



## 2017 AAD Annual Meeting

March 03-07, 2017

Orlando, Fla.

Orange County Convention Center



# “New therapies in Psoriasis and Eczema”

AAD Highlights 2017

30<sup>th</sup> March 2017

Dr. Oonagh Molloy

SpR in Dermatology

UCHG

# Introduction

- A paradigm shift in the treatment of atopic dermatitis
- A new era in translational research that shows promise in the chronic management of atopic dermatitis.
- In psoriasis we are raising the bar.
- Is PASI 75 passé?

# Hot topics in Atopic Dermatitis

- Translational research
- Abnormal cytokine profile
- Biomarkers of disease activity.
- New topical therapies
  - Crisaborole<sup>®</sup> (PDE-4 inhibitor) (not licensed in Ireland)
  - Topical JAK inhibitors
- Biologics
  - Dupilumab (Dupixent<sup>®</sup> approved FDA 29/03/2017)
  - Nemolizumab (not licensed in Ireland)
  - Tralokinumab (not licensed in Ireland)
  - Lebrikizumab (not licensed in Ireland)
- Role of the Microbiome

# What's coming on stream

| Drug Candidate                                          | Phase | Mechanism                           | Route of Administration | Sponsor                             | Study Location |
|---------------------------------------------------------|-------|-------------------------------------|-------------------------|-------------------------------------|----------------|
| BMS-981164                                              | 1     | biologic                            | injection               | Bristol-Myers Squibb                | Non-US         |
| CNTO 7160                                               | 1     |                                     | injection               | Janssen Research & Development, LLC | Non-US         |
| E6005                                                   | 1     | PDE-4 inhibitor                     | topical                 | Eisai Co., Ltd.                     | Non-US         |
| FURESTEM-AD                                             | 1     |                                     | injection               | Kang Stem Biotech Co., Ltd.         | Non-US         |
| OPA-15406                                               | 1     | PDE-4 inhibitor                     | topical                 | Otsuka Pharmaceutical Co., Ltd.     | Non-US         |
| Sodium Hypochlorite Solution                            | 1     | antimicrobial                       | topical                 | Makati Medical Center               | Non-US         |
| XmAb*7195                                               | 1     | biologic                            | injection               | Xencor, Inc.                        | US             |
| Apremilast (CC-10004)                                   | 2     | PDE-4 inhibitor                     | oral                    | Celgene Corporation                 | US/Non-US      |
| AQX-1125                                                | 2     | Activates SHIP1 pathway             | oral                    | Aquinox Pharmaceuticals, Inc.       | Non-US         |
| CIM331                                                  | 2     | Anti-IL-31 receptor                 | injection               | Chugai Pharmaceutical               | US             |
| CT327                                                   | 2     | anti-pruritic                       | topical                 | Creabilis SA                        | Non-US         |
| DS107G                                                  | 2     |                                     | oral                    | Dignity Sciences, Ltd.              | US/Non-US      |
| Dupilumab and Immune Responses                          | 2     | biologic IL-4R Antibody             | injection               | Regeneron Pharmaceuticals           | US             |
| IgE specific Immunoabsorption                           | 2     | removal of IgE                      | immunoabsorption        | Universitaire Ziekenhuizen Leuven   | Non-US         |
| ILV-094                                                 | 2     | anti-IL-22                          | injection               | Rockefeller University              | US             |
| KHK4577                                                 | 2     | interventional                      | oral                    | Kyowa Hakko Kirin Company, Ltd.     | Non-US         |
| KM110329                                                | 2     | dietary supplement                  | oral                    | Kyunghee University Medical Center  | Non-US         |
| MRX-6 Cream 2%                                          | 2     | anti-Inflammatory                   | topical                 | Celsus Therapeutics PLC             | Non-US         |
| OC000459                                                | 2     | DP2 antagonist                      | oral                    | Atopix Therapeutics, Ltd.           | Non-US         |
| SB011                                                   | 2     | cleaves GATA-3 mRNA                 | topical                 | Sterna Biologicals GmbH & Co. KG    | Non-US         |
| QAW039                                                  | 2     | (PGD2), DP2 (CRTH2)                 | oral                    | Novartis Pharmaceuticals            | Non-US         |
| Tralokinumab                                            | 2     | anti-IL13                           | injection               | MedImmune LLC                       | US             |
| VLY-686                                                 | 2     | anti-pruritic                       | oral                    | Vanda Pharmaceuticals               | Non-US         |
| Ustekinumab                                             | 2     | anti-IL12/23                        | injection               | Rockefeller University              | US             |
| Amino Acid Moisturizing Cream/<br>Desonide Cream        | 3     | hydrates skin/<br>anti-inflammatory | topical                 | NeoStrata Company, Inc.             | US             |
| AN2728 Topical Ointment, 2%                             | 3     | PDE-4 inhibitor                     | topical                 | Anacor Pharmaceuticals, Inc.        | US             |
| Clemastine Fumarate + Dexamethasone                     | 3     | anti-Inflammatory                   | topical                 | EMS                                 | Non-US         |
| Dupilumab Monotherapy<br>Efficacy and Safety            | 3     | biologic IL-4R Antibody             | injection               | Regeneron Pharmaceuticals           | US             |
| Dupilumab + Topical Corticosteroids<br>Long-term Safety | 3     | biologic IL-4R Antibody             | injection               | Regeneron Pharmaceuticals           | US             |
| Holly Mangrove Shower Gel                               | 3     | Improves skin barrier function      | topical                 | Mahidol University                  | Non-US         |

# Crisaborole 2%(EUCRISA®)

(not licensed in Ireland)

- PDE-4 inhibitor (phenoxybenoxaborole,  $C_{14}H_{10}BNO_3$ )
- Mode of action:
  - PDE-4B is responsible for inflammation, reducing TNF- $\alpha$ , IL-12, IL-23.
    - Non steroidal anti inflammatory with a boron ring. Boron enhances its binding activity and allows better penetration into the skin
- Achieved significant efficacy in 2 large phase 3 trials in AD.

- Amy S. Paller, Wynn L. Tom, Mark G. Lebwohl, Robin L. Blumenthal, Mark Boguniewicz, Robert S. Call, Lawrence F. Eichenfield, Douglass W. Forsha, William C. Rees, Eric L. Simpson, Mary C. Spellman, Linda F. Stein Gold...
- **Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults.**

Journal of the American Academy of Dermatology, Volume 75, Issue 3, 2016, 494–503.e6

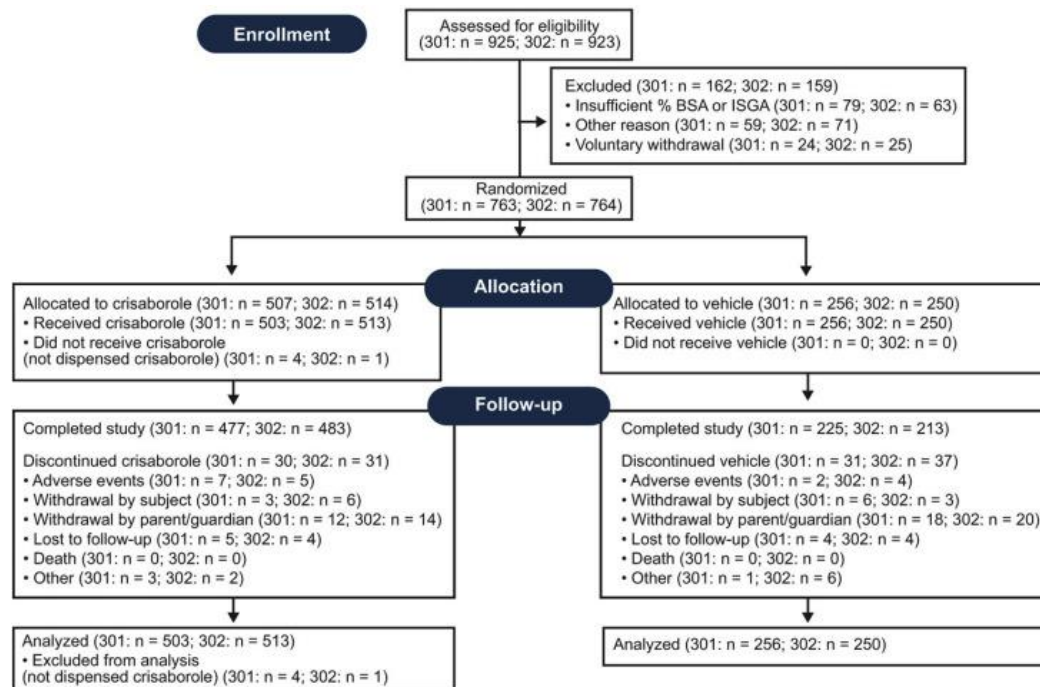


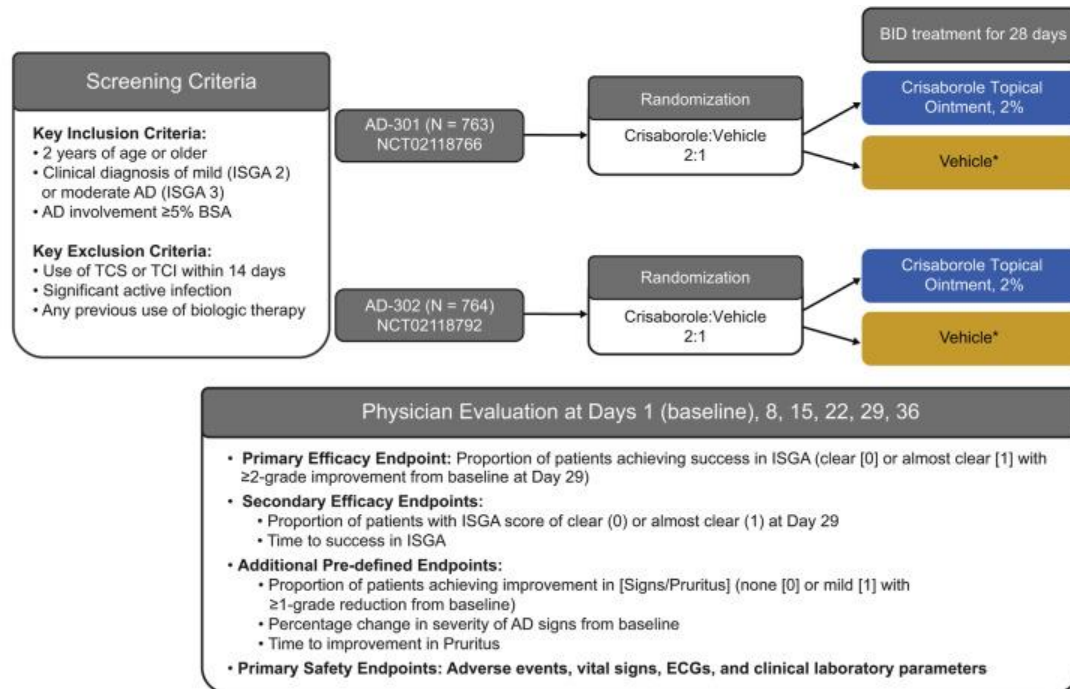
Fig 1. Atopic dermatitis. Enrollment, randomization, treatment, and follow-up. BSA, Body surface area; ISGA, Investigator's Static Global Assessment.

Amy S. Paller, Wynniss L. Tom, Mark G. Lebwohl, Robin L. Blumenthal, Mark Boguniewicz, Robert S. Call, Lawrence F. Eichenfield, Douglass W. Forsha, William C. Rees, Eric L. Simpson, Mary C. Spellman, Linda F. Stein Gold...

**Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults**

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<http://dx.doi.org/10.1016/j.jaad.2016.05.046>



Supplementary Fig 1. Atopic dermatitis (AD). Study design and treatment. Key screening criteria, patient enrollment, randomization, and assessments. AD, Atopic dermatitis; BID, twice daily; BSA, body surface area; ECG, electrocardiography; ISGA, Investigator's...

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### **Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults**

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# Clinical outcomes

- 1° endpoint @ day 29
- % success of clear or almost clear with a minimum of a  $\geq 2$  grade improvement
- 2° endpoint
- % patients almost clear @ day 29
- Crisaborole achieved success earlier than vehicle treated patients.

# Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults

Amy S. Paller, Wynn L. Tom, Mark G. Lebwohl, Robin L. Blumenthal, Mark Boguniewicz, Robert S. Call, Lawrence F. Eichenfield, Douglass W. Forsha, William C. Rees, Eric L. Simpson, Mary C. Spellman, Linda F. Stein Gold.

