Acne Vulgaris: Clinical Update

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EDUCATIONAL GOALS

Learning Objectives

Pathophysiology

Review evolving models: follicular hyperkeratinization, sebaceous dysfunction, microbial dysbiosis, and immune activation. Integrate genetics, epigenetics, and metabolic influences.

Therapeutics

Summarize trial data on novel topical agents, isotretinoin dosing, hormonal therapies, and microbiome-directed approaches. Evaluate emerging paradigms and their algorithmic integration.

Research Gaps

Discuss limitations: lack of long-term trials, outcome heterogeneity, and need for predictive biomarkers. Identify priority areas for future investigation.

By presentation's end, participants will have an updated, evidence-based approach to acne management, incorporating recent advances. These objectives align with the 2023 AAD Guidelines Update, translating science into improved clinical care.

AAD Guidelines Update 2023; Zaenglein AL et al. J Am Acad Dermatol. 2024

Epidemiology & Burden

Post-adolescent acne shows female predominance
- linked to hormonal factors
- Often refractory
- More persistent and psychologically distressing.

Beyond physical symptoms, acne carries significant psychological and social burdens: anxiety, depression, stigma, social withdrawal, impaired self-esteem, and scarring.

85%

Adolescent prevalence

Peak incidence age 12–24

40%

Persist to adulthood

Higher in females

9.4%

Global prevalence

8th most common disease

Bhate K et al. Br J Dermatol. 2022

Pathophysiology Revisited

Follicular Hyperkeratinization

Abnormal keratinocyte growth leads to comedogenesis, creating a microenvironment that precedes and facilitates subsequent events.

Sebum Dysregulation

Enlarged sebaceous glands and altered lipid composition provide inflammatory mediators. Sebum actively modulates immune signaling.

Microbial Trigger

C. acnes acts as an immune trigger. Specific strains activate pattern recognition receptors, starting inflammatory cascades.

Immune Activation

Innate immune responses drive acne formation. Inflammation now is understood to occur early in acne pathogenesis.

Dreno B et al. Clin Dermatol. 2022

Microbiome: Beyond Bacterial Load

→ Strain Specificity

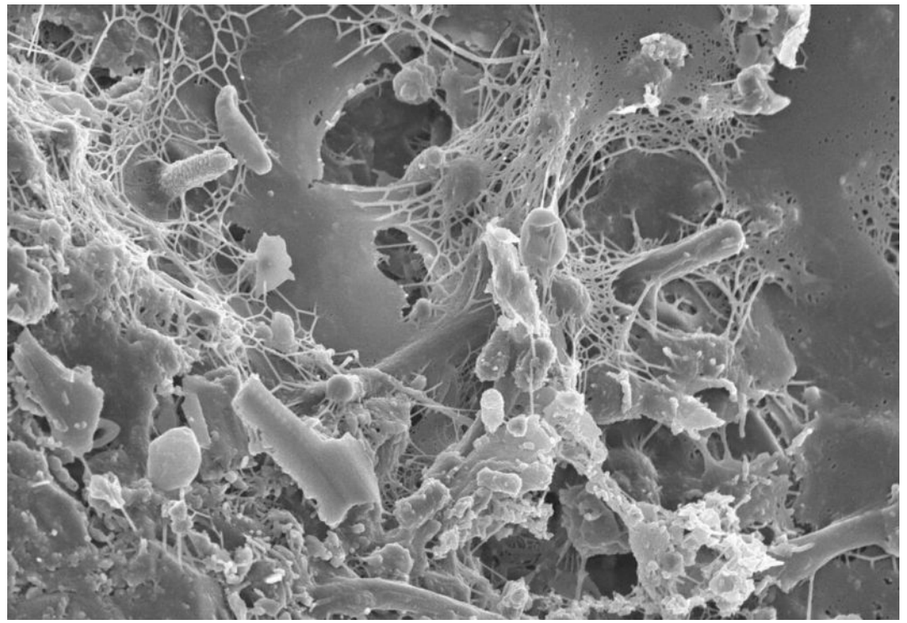
C. acnes phylotypes; Type IA is prevalent in lesions, Type II may be protective.

→ Biofilm Formation

C. acnes forms biofilms, contributing to chronic acne

→ Microbial Diversity

Greater diversity often correlates with healthier skin, suggesting therapeutic potential in restoring balance.



Nguyen JK et al. Br J Dermatol. 2024

Topical Retinoids: Updated Mechanism of Action

Normalization of Keratinization

Anti-Inflammatory Effects

RAR-γ Selectivity

→ **Clinical Implications**

Retinoids are effective for both comedonal and inflammatory lesions, making them first-line therapy across acne subtypes.

→ **Enhanced Efficacy**

Combination with benzoyl peroxide or topical antibiotics can boost efficacy and help prevent antibiotic resistance.

→ **Tolerability Challenges & Solutions**

Key challenges include erythema, dryness, and peeling. Strategies involve gradual titration, moisturizers, and enhanced formulations.

Thiboutot D et al. J Drugs Dermatol. 2023

New Generation Retinoids

Maximize efficacy while minimizing irritation and tolerability issues, improving patient adherence.

Tazarotene 0.045% Lotion

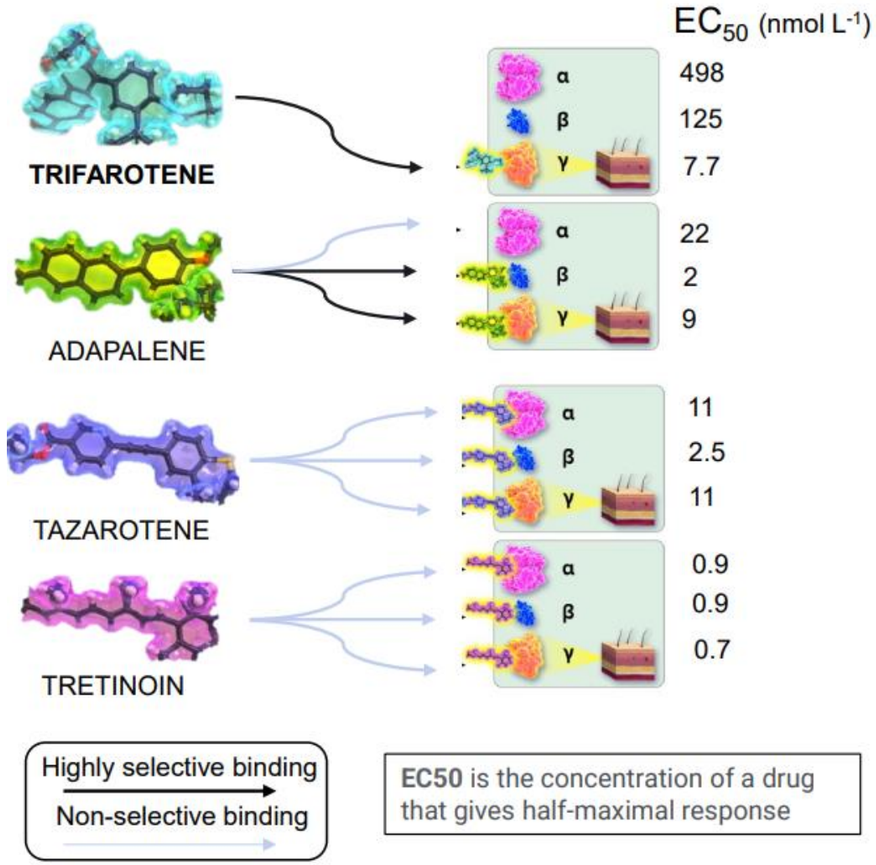
Third-generation retinoid with high RAR-β & RAR-γ selectivity.

