ASLAN 2022 R&D Day

September 15, 2022

St Regis, NY

Nasdaq: ASLN

ASLAN PHARMACEUTICALS

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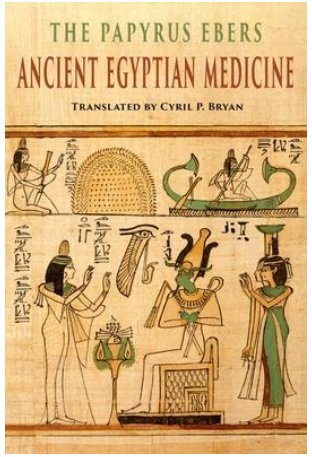
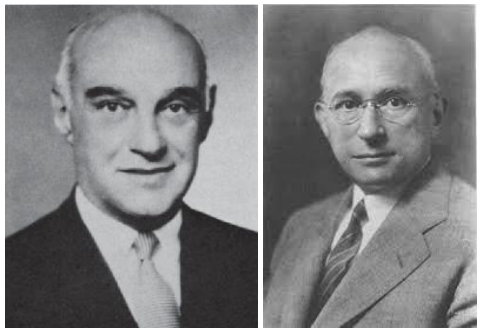
Dr Carl Firth
CEO

Welcome

ASLAN Pharmaceuticals is a clinical-stage, immunology-focused biopharmaceutical company developing innovative therapies to treat inflammatory disease, transforming the lives of patients

Atopic dermatitis has been around since ….





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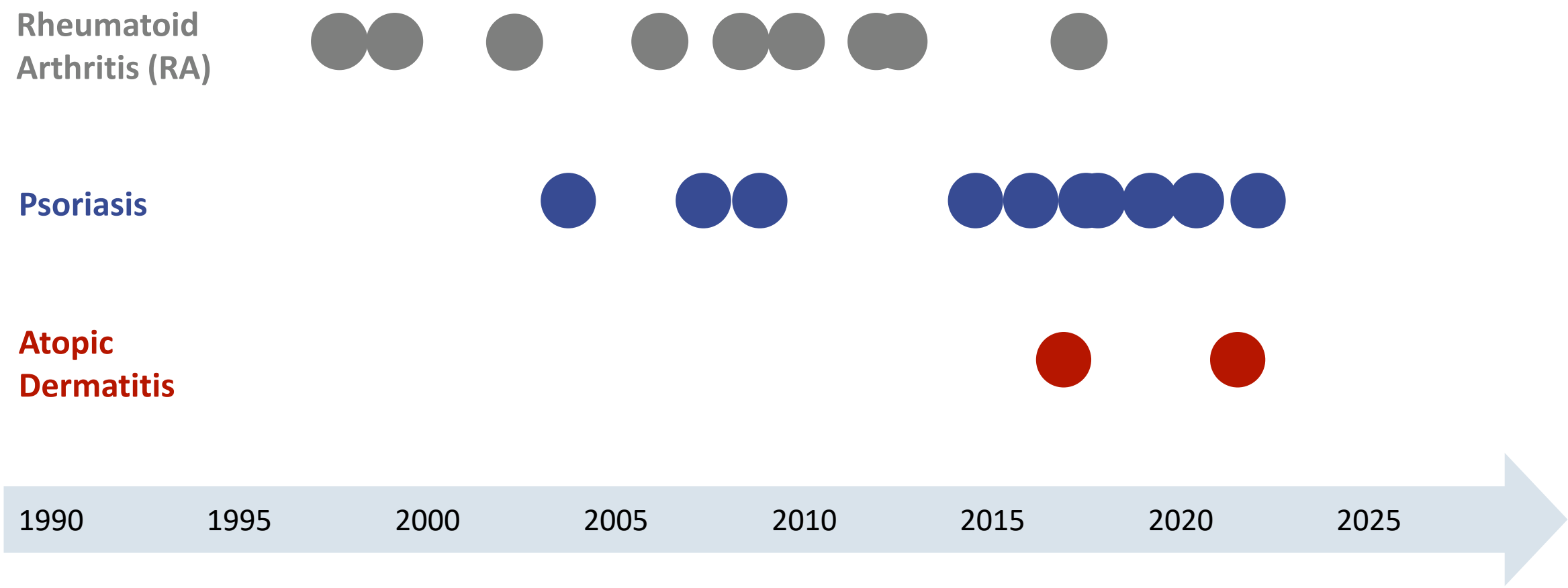
We’re at an inflection point in history for treatment of AD



Biomedtracker database, year of biologic therapy approval for listed indication

Agenda

Time	Presentation	Speaker	
10:00	Welcome		**Dr Carl Firth** CEO, ASLAN
10:10	Emerging unmet needs in Atopic Dermatitis (AD)		**Dr Peter Lio** Northwestern University
10:30	*Eblasakimab:* addressing the market needs and opportunities		**Stephen Doyle** Chief Business Officer, ASLAN
10:40	Promise of targeting the IL-13 receptor		**Dr Ferda Cevikbas** Head Translational Sciences, ASLAN
10:55	Type-2 inflammation and beyond		**Dr Shawn Kwatra** Johns Hopkins University
11:20	Q&A		

Agenda

Time	Presentation	Speaker	
11:40	New findings from the proof-of-concept study		**Dr Karen Veverka** VP Medical, ASLAN
12:00	*Eblasakimab* development program		**Dr Alex Kaoukhov** Chief Medical Officer, ASLAN
12:10	Company Q&A		
12:25	Panel discussion		**Dr Lio, Dr Kwatra, Dr Veverka** moderated by Dr Carl Firth
12:55	Closing remarks		**Dr Carl Firth** CEO, ASLAN

Developing innovative therapies to treat inflammatory disease

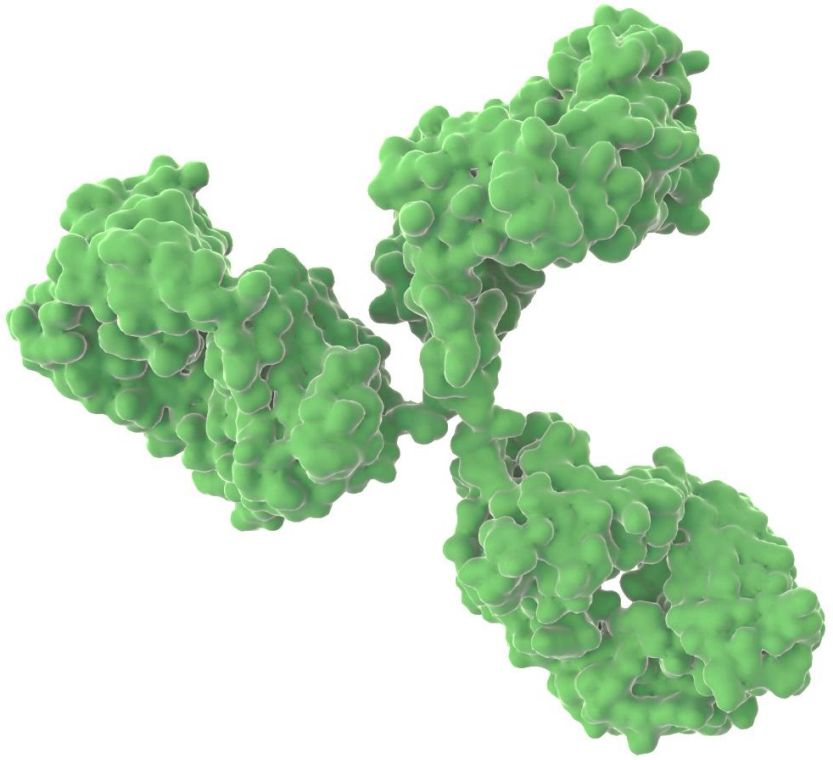
Program	Target	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated milestones
Eblasakimab	IL-13Rα1	Atopic dermatitis	Biologic naïve				Phase 2b topline data in 1H 2023
			Dupilumab experienced				Phase 2 initiation 4Q 2022
		Type 2-driven disease					
Farudodstat	DHODH	Autoimmune skin disease					

Past 12 months has seen tremendous advances in the development of *eblasakimab*

- **Positive topline** data readout from Phase 1b MAD study in Sep 2021
- Presentation of **results from MAD study**:
  Late Breaker Oral Presentation at AAD 2022 and 3 posters at EADV 2022
- TREK-AD: **Phase 2b study initiated**
- **Data supporting differentiation:** novel translational work on neuronal itch, late-breaker at SID 2022, 2 late-breakers accepted at ESDR 2022
- Initiating TREK-DX: **pioneering study for *dupilumab*-experienced** patients
- Built **world-class dermatology team** bringing experience from Regeneron, Dermira, Eli Lilly, Almirall and LEO Pharma

Takeaways from the R&D Day

- The **unmet needs and opportunities** in AD
- Mechanistic rationale supporting **differentiated profile** of *eblasakimab*
- Role of the IL-13 receptor in disease pathology and **advantages of directly blocking IL-13Rα1**
- How *eblasakimab* can directly reducing **neuronal itch responses**
- Clinical data supporting potential for **differentiated profile**



Dr Peter Lio
Northwestern University

Welcome

Emerging unmet needs in Atopic Dermatitis (AD)

Eblasakimab: addressing the market needs and opportunities

Promise of targeting the IL-13 receptor

Type-2 inflammation and beyond

Q&A

New findings from the proof-of-concept study

Eblasakimab development program

Company Q&A

Panel discussion

Closing remarks

EMERGING UNMET NEEDS IN ATOPIC DERMATITIS

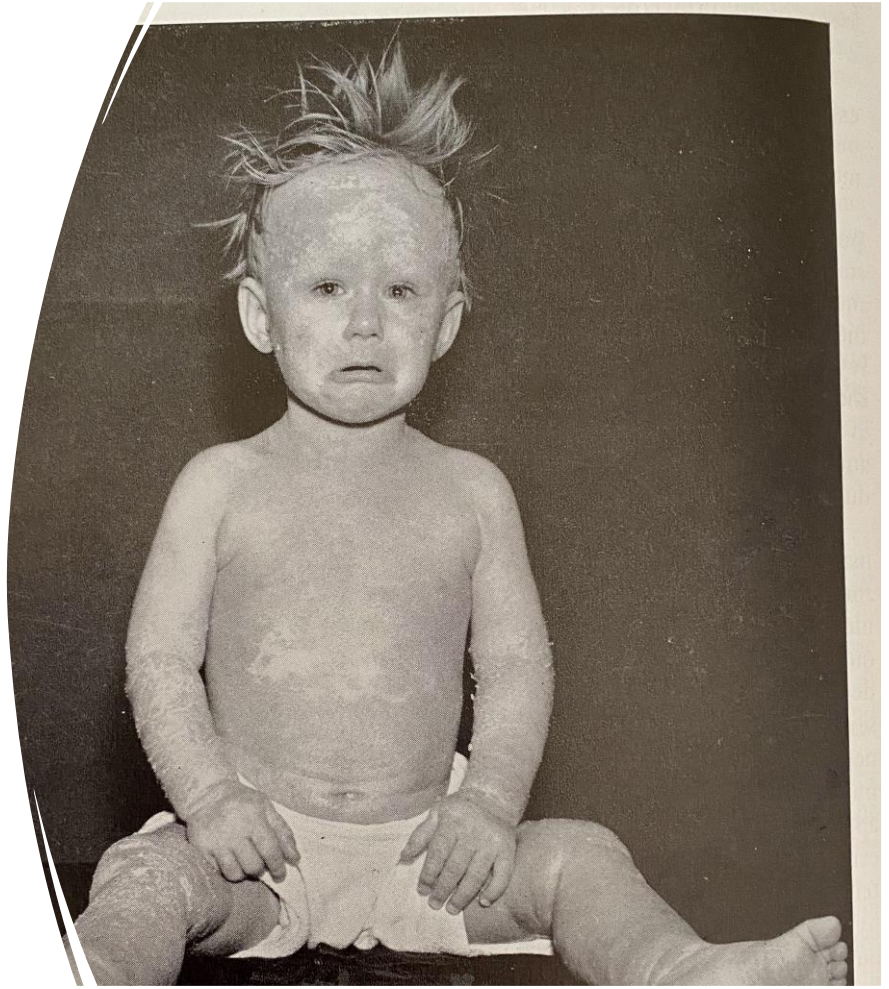
PETER A LIO, MD

ASSISTANT PROFESSOR CLINICAL DERMATOLOGY & PEDIATRICS

NORTHWESTERN UNIVERSITY FEINBERG SCHOOL OF MEDICINE

AD BACKGROUND

- Incredibly common, chronic inflammatory disease
- Up to 20% of children and up to 10% adults in developed countries
- Massive suffering for both patient and family



BURDEN OF AD IS HIGH

Increasing US Prevalence[1,2]

12% to 13% in children and adolescents and 7% in adults

- 90% of cases present by 5 years of age
- Among adults, 17% of cases develop after adolescence

Increasing Costs[3]

~$5.3 billion/year

- Doesn't include time, emotional cost, and presenteeism

Impact on QoL[4]

Greater than Type 1 diabetes

- Not "just a rash"

Sleep Deprivation[2,3-6]

- Exhaustion
- Mood changes
- Impaired psychosocial functioning

Social Isolation[2,3,5]

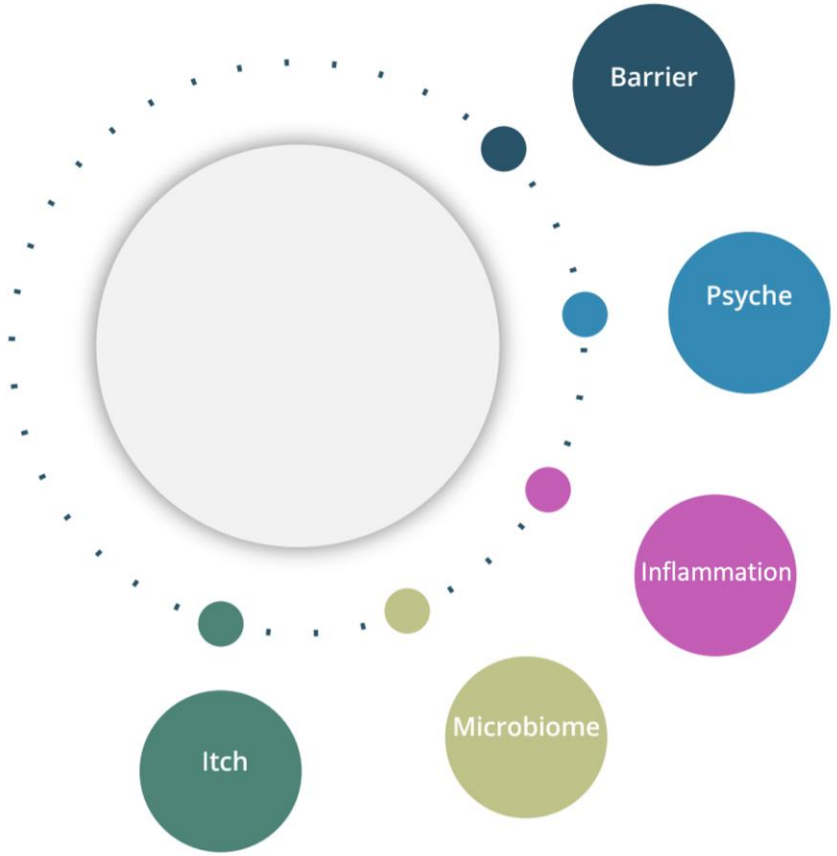
- School avoidance
- Depression

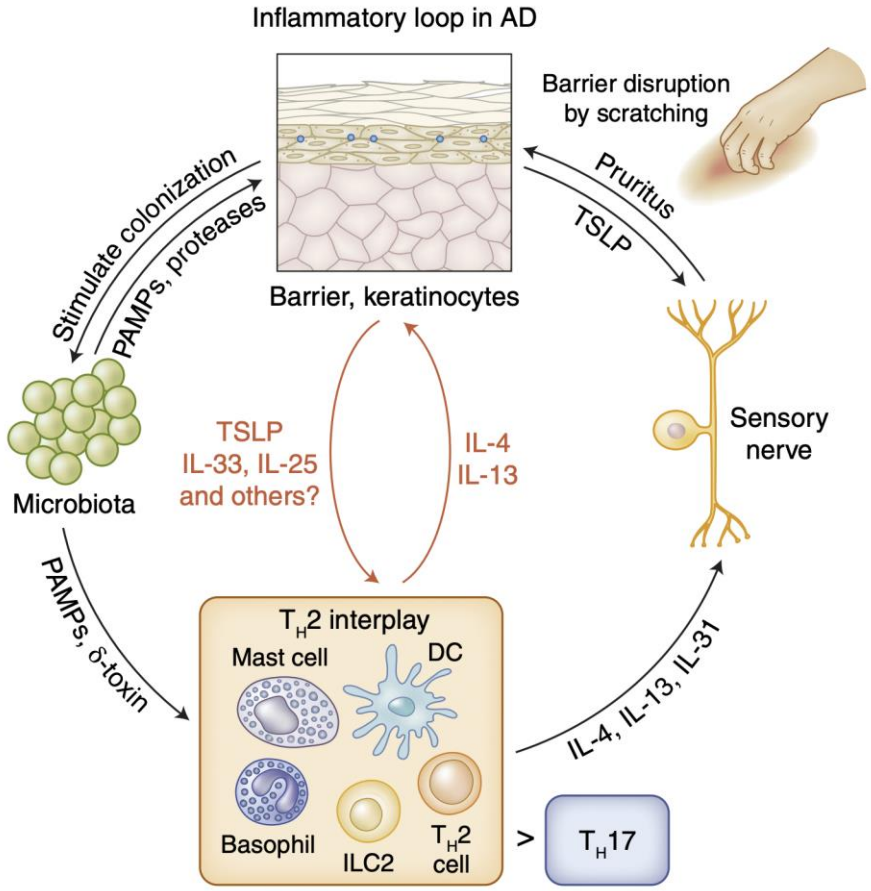
Restricted Choices[3,5]

- Clothing, holidays, socializing, owning pets, and participating in sports

1. Avena-Woods C. (2017). Overview of atopic dermatitis. *The American journal of managed care*, *23*(8 Suppl), S115–S123.
2. Silverberg J. I. (2019). Comorbidities and the impact of atopic dermatitis. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology*, *123*(2), 144–151.
3. Drucker, A. M., Wang, A. R., Li, W. Q., Sevetson, E., Block, J. K., & Qureshi, A. A. (2017). The Burden of Atopic Dermatitis: Summary of a Report for the National Eczema Association. *The Journal of investigative dermatology*, *137*(1), 26–30.
4. Silverberg, J. I., Gelfand, J. M., Margolis, D. J., Boguniewicz, M., Fonacier, L., Grayson, M. H., Simpson, E. L., Ong, P. Y., & Chiesa Fuxench, Z. C. (2018). Patient burden and quality of life in atopic dermatitis in US adults: A population-based cross-sectional study. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology*, *121*(3), 340–347.
5. Lewis-Jones S. (2006). Quality of life and childhood atopic dermatitis: the misery of living with childhood eczema. *International journal of clinical practice*, *60*(8), 984–992.
6. Arkwright, P. D., Motala, C., Subramanian, H., Spergel, J., Schneider, L. C., Wollenberg, A., & Atopic Dermatitis Working Group of the Allergic Skin Diseases Committee of the AAAAI (2013). Management of difficult-to-treat atopic dermatitis. *The journal of allergy and clinical immunology. In practice*, *1*(2), 142–151.

CAUSES OF AD





Dianichi T, Kitoh A, Otsuka A, Nakajima S, Nomura T, Kaplan D and Kabashima K (2018). The epithelial immune microenvironment (EIME) in atopic dermatitis and psoriasis. *Nature Immunology*, *19*, 1286-1298.

TREATMENT OPTIONS FOR AD PATIENTS: PAST AND PRESENT

Clinical Drug Investigation
https://doi.org/10.1007/s40261-020-00905-7

REVIEW ARTICLE

Revisiting Therapies for Atopic Dermatitis that Failed Clinical Trials

Gaurav Agnihotri[1] · Peter A. Lio[2,3]

Agent	Drug Class
Apremilast	PDE4 inhibitor
Roflumilast	PDE4 inhibitor
Fevipiprant	CRTH2 inhibitor
Timapiprant	CRTH2 inhibitor
Tezepelumab	Anti-TSLP
Ustekinumab	Anti-IL12/IL23/p40
Ustekinumab	Anti-IL12/IL23/p40

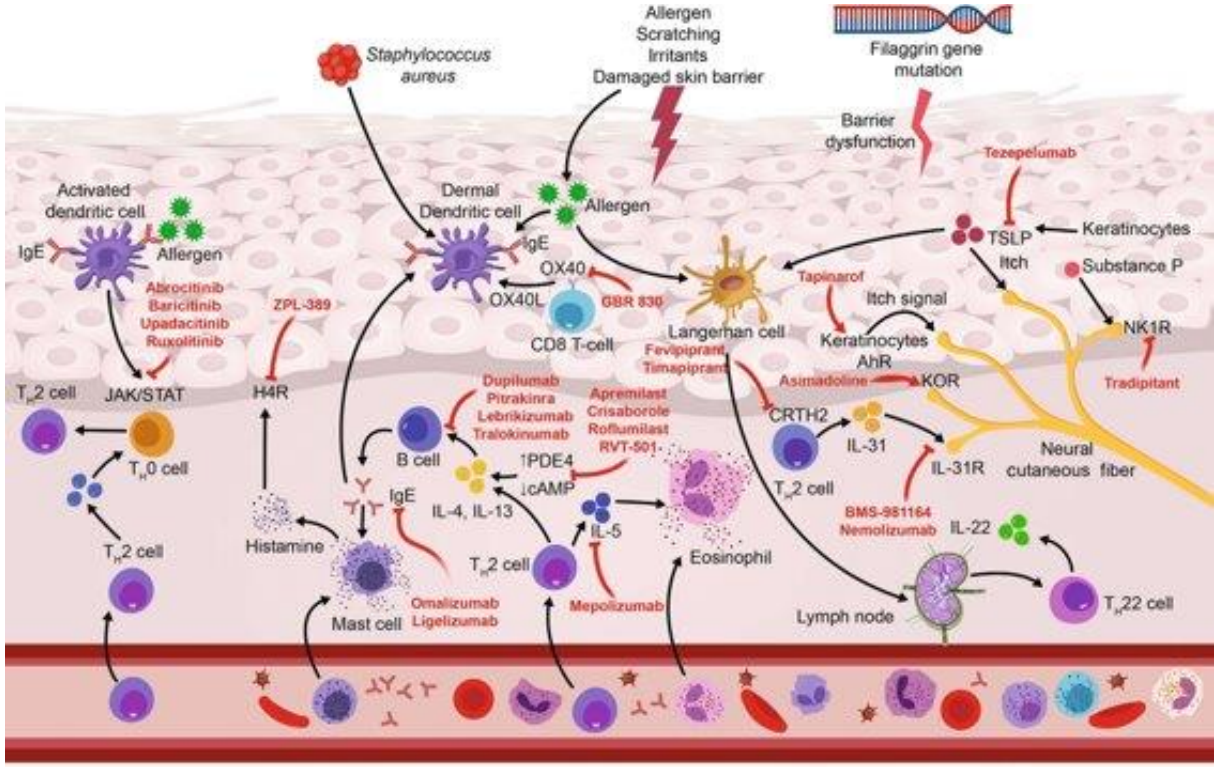
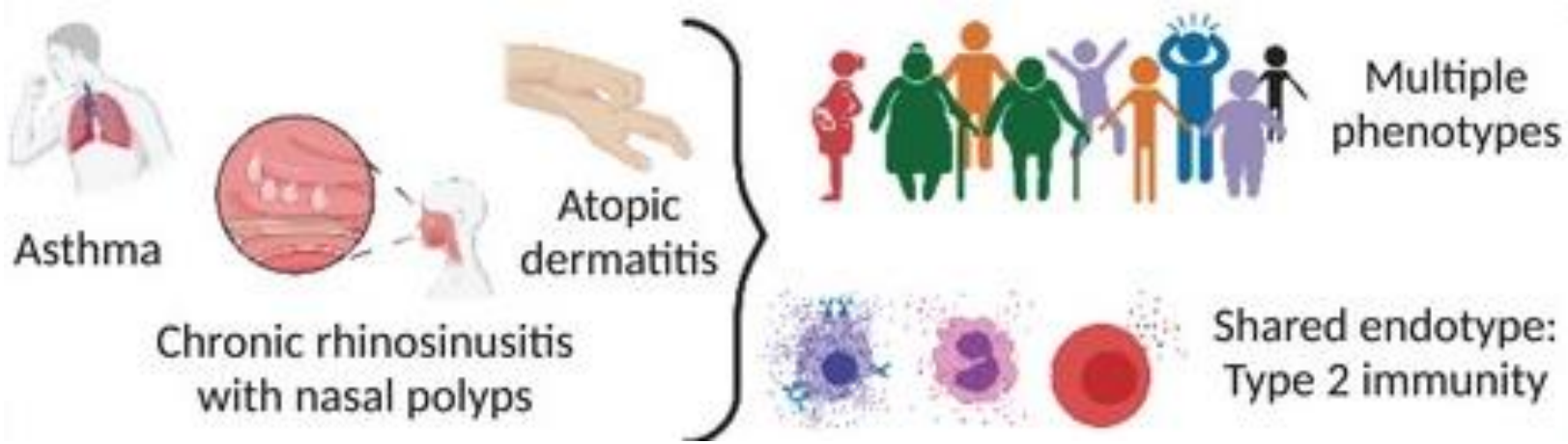


Image from: Eichenfield, L.F., *et al.* (2022). *Pediatr Drugs* 24, 293–305.

bid twice-daily, PDE4 phosphodiesterase-4, EASI Eczema Area and Severity Index, SCORAD SCORing Atopic Dermatitis, CRTH2 chemoattractant receptor-homologous molecules expressed on Th2 lymphocytes, IL interleukin, PBO placebo TSLP thymic stromal lymphopoietin, TCS topical corticosteroid, SC subcutaneous, SE standard error

Gaurav Agnihotri, Peter A. Lio. (2020) Revisiting Therapies for Atopic Dermatitis that Failed Clinical Trials. *Clinical Drug Investigation,* 40, 421–431.

ALLERGIC COMORBIDITIES



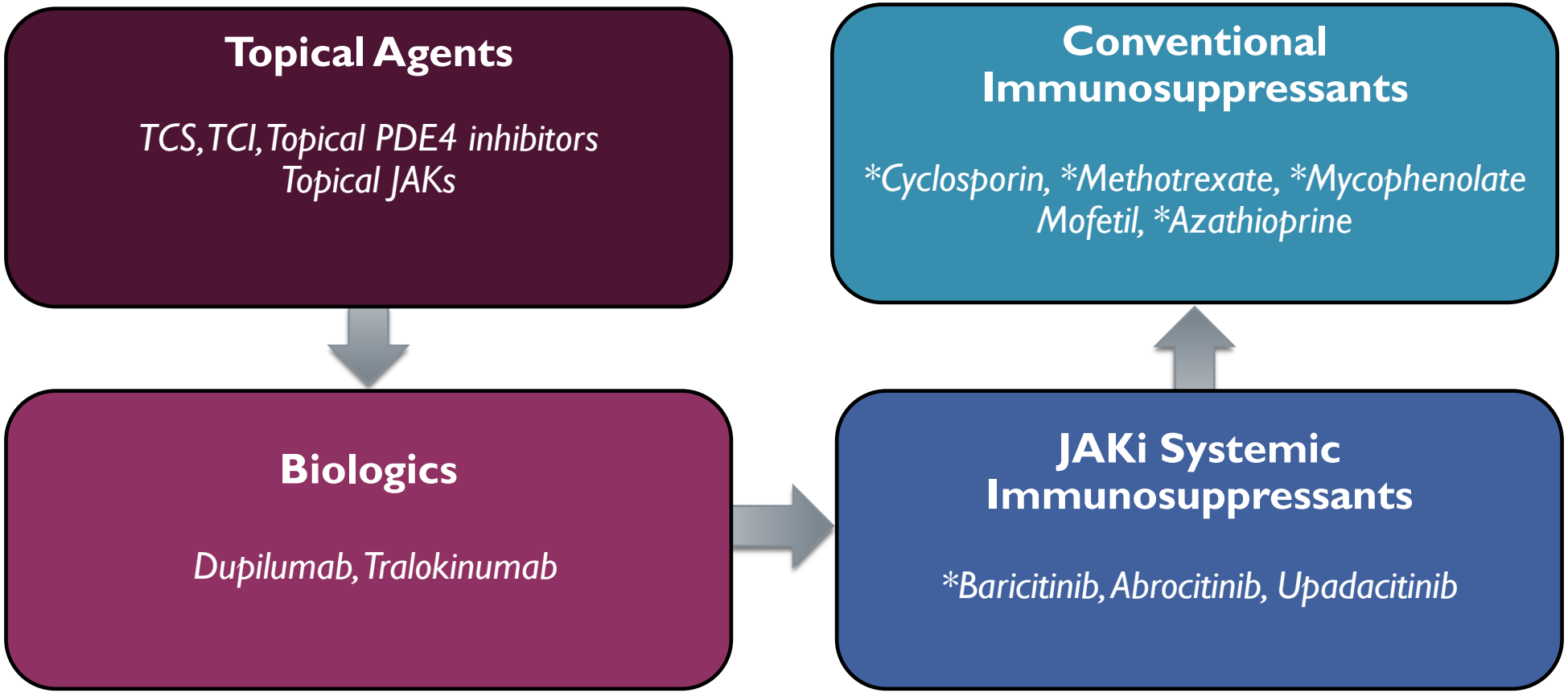
Adults with AD are 3 times more likely to have asthma

In a cross-sectional study of over 2200 children,

- ~80% had some form of allergy
- ~40% had asthma and allergic rhinitis

1. Appiah, M. M., Haft, M. A., Kleinman, E., Laborada, J., Lee, S., Loop, L., Geng, B., & Eichenfield, L. F. (2022). Atopic Dermatitis: Review of Comorbidities and Therapeutics. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology*, S1081-1206(22)00446-X. Advance online publication.
2. Hill, D. A., & Spergel, J. M. (2018). The atopic march: Critical evidence and clinical relevance. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology*, *120*(2), 131–137
3. Hassoun, D., Malard, O., Barbarot, S., Magnan, A., & Colas, L. (2021). Type 2 immunity-driven diseases: Towards a multidisciplinary approach. *Clinical & Experimental Allergy*, *51*(12), 1538–1552. https://doi.org/10.1111/cea.14029

CURRENTLY AVAILABLE TREATMENT OPTIONS



*Not approved in the United States for treatment of AD

1. Sidbury, R., Davis, D. M., Cohen, D. E., Cordoro, K. M., Berger, T. G., Bergman, J. N., Chamlin, S. L., Cooper, K. D., Feldman, S. R., Hanifin, J. M., Krol, A., Margolis, D. J., Paller, A. S., Schwarzenberger, K., Silverman, R. A., Simpson, E. L., Tom, W. L., Williams, H. C., Elmets, C. A., Block, J.A., Harrod, C.G., Eichenfield, Bego L. F. (2014). Guidelines of care for the management of atopic dermatitis. *Journal of the American Academy of Dermatology*, *71*(2), 327–349.
2. Boguniewicz, M., Fonacier, L., Guttman-Yassky, E., Ong, P. Y., Silverberg, J., & Farrar, J. R. (2018). Atopic dermatitis yardstick: Practical recommendations for an evolving therapeutic landscape. *Annals of allergy, asthma & immunology: official publication of the American College of Allergy, Asthma, & Immunology*, *120*(1), 10–22.e2. 3. U.S. Food and Drug Administration. (2021). *DUPIXENT® (dupilumab) Injection, for Subcutaneous Use*. Accessdata FDA. Retrieved June 7, 2022, from https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761055s020lbl.pdf

ADVERSE EVENTS

- Every drug has different levels of adverse events
- Characterising patient-specific adverse event profile can be the next frontier in precision medicine

System Agent	Common AEs (Clinical Trial Incidence of ≥ 1/100)
Clobetasol propionate	Burning, stinging, skin dryness, irritation, erythema, folliculitis, pruritus, skin atrophy, telangiectasia
Ruxolitinib	Bruising, dizziness, headache, UTI, herpes zoster, increased weight, flatulence, anemia, thrombocytopenia, neutropenia
Dupilumab	Nasopharyngitis, headache, URTI, injection site reactions, conjunctivitis, AD exacerbation, skin infections, herpes viral infections
Tralokinumab	Nasopharyngitis, URTI, headache, AD exacerbation, injection site reactions, arthralgia, syncope, pruritus, conjunctivitis, skin infections
Abrocitinib	Nasopharyngitis, nausea, headache, herpes simplex, Increased blood creatinine phosphokinase, dizziness, fatigue, UTI, acne, vomiting, impetigo, oropharyngeal pain, hypertension, influenza, gastroenteritis, dermatitis contact, abdominal pain upper, abdominal discomfort, herpes zoster, thrombocytopenia
Upadacitinib	UTRI, acne, herpes simplex, headache, increased blood creatinine phosphokinase, cough, hypersensitivity, folliculitis, nausea, abdominal pain, pyrexia, increased weight, herpes zoster, influenza, fatigue, neutropenia, myalgia, influenza like illness
Cyclosporin	Serum creatinine increase, hypertension, GI upset, infections, headache, fatigue, paranesthesia, lower limb oedema, hypertrichosis, gingival hyperplasia, anemia, leukopenia, pancytopenia, thrombocytopenia, ESR increase, liver enzyme increase, magnesium decrease, fever, malaise, AD exacerbation, dyslipidemia, tremor, flushing, metallic taste
Methotrexate	GI upset, infections, liver enzyme increase, skin infections, AD exacerbation, anaemia, leukopenia, pancytopenia, fatigue, headache, renal impairment, fever, malaise

AD, atopic dermatitis; AE, adverse event; CK, creatine kinase, ESR, erythrocyte sedimentation rate; GI, gastrointestinal; HSV, herpes simplex virus; HZV, herpes zoster virus; LRTI, lower respiratory tract infection; URTI, upper respiratory tract infection

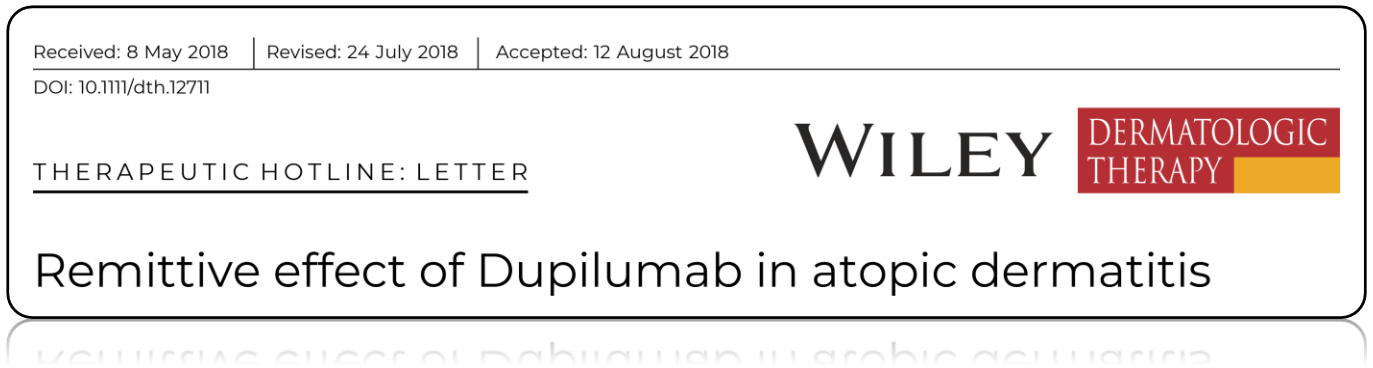
1. Adapted from Alexander, H., Patton, T., Jabbar-Lopez, Z. K., Manca, A., & Flohr, C. (2019). Novel systemic therapies in atopic dermatitis: what do we need to fulfil the promise of a treatment revolution?. *F1000Research*, *8*, F1000 Faculty Rev-132.
2. Nie, D., Tegtmeyer, K., Zhao, J., & Lio, P. A. (2020). Developing patient-specific adverse effect profiles: the next frontier for precision medicine in dermatology. *The Journal of dermatological treatment*, *31*(3), 211–212.