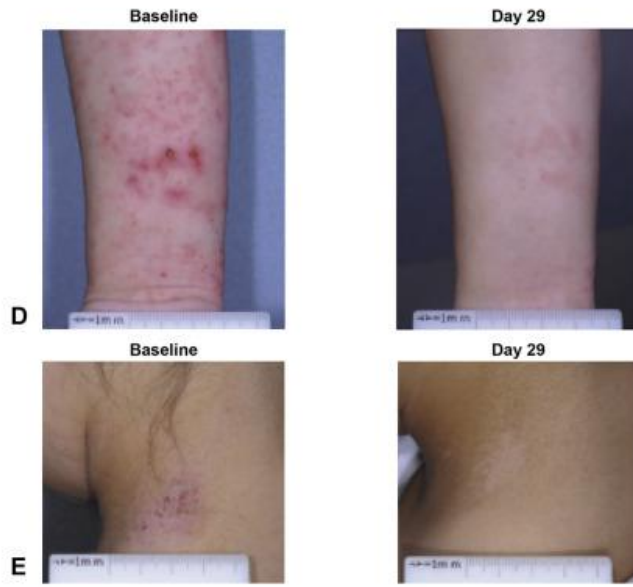
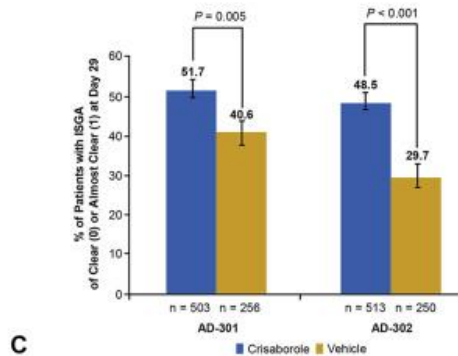
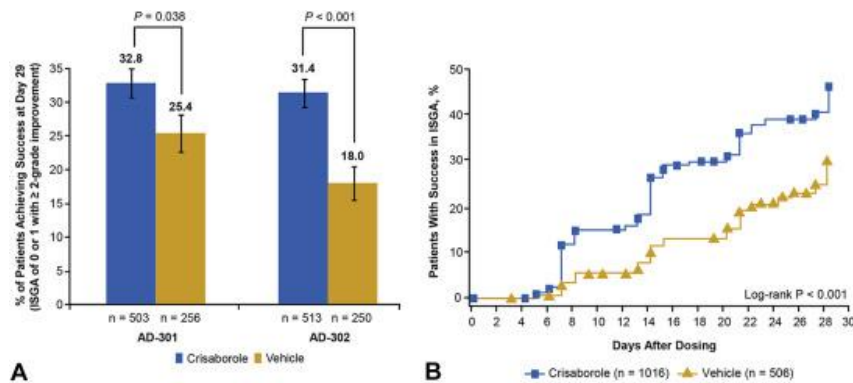


Fig 2. Atopic dermatitis (AD). Efficacy analysis. In studies AD-301 and AD-302, a greater proportion of crisaborole-treated patients achieved success in Investigator's Static Global Assessment (ISGA) score by day 29 (A). In addition, crisaborole-treated patien...

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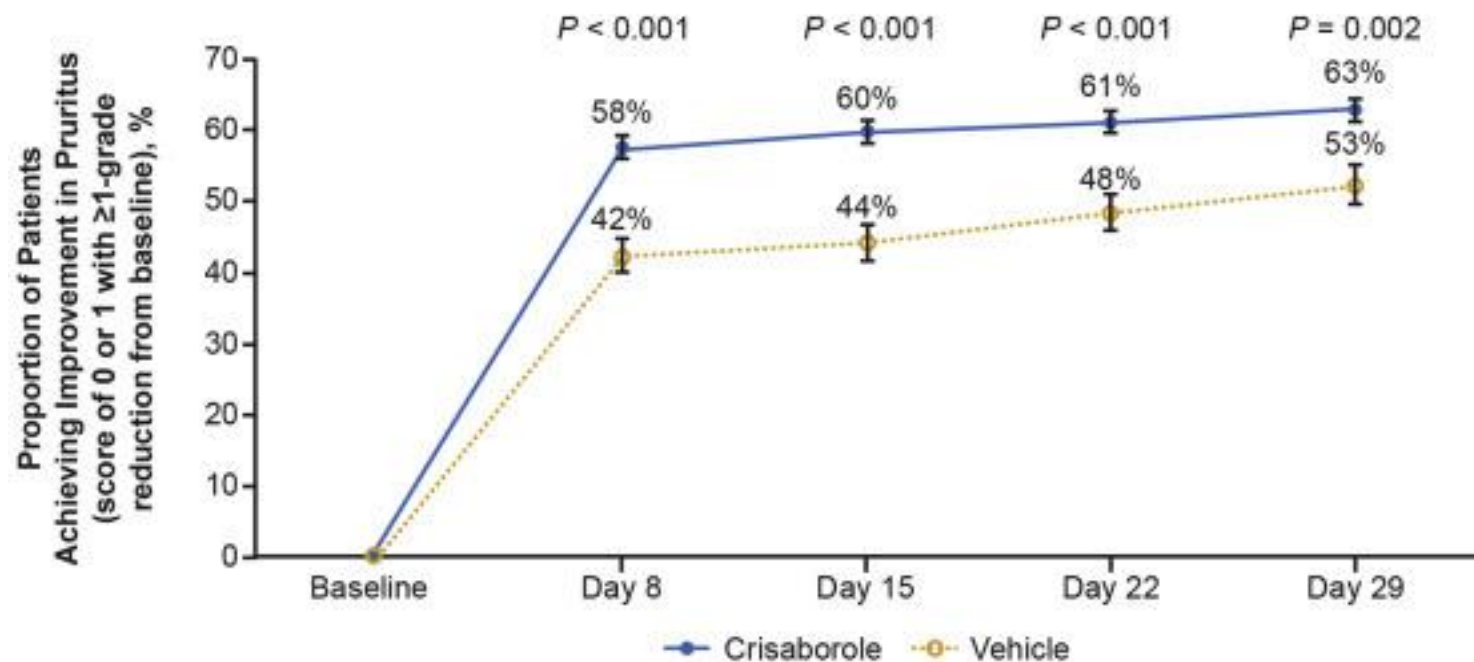


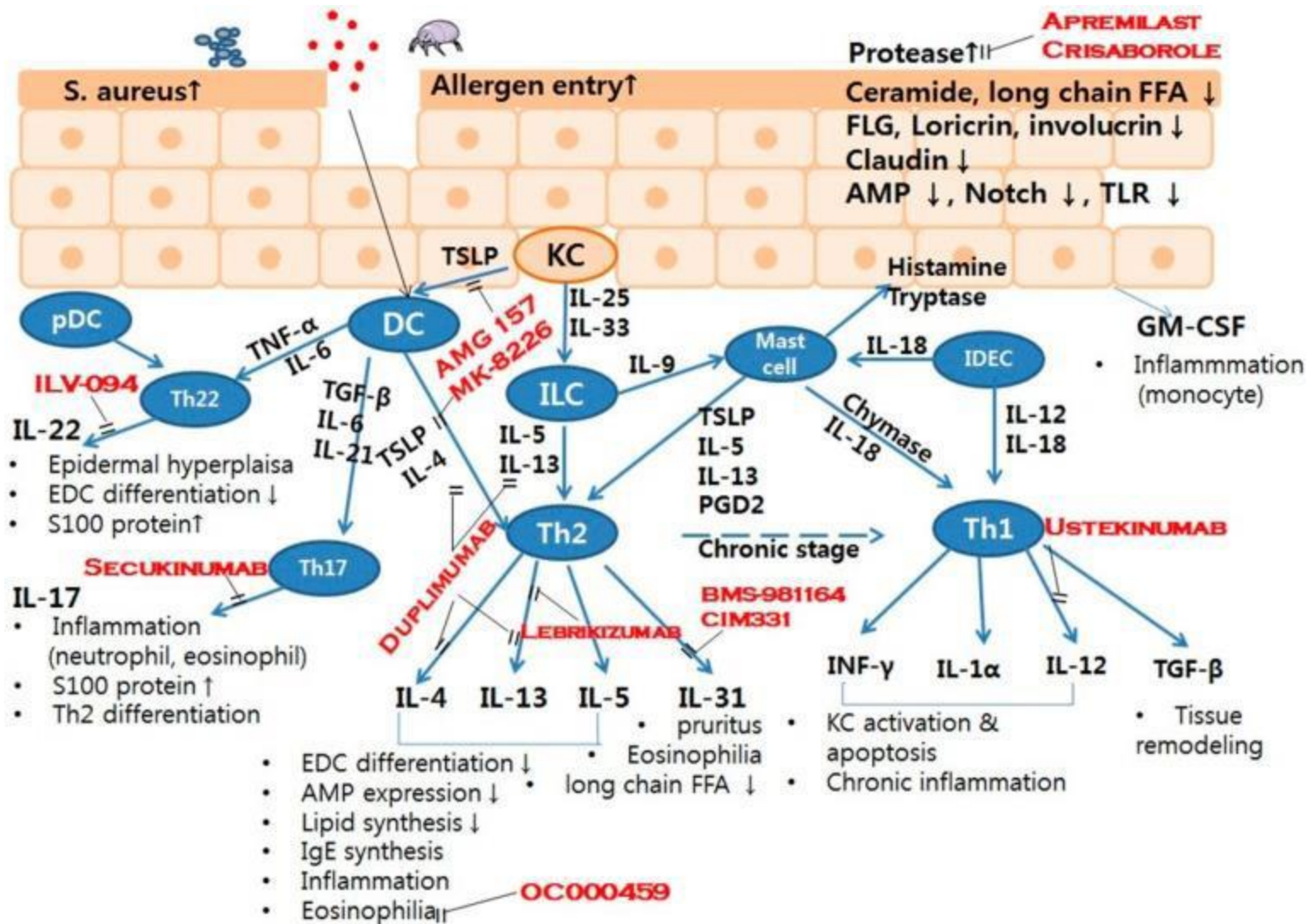
Fig 3. Atopic dermatitis (AD). Improvements in pruritus. In a pooled analysis of studies AD-301 and AD-302, a greater percentage of crisaborole-treated patients achieved improvement in pruritus at the earliest evaluation and throughout treatment compared with...

Amy S. Paller, Wynniss L. Tom, Mark G. Lebwohl, Robin L. Blumenthal, Mark Boguniewicz, Robert S. Call, Lawrence F. Eichenfield, Douglass W. Forsha, William C. Rees, Eric L. Simpson, Mary C. Spellman, Linda F. Stein Gold...

**Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults**

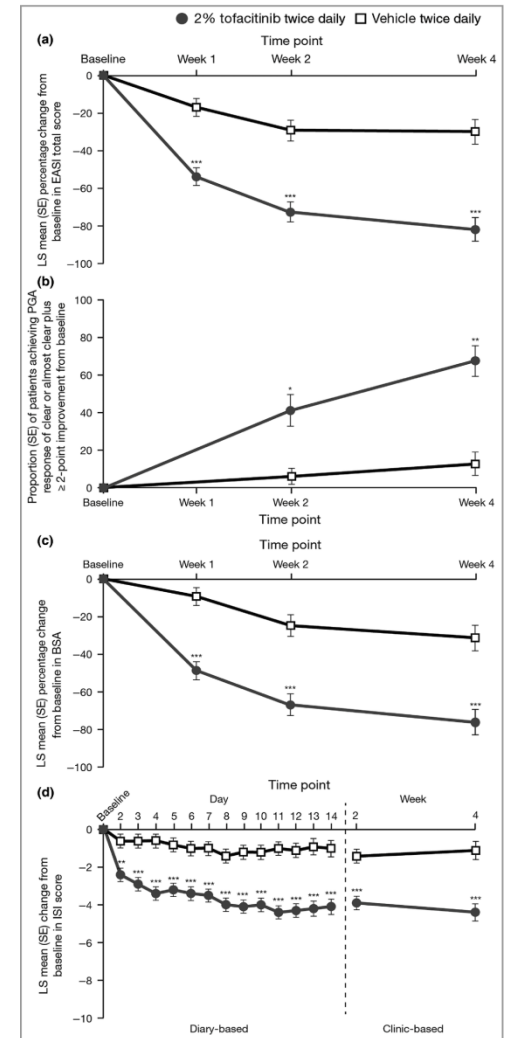
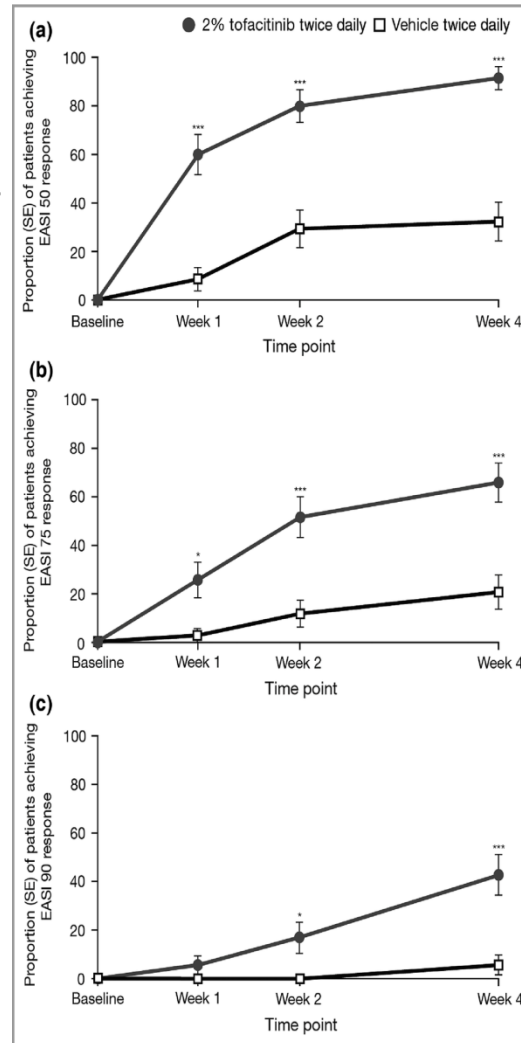
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<http://dx.doi.org/10.1016/j.jaad.2016.05.046>



# JAK inhibitors

- Topical tofacitinib 2%
- Janus kinase inhibitors.



