

Therapeutic Update: What's Approved for Teens with Acne?

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Disclosures

- Galderma – investigator and speaker
- Ortho-Dermatologics – advisory board
- Almirall - consultant

Outline

- Population and Adherence
- What medications can you use
- Oral Spironolactone
- Combined Oral Contraceptives
- Diet
- How to increase adherence
- Future

Adherence

Adherence in Acne patients

- A review of medical records from an outpatient university dermatology clinic
- Had acne
- Looked at whether they took used their treatments

- Anderson KL, Dothard EH, Huang KE, Feldman SR. Frequency of Primary Nonadherence to Acne Treatment. JAMA Dermatol. 2015 Jun;151(6):623-6

Results of Acne Adherence Study

- Overall, **27% of patients did not fill all their prescriptions.**
 - Of patients who were given 1, 2, or 3 or more treatments, 9%, 40%, and 31%, respectively, did not fill all their prescriptions.
 - There was no statistically significant difference by sex or age.
-
- Anderson KL, Dothard EH, Huang KE, Feldman SR. Frequency of Primary Nonadherence to Acne Treatment. JAMA Dermatol. 2015 Jun;151(6):623-6

Acne Treatment Adherence

- Primary Nonadherence was associated with:

Being prescribed a topical retinoid (odds ratio, 2.9; 95% CI, 1.0-8.0)

Recommending an over-the-counter product (odds ratio, 3.6; 95% CI, 1.1-12.3)

Acne Treatment Adherence

- In this study...
- There was **less primary nonadherence** with **electronic prescriptions** compared with paper prescriptions ($P < .001$).

Adherence

- Primary adherence to an acne treatment regimen is better **when only 1 treatment is prescribed.**
- Some patients may not complete acne treatment because medications were never obtained

- Anderson KL, Dothard EH, Huang KE, Feldman SR. Frequency of Primary Nonadherence to Acne Treatment. JAMA Dermatol. 2015 Jun;151(6):623-6

Pediatric Adherence to Acne Treatments

- The mean adherence rate to acne medication was significantly different between children (0.22) and adolescents (0.32).
- By the definition of adherence, **neither population was adherent to, but adolescents were more adherent.**
- Only 3.71% of children (ages 6-11 years) were adherent to acne medication while 13.38% of adolescents were adherent.
- Hester C Park C, Chung J, Balkrishnan R, Feldman S, Chang J Medication Adherence in Children and Adolescents with Acne Vulgaris in Medicaid: A Retrospective Study Analysis Dermatol. 2016 Jan;33(1):49-55.

Pediatric Adherence to Acne Treatments

- Adolescents:
- were 2.06 times more likely to get an **acne-related medication refilled**
- were 2.40 times more likely to be **adherent to acne-related medication**

Review of all the medications you can use for acne in teenagers

- Eichenfield DZ, Sprague J, Eichenfield LF. Management of Acne Vulgaris: A Review. JAMA. 2021 Nov 23;326(20):2055-2067

