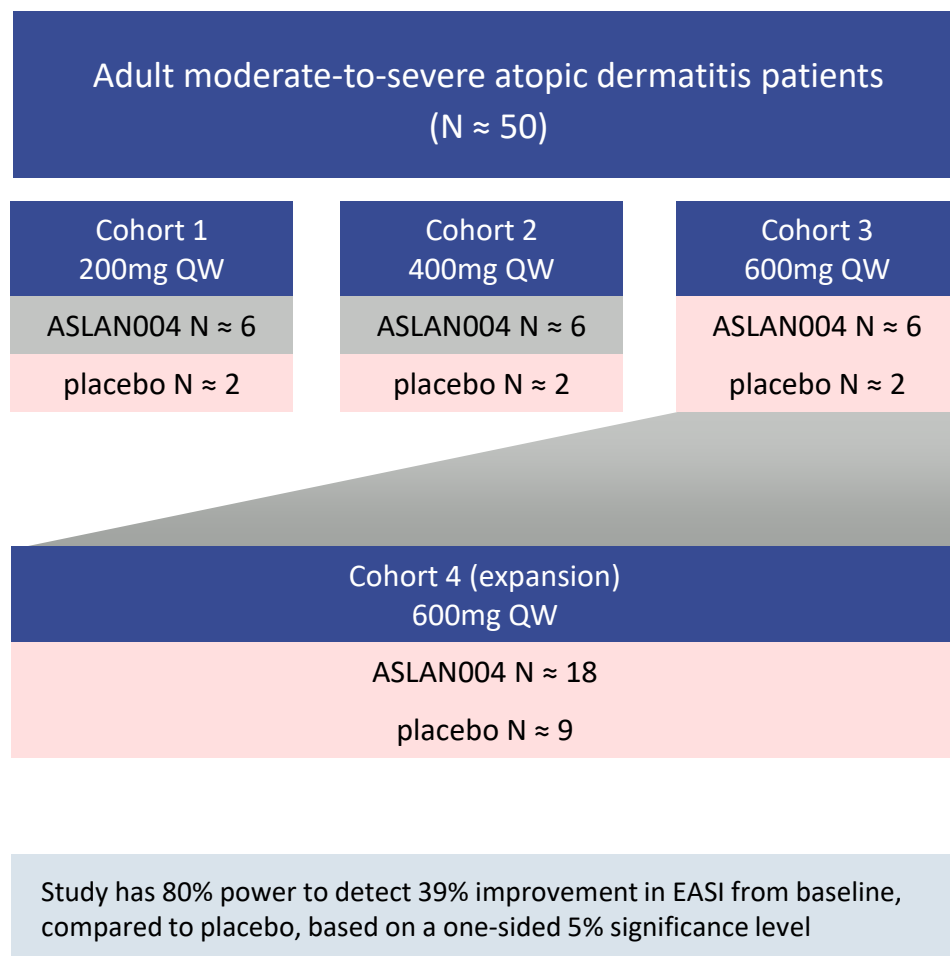
*Dupilumab*

Broad blockade of Type 1 and Type 2 receptors





# Completed Proof of Concept study in moderate-to-severe AD



- Double-blind, randomized, placebo-controlled Phase 1 MAD study
- Patients dosed weekly via subcutaneous injection for 8 weeks with a 12-week recovery period
- Analysis compares patients in cohorts 3 and 4 dosed with 600mg QW against all placebos

Primary endpoints are safety and tolerability

Secondary endpoints include percentage change from baseline in EASI (Eczema Area and Severity Index) score, pruritus score (numeric rating scale, NRS) and IGA (Investigator Global Assessment), and biomarkers TARC and IgE

Key inclusion criteria:

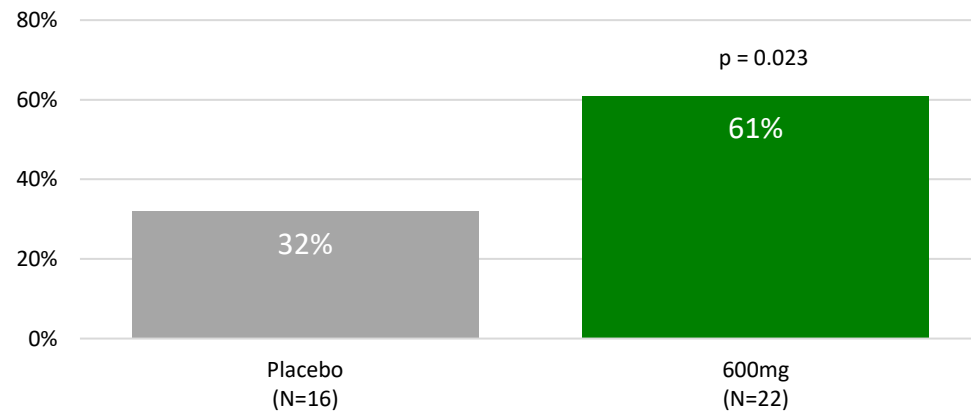
- Chronic AD present for ≥3 years before screening visit
- EASI score ≥16 at screening and baseline
- IGA score ≥3 (scale of 0 to 4) at screening and baseline
- ≥10% BSA (Body Surface Area) of AD involvement at screening and baseline



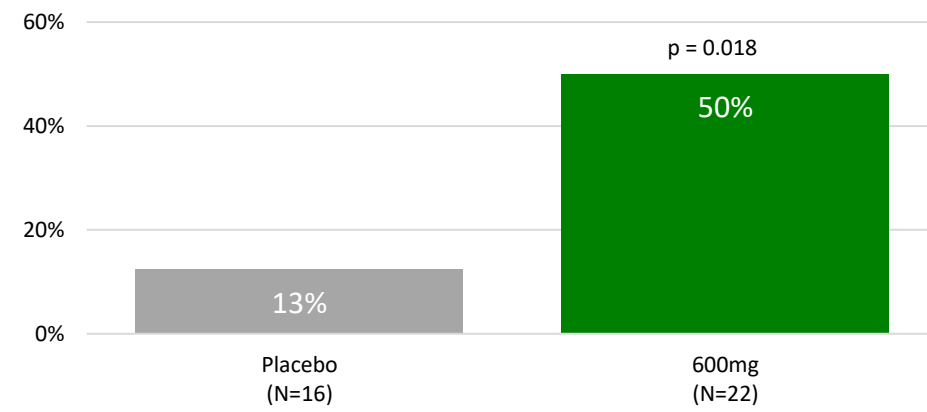
# Topline data demonstrate a competitive profile with the potential to differentiate in terms of efficacy and safety

- ASLAN004 demonstrated a statistically significant improvement of 61% versus 32% in placebo, in the primary efficacy endpoint of percent change from baseline in EASI
- ASLAN004 also showed statistically significant improvements in other key efficacy endpoints: EASI-50, EASI-75, peak pruritus, POEM.
- Well-tolerated with no emerging safety concerns
- Phase 2b expected to initiate in January 2022

Mean reduction in EASI from baseline (8 weeks)



EASI-75 (8 weeks)



# Comparison of proof of concept studies in atopic dermatitis

Drug	Study	Target	Patients	Efficacy assessment at	Reached statistical significance?		
					$\Delta$ EASI score (%)	EASI-75	IGA 0/1
<b>ASLAN004</b>	Phase 1B <sup>1</sup>	IL-13R	38	8 weeks	✓	✓	
<b>Dupilumab</b>	Phase 1B (M4A+ M4B) <sup>2</sup>	IL-4R	67	4 weeks	✓		
	Phase 2A (M12) <sup>2</sup>	IL-4R	109	4 weeks			
				12 weeks	✓		✓
<b>CBP201</b>	Phase 1B <sup>3</sup>	IL-4R	31	4 weeks			
<b>KHK4083</b>	Phase 1 <sup>4</sup>	OX-40	20	6 weeks			

Data from Phase 1 studies of *lebrikizumab* and *tralokinumab* were not published