The New England Journal of Medicine

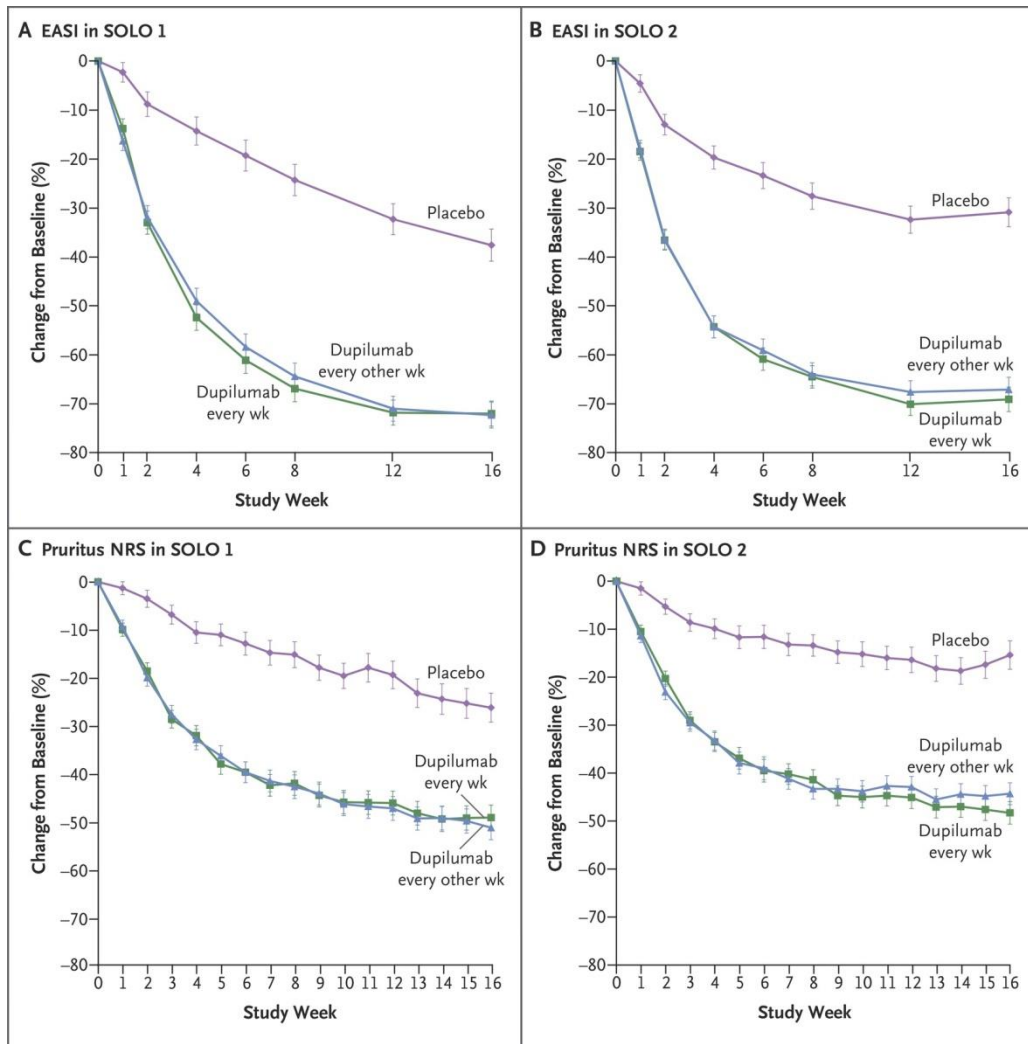
**ORIGINAL ARTICLE**

Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis

- Eric L. Simpson, M.D., Thomas Bieber, M.D., Ph.D., Emma Guttman-Yassky, M.D., Ph.D., Lisa A. Beck, M.D., Andrew Blauvelt, M.D., Michael J. Cork, M.B., Ph.D., Jonathan I. Silverberg, M.D., Ph.D., M.P.H., Mette Deleuran, M.D., D.M.Sc., Yoko Kataoka, M.D., Jean-Philippe Lacour, M.D., Külli Kingo, M.D., Ph.D., Margitta Worm, M.D., Yves Poulin, M.D., Andreas Wollenberg, M.D., Yuhwen Soo, Ph.D., Neil M.H. Graham, M.B., B.S., M.D., M.P.H., Gianluca Pirozzi, M.D., Ph.D., Bolanle Akinlade, M.D., Heribert Staudinger, M.D., Ph.D., Vera Mastey, M.S., Laurent Eckert, Ph.D., Abhijit Gadkari, Ph.D., Neil Stahl, Ph.D., George D. Yancopoulos, M.D., Ph.D., and Marius Ardeleanu, M.D., for the SOLO 1 and SOLO 2 Investigators\*
- N Engl J Med 2016; 375:2335-2348 [December 15, 2016](#)
- DOI:10.1056/NEJMoa1610.020
- **Not yet licensed in Ireland**

# Dupilumab

- A fully human Anti IL-4a inhibitor (Th2 cytokines)
- Phase 3 results are in!
- Recruiting teenage and paediatric population
- Reduction in itch
- Improved DQLI
- Reduction in EASI
- SOLO-1, SOLO-2, LIBERTY AD CHRONOS RCTs.



**Table 3. Adverse Events.\***

| Event                                              | SOLO 1               |                                            |                                      | SOLO 2               |                                            |                                      |
|----------------------------------------------------|----------------------|--------------------------------------------|--------------------------------------|----------------------|--------------------------------------------|--------------------------------------|
|                                                    | Placebo<br>(N = 222) | Dupilumab<br>Every Other Week<br>(N = 229) | Dupilumab<br>Every Week<br>(N = 218) | Placebo<br>(N = 234) | Dupilumab<br>Every Other Week<br>(N = 236) | Dupilumab<br>Every Week<br>(N = 237) |
| <i>number of patients (percent)</i>                |                      |                                            |                                      |                      |                                            |                                      |
| <b>Adverse or serious adverse event</b>            |                      |                                            |                                      |                      |                                            |                                      |
| At least 1 adverse event                           | 145 (65)             | 167 (73)                                   | 150 (69)                             | 168 (72)             | 154 (65)                                   | 157 (66)                             |
| At least 1 serious adverse event                   | 11 (5)               | 7 (3)                                      | 2 (1)                                | 13 (6)               | 4 (2)                                      | 8 (3)                                |
| Death†                                             | 0                    | 0                                          | 0                                    | 0                    | ➡ 1 (<1)                                   | ➡ 1 (<1)                             |
| Adverse event leading to treatment discontinuation | 2 (1)                | 4 (2)                                      | 4 (2)                                | 5 (2)                | 2 (1)                                      | 3 (1)                                |
| <b>Noninfectious adverse event‡</b>                |                      |                                            |                                      |                      |                                            |                                      |
| Injection-site reaction                            | 13 (6)               | 19 (8)                                     | 41 (19)                              | 15 (6)               | 32 (14)                                    | 31 (13)                              |
| Exacerbation of atopic dermatitis                  | 67 (30)              | 30 (13)                                    | 21 (10)                              | 81 (35)              | 32 (14)                                    | 38 (16)                              |
| Headache                                           | 13 (6)               | ➡ 21 (9)                                   | 11 (5)                               | 11 (5)               | 19 (8)                                     | 22 (9)                               |
| Allergic conjunctivitis                            | 2 (1)                | ➡ 12 (5)                                   | 7 (3)                                | 2 (1)                | 2 (1)                                      | 3 (1)                                |
| <b>Infectious adverse event‡</b>                   |                      |                                            |                                      |                      |                                            |                                      |
| Infections and infestations§                       | 63 (28)              | ➡ 80 (35)                                  | ➡ 74 (34)                            | 76 (32)              | 65 (28)                                    | 68 (29)                              |
| Nasopharyngitis                                    | 17 (8)               | ➡ 22 (10)                                  | ➡ 25 (11)                            | 22 (9)               | 20 (8)                                     | 20 (8)                               |
| Upper respiratory tract infection                  | 5 (2)                | 6 (3)                                      | 11 (5)                               | 5 (2)                | 7 (3)                                      | 9 (4)                                |
| Conjunctivitis¶                                    | 2 (1)                | 11 (5)                                     | 7 (3)                                | 1 (<1)               | 9 (4)                                      | 9 (4)                                |
| Any herpes viral infection                         | 9 (4)                | 15 (7)                                     | 9 (4)                                | 8 (3)                | 10 (4)                                     | 12 (5)                               |
| Oral herpes                                        | 4 (2)                | 9 (4)                                      | 4 (2)                                | 4 (2)                | 8 (3)                                      | 9 (4)                                |
| Herpes simplex                                     | 3 (1)                | 7 (3)                                      | 2 (1)                                | 1 (<1)               | 0                                          | 1 (<1)                               |
| Eczema herpeticum                                  | 2 (1)                | 1 (<1)                                     | 1 (<1)                               | 1 (<1)               | 2 (1)                                      | 0                                    |
| Herpes virus infection                             | 0                    | 0                                          | 1 (<1)                               | 1 (<1)               | 0                                          | 0                                    |
| Herpes zoster                                      | 1 (<1)               | 1 (<1)                                     | 0                                    | 1 (<1)               | 0                                          | 0                                    |
| Ophthalmic herpes simplex                          | 0                    | 0                                          | 1 (<1)                               | 0                    | 0                                          | 0                                    |
| Genital herpes                                     | 1 (<1)               | 0                                          | 0                                    | 0                    | 0                                          | 1 (<1)                               |
| Herpes ophthalmic                                  | 0                    | 0                                          | 0                                    | 1 (<1)               | 0                                          | 1 (<1)                               |
| Herpes simplex otitis externa                      | 0                    | 0                                          | 0                                    | 0                    | 1 (<1)                                     | 0                                    |
| Adjudicated skin infection                         | 18 (8)               | 13 (6)                                     | 14 (6)                               | 26 (11)              | 13 (6)                                     | 15 (6)                               |
| Non-skin infection                                 | 49 (22)              | 69 (30)                                    | 67 (31)                              | 57 (24)              | 58 (25)                                    | 61 (26)                              |

\* Patients are listed according to the study drug received, which may differ from the randomized group. Adverse events that were reported at the level of preferred terms occurred in at least 5% of the patients in any randomized group, with the exception that all adverse events with preferred terms related to herpes virus infection are reported here. Included in the safety analysis were all the patients who underwent randomization and received at least one dose of dupilumab or placebo.

† Details regarding the two deaths are provided in the Supplementary Appendix.

‡ Adverse events are reported at the preferred term level of the *Medical Dictionary for Regulatory Activities* (MedDRA) hierarchy, unless otherwise indicated.

§ This adverse event is reported at the system organ class level in the MedDRA hierarchy.

¶ This MedDRA preferred term includes conjunctivitis of unspecified cause.

|| This adverse event is reported at the high-level term in the MedDRA hierarchy.

# LIBERTY AD CHRONOS

|                                |                                                                                                                                                |
|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| ClinicalTrials.gov Identifier: | NCT02260986                                                                                                                                    |
| Study Title:                   | Study to Assess the Efficacy and Long-term Safety of Dupilumab (REGN668/SAR231893) in Adult Patients With Moderate-to-Severe Atopic Dermatitis |
| First Received:                | October 6, 2014                                                                                                                                |
| Last Updated:                  | February 7, 2017                                                                                                                               |

- RCT: Dupilumab & concomitant TCS
- Dup 300mgs weekly + TCS
- Dup 300mgs q2weekly +TCS
- Placebo + TCS
- IGA & EASI 75
- 1°endpoint Clear at 16 weeks
- Wk 16-52 40% maintained a response.
- Rescue rate ~15%;with CyA

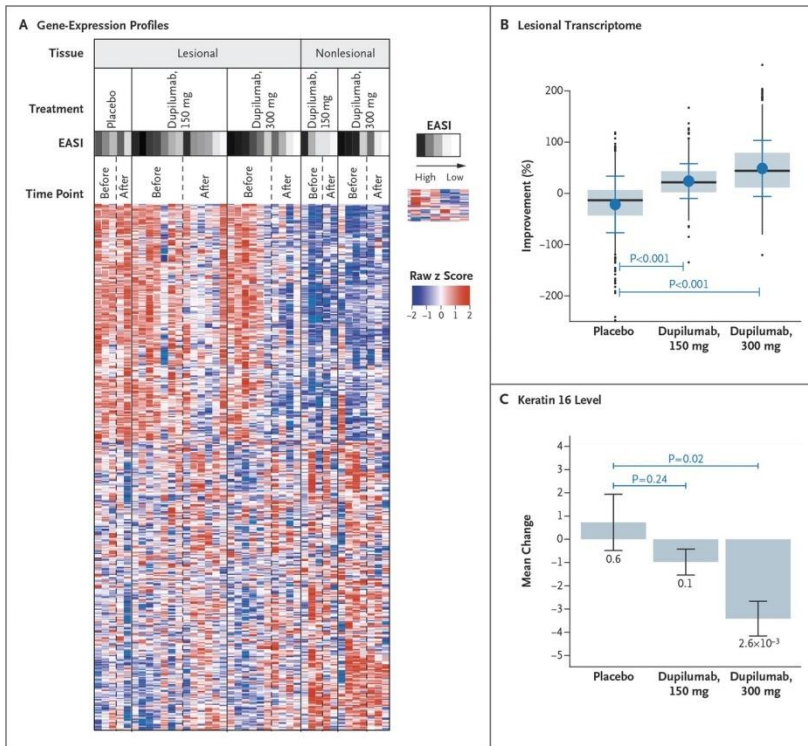
# Study details

- Inclusion criteria BSA > 50%
- 34-40 years
- High DLQI
- Safety data : no parasitic infections
- More flares in TCS group
- More injection site reactions.
- Met primary endpoints.
- 1<sup>st</sup> placebo controlled trial blocking Th2, key for treating atopic dermatitis.
- Also may have a role in Asthma

# Other trials

- Guttman:
- Role of IL-17, IL-22 in AD.
- Markers of epidermal hyperplasia -keratin 16
- Down-regulation of biomarkers in patients treated with Dupilumab 300mgs, up-regulation in placebo groups. Dupilumab appears to impact the inflammation plus the barrier dysfunction of AD.
- SKIN BIOPSIES;

Skipped expression seen in FLG normalised on Dupilumab by week 16 & there was a 40% reduction of epidermal thickness