- Polymeric emulsion enhances delivery & tolerability.
- Reduces inflammatory & non-inflammatory lesions.
- Improves skin oiliness; well-tolerated.

Trifarotene 50 µg/g Cream (Aklief)

First topical retinoid engineered for RAR-γ selectivity (predominant in skin).

- Robust efficacy for facial & truncal acne.
- Minimizes off-target effects.
- Sustained efficacy & favorable safety profile in long-term studies.



Tanghetti EA et al. J Dermatolog Treat. 2023; Blume-Peytavi U et al. J Eur Acad Dermatol Venereol. 2020; Baldwin H et al. J Drugs Dermatol. 2024

Safety of Tazarotene 0.045% Lotion and Hyperpigmentation Improvements in Black Participants With Moderate-to-Severe Acne

Fran E Cook-Bolden, MD[1,2]; Linda Stein Gold, MD[3]; Hilary Baldwin, MD[4,5]; Valerie Callender, MD[6,7]; Andrew F Alexis, MD, MPH[1]; Neal Bhatia, MD[8]; Joshua A Zeichner, MD[9]; Emil A Tanghetti, MD[10]; Eric Guenin, PharmD, PhD, MPH[11]

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*Ortho Dermatologics is a division of Bausch Health US, LLC

SYNOPSIS

- Acne is one of the major causes of post-inflammatory hyperpigmentation (PIH) in patients with skin of color[1]
- PIH may be more distressing than the acne itself, and patients with higher skin phototypes may be impacted more greatly than those with lower skin phototypes[2]
- Topical retinoids, a mainstay of acne treatment, can also reduce hyperpigmentation via multiple mechanisms, including downregulation of cell proliferation and inflammation[3]
- In a review of studies including patients with PIH and/or acne, tazarotene treatment led to significant reductions in hyperpigmented lesions[3]
  - For example, significant reductions in the severity, intensity, and/or extent of hyperpigmented lesions were observed after 16–18 weeks of treatment with tazarotene vs adapalene or vehicle[4,5]
- To minimize skin irritation and other skin reactions associated with tazarotene gel and cream formulations, a hydrating, lower-dose tazarotene 0.045% lotion formulation was developed utilizing proprietary polymeric emulsion technology to allow for more efficient delivery of tazarotene into dermal layers

OBJECTIVE AND METHODS

- The objective of this pooled, post hoc analysis was to evaluate the safety of tazarotene 0.045% lotion and its effect on hyperpigmentation in Black individuals with acne
- In two identical phase 3 randomized, double-blind, vehicle-controlled studies (NCT03168321; NCT03168334), participants aged ≥9 years with moderate-to-severe acne (score of 3 or 4 on the Evaluator's Global Severity Score) were randomized (1:1) to once-daily tazarotene 0.045% lotion or vehicle lotion for 12 weeks
  - CeraVe® hydrating cleanser and CeraVe® moisturizing lotion (L'Oreal, NY) were provided as needed for optimal moisturization/cleaning of the skin
- Safety evaluations included reports of treatment-emergent adverse events (TEAEs) and investigator-assessed hyperpigmentation (graded on a 4-point scale from 0 [none] to 3 [severe])
- Post hoc analyses were based on participants' self-identification of race, including 'Black or African American' (herein referred to as Black)

RESULTS

Participants

- The pooled intent-to-treat population included 1614 participants, of whom 262 (16.2%) self-identified as Black; the safety population included 253 Black participants
- At baseline, over three-fourths of Black participants in the study were female and ~95% had an EGSS score of 3 ('moderate')

Hyperpigmentation

- Rates of investigator-assessed hyperpigmentation in Black participants were high at baseline; approximately 40% of participants in both the tazarotene 0.045% lotion and vehicle arms had mild or moderate hyperpigmentation (mild [score=1]: tazarotene=28.1%, vehicle=22.7%; moderate [score=2]: tazarotene=11.6%, vehicle=13.6%)
- Rates of hyperpigmentation decreased by week 12 with tazarotene treatment (from 40.5% to 31.4%), but remained relatively unchanged with vehicle (37.9% to 37.2%) (**Figure 1**)
- Images depicting hyperpigmentation improvement in tazarotene-treated Black participants are shown in **Figure 2**

Safety

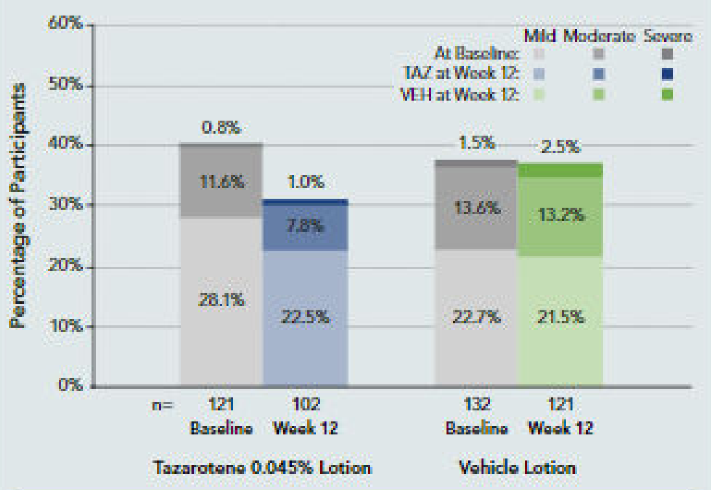
- TEAEs were mild to moderate in severity in almost all Black tazarotene-treated participants (**Table 1**)
- The most common TEAEs with tazarotene 0.045% lotion were at the application site: pain (6.6%), exfoliation (5.0%), dryness (3.3%), and pruritus (2.5%)
- No Black participants reported application site irritation or dermatitis with tazarotene 0.045% lotion
- A full report on safety and tolerability of tazarotene 0.045% lotion in Black participants has been published[6]