BIOLOGICS

- Dupilumab has been a revolutionary therapy in treatment of AD
- Opened the space for biologics in AD
- Stopping dupilumab can have a remittive effect: different to TCS

PATIENTS DISCONTINUING BIOLOGICS

- Primary failure /loss of response
- Adverse events
- Access issues


Received: 8 May 2018 | Revised: 24 July 2018 | Accepted: 12 August 2018
DOI: 10.1111/dth.12711

THERAPEUTIC HOTLINE: LETTER

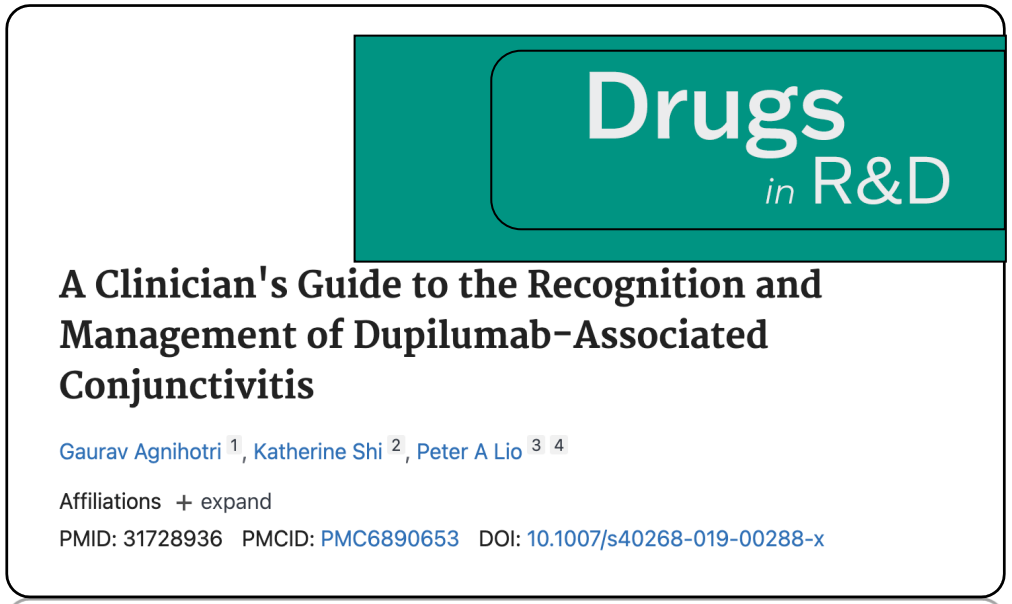
WILEY DERMATOLOGIC THERAPY

Remittive effect of Dupilumab in atopic dermatitis

Treister, A. D., & Lio, P. A. (2018). Remittive effect of Dupilumab in atopic dermatitis. *Dermatologic therapy*, *31*(6), e12711.

DUPILIMAB ASSOCIATED CONJUNCTIVITIS

- Dupilumab Associated Conjunctivitis (DAC) has been characterised as a specific adverse event related to treatment
- A review of 2629 patients treated with dupilumab showed a higher incidence of conjunctivitis in dupilumab-treated patients (8.6-22.1%) vs placebo (2.1-11.1%)[1]
- Patients with severe AD at baseline were more likely to report higher incidence of DAC
- Pathogenesis of conjunctivitis in dupilumab-treated patients is not well understood although several theories have been postulated



1. Agnihotri, G., Shi, K., & Lio, P. A. (2019). A Clinician's Guide to the Recognition and Management of Dupilumab-Associated Conjunctivitis. *Drugs in R&D*, *19*(4), 311–318.

FACE AND NECK ERYTHEMA

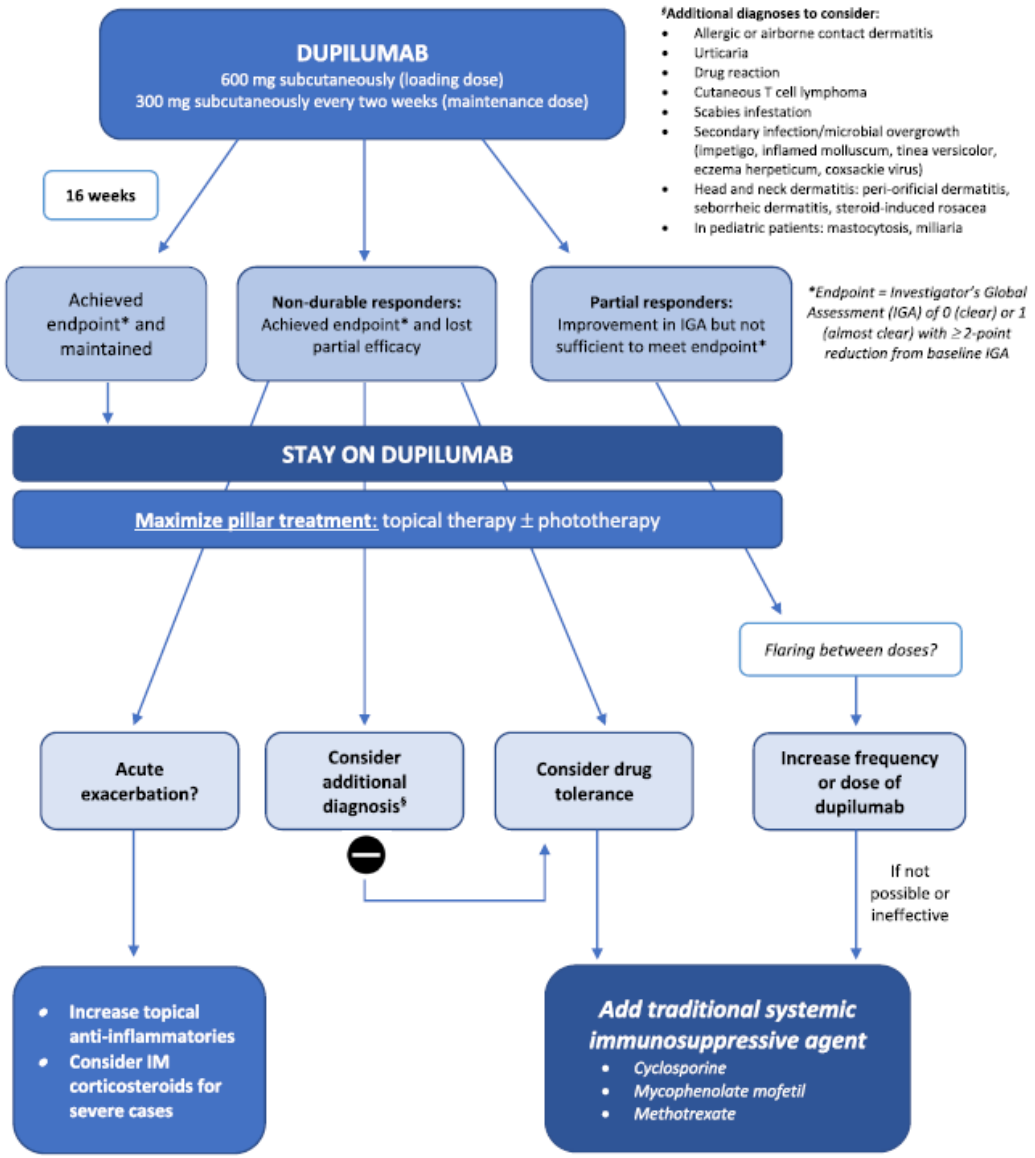
Facial and neck erythema associated with dupilumab treatment: A systematic review

Christine E. Jo, BSc,[a] Alexandra Finstad, BScH, BAH,[a] Jorge R. Georgakopoulos, MD,[b] Vincent Piguet, MD, PhD, FRCP,[b,c] Jensen Yeung, MD, FRCPC,[b,c,d,e] and Aaron M. Drucker, MD, ScM, FRCPC[b,c]

Ottawa, Toronto, and Waterloo, Ontario, Canada

- Broad, complex differential diagnosis
- Increasing awareness of DFAND in scientific literature and clinical experince
- At-risk patients should be identified and counseled accordingly

DEFINING THE DUPILUMAB NON-RESPONDER POPULATION



Management algorithm for dupilumab partial and non-durable responders. *IM* intramuscular

Hendricks, A. J., Lio, P. A., & Shi, V. Y. (2019). Management Recommendations for Dupilumab Partial and Non-durable Responders in Atopic Dermatitis. *American journal of clinical dermatology*, *20*(4), 565–569.

JAK INHIBITOR AND SAFETY CONCERNS

- Received recent approval in AD
- Effective therapies for flares and disease uncontrolled by biologics
- Black Box warnings
- Potential implications of long-term use for chronic condition such as AD

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE), and THROMBOSIS

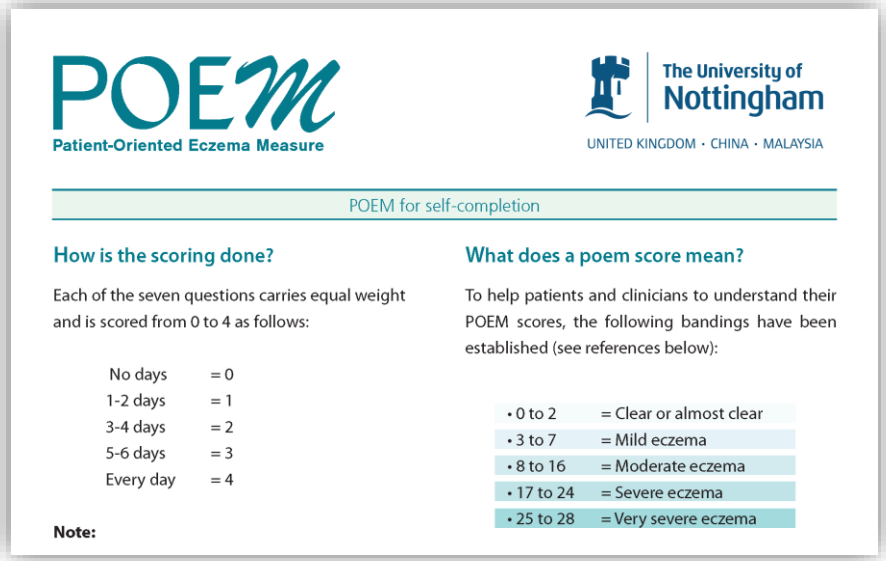
See full prescribing information for complete boxed warning.

- **Increased risk of serious bacterial, fungal, viral and opportunistic infections leading to hospitalization or death, including tuberculosis (TB). Discontinue treatment with CIBINQO if serious or opportunistic infection occurs. Test for latent TB before and during therapy; treat latent TB prior to use. Monitor all patients for active TB during treatment, even patients with initial negative latent TB test. (5.1)**
- **Higher rate of all-cause mortality, including sudden cardiovascular death, with another JAK inhibitor vs. TNF blockers in rheumatoid arthritis (RA) patients. CIBINQO is not approved for use in RA patients. (5.2)**
- **Malignancies have occurred with CIBINQO. Higher rate of lymphomas and lung cancers with another JAK inhibitor vs. TNF blockers in RA patients. (5.3)**
- **MACE has occurred with CIBINQO. Higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) with another JAK inhibitor vs. TNF blockers in RA patients. (5.4)**
- **Thrombosis has occurred with CIBINQO. Increased incidence of pulmonary embolism, venous and arterial thrombosis with another JAK inhibitor vs. TNF blockers. (5.5)**

Cibinqo full prescribing information

EFFICACY FROM PATIENT REPORTED OUTCOMES

- Patient-Oriented Eczema Measure (POEM), focuses on the illness severity as experienced by the patient (sleep loss, itch, and skin assessments)



POEM
Patient-Oriented Eczema Measure

The University of Nottingham
UNITED KINGDOM · CHINA · MALAYSIA

POEM for self-completion

How is the scoring done?

Each of the seven questions carries equal weight and is scored from 0 to 4 as follows:

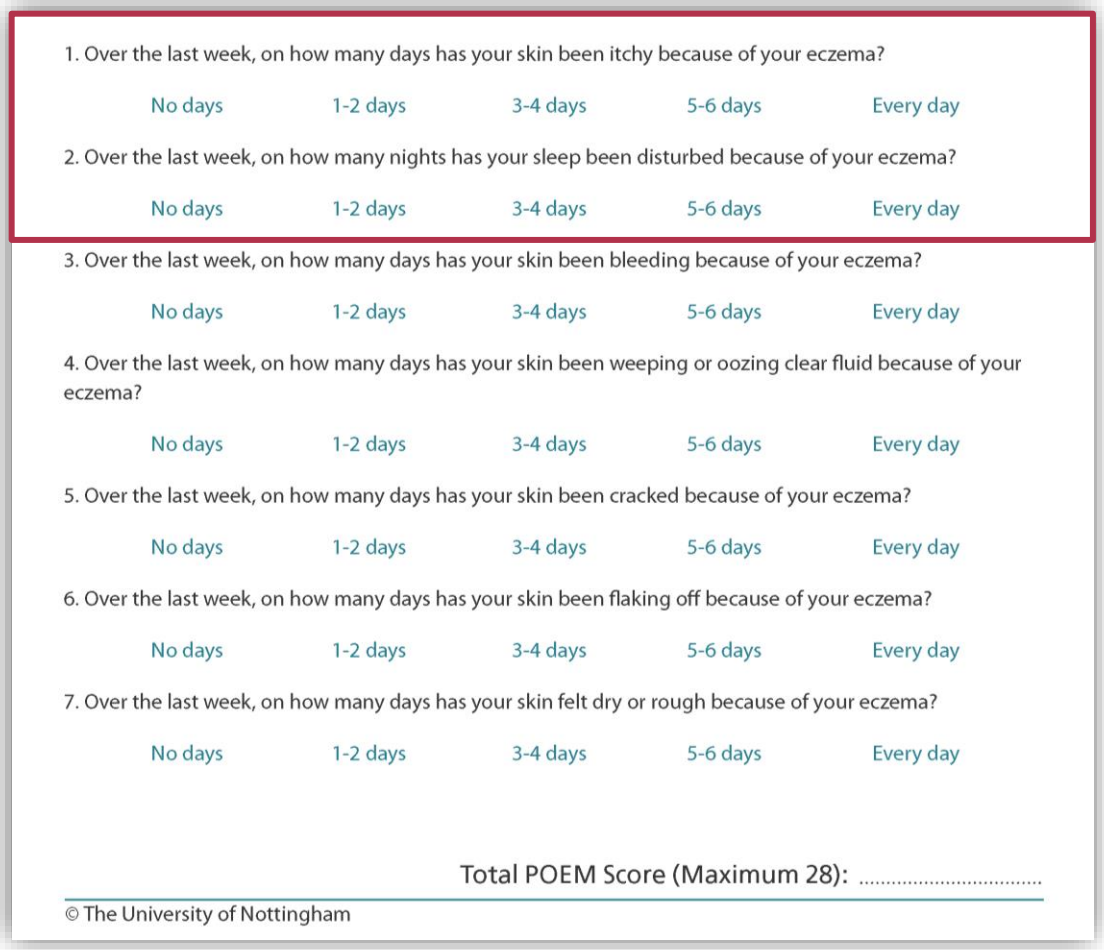
No days	= 0
1-2 days	= 1
3-4 days	= 2
5-6 days	= 3
Every day	= 4

Note:

What does a poem score mean?

To help patients and clinicians to understand their POEM scores, the following bandings have been established (see references below):

• 0 to 2	= Clear or almost clear
• 3 to 7	= Mild eczema
• 8 to 16	= Moderate eczema
• 17 to 24	= Severe eczema
• 25 to 28	= Very severe eczema



1. Over the last week, on how many days has your skin been itchy because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

2. Over the last week, on how many nights has your sleep been disturbed because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

3. Over the last week, on how many days has your skin been bleeding because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

4. Over the last week, on how many days has your skin been weeping or oozing clear fluid because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

5. Over the last week, on how many days has your skin been cracked because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

6. Over the last week, on how many days has your skin been flaking off because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

7. Over the last week, on how many days has your skin felt dry or rough because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

Total POEM Score (Maximum 28): .....

https://www.nottingham.ac.uk/research/groups/cebd/documents/methodological-resources/poem-for-self-completion.pdf.

CONCLUSIONS

- The past 50 years have been relatively quiet for AD… but that does not seem to be predictive of the next 5-10!
- We are on the verge of a giant leap in both understanding and treating AD
- Current treatment options have varying efficacy and safety profiles and not all treatments are suitable for all populations
- Additional treatment options are needed for AD patients and emerging treatments have the potential to address the unmet needs that remain

Stephen Doyle
Chief Business Officer

Welcome

Emerging unmet needs in Atopic Dermatitis (AD)

***Eblasakimab*: addressing the market needs and opportunities**

Promise of targeting the IL-13 receptor

Type-2 inflammation and beyond

Q&A

New findings from the proof-of-concept study

Eblasakimab development program

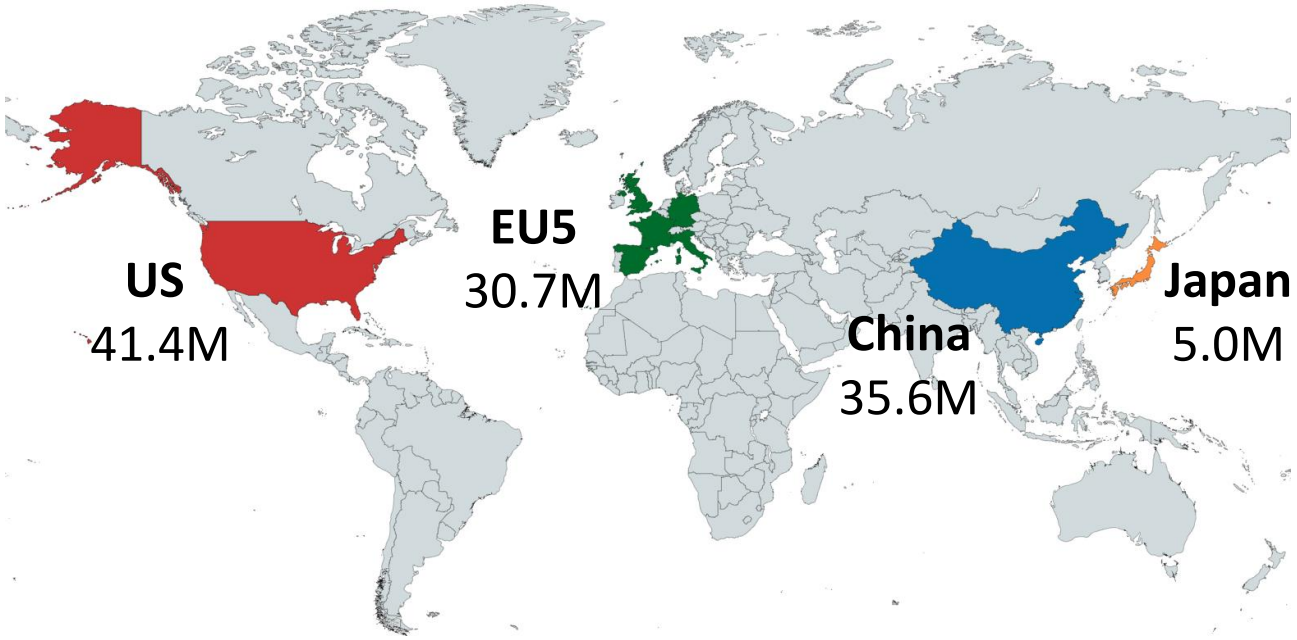
Company Q&A

Panel discussion

Closing remarks

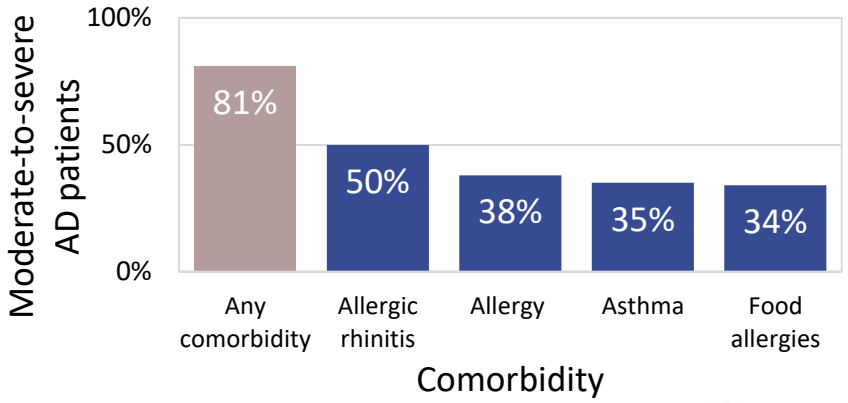
AD is a chronic disease that can severely impact quality of life

Total AD prevalent cases, 2019



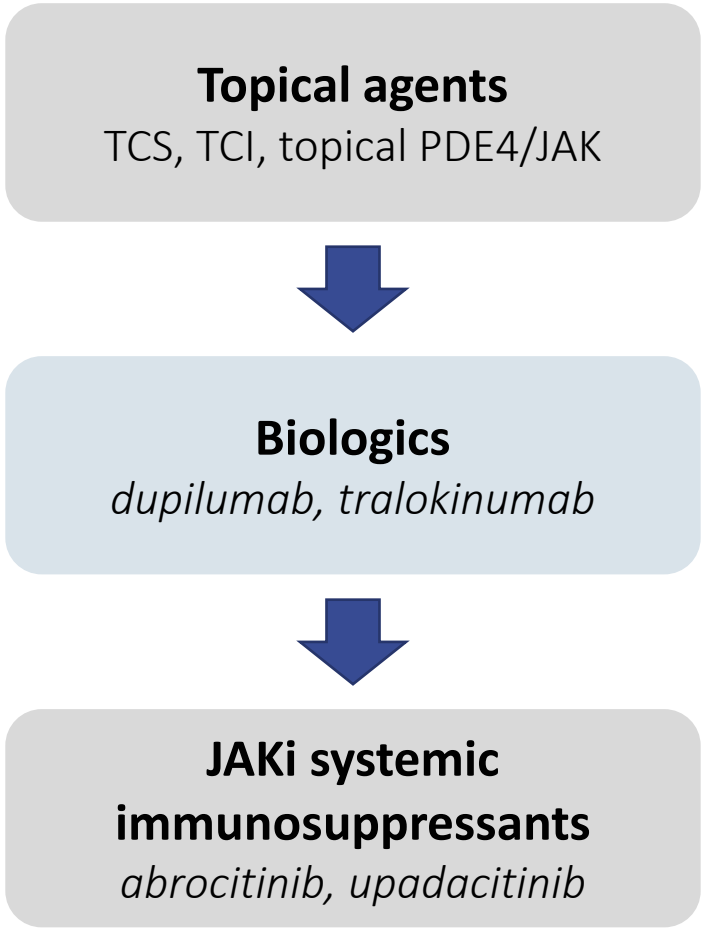
Over 200 million AD patients worldwide

- Prevalence estimated at 1-3% of adults worldwide
- Over 30% of patients have moderate-to-severe disease
- Around 80% of these have other allergic comorbidities:



Wen-Ian Dong et al (2021) WAO Journal 14(11):100604.
Divekar et al (2021) Atopic Dermatitis/Atopic Eczema: Disease Landscape & Forecast. Decision Resources Group (DRG)
Calzavara-Pinton et al (2022) AAD Annual Meeting poster presentation, Baseline patient demographics and comorbidities in patients with atopic dermatitis from the GLOBOSTAD registry (237 patients)

Dupilumab has advanced the standard of care for atopic dermatitis but a significant unmet need remains



- There are few safe and effective treatments for moderate-to-severe AD
- Treatment is traditionally focused on topical corticosteroids but steroid use can be associated with safety risks
- *Dupilumab* has established dual blockade of IL-4/IL-13 biologic therapy as the new standard of care[1]
  - Launch of *dupilumab* in 2017 helped drive a large market for systemic AD therapy with 2021 sales of $5.2B
  - Sanofi expects to grow sales to over $14B
- However, only 8% of eligible patients receive *dupilumab* today[1] and there remains a significant unmet need:
  - Only 35% of patients treated with *dupilumab* achieved an optimal response[2]
  - Conjunctivitis is common and can lead to treatment discontinuations
  - Opportunity to improve upon biweekly dosing regimen

1 Sanofi's quarterly financials and annual reports
2 Spherix (2018) Atopic dermatitis ATU study

High unmet need in biologic eligible and experienced population

AD patients 41M[1]

Drug treated Mod-to-sev 3.3M[2]

TARGET MARKET

Biologic eligible 2M[3]

- Biologic naïve population seeking safe long-term treatment
- *Dupilumab* is standard of care for these patients

8%[4]

Dupi-treated 220k[5]

Dupilumab experienced 150k[6]

- Patients who show sub-optimal response
- Response declines over time
- Discontinuations due to conjunctivitis

Numbers are only meant to be illustrative of estimated relative market sizes

1 Divekar et al (2021) Atopic Dermatitis/Atopic Eczema: Disease Landscape & Forecast, DRG
2 Drug treated diagnosed prevalence, assuming one-third moderate and all severe patients, Divekar et al (2021) DRG
3 Calculated assuming 220K patients represent 8% of the biologic eligible market
4 Sanofi's investor presentations
5 Estimated based on Dupixent annual US sales from Sanofi Annual Report 2021
6 Spherix (2018) Atopic dermatitis ATU study

The number of biologics in development is limited due to several notable failures in recent years

Topical agents
TCS, TCI, topical PDE4/JAK

Biologics
dupilumab, tralokinumab

JAKi systemic immunosuppressants
abrocitinib, upadacitinib

Target	Biologic	Current status
IL-4Rα	*Dupilumab*	Approved
IL-13	*Tralokinumab* *Lebrikizumab*	Suboptimal efficacy (approved) Phase 3 completed
IL-31	*Nemolizumab*	Suboptimal efficacy (phase 3)
OX-40 OX-40L	KHK4083 KY1005	KHK4083 trial paused (phase 3)

Eblasakimab has the potential to be a differentiated therapy in AD

Ideal target product profile

Efficacy	Dosing	Safety	Treats comorbidities
			
Better efficacy over current standard-of-care with rapid control of itch	Less frequent and more convenient dose regimen	Addresses physician concerns on safety with lower rate of discontinuation	Able to address allergic comorbidities such as asthma and rhinitis

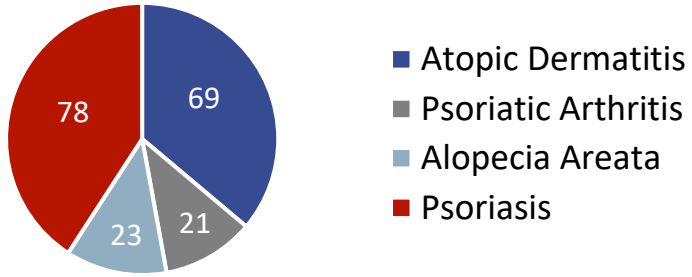
Preference for *eblasakimab* profile tested through market survey of US dermatologists