# Nemolizumab

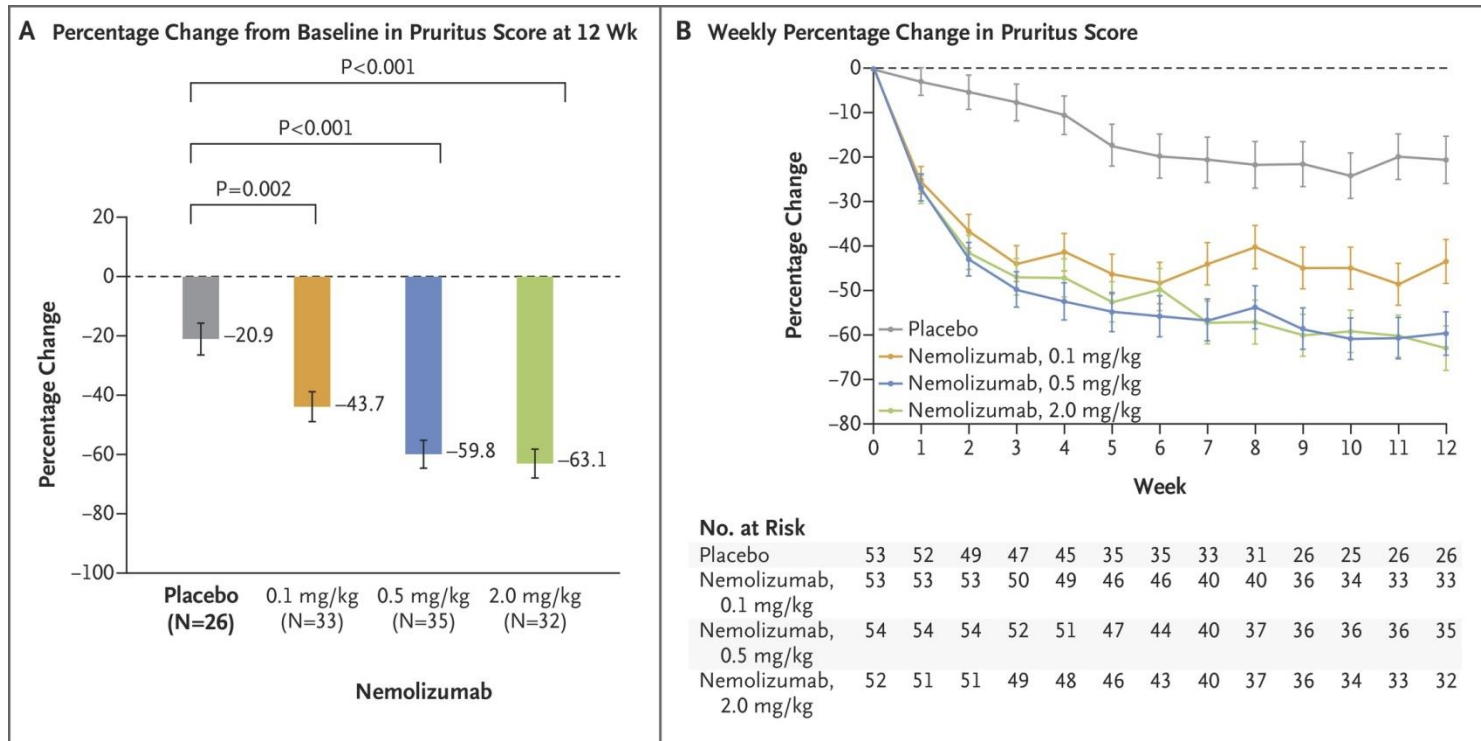
Original Article

## **Anti-Interleukin-31 Receptor A Antibody for Atopic Dermatitis**

Thomas Ruzicka, M.D., Jon M. Hanifin, M.D., Masutaka Furue, M.D., Ph.D., Grazyna Pulka, M.D., Izabela Mlynarczyk, M.D., Andreas Wollenberg, M.D., Ryszard Galus, M.D., Ph.D., Takafumi Etoh, M.D., Ryosuke Mihara, M.S., Hiroki Yoshida, M.S., Jonathan Stewart, M.B., Ch.B., and Kenji Kabashima, M.D., Ph.D., for the XCIMA Study Group<sup>\*</sup>  
N Engl J Med 2017; 376:826-835 [March 2, 2017](#) DOI: 10.1056/NEJMoa1606490

- Anti IL-31 inhibitor.
- Pruritus in AD
- Pro-inflammatory role.
- DB RCT trial 5 arms over 64 weeks.
- Part B Placebo group crossed over at 12 weeks and TCS were used prn.

- In a phase 2, placebo-controlled trial, Nemolizumab, an antibody against interleukin-31 receptor A, reduced pruritus in patients with moderate-to-severe atopic dermatitis.
- These findings support the role of interleukin-31 in the pathophysiology of atopic dermatitis.



# Results

- 50% of patients didn't need TCS even though allowed.
- Limitations: no placebo controlled group in part B.
- Phase 2 trial.

**Table 3. Adverse Events (Safety Population).\***

| Event                                                                            | Placebo<br>(N = 53) | Nemolizumab           |                       |                       |                                     |
|----------------------------------------------------------------------------------|---------------------|-----------------------|-----------------------|-----------------------|-------------------------------------|
|                                                                                  |                     | 0.1 mg/kg<br>(N = 53) | 0.5 mg/kg<br>(N = 54) | 2.0 mg/kg<br>(N = 52) | 2.0 mg/kg<br>Every 8 Wk<br>(N = 52) |
| Total no. of adverse events                                                      | 105                 | 110                   | 80                    | 99                    | 90                                  |
| Patients with ≥1 adverse event —<br>no. (%)                                      | 36 (68)             | 38 (72)               | 36 (67)               | 40 (77)               | 37 (71)                             |
| Patients with ≥1 serious adverse<br>event — no. (%)                              | 1 (2)               | 1 (2)                 | 0                     | 3 (6)                 | 2 (4)                               |
| Related to atopic dermatitis                                                     | 0                   | 0                     | 0                     | 2 (4)                 | 1 (2)                               |
| Not related to atopic dermatitis                                                 | 1 (2)               | 1 (2)                 | 0                     | 1 (2)                 | 1 (2)                               |
| Patients with adverse event leading to<br>withdrawal from treatment —<br>no. (%) | 1 (2)               | 5 (9)                 | 3 (6)                 | 4 (8)                 | 3 (6)                               |
| Related to atopic dermatitis                                                     | 0                   | 2 (4)                 | 3 (6)                 | 2 (4)                 | 3 (6)                               |
| Not related to atopic dermatitis                                                 | 1 (2)               | 3 (6)                 | 0                     | 2 (4)                 | 0                                   |
| Exacerbation of atopic dermatitis —<br>no. (%)†                                  | 7 (13)              | 11 (21)               | 10 (19)               | 11 (21)               | 9 (17)                              |
| Nasopharyngitis — no. (%)†                                                       | 8 (15)              | 9 (17)                | 6 (11)                | 5 (10)                | 7 (13)                              |
| Upper respiratory tract infection —<br>no. (%)†                                  | 6 (11)              | 4 (8)                 | 1 (2)                 | 4 (8)                 | 5 (10)                              |
| Peripheral edema — no. (%)†                                                      | 0                   | 2 (4)                 | 3 (6)                 | 5 (10)                | 2 (4)                               |
| Elevation in blood creatine kinase —<br>no. (%)†                                 | 3 (6)               | 2 (4)                 | 2 (4)                 | 4 (8)                 | 3 (6)                               |

\* Nemolizumab or placebo was administered once every 4 weeks, unless otherwise indicated.

† This adverse event was reported in at least 5% of the patients who received nemolizumab.



# IL-13 Inhibitors

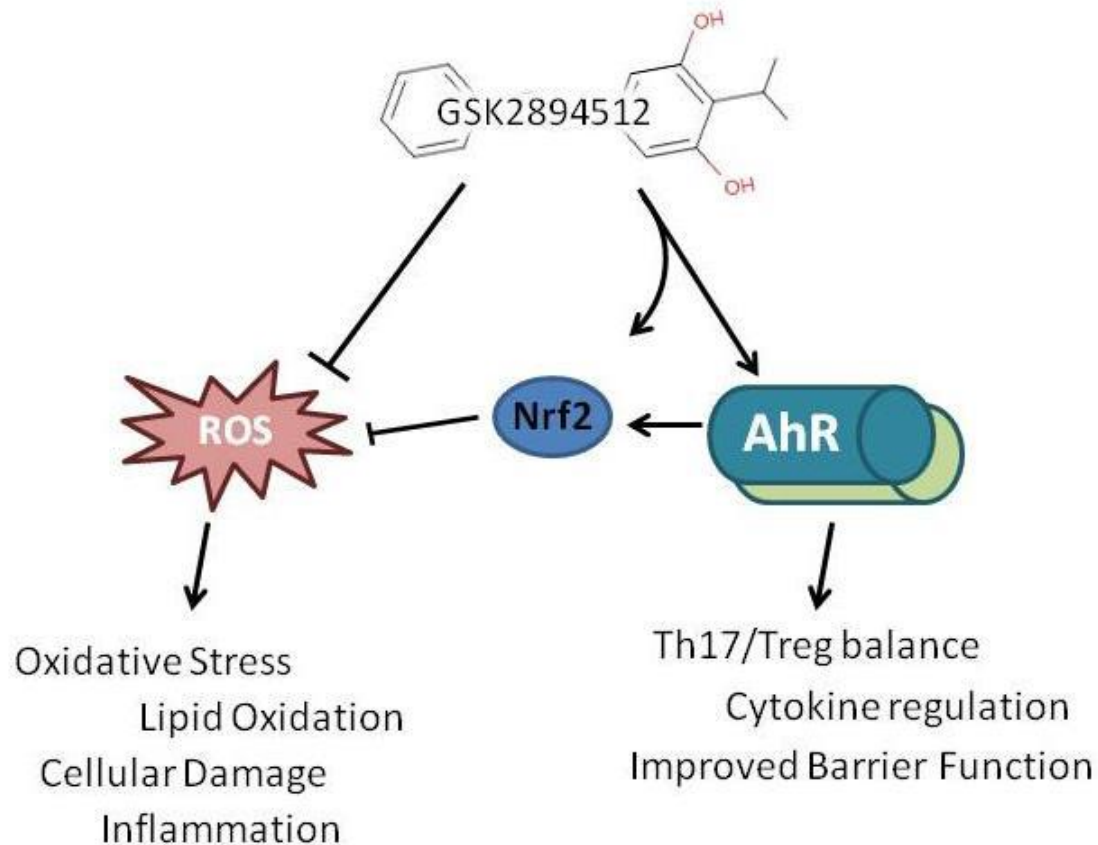
- Lebrikizumab
- Tralokinumab
- Narrower therapeutic target.

1.Noda S, Suárez-Fariñas M, Ungar B, Kim SJ, de Guzman Strong C, Xu H, Peng X, Estrada YD, Nakajima S, Honda T, Shin JU. The Asian atopic dermatitis phenotype combines features of atopic dermatitis and psoriasis with increased T H 17 polarization. *Journal of Allergy and Clinical Immunology*. 2015 Nov 30;136(5):1254-64.

2.Howell MD, Parker ML, Mustelin T, Ranade K. Past, present, and future for biologic intervention in atopic dermatitis. *Allergy*. 2015 Aug 1;70(8):887-96.

# Tapinarof ( AhR)

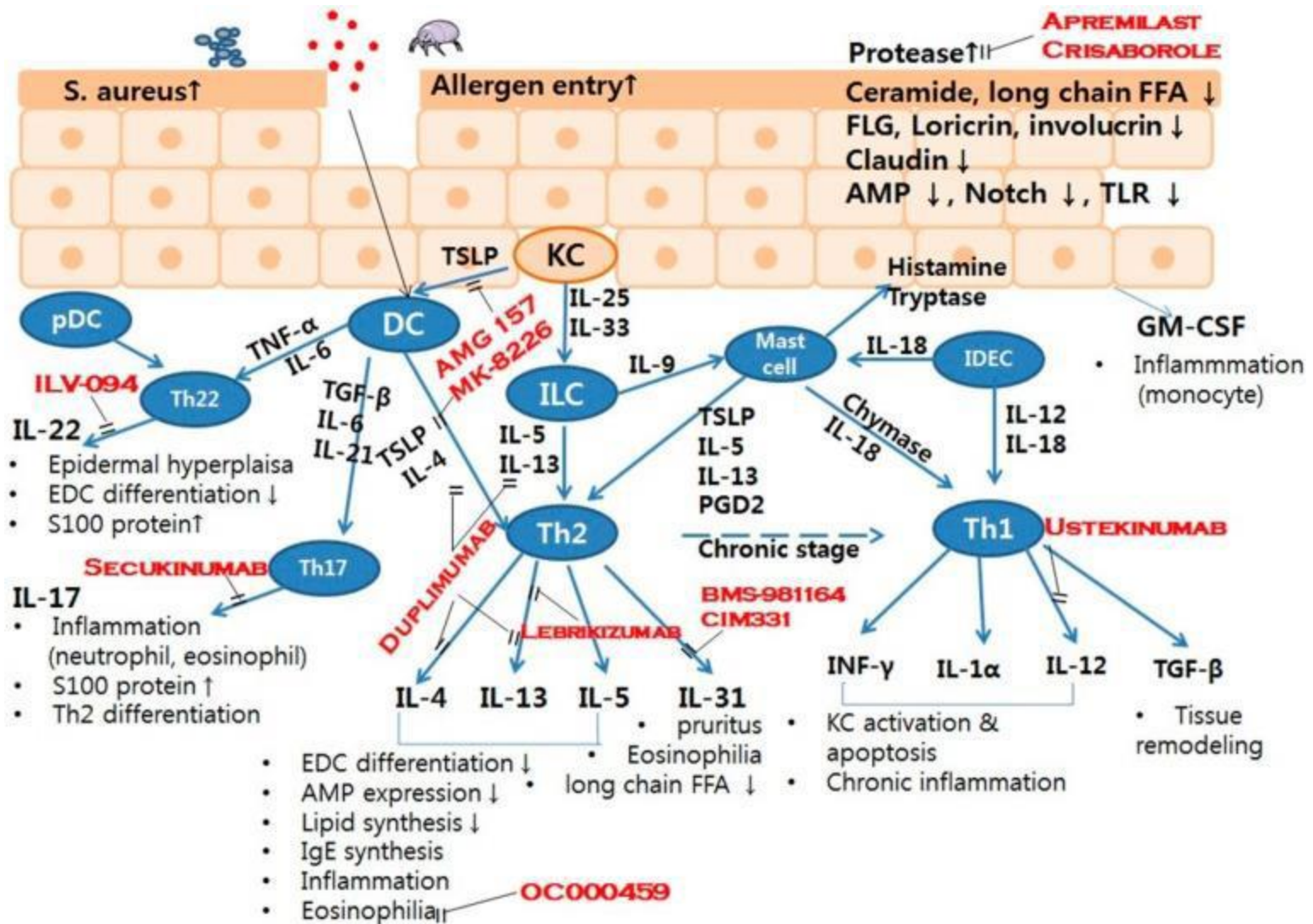
## Aryl Hydrocarbon receptor agonist



# Tapinarof

GSK 2894512 Clinical trial unlicensed.