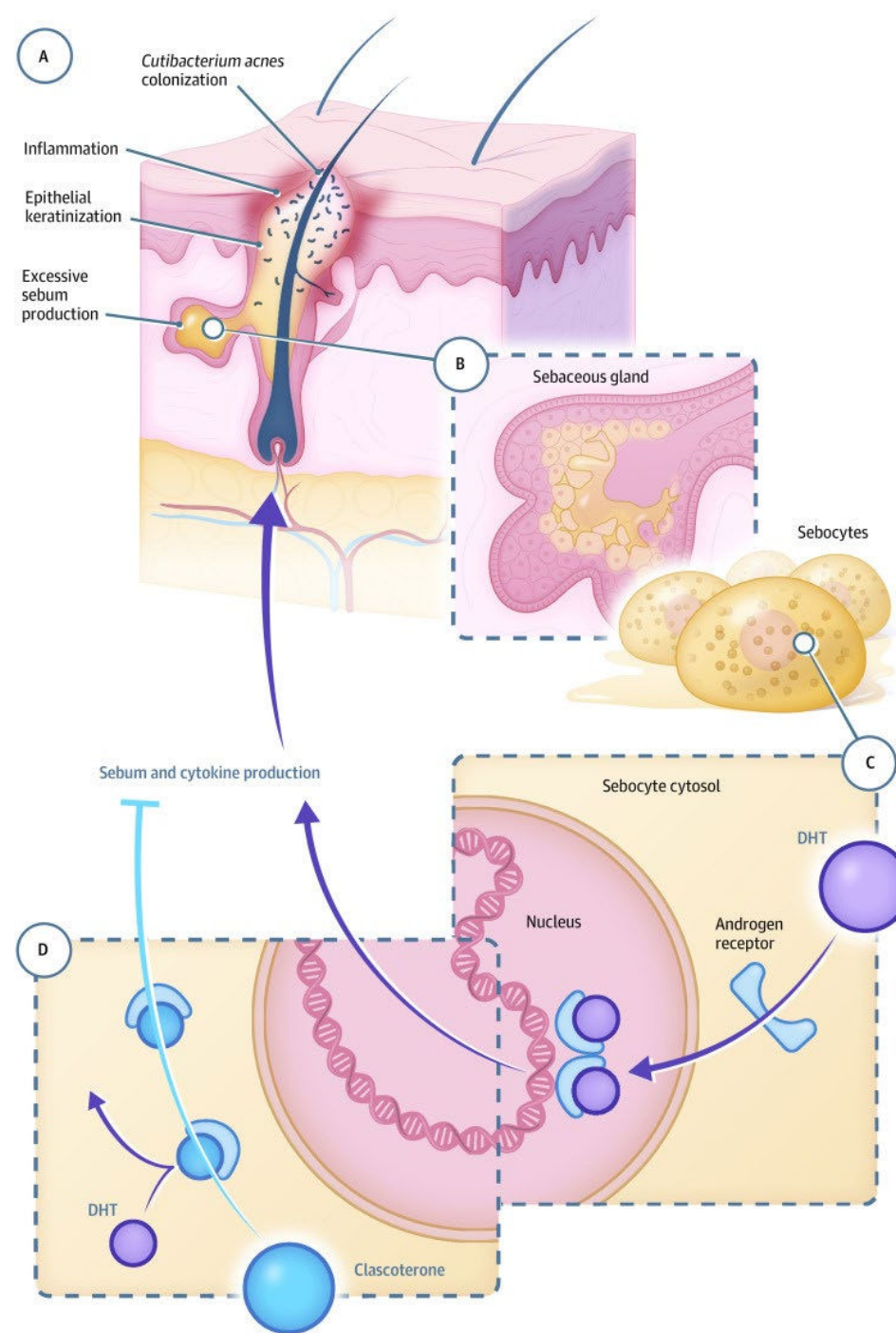
Approved newer medications

- For what age are they approved?

Newer topical antiandrogen - clascoterone

- To what age?
 - **12 years and above**
 - **Males and females**

Exact mechanism of action is unknown.
The drug is believed to compete with the dihydrotestosterone (DHT) for binding to androgen receptors in the sebaceous gland and hair follicles to attenuate signaling necessary for acne pathogenesis



- Hebert A, Thiboutot D, Stein Gold L, Cartwright M, Gerloni M, Fragasso E, Mazzetti A. Efficacy and Safety of Topical Clascoterone Cream, 1%, for Treatment in Patients With Facial Acne: Two Phase 3 Randomized Clinical Trials. JAMA Dermatol