✓ represents two-sided p-value <0.05

1. Refers to ITT

2. Beck et al (2014) NEJM 371(2):130-139

3. Wang et al (2020), 29<sup>th</sup> EADV Congress, Oct 28- Nov 1, 2020, p-value not disclosed

4. Nakagawa et al (2020) J Derm Sci 99:82-89, p-value not applicable (single-arm study)





# A Closer Look: Key Factors Impacting Responses In Atopic Dermatitis Clinical Trials

**April W. Armstrong, MD MPH**

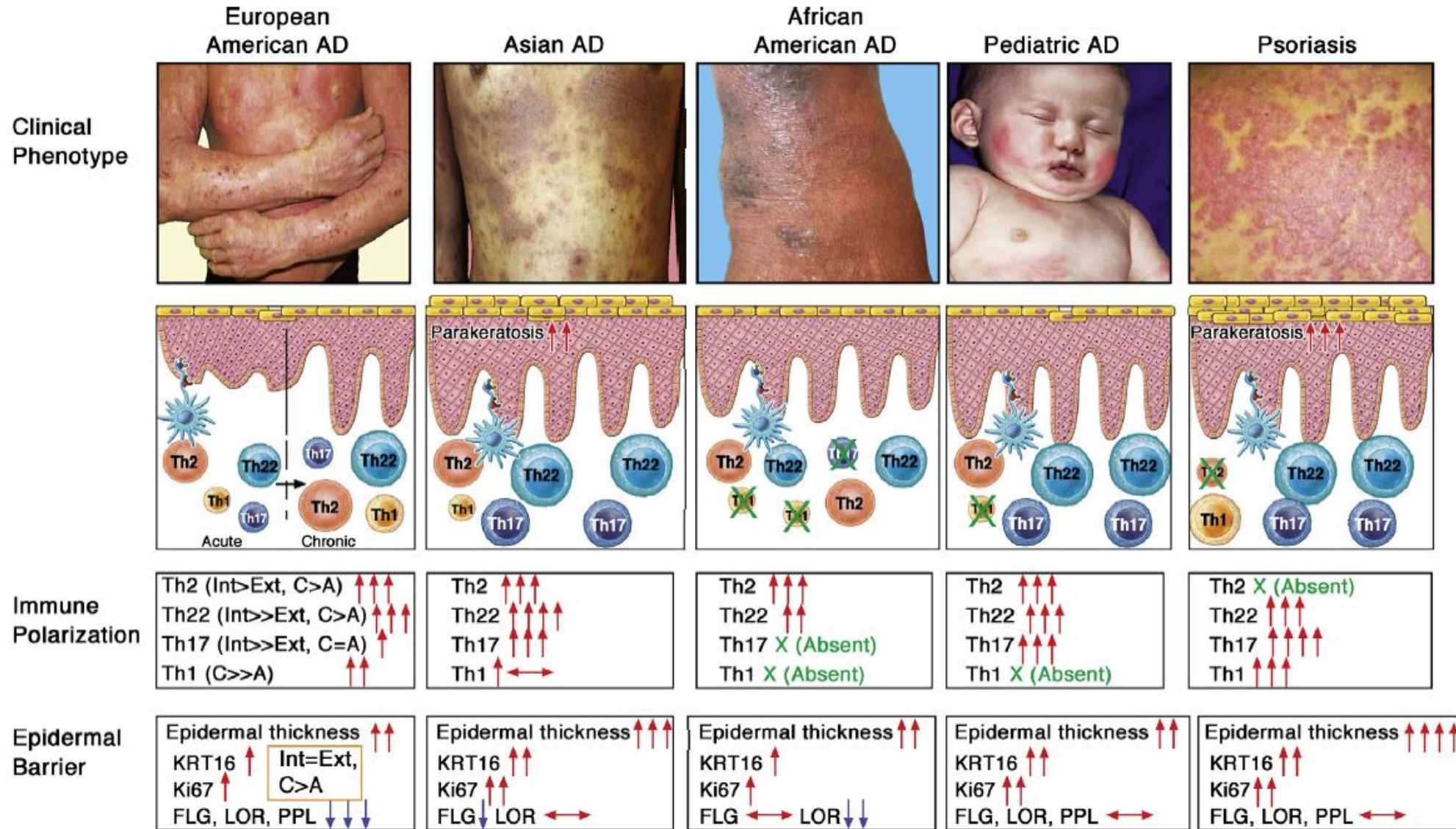
Professor of Dermatology

Associate Dean of Clinical Research

University of Southern California

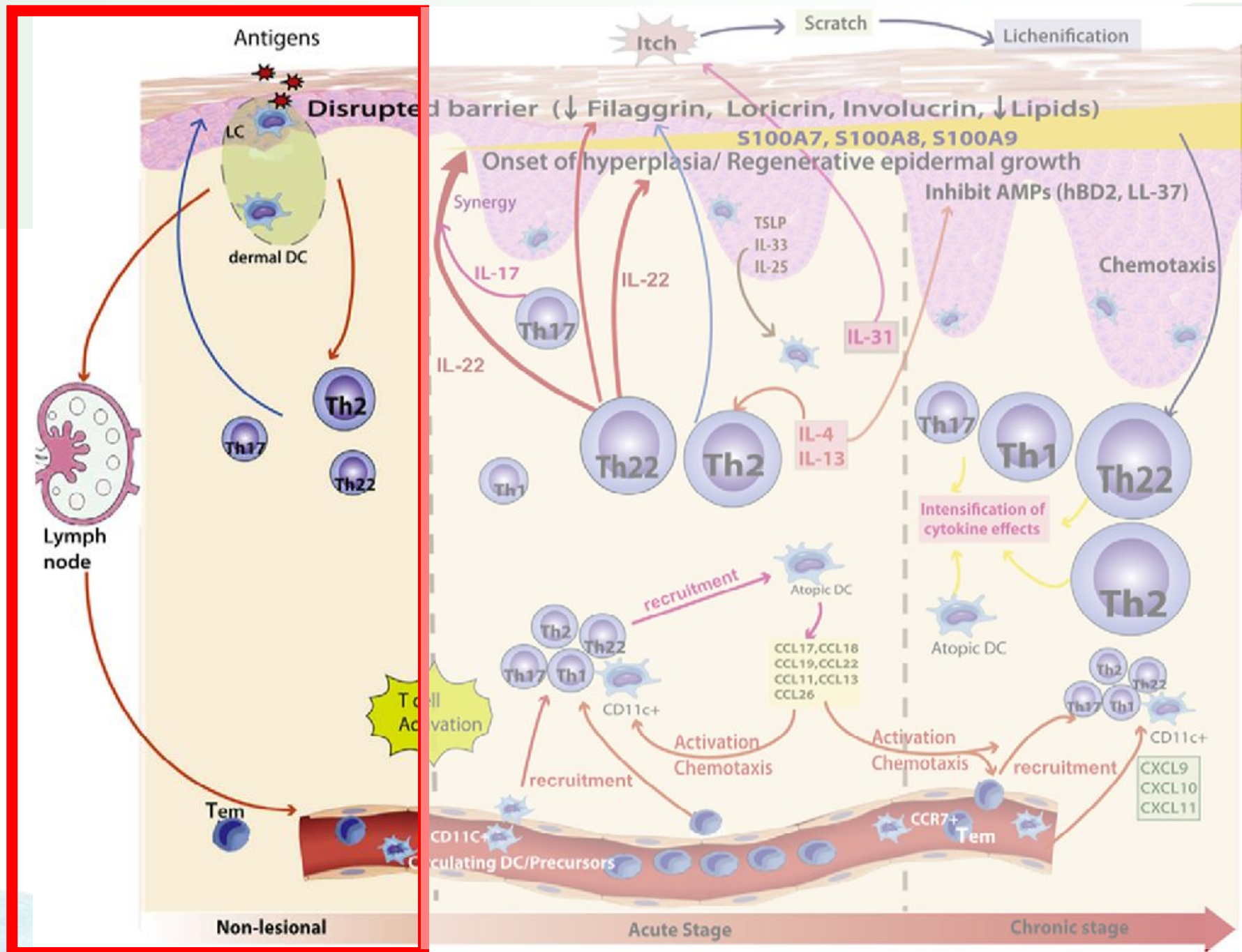


# Atopic Dermatitis (AD) clinical phenotypes and molecular pathways

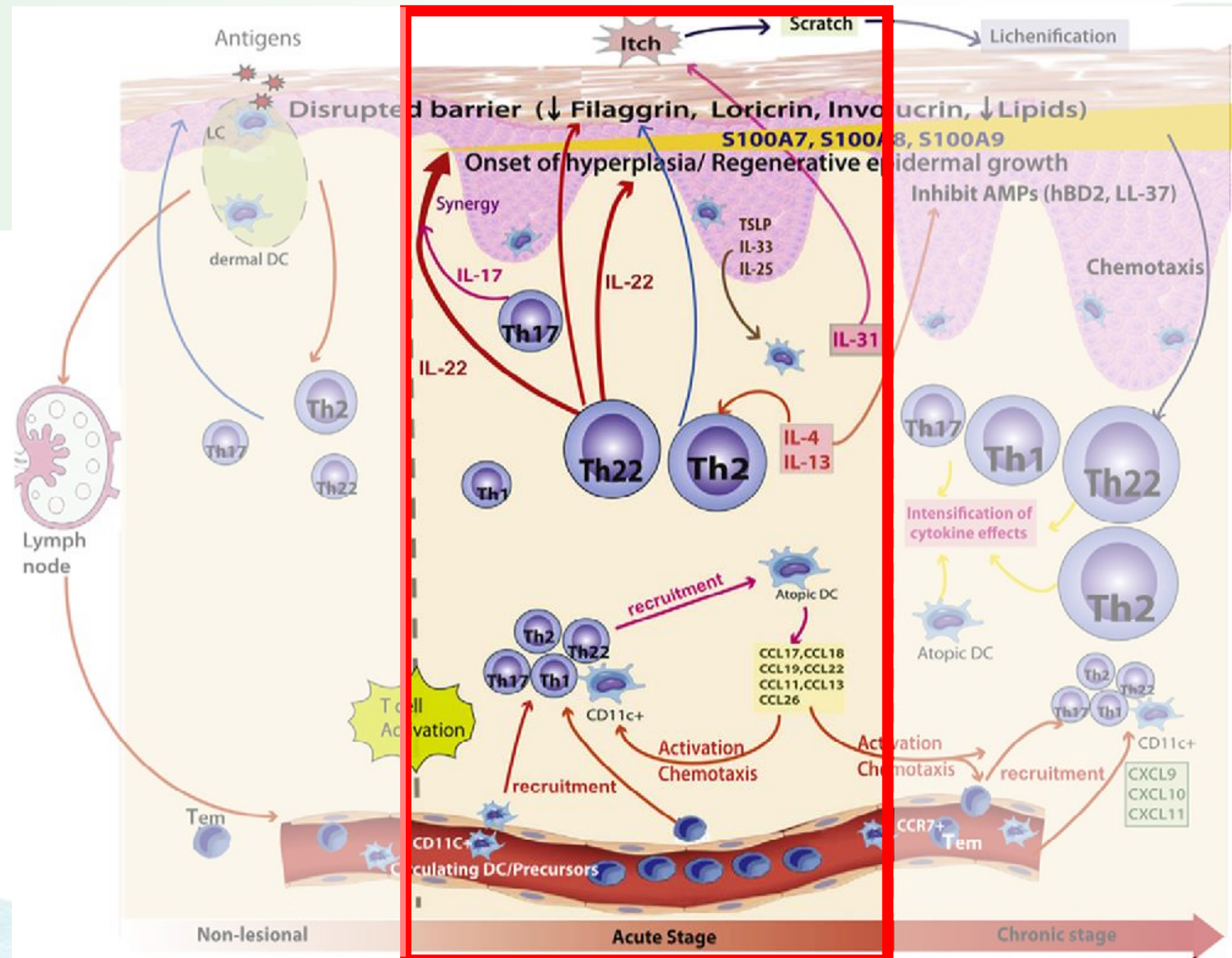




# AD pathways

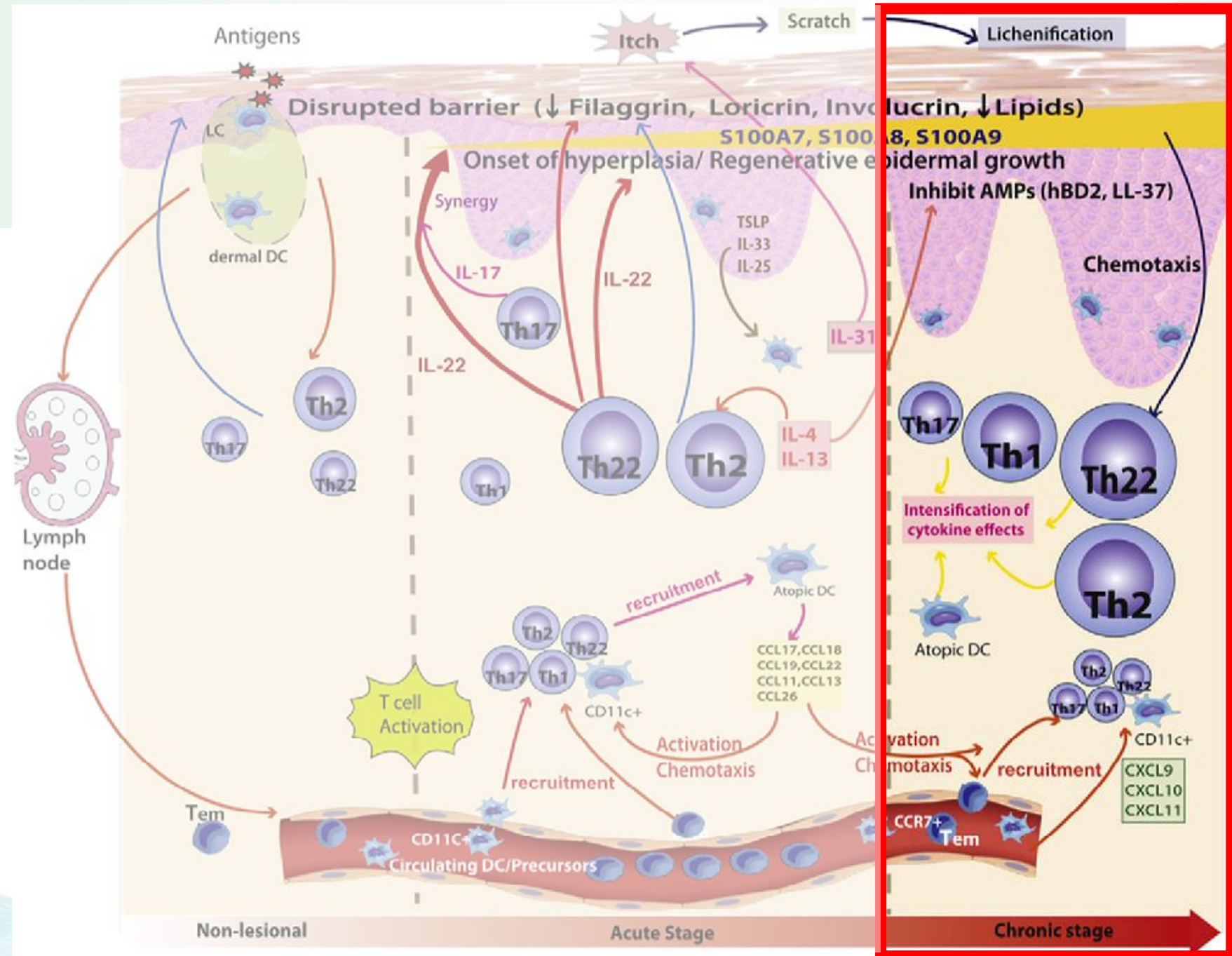


# AD pathways



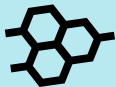







# AD pathways



# Emerging therapies

Drug Class	Route	Target	Drug Names	Latest Phase	Sponsor
<div>Biologic</div> <div></div>	<div>Systemic-Subcutaneous</div> <div></div>	IL-4Rα	<i>Dupilumab</i>	Approved	Sanofi/ Regeneron
		IL-4Rα	CBP-201	Phase 2	Connect Bio
		IL-13	<i>Tralokinumab</i>	Approved	LEO Pharma
		IL-13	<i>Lebrikizumab</i>	Phase 3	Eli Lilly/ Dermira
		IL-13Rα1	ASLAN004	Phase 2b	ASLAN Pharma
		IL-31	<i>Nemolizumab</i>	Phase 3	Galderma
		OX-40/ OX-40L	KHK4083/ISB830 (GBR-830)/ KY1005	Phase 2	Kyowa Kirin, Glenmark/ Ichnos, Kymab/ Sanofi
<div>Small Molecule</div> <div></div>	<div>Systemic-Oral</div> <div></div>	JAK1/JAK2	<i>Baricitinib</i>	Approved (EU)	Eli Lilly
		JAK1	<i>Upadacitinib/ Abrocitinib</i>	Approved	AbbVie/ Pfizer
		S1PR1, S1PR4, S1PR5	<i>Etrasimod</i>	Phase 3	Arena Pharma/Pfizer
		H4R	<i>Adriforant</i>	Phase 2b	Novartis
<div>Small Molecule</div> <div></div>	<div>Topical</div> <div></div>	JAK1/JAK2	<i>Ruxolitinib</i>	Approved	Incyte
		JAK1/TYK2	<i>Brepocitinib</i>	Phase 2b	Pfizer
		PDE4	<i>Lotamilast/ Difamilast/ DRM02</i>	Phase 2	Dermavant/ Otsuka/ Dermira
		S1PR1	AKP-11	Phase 2	Akaal Pharma

# Key Factors Impacting Interpretation of Randomized Clinical Trials in Atopic Dermatitis

Current Opinion | [Open Access](#) | [Published: 26 October 2021](#)