- Reduces IL-17
- NSAID topical anti-inflammatory with a NOVEL mode of action.
- Phase 2 trial : 1% qid /1%bd/ 0.5% be/ 0.5% od.
- Adverse events: SAE Contact dermatitis /folliculitis
- Primary endpoint PGA 0/1
- 12 weeks , follow up data up-to 16 weeks
- Clear difference between active arm vehicle arms.
- 1% higher efficacy and quicker onset of action.
- 1% qd is proposed for phase 3 trials
- 10% discontinued due to AEs.
- Phase 2 no patch testing, phase 3 patch testing



# Hot topics in Psoriasis

- Translational research
- Topical therapies from late breaking abstracts
- Update on
  - IL-17 inhibitors
  - IL-23 inhibitors
  - Ps and PsA
  - Palmoplantar and nail disease
  - Paediatric Psoriasis
  - Biosimilars

# Certolizumab<sup>®</sup>

(not licensed in Ireland for psoriasis)

- Anti –TNF Fab fragment
- CIMPASI 1+2 Phase 3 studies 152 weeks

- **CIMPASI\_1**

the efficacy and safety of two dose levels of certolizumab pegol in adults with moderate to severe chronic plaque psoriasis when administered every 2 weeks.

- **CIMPASI-2**

efficacy and safety of two dose levels of certolizumab pegol in adults with moderate to severe chronic plaque psoriasis.

- A Phase 3 Multicenter, Randomized, Double Blind, Parallel Group Study Followed by Dose Blind Period and Open Label Follow Up to Evaluate Efficacy and Safety of Certolizumab Pergola in Subjects With Moderate to Severe Chronic Plaque Psoriasis.
- Results due in Sept 2018

- 1.Campanati A, Benfaremo D, Luchetti MM, Ganzetti G, Gabrielli A, Offidani A. Certolizumab pegol for the treatment of psoriasis. Expert Opinion on Biological Therapy. 2017 Feb 4;1-8.

# Results

- 2 Co primary endpoints: PASI 75+ PGA 0/1
- Cohorts
- CTS 400mgs q2weekly
- CTS 200mgs q 2weekly
- placebo
- Responder rate @wk 16 66.75% CIMPASI 1
- 66.7% CIMPASI 2
- Statistically meaningful
- clear /almost clear PGA score

# **1% Benvitimod for Mild to moderate plaque Psoriasis.**

**RCT double blind placebo controlled phase 3 trial.  
(not licensed in Ireland)**

- AhR pathway.
- 3 Cohorts
  - Benvitimod
  - Calcipotriol
  - Placebo
- 12 weeks
- Safety profile: AEs 44%
- 8.4% discontinuation due to pruritus/contact dermatitis/folliculitis.
- 40 week follow up period
- 59 had remission.
- Benvitimod 1%
  - PASI 75 at 12:weeks higher than calcipotriol.
- ? Are the Benvitimod and Tapinarof the same molecule??

# Secukinumab <sup>®</sup>

IL-17 a , humanized mAb

FUTURE -2 trial ( PsA)

TRANSFIGURE –nail psoriasis

16 weeks

GESTURE-palmoplantar psoriasis

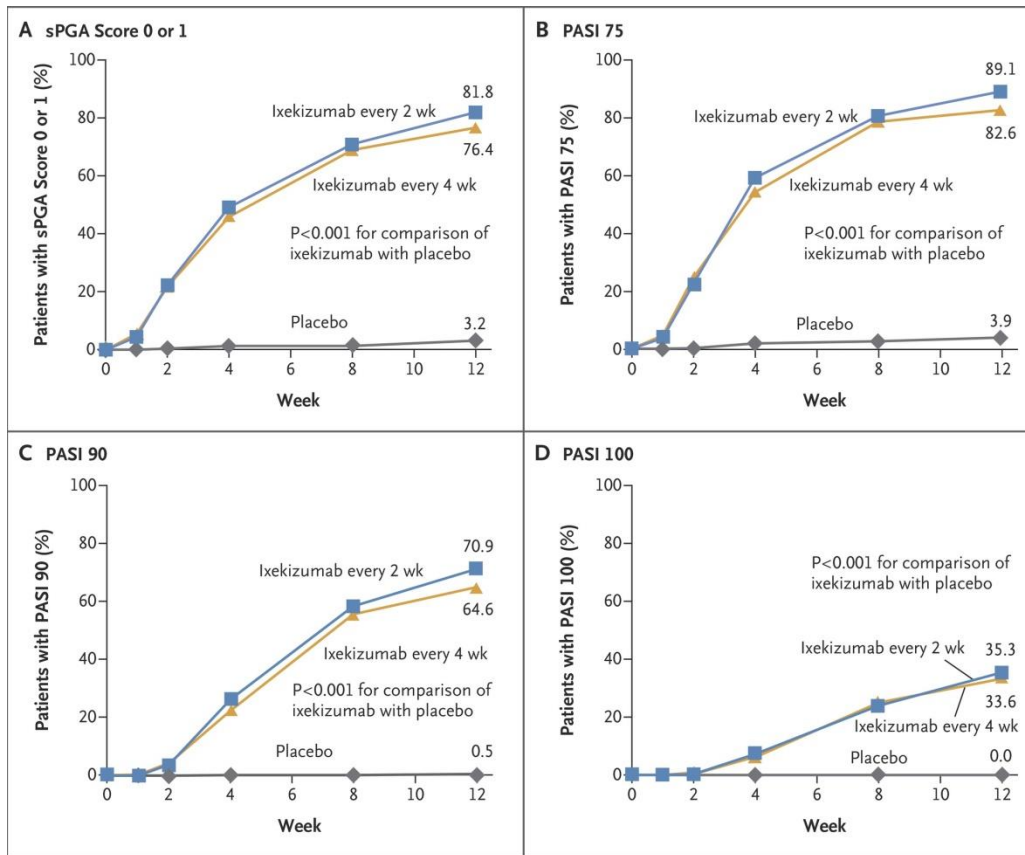
16 weeks

1. Reich K, Sullivan J, Arenberger P. Secukinumab is effective in subjects with moderate to severe plaque psoriasis with significant nail involvement: 16 week results from the TRANSFIGURE study. In 23rd World Congress of Dermatology. Vancouver, Canada 2015 Jun 8 (Vol. 11).

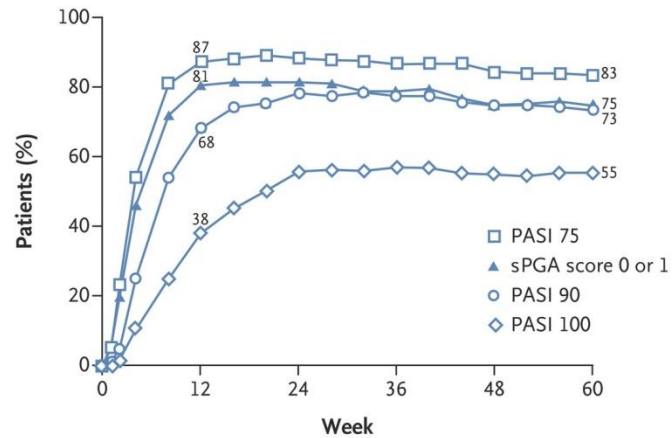
2. Gottlieb AB, Sullivan J, van Doorn MB. Secukinumab is effective in subjects with moderate to severe palmoplantar psoriasis: 16 week results from the GESTURE study 23rd World Congress of Dermatology. Vancouver, Canada. 2015;11.

# Ixekizumab

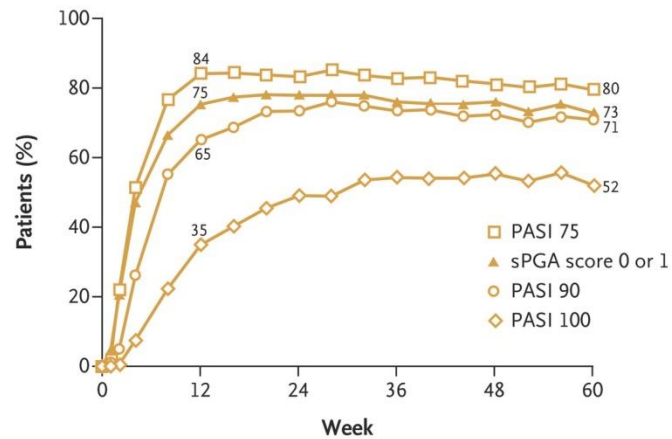
- Anti IL-17a human mAb UNCOVER 1, 2, 3



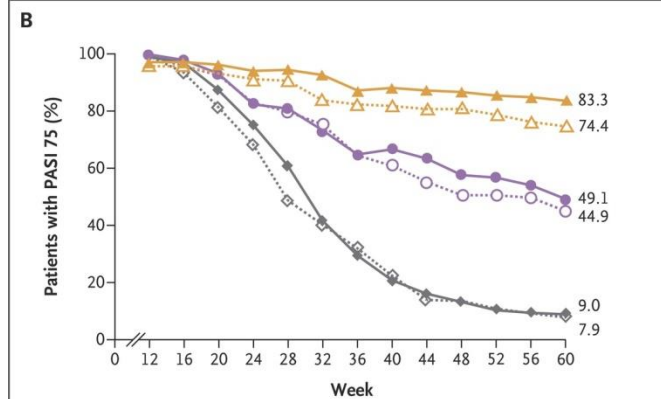
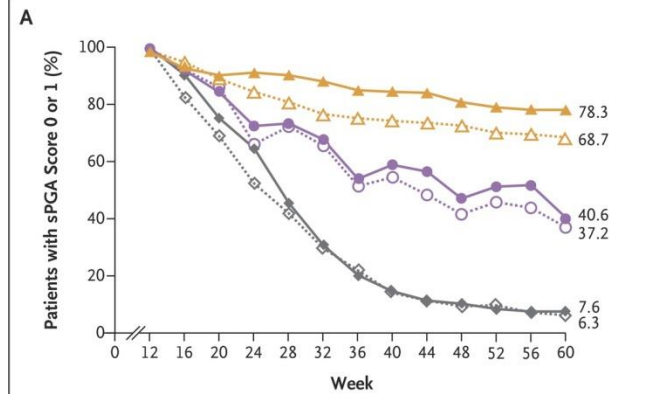
**A** Ixekizumab Every 2 Weeks (Weeks 0–12), Followed by Ixekizumab Every 4 Weeks (Weeks 12–60)



**B** Ixekizumab Every 4 Weeks, Weeks 0 through 60



- ◆— Ixekizumab every 2 wk (weeks 0–12)  
→placebo (weeks 12–60) (N=211)
- Ixekizumab every 2 wk (weeks 0–12)  
→Ixekizumab every 12 wk  
(weeks 12–60) (N=212)
- ▲— Ixekizumab every 2 wk (weeks 0–12)  
→Ixekizumab every 4 wk  
(weeks 12–60) (N=221)
- ◇— Ixekizumab every 4 wk (weeks 0–12)  
→placebo (weeks 12–60) (N=191)
- Ixekizumab every 4 wk (weeks 0–12)  
→Ixekizumab every 12 wk  
(weeks 12–60) (N=196)
- △— Ixekizumab every 4 wk  
(weeks 0–60) (N=195)



# Ixekizumab®

- IXORA-S RCT IXE vs USTE
- 1° endpoint patients achieving PASI 90 @12 wks follow on through to 24wks
- Inclusion criteria of PASI 10, mean 19.9
- IXE PASI 90 Achieved in 83% @wk 24
- ?Under dosing of Ustekinumab
- No difference in safety data @24 weeks between IXE & USTE

- IXORA-S Clinical trials.gov. NCT02561806 Ongoing. Eli Lilly.
- Griffiths CE, Reich K, Lebwohl M, van de Kerkhof P, Paul C, Menter A, Cameron GS, Erickson J, Zhang L, Secrest RJ, Ball S. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. The Lancet. 2015 Aug 14;386(9993):541-51.

# Brodalumab

- IL-17 Receptor antagonist.
- Wider blockage:IL-25, IL-17& IL-17c
- AMAGINE-2 /AMAGINE-3
- PASI 75 of 86% @ week 12
- In a head to head comparison with Ustekinumab
- PASI 100 of 51% maintained over 1 year compared to 28% in Ustekinumab.

# Brodalumab labelling

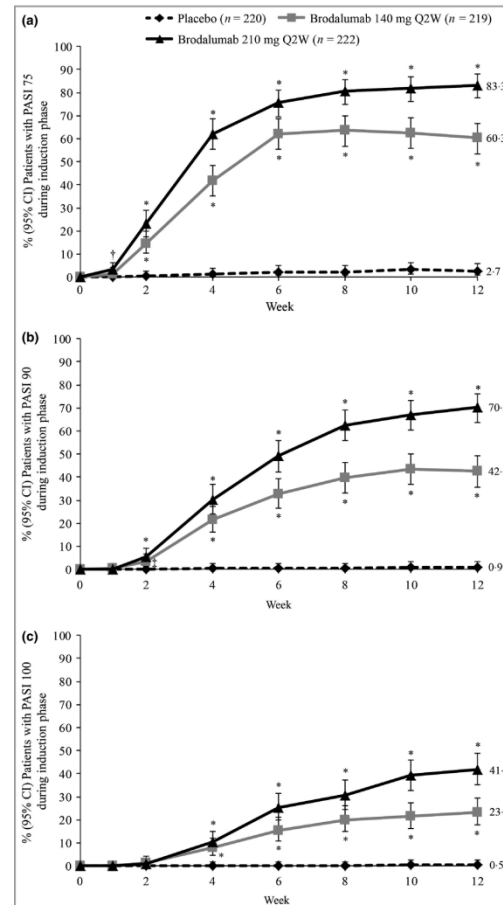
FDA approved

- *A causal relationship between suicidal ideation and behaviour has not been established.*
- 4 completed suicides & 10 attempts in the active arm.
- SILIQ users with a history of depression/suicidal ideation had an increased risk of suicidal ideation.
- Ixekizumab: 10 suicide attempts in the active arm
- Increased rate of suicide & depression in the psoriasis population.
- Middle aged white males represent the demographic most at risk for suicide.

