

Update in Treatment of Acne Patients

Jonette E. Keri, M.D., Ph.D.

Professor, Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery,
University of Miami, Miller School of Medicine

Chief, Dermatology Service, Bruce W. Carter VAMC (Miami VA)

Disclosures

- Galderma – investigator and speaker
- Ortho Dermatologics – advisory board, author
- Almirall – advisory board and author
- L’Oreal – advisory board and author

Outline

- New Triple Drug Topical
- Trifarotene for Scarring
- Barrier is Important in Acne
- New Lasers
- Jak Inhibitor Induced Acne
- Ipledge Program Changes Now and Coming in the Next Year

Fixed-Dose Clindamycin Phosphate 1.2%, Benzoyl Peroxide 3.1%, and Adapalene 0.15% Gel (Cabtreo™)

- Triple drug combination
- Approval by FDA in October 2023
- Study looked at all double combinations versus triple combination
- Triple combination did the best

- Linda Stein Gold, Hilary Baldwin, Leon H Kircik, Jonathan S Weiss et al. Efficacy and Safety of a Fixed-Dose Clindamycin Phosphate 1.2%, Benzoyl Peroxide 3.1%, and Adapalene 0.15% Gel for Moderate-to-Severe Acne: A Randomized Phase II Study of the First Triple-Combination Drug. *Am J Clin Dermatol.* 2022 Jan;23(1):93-104.

Fixed-Dose Clindamycin Phosphate 1.2%, Benzoyl Peroxide 3.1%, and Adapalene 0.15% Gel

