

# ACNE

## PEER-TO-PEER EDUCATIONAL TOOLKIT

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A compilation of key content from select presentations at the 2021 South Beach Symposium Part I: Medical Dermatology Summit and the Masters of Pediatric Dermatology

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# Acne Vulgaris

- Acne vulgaris is one of the most common skin conditions in children and adolescents, affecting up to 93% of adolescents
- The mainstay of acne treatment includes topical gels and/or antibiotics, off-label use of oral antibiotics, hormonal medications for females, or oral isotretinoin for moderate to severe or refractory cases
- Great need for new oral and topical antibiotics specifically targeting acne vulgaris

<sup>1</sup>Husein-ElAhmed H. *Dermatol Ther.* 2015, 28(3):166-72.

**TABLE. TREATMENT ALGORITHM FOR THE MANAGEMENT OF ACNE VULGARIS IN ADOLESCENTS AND YOUNG ADULTS<sup>4</sup>**

	Mild	Moderate	Severe
First-line treatment	Benzoyl peroxide (BP) OR topical retinoid OR topical combination therapy <sup>a</sup> (BP + antibiotic) OR (retinoid + BP) OR (retinoid + BP + antibiotic)	Topical combination therapy <sup>a</sup> (BP + antibiotic) OR (retinoid + BP) OR (retinoid + BP + antibiotic) OR (oral antibiotic + topical retinoid + BP) OR (oral antibiotic + topical retinoid + BP + topical antibiotic)	Oral antibiotic plus topical combination therapy <sup>a</sup> (BP + antibiotic) OR (retinoid + BP) OR (retinoid + BP + antibiotic) OR Oral isotretinoin
Alternative treatment	Add topical retinoid or BP (if not already applied) OR Consider alternate retinoid OR Consider topical dapsone	Consider alternate combination therapy OR Consider change in oral antibiotic OR Add combined oral contraceptive or oral spironolactone (females) OR Consider oral isotretinoin	Consider change in oral antibiotic OR Add combined oral contraceptive or oral spironolactone (females) OR Consider oral isotretinoin

<sup>a</sup>May be prescribed as a fixed combination product or as a separate component.

Reprinted with permission from Zaenglein AL, Pathy AL, Schlosser BJ, et al. *J Am Acad Dermatol*. 2016;74(5):945-973.e33.

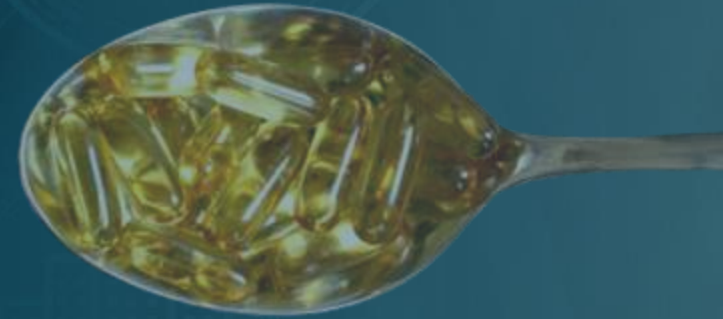
Reprinted from the *Journal of the American Academy of Dermatology*, 74(5), Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris, 945-973.e33. © 2016, with permission from Elsevier.

# Antibiotics



# Antibiotics for Acne

- Tetracyclines (minocycline, doxycycline) - 1<sup>st</sup> Line
- Macrolides
- Trimethoprim/ Sulfamethoxazole
- Topicals: Clindamycin, erythromycin



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# RESISTANCE

Erythromycin > Clindamycin > TCN > Doxycycline > Minocycline

- Can be transmitted to personal contacts

# Systemic Antibiotics – Antibiotic Stewardship

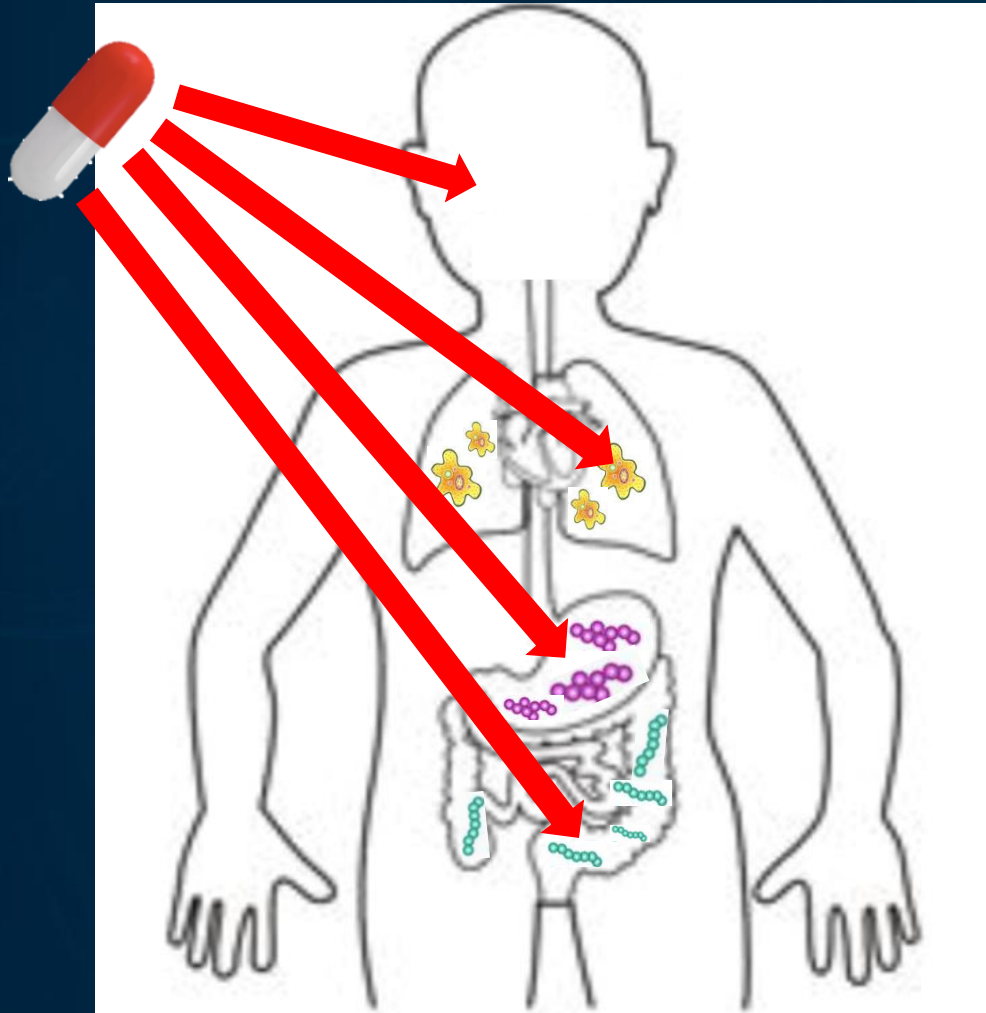
- Minocycline, doxycycline
- Limit 3-6 months
- Use with topical BP
- Avoid topical antibiotic monotherapy
- Topicals for maintenance