## Expert Perspectives on Key Parameters that Impact Interpretation of Randomized Clinical Trials in Moderate-to-Severe Atopic Dermatitis

[Jonathan I. Silverberg](#) , [Eric L. Simpson](#), [April W. Armstrong](#), [Marjolein S. de Bruin-Weller](#), [Alan D. Irvine](#) & [Kristian Reich](#)

[American Journal of Clinical Dermatology](#) (2021) | [Cite this article](#)

Inclusion/Exclusion  
Criteria

Washout Period  
Duration

Comparator

Use of Rescue  
Treatment

Missing Data  
Handling and Data  
Censoring



# Stages of clinical trial

## ECZTRA 1 AND ECZTRA 2 TRIAL DESIGN

Patients with moderate-to severe atopic dermatitis who were candidates for systemic therapy

### Screening

Washout of TCS  
and other atopic  
dermatitis  
medication

### Initial treatment

300 mg Q2W after initial  
loading dose (600mg)

### Maintenance treatment

Patients with clinical response of  
IGA 0/1 or EASI 75

2:2:1 randomization

**Tralokinumab 300 mg Q2W**

Tralokinumab 300 mg Q4W  
Alternating with placebo

**Placebo Q2W**

**Placebo Q2W**

### Safety follow up

#### Primary endpoints

- IGA 0/1 at week 16
- EASI 75 at week 16

#### Secondary endpoints

- Reduction of worst daily pruritus NRS (weekly average)  $\geq 4$  to week 16
- Change in SCORAD to week 16
- Change in DLQI to week 16

#### Maintenance endpoints

- IGA 0/1 at week 52
- EASI 75 at week 52

### Open-label treatment

**Tralokinumab 300 mg Q2W**  
Optional TCS and optional home use

3:1  
randomization

**Tralokinumab 300 mg Q2W**

ECZTRA 1 ( n = 603) and ECZTRA 2 (n=593)

**Placebo Q2W**

ECZTRA 1 ( n = 199) and ECZTRA 2 (n=201)

-6 weeks

0

16 weeks

52 weeks

66 weeks



# Inclusion and Exclusion Criteria

---

# Inclusion/Exclusion criteria vary across AD RCTs

Baseline I/E criteria:	JADE-Mono-1 Ph.3 <sup>1</sup>	JADE-Mono-2 Ph.3 <sup>2</sup>	SOLO1 Ph.3 <sup>3</sup>	SOLO2 Ph.3 <sup>3</sup>	Lebrikizumab Ph.2b <sup>4</sup>	ECZTRA 1 Ph.3 <sup>5</sup>	ECZTRA 2 Ph.3 <sup>5</sup>	ECZTRA 3 (+TCS) Ph.3 <sup>6</sup>
Drug	<i>abrocitinib</i>		<i>dupilumab</i>		<i>lebrikizumab</i>	<i>tralokinumab</i>		
IGA severity	3 or 4		3 or 4		3 or 4	3 or 4		3 or 4
EASI score (screening/ baseline)	16		16		16	12/16		12/16