13-Year-Old Female - Black

Baseline: EGSS 3

Week 12: EGSS 1



14-Year-Old Male - Asian

Baseline: EGSS 3

Week 12: EGSS 0



26-Year-Old Female - White

Baseline: EGSS 3

Week 12: EGSS 1



27-Year-Old Female - Black/White

Baseline: EGSS 3

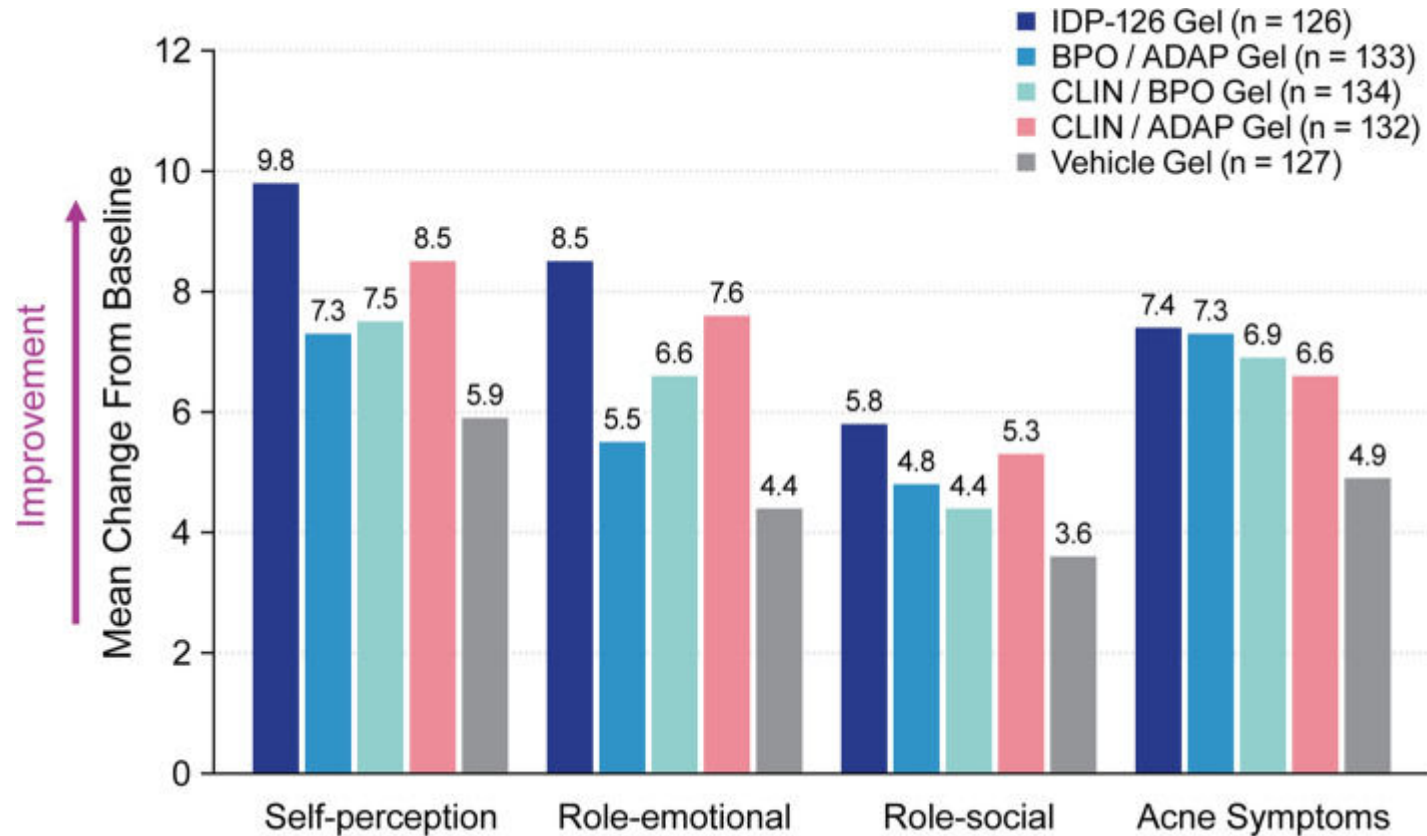
Week 12: EGSS 1



Linda Stein Gold,
Hilary Baldwin,
Leon H Kircik,
Jonathan S Weiss
et al. Drug. Am J
Clin Dermatol.
2022
Jan;23(1):93-104.

Fixed-Dose Clindamycin Phosphate 1.2%, Benzoyl Peroxide 3.1%, and Adapalene 0.15% Gel

Linda Stein
Gold, Hilary
Baldwin, Leon H
Kircik, Jonathan
S Weiss et al.
Drug. Am J Clin
Dermatol. 2022
Jan;23(1):93-
104.



Trifarotene for Scarring

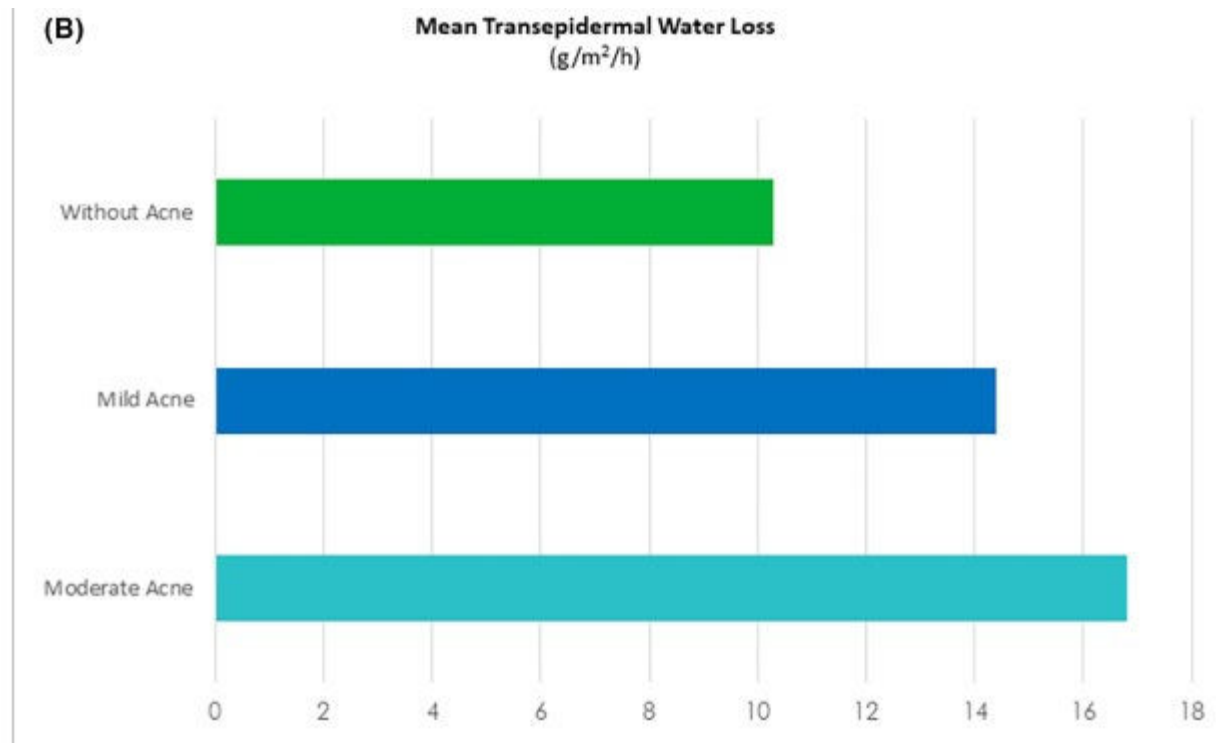
- Trifarotene was **effective reducing atrophic acne scars**, with reduction of total atrophic scar count as early as week 2.
- Schleicher S, Moore A, Rafal E, Gagne-Henley A, Johnson SM, Dhawan S, Chavda R, York JP, Sforzolini B, Holcomb K, Ablon G, Del Rosso J, Dreno B. Trifarotene Reduces Risk for Atrophic Acne Scars: Results from A Phase 4 Controlled Study. *Dermatol Ther (Heidelb)*. 2023 Dec;13(12):3085-3096.