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## Broad Spectrum Antibiotics:

**Tetracycline, Doxycycline, Minocycline**

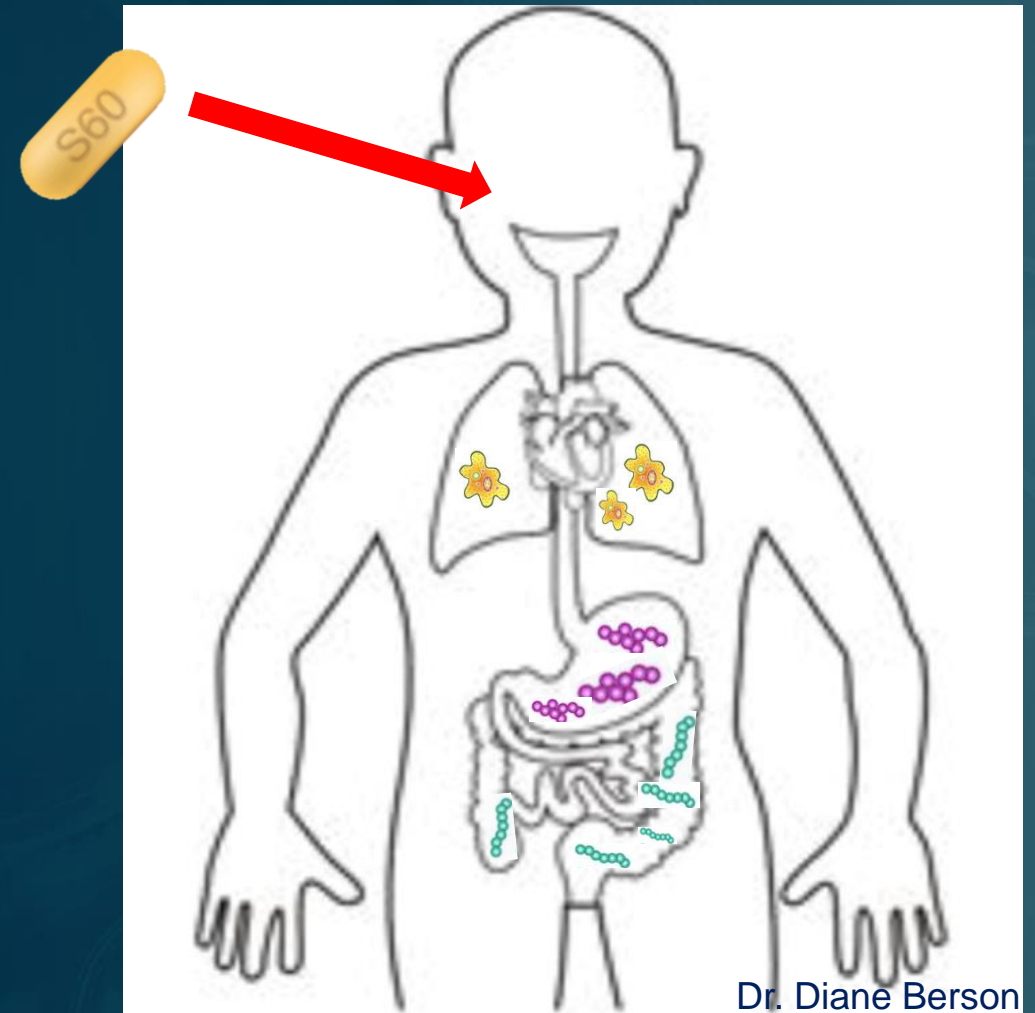
Inhibit many types of bacteria throughout the body



## Narrow Spectrum Antibiotics:

**Sarecycline**

Inhibit a limited number of bacteria in specific locations



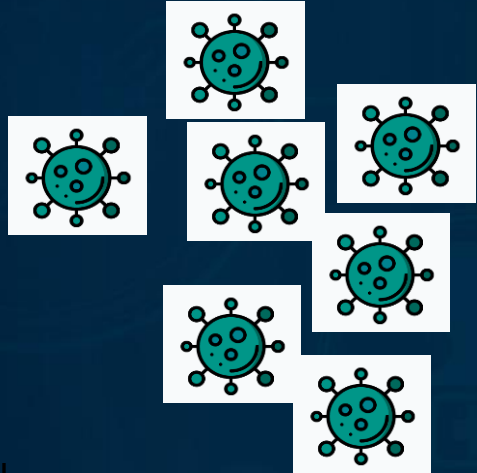
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**Narrow spectrum**