Baseline itch requirement	PP-NRS $\geq$ 4		PP-NRS $\geq$ 3		--	PP-NRS $\geq$ 4		PP-NRS $\geq$ 4
Topical Washout Period (minimum)	72 hours		1 Week		1 Week	2 Weeks		2 Weeks

1. Simpson et al Lancet 2020 396(10246):255-266

2. Silverberg et al JAMA Dermatol 2020 156(8):863-873

3. Simpson et al NEJM 2016 375:2335-2348

4. Guttman-Yassky et al JAMA Dermatol 2020 156(4):411-420

5. Wollenberg et al BJD 2021 184:437-449

6. Silverberg et al BJD 2021 184:386-387



# Inclusion and Exclusion parameters impact trial outcomes

## Proportion with moderate disease

- With topical drugs, may see greater efficacy than when a more moderate patient population is enrolled; for biologic drugs the opposite might occur

## Response to prior therapies

- Trials with non-responders or prior use of multiple other systemic therapies may enroll a more severe population than a trial that excluded such populations
- Head-to-head studies must exclude those who had prior experience with the Investigational Product for a fair comparison

## Comorbidities

- A trial that included asthma patients versus those that excluded such patients

# Meta-analysis of 64 AD RCTs shows lower baseline EASI scores have greater placebo response rates



Predictor	Least mean square estimate (95% CI)		Difference in estimates	p-value
	Cochran D EASI (n=64)			
	n<50%	n≥50%		
Proportion of females	1.055 (0.631 to 1.478)	0.743 (0.476 to 1.010)	-0.312 (-0.577 to -0.047)	0.219
	No	Yes		
Prescription topical therapy use	0.825 (0.488 to 1.161)	0.973 (0.636 to 1.310)	0.148 (0.001 to 0.296)	.0493
	<18	≥18		
Mean age (yr)	0.658 (0.294 to 1.022)	1.140 (0.614 to 1.666)	0.482 (-0.140 to 1.104)	.1256
	<3	≥3		
Study endpoint (months)	0.787 (0.471 to 1.103)	1.011 (0.656 to 1.366)	0.224 (0.080 to 0.368)	.0030
	2	≥3		
Number of treatment arms	1.103 (0.640 to 1.567)	0.694 (0.442 to 0.947)	-0.409 (-0.763 to -0.055)	.0246
	Moderate (<21)	Severe (≥21)		
Baseline severity	1.341 (0.620 to 2.062)	0.457 (0.171 to 0.743)	-0.864 (-1.762 to -0.006)	.0485
	Double or Triple	Unspecified, None, or Single		
Blinding	0.660 (0.380 to 0.939)	1.138 (0.738 to 1.538)	0.479 (0.268 to 0.689)	<.0001