TABLE 1. Black Participants Reporting any Treatment-Emergent Adverse Event (Safety Population, Pooled)

	TAZ 0.045% Lotion (n=121)	Vehicle Lotion (n=132)
Any TEAE	30 (24.8)	17 (12.9)
Any SAE[a]	1 (0.8)	1 (0.8)
Severity of TEAEs		
Mild	22 (18.2)	8 (6.1)
Moderate	7 (5.8)	7 (5.3)
Severe	1 (0.8)	2 (1.5)
Most common TEAEs[b]		
Application site pain	8 (6.6)	0
Application site dryness	4 (3.3)	0
Application site exfoliation	6 (5.0)	0
Application site pruritus	3 (2.5)	0
Viral upper respiratory tract infection[a]	6 (5.0)	2 (1.5)

[a]No instances were considered by the investigator to be treatment related.
[b]Reported in ≥2% of participants in any treatment arm.
SAE, serious adverse event; TAZ, tazarotene; TEAE, treatment-emergent adverse event.

FIGURE 1. Rates and Severity of Hyperpigmentation in Black Participants (Safety Population, Pooled)



Data for "none" are not shown.
TAZ, tazarotene 0.045%; VEH, vehicle.

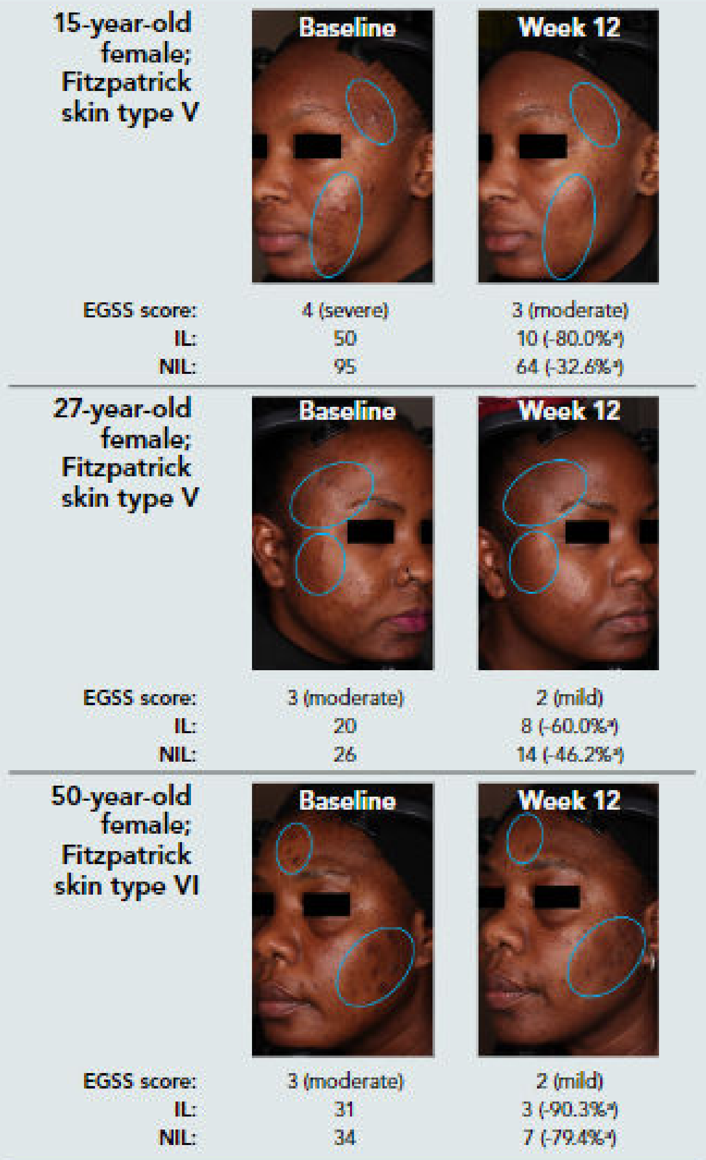
CONCLUSIONS

- Maximizing efficacy while mitigating irritation is a key goal in managing acne in patients with skin of color, given the higher risk of pigmentary alterations in melanin-rich skin[2,7]
- Tazarotene 0.045% lotion was safe and well tolerated, with no reports of application-site irritation or dermatitis in Black participants after 12 weeks of once-daily treatment
- Tazarotene treatment led to improvements in hyperpigmentation, an inflammation-associated sequela of acne
- As PIH can persist for up to 12 months,[1] additional improvement in hyperpigmentation may be expected with continued tazarotene use

REFERENCES

AUTHOR DISCLOSURES

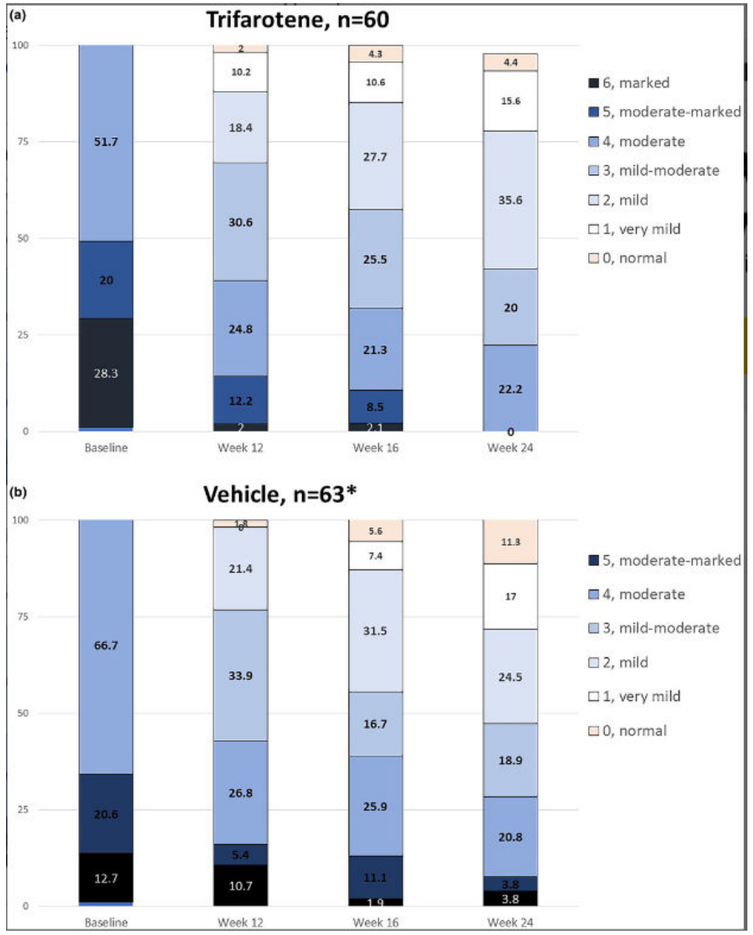
FIGURE 2. Hyperpigmentation Improvements in Black Participants Treated With Tazarotene 0.045% Lotion