Barrier is important in acne

- **Patient with acne (before any treatment) have increased transepidermal water loss versus those without acne**
- Schachner LA, Alexis AF, Andriessen A, Berson D, Gold M, Goldberg DJ, Hu S, Keri J, Kircik L, Woolery-Lloyd H. Insights into acne and the skin barrier: Optimizing treatment regimens with ceramide-containing skincare. *J Cosmet Dermatol.* 2023 Nov;22(11):2902-2909.

Transepidermal Water Loss in Acne Patients

- Schachner LA, Alexis AF, Andriessen A, Berson D, Gold M, Goldberg DJ, Hu S, Keri J, Kircik L, Woolery-Lloyd H. Insights into acne and the skin barrier: Optimizing treatment regimens with ceramide-containing skincare. J Cosmet Dermatol. 2023 Nov;22(11):2902-2909.



Barrier is important in acne

- Inflammation plays an important role in acne
 - Educate patients and clinicians about inflammation and acne.
-
- Schachner LA, Alexis AF, Andriessen A, Berson D, Gold M, Goldberg DJ, Hu S, Keri J, Kircik L, Woolery-Lloyd H. Insights into acne and the skin barrier: Optimizing treatment regimens with ceramide-containing skincare. *J Cosmet Dermatol.* 2023 Nov;22(11):2902-2909.

Barrier is important in acne

- **Daily skin care regimens** should be used to treat skin irritation and xerosis from acne and acne treatments.
- Goal to improve adherence.
- Schachner LA, Alexis AF, Andriessen A, Berson D, Gold M, Goldberg DJ, Hu S, Keri J, Kircik L, Woolery-Lloyd H. Insights into acne and the skin barrier: Optimizing treatment regimens with ceramide-containing skincare. J Cosmet Dermatol. 2023 Nov;22(11):2902-2909.

Sunscreen and acne

- The use of specifically formulated sunscreens **could enhance adherence** to topical or systemic therapy, camouflage lesions (tinted sunscreens), **decrease inflammation**, and **reduce the incidence of post-inflammatory hyperpigmentation/erythema**.
- J Piquero-Casals, D Morgado-Carrasco, E Rozas-Muñoz, J F Mir-Bonafé, C Trullàs, E Jourdan, J Piquero-Martin, C Trull's Zouboulis, J Krutmann. Sun exposure, a relevant exposome factor in acne patients and how photoprotection can improve outcomes. *Cosmet Dermatol.* 2023 Jun;22(6):1919-1928

Lasers for Acne

Laser for Acne

- The 1726 nm laser is safe and effective for treating mild to severe acne in **all Fitzpatrick skin types**.
- Acne resolution is apparent within the first month and improves for **up to 2 years beyond treatment**.
- Represents a safe alternative to traditional acne therapies
- Cutera AviClear laser
- Goldberg DJ, Andriessen A, Bhatia AC, Gold MH, Lewis AB, Lolis MS, Miller JH, Ros A. Treatment of mild to severe acne with 1726 nm laser: A safe alternative to traditional acne therapies. J Cosmet Dermatol. 2023 Nov;22(11):3026-3032. doi: 10.1111/jocd.15964. Epub 2023 Aug 18.