- Systematic study of 64 RCTs conducted between 2007-2018
- Baseline mild-moderate disease severity scores were independently and significantly associated with increased responses in the placebo group
- In fact, the most consistent factor for increased placebo response was lower baseline severity

Adapted from Lee et al JAAD 2020 82(1):62-71



# Washout Period Duration



# Washout Period Duration



- **Washout Period:** time prior to baseline when previous treatments are cleared from a patient's system, such that effects of an investigational drug are not confounded by the previous treatment
- **Systemic medications** require longer washout period compared to topical medications



# Potential implications of topical washout period

In various trials, topical washout ranges from 72 hours to 2 weeks

No anti-inflammatory treatment for patients with moderate to severe atopic dermatitis for longer periods of time may:

- Increase flares and exacerbations related to uncontrolled disease
- Increase likelihood of early rescue use

# Varying washout periods across different treatments

Trial	Phase	Drug	Drug Class	Wash Out Period		
				Systemic Cortico-steroids	Systemic Biologics	Topical Cortico-steroids (TCS)
JADE Mono-2	3	<i>abrocitinib</i> <sup>1</sup>	JAK inhibitor	4 weeks	6 weeks	72 hrs
Measure Up 1/2	3	<i>upadacitinib</i> <sup>2</sup>	JAK inhibitor	4 weeks	4 weeks	1 week
ADvocate-1/2	3	<i>lebrikizumab</i> <sup>3</sup>	Biologic	4 weeks	8 weeks	1 week
BREEZE-AD 1/2	3	<i>baricitinib</i> <sup>4</sup>	JAK inhibitor	4 weeks	4 weeks	2 weeks
ECZTRA 1/2	3	<i>tralokinumab</i> <sup>5</sup>	Biologic	4 weeks	12 weeks	2 weeks



**Shorter  
patient  
recruitment  
timeline**



**Higher use of  
Rescue  
therapy**

1. Silverberg et al JAMA Dermatol 2020 156(8):863-873

2. Guttman-Yassky et al Lancet 2021 297(10290):2151-2168

3. <https://clinicaltrials.gov/ct2/show/NCT04146363>

4. Simpson et al BJD 2020 182(2):242-255

5. Wollenberg et al BJD 2021 184:437-449

# Association of topical washout duration on baseline disease scores in AD trial populations

Disease Characteristic	JADE-Mono-2 Ph.3 <sup>2a</sup> <i>abrocitinib</i>			JADE-Mono-1 Ph.3 <sup>1a</sup> <i>abrocitinib</i>			SOLO1 Ph.3 <sup>3b</sup> <i>dupilumab</i>			SOLO2 Ph.3 <sup>3b</sup> <i>dupilumab</i>			Iebrikizumab Ph.2b <sup>4a</sup> <i>Iebrikizumab</i>				ECZTRA 1 Ph.3 <sup>5b</sup> <i>tralokinumab</i>		ECZTRA 2 Ph.3 <sup>5b</sup> <i>tralokinumab</i>		ECZTRA 3 (+TCS) Ph.3 <sup>6b</sup> <i>tralokinumab</i>		
Topical washout duration	72 hours			72 hours			1 week			1 week			1 week				2 weeks				2 weeks		
ARM	PBO	100	200	PBO	100	200	PBO	q2w	qw	PBO	q2w	qw	PBO	125 q4w	250 q4w	250 q2w	PBO	300	PBO	300	ALL	PBO	300
Duration	21.7	21.1	20.5	22.5	24.9	22.7	28.0	26.0	26.0	26.0	24.5	24.0	24.4	22.8	23.3	22.1	28.0	27.0	25.0	25.5	26.0	26.0	27.0
IGA score of 4, %	33.3	32.3	31.6	40.0	41.0	41.0	49.1	48.2	47.5	48.7	49.4	46.9	38.5	41.1	32.5	29.3	51.3	50.6	50.2	48.2	46.3	47.2	45.8
EASI	28.0	28.4	29.0	28.7	31.3	30.6	31.8	30.4	29.8	30.5	28.6	29.0	28.9	29.9	26.2	25.5	30.3	28.2	29.6	28.2	25.5	26.5	24.7
BSA	48.2	48.7	47.7	47.4	50.8	49.9	57.0	53.4	54.5	53.0	50.0	50.0	46.5	45.5	41.1	39.4	52.5	50.0	50.0	50.0	41.0	40.0	41.0
PP-NRS	6.7	7.1	7.0	7.0	6.9	7.1	7.7	7.6	7.7	7.7	7.8	7.8	7.4	7.6	7.1	7.6	7.9	7.9	8.1	8.0	8.0	8.0	8.0

1. Simpson et al Lancet 2020 396(10246):255-266  
2. Silverberg et al JAMA Dermatol 2020 156(8):863-873  
3. Simpson et al NEJM 2016 375:2335-2348

4. Guttman-Yassky et al JAMA Dermatol 2020 156(4):411-420  
5. Wollenberg et al BJD 2021 184:437-449  
6. Silverberg et al BJD 2021 184:386-387

a. Variables reported as means  
b. Variables reported as medians



# Washout Period Duration

## Longer washout period

- reduces likelihood of “carryover treatment effect”
- deterrent to participation due to fear of severe AD flare
- greater disease severity at baseline
- increased rescue treatment use, especially early in a study

## Shorter washout period

- prior treatment may still impact the patient
- reduces the likelihood of needing rescue treatment after randomization



Comparator

# Comparator



## Monotherapy trials

- experimental drug A versus placebo
  - If TCS use is permitted on an as needed basis for both arms, those in the placebo arm may use more TCS than those in the active treatment arm--> underestimate of perceived placebo-adjusted treatment effect of the experimental drug
- head-to-head trials

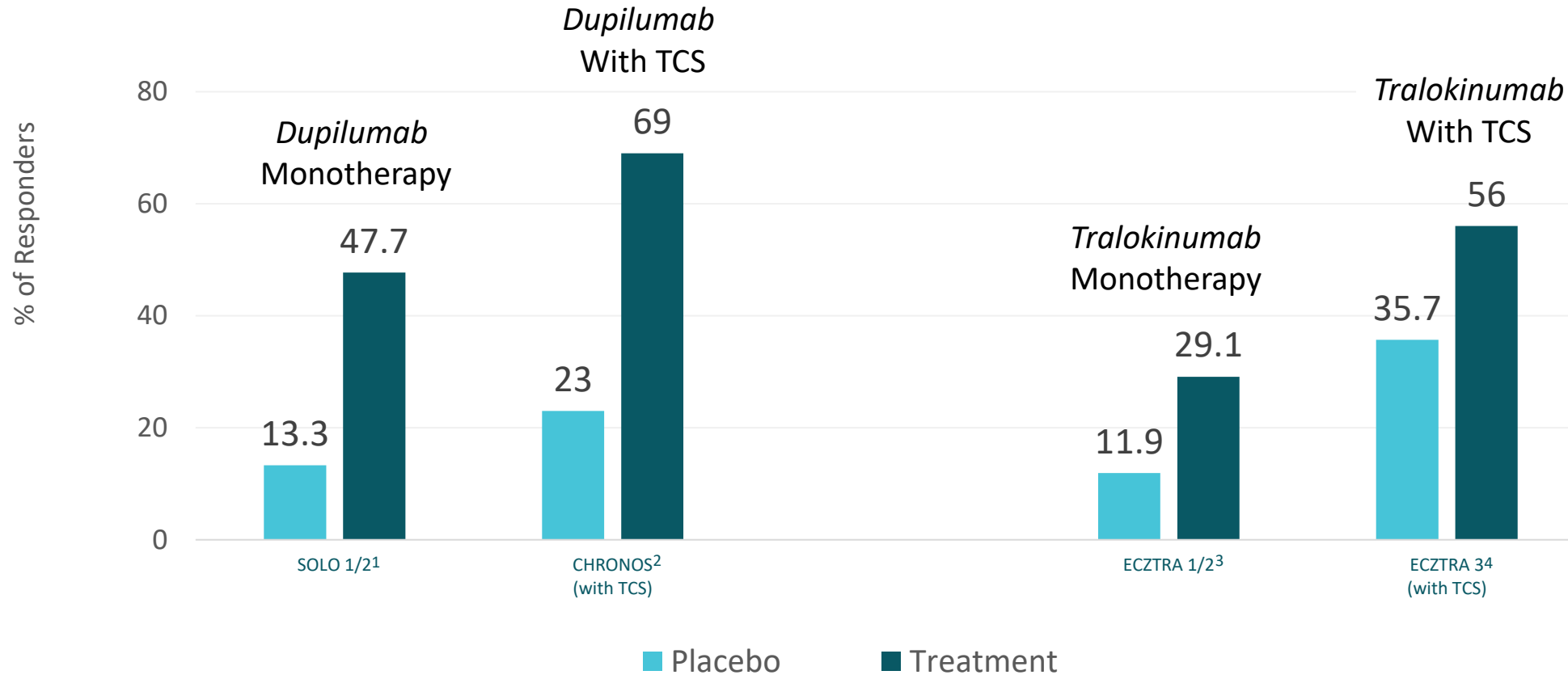
## Topical corticosteroid (TCS) combination trials