Newer retinoid – trifarotene

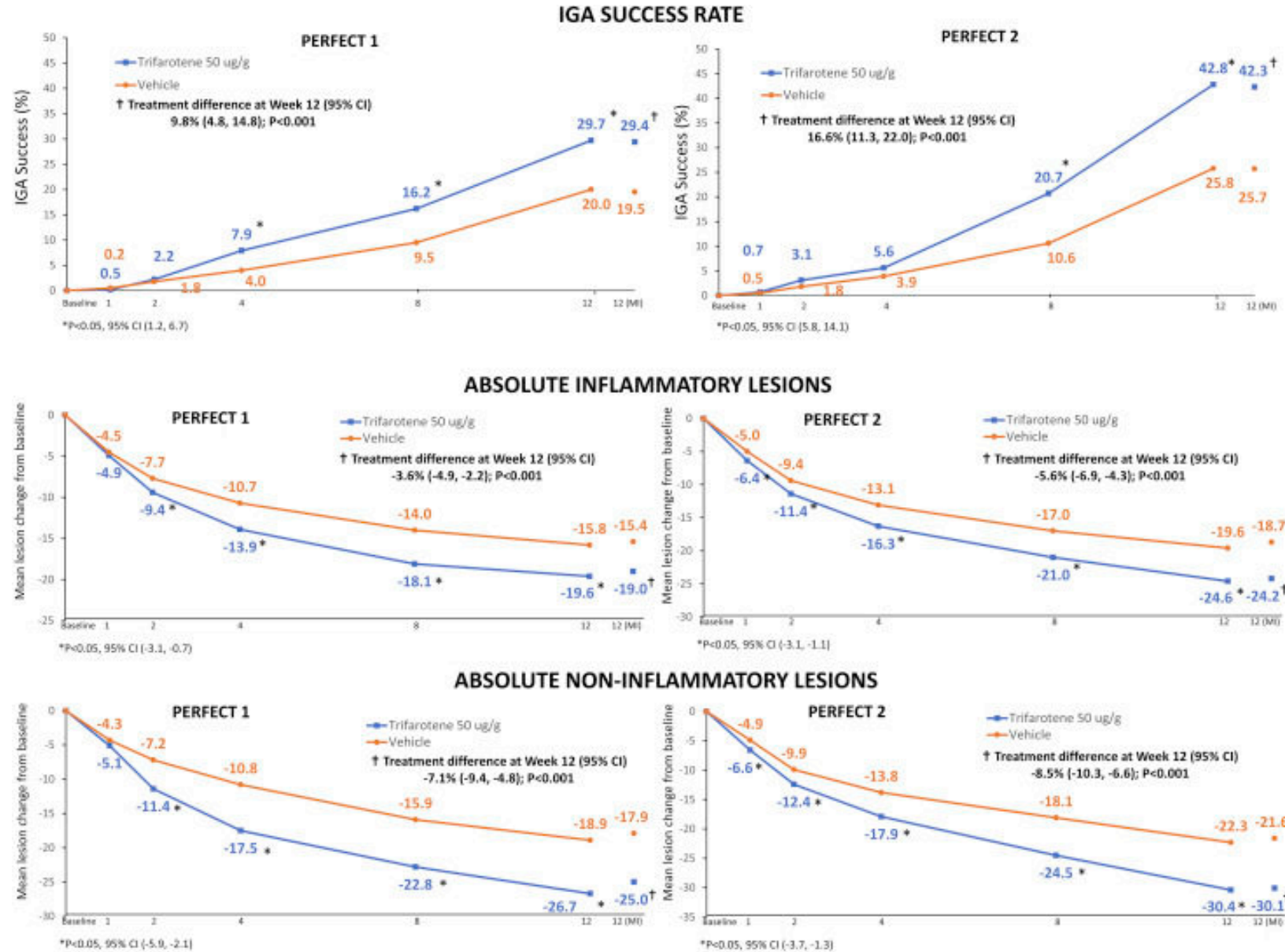
- Trifarotene .0005% cream
- Agonist of the Retinoic Acid Receptor (RAR)
- Trifarotene 50 µg/g cream is for the treatment of moderate acne on the **face and trunk**.
- Approved from age 9 years and up
- Tan J, Thiboutot D, Popp G, Gooderham M, Lynde C, Del Rosso J, Weiss J, Blume-Peytavi U, Weglovská J, Johnson S, Parish L, Witkowska D, Sanchez Colon N, Alió Saenz A, Ahmad F, Graeber M, Stein Gold L. Randomized phase 3 evaluation of trifarotene 50 µg/g cream treatment of moderate facial and truncal acne. J Am Acad Dermatol. 2019 Jun;80(6):1691-1699.