Laser for Acne

- Accure Laser System, manufactured by Quantas System,
- Utilizes a 1726nm wavelength that uniquely targets sebum within the overactive sebaceous glands.
- Instead of treating to power, the groundbreaking technology within the Accure system treats to temperature, providing a reproducible, safe and efficacious treatment every time.

New Medications

New side effects

JAK Inhibitor induced Acne

- Based on the current evidence, there is an increased risk of acne related to systemic JAK inhibitors:
 - Abrocitinib 200mg
 - Upadacitinib (15mg and 30mg)

- Consider balance between the benefits of symptomatic relief from AD and the potential risk of acne may need to be carefully considered.

- Chen Sun, Zheng Su, Yue-Ping Zeng. Association of risk of incident acne and treatment with systemic Janus kinase inhibitors in atopic dermatitis: a systematic review and meta-analysis. *Inflamm Res.* 2023 Sep;72(9):1861-1871.

JAK Inhibitor induced Acne

- 25 unique studies (10 839 unique participants; 54% male and 46% female)
- Increased Odds ratios
 - Abrocitinib (13.47 [95% CI, 3.25-55.91])
 - Baricitinib (4.96 [95% CI, 2.52-9.78])
 - Upadacitinib (4.79 [95% CI, 3.61-6.37]),
 - Deucravacitinib (2.64 [95% CI, 1.44-4.86])
 - Deuruxolitinib (3.30 [95% CI, 1.22-8.93])
- Estimated ORs were higher across studies investigating the use of JAK inhibitors for the **management of dermatologic compared with nondermatologic conditions** (4.67 [95% CI, 3.10-7.05])
- **So we will most likely be seeing these patients with both conditions**
- Martinez J, Manjaly C, Manjaly P, Ly S, Zhou G, Barbieri J, Mostaghimi A. Janus Kinase Inhibitors and Adverse Events of Acne: A Systematic Review and Meta-Analysis. JAMA Dermatol. 2023 Oct 18:e233830.

Upadacitinib and Acne

- This was a post hoc integrated analysis of 3 phase 3 randomized, double-blind, placebo-controlled trials of upadacitinib
- Data included were from the 16-week placebo-controlled period.
- Pedro Mendes-Bastos , Barry Ladizinski , et al. Characterization of acne associated with upadacitinib treatment in patients with moderate-to-severe atopic dermatitis: A post hoc integrated analysis of 3 phase 3 randomized, double-blind, placebo-controlled trials. J Am Acad Dermatol 2022 Oct;87(4):784-791

Acne and Upadacitinib

- **Acne frequency** at 16 weeks:
 - Upadacitinib **15 mg** – **(9.8%)** 84/857
 - Upadacitinib **30 mg** – **(15.2%)** 131/864
 - Placebo **(2.2%)** 19/862
-
- Pedro Mendes-Bastos , Barry Ladizinski , et al. Characterization of acne associated with upadacitinib treatment in patients with moderate-to-severe atopic dermatitis: A post hoc integrated analysis of 3 phase 3 randomized, double-blind, placebo-controlled trials. J Am Acad Dermatol 2022 Oct;87(4):784-791

Acne and Upadacitinib

- All cases of acne, except 1, were mild/moderate
- 2 patients discontinued treatment due to moderate acne.
- Acne occurred at higher rates among younger, female, and non-White patients.
- Pedro Mendes-Bastos, Barry Ladizinski, et al. Characterization of acne associated with upadacitinib treatment in patients with moderate-to-severe atopic dermatitis: A post hoc integrated analysis of 3 phase 3 randomized, double-blind, placebo-controlled trials. J Am Acad Dermatol 2022 Oct;87(4):784-791