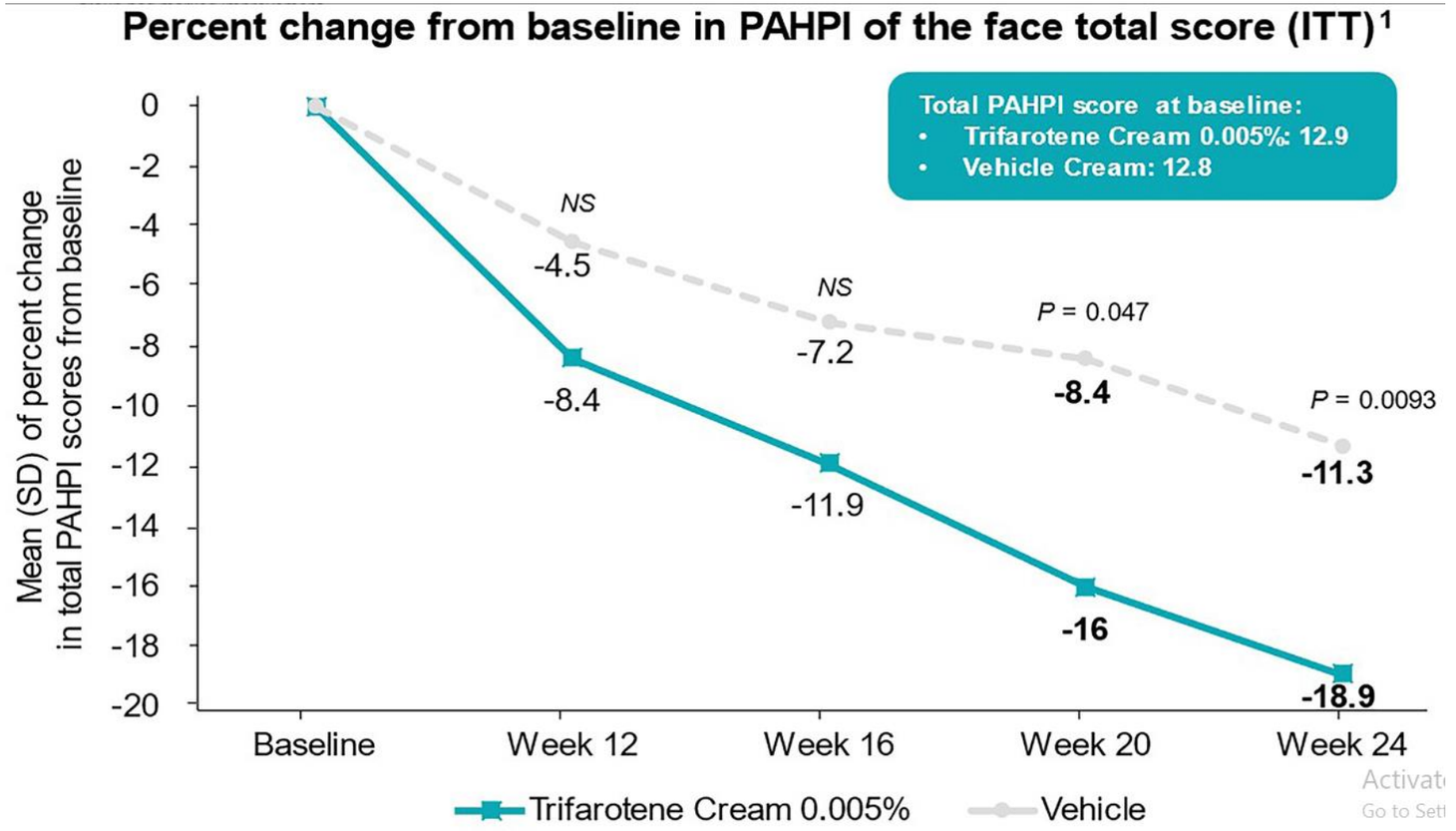


[a]Indicates percent change from baseline.
All three participants self-reported ethnicity as not Hispanic/Latino. Fitzpatrick skin types were assessed post hoc from participant photographs. Individual results may vary.
EGSS, Evaluator's Global Severity Score for acne; IL, inflammatory lesions; NIL, noninflammatory lesions.

ACKNOWLEDGEMENTS: Medical writing support was provided by Prescott Medical Communications Group (Chicago, IL) with financial support from Ortho Dermatologics; Ortho Dermatologics is a division of Bausch Health US, LLC • *Presented at the PA & NP Fall Clinical Dermatology Conference • June 9-11, 2023 • Orlando, FL*

Importance of treating acne sequelae in skin of color: 6-month phase IV study of trifarotene with an appropriate skincare routine including UV protection in acne-induced post-inflammatory hyperpigmentation





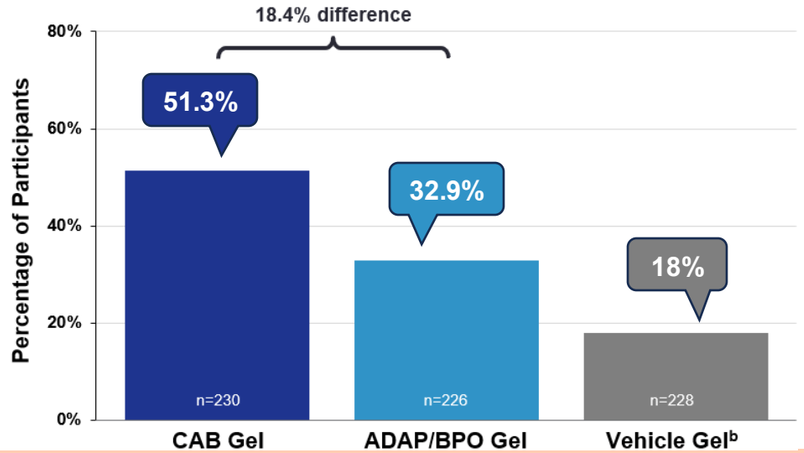
Alexis, A., et al. Int J Dermatol. 2024.