- Greig SL. Brodalumab: First Global Approval. *Drugs*. 2016 Sep 1;76(14):1403-12.

- **British Journal of Dermatology**  
Volume 175, Issue 2, pages 273-286, 23 JUN 2016 DOI: 10.1111/bjd.14493  
<http://onlinelibrary.wiley.com/doi/10.1111/bjd.14493/full#bjd14493-fig-0002>

# A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis



# IL-23 inhibitors

- Ustekinumab
- IL-23 p40 subunit: mediates its effect through IL-23, IL-12
- Guselkumab, Tildrakizumab & Risankizumab
- IL-23 p19 subunit : IL-12 pathway is unaffected.

# Guselkumab

- Guselkumab (VOYAGE-1) with active comparator Adalimumab

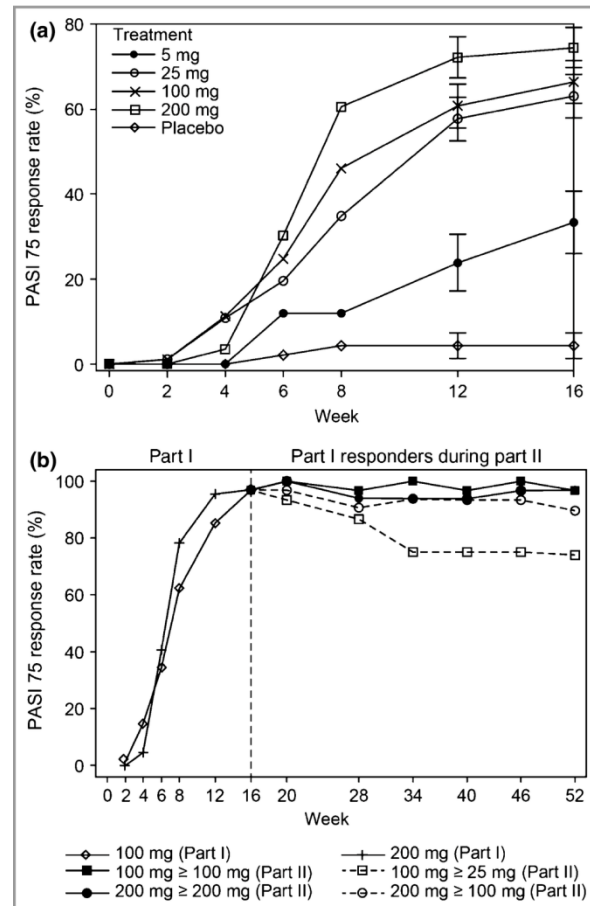
1. Tausend W, Downing C, Tying S. Systematic review of interleukin-12, interleukin-17, and interleukin-23 pathway inhibitors for the treatment of moderate-to-severe chronic plaque psoriasis: ustekinumab, briakinumab, tildrakizumab, guselkumab, secukinumab, ixekizumab, and brodalumab. *Journal of cutaneous medicine and surgery*. 2014 May;18(3):156-69.

2. Gordon KB, Duffin KC, Bissonnette R, Prinz JC, Wasfi Y, Li S, Shen YK, Szapary P, Randazzo B, Reich K. A phase 2 trial of guselkumab versus adalimumab for plaque psoriasis. *New England Journal of Medicine*. 2015 Jul 9;373(2):136-44.

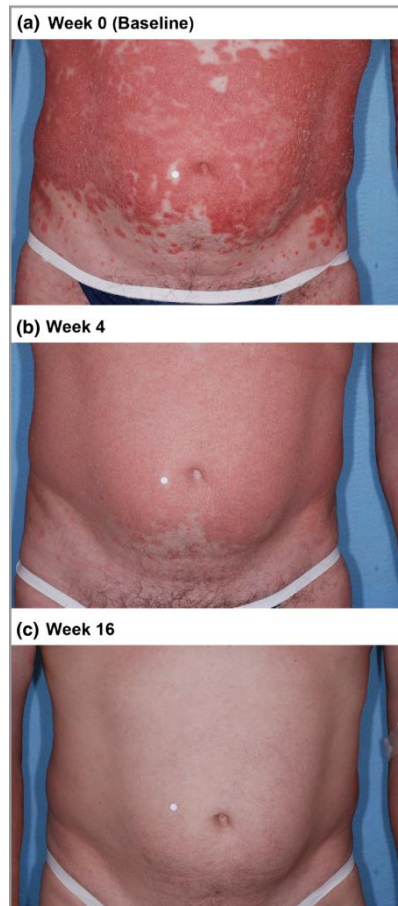
# Tildrakizumab

- Tildrakizumab (reSURFACE-1 & reSURFACE-2) with active comparator Etanercept.

# Tildrakizumab (MK-3222), an anti-interleukin-23p19 monoclonal antibody, improves psoriasis in a phase IIb randomized placebo-controlled trial



## Tildrakizumab (MK-3222), an anti-interleukin-23p19 monoclonal antibody, improves psoriasis in a phase IIb randomized placebo-controlled trial



# Risankizumab

not licensed in Ireland

- IL-23a BI 655066 Acquired by Abbvie
- Active comparator Ustekinumab
- Kaplan Meier analysis after stopping Risankizumab, it took 225 days to lose PASI 90

A Study to Assess the Safety and Efficacy of Risankizumab for Maintenance in Moderate to Severe Plaque Type Psoriasis. ACTIVE ENROLLING .  
NCT03047395 Clinical trials .gov

BI 655066 (Risankizumab) Compared to Placebo and Active Comparator (Ustekinumab) in Patients With Moderate to Severe Chronic Plaque Psoriasis. ( complete) NCT02684370 Clinical Trials.gov

Krueger, J; et al. (July 2015). "Anti-IL-23A mAb BI 655066 for treatment of moderate-to-severe psoriasis: Safety, efficacy, pharmacokinetics, and biomarker results of a single-rising-dose, randomized, double-blind, placebo-controlled trial.". *J Allergy Clin Immunol.* **136** (1): 116–127. [doi:10.1016/j.jaci.2015.01.018](https://doi.org/10.1016/j.jaci.2015.01.018).

# Methotrexate (METOP) RCT 52 weeks

- 120 PATIENTS
- 3:1 RANDOMISATION MTX : Placebo for 16 weeks
- Sub cutaneous MTX 17.5mgs weekly , dose escalation allowed after 8 weeks if PASI 50 not achieved.
- Cross over at 16 week OPEN label
- Primary endpoint % patients achieving PASI 75 at week 16
- Results: PASI 75 41%, PASI 90 achieved in 27%
- 40% achieved IGA 0/1

- Warren RB, Mrowietz U, von Kiedrowski R, Niesmann J, Wilsmann-Theis D, Ghoreschi K, Zschocke I, Falk TM, Blödorn-Schlicht N, Reich K. An intensified dosing schedule of subcutaneous methotrexate in patients with moderate to severe plaque-type psoriasis (METOP): a 52 week, multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *The Lancet*. 2017 Feb 10;389(10068):528-37.

# Biosimilars and Interchangeability

- Infliximab is already here
- Adalimumab<sup>®</sup>
- Etanercept<sup>®</sup>
- Safety and efficacy data similar to biologics.
- No suggestion of loss of efficacy with interchangeability between biologics and biosimilars.
- No suggestion of antibody formation.

- Strober BE, Armour K, Romiti R, Smith C, Tebbey PW, Menter A, Leonardi C. Biopharmaceuticals and biosimilars in psoriasis: what the dermatologist needs to know.
- Radtke MA, Augustin M. Biosimilars in psoriasis: what can we expect?. JDDG: Journal der Deutschen Dermatologischen Gesellschaft. 2014 Apr 1;12(4):306-12.

# Paediatric psoriasis

- Etanercept licensed for use in paediatric psoriasis 20 years after licensing for Juvenile Idiopathic Arthritis.
- Tips :
- Check for sources of strep including perianal strep.

# Choosing a therapy?

[illegible]