Acne and Upadacitinib

- Treatment – generally TOPICALS
 - topical antibiotics, benzoyl peroxide, and/or retinoids.
- No intervention in 40.5% and 46.6% of patients receiving upadacitinib 15 and 30 mg, respectively.
- Acne also had no impact on patient-reported outcomes

- One patient treated with isotretinoin
 - Pedro Mendes-Bastos , Barry Ladizinski , et al. Characterization of acne associated with upadacitinib treatment in patients with moderate-to-severe atopic dermatitis: A post hoc integrated analysis of 3 phase 3 randomized, double-blind, placebo-controlled trials. J Am Acad Dermatol 2022 Oct;87(4):784-791

Class effect – JAK inhibitors

- Tofacitinib also associated with acne – up to 13% in recent review¹

¹Guo L, Feng S, Sun B, Jiang X, Liu Y. Benefit and risk profile tofacitinib for the treatment of alopecia areata: a systemic review and meta-analysis. *J Eur Acad Dermatol Venereol.* 2020;34:192-201

Acne and JAK inhibitors

- Topical Ruxolitinib for Vitiligo
- Most common adverse events in these 2 phase 3 studies were **application-site acne 6.3% - 6.6%.**

- David Rosmarin, Thierry Passeron, et al. Two Phase 3, Randomized, Controlled Trials of Ruxolitinib Cream for Vitiligo. N Engl J Med. 2022 Oct 20;387(16):1445-1455.

JAK Inhibitor to treat Acne associated condition

- Case report: successful treatment of refractory SAPHO syndrome with the JAK inhibitor tofacitinib
 - (Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is an autoinflammatory disorder without standardized treatment.)
-
- Qiao Yang, Yumo Zhao, Chen Li, Yaping Luo, Weixin Hao, Wen Zhang *Medicine (Baltimore)* Case report: successful treatment of refractory SAPHO syndrome with the JAK inhibitor tofacitinib. 2018 Jun;97(25):e11149.

Ipledge Program Changes

Ipledge Changes Now



Important – Changes to the iPLEDGE REMS

Changes to the iPLEDGE REMS have been implemented. These changes include:

- Designees can now initiate Patient Enrollment.
- A Patient Calendar will display the patient's program status for patients, prescribers, and designees. The calendar will also display the required actions to be completed in order for the patient to become Qualified to Receive Drug.

All iPLEDGE REMS materials have been updated to align with these changes.

Ipledge Changes Now



Important – Effective November 8, 2023, all pre-treatment pregnancy tests must be completed in a medical setting (e.g., prescriber’s office, laboratory)

Per the FDA’s [iPLEDGE REMS Enforcement Discretion communication](#), the Agency will continue to exercise flexibility and allow prescribers to:

- Assess a patient’s pregnancy status using pregnancy tests that are not performed in a CLIA-certified laboratory.
- Rely on the patient to perform home pregnancy tests and report the dates and results of these tests to the prescriber during and after isotretinoin treatment.

All pre-treatment pregnancy tests must be completed in a medical setting (e.g., prescriber’s office, laboratory).

Prescribers will continue to be responsible for interpreting and documenting all pregnancy test results in the iPLEDGE REMS system. Prescribers who rely on the patient to perform a home pregnancy test need to take steps to minimize patients falsifying the results of these tests. All other iPLEDGE REMS requirements are in effect.

Ipledge Changes Coming

- **Remove the "19-day lockout"** for patients if they do not obtain isotretinoin within the first 7-day prescription window. Before initiating isotretinoin treatment, a repeat confirmatory pregnancy test must be completed in a medical setting (as described above) **without any required waiting period.**
- Revise the pregnancy registry requirement to remove the objective to document pregnancy and fetal outcomes (and associated data collection) for each pregnancy.