Fixed-Dose Triple Combination

Phase 2 Clinical Data – CAB vs Epiduo Forte

Superior Efficacy, comparable tolerability
Less than 3% of CAB-treated participants discontinued due to AEs

	Study 202		
	CABTREO™ (n = 230)	ADAP/BPO Gel (n=226)	Vehicle Gel (n = 228)
Treatment success[a]	**51.3%*****	32.9%***###	18%
Percent change from baseline, LS mean			
Inflammatory lesions	**-76.8%*****	-73%***	-51.5%
Noninflammatory lesions	**-71.8%*****	-67.2%***	-46.4%



Tanghetti EA et al. J Dermatolog Treat. 2023; Blume-Peytavi U et al. J Eur Acad Dermatol Venereol. 2020; Baldwin H et al. J Drugs Dermatol. 2024;

Fixed-Dose Triple Combination

Phase 2 Clinical Data – CAB vs Epiduo Forte

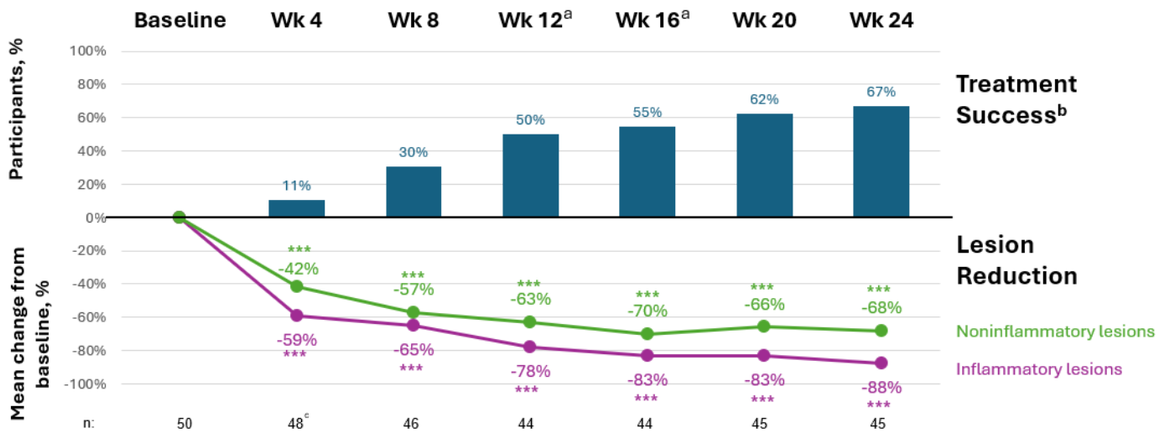
Superior Efficacy, comparable tolerability
<3% of CAB-treated participants discontinued due to AEs

Long-term efficacy and tolerability of CAB

At week 24, 67% of CAB-treated participants achieved treatment success, 88% reductions in inflammatory and 68% reductions in noninflammatory lesions (P<0.001)

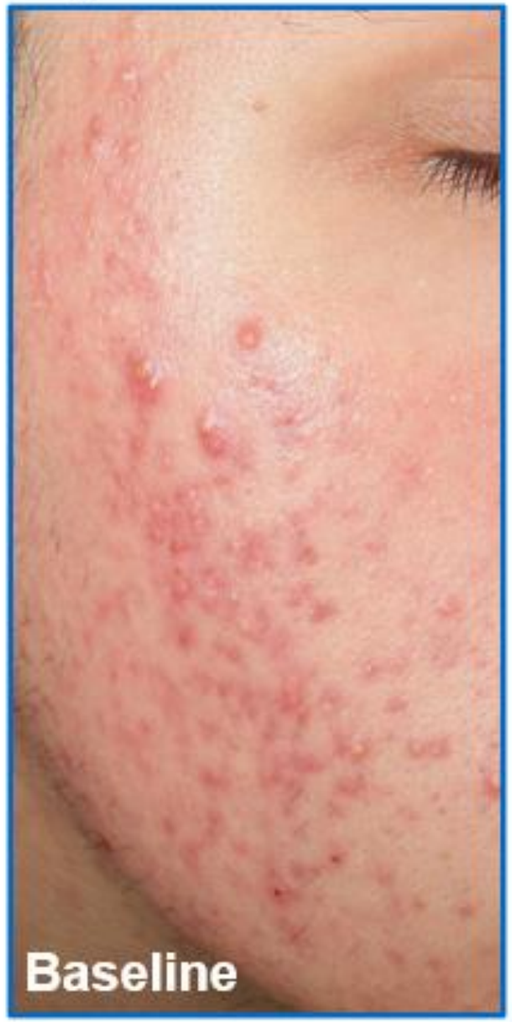
33% reduction in acne scarring from baseline by week 24

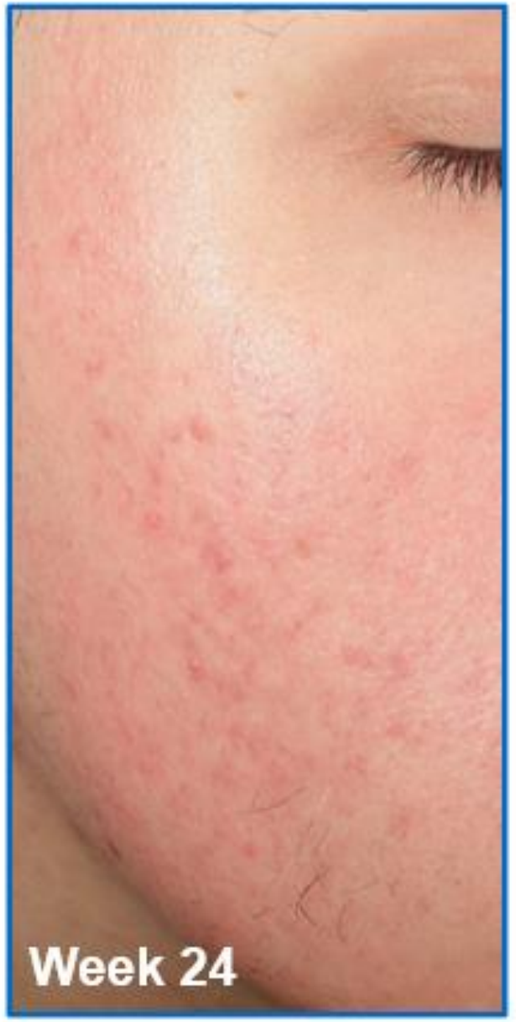
71% and 77% reductions from baseline at week 24 in PIH and PIE, respectively



Draelos ZD et al. J Drugs Dermatol. 2025

Right Cheek





Fixed-Dose Triple Combination

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33% reduction in acne scarring from baseline by week 24

71% and 77% reductions from baseline at week 24 in PIH and PIE, respectively

Reduced Bleaching

95%+ agreement that CAB did not produce bleaching of the skin or clothing

Fixed-Dose Triple Combination

These advances highlight ongoing innovation in retinoid therapy. Selection depends on disease severity, distribution, skin sensitivity, and prior treatment responses. Vehicle formulation can be tailored to patient preference for optimal tolerability.