Methodology

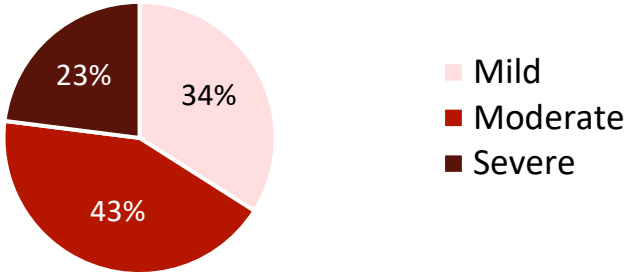
20 mins online survey, n=150

20-30 mins phone interviews, n =15

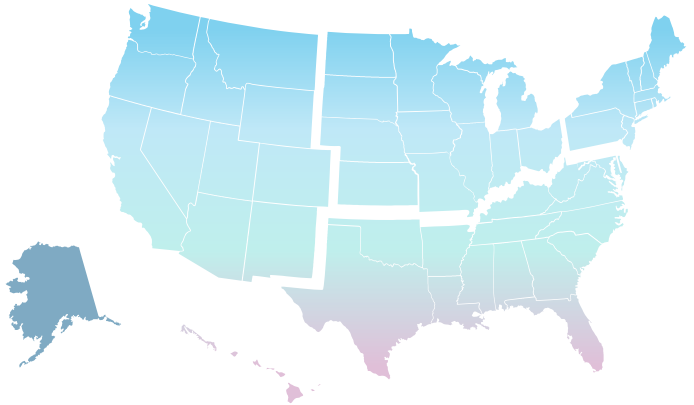
Indications treated by dermatologists



Atopic Dermatitis patients

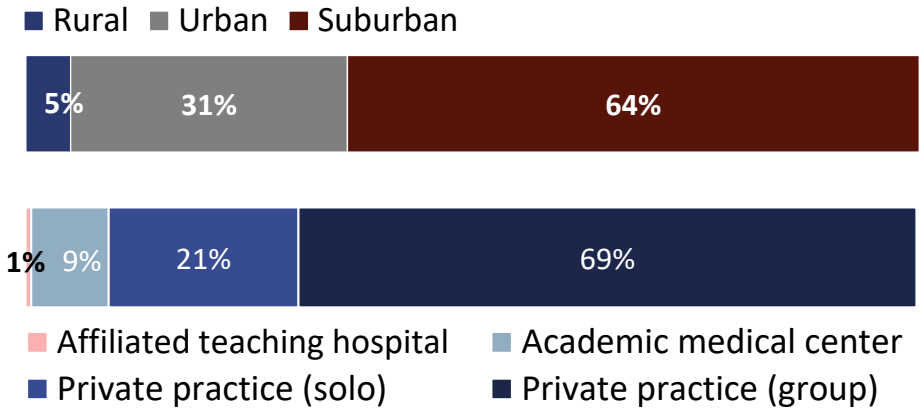


Board-certified US dermatologists



West 23%
Midwest 19%
South 31%
Northeast 27%

Representation of dermatologists in US



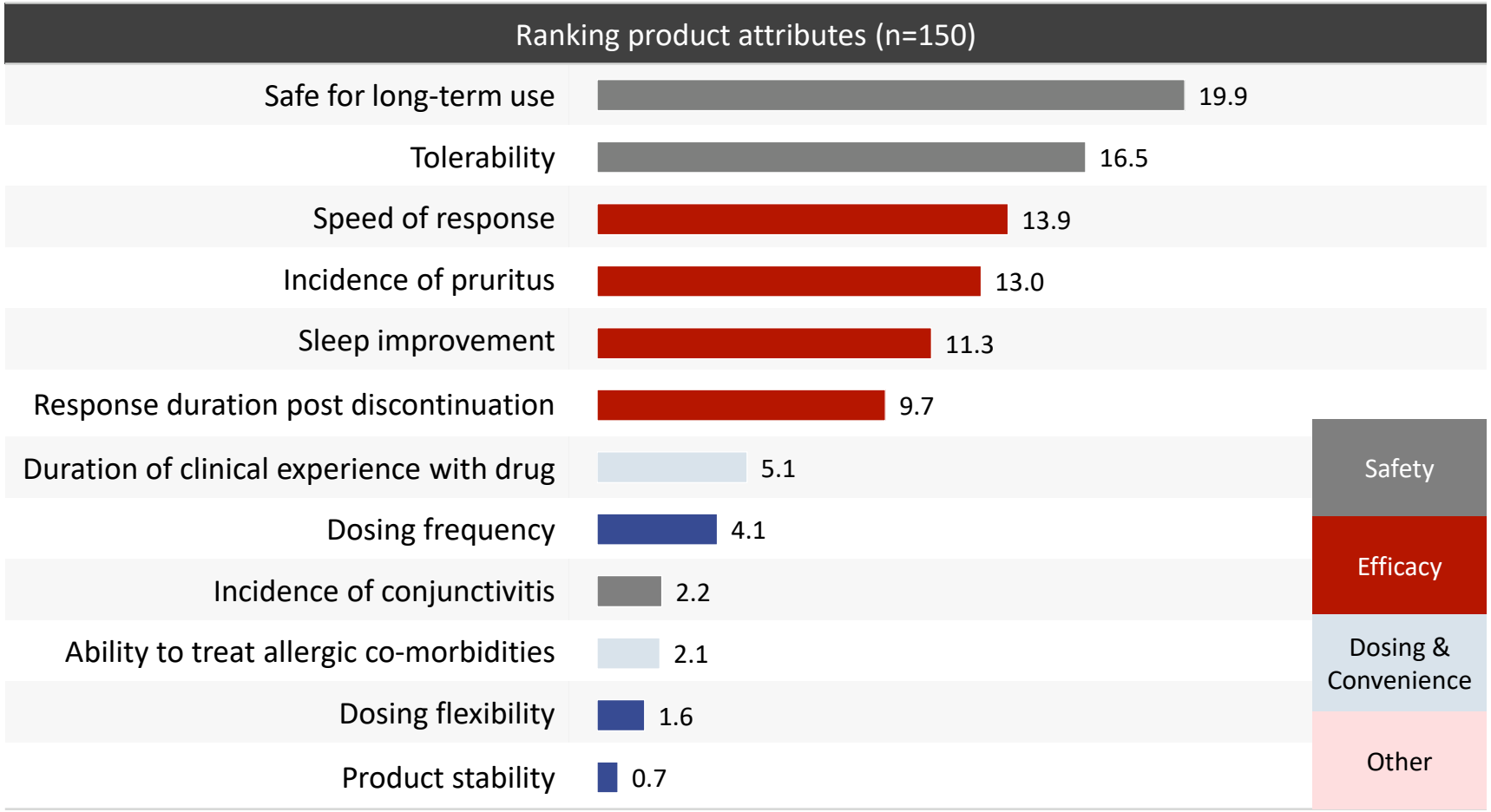
Topical steroids and *dupilumab* are the mainstays of AD treatment

Current prescribing for moderate-to-severe atopic dermatitis *(% of Patients)*	
Topical Corticosteroids (TCS)	70%
Dupixent (*dupilumab*)	30%
Topical immunomodulators[1]	23%
Opzelura (*ruxolitinib*)	7%
Phototherapy	6%
Systemic immunomodulators[2]	5%
Rinvoq (*upadacitinib*)	2%
Adbry (*tralokinumab*)	2%
Cibinqo (*abrocitinib*)	1%

Product	% overall satisfaction
Dupixent (*dupilumab*)	83%
Adbry (*tralokinumab*)	45%
Opzelura (*ruxolitinib*)	39%
Rinvoq (*upadacitinib*)	32%
Cibinqo (*abrocitinib*)	29%
Eucrisa (*crisaborole*)	11%

1 Topical immunomodulators: Eidel, protopic
2 Systemic immunomodulators include methotrexate, CellCept, Immuran

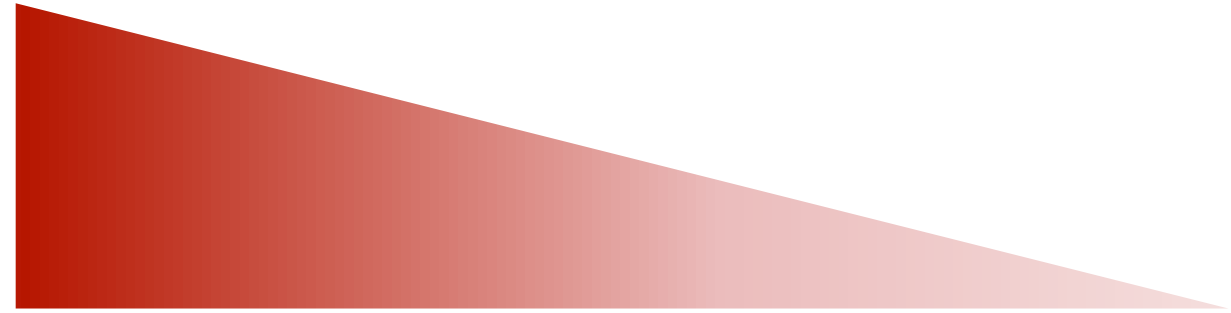
Safety, speed of response, itch relief and sleep improvement prioritised attributes for treatment decisions



Eblasakimab profiles created to test the product attributes

	Efficacy	Dosing	Safety	Treats comorbidities
Ideal target product profile				
Profile A	+++	+++	+++	+++
	8% increase to SOC	Q4W dosing		
Profile B	+++	++	+++	+++
	8% increase to SOC	Q2W dosing		
Profile C	++	+	+++	+++
	Comparable to SOC	QW dosing		

Eblasakimab could be the favoured biologic, despite dermatologists' long experience with *dupilumab*



+ Efficacy
+ Monthly

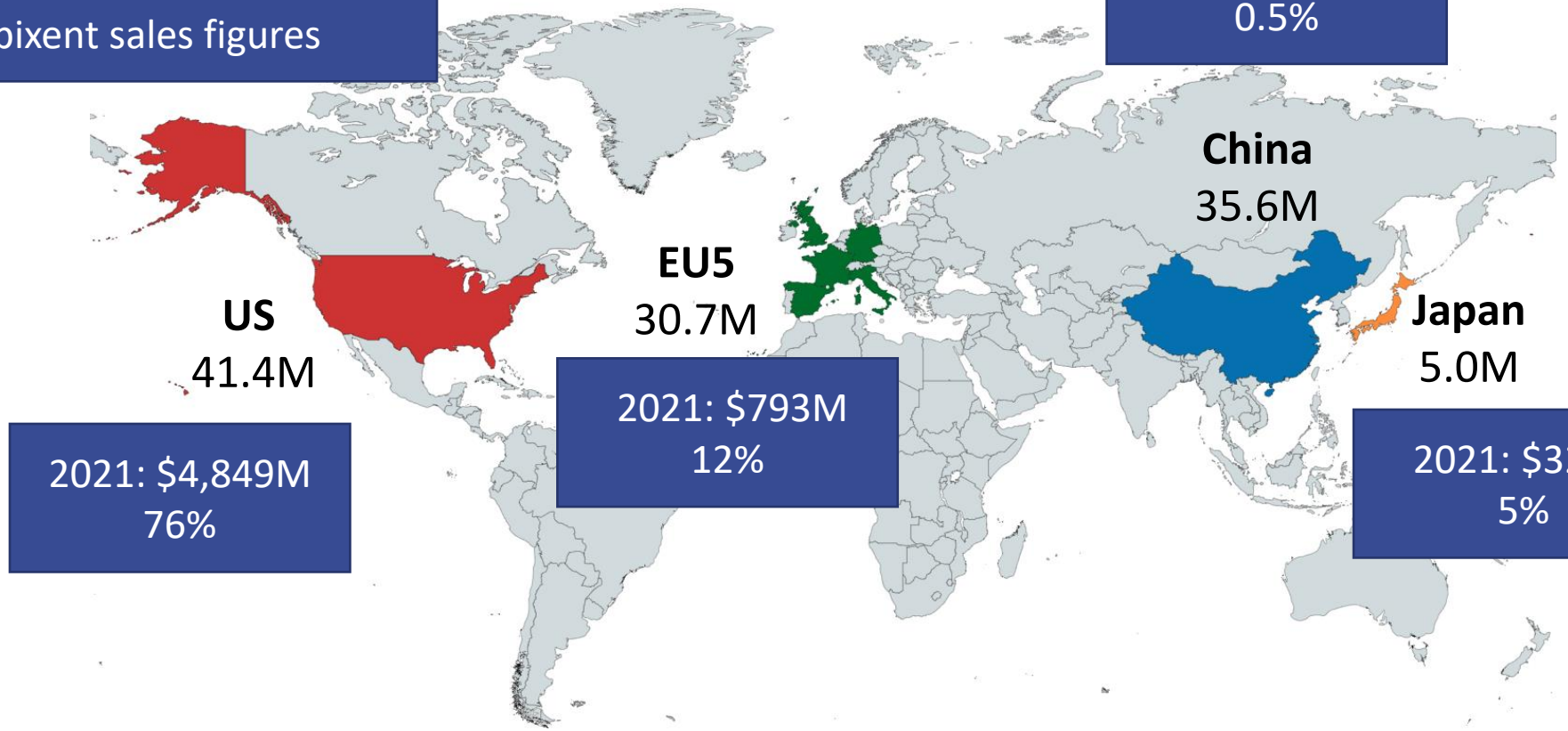
+ Efficacy
+ Biweekly

Patient populations	Profile A	Profile B	Profile C
Biologic-naive (selected against *dupilumab*)	51%	44%	20%
Dupilumab-experienced (selected against *upadacitinib*)	55%	54%	47%

Commercialization of *eblasakimab* has potential in different regional markets

Total AD prevalent cases, 2019

Dupixent sales figures



Wen-Ian Dong, et al (2021) *WAOjournal*: 14(11):100604.
Divekar et al (2021) Atopic Dermatitis/Atopic Eczema: Disease Landscape & Forecast. Decision Resources Group
Sanofi's quarterly financials and annual reports and IMS data

Dr Ferda Cevikbas
Head Translational Sciences

Welcome

Emerging unmet needs in Atopic Dermatitis (AD)

Eblasakimab: addressing the market needs and opportunities

Promise of targeting the IL-13 receptor

Type-2 inflammation and beyond

Q&A

New findings from the proof-of-concept study

Eblasakimab development program

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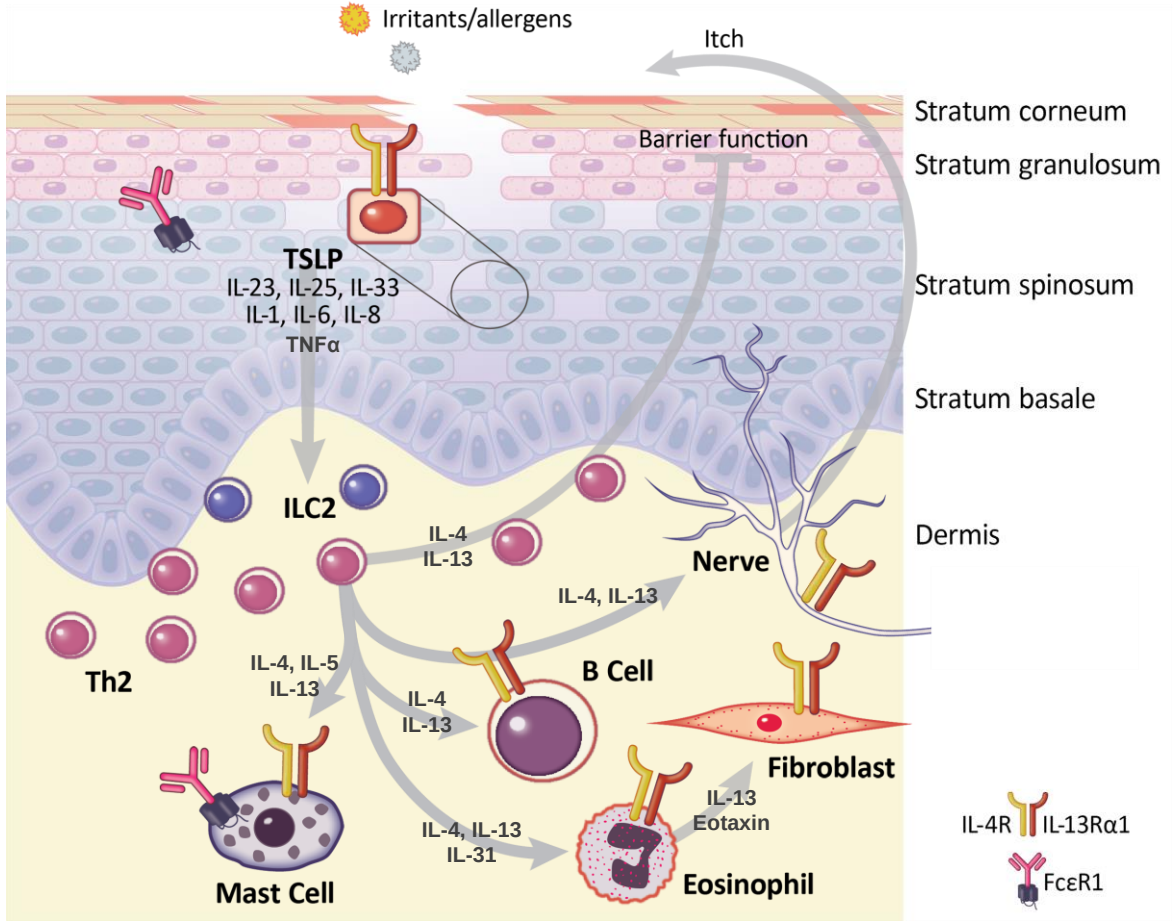
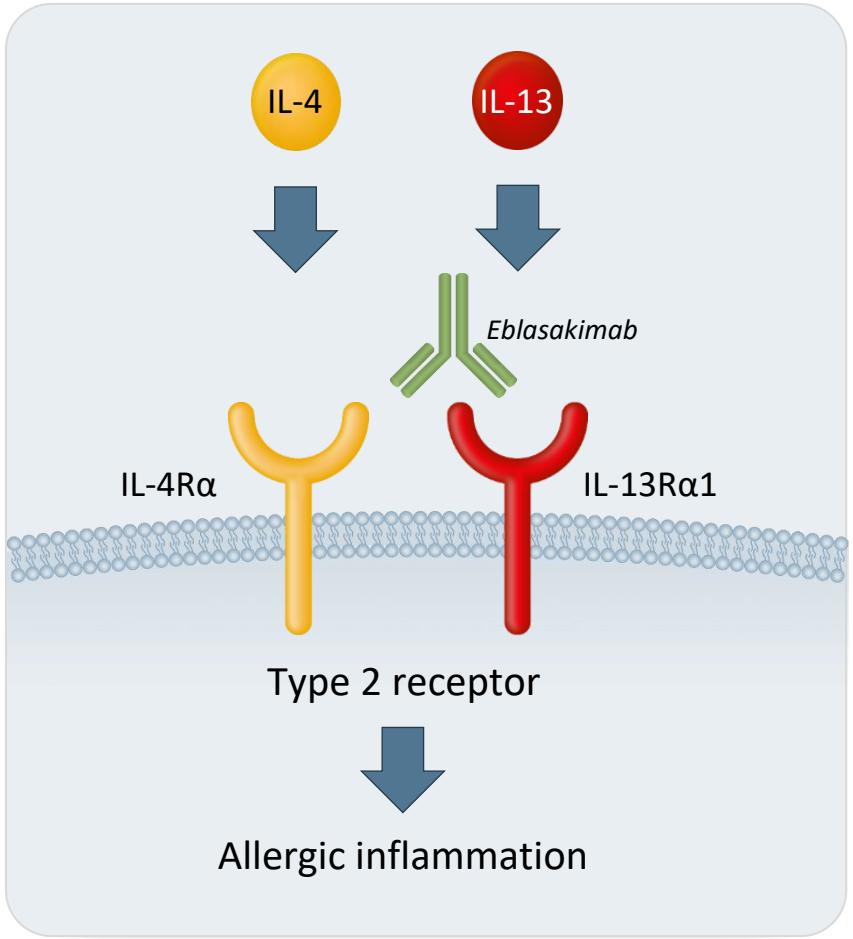
Atopic dermatitis is a chronic inflammatory skin disease with Th2 cell polarization



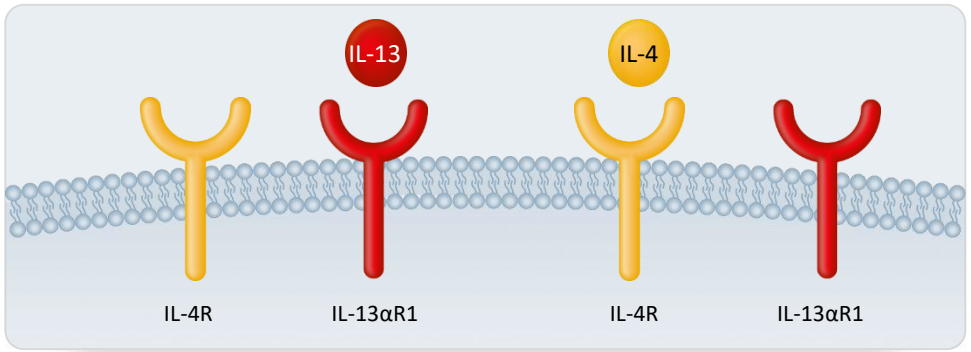
- Skin barrier disruption allows for the entry of irritants and allergens which leads to immune cell activation
- Th2 cells produce IL-4 and IL-13. IL-13 is the key effector cytokine in AD
- Signaling of both cytokines occurs through the Type 2 receptor ( ) which is expressed on a range of immune and non-immune cells including mast cells, B cells, eosinophils, fibroblasts and neurons
- On itch specific sensory neurons, the Type 2 receptor can amplify itch signals

Eblasakimab is the only monoclonal antibody in the clinic targeting the IL-13 receptor



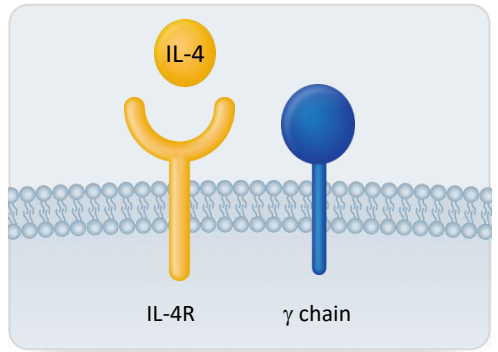
- The Type 2 receptor complex comprises the IL-4 receptor and IL-13 receptor
- When either cytokine binds its respective receptor, the receptors form an active heterodimer
- By targeting the IL-13 receptor, *eblasakimab* blocks the Type 2 receptor complex, preventing signaling through **both** IL-4 and IL-13

Eblasakimab selectively blocks the Type 2 receptor



Type 2 receptor

Blocks IL-13 signaling | Blocks IL-4 signaling



Type 1 receptor

Blocks IL-4 signaling

Eblasakimab: Specific and complete blockade of Type 2 receptor

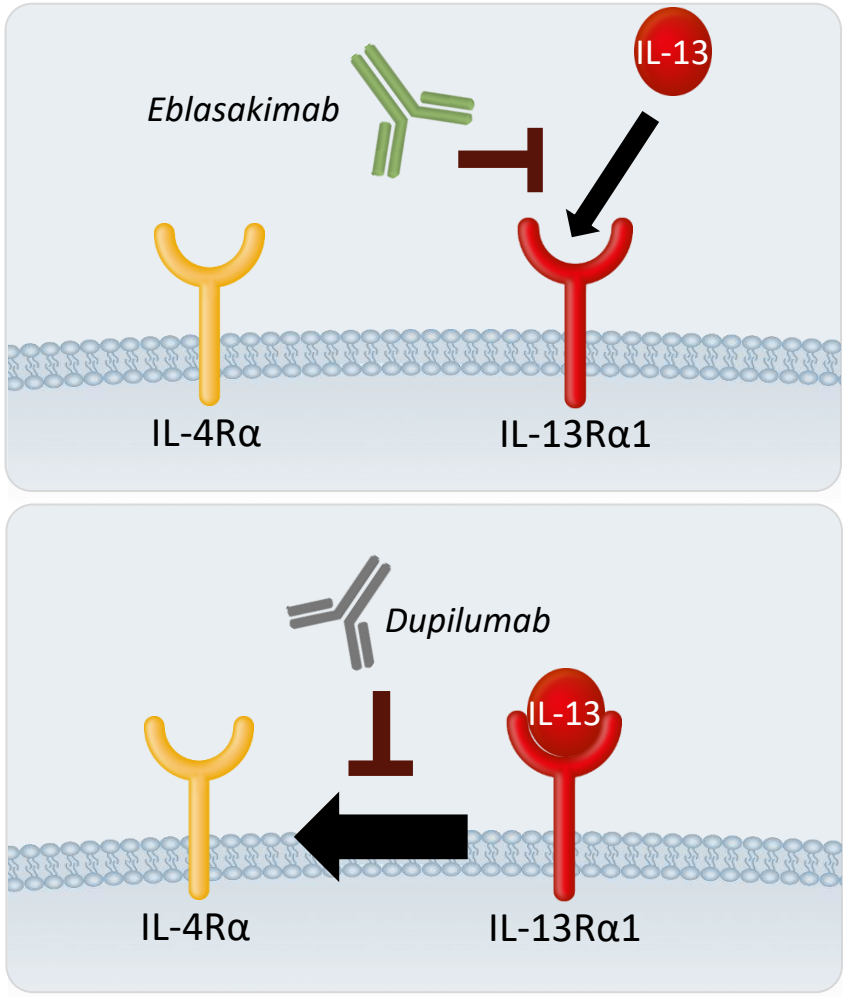
Lebrikizumab: Partial blockade of Type 2 receptor signaling

Dupilumab: Broad blockade of Type 1 and Type 2 receptors

Eblasakimab has the potential to be a differentiated therapy in AD

	Efficacy	Dosing	Safety	Treats comorbidities
				
Ideal target product profile	Better efficacy over current standard-of-care with rapid control of itch	Less frequent and more convenient dose regimen	Addresses physician concerns on safety with lower rate of discontinuation	Able to address allergic comorbidities such as asthma and rhinitis

Eblasakimab directly binds the IL-13Rα1, which has the potential for more efficient blockade of the Type 2 receptor



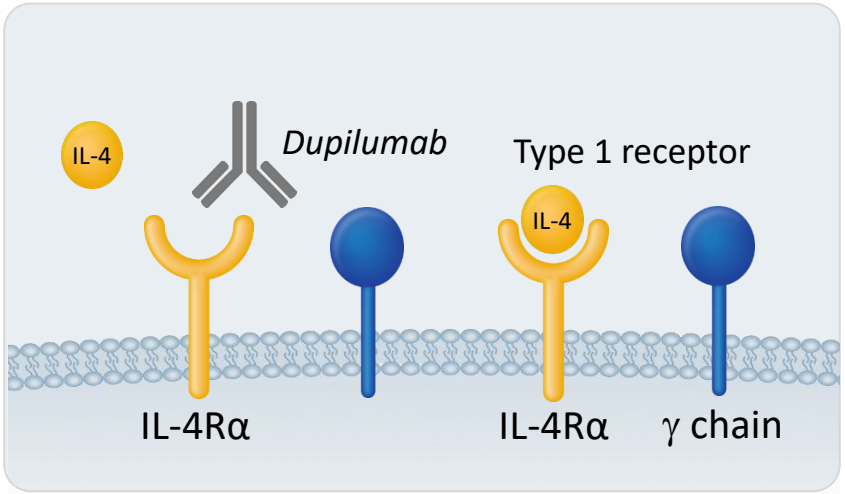
- Formation of the Type 2 receptor complex occurs in 2 steps:
  1. Ligand binding to its receptor (IL-13 to IL-13Rα1)
  2. Bound receptor binding to the partner receptor (IL-4Rα)
- Step 1 is a weaker, lower affinity interaction and a rate limiting step while Step 2 is a high affinity interaction
- By directly blocking the rate limiting step, *eblasakimab* has the potential to provide more efficient blockade of IL-13 signaling versus *dupilumab* which interferes with Step 2, a high affinity interaction
- This may translate to lower required concentration *in vivo* and may provide improved dosing frequency and efficacy

1 Ito et al (2009) JBC 284(36): 24289-24296
2 Andrews et al (2002) JBC 277(48):46073-46078.

Certain side effects, such as conjunctivitis, may be driven by inhibition of Type 1 receptor, which *eblasakimab* does not bind

Dupilumab study	Rate of conjunctivitis
Phase 3 mono[1]	**8%** (placebo-adjusted)
Open label extension[1]	**20%**
Real world experience[2]	**26%**

- Rates of conjunctivitis are higher in *dupilumab* treated patients[1]
- *Lebrikizumab,* which targets IL-13 and does not block the Type 1 receptor, may have a lower rate of conjunctivitis (5% placebo-adjusted)[3]

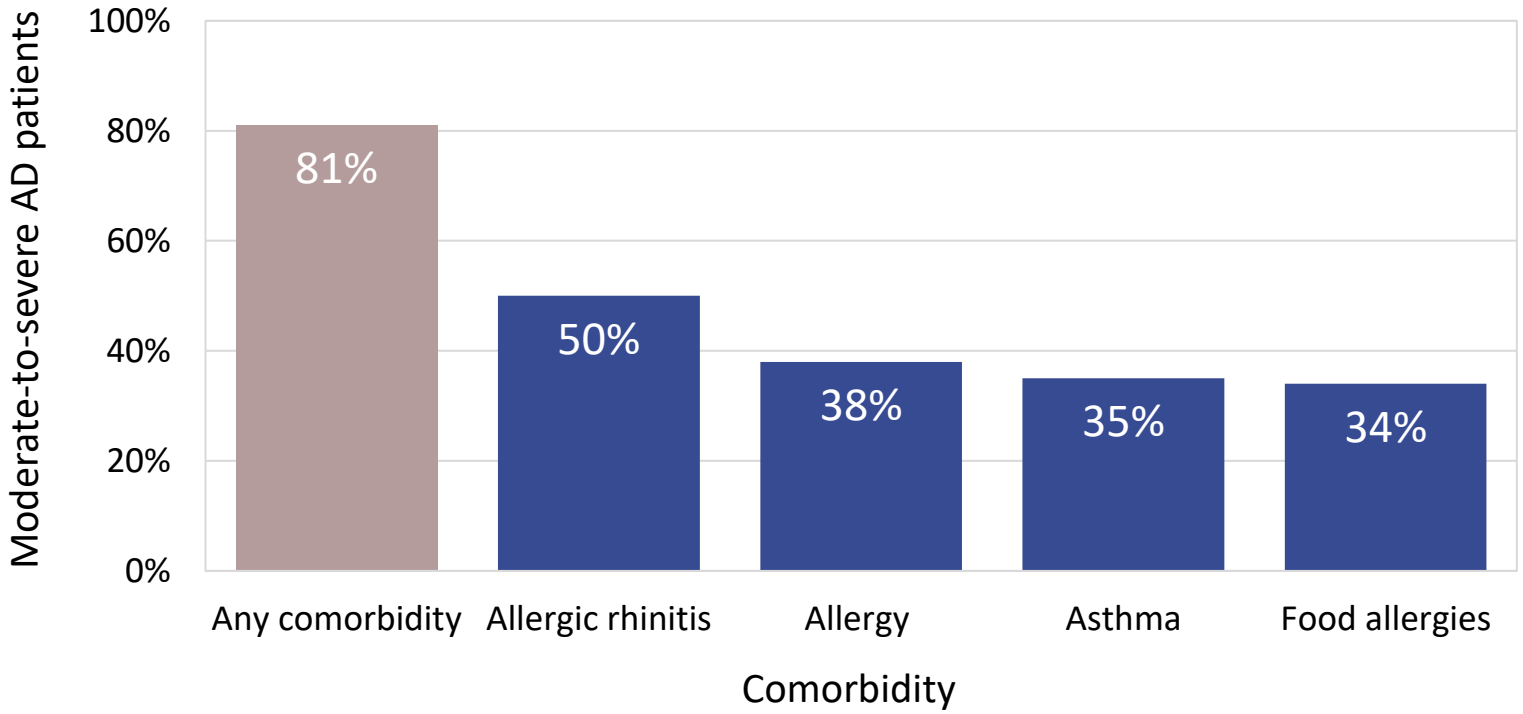


- Blockade of the Type 1 receptor may drive T-cells to a pro-inflammatory T_H1 phenotype
- This may lead to unwanted side effects, such as conjunctivitis

1 Dupixent full prescribing information
2 Halling et al (2021) JAAD 84:139-147
3 Simpson et al (2022) AAD Annual Meeting, 25-29 March 2022.

Eblasakimab may be efficacious against a wide range of AD comorbidities, such as asthma and allergy

81% of moderate-to-severe AD patients have Type 2 inflammatory comorbidities:



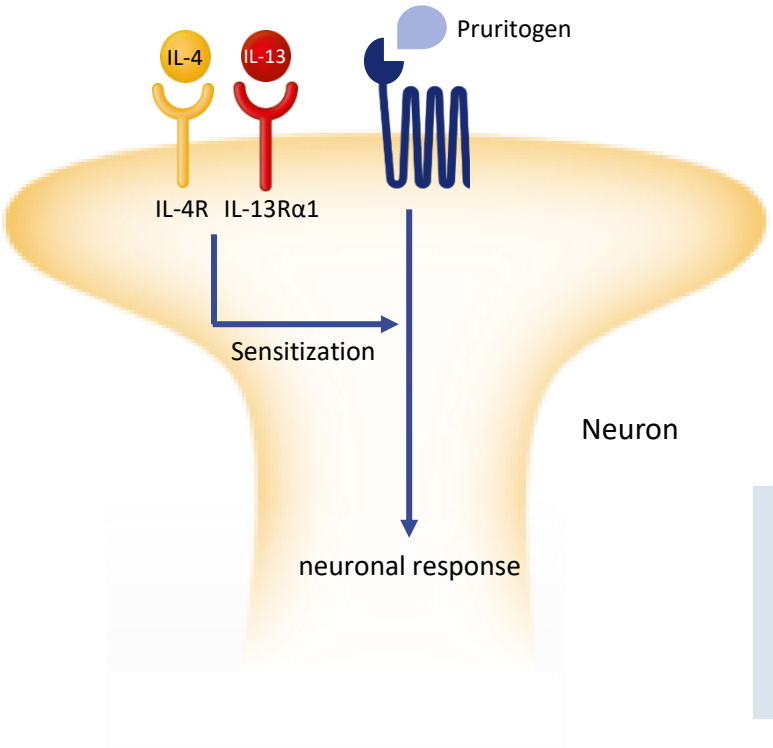
Blockade of IL-4 and IL-13 signaling through the Type 2 receptor will be important to address both IL-4 and IL-13 driven comorbidities in AD patients.