New retinoid – trifarotene

- Trifarotene .0005% cream
- The onset of effect was **rapid versus vehicle:**
 - inflammatory and noninflammatory lesion counts decreased as early as **1 week after treatment on the face**
 - as early as **2 weeks** after treatment on the **trunk**
- Side effect profile was mostly mild to moderate when applied not only to the face but the trunk which is a large surface area.
 - skin dryness, erythema, scaling, stinging, and burning
- Tan J, Thiboutot D, Popp G, Gooderham M, Lynde C, Del Rosso J, Weiss J, Blume-Peytavi U, Weglovská J, Johnson S, Parish L, Witkowska D, Sanchez Colon N, Alió Saenz A, Ahmad F, Graeber M, Stein Gold L. Randomized phase 3 evaluation of trifarotene 50 mug/g cream treatment of moderate facial and truncal acne. J Am Acad Dermatol. 2019 Jun;80(6):1691-1699.



Trifarotene treatment responses



Sarecycline

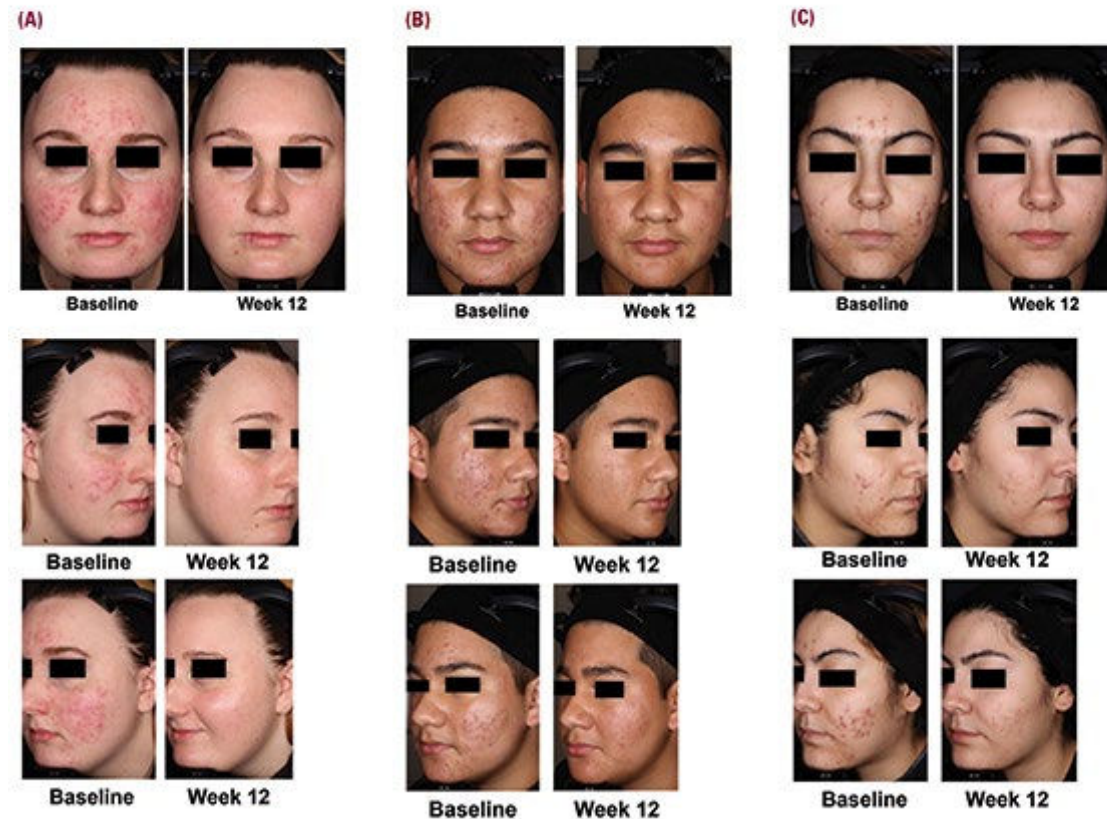
- Newer tetracycline class oral antibiotic
- Only narrow spectrum tetracycline antibiotic
- Approved for acne
- Daily dosing
- Weight based dosing
- 1.5mg/kg/day
- FDA Approved ages **9 years and up**
- *Cutibacterium acnes* has a low propensity to develop resistance