Tanghetti EA et al. J Dermatolog Treat. 2023; Blume-Peytavi U et al. J Eur Acad Dermatol Venereol. 2020; Baldwin H et al. J Drugs Dermatol. 2024

Topical Antiandrogens

1

Mechanism of Action

- Competitive androgen receptor (AR) antagonist (cortexolone derivative).
- Reduces sebum synthesis and blocks androgen-induced inflammatory pathways.

2

Clinical Efficacy

- Pivotal Phase 3 trials showed significant reductions in inflammatory and non-inflammatory lesions at 12 weeks BID.
- Draelos et al reported reduced sebum production 27% at week 12, 47% at week 52 ($p<0.001$)
- Efficacy observed across male, female, and varied age groups.

3

Safety Profile

- Minimal systemic absorption
- Local adverse effects are generally mild (erythema, dryness, scaling).
- Low systemic bioavailability avoids hormonal side effects seen with oral antiandrogens.

Hebert A et al. J Am Acad Dermatol. 2022; Draelos et al. Dermatology and therapy. 2025.

Oral Antiandrogens

Mechanism of Action

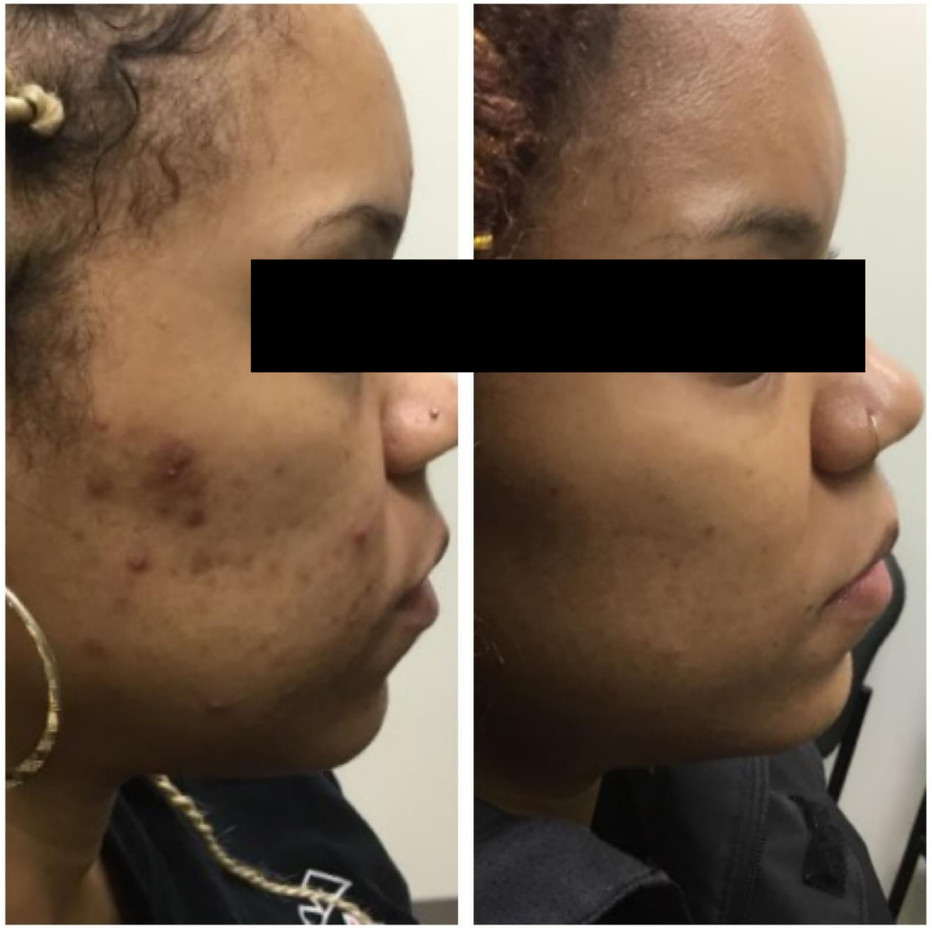
Inhibition of androgen production competitive binding to androgen receptors in sebaceous glands, reducing sebum secretion and inflammation.

Dosage Recommendations

Range from 50-100 mg/day. Clinical improvement usually noted after 3-6 months of consistent use.

Safety & Monitoring

Common side effects include menstrual irregularities, breast tenderness, and mild diuresis. *Baseline and periodic potassium level monitoring is recommended for at-risk patients.



Eichenfield LF et al. J Drugs Dermatol. 2021; Zaenglein AL et al. J Am Acad Dermatol. 2016

Oral Contraceptives

Mechanism of Action

COCs reduce ovarian androgen production and increase SHBG, lowering free androgens. Lowering sebum output.

Treatment Guidelines

Females with moderate to severe acne, or with hyperandrogenism (e.g., hirsutism, irregular menses). Contraindications include thromboembolic events, uncontrolled hypertension, or certain migraines.

FDA-Approved Options

Contain ethinyl estradiol with progestins like norgestimate (e.g., Ortho Tri-Cyclen) or drospirenone (e.g., Yaz).

Zaenglein AL et al. J Am Acad Dermatol. 2016; Eichenfield LF et al. J Am Acad Dermatol. 2021

Thromboembolic Risk with Hormonal Therapies

1-5

General Population

Annual VTE events per 10,000 women-years.

3-9

Oral Contraceptives

Annual VTE events per 10,000 women-years, varying by progestin type.

2-4

Hormone Replacement Therapy (HRT)

Annual VTE events per 10,000 women-years.

5-20

Pregnancy

Annual VTE events per 10,000 women-years.

40-65

Postpartum Period

Highest risk of VTE events per 10,000 women-years.

Patient risk factors (e.g., smoking, obesity, personal or family history of VTE, age >35) should be thoroughly assessed before initiating.

Tepper NK et al. Contraception. 2016; Committee Opinion No. 713: Use of Hormonal Contraception in Women at Risk for Venous Thromboembolism. Obstet Gynecol. 2017

Antibiotic Stewardship

⚠ CRITICAL ISSUE

1

Rising Resistance Patterns

- Widespread macrolide and lincosamide resistance.
- Increasing, though less common, tetracycline resistance.
- Geographic variations link higher rates to liberal prescribing.