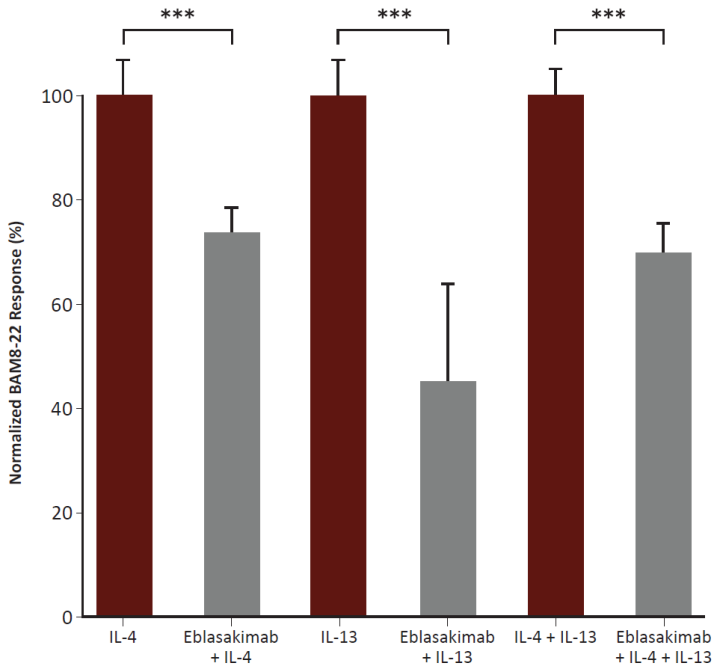
Physicians would prefer treatment options that can address these other conditions.

Calzavara-Pinton et al (2022) AAD Annual Meeting poster: Baseline patient demographics and comorbidities in patients with atopic dermatitis from the GLOBOSTAD registry (237 patients).

Eblasakimab blocks the Type 2 receptor on itch neurons supporting the potential for rapid itch relief

The Type 2 receptor is expressed on certain itch-specific neurons. IL-13 and IL-4 believed to amplify itch responses





- *Ex vivo* studies performed on human sensory neurons
- IL-4 and IL-13 enhanced the neuronal itch response via the Type 2 receptor
- *Eblasakimab* significantly reduced neuronal responses to IL-4, IL-13, and their combination by an average of up to 50% ($p<0.0001$)

These results suggest a molecular basis for the significant reduction of pruritus scores observed in *eblasakimab*-treated moderate-to-severe AD patients in the Phase 1b clinical trial

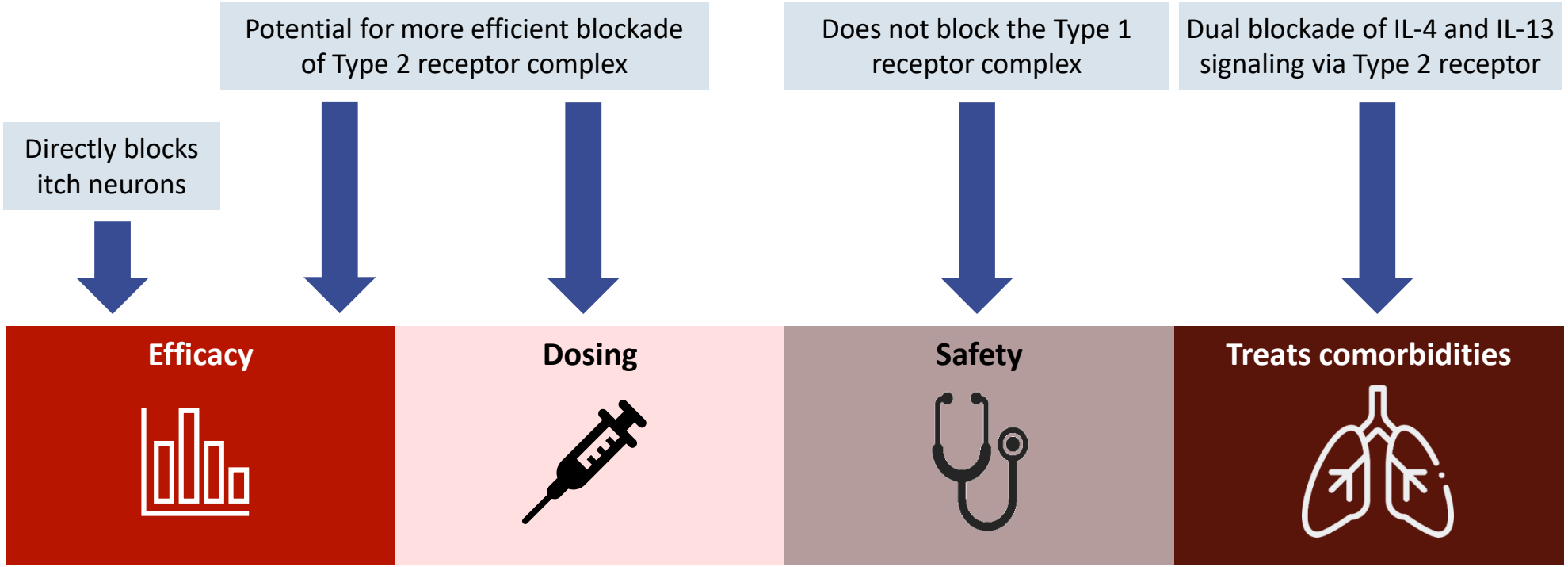
Total N=11 across four tested conditions, at 24hr timepoint.

New data on neuronal itch at ESDR

New data on neuronal itch and differentiated neuromodulation will be shared at ESDR, Amsterdam, Netherlands, late breaker session

Eblasakimab has the potential to be a differentiated therapy in AD

What makes *eblasakimab* different?



Ideal target product profile	Better efficacy over current standard-of-care with rapid control of itch	Less frequent and more convenient dose regimen	Addresses physician concerns on safety with lower rate of discontinuation	Able to address allergic comorbidities such as asthma and rhinitis

Dr Shawn Kwatra
Johns Hopkins School of Medicine

Welcome

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Type 2 inflammation and beyond

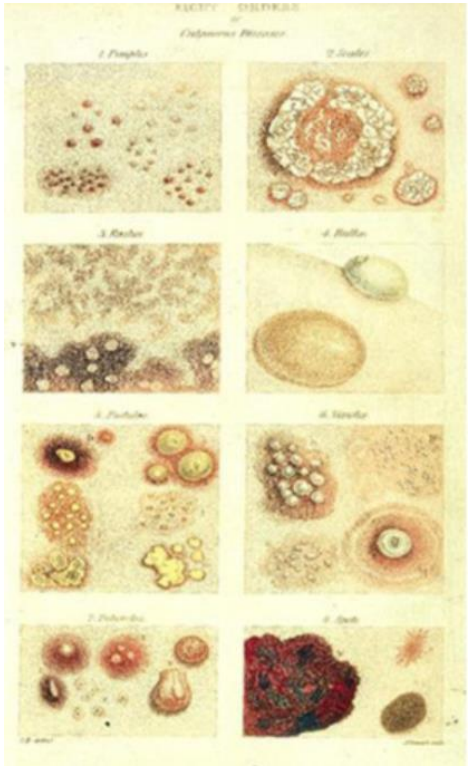
DR SHAWN KWATRA

DIRECTOR, JOHNS HOPKINS ITCH CENTER

ASSOCIATE PROFESSOR OF DERMATOLOGY

JOHNS HOPKINS SCHOOL OF MEDICINE

A brief molecular history of dermatology



Centuries of non-specific therapies until the last few decades

Psoriasis heralded a new era in targeted therapeutics

Journal of *Clinical Medicine*

MDPI

Review

Translational Relevance of Mouse Models of Atopic Dermatitis

Justin Choi [1,2], Nishadh Sutaria [1], Youkyung Sophie Roh [1], Zachary Bordeaux [1], Martin P. Alphonse [1], Shawn G. Kwatra [1,*] and Madan M. Kwatra [2]

The revolution in atopic dermatitis, inflammatory skin diseases & itch is driven by translational human research

Lessons from psoriasis treatment

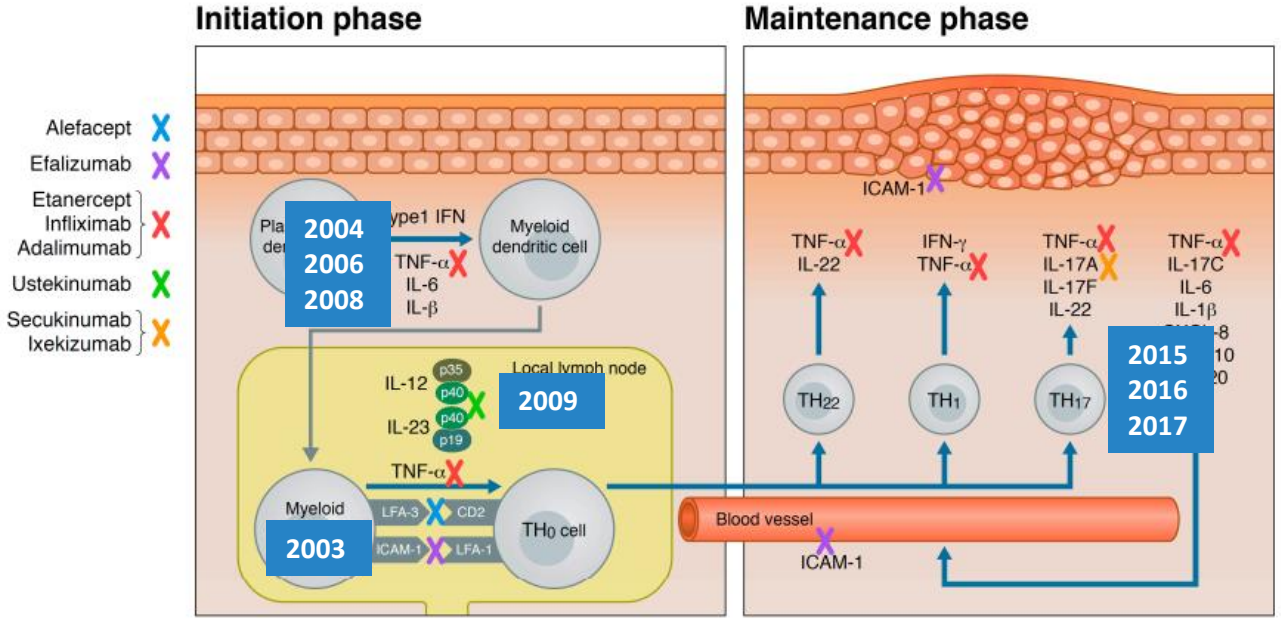
International Journal of *Molecular Sciences*

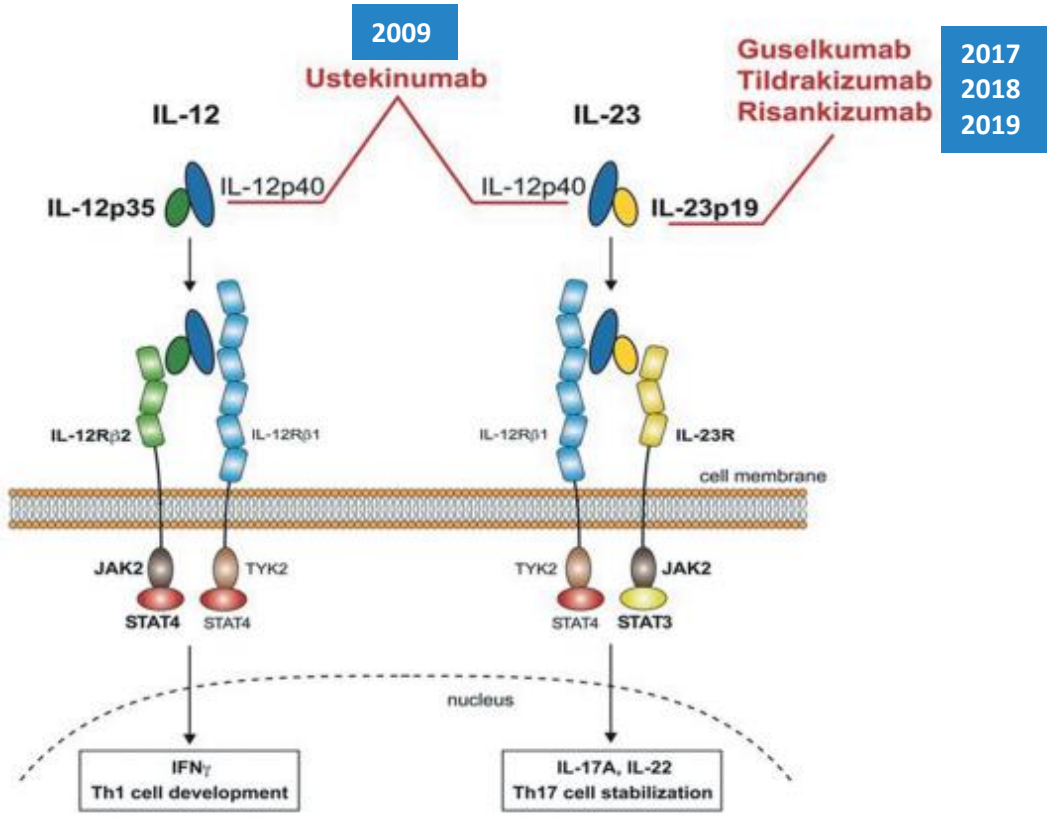
MDPI

Review

Old and New Biological Therapies for Psoriasis

Kirsten Rønholt * and Lars Iversen





THE LANCET

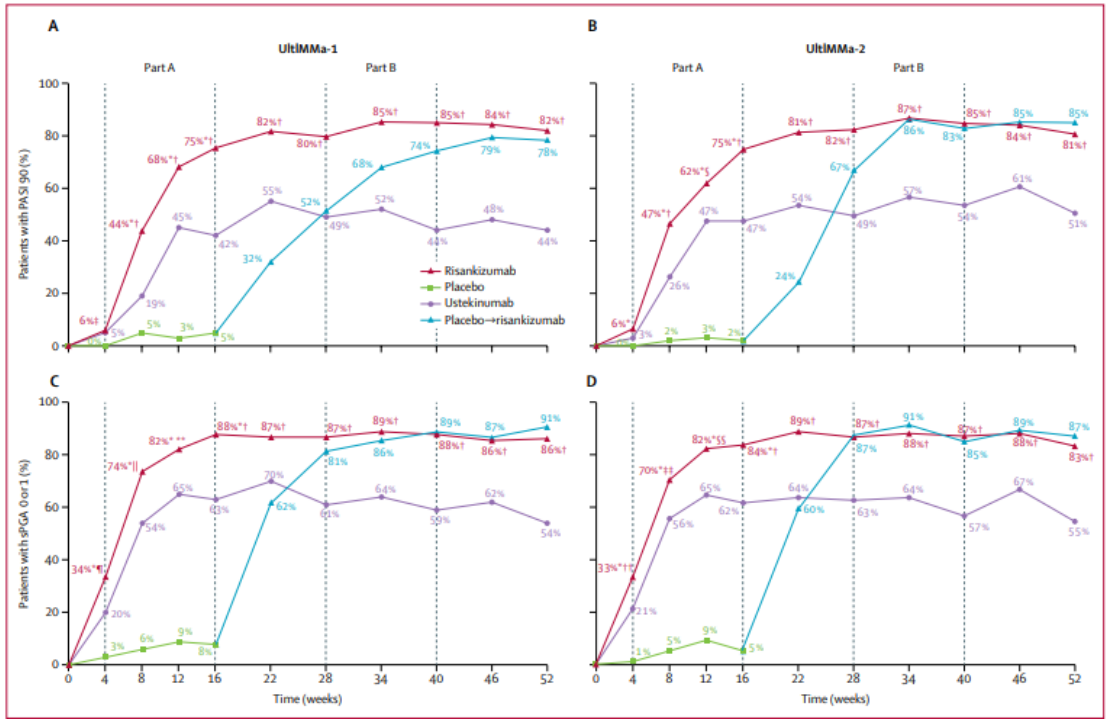
Efficacy and safety of risankizumab in moderate-to-severe plaque psoriasis (UltIMMa-1 and UltIMMa-2): results from two double-blind, randomised, placebo-controlled and ustekinumab-controlled phase 3 trials

Kenneth B Gordon, Bruce Strober, Mark Lebwohl, Matthias Augustin, Andrew Blauvelt, Yves Poulin, Kim A Papp, Howard Sofen, Lluís Puig, Peter Foley, Mamitaro Ohtsuki, Mary Flack, Ziqian Geng, Yihua Gu, Joaquin M Valdes, Elizabeth H Z Thompson, Hervé Bachelez

	UltIMMA-1			UltIMMA-2		
	Risankizumab (n=304)	Ustekinumab (n=100)	Placebo (n=102)	Risankizumab (n=294)	Ustekinumab (n=99)	Placebo (n=98)
Any adverse event	151 (49·7%)	50 (50·0%)	52 (51·0%)	134 (45·6%)	53 (53·5%)	45 (45·9%)
Serious adverse events	7 (2·3%)	8 (8·0%)	3 (2·9%)	6 (2·0%)	3 (3·0%)	1 (1·0%)
Severe adverse events	6 (2·0%)	3 (3·0%)	5 (4·9%)	7 (2·4%)	6 (6·1%)	1 (1·0%)
Adverse event leading to drug discontinuation	2 (0·7%)	2 (2·0%)	4 (3·9%)	1 (0·3%)	0	1 (1·0%)
Infections	75 (24·7%)	20 (20·0%)	17 (16·7%)	56 (19·0%)	20 (20·2%)	9 (9·2%)
Serious infections	1 (0·3%)	3 (3·0%)	0	3 (1·0%)	1 (1·0%)	0
Active tuberculosis	0	0	0	0	0	0
Latent tuberculosis	0	0	0	0	0	0
Adjudicated major adverse cardiovascular event	0	0	0	0	0	0
Malignancies	1 (0·3%)	0	1 (1·0%)	1 (0·3%)	0	0
Malignancies excluding non-melanoma skin cancer	0	0	0	0	0	0
Serious hypersensitivity	0	0	0	0	0	0
Deaths (including non-treatment emergent)	0	0	0	1 (0·3%)*	0	0

Any adverse event with grade 3 or grade 4 on Rheumatology Common Toxicity Criteria severity grading was considered severe. *One non-treatment emergent death of unknown cause on study day 189 occurred 161 days after last dose of study drug and fell outside of the treatment-emergent window.

Table 3: **Treatment-emergent adverse events during part A in UltIMMa-1 and UltIMMa-2**



Risankizumab: clinical considerations in moderate to severe plaque psoriasis

- Humanized IgG1 monoclonal antibody that binds to and blocks the proinflammatory effects of IL-23
- More effective than placebo, ustekinumab, adalimumab, secukinumab and fumaric acid esters in reducing the severity and extent of plaque psoriasis
- Improves health-related quality of life
- Generally well tolerated

Lessons from psoriasis

JOURNAL OF DERMATOLOGICAL TREATMENT
https://doi.org/10.1080/09546634.2022.2095328

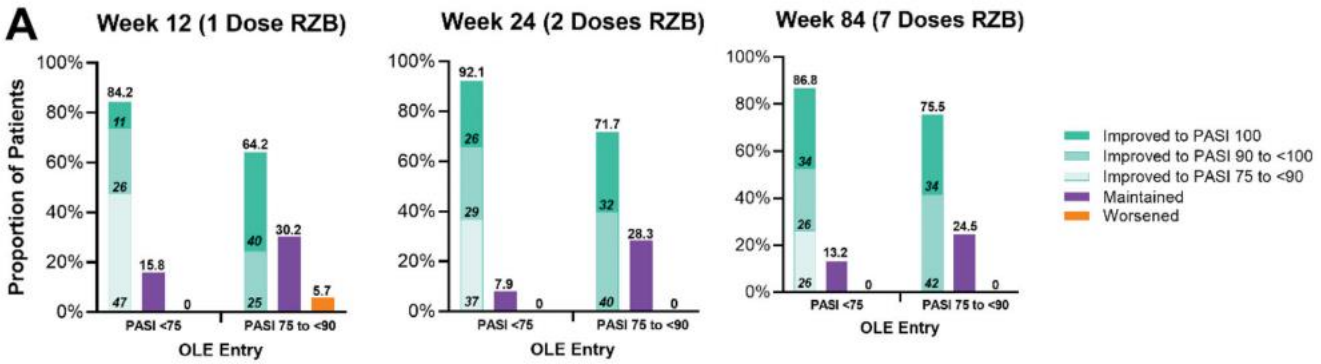
Taylor & Francis
Taylor & Francis Group

ARTICLE

OPEN ACCESS Check for updates

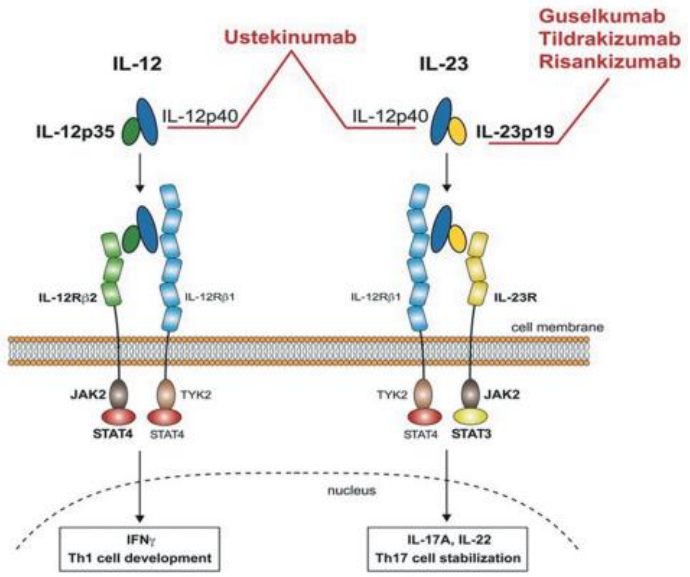
Switching to risankizumab from ustekinumab or adalimumab in plaque psoriasis patients improves PASI and DLQI outcomes for sub-optimal responders

Bruce Strober[a], April Armstrong[b], Simone Rubant[c], Manish Patel[c], Tianshuang Wu[c], Huzefa Photowala[c] and Jeffrey Crowley[d]

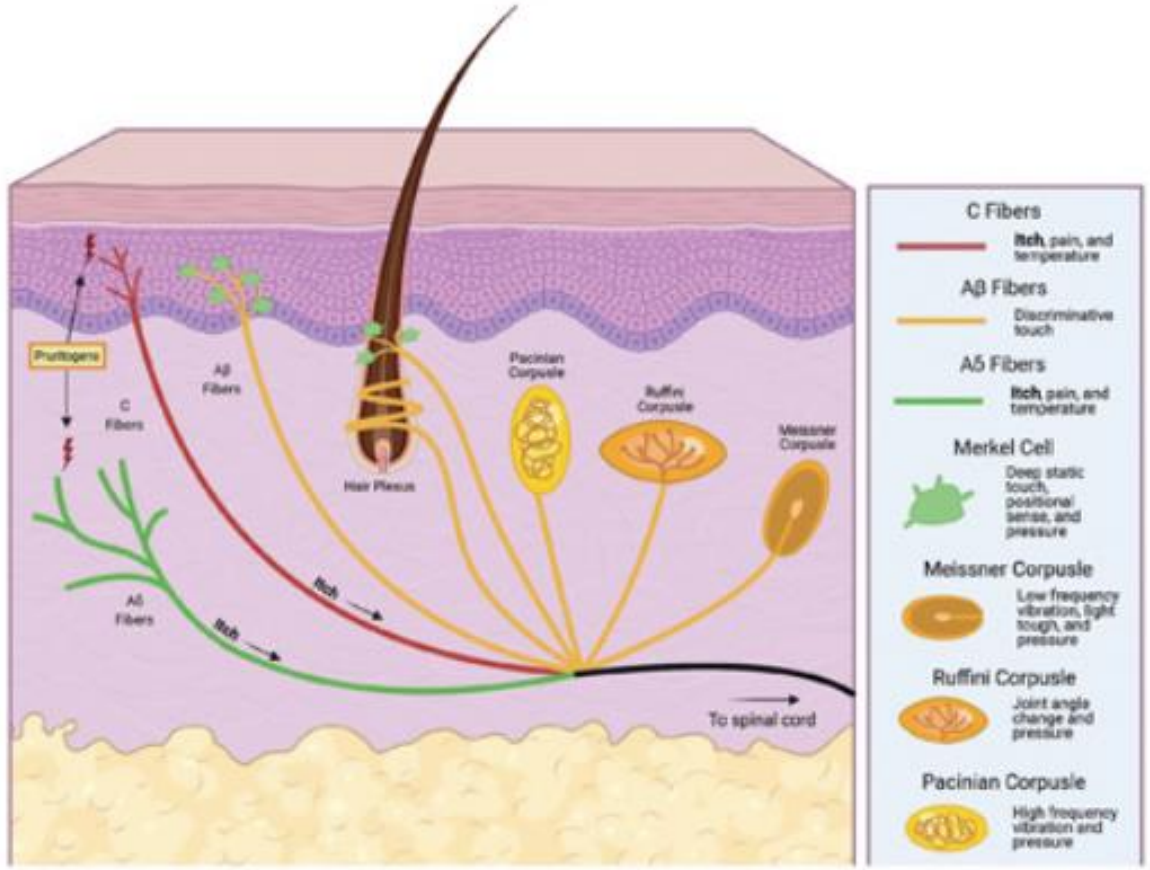


Patients with inadequate response to ustekinumab had improved response with risankizumab

Targeting different subunits of the same molecular pathway can lead to different clinical outcomes



Atopic Dermatitis and Itch



Helping dermatologists improve patient outcomes

Pruritus

Clinical & Translational Immunology

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REVIEW

Molecular and cellular mechanisms of itch and pain in atopic dermatitis and implications for novel therapeutics

Shawn G Kwatra[1], Laurent Misery[2], Claire Clibborn[3] & Martin Steinhoff[4,5,6,7,8,9]

Itch: Pathogenesis and treatment

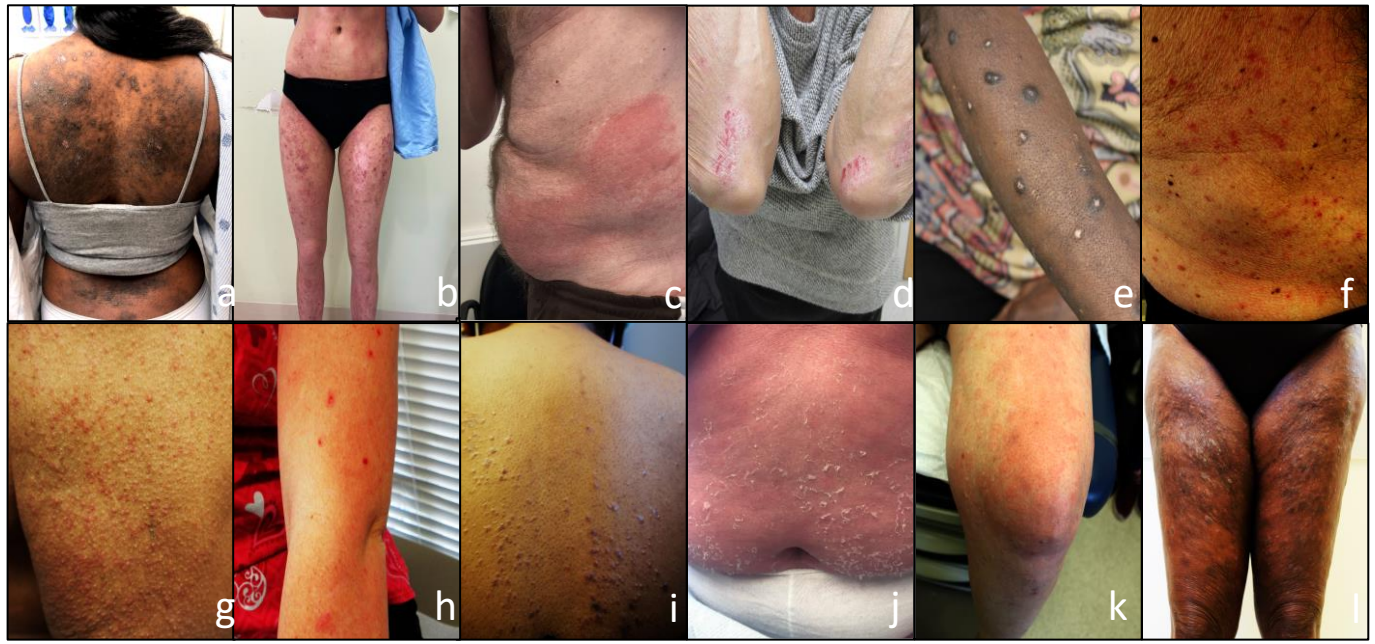
Nishadh Sutaria, BS,[a] Waleed Adawi, MS,[a] Rebecca Goldberg, BS,[a] Youkyung S. Roh, BA,[a] Justin Choi, BA,[a] and Shawn G. Kwatra, MD[a,b]
Baltimore, Maryland

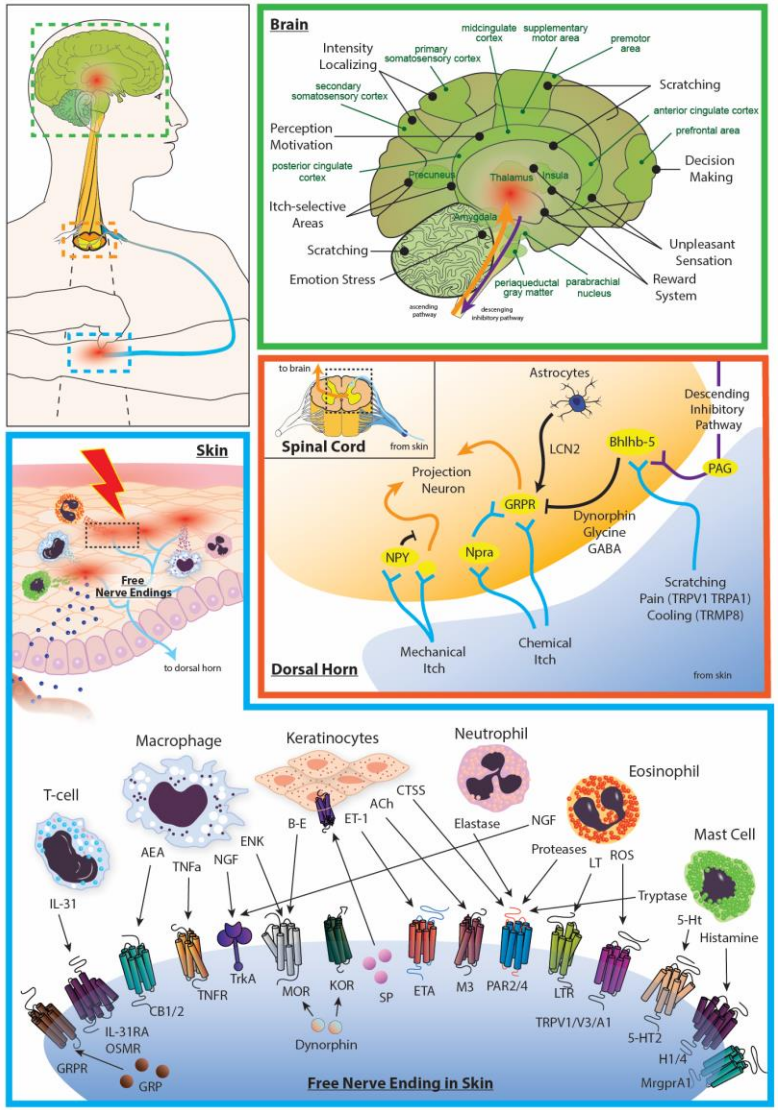
CONTINUING MEDICAL EDUCATION

Itch: Epidemiology, clinical presentation, and diagnostic workup

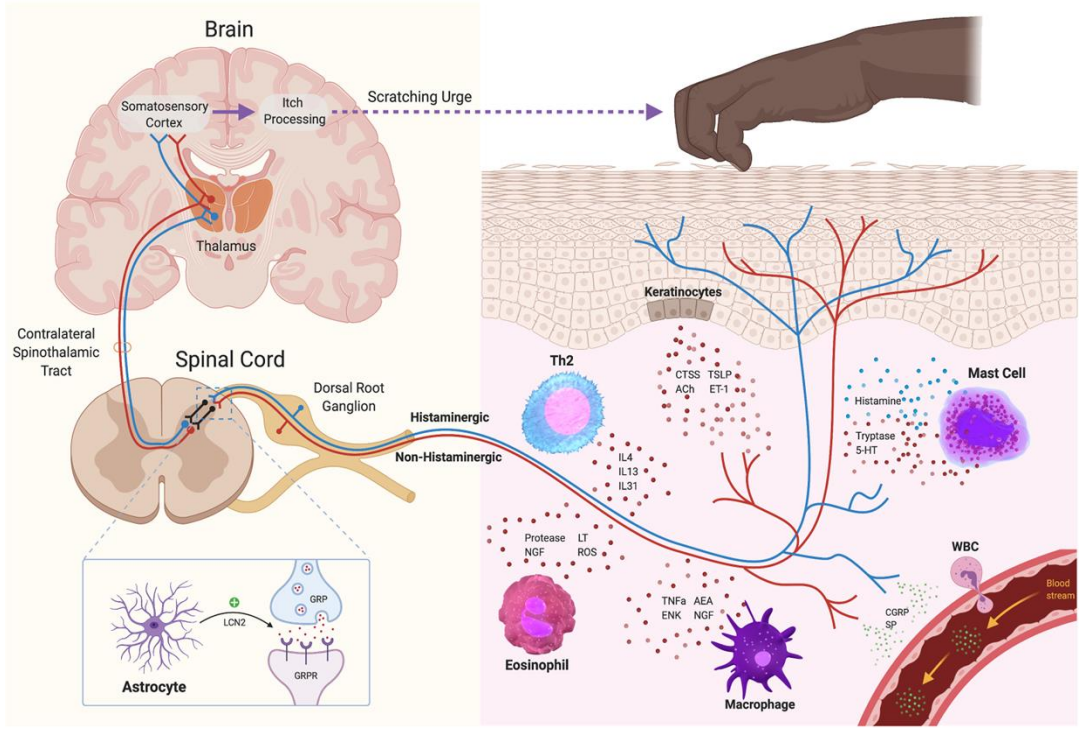
Youkyung S. Roh, BA,[a] Justin Choi, BA,[a] Nishadh Sutaria, BS,[a] and Shawn G. Kwatra, MD[a,b]
Baltimore, Maryland