- Experimental drug A + TCS versus TCS

# Monotherapy versus combination with TCS



## Patients achieving EASI-75 at Week 16



Inclusion/ exclusion criteria of monotherapy and combination therapy were similar for both drugs

1. Simpson et al NEJM 2016 375(24):2335-48
2. Blauvelt et al Lancet 2017 389(10086):2287-2203
3. Wollenberg et al BJD 2021 184:437-449
4. Silverberg et al BJD 2020 184(3):450-463



# Use of topical combination therapy in RCTs also increases placebo rates

Predictor	Least mean square estimate (95% CI)		Difference in estimates	p-value
	Cochran D EASI (n=64)			
	n<50%	n≥50%		
Proportion of females	1.055 (0.631 to 1.478)	0.743 (0.476 to 1.010)	-0.312 (-0.577 to -0.047)	0.219
	No	Yes		
Prescription topical therapy use	0.825 (0.488 to 1.161)	0.973 (0.636 to 1.310)	0.148 (0.001 to 0.296)	.0493
	<18	≥18		
Mean age (yr)	0.658 (0.294 to 1.022)	1.140 (0.614 to 1.666)	0.482 (-0.140 to 1.104)	.1256
	<3	≥3		
Study endpoint (months)	0.787 (0.471 to 1.103)	1.011 (0.656 to 1.366)	0.224 (0.080 to 0.368)	.0030
	2	≥3		
Number of treatment arms	1.103 (0.640 to 1.567)	0.694 (0.442 to 0.947)	-0.409 (-0.763 to -0.055)	.0246
	Mild to moderate (<21)	Severe (≥21)		
Baseline severity	1.341 (0.620 to 2.062)	0.457 (0.171 to 0.743)	-0.864 (-1.762 to -0.006)	.0485
	Double or Triple	Unspecified, None, or Single		
Blinding	0.660 (0.380 to 0.939)	1.138 (0.738 to 1.538)	0.479 (0.268 to 0.689)	<.0001

- Concomitant use of prescription topical therapy in AD randomized clinical trials increases placebo response rates

Extracted from Lee H et al JAAD 2020 82(1):62-71



Rescue Therapy

# Rescue Therapy



- Topical steroids are the most common rescue treatment in AD monotherapy trials
  - Permit use throughout the active trial period
  - Limit use to a defined period (only after 2 weeks of treatment)
- Different rescue treatment regimen
- If TCS use is not permitted during screening → experience more disease exacerbation at study initiation than those in trials permitting TCS.



# Rescue regimens vary across studies

Trial Name	Ph	Drug	Rescue regimen	% Dropout (average)	Δ (Drop-out)
<u>PROHIBITED</u>					
Upadacitinib Ph 2b	2	Upadacitinib <sup>3</sup>	Rescue prohibited	50% placebo, 16% treatment	34%
JADE-MONO 1	3	Abrocitinib <sup>1</sup>	Rescue prohibited	21% placebo, 12% treatment	9%
JADE-MONO 2	3	Abrocitinib <sup>2</sup>	Rescue prohibited	33% placebo, 11% treatment	22%
<u>ALLOWED</u>					
BREEZE-AD 1/2	3	Baricitinib <sup>4</sup>	Topical and systemic rescue throughout treatment period	8.5% placebo 7% treatment	1.5%
Measure Up 1/2	3	Upadacitinib <sup>5</sup>	Topical rescue allowed from Week 4 if disease activity criteria met	14% placebo, 5% treatment	9%
ECZTRA 1/2	3	Tralokinumab <sup>6</sup>	Topical then systemic rescue throughout treatment period	8.5% placebo, 6.5% treatment	2%

Higher dropout rates in both arms and larger delta

Lower dropout and lower delta

1. Simpson et al Lancet 2020 396(10246):255-266  
2. Silverberg et al JAMA Dermatol 2020156(8):863-873  
3. Guttman-Yassky et al JACI 2020 145(3): 877-884

4. Simpson et al BJD 2020 182(2):242-255  
5. Guttman-Yassky et al Lancet 2021 297(10290):2151-2168  
6. Wollenberg et al BJD 2021 184:437-449

All above trials are monotherapies  
Patient baseline characteristics (EASI, % IGA and BSA) similar across all studies



# Rescue regimens vary across studies

Trial Name	Ph	Drug	Rescue regimen	% Dropout (average)	Δ (Drop-out)
<b><u>PROHIBITED</u></b>					
<i>Upadacitinib</i> Ph 2b	2	<i>Upadacitinib</i> <sup>3</sup>	Rescue prohibited	50% placebo, 16% treatment	<b>34%</b>
JADE-MONO 1	3	<i>Abrocitinib</i> <sup>1</sup>	Rescue prohibited	21% placebo, 12% treatment	<b>9%</b>
JADE-MONO 2	3	<i>Abrocitinib</i> <sup>2</sup>	Rescue prohibited	33% placebo, 11% treatment	<b>22%</b>
<b><u>ALLOWED</u></b>					
BREEZE-AD 1/2	3	<i>Baricitinib</i> <sup>4</sup>	Topical and systemic rescue throughout treatment period	8.5% placebo 7% treatment	<b>1.5%</b>
Measure Up 1/2	3	<i>Upadacitinib</i> <sup>5</sup>	Topical rescue allowed from Week 4 if disease activity criteria met	14% placebo, 5% treatment	<b>9%</b>
ECZTRA 1/2	3	<i>Tralokinumab</i> <sup>6</sup>	Topical then systemic rescue throughout treatment period	8.5% placebo, 6.5% treatment	<b>2%</b>

Higher dropout rates in both arms and larger delta

Lower dropout and lower delta

1. Simpson EL et al Lancet 2020 396(10246):255-266

2. Silverberg JI et al JAMA Dermatol 2020;156(8):863-873

3. Guttman-Yassky et al JACI 2020 145(3): 877-884

4. Simpson et al BJD 2020 182(2):242-255

5. Guttman-Yassky et al Lancet 2021 297(10290):2151-2168

6. Wollenberg et al BJD 2021 184:437-449

All above trials are monotherapies  
Patient baseline characteristics (EASI, % IGA and BSA) similar across all studies

## Rescue **PROHIBITED**<sup>15, 18</sup>

May result in greater rate of **trial discontinuation**

May result in **fewer participants being imputed as non-responders** for studies with NRI analyses