2

Avoiding Monotherapy

- Antibiotic monotherapy is strongly discouraged due to rapid resistance selection.
- Combine with benzoyl peroxide (BPO) for bactericidal effects.
- Retinoids complement antibiotics by addressing non-antimicrobial aspects.

3

Limiting Duration

- Avoid prolonged courses (>3–6 months) to reduce resistance risk.
- Extended use disrupts cutaneous and gut microbiomes.
- Transition to non-antibiotic maintenance therapies is essential.

Barbieri JS et al. JAMA Dermatol. 2023

Sarecycline

Narrow-spectrum tetracycline, FDA-approved in 2018. Targets C. acnes, minimizes resistance and microbiota disruption.

1

Targeted Activity

Preferential activity against Gram-positive C. acnes. Reduced potency against Gram-negative gut flora (e.g., Bacteroides)

1

Mechanism

Binds to bacterial 30S ribosomal subunit, inhibiting protein synthesis.

2

Efficacy

Phase 3 trials showed significant reductions in inflammatory lesion counts and high Investigator's Global Assessment success rates.

3

Safety

Well tolerated; lower GI adverse effects than doxycycline. Minimal photosensitivity risk.

4

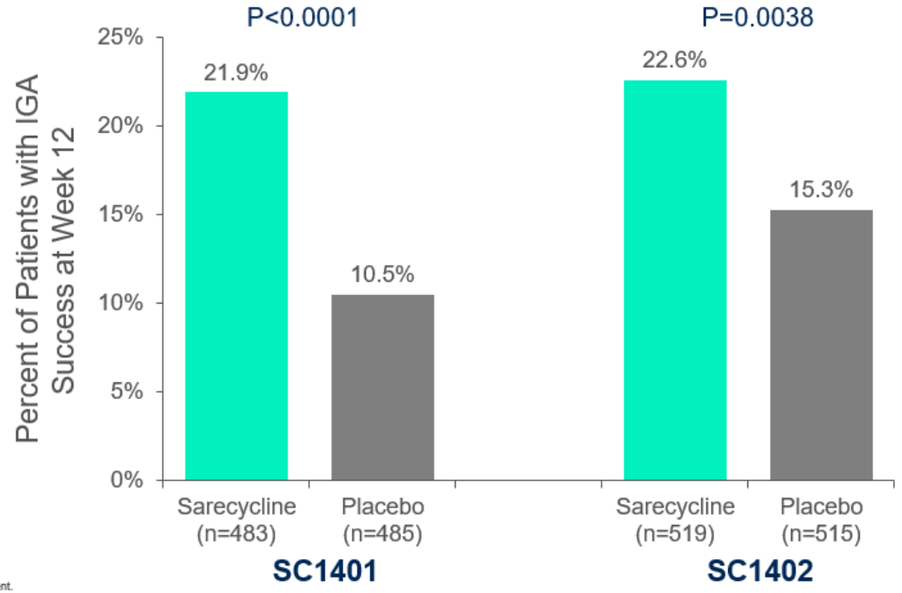
Stewardship

Spares Gram-negative gut flora, reducing dysbiosis and potential for resistance.

Zhanel G et al. Antimicrob Agents Chemother. 2018

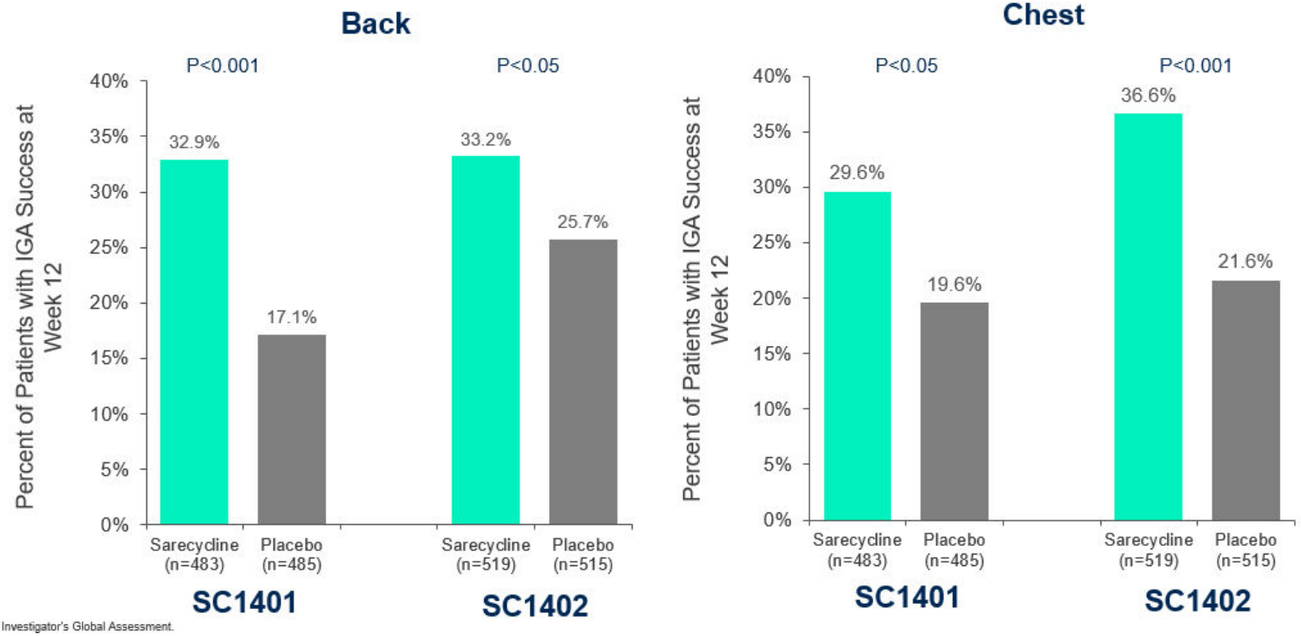
Sarecycline: Phase 3

Facial IGA success was defined as a ≥2-point decrease (improvement) in facial IGA score from baseline and a score of clear/almost clear



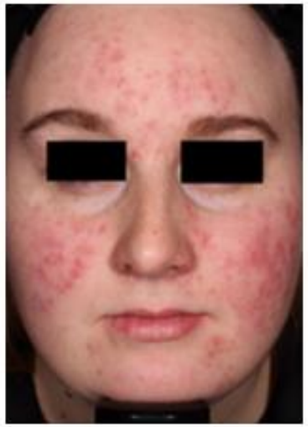
IGA, Investigator's Global Assessment.