Systemic Antibiotics

- Sarecycline 60-150mg orally daily
 - <54kg = 60mg po daily
 - 55-84kg = 100mg po daily
 - 85-136 = 150mg po daily
- Approved for moderate to severe acne
- Used in patients **≥ 9 years of age**
- Main side effect – nausea (3.1%), vaginal candidiasis (<1%)

Sarecycline

FIGURE 7. Response to sarecycline in (A) a 23-year-old female patient in SC1401[†]; (B) a 14-year-old male patient in SC1402[‡]; (C) a 19-year-old female patient in SC1401.[†] IGA, Investigator's Global Assessment. [†]IGA score: 4 at baseline, 1 at week 12. Inflammatory lesions: 50 at baseline, 4 at week 12. Noninflammatory lesions: 22 at baseline, 17 at week 12. [‡]IGA score: 4 at baseline, 1 at week 12. Inflammatory lesions: 42 at baseline, 8 at week 12. Noninflammatory lesions: 74 at baseline, 31 at week 12. [§]IGA score: 4 at baseline, 1 at week 12. Inflammatory lesions: 33 at baseline, 8 at week 12. Noninflammatory lesions: 33 at baseline, 5 at week 12.



Moore A, Green LJ, Bruce S, et al. Once-Daily Oral Sarecycline 1.5 mg/kg/day Is Effective for Moderate to Severe Acne Vulgaris: Results from Two Identically Designed, Phase 3, Randomized, Double-Blind Clinical Trials. J Drugs Dermatol. 2018 Sep 1;17(9):987-996.

Minocycline foam 4%

- Once daily minocycline foam 4%
- Minimal systemic minocycline exposure
- 730 to 765 times LOWER than what is seen in oral minocycline ¹
- Approved for ages 9 and up
- Watch the foam can be flammable

- ¹Jones, MT, Eliman H, DeVries T., Pharmacokinetic comparison of once-daily topical minocycline foam 4% vs oral minocycline for moderate to severe acne. J Drugs Dermatol 2017;16(10):1022.

Minocycline Foam

- **Effective for up to 52 weeks of therapy**

- Linda Stein Gold, Sunil Dhawan, Jonathan Weiss Zoe Diana Draelos, et al. Open-label Extension Study Evaluating Long-term Safety and Efficacy of FMX101 4% Minocycline Foam for Moderate-to-Severe Acne Vulgaris. J Clin Aesthet Dermatol. . 2019 Oct;12(10):16-23.

New Retinoid formulations.... old retinoid

- Tazarotene 0.045% lotion with polymeric emulsion technology
- Tretinoin 0.05% lotion with polymeric emulsions technology

Tazarotene 0.045% lotion

- Tazarotene 0.045% lotion with polymeric emulsion technology
- Similar efficacies with respect to inflammatory and noninflammatory lesions in moderate to severe acne
- Take home: **As effective as the Tazarotene 0.1% cream but with less adverse effects**
- Tanghetti EA, Kircik LH, Green LJ, Guenin E, Harris S, Martin G, Pillai R. A Phase 2, Multicenter, Double-Blind, Randomized, Vehicle-Controlled Clinical Study to Compare the Safety and Efficacy of a Novel Tazarotene 0.045% Lotion and Tazarotene 0.1% Cream in the Treatment of Moderate-to-Severe Acne Vulgaris. J Drugs Dermatol. 2019 Jun 1;18(6):542.

Before and After Pictures

12-year-old ARAZLO- treated female



Baseline
EGSS 3 (Moderate)



Week 12
EGSS 1 (Almost Clear)

14-year-old ARAZLO-treated male



Baseline
EGSS 3 (Moderate)



Week 12
EGSS 1 (Almost Clear)