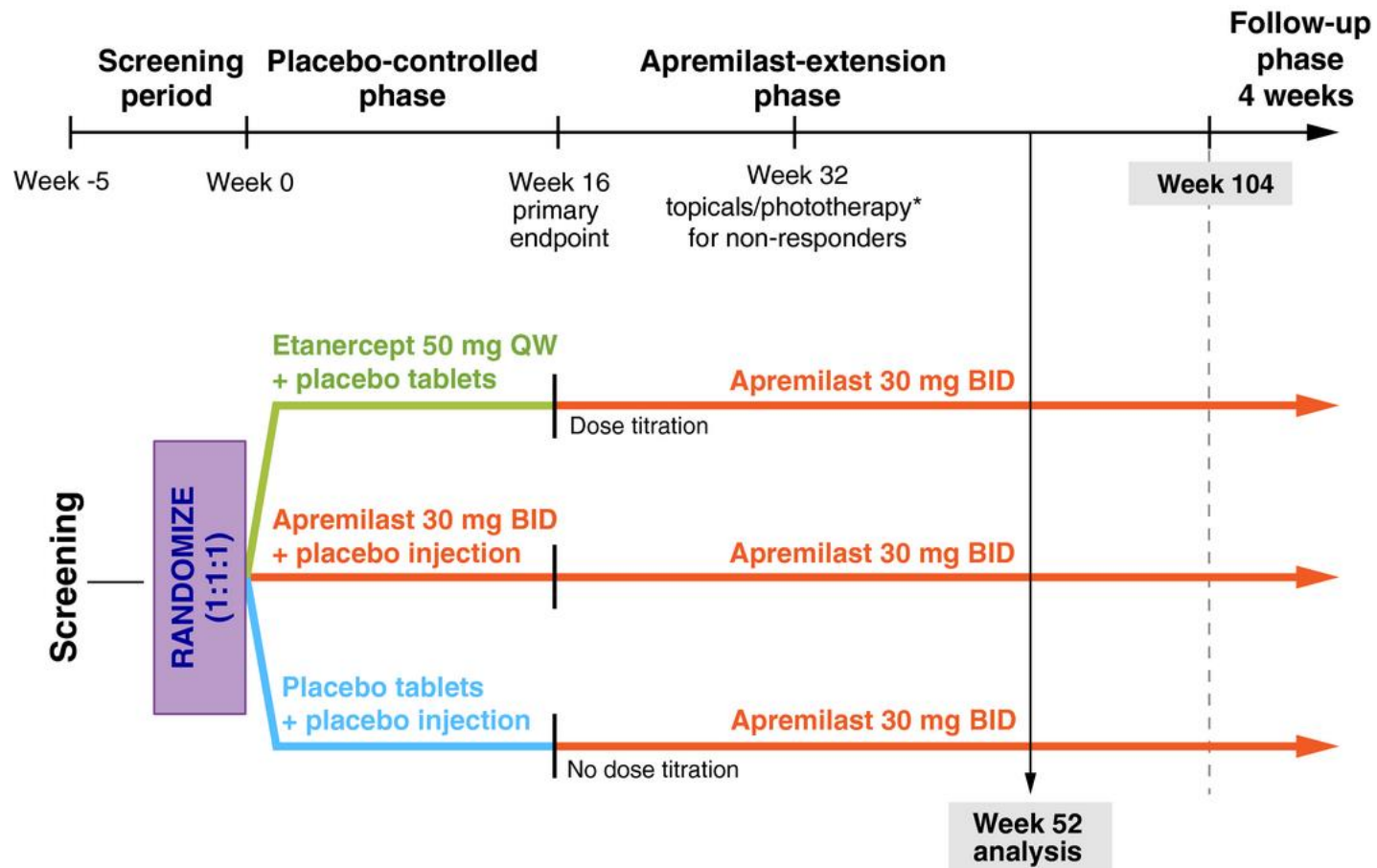
# References

- Beck LA, Thaçi D, Hamilton JD, Graham NM, Bieber T, Rocklin R, Ming JE, Ren H, Kao R, Simpson E, Ardeleanu M. Dupilumab treatment in adults with moderate-to-severe atopic dermatitis. *New England Journal of Medicine*. 2014 Jul 10;371(2):130-9.
- Thaçi D, Simpson EL, Beck LA, Bieber T, Blauvelt A, Papp K, Soong W, Worm M, Szepietowski JC, Sofen H, Kawashima M. Efficacy and safety of dupilumab in adults with moderate-to-severe atopic dermatitis inadequately controlled by topical treatments: a randomised, placebo-controlled, dose-ranging phase 2b trial. *The Lancet*. 2016 Jan 8;387(10013):40-52.
- Simpson EL, Bieber T, Guttman-Yassky E, Beck LA, Blauvelt A, Cork MJ, Silverberg JI, Deleuran M, Kataoka Y, Lacour JP, Kingo K. Two phase 3 trials of Dupilumab versus placebo in atopic dermatitis. *New England Journal of Medicine*. 2016 Dec 15;375(24):2335-48.
- Murrell DF, Gebauer K, Spelman L, Zane LT. Crisaborole Topical Ointment, 2% in Adults With Atopic Dermatitis: A Phase 2a, Vehicle-Controlled, Proof-of-Concept Study. *Journal of drugs in dermatology: JDD*. 2015 Oct;14(10):1108-12.
- Paller AS, Tom WL, Lebwohl MG, Blumenthal RL, Boguniewicz M, Call RS, Eichenfield LF, Forsha DW, Rees WC, Simpson EL, Spellman MC. Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults. *Journal of the American Academy of Dermatology*. 2016 Sep 30;75(3):494-503.
- Mansouri Y, Guttman-Yassky E. Immune pathways in atopic dermatitis, and definition of biomarkers through broad and targeted therapeutics. *Journal of clinical medicine*. 2015 Apr 29;4(5):858-73.
- Beck LA, Thaçi D, Hamilton JD, Graham NM, Bieber T, Rocklin R, Ming JE, Ren H, Kao R, Simpson E, Ardeleanu M. Dupilumab treatment in adults with moderate-to-severe atopic dermatitis. *New England Journal of Medicine*. 2014 Jul 10;371(2):130-9. Gottlieb AB. Foreword. *American journal of clinical dermatology*. 2014 Feb 1;15(1):3-4.
- Campanati A, Benfaremo D, Luchetti MM, Ganzetti G, Gabrielli A, Offidani A. Certolizumab pegol for the treatment of psoriasis. *Expert Opinion on Biological Therapy*. 2017 Feb 4:1-8.
- Griffiths CE, Reich K, Lebwohl M, van de Kerkhof P, Paul C, Menter A, Cameron GS, Erickson J, Zhang L, Secrest RJ, Ball S. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. *The Lancet*. 2015 Aug 14;386(9993):541-51.
- Warren RB, Mrowietz U, von Kiedrowski R, Niesmann J, Wilschmann-Theis D, Ghoreschi K, Zschocke I, Falk TM, Blödmann-Schlicht N, Reich K. An intensified dosing schedule of subcutaneous methotrexate in patients with moderate to severe plaque-type psoriasis (METOP): a 52 week, multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *The Lancet*. 2016 Dec 22.
- Gordon KB, Duffin KC, Bissonnette R, Prinz JC, Wasfi Y, Li S, Shen YK, Szapary P, Randazzo B, Reich K. A phase 2 trial of guselkumab versus adalimumab for plaque psoriasis. *New England Journal of Medicine*. 2015 Jul 9;373(2):136-44.
- Papp K, Thaçi D, Reich K, Riedl E, Langley RG, Krueger JG, Gottlieb AB, Nakagawa H, Bowman EP, Mehta A, Li Q. Tildrakizumab (MK-3222), an anti-interleukin-23p19 monoclonal antibody, improves psoriasis in a phase IIb randomized placebo-controlled trial. *British Journal of Dermatology*. 2015 Oct 1;173(4):930-9.
- Mullard A. New plaque psoriasis approval carries suicide warning. *Nature Reviews Drug Discovery*. 2017 Mar 1;16(3):155-.
- Berry N. AbbVie adds Boehringer Ingelheim's BI 655066 to its Autoimmune Portfolio. *PharmaDeals Review*. 2016 Mar 24;2016(3).
- Politiek K, Schaft J, Coenraads PJ, Bruin-Weller MS, Schuttelaar ML. Drug survival for methotrexate in a daily practice cohort of adult patients with severe atopic dermatitis. *British Journal of Dermatology*. 2016 Jan 1;174(1):201-3.e

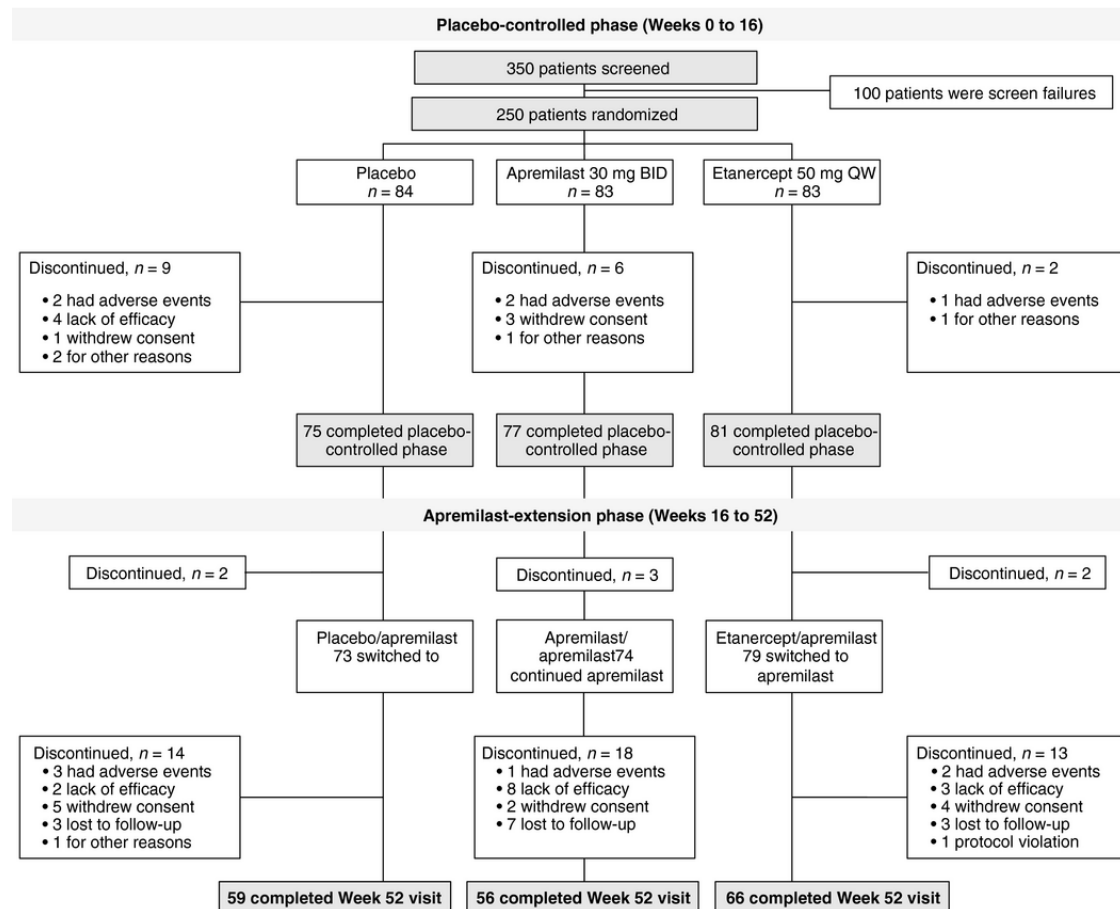
# References continued

- Corren J, Lemanske Jr RF, Hanania NA, Korenblat PE, Parsey MV, Arron JR, Harris JM, Scheerens H, Wu LC, Su Z, Mosesova S. Lebrikizumab treatment in adults with asthma. *New England Journal of Medicine*. 2011 Sept 22;365(12):1088-98.
- Noda S, Suárez-Fariñas M, Ungar B, Kim SJ, de Guzman Strong C, Xu H, Peng X, Estrada YD, Nakajima S, Honda T, Shin JU. The Asian atopic dermatitis phenotype combines features of atopic dermatitis and psoriasis with increased TH 17 polarization. *Journal of Allergy and Clinical Immunology*. 2015 Nov 30;136(5):1254-64.

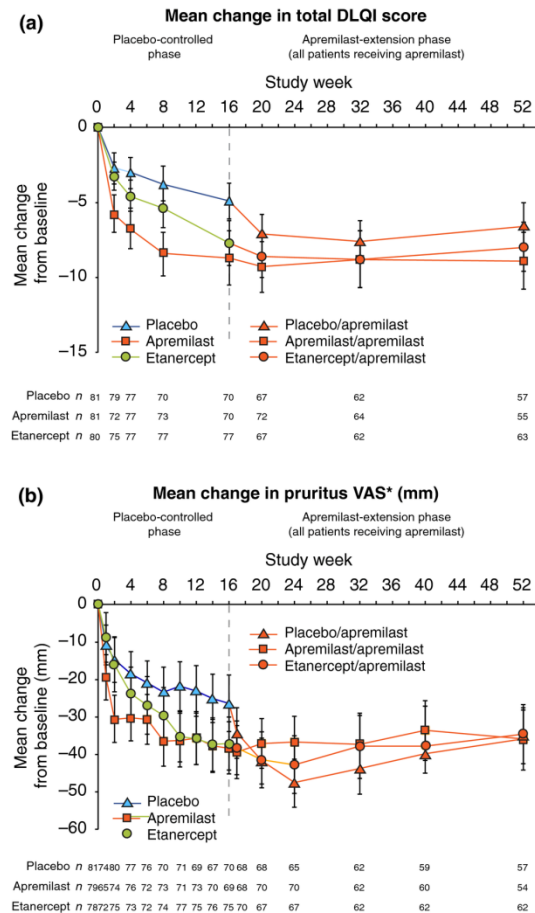
**The efficacy and safety of apremilast, etanercept and placebo in patients with moderate-to-severe plaque psoriasis: 52-week results from a phase IIIb, randomized, placebo-controlled trial (LIBERATE)**



# The efficacy and safety of apremilast, etanercept and placebo in patients with moderate-to-severe plaque psoriasis: 52-week results from a phase IIIb, randomized, placebo-controlled trial (LIBERATE)



# The efficacy and safety of apremilast, etanercept and placebo in patients with moderate-to-severe plaque psoriasis: 52-week results from a phase IIIb, randomized, placebo-controlled trial (LIBERATE)



- In three phase 3 trials involving patients with psoriasis, Ixekizumab was effective through 60 weeks of treatment.
- As with any treatment, the benefits need to be weighed against the risks of adverse events.
- The efficacy and safety of Ixekizumab beyond 60 weeks of treatment are not yet known.

| Variable                                       | UNCOVER-1          |                                     |                                     | UNCOVER-2 <sup>†</sup> |                       |                                     |                                     | UNCOVER-3 <sup>‡</sup> |                       |                                     |                                     |
|------------------------------------------------|--------------------|-------------------------------------|-------------------------------------|------------------------|-----------------------|-------------------------------------|-------------------------------------|------------------------|-----------------------|-------------------------------------|-------------------------------------|
|                                                | Placebo<br>(N=431) | Ixekizumab<br>Every 4 wk<br>(N=432) | Ixekizumab<br>Every 2 wk<br>(N=433) | Placebo<br>(N=168)     | Etanercept<br>(N=358) | Ixekizumab<br>Every 4 wk<br>(N=347) | Ixekizumab<br>Every 2 wk<br>(N=351) | Placebo<br>(N=193)     | Etanercept<br>(N=382) | Ixekizumab<br>Every 4 wk<br>(N=386) | Ixekizumab<br>Every 2 wk<br>(N=385) |
| Age — yr <sup>†</sup>                          | 46±13              | 46±13                               | 45±12                               | 45±12                  | 45±13                 | 45±14                               | 45±13                               | 46±12                  | 46±14                 | 46±13                               | 46±13                               |
| Male sex — no. (%)                             | 303 (70.3)         | 289 (66.9)                          | 291 (67.2)                          | 120 (71.4)             | 236 (65.9)            | 244 (70.3)                          | 221 (63.0)                          | 137 (71.0)             | 269 (70.4)            | 258 (66.8)                          | 254 (66.0)                          |
| White race — no./total no.<br>(%) <sup>‡</sup> | 401/431<br>(93.0)  | 397/432<br>(91.9)                   | 401/433<br>(92.6)                   | 149/168<br>(88.7)      | 331/354<br>(93.5)     | 315/343<br>(91.8)                   | 330/350<br>(94.3)*                  | 176/193<br>(91.2)      | 351/382<br>(91.9)     | 360/386<br>(93.3)                   | 361/385<br>(93.8)                   |
| Weight — kg <sup>§</sup>                       | 92±25              | 92±24                               | 92±23                               | 92±22                  | 93±22                 | 93±23                               | 89±22*                              | 91±21                  | 92±24                 | 91±24                               | 90±23                               |
| <100 kg — no. (%)                              | 289 (67.1)         | 290 (67.1)                          | 288 (66.5)                          | 111 (66.9)             | 232 (65.0)            | 227 (65.6)                          | 256 (72.9)*                         | 138 (71.9)             | 256 (67.0)            | 274 (71.9)                          | 275 (71.6)                          |
| ≥100 kg — no. (%)                              | 142 (32.9)         | 142 (32.9)                          | 145 (33.5)                          | 55 (33.1)              | 125 (35.0)            | 119 (34.4)                          | 95 (27.1)*                          | 54 (28.1)              | 126 (33.0)            | 107 (28.1)                          | 109 (28.4)                          |
| Duration of psoriasis — yr                     | 20±12              | 19±12                               | 20±12                               | 19±13                  | 19±12                 | 19±13                               | 18±12                               | 18±13                  | 18±12                 | 18±12**                             | 18±12                               |
| Percent of body-surface area<br>involved       | 27±18              | 27±16                               | 28±18                               | 27±18                  | 25±16                 | 27±17                               | 25±16                               | 29±17                  | 28±17                 | 28±16**                             | 28±17                               |
| sPGA score ≥4 — no. (%) <sup>¶</sup>           | 227 (52.7)         | 235 (54.4)                          | 202 (46.7)                          | 82 (48.8)              | 172 (48.0)            | 181 (52.2)                          | 173 (49.3)                          | 101 (52.3)             | 192 (50.3)            | 177 (46.2)**                        | 178 (46.2)                          |
| PASI score <sup>  </sup>                       | 20±9               | 20±7                                | 20±8                                | 21±8                   | 19±7*                 | 20±7                                | 19±7                                | 21±8                   | 21±8                  | 21±8**                              | 21±8                                |
| Previous therapy — no. (%)                     | 418 (97.0)         | 419 (97.0)                          | 424 (97.9)                          | 164 (97.6)             | 344 (96.1)            | 338 (97.4)                          | 340 (96.9)                          | 181 (93.8)             | 368 (96.3)            | 360 (93.3)                          | 361 (93.8)                          |
| Phototherapy                                   | 185 (42.9)         | 205 (47.5)                          | 201 (46.4)                          | 74 (44.0)              | 173 (48.3)            | 160 (46.1)                          | 163 (46.4)                          | 60 (31.1)              | 157 (41.1)*           | 154 (39.9)*                         | 151 (39.2)                          |
| Nonbiologic systemic                           | 224 (52.0)         | 213 (49.3)                          | 247 (57.0)                          | 80 (47.6)              | 170 (47.5)            | 178 (51.3)                          | 178 (50.7)                          | 82 (42.5)              | 182 (47.6)            | 181 (46.9)                          | 170 (44.2)                          |
| Biologic                                       | 181 (42.0)         | 168 (38.9)                          | 173 (40.0)                          | 43 (25.6)              | 76 (21.2)             | 85 (24.5)                           | 84 (23.9)                           | 33 (17.1)              | 60 (15.7)             | 58 (15.0)                           | 58 (15.1)                           |

\* Plus-minus values are means ±SD. The following baseline variables differed significantly between the groups: white race (UNCOVER-2: ixekizumab every 2 weeks [80 mg of ixekizumab every 2 weeks after a starting dose of 160 mg] vs. placebo,  $P=0.02$ ); mean weight (UNCOVER-2: ixekizumab every 2 weeks vs. etanercept,  $P=0.03$ ); <100-kg group and ≥100-kg group (UNCOVER-2: ixekizumab every 2 weeks vs. etanercept,  $P=0.02$ ); baseline Psoriasis Area Severity Index (PASI) score (UNCOVER-2: etanercept vs. placebo,  $P=0.03$ ); and phototherapy (UNCOVER-3: ixekizumab every 4 weeks [80 mg of ixekizumab every 4 weeks after a starting dose of 160 mg] vs. placebo and etanercept vs. placebo,  $P<0.05$  for both comparisons).