IGA success was defined as a ≥2-point decrease (improvement) in non-facial IGA score from baseline and a score of clear/almost clear

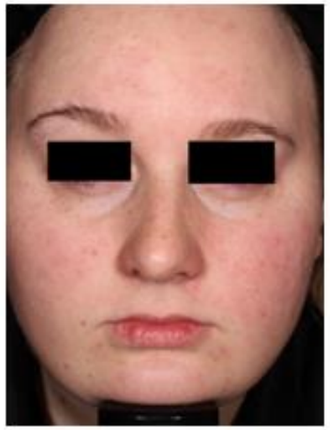


IGA, Investigator's Global Assessment.

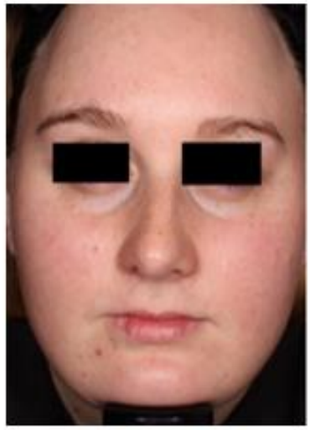
Moore A, et al. J Drugs Dermatol. 2018.;



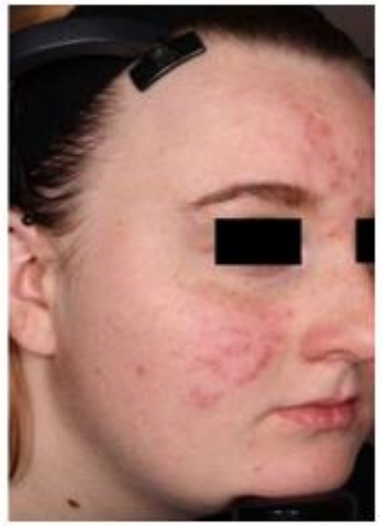
Baseline

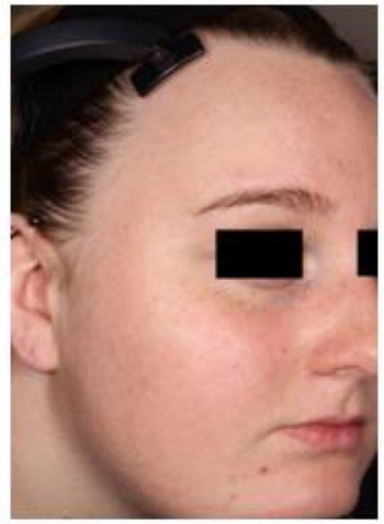


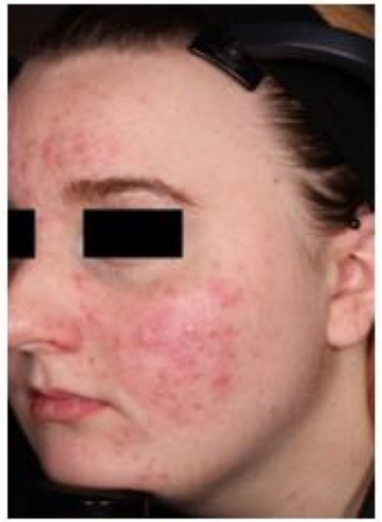
Week 3



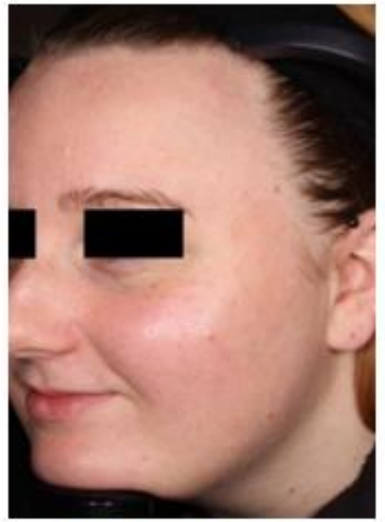
Week 12







Baseline



Week 12

Isotretinoin: Dosing Reconsidered

Isotretinoin remains the most effective therapy for severe, recalcitrant acne, offering long-term remission for many. Dosing strategies have evolved from rigid cumulative dose targets to more flexible, patient-tailored approaches.

Historical Dosing Paradigm

Traditional guidelines recommended a cumulative dose of 120–150 mg/kg, leading to protracted treatment at lower daily doses. Strict adherence to these cumulative targets is now being questioned.

- Cumulative dose: 120-150 mg/kg
- Protracted treatment (6-9+ months)

Low-Dose Efficacy

Low-dose regimens (0.25–0.5 mg/kg/day) are effective, especially for moderate acne or when higher doses are contraindicated. They are associated with reduced adverse effects and improved tolerability.

- Effective for moderate acne
- Reduced adverse effects
- Improved tolerability

Layton AM et al. Isotretinoin for acne vulgaris - 10 years later: a safe and successful treatment. Br J Dermatol. 1993;129(3):292-6.

Microbiome-Directed Therapies

Topical Probiotics

Live or inactivated probiotic bacteria modulate immunity and act as antimicrobials. They reduce inflammatory lesions and improve skin barrier function. More research is needed to confirm efficacy.

Prebiotics

Non-digestible substrates that promote beneficial microorganisms. They enhance microbial diversity and suppress pathogenic C. acnes strains..

Bacteriophages

Viruses that selectively target pathogenic C. acnes while sparing commensal bacteria. Preclinical models show promise, but manufacturing challenges exist.

Nakatsuji T et al. Front Cell Infect Microbiol. 2023

Acne Vaccine: A Prophylactic Strategy

nature

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nature › outlook › article

OUTLOOK | 27 August 2025 | Correction 14 October 2025

Acne vaccines could offer robust defence

Researchers are hoping to trick the immune system into fighting back against the bane of adolescents everywhere.

KEY TAKEAWAYS

Take-Home Messages

Complex Inflammatory Disease

Acne is a multifactorial inflammatory disease. Key factors include:

- Follicular hyperkeratinization
- Sebaceous gland dysregulation
- Microbial dysbiosis
- Innate immune activation
- Genetic, hormonal, and environmental influences

This complexity drives mechanism-based therapeutic strategies.

Expanding Treatment Options

The therapeutic landscape for acne is growing, with:

- Novel topical agents
- Refined retinoid formulations
- Microbiome-directed therapies
- Hormonal options

Guidelines emphasize combination therapy, antibiotic stewardship, and individualized selection.

Personalized Care Future

Future management will adopt precision medicine, integrating:

- Genetic and microbiomic data
- Biomarker-guided selection
- Targeted anti-inflammatory therapies
- Smart drug delivery systems

This approach aims to optimize outcomes, minimize adverse effects, and prioritize patient-centered care.

Thank You

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