From the clinical trial

Tretinoin 0.05% Lotion

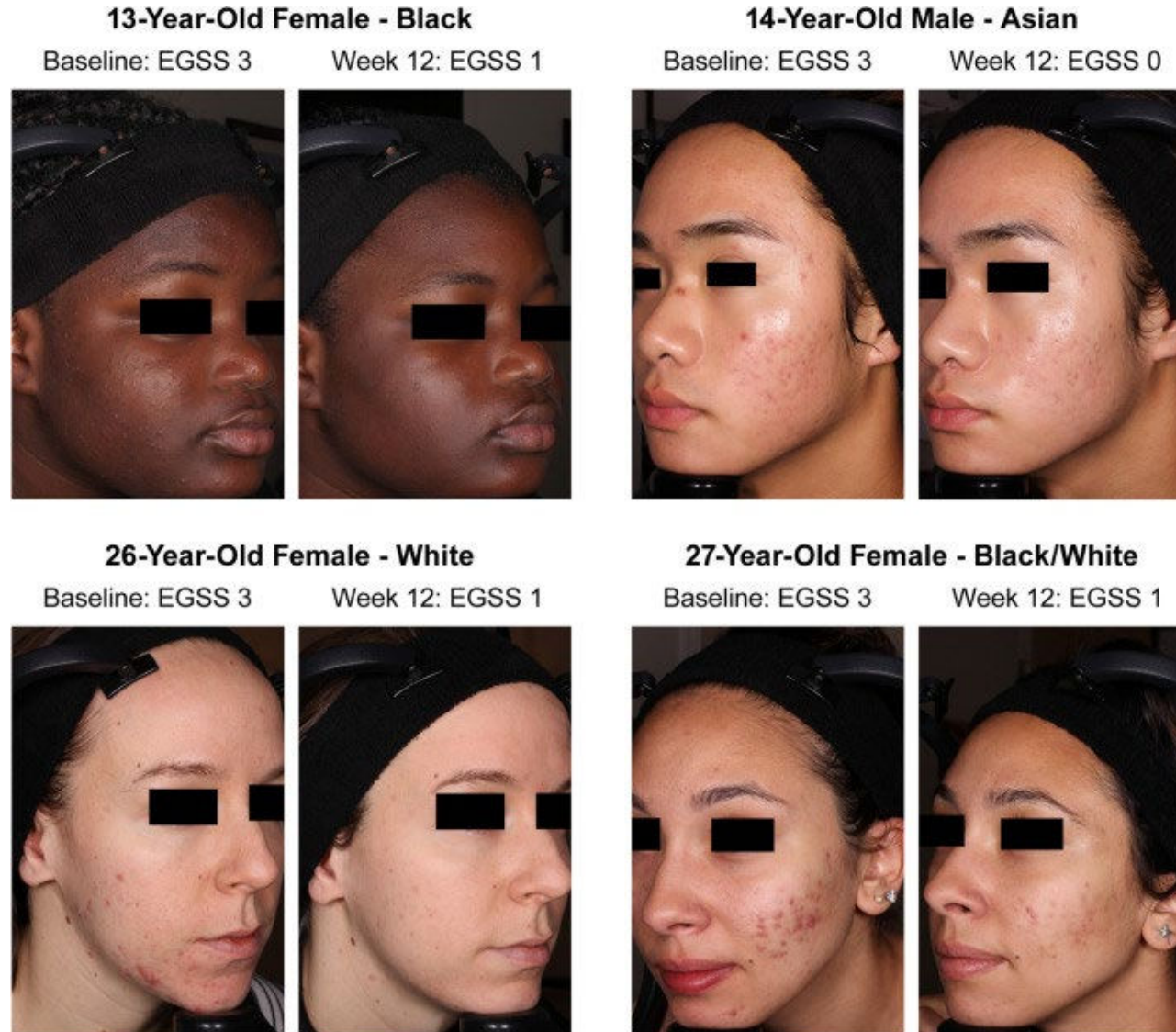
- Tretinoin 0.05% lotion with polymeric emulsions technology (Altreno)
- Low side effect profile

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

- 741 participants – double blind
- At week 12
- 52.5% of participants success over vehicle (8.1%) and over dyads (range 27.8-30.5%; $P \leq 0.001$, all).
- Once daily
- Novel fixed-dose triple-combination clindamycin phosphate 1.2%/BPO 3.1%/adapalene 0.15% gel demonstrated superior efficacy to vehicle and all three dyad component gels
- Well tolerated over 12 weeks in pediatric, **adolescent**, and adult participants with moderate-to-severe acne.