Ipledge Changes coming

- Revise the requirement for prescribers to document patient counseling in patients **who cannot become pregnant from monthly to only at enrollment.**
- **Remove the requirement that pregnancy tests must be performed in a CLIA-certified laboratory;** however, all pregnancy testing before isotretinoin treatment initiation must be completed in a medical setting (e.g., prescriber's office, clinic laboratory).
- Allow prescribers the option of using home pregnancy testing for their patients during and after isotretinoin treatment. Prescribers who rely on the patient to perform a home pregnancy test need to take steps to minimize patients falsifying the results of these tests. As of November 7, 2023, all pre-treatment pregnancy tests must be performed in a medical setting (e.g., office, laboratory).

New ideas in Acne

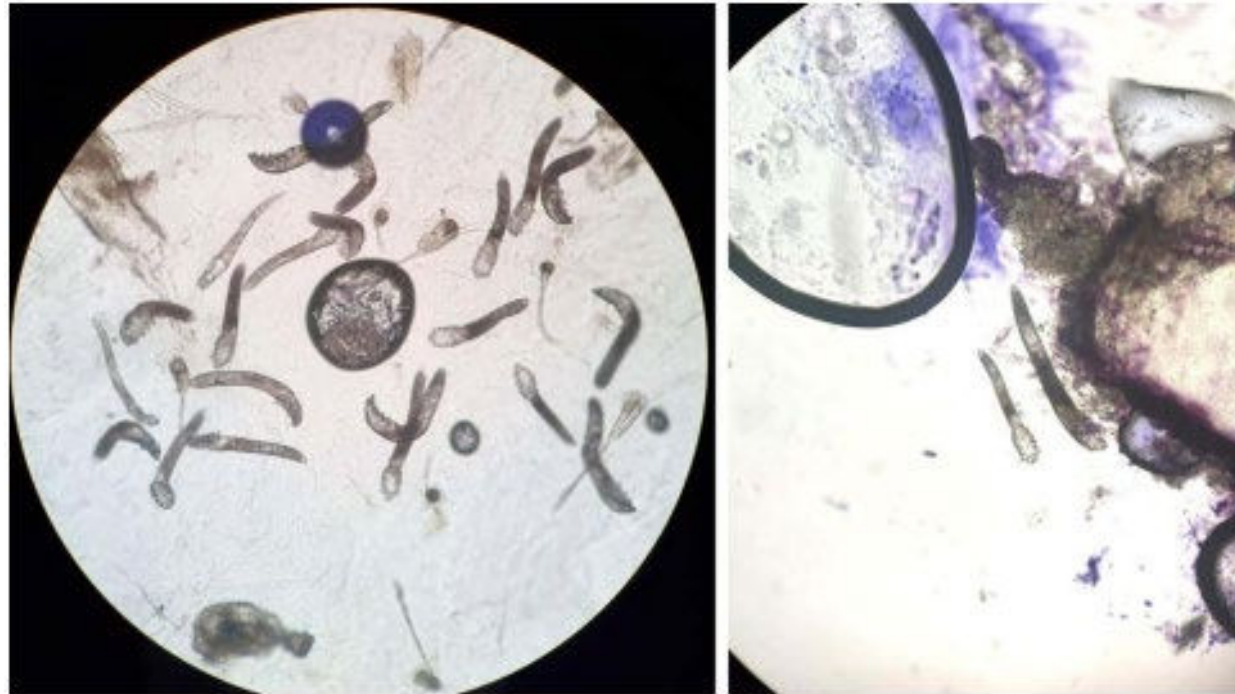
- *Demodex* mites, in acne?
- Most people have demodex mites but when the numbers become abnormally high they contribute to:
 - Rosacea
 - Perioral Dermatitis
 - Folliculitis
- Anon Paichitrojjana, Anand Paichitrojjana. Case Series of Demodicosis in Acne Vulgaris Patients. Clin Cosmet Investig Dermatol. 2023 Nov 18:16:3363-3368.

Acne patient with Increased *Demodex* mites



Anon Paichitrojjana ,
Anand Paichitrojjana.
Case Series of
Demodicosis in Acne
Vulgaris Patients. Clin
Cosmet Investig
Dermatol. 2023 Nov
18:16:3363-3368.

Same acne patient's *Demodex* mite scraping



Anon Paichitrojjana ,
Anand Paichitrojjana.
Case Series of
Demodicosis in Acne
Vulgaris Patients. Clin
Cosmet Investig
Dermatol. 2023 Nov
18:16:3363-3368.