CDC recommends the use of **narrow-spectrum** antibiotics when the causative organism is known

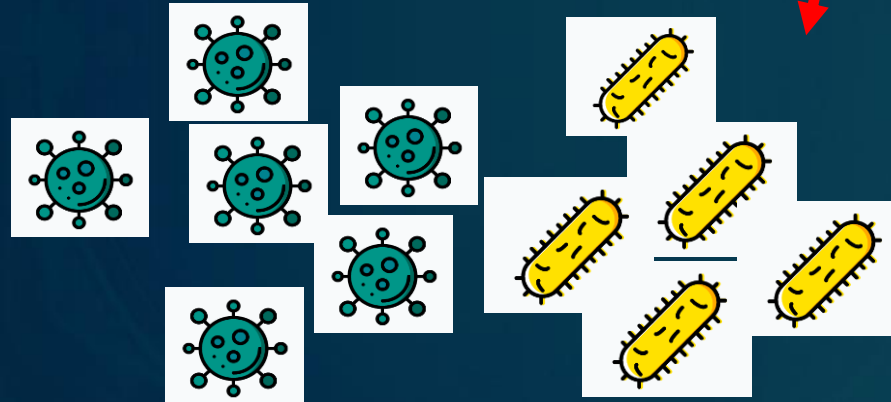


Specific pathogenic bacteria

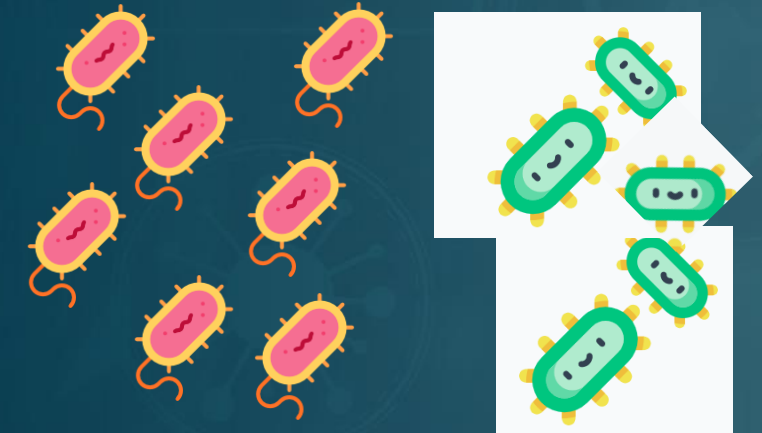
**Broad spectrum**



FDA recommends reducing the use of **broad-spectrum** antibiotics when more targeted therapies are appropriate



Pathogenic bacteria



Beneficial bacteria in human body

# Oral Therapies

# Sarecycline

- **NEW** tetracycline-class oral antibiotic for acne that target cutaneous *P. acnes* but **LOW activity against healthy gram-negative gut bacteria**
- **FDA-approved** for non-nodular moderate to severe acne on October 2018
- Once-daily dosage at 1.5 mg/kg/day
- Safe and effective in children **9 years and older**<sup>1</sup>
- Highly active against *C. acnes* strains, *S. epidermidis*, and *S. aureus*

<sup>1</sup>Deeks, E. Sarecycline: First Global Approval. 2019;79. 325-39.

<sup>2</sup>Zhanel G, Critchley I, Lin LY, Alvandi N. Microbiological Profile of Sarecycline, A Novel Targeted Spectrum Tetracycline for the Treatment of Acne Vulgaris. Antimicrob Agents Chemother. 2019;63 (1): e01297-18.

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

**TABLE 3.**

**Treatment-Emergent Adverse Events Common to Tetracycline-Class Antibiotics (Safety Population)**

Event, n (%)	SC1401		SC1402	
	Sarecycline (n=481)	Placebo (n=483)	Sarecycline (n=513)	Placebo (n=513)
Gastrointestinal effects in ≥1% of patients in any group				
Nausea	22 (4.6)	12 (2.5)	10 (1.9)	5 (1.0)
Vomiting	10 (2.1)	7 (1.4)	3 (0.6)	2 (0.4)
Abdominal pain	6 (1.2)	6 (1.2)	3 (0.6)	1 (0.2)
Abdominal discomfort	5 (1.0)	1 (0.2)	2 (0.4)	2 (0.4)
Diarrhea	5 (1.0)	8 (1.7)	6 (1.2)	6 (1.2)
Vestibular effects				
Dizziness	3 (0.6)	7 (1.4)	2 (0.4)	4 (0.8)
Motion sickness	0	0	1 (0.2)	1 (0.2)
Tinnitus	0	0	0	0
Vertigo	0	0	0	0
Phototoxic effects				
Photosensitivity	0	0	1 (0.2)	0
Sunburn	3 (0.6)	2 (0.4)	4 (0.8)	1 (0.2)
Vaginal yeast infections in females				
Vulvovaginal candidiasis <sup>a</sup>	3 (1.1)	0	1 (0.3)	0
Vulvovaginal mycotic infection <sup>a</sup>	2 (0.7)	0	3 (1.0)	0