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

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



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

Spironolactone

Spironolactone

- Potent antiandrogen
- Use most often in conjunction with oral contraceptives
- Dose 25-100mg (sometimes 150-200mg) daily
- Age of use - 15 years or up in most cases. Have rarely used under this age
- **Drospirenone containing oral contraceptives are equivalent to 25mg of spironolactone**



- ¹ Thiede RM, Rastogi S, Nardone B, Sadowsky LM, Rangel SM, West DP, Schlosser BJ. Hyperkalemia in women with acne exposed to oral spironolactone: A retrospective study from the RADAR (Research on Adverse Drug Events and Reports) program. Int J Womens Dermatol. 2019 Apr 25;5(3):155-157



Spironolactone in Adolescents

- Eighty patients (80) with a median age of 19 years (range, **14-20 years**) met study inclusion criteria.
- Patients received spironolactone:
 - median duration of 7 month (range, 3-45 months)
 - mean follow-up time was 16 months.
- The median dose of spironolactone was 100 mg daily (range, 25-200 mg).
- Approximately 15-25% of pediatric patients with grade 3 to 4 acne had no response to spironolactone.
- **Only 3.8%** of pediatric patients had side effects from spironolactone and discontinued therapy (rash, breast tenderness, diarrhea, and headache).



Combined Oral Contraceptives

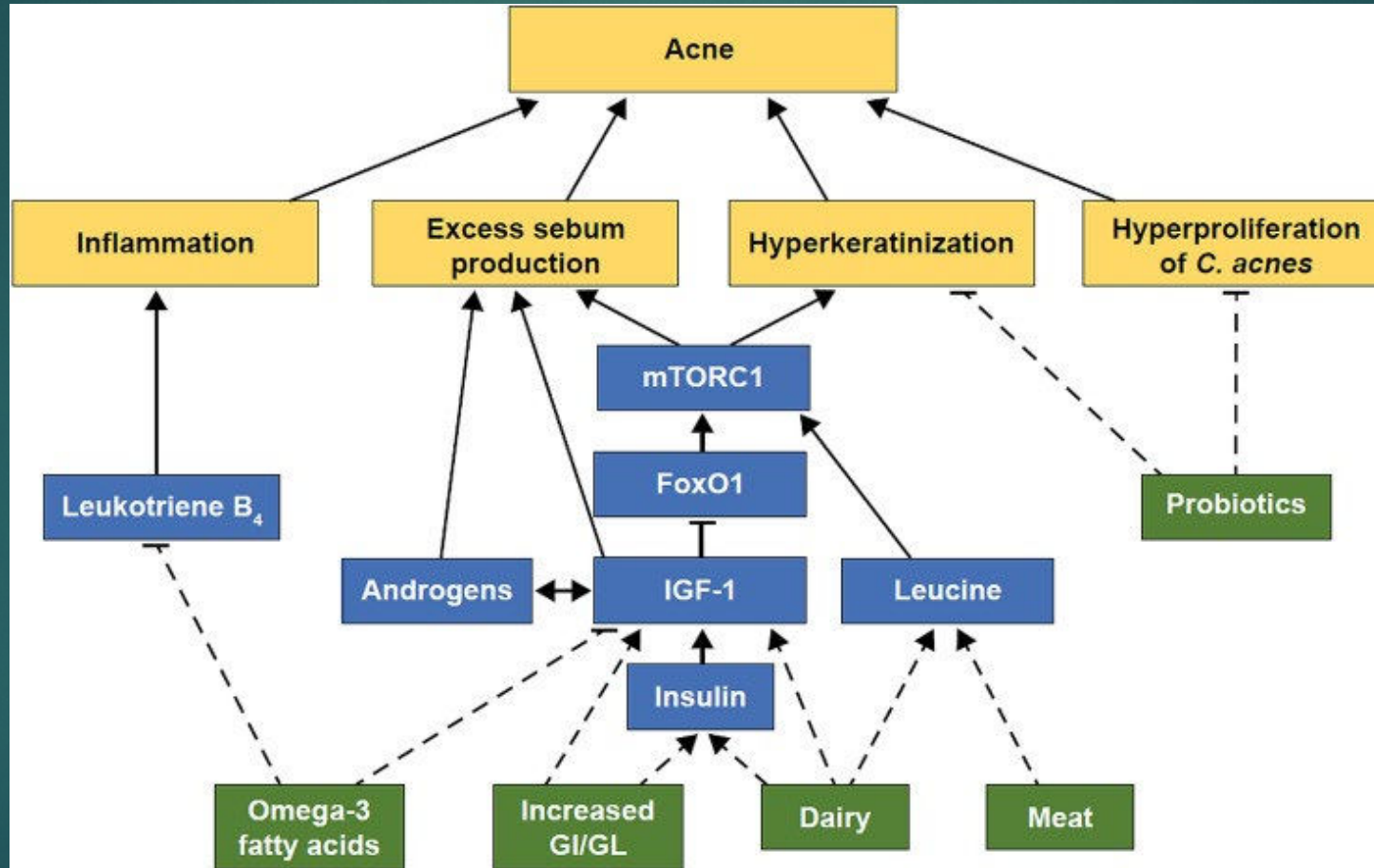
- When can we use?
- No exact age
- Once they have established menstrual cycles
- Careful with early teens
- Desire contraception