Itch Translational Perspectives

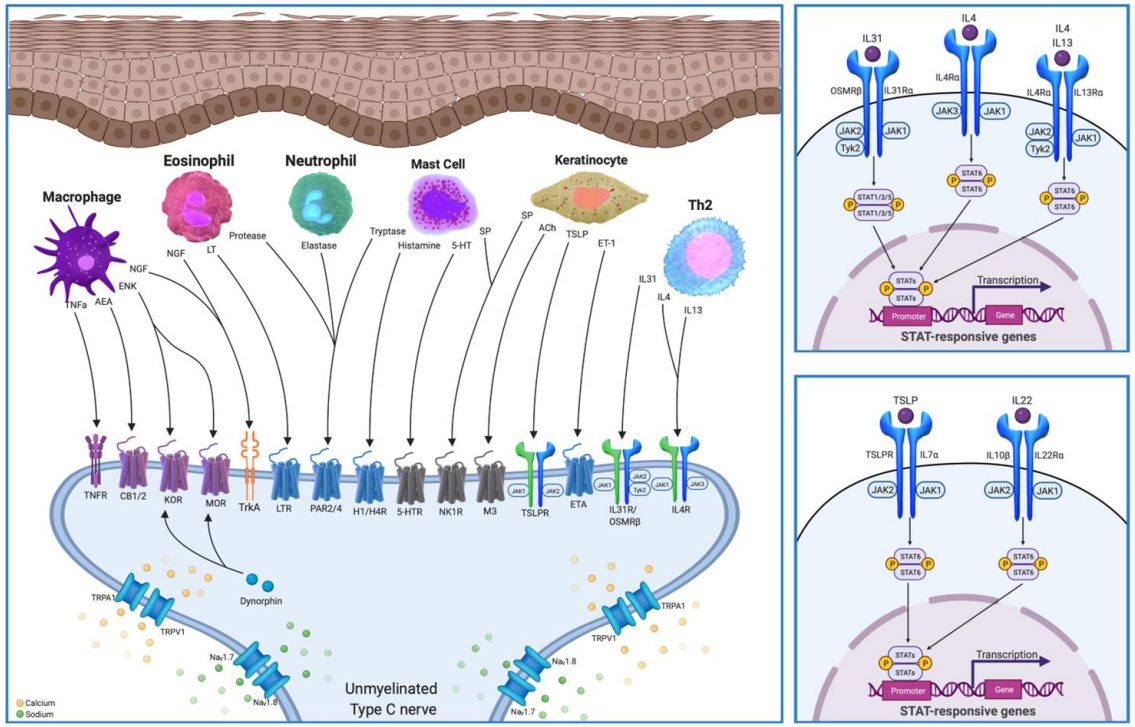




Itch pathway and Type 2 inflammation

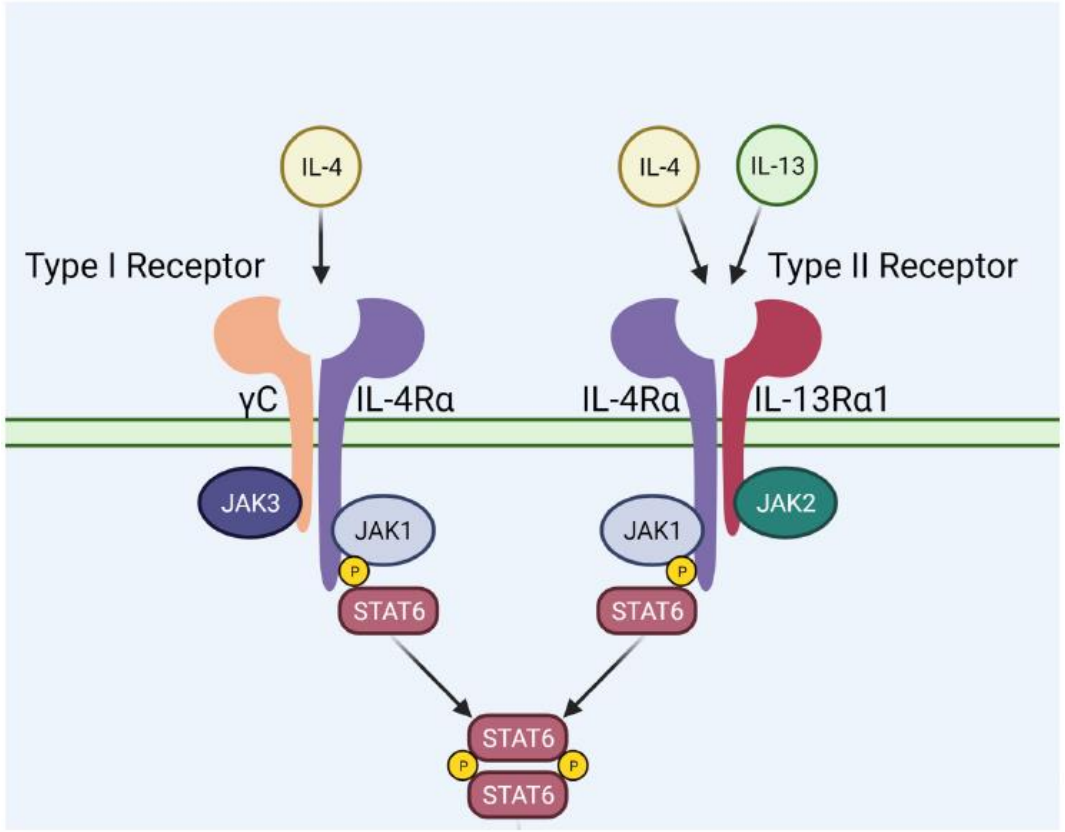


Sutaria et al, Kwatra SG. *J Am Acad Dermatol*. 2022.



Sutaria et al., Kwatra SG. *J Am Acad Dermatol*. 2022.

Understanding downstream molecular effects of eblasakimab

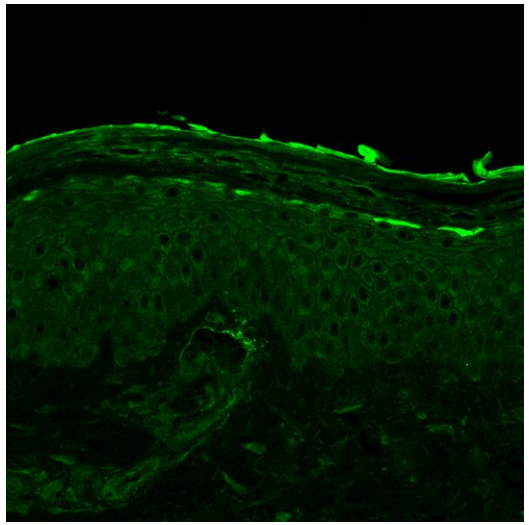


Research collaboration to investigate the differentiated functional roles of Type 1 and Type 2 signaling by selective targeting different receptor subunits

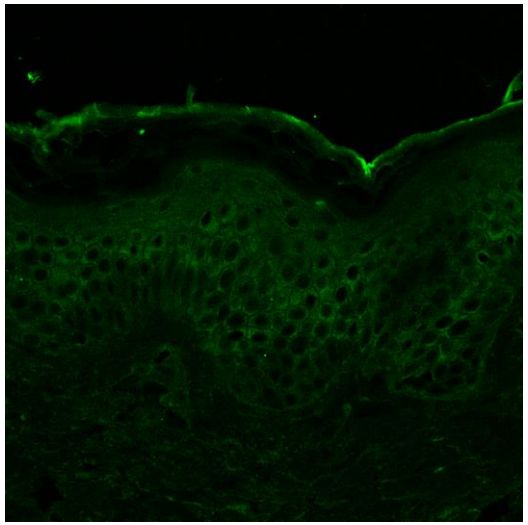
Studies will be conducted with AD patient-derived PBMCs and samples will be analysed by transcriptomic and proteomic approaches

Determining the distribution and intensity of IL-13Rα1 expression in lesional and nonlesional AD skin

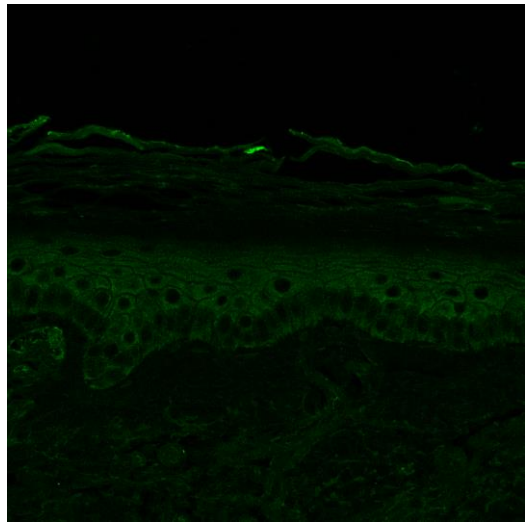
AD Lesional



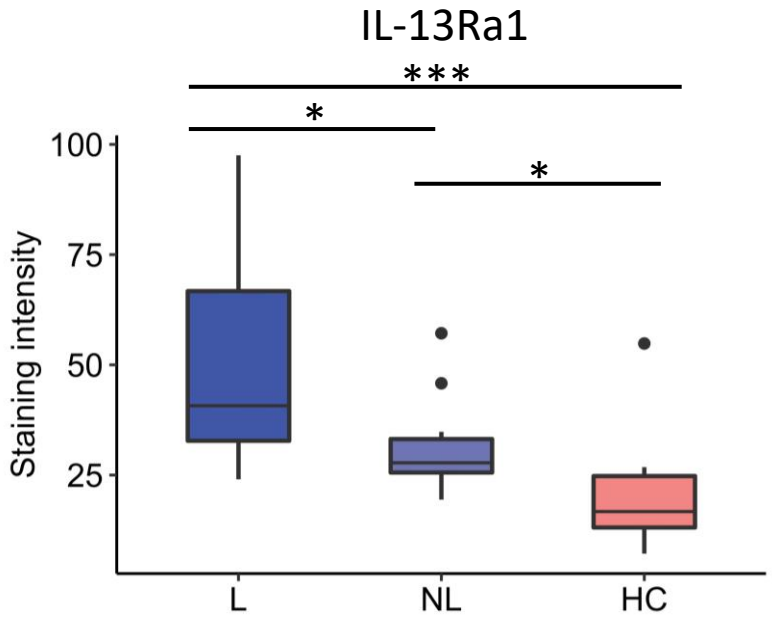
AD Non-lesional



Healthy Control (HC)



Immunofluorescent staining of IL-13Rα1 in lesional AD, non-lesional AD and healthy control skin. Images are shown at 40X magnification.

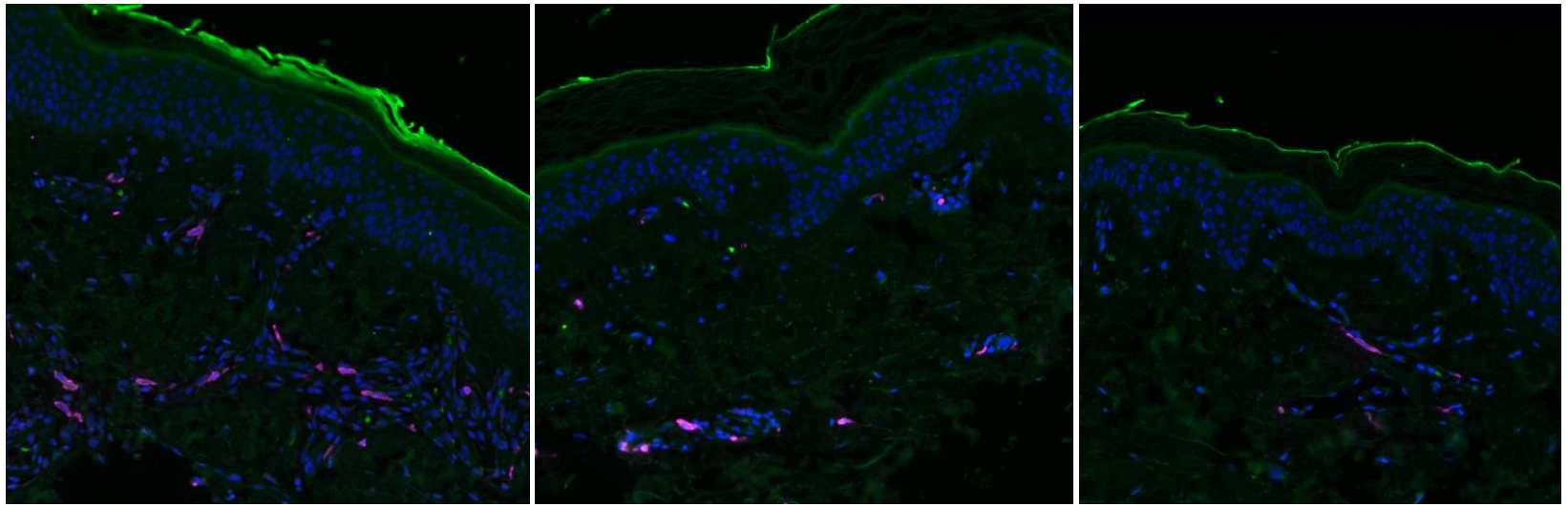


Quantification of IL-13Rα1 shows increased expression in lesional AD skin compared to non-lesional AD and control skin. IL-13Rα1 expression is also increased in non-lesional AD compared to control skin. *p<.05; **p<.01; ***p<.001

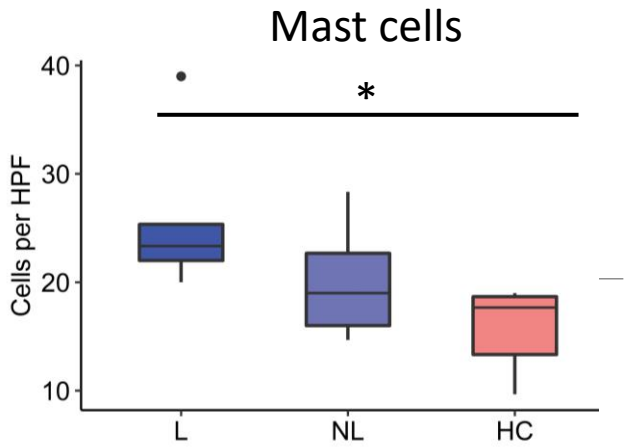
IL-13Rα1 expression is increased in atopic dermatitis

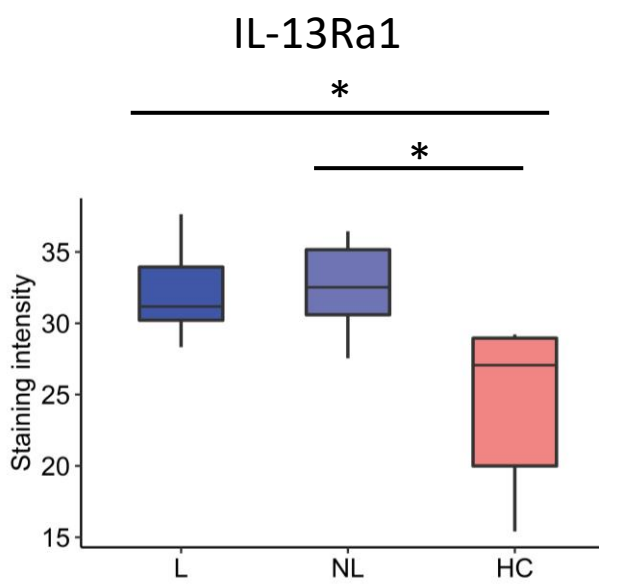
Mast cells

Lesional | Non-Lesional | Healthy control



Immunofluorescent staining of IL-13Rα1 and tryptase in lesional AD, non-lesional AD and healthy control skin. Images are shown at 20X magnification.





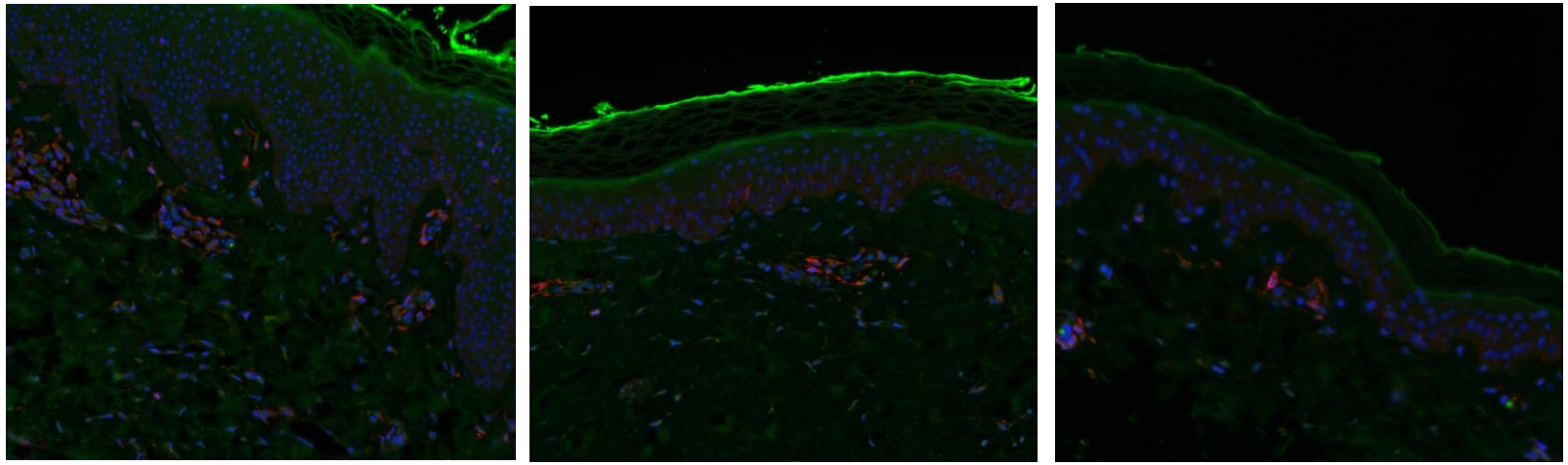
Mast cell number is increased in L AD compared to HC. Compared to HC, L and NL AD mast cells show increased average IL-13Ra1 staining. *p<.05

Eosinophil numbers

Lesional

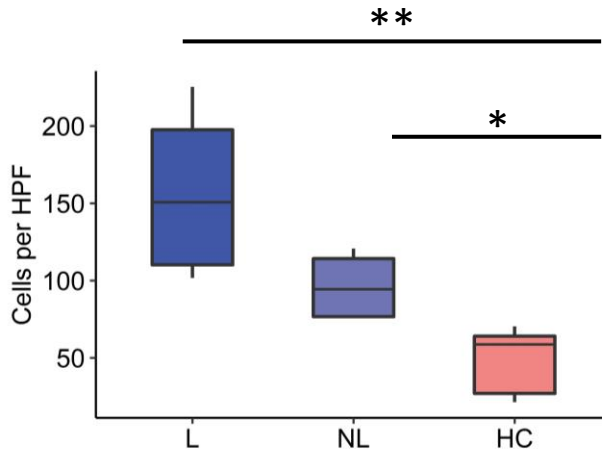
Non-Lesional

HC

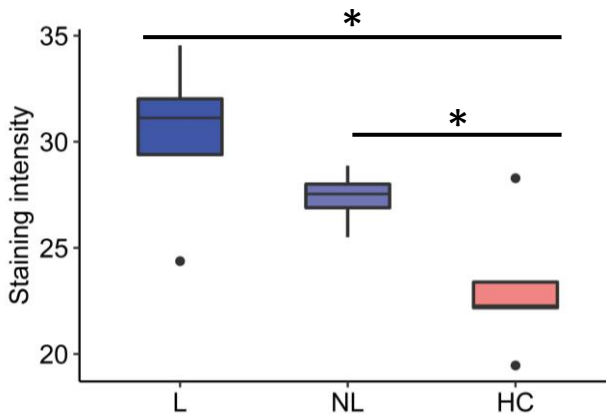


Immunofluorescent staining of IL-13Rα1 and major basic protein in lesional AD, non-lesional AD and healthy control skin. Images are shown at 20X magnification.

Eosinophils



IL-13Ra1

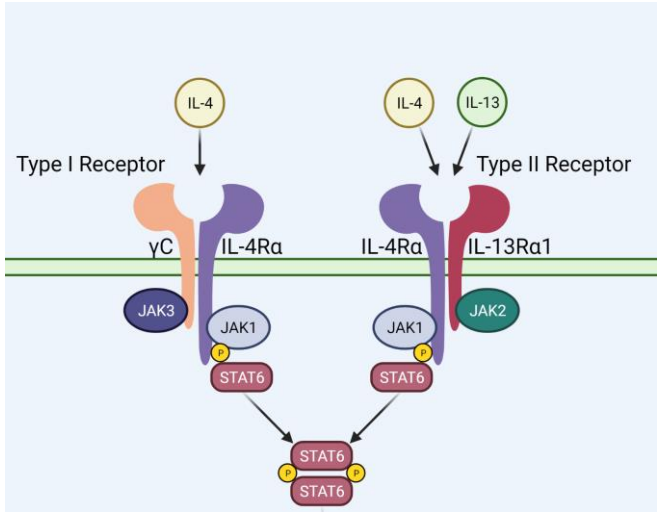


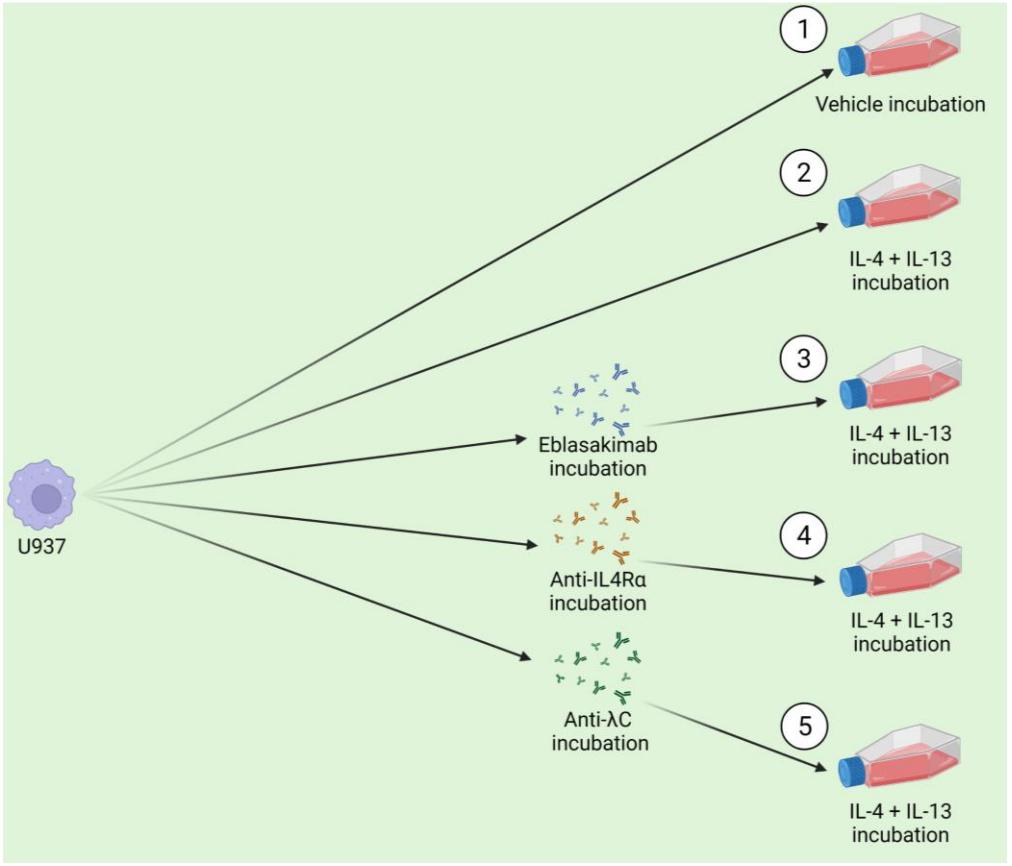
Eosinophil number is increased in L and NL AD compared to HCs. Average eosinophil IL-13Ra1 staining is increased in L and NL AD compared to HCs. *p<.05; **p<.01

Determining signaling differences between type I and type II receptors in cell culture models

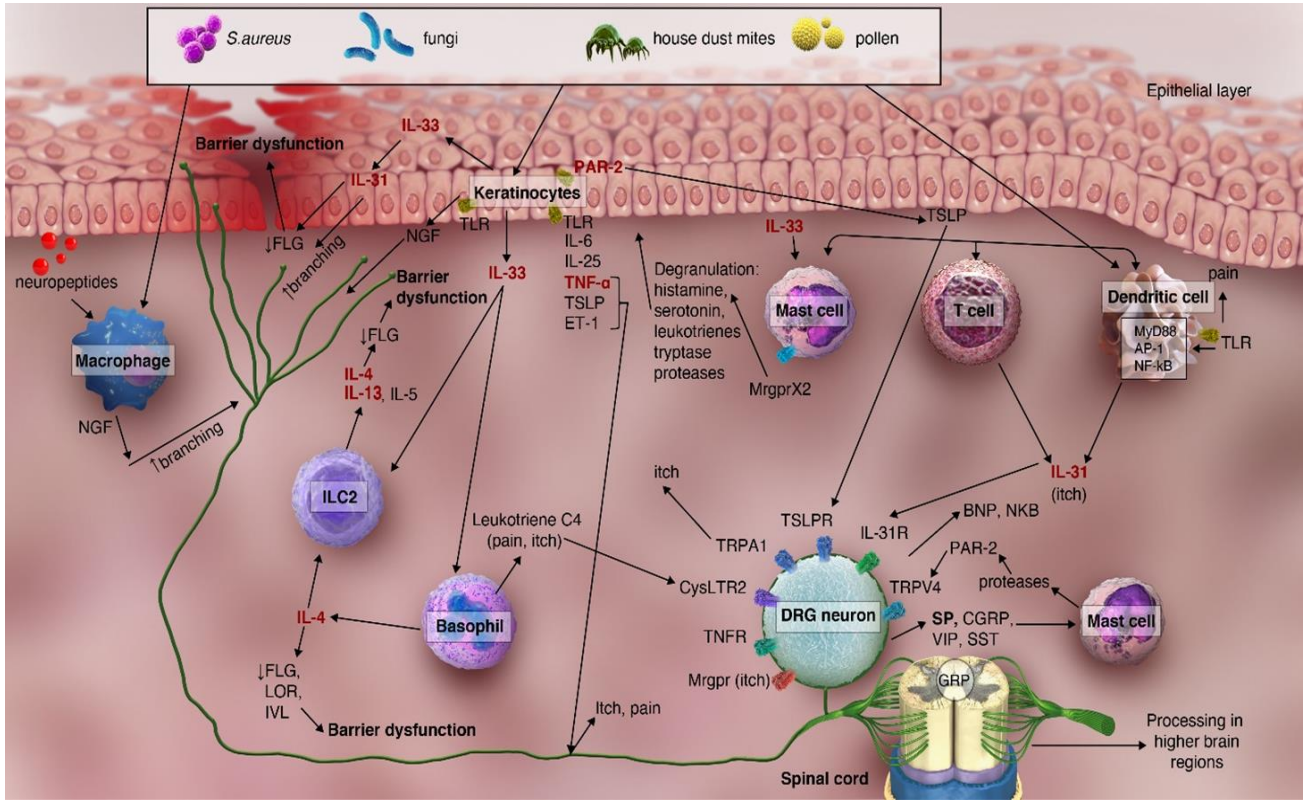
Approach

We used U937 Cells, a monocyte cell line, that expresses both type I and type II receptors





Shared mechanisms of Type 2 inflammation and itch across different indications



Kwatra et al. *Clin Transl Immunology. 2022.*

- ✓You scratch off the intraepidermal nerve fibers
- ✓The nerve fibers need to regrow
- ✓This “activates” the itch nerves
- ✓It takes time to regrow the intraepidermal nerve fibers- NEURAL Healing
- ✓Treating the itch to stop the scratching is critical to breaking the “ITCH-SCRATCH CYCLE”
- ✓Similar for chronic itch in AD, PN, CU, BP, CPUO
- ✓Key itch mediators are shared across these diseases
- ✓Targeting IL-4 and IL-13 as sensitizers might provide relief across type-2 underlining diseases

Type 2 Inflammatory Diseases

bioRχiv
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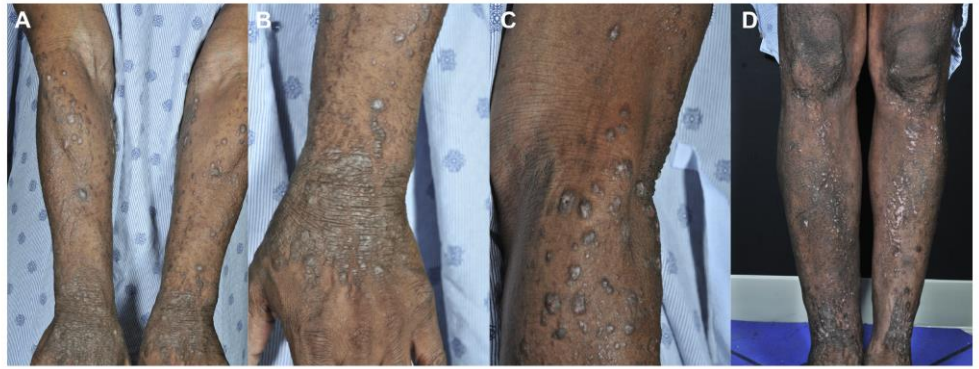
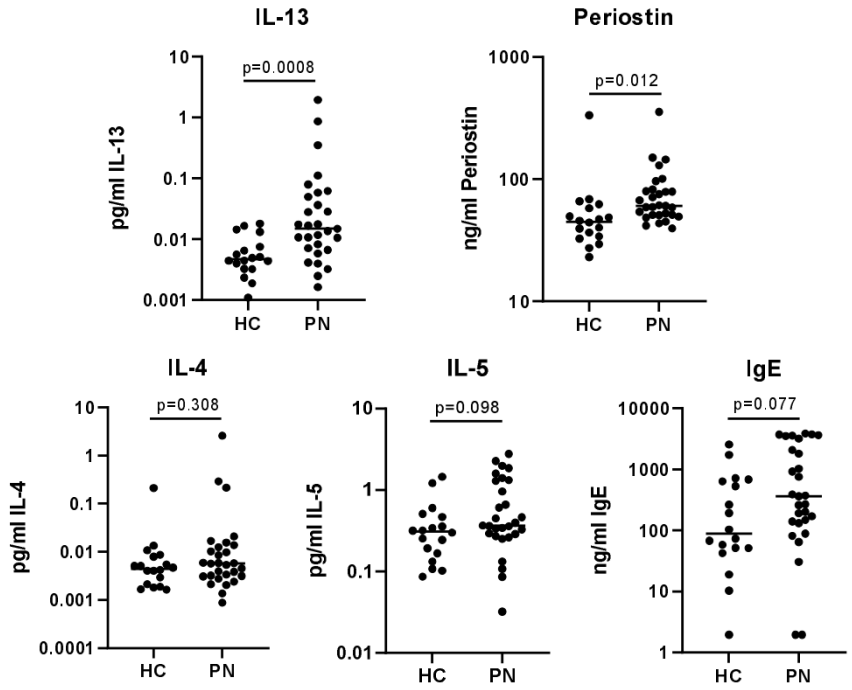
Circulating plasma IL-13 and periostin are dysregulated type 2 inflammatory biomarkers in prurigo nodularis: a cluster analysis

Varsha Parthasarathy, Karen Cravero, Junwen Deng, Zhe Sun, Sarah Engle, Autum Auxier, Nathan Hahn, Jonathan T. Sims, Angela Okragly, Martin P. Alphonse, Shawn G. Kwatra

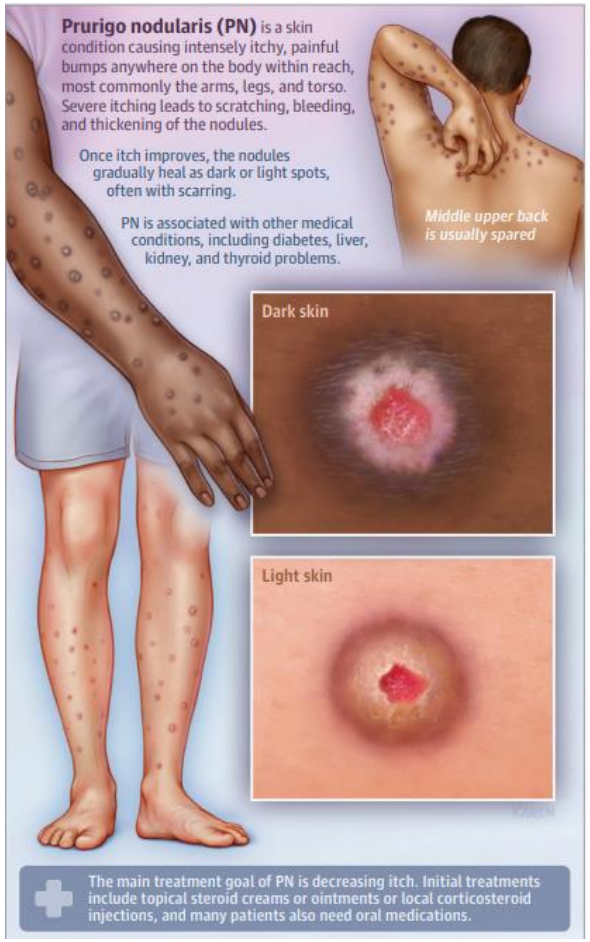
doi: https://doi.org/10.1101/2022.06.07.495051





McColl et al. *J Natl Med Assoc*. 2021.