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# Topicals



# Minocycline foam 4%

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

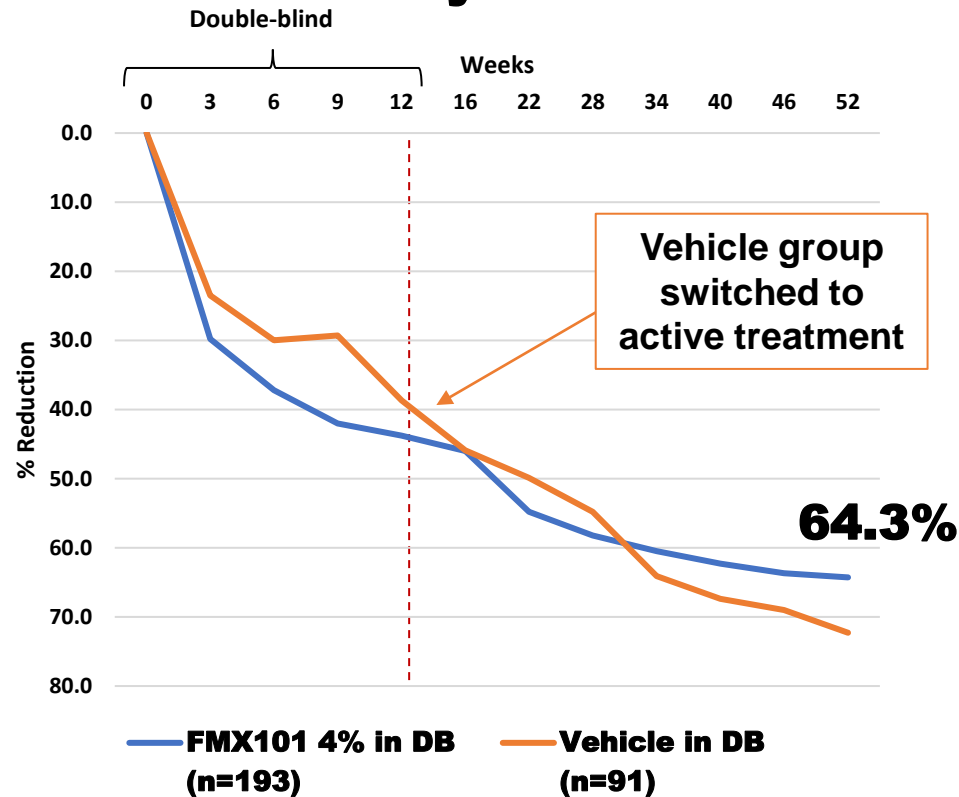
<sup>1</sup>Jones, MT, Eliman H, DeVries T., Pharmacokinetic comparison of once-daily topical minocycline foam 4% vs oral minocycline for moderate to severe acne. J Drugs Dermatol 2017;16(10):1022.

# MINOCYCLINE 4% FOAM ONCE DAILY

LONG TERM SAFETY DATA – MODERATE/SEVERE ACNE

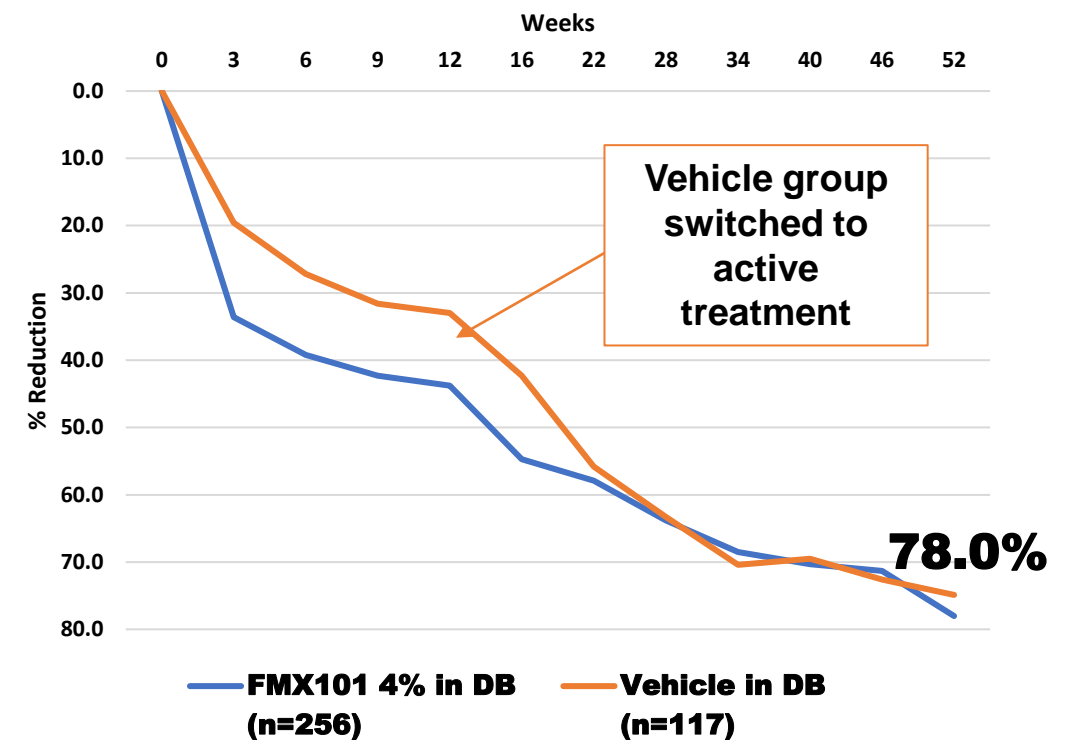
≥9 YEARS OF AGE – CHANGE IN INFLAMMATORY LESIONS (ILs)

## Study 04



\* $P \leq .0001$ ;  $^{\dagger}P \leq .001$ ;  $^{\ddagger}P \leq .01$ .