When can you use combined oral contraceptives in adolescents?

- Age 16-17 but have used earlier and can use after having menses for 2 years
- But if sexually active have to consider risk of contraceptive pill versus unwanted pregnancy
- Thromboembolic events remain the most concerning
 - Pregnancy test prior to starting
 - Review side effects (hypertension, migraine with aura, stroke risk)
 - Don't need to see OB/GYN before starting, but encourage

Diet?

Pathways proposed for diet and acne



Baldwin H, Tan J.
Effects of Diet on
Acne and Its
Response to
Treatment. Am J
Clin Dermatol.
2021
Jan;22(1):55-65.

Dietary impact
on mammalian
target of
rapamycin
complex 1
(mTORC1)
signaling.
Dashed lines
represent
associations
under discussion
in this review.
FoxO1 forkhead
box class O
transcription
factor 1, GI
glycemic index,
GL glycemic

What is a low glycemic load diet?
How can we do it inexpensively

- Less sugar
- Less sugary drinks

Face Washing

- Twice a day is best
- Study looked at 1,2, and 4 times a day
- Joanna Mimi Choi 1, Vincent K Lew, Alexa B Kimball. A single-blinded, randomized, controlled clinical trial evaluating the effect of face washing on acne vulgaris. . Pediatr Dermatol. 2006 Sep-Oct;23(5):421-7.

Which Cleanser?

- English-language articles indexed in MEDLINE (1951-March 2017) and EMBASE (1974-March 2017).
 - Single over-the-counter cleanser or washing intervention
 - 14 prospective studies representing 671 participants
 - Difficult to formulate reliable recommendations
-
- Thomas Stringer Arielle Nagler, Seth J Orlow, Vikash S Oza. Clinical evidence for washing and cleansers in acne vulgaris: a systematic review. J Dermatolog Treat. . 2018 Nov;29(7):688-693.

How can we increase adherence?

Adherence is issue in adolescent population

- Listen
- Which formulations - Pads/Swabs/Once a day/Combination products
- How to ask questions? “How many days a week do you use your meds OR how do you use your meds”
- Listen
- Find out what they like and dislike
- Expectations – slower process than they think
- Show interest
- Listen

Adolescents

- **Address Adherence**
- They will be honest
- Evaluate what they have used and then move forward with an algorithm
- Understand the pediatric approach to care is important in this population
- Electronic visits
- Remember diverse populations

Future...

- In the pipeline:
 - Bacteriocidal agents
 - Anti-sebum agents
- Lasers and Lights?
- Accure Acne's Laser System Cleared - November 29, 2022 by FDA
Treat mild-to-severe inflammatory acne vulgaris

1726 nanometer laser wavelength which selectively targets sebaceous glands (photothermolysis) using a proprietary pulsing algorithm that controls the thermal depth

Wrap up

- Listen
- Have plan
- For medications
- For washes
- For diet
- For future/alternative treatments

Thank you!