## Rescue **PERMITTED**<sup>10-14, 16, 17, 19, 21</sup>

May incentivize **greater trial participation** rates given eventual access to rescue treatment (eg, 2 weeks following treatment initiation), if needed

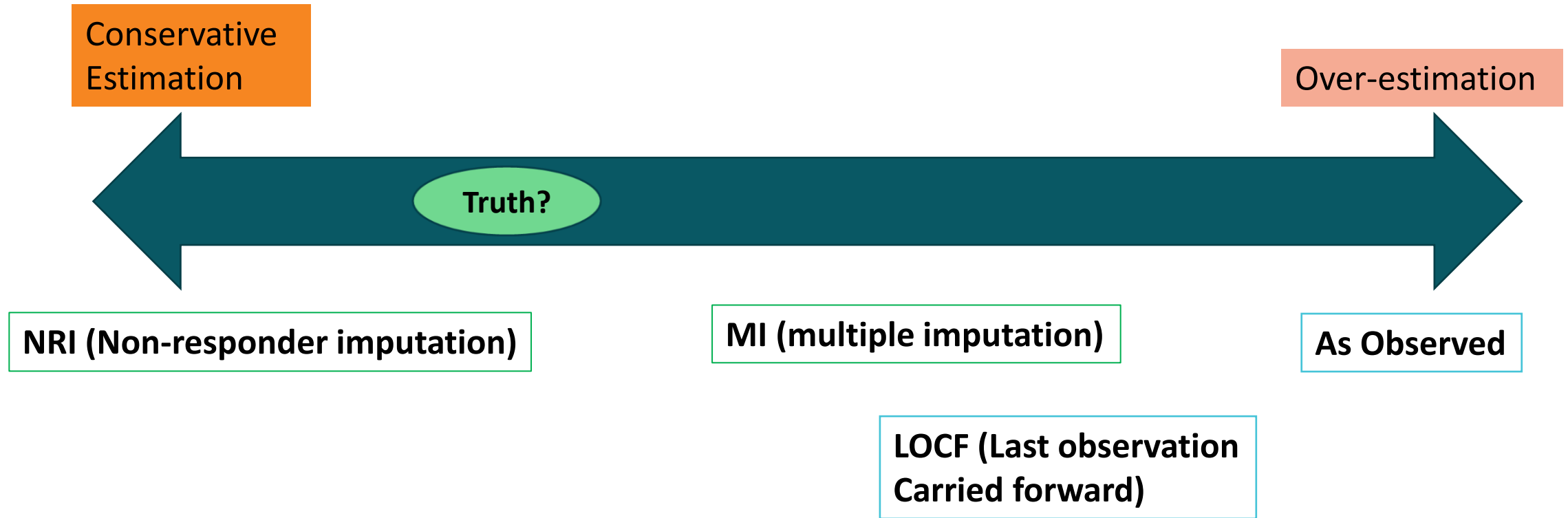
May result in **more participants being imputed as non-responders** for studies with NRI analyses, lowering the reported response rates





Missing Data

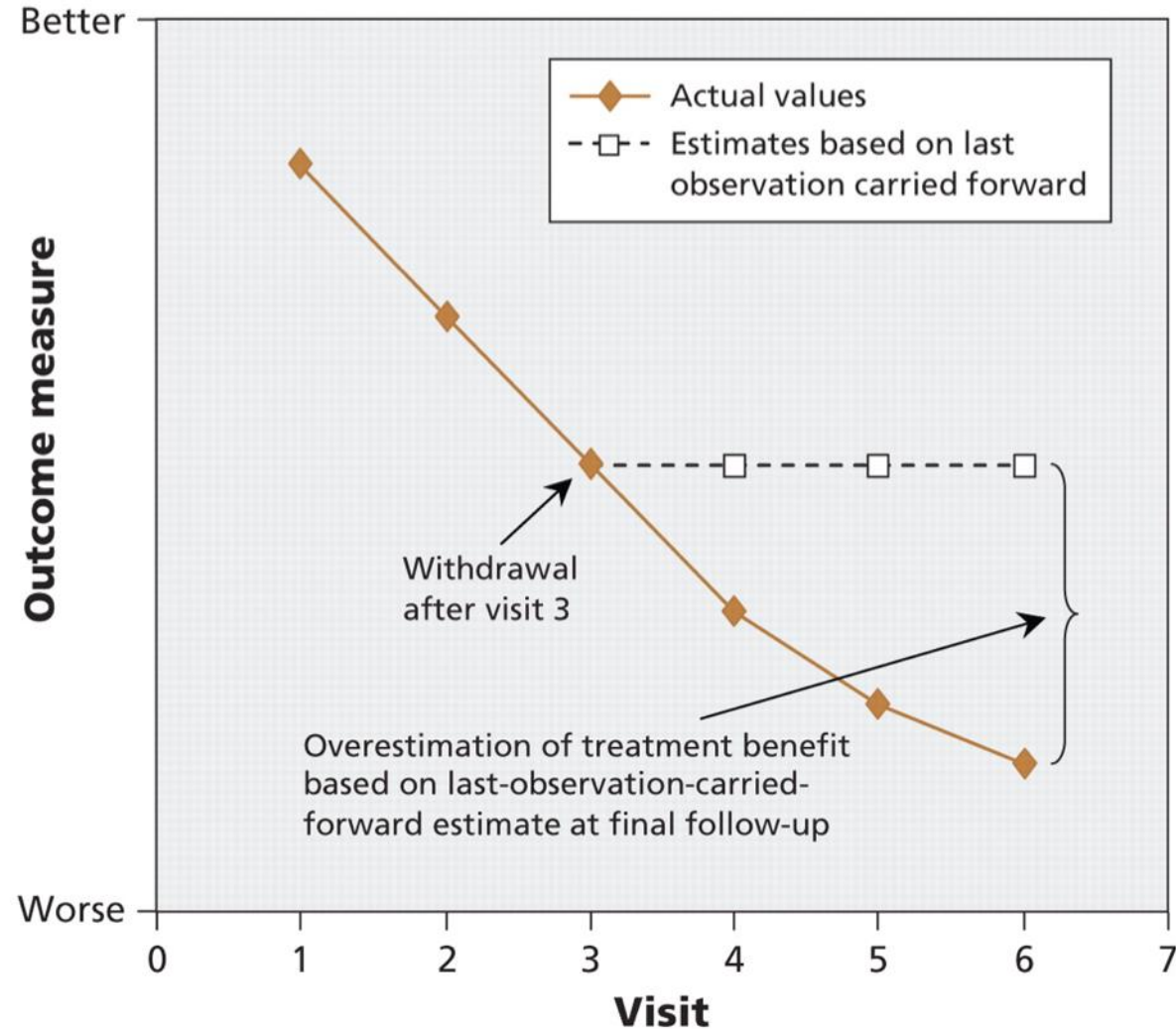
# Handling missing data for long-term extension studies