New, but yet old treatment

The Clay Mask

(A little fun at the end of the talk)

Results

- Number of acne lesions decreased
- Sebum content decreased
- Transepidermal water loss decreased
- Skin hydration increased

Results of the study

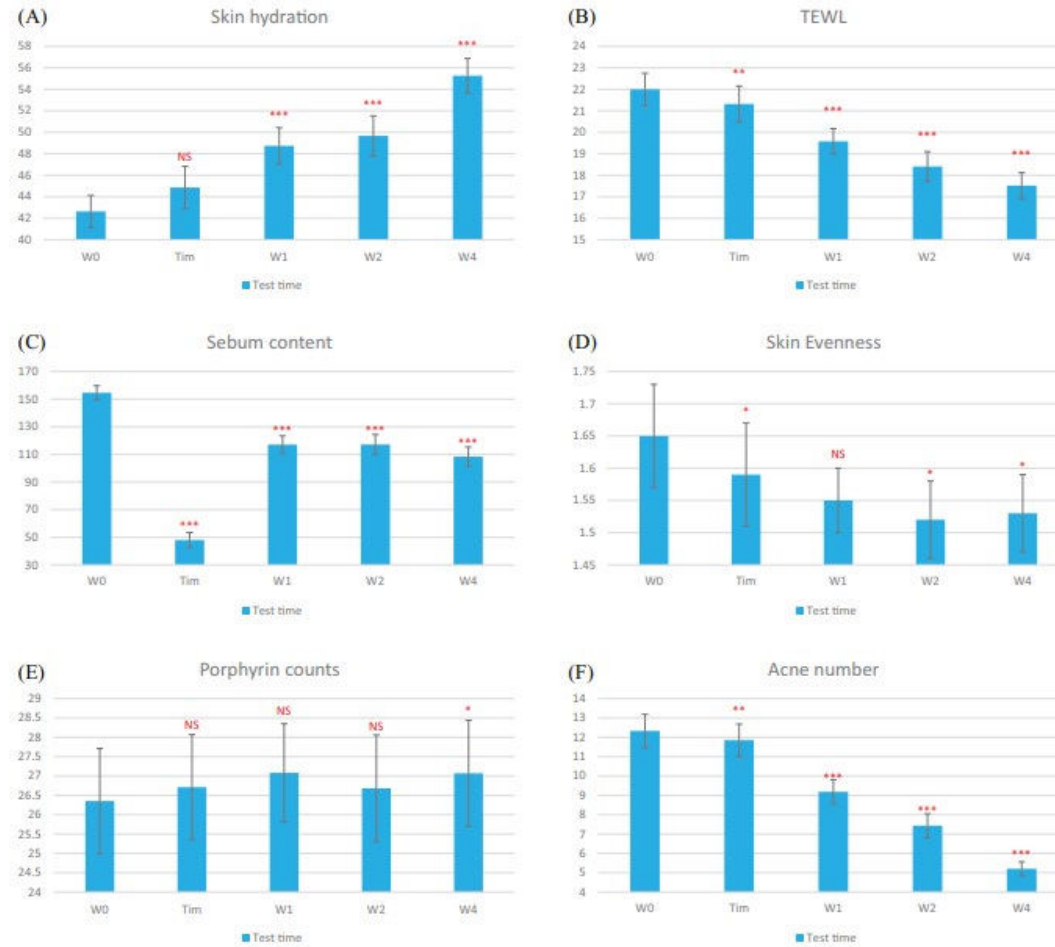


FIGURE 1 Changes from baseline in investigator global assessment (IGA) score of acne severity (A), Skin hydration (B), TEWL (C), Sebum content (D), Skin evenness (E), Porphyrin counts (F), Acne number.

Xianghua Zhang, Zhongxing Zhang et al.
Comprehensive assessment of the efficacy
and safety of a clay mask in oily and acne
skin. *Skin Res Technol.* 2023
Nov;29(11):e13513.

Oldy but Goody Face Mask



Conclusion

- Newer concepts around acne – lasers, demodex
- New takes on older ideas – 3 active ingredients in one
- Old ideas can still work – clay masks

Thank you!