<sup>†</sup> Data were not available for 1 patient in the placebo group, the etanercept group, and the ixekizumab-every-2-week group in the UNCOVER-2 trial, and were not available for 4 patients in the ixekizumab-every-4-week group and 1 patient in the ixekizumab-every-2-week group in the UNCOVER-3 trial.

<sup>‡</sup> Race was self-reported.

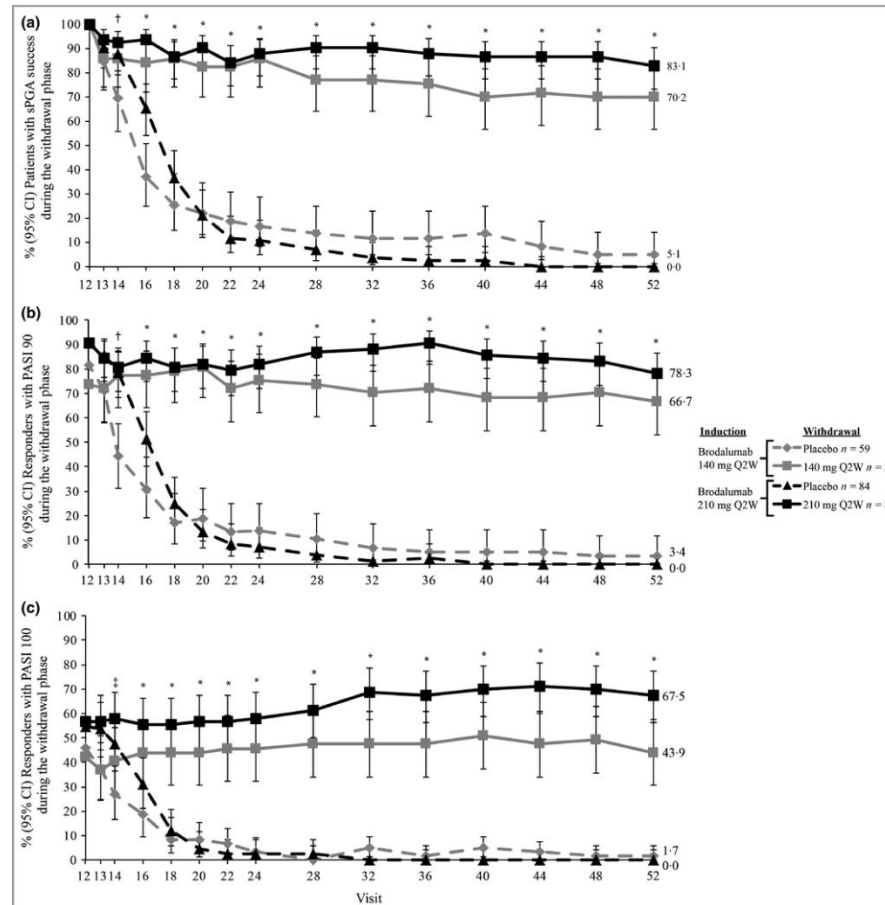
<sup>§</sup> Data were not available for 2 patients in the placebo group, 1 patient in the etanercept group, and 1 patient in the ixekizumab-every-4-week group in the UNCOVER-2 trial, and were not available for 1 patient in the placebo group, 5 patients in the ixekizumab-every-4-week group, and 1 patient in the ixekizumab-every-2-week group in the UNCOVER-3 trial.

<sup>¶</sup> Scores on the static Physician's Global Assessment (sPGA) range from 0 (clear) to 5 (very severe); a score of 3 indicates moderate disease.

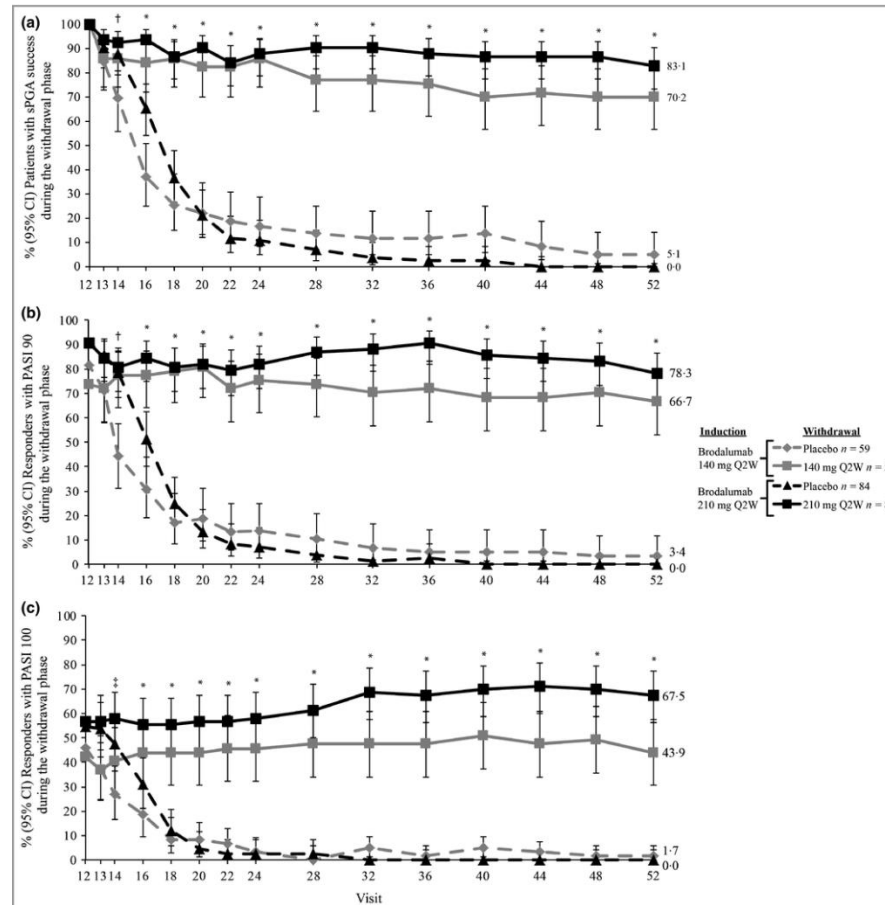
<sup>||</sup> Overall PASI ranges from 0 (clear skin) to 72 (worst possible psoriasis); a score of 12 indicates moderate disease.

\*\* Data were available for 383 patients.

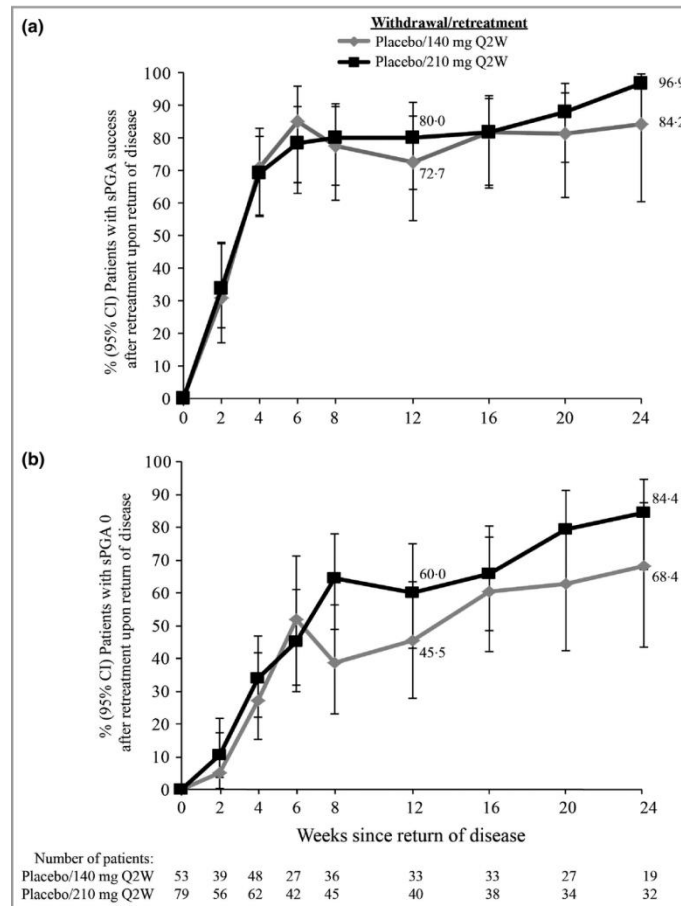
# A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis



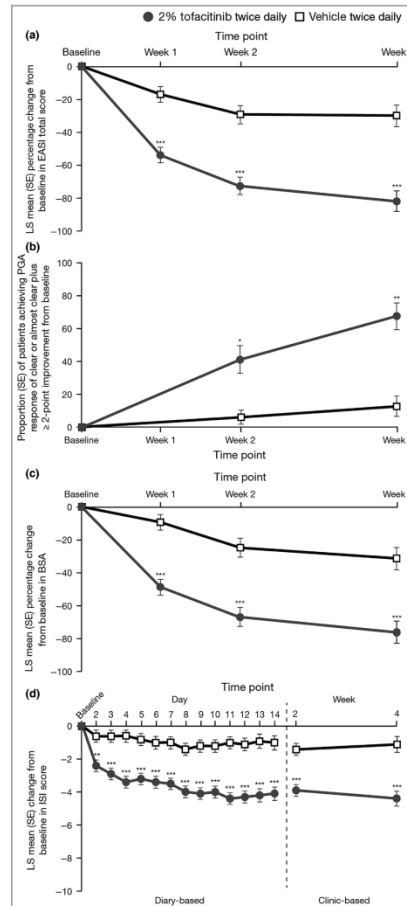
# A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis



# A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis



# Topical tofacitinib for atopic dermatitis: a phase IIa randomized trial



**Table 2. Changes from Baseline in Secondary Outcome Measures at 12 Weeks.\***

| Outcome Measure                                                              | Placebo<br>(N = 53) | Nemolizumab           |                       |                       |
|------------------------------------------------------------------------------|---------------------|-----------------------|-----------------------|-----------------------|
|                                                                              |                     | 0.1 mg/kg<br>(N = 53) | 0.5 mg/kg<br>(N = 54) | 2.0 mg/kg<br>(N = 52) |
| Change in score on pruritus visual-analogue scale                            |                     |                       |                       |                       |
| No. of patients                                                              | 26                  | 33                    | 35                    | 32                    |
| Percent change                                                               | -20.9±5.3           | -43.7±4.9             | -59.8±4.8             | -63.1±5.0             |
| Change in EASI score                                                         |                     |                       |                       |                       |
| No. of patients                                                              | 26                  | 33                    | 35                    | 32                    |
| Percent change                                                               | -26.6±8.1           | -23.0±7.5             | -42.3±7.3             | -40.9±7.5             |
| Change in SCORAD score†                                                      |                     |                       |                       |                       |
| No. of patients                                                              | 23                  | 27                    | 30                    | 27                    |
| Percent change                                                               | -18.5±5.2           | -27.5±4.9             | -37.7±4.8             | -39.8±4.9             |
| Improvement of ≥2 points in score on static Investigator's Global Assessment |                     |                       |                       |                       |
| No. of patients                                                              | 26                  | 33                    | 35                    | 32                    |
| Patients with improvement — %                                                | 11                  | 14                    | 38                    | 25                    |
| Change in body-surface area affected by atopic dermatitis                    |                     |                       |                       |                       |
| No. of patients                                                              | 26                  | 33                    | 35                    | 32                    |
| Percent change                                                               | -15.7±10.5          | -7.5±9.7              | -20.0±9.6             | -19.4±9.7             |
| Change in sleep-disturbance score on visual-analogue scale‡                  |                     |                       |                       |                       |
| No. of patients                                                              | 26                  | 33                    | 34                    | 32                    |
| Percent change                                                               | -31.9±6.3           | -52.3±5.8             | -59.1±5.8             | -62.6±5.9             |

\* Plus-minus values are means ±SE. Nemolizumab or placebo was administered once every 4 weeks in each group.

† Scores on Scoring Atopic Dermatitis (SCORAD) range from 0 to 103, with higher scores indicating greater disease severity. SCORAD assesses the extent and severity of signs of atopic dermatitis through area and intensity assessment by the investigator and subjective symptoms reported by the patient.

‡ Sleep-disturbance scores on the visual-analogue scale range from 0 to 100 mm, with higher scores indicating greater sleep disturbance.