Unmet needs in prurigo nodularis and chronic pruritus of unknown origin



JID JOURNAL OF INVESTIGATIVE DERMATOLOGY

A Nationwide Study of Prurigo Nodularis: Disease Burden and Healthcare Utilization in the United States

Shannon Wongvibulsin • Nishadh Sutaria • Kyle A. Williams • ... Anant Walia • Yevgeniy R. Semenov [6]
Shawn G. Kwatra [6] • Show all authors • Show footnotes

Published: April 03, 2021 • DOI: https://doi.org/10.1016/j.jid.2021.02.756 • Check for updates

Chronic pruritus of unknown origin

Clinical Communications

Circulating blood eosinophils as a biomarker for variable clinical presentation and therapeutic response in patients with chronic pruritus of unknown origin

Youkyung S. Roh, BA[a,*], Raveena Khanna, BA[a,*], Sagar P. Patel, MD[a], Shilpa Gopinath, MPH[a], Kyle A. Williams, BS[a], Ravya Khanna, BA[a], Thomas Pritchard, MPH[a], Nishadh Sutaria, BS[a], Justin Choi, BA[a], Martin P. Alphonse, PhD[a], Madan M. Kwatra, PhD[b], and Shawn G. Kwatra, MD[a,c]

Several conditions affected by inflammation and itch including prurigo nodularis (PN), Chronic Spontaneous Urticaria (CSU), Bullous Pemphigoid (BP), etc

These conditions have high unmet needs, no targeted therapies, further discovery of molecular pathways holds future promise

1. Kwatra SG. *JAMA Dermatol*. 2022.
2. Wongvibulsin S, et al. *J Invest Dermatol*. 2021.

Conclusion

- Characterisation of molecular pathways in disease has been revolutionary for patients with dermatological conditions
- Targeting different molecular pathways can make an impact on clinical outcomes
- Type 2 receptor plays an important role in driving inflammation and itch pathways
- IL-13R is expressed on AD skin and upcoming research to highlight its distinct role in AD versus the other subunits of the Type 2 receptor
- Discoveries in itch mechanisms can extend to a number of conditions with high unmet needs

Q&A

Dr Carl Firth
CEO
ASLAN

Dr Peter Lio
Northwestern University

Stephen Doyle
Chief Business Officer
ASLAN

Dr Ferda Cevikbas
Head of Translational Science
ASLAN

Dr Shawn Kwatra
Johns Hopkins University

Program will continue after a short break

Dr Karen Veverka
VP Medical

Welcome

Emerging unmet needs in Atopic Dermatitis (AD)

Eblasakimab: addressing the market needs and opportunities

Promise of targeting the IL-13 receptor

Type-2 inflammation and beyond

Q&A

New findings from the proof-of-concept study

Eblasakimab development program

Company Q&A

Panel discussion

Closing remarks

New clinical data presented at EADV (September 7-10, 2022)

P0343

Eblasakimab improves multiple disease measures in adult patients with moderate-to-severe atopic dermatitis in a randomized, double-blinded, placebo-controlled, Phase 1 study

Karen A. Veverka[1], Josemund Menezes[1], Steven Tien Guan Thng[2], Melinda Gooderham[3], Eric Simpson[4]
1. ASLAN Pharmaceuticals, Menlo Park, CA, and Singapore. 2. Skin Research Institute of Singapore, Agency for Science Technology & Research, Singapore; National Skin Center, Singapore. 3. SKiN Centre for Dermatology, Peterborough, ON, Canada; Queens University, Kingston, ON, Canada; Probity Medical Research, Waterloo, ON, Canada.
4. Department of Dermatology, Oregon Health & Science University, Portland, OR, USA

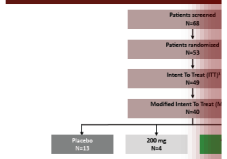
Background

- Interleukin (IL)-4 and IL-13 are key drive
(AD). Both signal through a shared type
comprised of IL-4Rα and IL-13Rα1.
- Eblasakimab (ASLAN004), a first-in-class
antibody binds IL-13Rα1 with high affini
IL-4 and IL-13 through the type-2 recept
- A randomized, double-blind, placebo-c
ascending dose monotherapy study [N
safety, tolerability, and clinical properti
in adult patients with moderate-to-seve
been reported previously (Blauvelt 202
- The objective of this study was to furth
endpoints of clinical relevance and post
Observations on patient reported outc
pharmacodynamic (PD) markers and ar
[**Posters P0342 & P0243**].

Methods

- Three patient cohorts were randomized
600 mg eblasakimab or placebo subcuta
weeks in a multiple ascending dose stud
methodology has been presented previo
- Adult patients were included with chron
before screening, and the following AD p
baseline: eczema area and severity inde
Global Assessment (IGA) score ≥3 (scale
surface area (BSA) of AD involvement. R
with active ingredient, topical corticoste
inhibitors) was not allowed; LOCF was us
rescue med.
- Efficacy assessments included percent cl
in EASI, proportions of patients with 50
EASI score (EASI 50 or EASI 75) or IGA 0/
involvement. Further data are presente
of patients from an excluded site with at
- Inferential statistical analysis was perfor
groups at week 8 only; results for 200 an
descriptively described due to small sam

*Analysis



- Efficacy analysis in the Phase 1b study
Treat (mITT) population in which 9 stu
were excluded from the ITT analysis p
participants did not have disease chara
moderate to severe AD.

P0342

Eblasakimab improves itch and sleep loss in adult patients with moderate-to-severe atopic dermatitis in a randomized, double-blinded, placebo-controlled, Phase 1 study

Karen A. Veverka[1], Josemund Menezes[1], Steven Tien Guan Thng[2], Eric Simpson[3]
1. ASLAN Pharmaceuticals, Menlo Park, CA, and Singapore. 2. Skin Research Institute of Singapore, Agency for Science Technology & Research, Singapore; National Skin Center, Singapore. 3. Department of Dermatology, Oregon Health & Science University, Portland, OR, USA

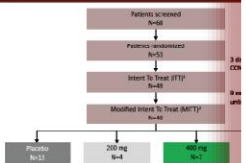
Background

- Interleukin-4 (IL-4) and IL-13 are key drivers of atop
(AD). Both signal through a shared type-2 receptor
comprised of IL-4Rα and IL-13Rα1.
- Eblasakimab (ASLAN004), a first-in-class, fully hum
antibody binds IL-13Rα1 with high affinity and bloc
IL-4 and IL-13 through the type-2 receptor.
- A randomized, double-blind, placebo-controlled, P
ascending dose monotherapy study [NCT0409022
safety, tolerability, and clinical properties for eblas
in adult patients with moderate-to-severe AD. Key
and observations on pharmacodynamic (PD) mark
separately [Veverka *et al.* EADV **Poster P0343**; Ce
Poster 243].
- The objective of this study was to evaluate the eff
eblasakimab on itch and sleep scores in AD.

Methods

- Three patient cohorts were randomized to receive
or 600 mg eblasakimab or placebo subcutaneous
8 weeks in a multiple ascending dose study design
AAD).
- Adult patients were included with chronic AD pres
before screening, and the following AD parameter
baseline: eczema area and severity index (EASI) ≥1
Global Assessment (IGA) score ≥3 (scale of 0 to 4),
body surface area (BSA) of AD involvement. Rescu
(moisturizer with active ingredient, topical corticos
topical calcineurin inhibitors) was not allowed; LOC
participants who used rescue medication.
- Patient reported outcomes were measured, includ
numeric rating scale (P-NRS) for both worst and a
Patient-Oriented Eczema Measure (POEM), which
item sleep loss component.
- Inferential statistical analysis was performed for 6
groups at week 8 only; results for 200 and 400 mg
descriptively described due to small sample size.

*Analysis



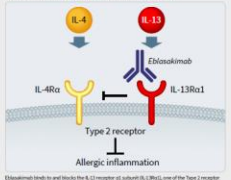
Eblasakimab, a Monoclonal Antibody Targeting IL-13Rα1 Reduces Serum Biomarkers Associated with Atopy and Correlated with Disease Severity in Patients With Moderate-to-Severe Atopic Dermatitis

Ferda Cevikbas[1], Jacob P. Thyssen[2], Eric Simpson[3], Alison Ward[1], Steven Tien Guan Thng[4], Karen A. Veverka[1]
[1]ASLAN Pharmaceuticals, California and Singapore, [2]Department of Dermatology, Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark
[3]Department of Dermatology, Oregon Health & Science University, Portland, OR, USA. [4]Skin Research Institute of Singapore, Agency for Science Technology & Research, Singapore; National Skin Center, Singapore

BACKGROUND

- Key inflammatory mediators of atopic dermatitis (AD) include interleukin-4 (IL-4) and IL-13, which both signal through a shared type 2 receptor, a heterodimer comprising IL-4Rα and IL-13Rα1.[1,2]
- Eblasakimab, a first-in-class, fully human monoclonal antibody binds IL-13Rα1 with high affinity and blocks the signaling of IL-4 and IL-13 through the type 2 receptor[3] (Figure 1).
- Elevated serum levels of specific biomarkers are associated with increased disease severity and exacerbations of AD.[4-6]
  - These biomarkers include thymus and activation regulated chemokine (TARC/CCL17), total immunoglobulin E (IgE), lactate dehydrogenase (LDH).
  - Reference range levels for these biomarkers in individuals without AD have been reported in the range of:
    - TARC/CCL17: 200 pg/mL[6]
    - Total IgE: 150 to 1,000 UI/mL (usually accepted upper limit is between 150 and 300 UI/mL)[6]
    - LDH: 105 to 333 U/L[7]
  - TARC/CCL17 is a chemokine involved in developing acute and chronic lesions in AD and serves as a biomarker for disease severity.[5]
  - IgE binds several immune cells and plays a role in the release of inflammatory mediators and antigen presentation in atopic dermatitis.[5]
  - LDH is an enzyme found in most cells and is known to be a marker of inflammation, but it also has been shown to correlate with levels of TARC/CCL17 and total IgE in patients with AD.[7]
- In a recent randomized multiple ascending dose (MAD) study (NCT04090229) eblasakimab demonstrated significant improvements in key measures of disease severity vs. placebo in patients with moderate-to-severe AD.[3]
  - Clinically relevant primary and secondary endpoint data are presented in poster #P0343, while patient reported outcomes are presented in poster #P0342.
- In the same study, pharmacodynamic assessments were performed to analyze AD biomarker levels in response to eblasakimab treatment in patients with moderate-to-severe AD.

Figure 1. Eblasakimab Mechanism of Action



Eblasakimab binds to and blocks the IL-13 receptor α1 subunit (IL-13Rα1), one of the Type 2 receptor components, thereby preventing signaling through both interleukin-4 (IL-4) and interleukin-13 (IL-13), key drivers of allergic inflammation in atopic dermatitis.
IL-4, interleukin-4; IL-4Rα, interleukin-4 receptor α; IL-13, interleukin-13; IL-13Rα1, interleukin-13 receptor α1 subunit

OBJECTIVE

RESULTS

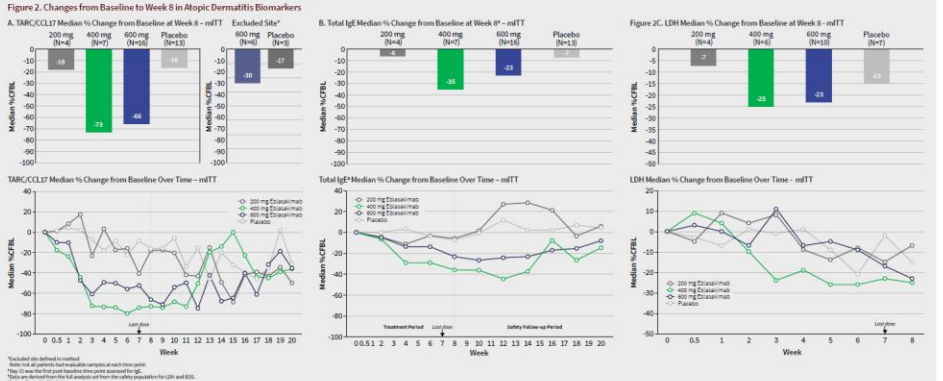
- A total of 40 patients were included in the mITT population analysis and received either eblasakimab at 200 mg (N=4), 400 mg (N=7), 600 mg (N=16), or placebo (N=13) (Table 1).
- Patient demographics and baseline characteristics for the mITT population were generally similar across dose cohorts, with a slightly younger population in the 400 mg group, a higher proportion of Asian patients in the 200 mg and 400 mg groups, and some differences in the level of elevation of biomarkers, particularly for TARC/CCL17 and total IgE (Table 1).
- The Excluded site* set was markedly different from the mITT set at baseline with substantially lower serum TARC/CCL17 (Table 1), serum IgE (Table 1), and EASI scores (Poster #0343) showing lower extent and severity of disease. Other notable differences included older age and lower IGA and BSA. Participants at this site had no atopic disease history but reported other comorbidities including diabetes and hypertension (Poster #0342).
- Baseline biomarker levels from the Excluded site* were, on average, within the reference range for individuals without AD, except for TARC/CCL17 levels, which were slightly elevated (Table 1).
- In the mITT population, eblasakimab reduced levels of pharmacodynamic markers IgE, TARC/CCL17, and LDH in the 400 mg and 600 mg dose groups after 8 weeks of once-weekly treatment, with a significant difference between 600 mg vs placebo for TARC/CCL17 (least squares [ls]-mean of -62.23 vs -17.83, P<0.001) (Figure 2A-C).
  - Reductions from baseline were observed as early as the first post-baseline assessment for TARC/CCL17 (day 4), IgE (day 15) and LDH (day 15).
  - In general, serum biomarkers remained suppressed in the eblasakimab groups for 4-6 weeks following the last dose.
  - End-of-study values for total IgE and TARC/CCL17 were no different than placebo, a trend also observed for LDH (data not shown).
- At the Excluded site* median % changes from baseline in total IgE, TARC/CCL17, and LDH level with 600 mg eblasakimab were substantially less than those of the corresponding mITT 600 mg dose group and similar to placebo at week 8 (P=0.272 vs. placebo for TARC/CCL17; Figure 2A and data not shown).

Table 1. Patient Demographics and Baseline Characteristics

		mITT				Excluded site*	
		Eblasakimab 200mg (N=4)	Eblasakimab 400mg (N=7)	Eblasakimab 600mg (N=16)	Placebo (N=13)	Eblasakimab 600mg (N=6)	Placebo (N=3)
Age, Mean (SD)		32.5 (5.26)	29.4 (4.89)	34.0 (13.39)	34.2 (11.27)	56.7 (17.92)	59.0 (22.27)
Male, n (%)		3 (75.0%)	5 (71.4%)	12 (75.0%)	10 (76.9%)	1 (16.7%)	1 (33.3%)
Race, n (%)	Asian	4 (100%)	7 (100%)	7 (43.8%)	8 (61.5%)	0	0
	Black	0	0	1 (6.2%)	0	1 (16.7%)	0
	White	0	0	8 (50.0%)	3 (23.1%)	5 (83.3%)	3 (100.0%)
	Other	0	0	0	2 (15.4%)	0	0
Ethnicity, n (%)	Not Hispanic or Latino	4 (100%)	7 (100%)	15 (93.8%)	13 (100.0%)	0	2 (66.7%)
BMI (kg/m²), Mean		25.8 (2.95)	25.3 (5.08)	26.3 (8.23)	25.8 (4.48)	30.8 (6.17)	25.2 (1.98)
Total IgE (kU/L)[a,b]	Mean (SD) Median	15,891 (14,993) 12,278	23,297 (28,508) 10,660	8,660 (7,178) 6,468	8,706 (8,175) 7173	677 (1,126) 268	76 (88) 70
TARC/CCL17 (pg/mL)[b]	Mean (SD) Median	6,097 (6,347) 5,556	18,310 (40,556) 2262	4,223 (5,186) 2128	5,056 (6,842) 2398	466 (340) 366	446 (344) 446
LDH (U/L)	Mean (SD)[c,d] Median	571.8 (378.07) 429	679.1 (255.46) 687	418.9 (290.32) 306	432.4 (187.07) 419	180.3 (37.68) 173	143.3 (36.30) 138

BMI, body mass index; IgE, immunoglobulin E; TARC/CCL17, thymus and activation regulated chemokine; LDH, lactate dehydrogenase; SD, standard deviation.
*Excluded site.
†Each subject had 200 mg (n=4), 400 mg (n=7), 600 mg (n=16), Placebo (n=13); Excluded site: Placebo (n=3).
[a]Data are derived from the full analysis set from the safety population for LDH and IL6.
[b]mITT: eblasakimab 200 mg (n=4), eblasakimab 400 mg (n=7), eblasakimab 600 mg (n=16), Placebo (n=13); Excluded site: Placebo (n=3).

Figure 2. Changes from Baseline to Week 8 in Atopic Dermatitis Biomarkers



CONCLUSIONS

- In this small Phase 1b multiple ascending dose study, eblasakimab, a monoclonal IL-13Rα1 directed antibody, reduced circulating levels of AD-associated pharmacodynamic biomarkers TARC/CCL17, total IgE and LDH.
  - In this study, biomarker responses were greatest in the 400 mg and 600 mg dose groups and were not further reduced at the higher dose group.
  - Among the biomarkers analyzed, TARC/CCL17 and LDH showed the greatest decrease from baseline levels with eblasakimab treatment.
  - This general suppression of biomarker levels supports the clinical responses and improvements in patient-reported outcomes observed in this trial, as evidenced by reductions in measures of AD severity[8] (see also Poster #P0343), itch and sleep loss (see Poster #P0342).
  - Limitations of the analysis include differences in baseline levels of biomarkers between groups, small n values, the presence of outliers, and a non-homogenous patient population.
- These biomarker results are consistent with findings in the literature reported for other approved AD treatments[9] and show the utility of these markers for characterizing reductions in disease severity in a moderate-to-severe AD population.
  - These data along with the clinical results of the trial support the further investigation of eblasakimab for the treatment of moderate-to-severe AD.
  - A phase 2b dose-finding trial is currently underway to evaluate the safety and efficacy of eblasakimab to treat moderate-to-severe atopic dermatitis.

REFERENCES
1. Dubin C, et al. *Expert Rev Clin Immunol.* 2021;17(8):835-852.
2. Jumblatt G. *Front Immunol.* 2018;9:693.
3. Redpath NT, et al. *Biochem J.* 2013;452(2):165-175.
4. Liddiard K, et al. *BMC Mol Biol.* 2006;7:45.
5. Wollenberg A, et al. *World Allergy Organ J.* 2021;14(3):100519.
6. Punnonen J, Yet al. *J Allergy Clin Immunol.* 1997;2008 Pt 1):795-801.
7. Kogawa K, et al. *J Cutan Immunol Allergy.* 2022;5:133-135.
8. Simon D, et al. *Allergy.* 2014;69(8):561-570.
9. Kakimuna, T, et al. *J Allergy Clin Immunol.* 2001;107(6):935-941.
10. Laurent, J, et al. *Ann Med Interne (Paris).* 1985;136(5):419-422.
11. Https://www.uccfhealth.org/medical-tests/lactate-dehydrogenase-test#:~:text=Normal%20Results,vary%20slightly%20among%20different%20laboratories.
12. Katsoka Y. *J Dermatol.* 2014 Mar;41(3):221-9
13. Blauvelt A, et al. *American Academy of Dermatology;* 2022; Boston, MA.
14. Hamilton, JD, et al. *Clin Exp Allergy.* 2021;51(7):915-931.

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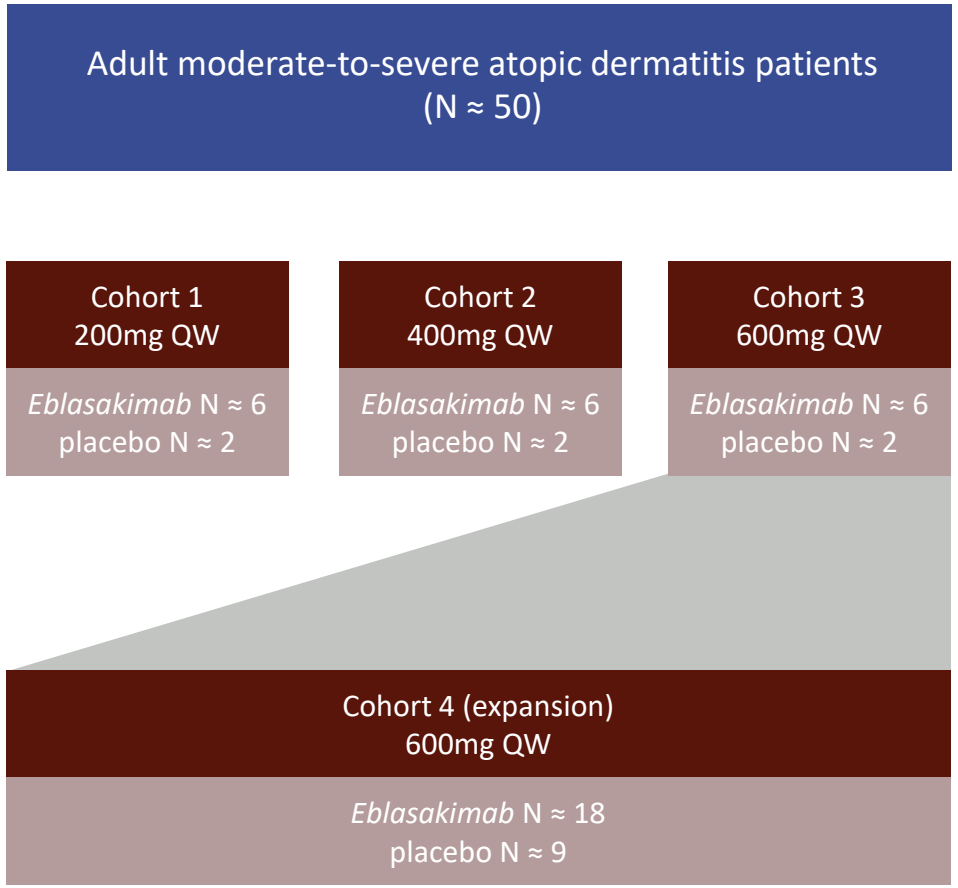
Completed Proof of Concept study in moderate-to-severe AD



- Double-blind, randomized, placebo-controlled Phase 1 MAD study
- Patients dosed weekly via subcutaneous injection for 8 weeks with a 12-week recovery period
- Positive interim data from dose escalation (cohorts 1 to 3) announced in March 2021
- Positive data from full study (cohorts 1 to 4) presented at AAD (2022)

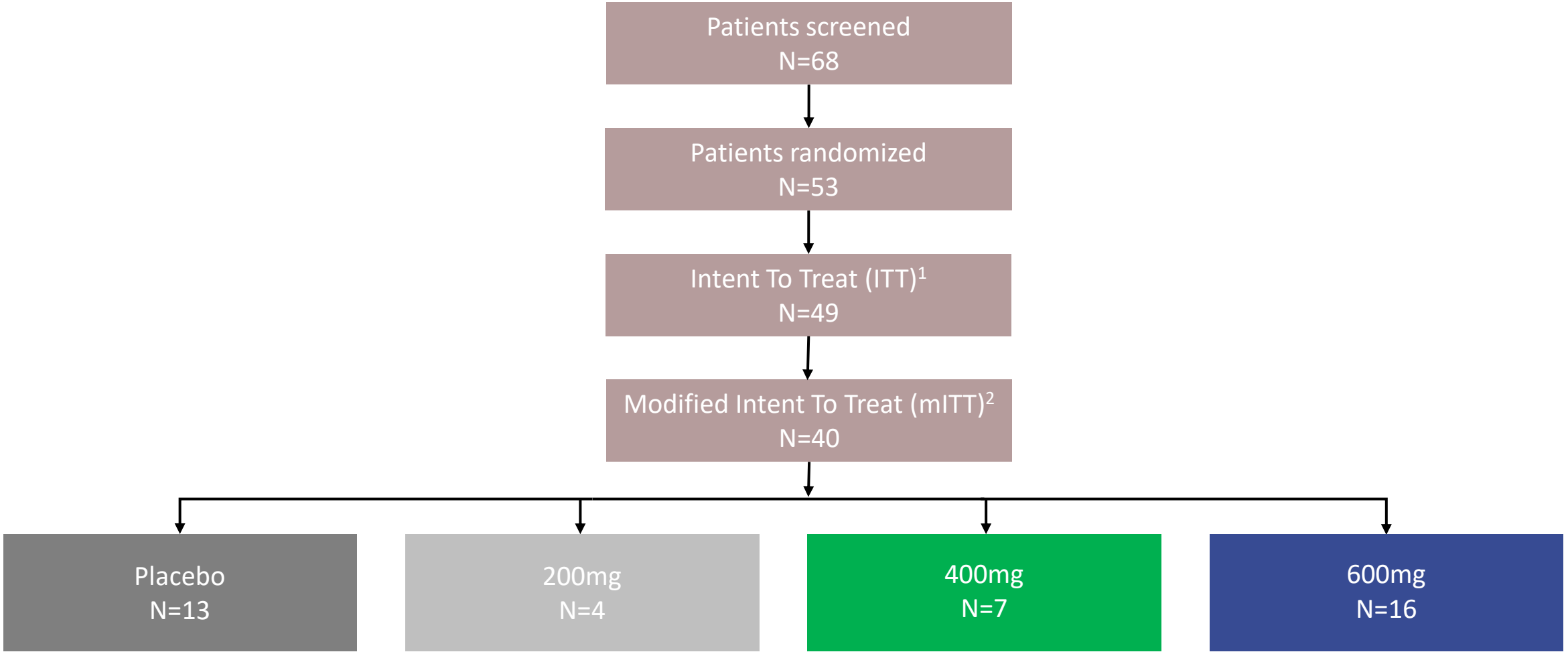
Primary endpoints are safety and tolerability

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

Patients recruited from 10 sites in US, Australia and Singapore



1 All patients excluding 3 who discontinued from the study prematurely due to COVID-19 restrictions (1 from placebo, 1 from 200mg, 1 from 400mg cohorts) and 1 patient who was randomized but not dosed (600mg cohort).
2 9 patients at one clinical site (Excluded Site) appeared atypical of moderate-to-severe AD patient population and were excluded in a pre-specified sensitivity analysis that was defined prior to unblinding

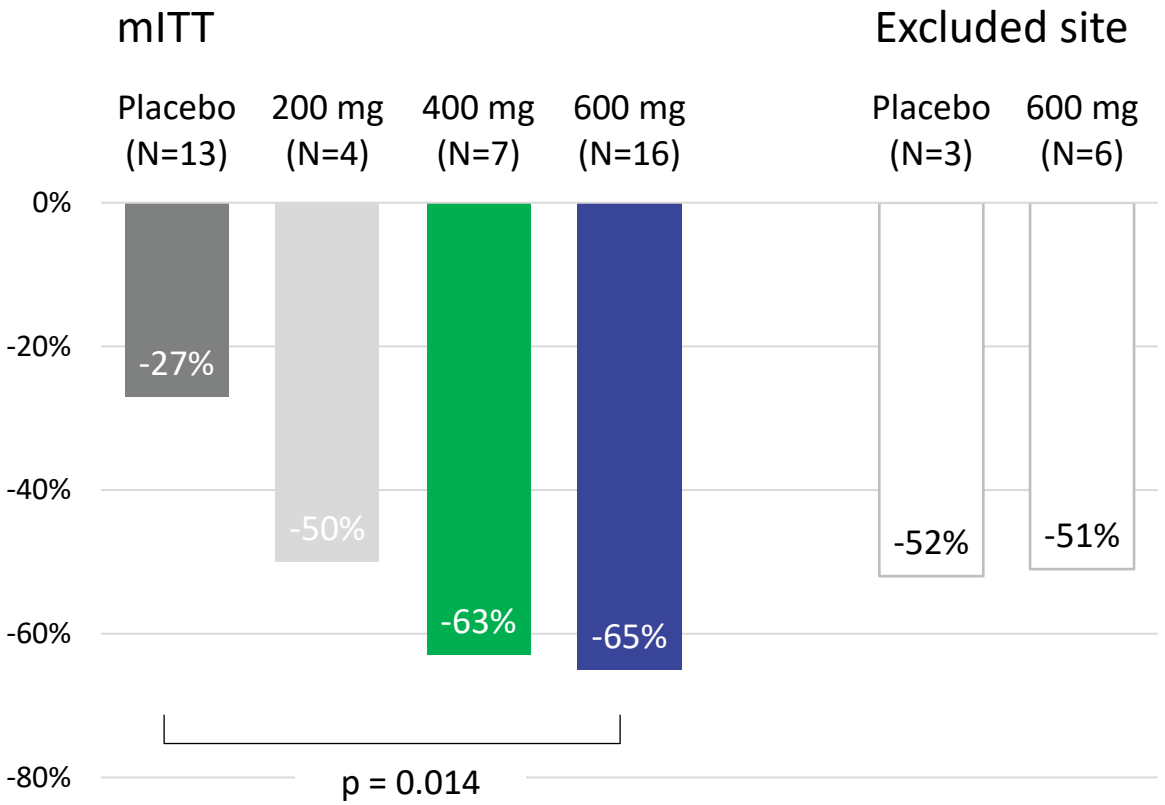
Selected baseline patient characteristics

	mITT (n=40)				Excluded site (N=9)
	Placebo (N=13)	200mg (N=4)	400mg (N=7)	600mg (N=16)	
Age (years)	37.8	30.4	29.4	40.2	57.4
Mean EASI score	28.3	29.6	30.5	27.6	19.3
Patients with IGA 3 / IGA 4	65% / 35%	60% / 40%	75% / 25%	68% / 32%	100% / 0%
Mean BSA	44.8%	47.8%	59.9%	41.0%	28.4%
Mean peak pruritus NRS score	7.7	7.4	7.7	7.9	7.2
Median TARC/CCL17 (pg/mL)	2,398	5,556	2,262	2,128	366
Median Total IgE (kU/l)	419	429	687	306	95