## Study 05



# Minocycline Distribution

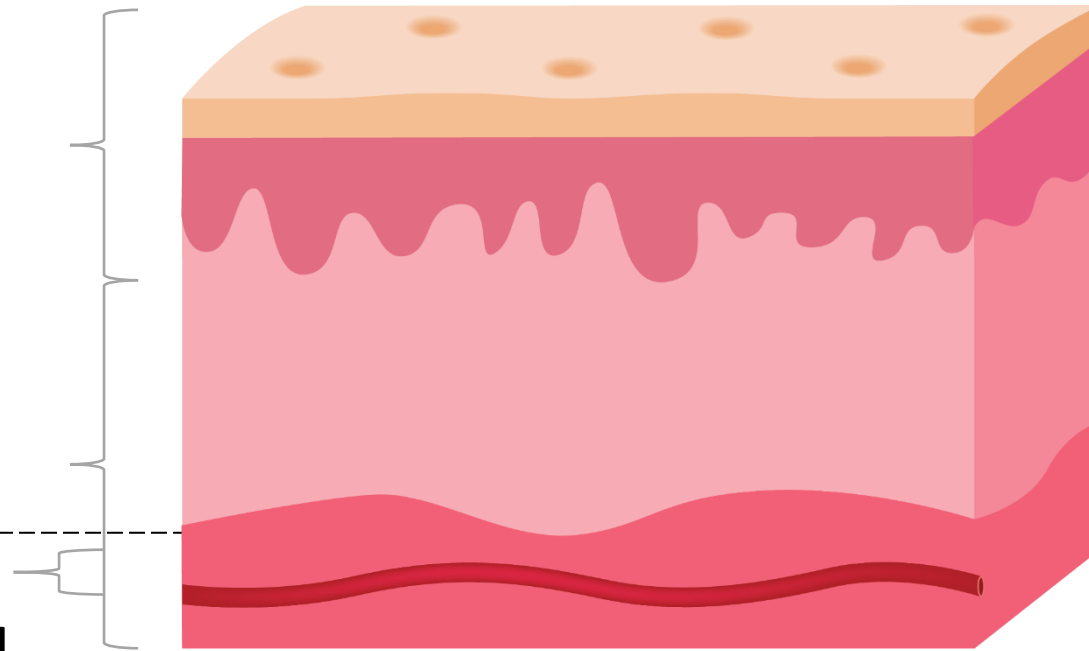
PREFERENTIAL CONCENTRATIONS IN SKIN >>> PLASMA

ORAL MINOCYCLINE  
(1mg/kg) at Day 21

EPIDERMIS<sup>1</sup>:  
3.7 µg/mL

DERMIS<sup>1</sup>:  
2.3 µg/mL

PLASMA<sup>2</sup>  
Mean C<sub>max</sub> = 850 ng/mL

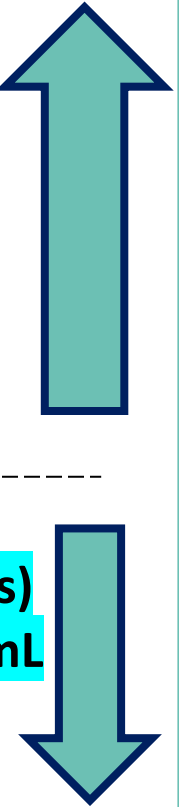


TOPICAL MINOCYCLINE 4% FOAM  
(10mg/cm<sup>2</sup>)

EPIDERMIS<sup>3</sup>:  
560.21 µg/mL

DERMIS<sup>3</sup>:  
17.50 µg/mL

PLASMA<sup>2</sup> (4g/day for 21 days)  
Mean C<sub>max</sub> = 1.3 ng/mL



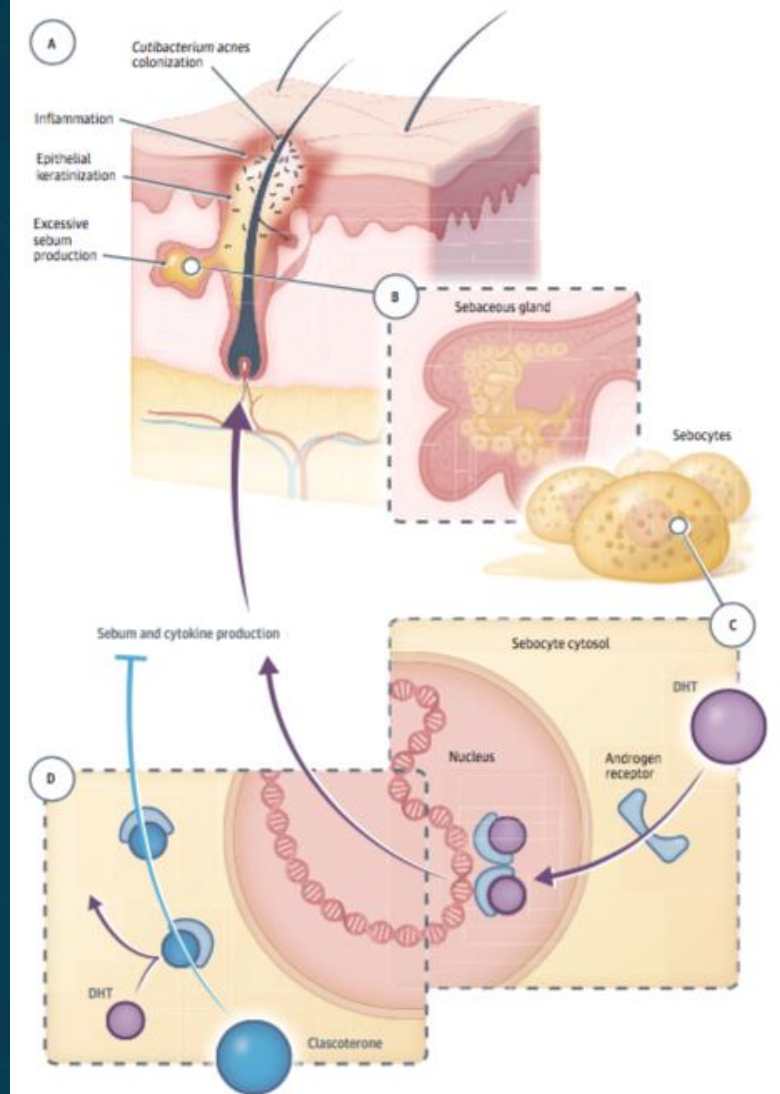
Approximately half of minocycline delivered to the epidermis was recovered from the sebaceous appendages<sup>1</sup>

1 Macdonald H et al. *Clin Pharmacol Ther.* 1973;14(5):852-861 2 Jones TM. *J Drugs Dermatol.* 2017;16(10):1022-1028. 3 Data on file: MedPharm Study No. 474-1701-1702.