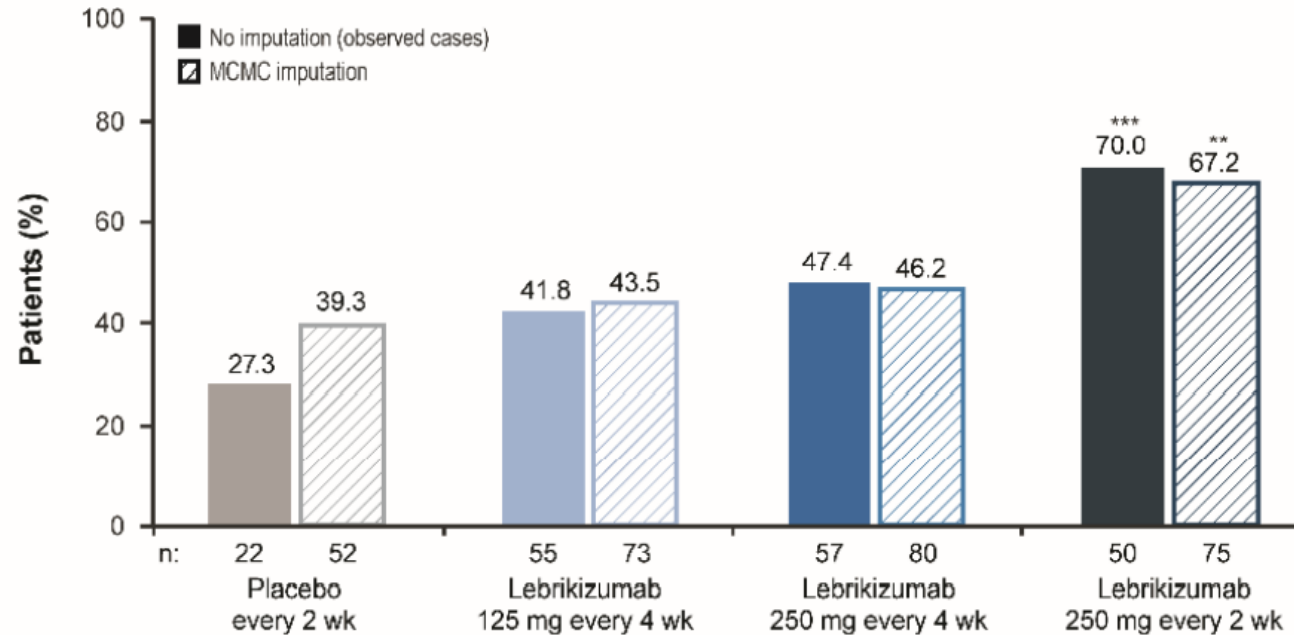
# Last Observation Carried Forward (LOCF)

Definition of “LOCF”: All missing data imputed with the **last available response** for a subject, which is carried forward as final response value



# Example of missing data handling on outcomes

## B. Improvement of $\geq 4$ Points



Abbreviations: BL, Baseline; CMH, Cochran-Mantel-Haenszel; LD, loading dose; LS, least squares; MCMC, Markov chain Monte Carlo; mITT, modified intent-to-treat; NRS, numeric rating scale; SD, standard deviation

\* $P < 0.05$ , \*\* $P < 0.01$ , and \*\*\* $P < 0.001$  versus placebo from pairwise CMH tests

# Summary



## Inclusion/Exclusion Criteria



Can influence patient baseline characteristics and severity of disease

Severity of disease might impact

- response to therapy
- use of rescue treatment

## Washout Period Duration



## Comparator



Comparator affects placebo rates

Combination therapy can result in lower rescue use

## Use of Rescue Treatment



Lack of rescue regimen can increase dropout and non-responders

Are rescued patients treated as non-responders?

## Missing Data Handling and Data Censoring



Data interpretation affected by models and non responder imputations

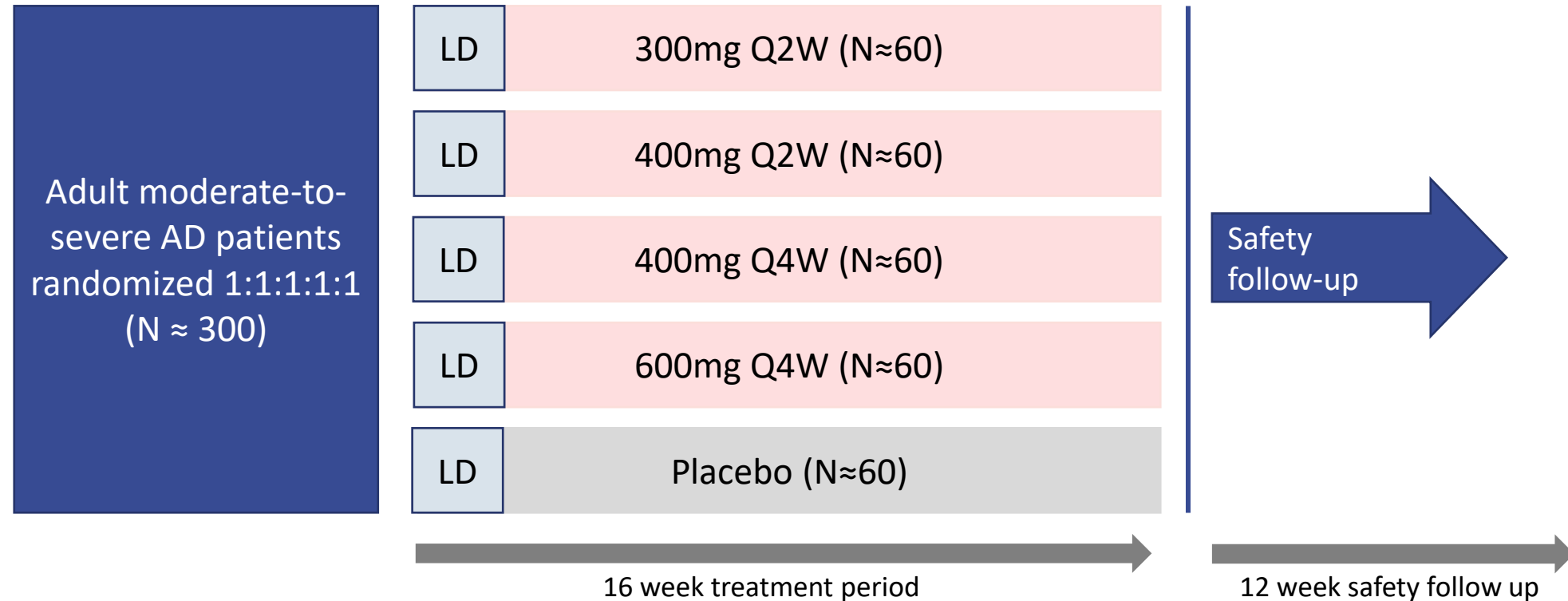
# ASLAN004: Phase 2b study design

Dr Karen Veverka  
VP Medical





# Phase 2b expected to initiate in January 2022



- Loading dose of 600mg for the Q2W dose groups at week 1 and week 2
- Loading dose of 600mg for the Q4W dose groups at week 1, week 2 and week 3



# Key parameters of phase 2b design

## Select inclusion criteria:

- vIGA  $\geq 3$
- $\geq 10\%$  BSA
- EASI  $\geq 16$
- Inadequate response or contraindication to TCS/TCI within 3 months of Screening
- Twice daily application of topical emollient for at least 7 days prior to randomization

## Select exclusion criteria:

- *dupilumab* if discontinued due to lack of efficacy or AE
- Other agents targeting IL-4 or IL-13 (eg lebrikizumab, tralokinumab or ASLAN004)
- Other AD treatments unless appropriate washout
- Washout periods: immunosuppressants/phototherapy 4 weeks, TCS/TCI 1 week



# Study Endpoints

## PRIMARY

- Percentage change in EASI score from Baseline to Week 16

## SECONDARY

- vIGA 0/1, EASI 50/75/90, EASI<7 at Week 16
- Change in EASI score from Baseline over time
- Absolute and percent change in peak P-NRS from Baseline to Week 16
- % of patients achieving ≥4-point reduction in peak P-NRS, SD-NRS at Week 16
- Change in BSA affected with AD from Baseline to Week 16
- Change in SCORAD, DLQI, POEM, EQ-5D-5L and HADS from Baseline to Week 16
- Proportion of patients achieving a 4-point reduction in SD-NRS from Baseline to Week 16
- TEAEs and TESAEs, including incidence of clinically significant changes in vital signs, clinical laboratory tests, and ECGs.

## EXPLORATORY

- AD flare(s) during the study period
- Asthma flare(s) (only for patients with asthma co-morbidity) during the study period
- Change from Baseline in biomarkers



# Fireside Chat & QnA





# ASLAN A<sup>4</sup> Series: Aspects of Atopic Dermatitis and ASLAN004

NASDAQ: ASLN