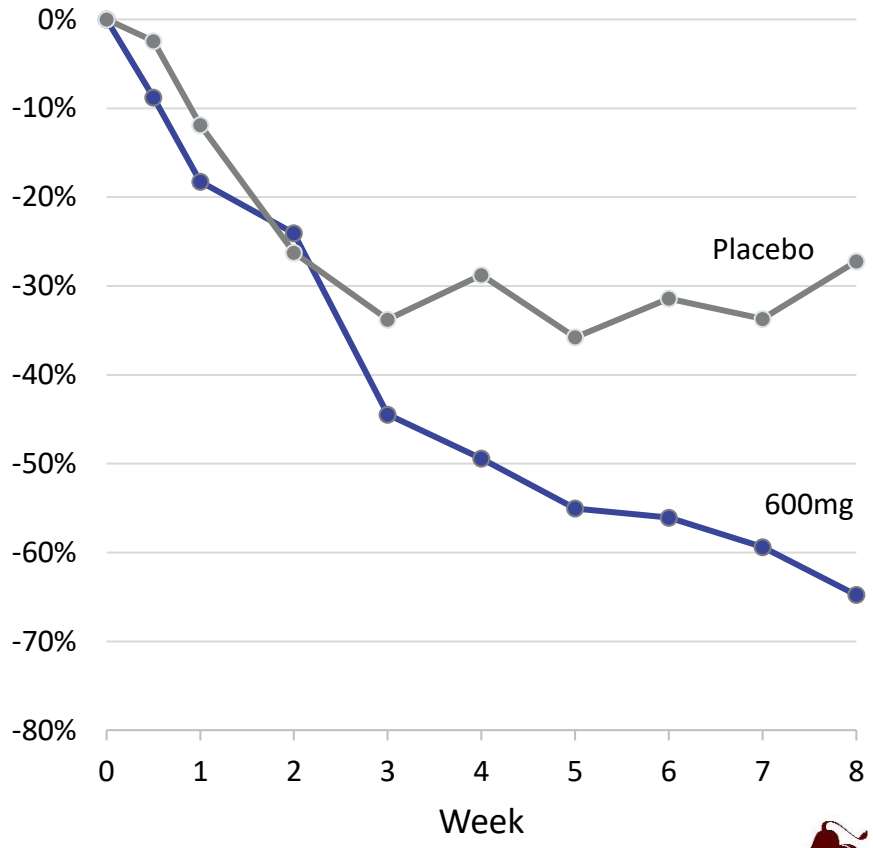
Selected baseline disease history

Disease history		**mITT** (N=40) N (%)	**Excluded site** (N=9) N (%)
Average age of diagnosis		9 years	44 years
Any comorbidities		33 (82.5%)	8 (88.9%)
Atopy-associated	Asthma	18 (45.0%)	1 (11.1%)
	Allergy (dust, pet, seasonal, etc.)	12 (30.0%)	0
	Allergic rhinitis	9 (22.5%)	0
	Allergic conjunctivitis/dry eye	2 (5.0%)	0
	Drug hypersensitivity	8 (20.0%)	0
	Psoriasiform dermatitis	2 (5.0%)	0
	Eczema herpeticum	1 (2.5%)	0
General	Diabetes	0	4 (44.4%)
	Anxiety/depression	4 (10%)	3 (33.3%)
	Hypertension	3 (7.5%)	4 (44.4%)
Other		22 (55.0%)	5 (55.6%)
None documented		6 (15.0%)	1 (11.1%)

Primary efficacy endpoint: change in EASI from baseline (week 8)



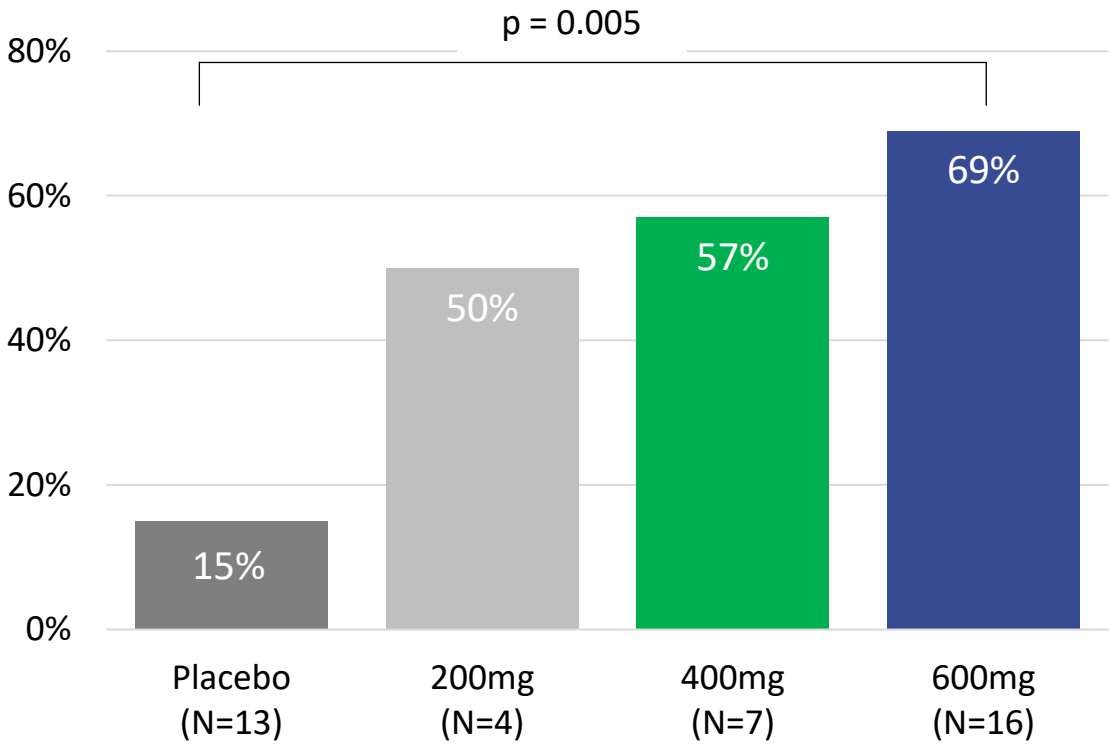
Mean change from baseline



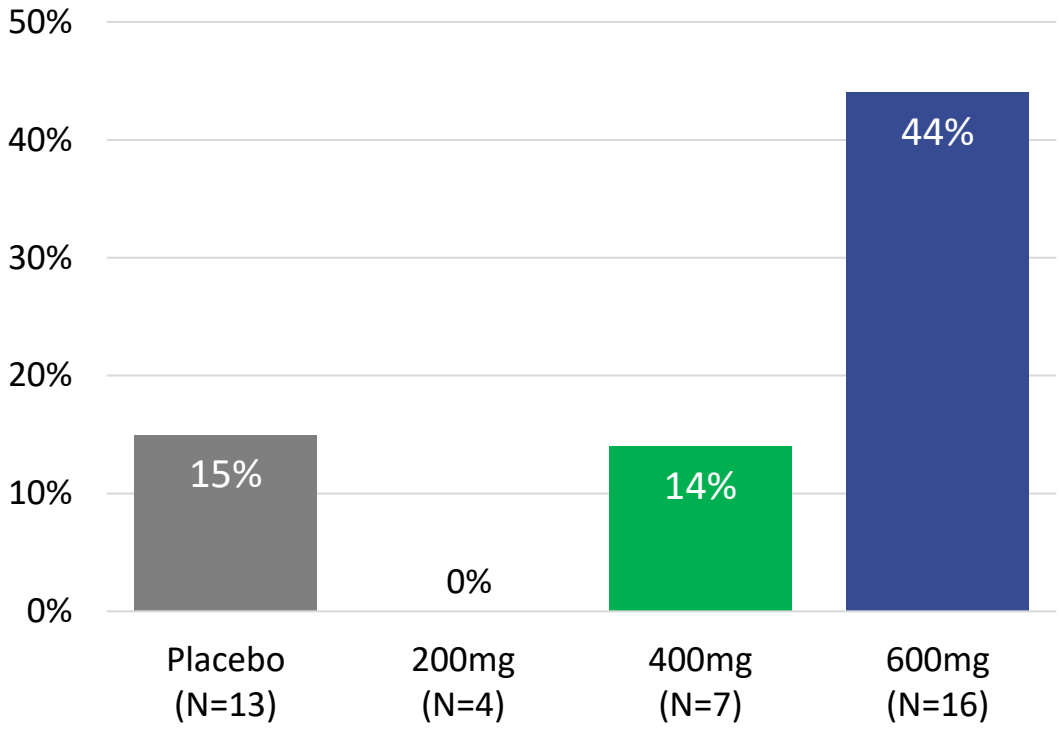
Data from mITT population, presented at 31st EADV Congress, September 7-10, 2022
p-values are one-sided

Other efficacy endpoints (week 8)

EASI-75



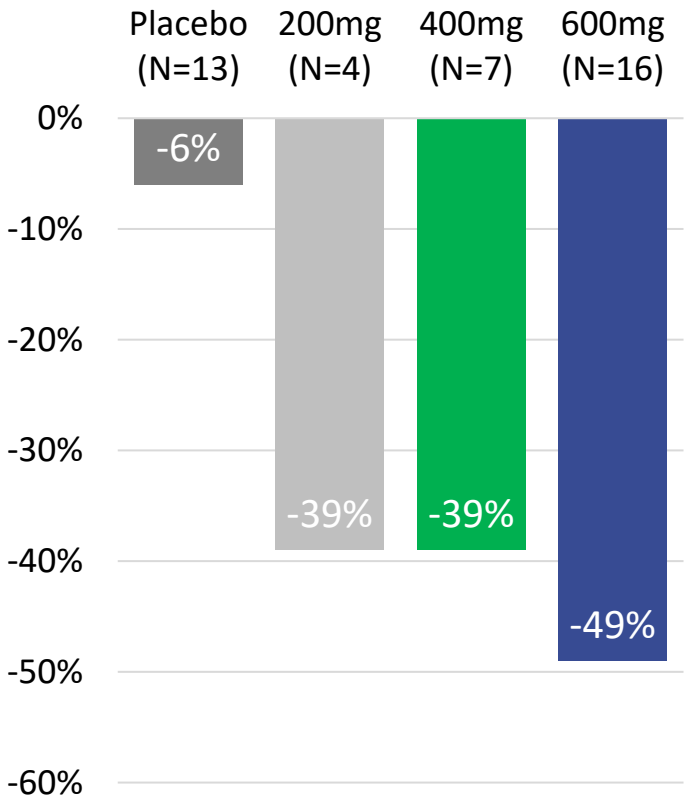
Patients achieving IGA 0/1



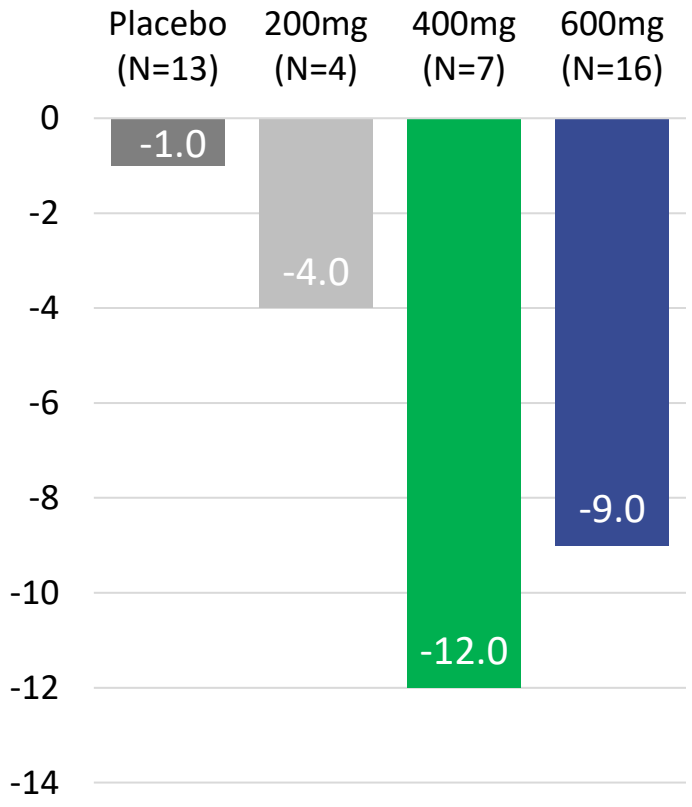
Data from mITT population, presented at 31st EADV Congress, September 7-10, 2022
p-values are one-sided

Patient reported outcomes (week 8)

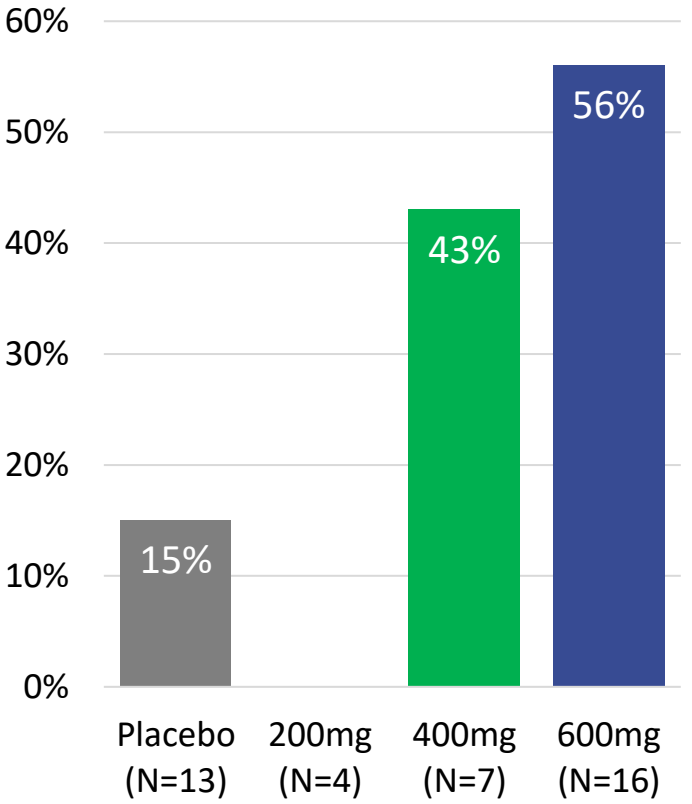
Peak P-NRS[1]



POEM[1]



Patients with 2-point improvement in sleep loss

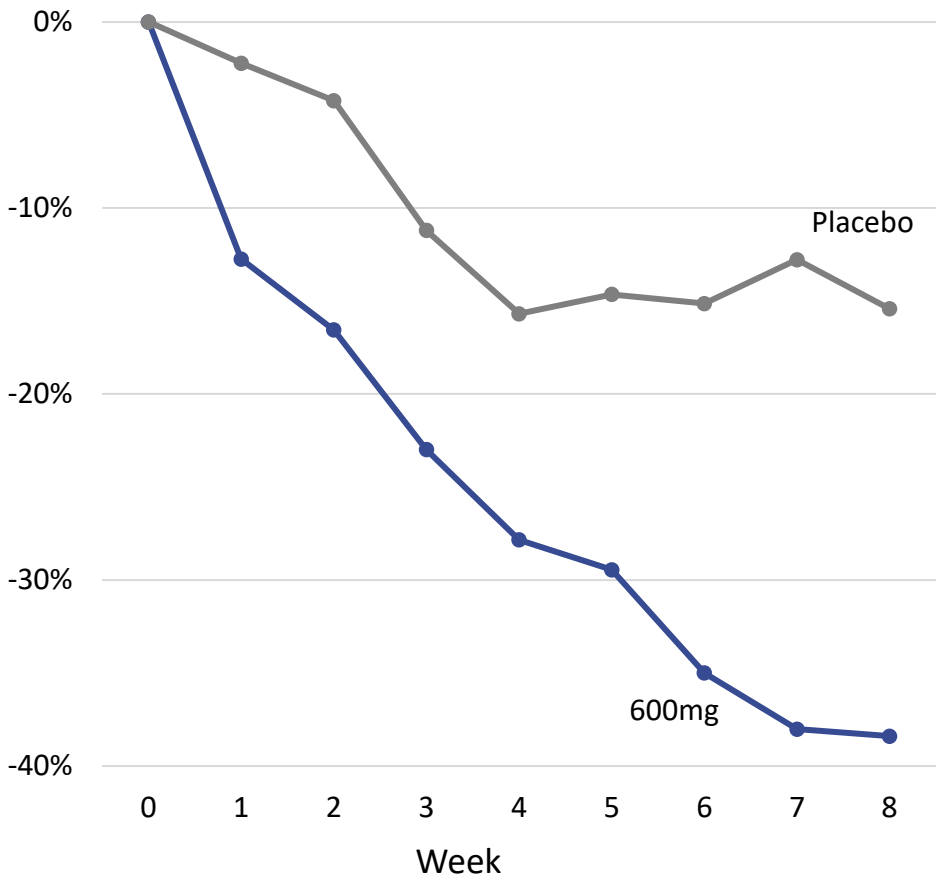


Data from mITT population, presented at 31st EADV Congress, September 7-10, 2022

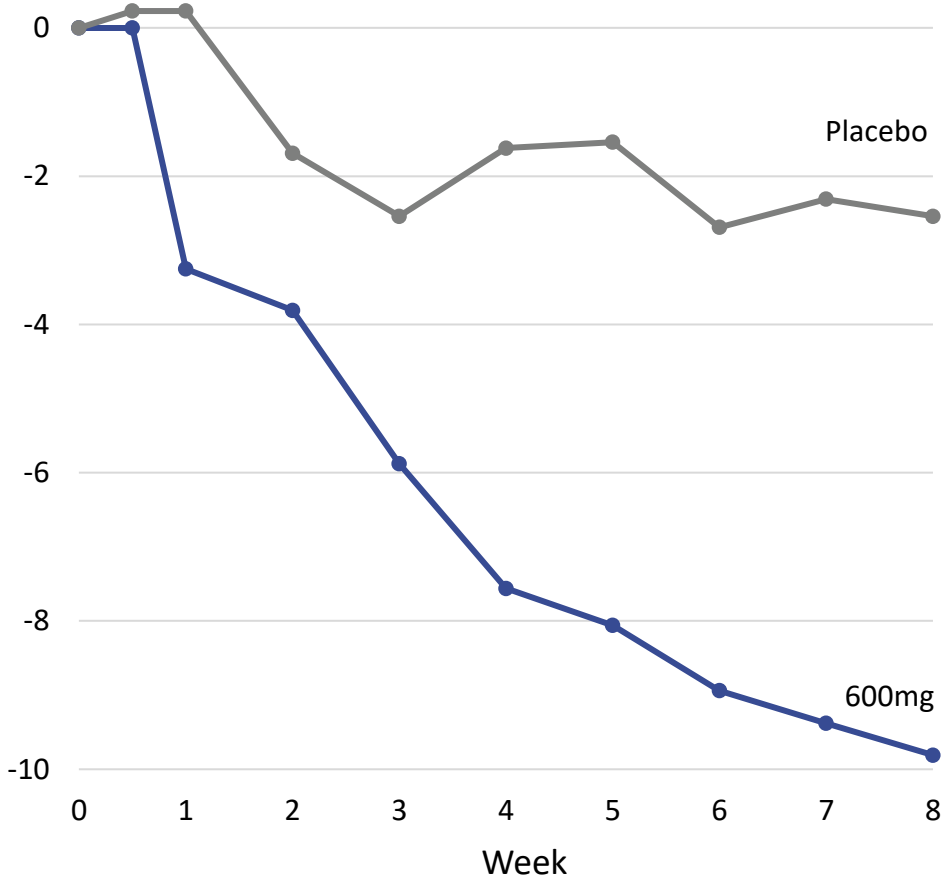
1 median change from baseline

Time course (mean change from baseline)

Peak P-NRS

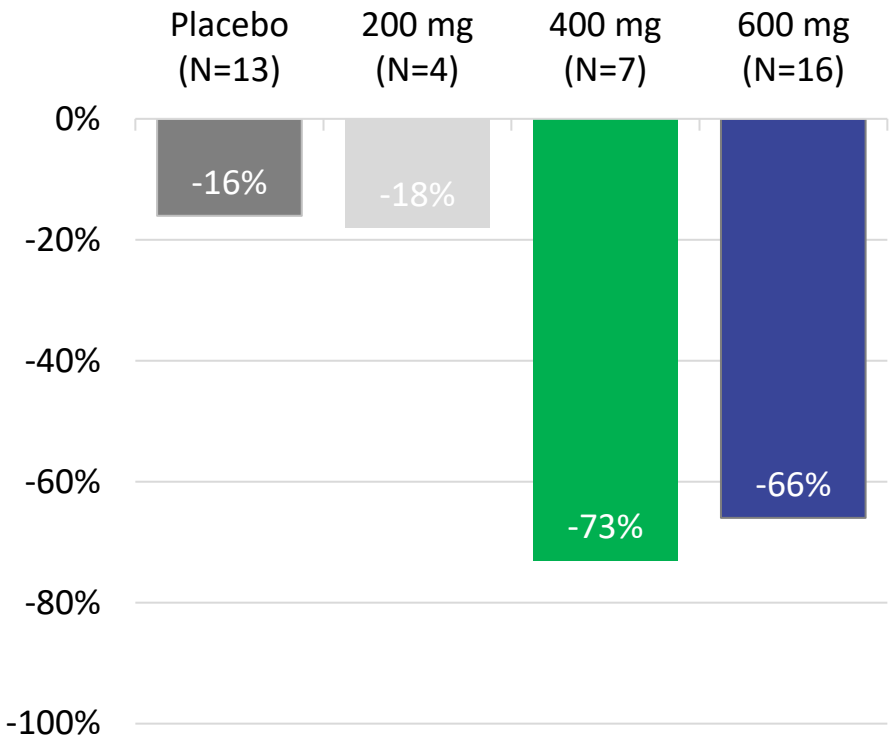


POEM



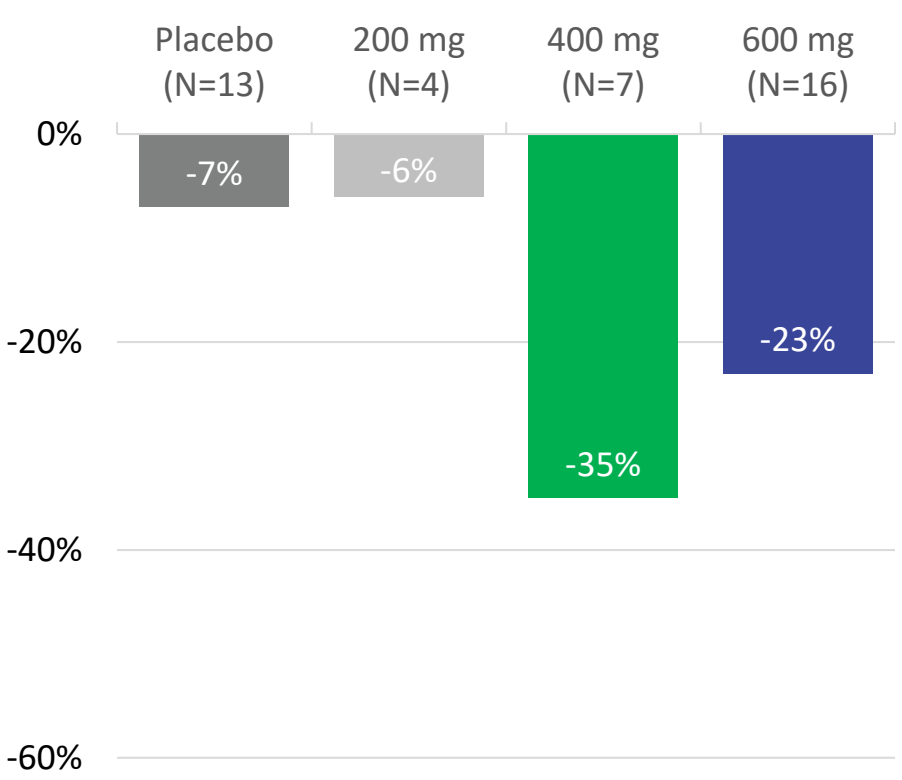
Data from mITT population, presented at 31st EADV Congress, September 7-10, 2022
p-values are one-sided

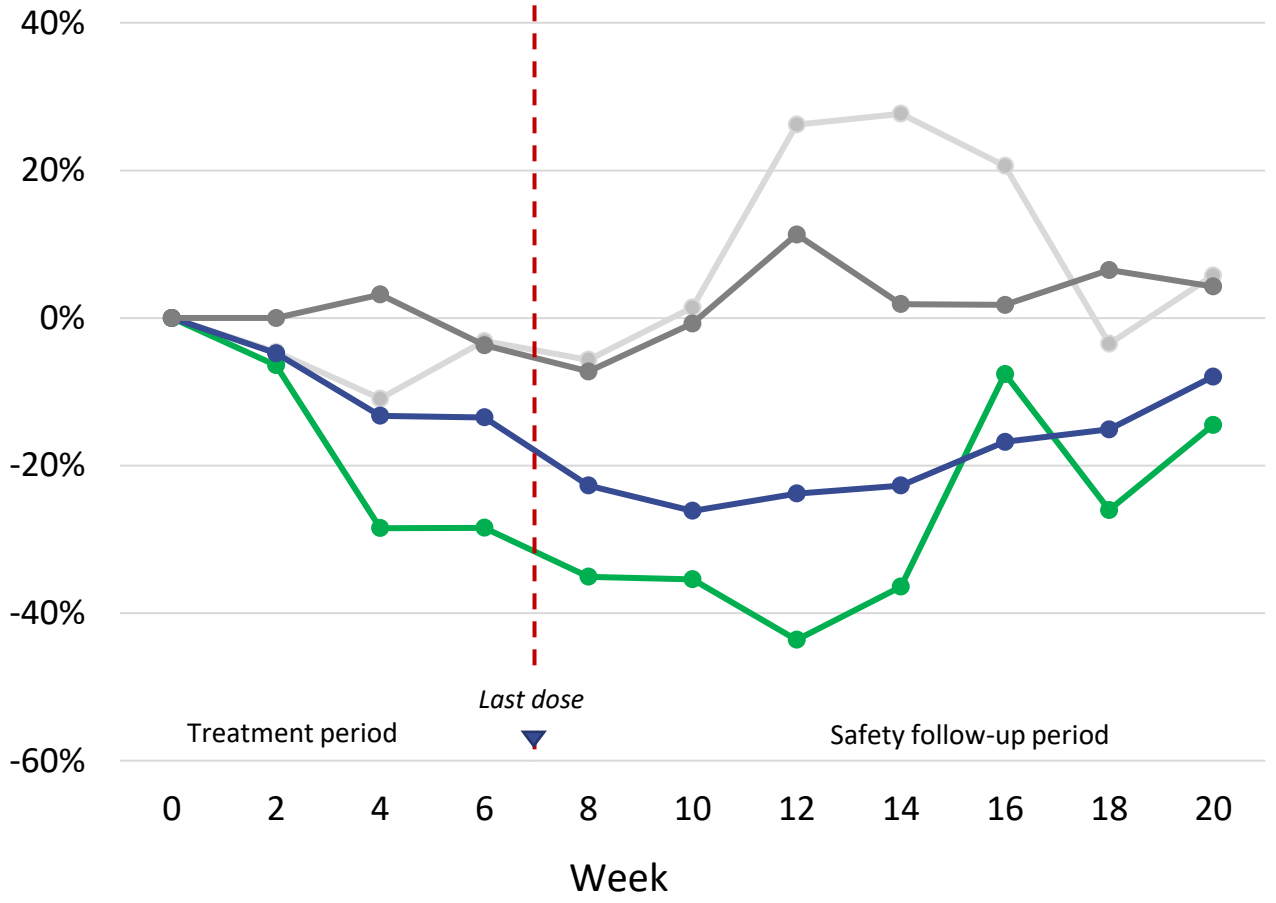
TARC median change from baseline at 8 weeks and over time



Data from mITT population, presented at 31st EADV Congress, September 7-10, 2022

Total IgE median change from baseline at week 8 and over time





Data from mITT population, presented at 31st EADV Congress, September 7-10, 2022

Eblasakimab well-tolerated with low incidence of conjunctivitis

Treatment Emergent Adverse Event (TEAE) by category[1]	All patients dosed (N=52)		
	600mg (N=22)	200-600mg (N=35)	Placebo (N=17)
Any	12 (55%)	25 (71%)	8 (47%)
Related	8 (36%)	19 (54%)	7 (41%)
Moderate/severe	6 (27%)	11 (31%)	5 (29%)
Serious adverse event (SAE)	0 (0%)	1 (3%)	0 (0%)
Drug-related AEs of interest[2]:			
• Injection site reaction	5 (23%)	9 (26%)	2 (12%)
• Conjunctivitis	1 (5%)	2 (6%)	0 (0%)

- Conjunctivitis was classified as mild. Patients had prior history of allergy or allergic conjunctivitis
- Rescue medication use: 3 patients on placebo arm, 1 patient on 600mg arm

1 Presented at AAD Annual Meeting, 25-29 March 2022
2 Drug-related AEs defined by the investigators as definitely related, probably related or possibly related

Newly published PRO and biomarker data supports previously published clinical data and potential for differentiated profile

Clinical data	*Eblasakimab* was **well-tolerated with statistically significant improvements** for compared to placebo for EASI %CFBL, EASI-50, EASI-75 at week 8. Potential for a greater magnitude of effect with treatment beyond 8 weeks.
Patient reported outcomes	New data presented at EADV 2022 demonstrate **further benefits in itch reduction** and **improvements in sleep loss for patients** with significant sleep disturbance at baseline
Biomarkers	**Circulating levels of TARC, IgE and LDH were reduced** with *eblasakimab* treatment and remained suppressed for 4-6 weeks after the last dose

Dr Alex Kaoukhov
Chief Medical Officer

Welcome

Emerging unmet needs in Atopic Dermatitis (AD)

Eblasakimab: addressing the market needs and opportunities

Promise of targeting the IL-13 receptor

Type-2 inflammation and beyond

Q&A

New findings from the proof-of-concept study

Eblasakimab **development program**

Company Q&A

Panel discussion

Closing remarks

High unmet need in biologic eligible and experienced population

AD patients 41M[1]

Drug treated Mod-to-sev 3.3M[2]

TARGET MARKET

Biologic eligible 2M[3]

- Biologic naïve population seeking safe long-term treatment
- *Dupilumab* is standard of care for these patients

8%[4]

Dupi-treated 220k[5]

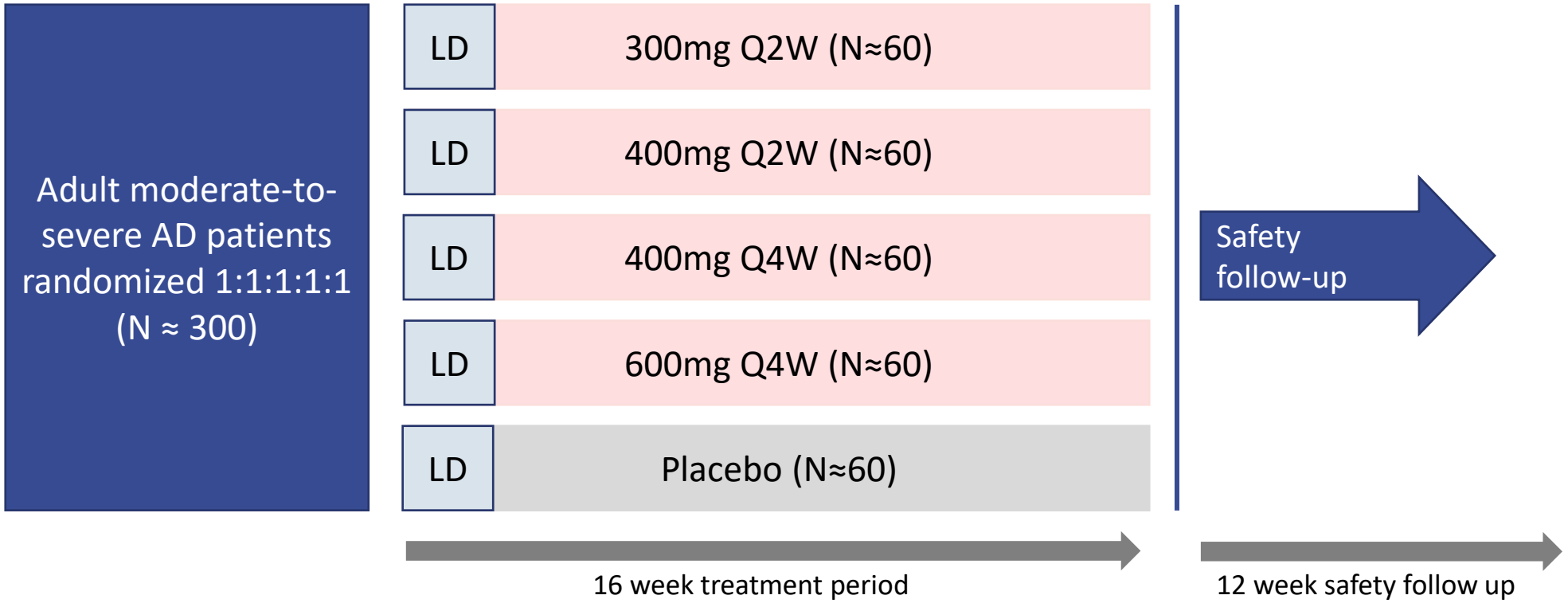
Dupilumab experienced 150k[6]

- Patients who show sub-optimal response
- Response declines over time
- Discontinuations due to conjunctivitis