# Clascoterone Cream, 1%

- First topical androgen receptor inhibitor
- FDA-approved in August 2020 for acne vulgaris in ages 12+
- Unlike systemic anti-androgens, may be used in males as well as female
  - Drug is metabolized to cortexolone (inactive), limiting systemic absorption
- Application is 1g twice per day

Figure 1. Proposed Mechanism of Action of Clascoterone



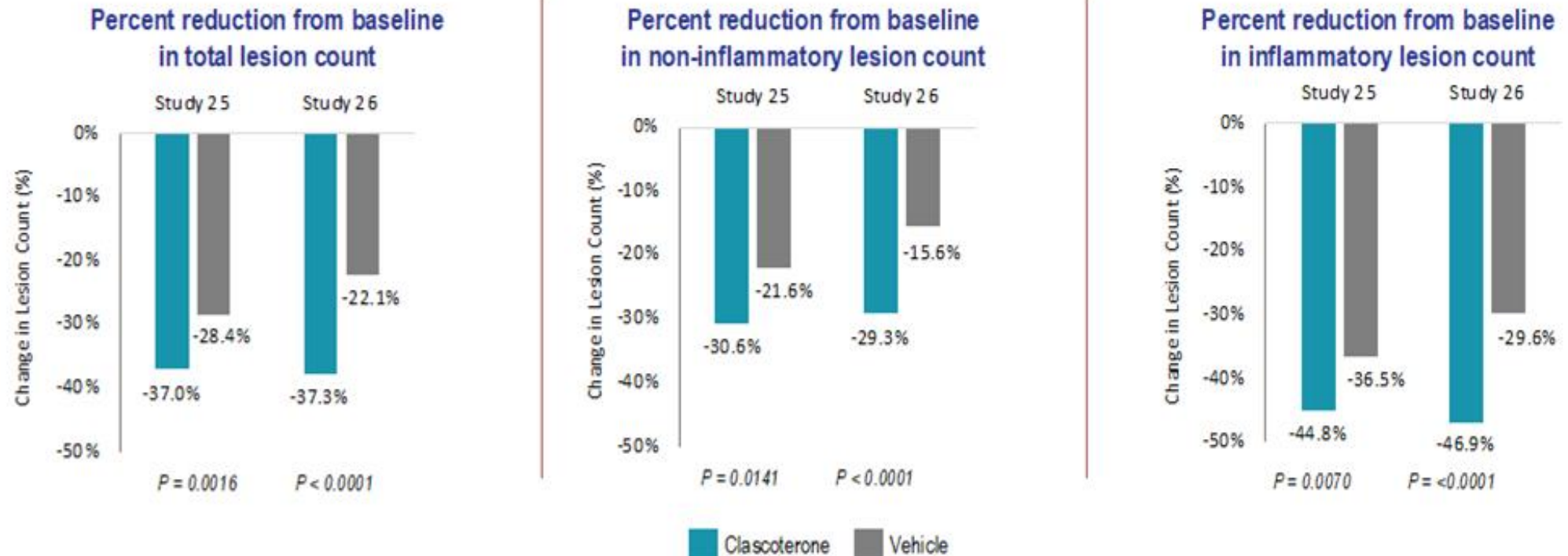
<sup>1</sup>Hebert A, Thiboutot D, Stein Gold L, Cartwright M, et al. Efficacy and Safety of Topical Clascoterone Cream, 1%, for Treatment in Patients With Facial Acne: Two Phase 3 Randomized Clinical Trials. *JAMA Dermatol.* 2020;156(6):621-630. doi: 10.1001/jamadermatol.2020.0465.



# Clascoterone 1% Cream 1% vs Vehicle Cream Twice Daily

Phase III Trials - Percent Reductions in Acne Lesions – Baseline Week 12

Safety and Efficacy (Secondary Endpoints) ITT (Week 12)