Numbers are only meant to be illustrative of estimated relative market sizes

1 Divekar et al (2021) Atopic Dermatitis/Atopic Eczema: Disease Landscape & Forecast, DRG
2 Drug treated diagnosed prevalence, assuming one-third moderate and all severe patients, Divekar et al (2021) DRG
3 Calculated assuming 220K patients represent 8% of the biologic eligible market
4 Sanofi's investor presentations
5 Estimated based on Dupixent annual US sales from Sanofi Annual Report 2021
6 Spherix (2018) Atopic dermatitis ATU study

Phase 2b (TREK-AD): initiated early 2022, topline expected 1H 2023



- 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 ≥3
- ≥10% BSA
- EASI ≥16
- Inadequate response or contraindication to TCS/TCI
- Twice daily application of topical emollient for at least 7 days prior to randomization

Select exclusion criteria:

- Other agents targeting IL-4 or IL-13 (eg *lebrikizumab*, *tralokinumab* or *eblasakimab*) except for *dupilumab* provided it was not discontinued due to lack of efficacy or AE
- Other AD treatments unless appropriate washout
- Washout periods: immunosuppressants/phototherapy 4 weeks, TCS/TCI 1 week

Study Endpoints

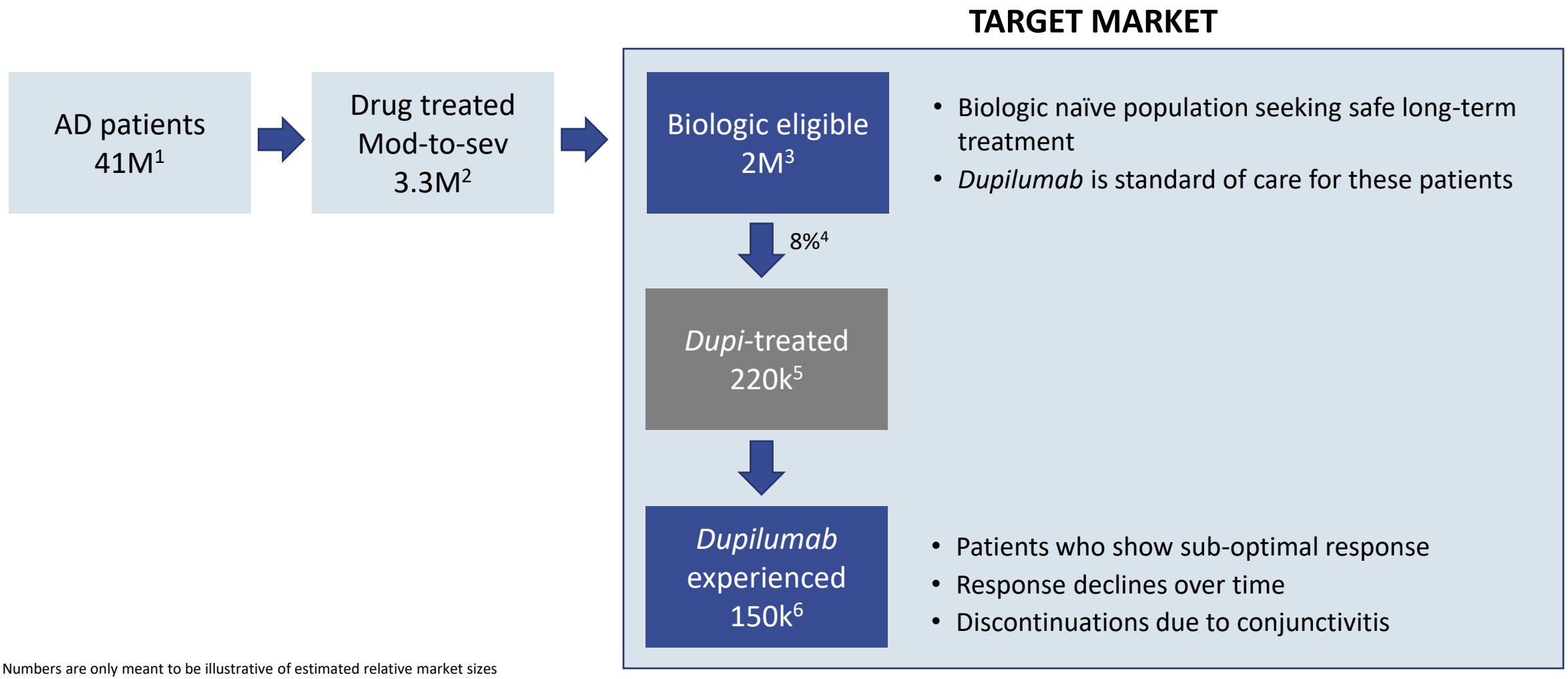
Primary

- 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

High unmet need in biologic eligible and experienced population



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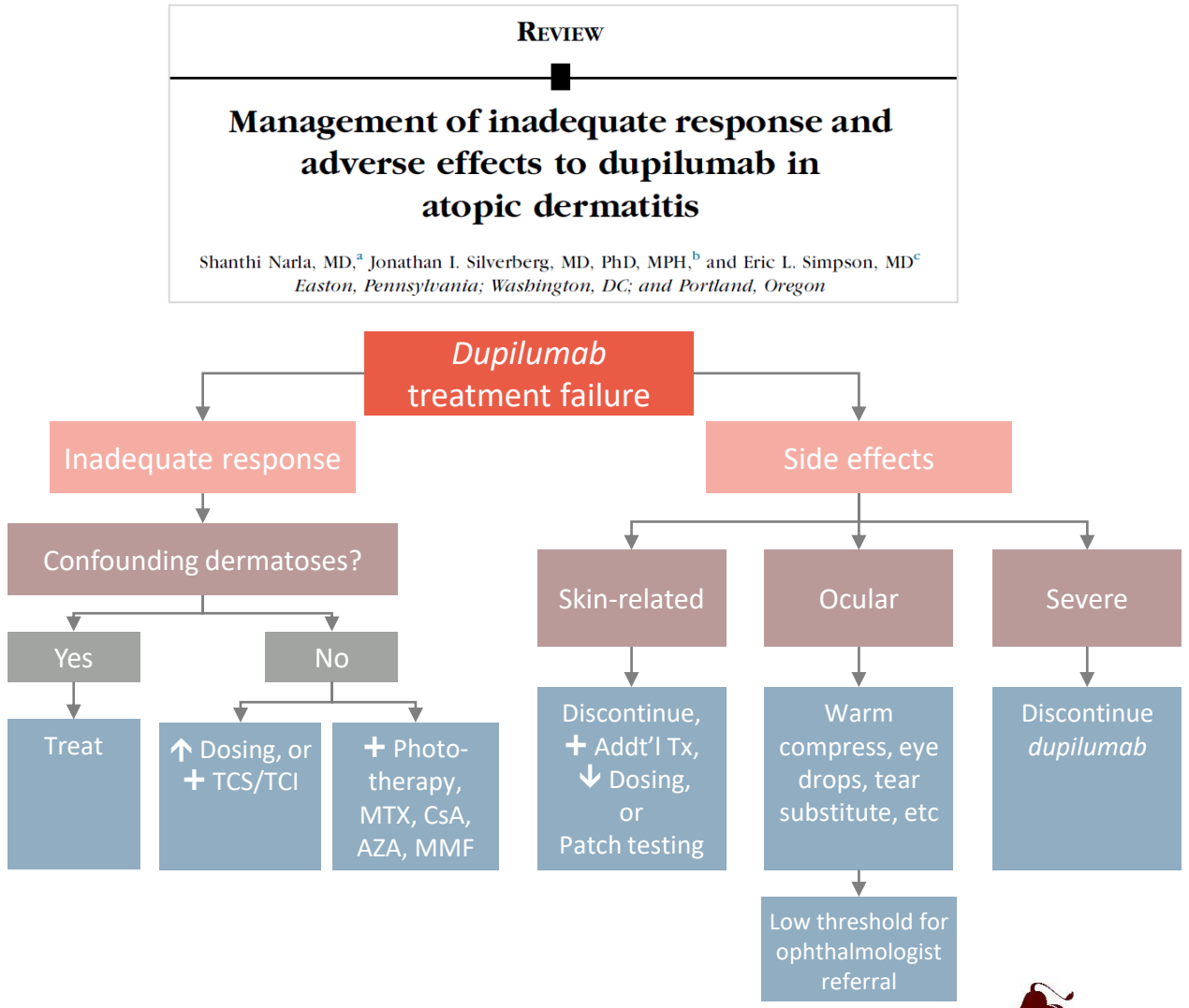
Dupilumab experienced patients lack safe long-term treatments

- *Dupilumab* has established standard-of-care for AD patients with high efficacy and good safety profile
- Various reasons for discontinuation of treatment and unique management for these patients is required[1,2]
  - Efficacy (heterogenous pool of non-response, partial response and non-durable response)
  - Adverse events
  - Access issues
- 37% of *dupilumab*-treated patients achieved IGA 0/1 with 54% maintained the response at wk 52
- *Dupilumab* experienced population seeking additional treatment options

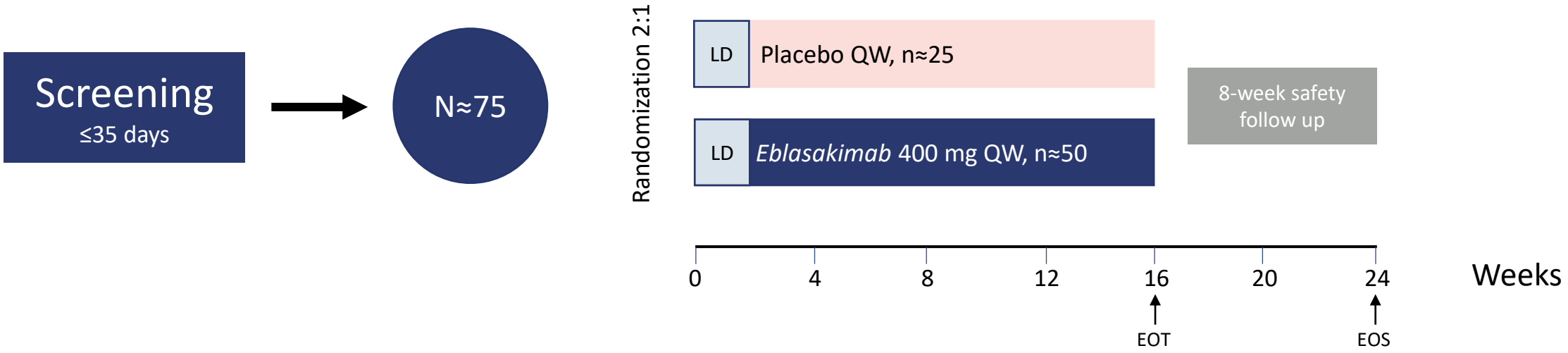


1. Narla et al (2022) JAAD 86(3):628–636.
2. Hendricks et al (2019) Am J Clin Derm 20(4):565–569.
3. ASLAN market research data 2022, quantitative survey of 150 US dermatologists.

TREK-DX: Phase 2 study in *dupilumab*-experienced patients

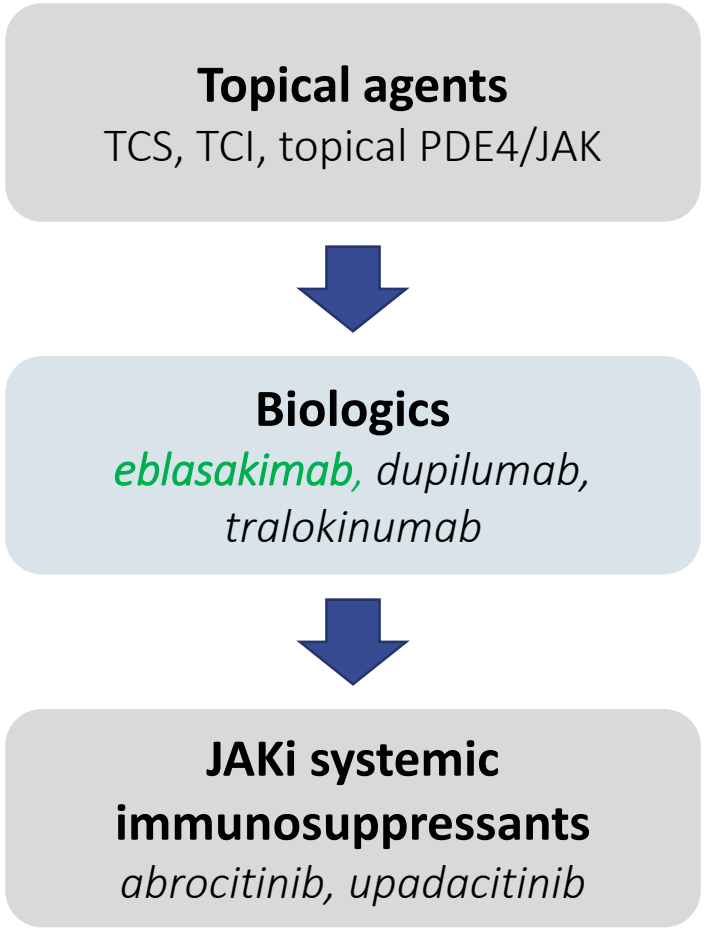
- TREK-DX: TRials in *EblasaKimab* in *Dupilumab*-eXperienced patients
- A randomized, double-blind, placebo-controlled, multicenter trial to evaluate the efficacy and safety of *eblasakimab* in patients with moderate to severe AD previously treated with *dupilumab*
- This study will allow to evaluate the efficacy of *eblasakimab* in participants with moderate-to-severe AD previously treated with *dupilumab*:
  - Assess the impact of prior failure to respond to *dupilumab* on *eblasakimab* efficacy
  - Assess the risk of conjunctivitis in patients reporting conjunctivitis associated with prior *dupilumab* use

TREK-DX: study design



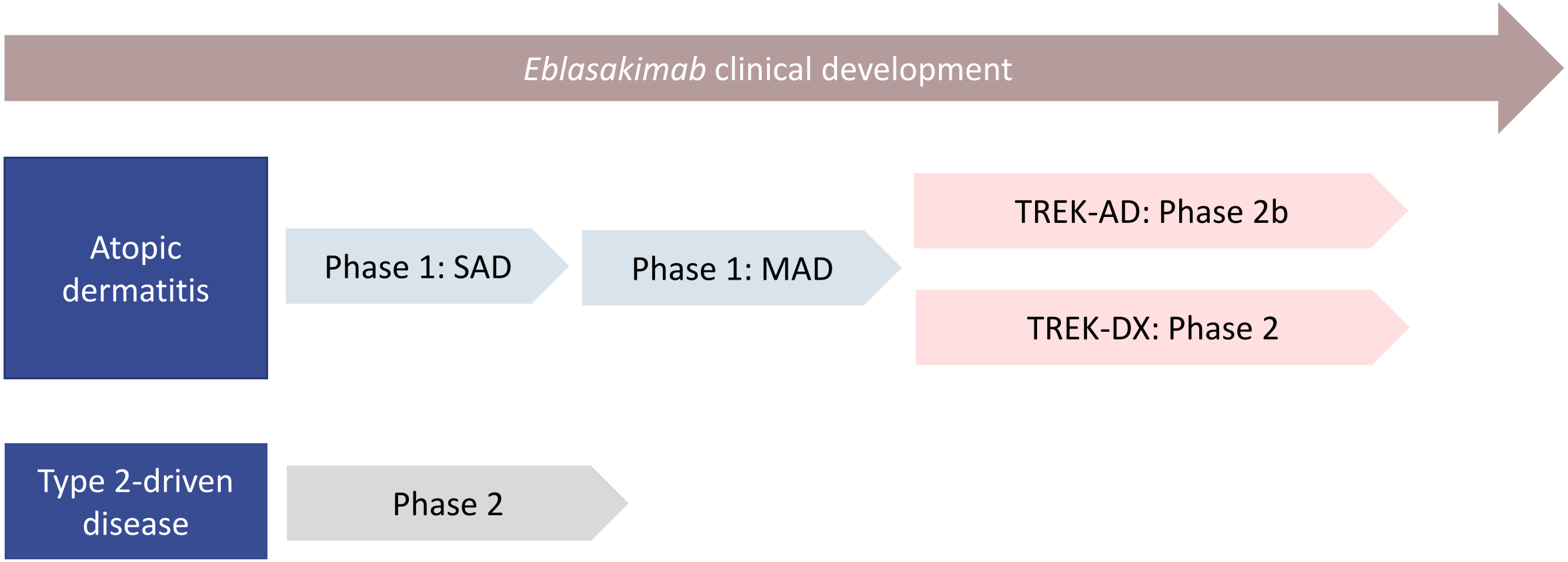
- Randomization will be stratified by the baseline vIGA score (3 or 4), and *dupilumab* discontinuation reason (failure or "all other")
- Loading dose of 400mg at week 1 and week 2, matching loading dose for placebo
- With exception of requirement of prior *dupilumab* exposure, inclusion/exclusion criteria and endpoints are virtually identical to TREK-AD study

Outcomes of the TREK-DX study could help position *eblasakimab* at the forefront of biologic treatment options



- The TREK-DX study is crucial for testing biologics in a patient population with few safe treatment options
- A positive outcome of the study will increase preference for *eblasakimab* as the first choice of biologic for AD treatment

Eblasakimab clinical program is initially focused on AD



Company Q&A

Dr Carl Firth
CEO
ASLAN

Dr Alex Kaoukhov
Chief Medical Officer
ASLAN

Dr Karen Veverka
VP Medical
ASLAN

Stephen Doyle
Chief Business Officer
ASLAN

Dr Ferda Cevikbas
Head Translational Sciences
ASLAN

Panel Discussion:
Eblasakimab's potential and positioning in treating AD

Dr Peter Lio

Dr Shawn Kwatra

Dr Karen Veverka

Dr Carl Firth
(moderator)

Dr Carl Firth
CEO

Welcome

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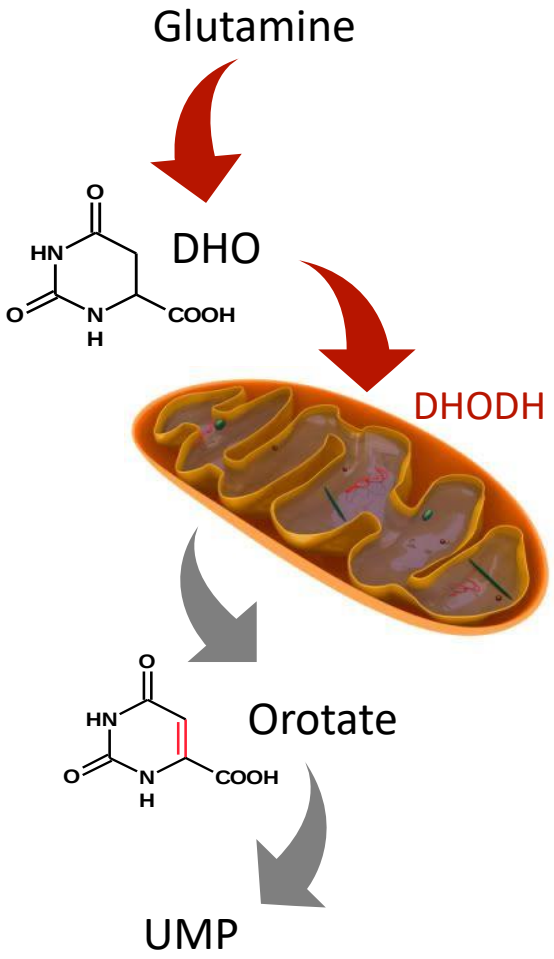
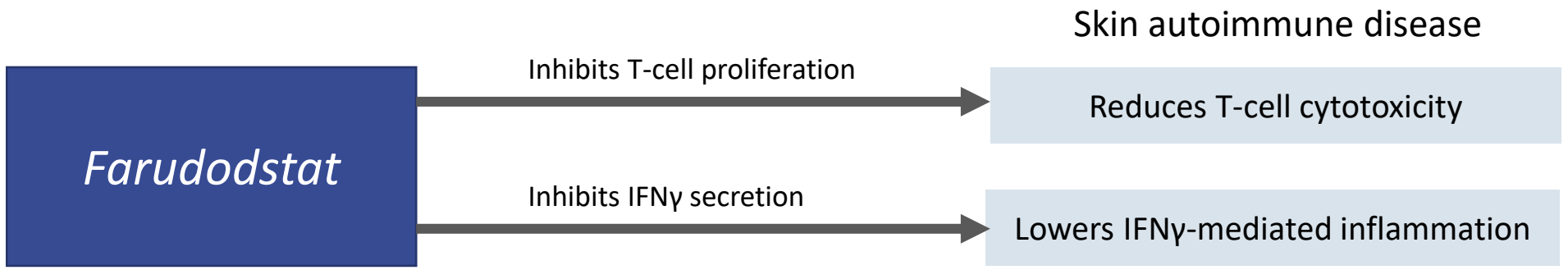
DHODH is a validated target for autoimmune disease



- Cells synthesise pyrimidines via
  - *De novo* pathway (DHODH dependent)
  - Salvage pathway (DHODH independent)
- DHODH inhibition will block *de novo* synthesis, impacting rapidly dividing cells eg lymphocytes.
- Other cells can continue to use the salvage pathway and are unaffected
- First generation inhibitors are approved in MS (Aubagio) and RA (Arava), however they have limited potency and significant safety liabilities
- *Farudodstat* was designed to be more potent and to address the toxicities associated with first generation inhibitors

DHODH is an attractive target for the treatment of autoimmune skin disease

- AA and vitiligo estimated to affect around 3% of the US population combined[1,2]
- JAK inhibitors carry 3 black box warnings presenting an opportunity for a safe, once-daily oral therapy
- *Farudodstat* targets the key mechanisms associated with autoimmune skin disease[3,4]



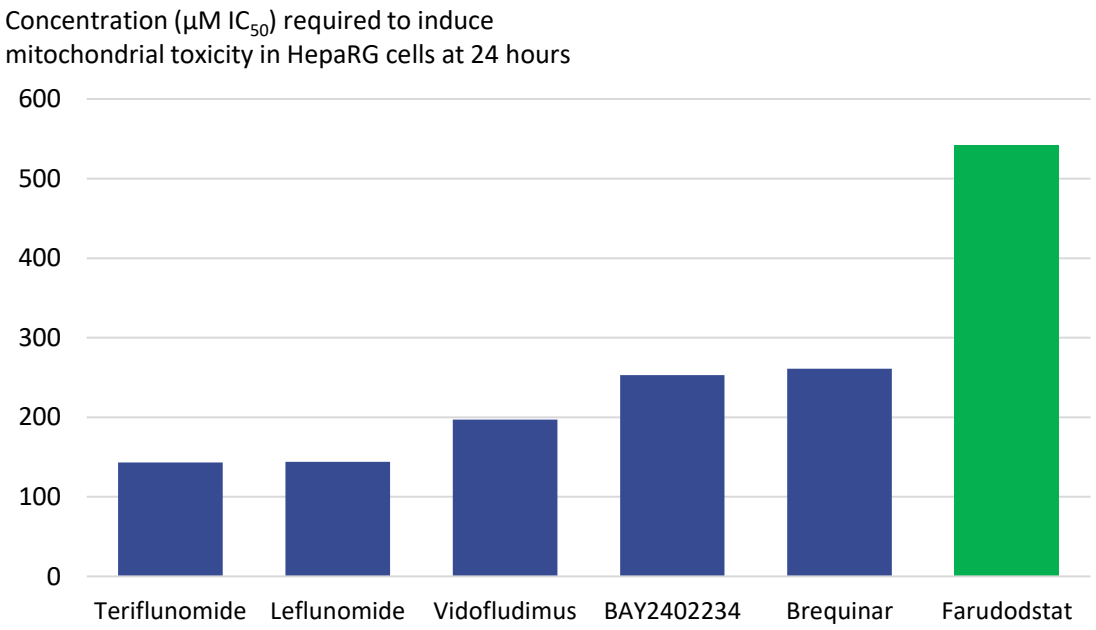
1 National Alopecia Areata Foundation
2 Vitiligo Research Foundation
3 Xing et al 2014 Nat Med 20(9):1043-1049
4 Van der Boorn 2009 J Inv Derm 129(9):2220-2232

Farudodstat has the potential to be best-in-class for autoimmune disease

- Stronger *in vitro* potency as compared with other DHODH inhibitors
- Selective against a panel of 195 enzymes, ion channels and receptor binding assays

Assay used to measure IC_{50}	*Farudodstat* (µM)	*Teriflunomide* (µM)
Enzymatic DHODH inhibition	0.035	1.1
Human PBMC proliferation inhibition	1.4	46
IFN_{γ} inhibition in human whole blood	2.5	259

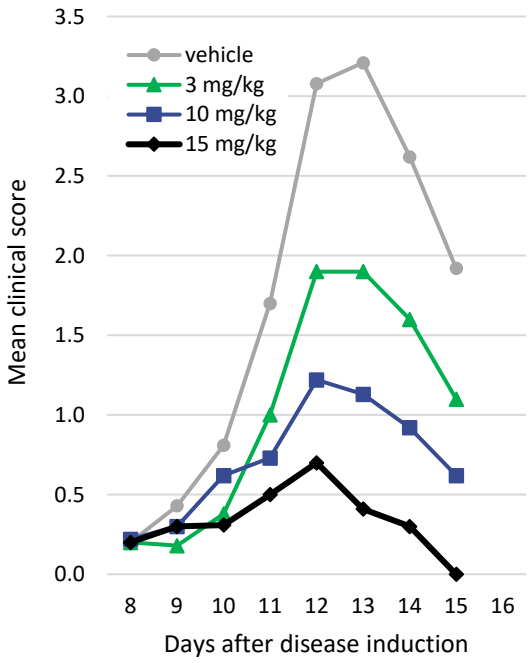
- *In vitro* studies demonstrated *farudodstat* has lowest potential for hepatotoxicity out of 6 approved and clinical stage DHODH inhibitors



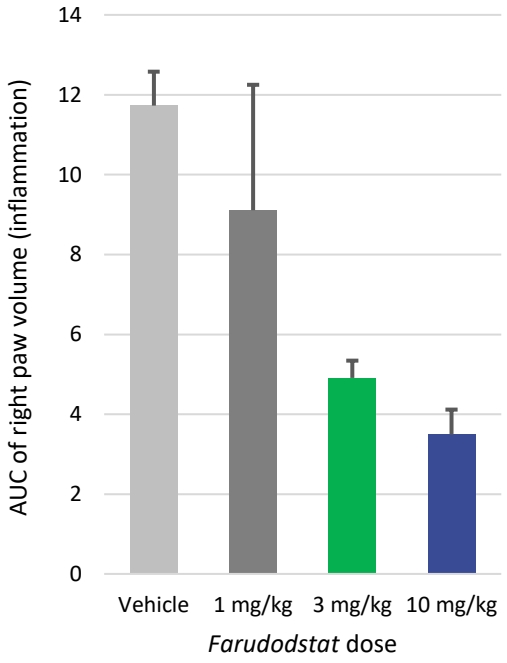
Jones et al (2021) Toxicology in Vitro 72:105096

Farudodstat has the potential to be best-in-class for autoimmune disease

- Active in the multiple sclerosis EAE model and rheumatoid arthritis AIA model

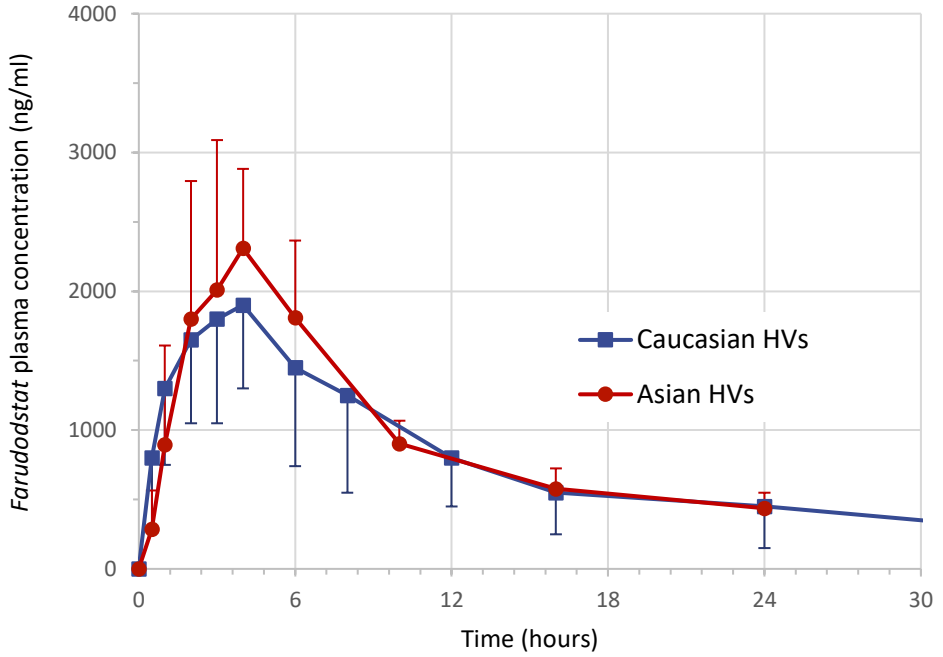


MS model in rat (EAE)



RA model in rat (AIA)

- Well-tolerated in 119 subjects in Phase 1 and Phase 2 clinical trials
- PK profile suitable for once-daily dosing



Single dose pharmacokinetics

Summary of *farudodstat*

Farudodstat has the potential to be best-in-class for autoimmune disease

- Stronger *in vitro* potency as compared with other DHODH inhibitors
- Selective against a panel of 195 enzymes, ion channels and receptor binding assays
- *In vitro* studies demonstrated *farudodstat* has lowest potential for hepatotoxicity out of 6 approved and clinical stage DHODH inhibitors
- Well-tolerated in 119 subjects in Phase 1 and Phase 2 clinical trials
- PK profile suitable for once-daily dosing

Next steps

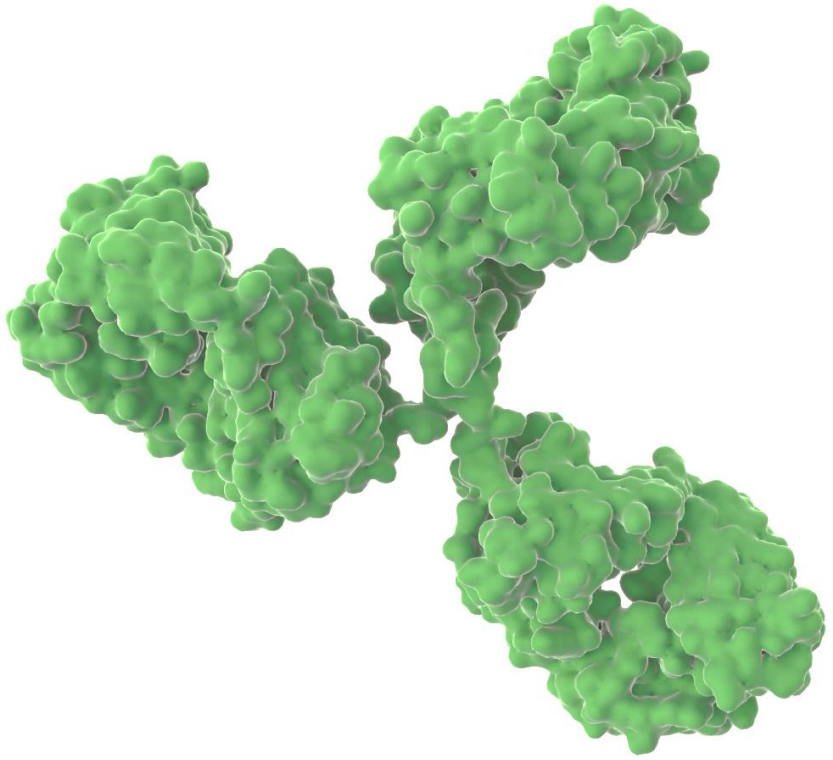
- Exploring applications in skin autoimmune diseases such as alopecia areata

An exciting year ahead for *eblasakimab*

- **TREK-AD topline data** readout from Phase 2b study in 1H 2023
- **TREK-DX first patient in** 4Q 2022
- Characterization of the **unique molecular profile of IL-13Rα1** signaling in AD, with Dr Shawn Kwatra and Dr Madan Kwatra (late-breaker at ESDR 2022)
- Advancing insights into **IL-13Rα1 specific neuronal itch pathways** (late-breaker at ESDR 2022)
- **Exploration of biomarker signatures** from TREK-AD patients in collaboration with Dr Emma Guttman-Yassky (Mount Sinai)

Takeaways from the R&D Day

- The **unmet needs and opportunities** in AD
- Mechanistic rationale supporting **differentiated profile** of *eblasakimab*
- Role of the IL-13 receptor in disease pathology and **advantages of directly blocking IL-13Rα1**
- How *eblasakimab* can directly reducing **neuronal itch responses**
- Clinical data supporting potential for **differentiated profile**



Thank you