**MODERATE TO SEVERE ACNE VULGARIS / AGES  $\geq 9$  YEARS / 12-WEEK STUDY**

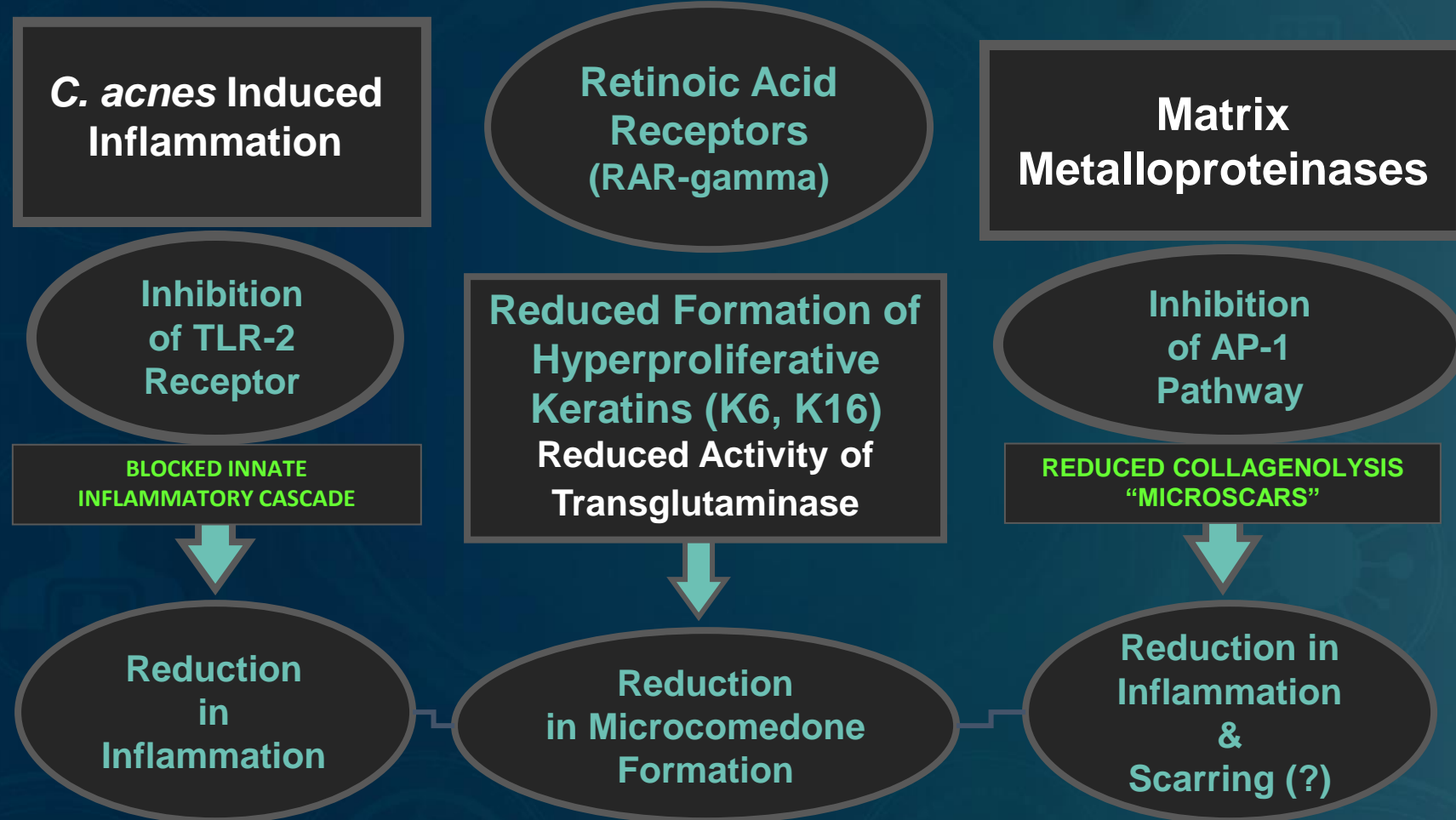
## Adverse Events

- There were no treatment-related serious adverse events among patients treated with clascoterone
- Local skin reactions, if present, were predominantly classified as mild

## Sample Size

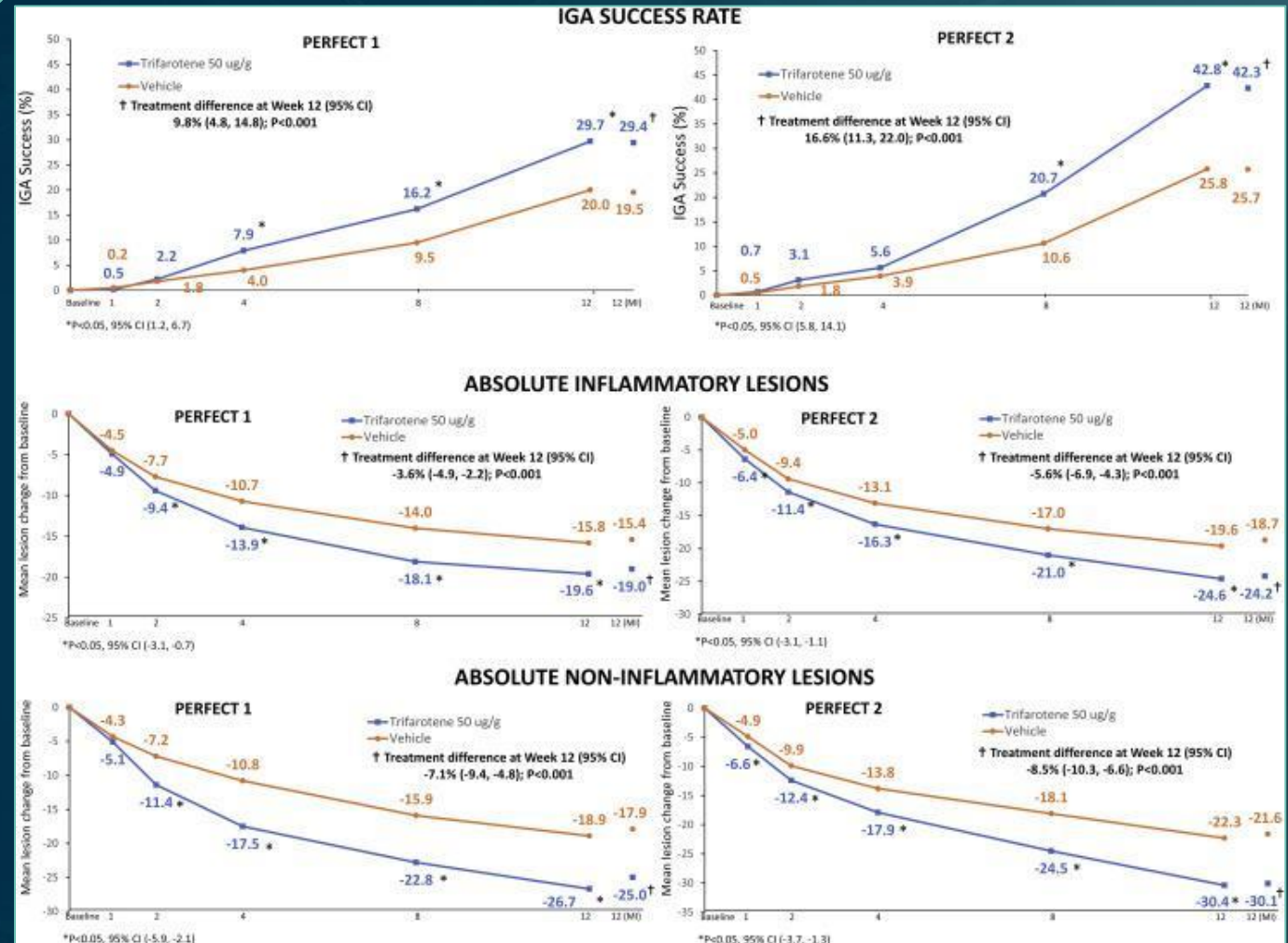
- Study 25: N = 708
- Study 26: N = 732

# Topical Retinoids Mechanism of Action and Impact on Pathophysiology



# Trifarotene, .0005%

- Trifarotene .0005% cream (RARγ-selective)
- FDA-approved in 2019 for acne vulgaris in ages 9+
- Safety and efficacy shown in both facial and truncal acne
- 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.

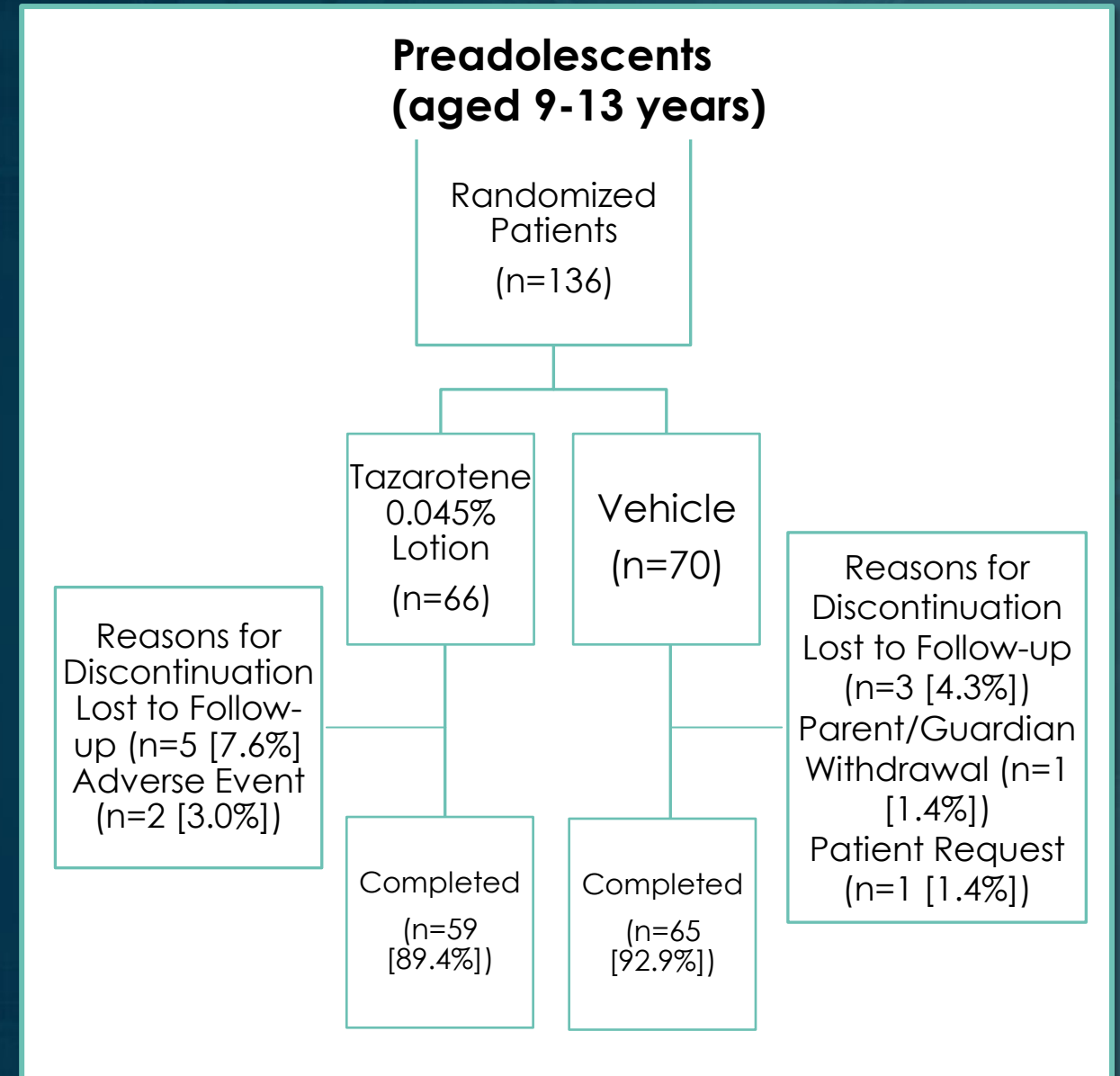
Dr. Jonette Keri

# New Retinoid Formulations



# Tazarotene, 0.045%

- Tazarotene 0.045% lotion with polymeric emulsion technology
- FDA-approved in 2019 for acne vulgaris in ages 9+
- 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.

Dr. Jonette Keri

# Tazarotene 0.045% Lotion in Acne Vulgaris

Once Daily – 12-Week Phase 2 Comparative Study

≥12 Years of Age  
with Facial Acne  
(N=210)

Moderate to Severe  
Acne at Baseline

TAZAROTENE 0.045%  
LOTION (n=69)

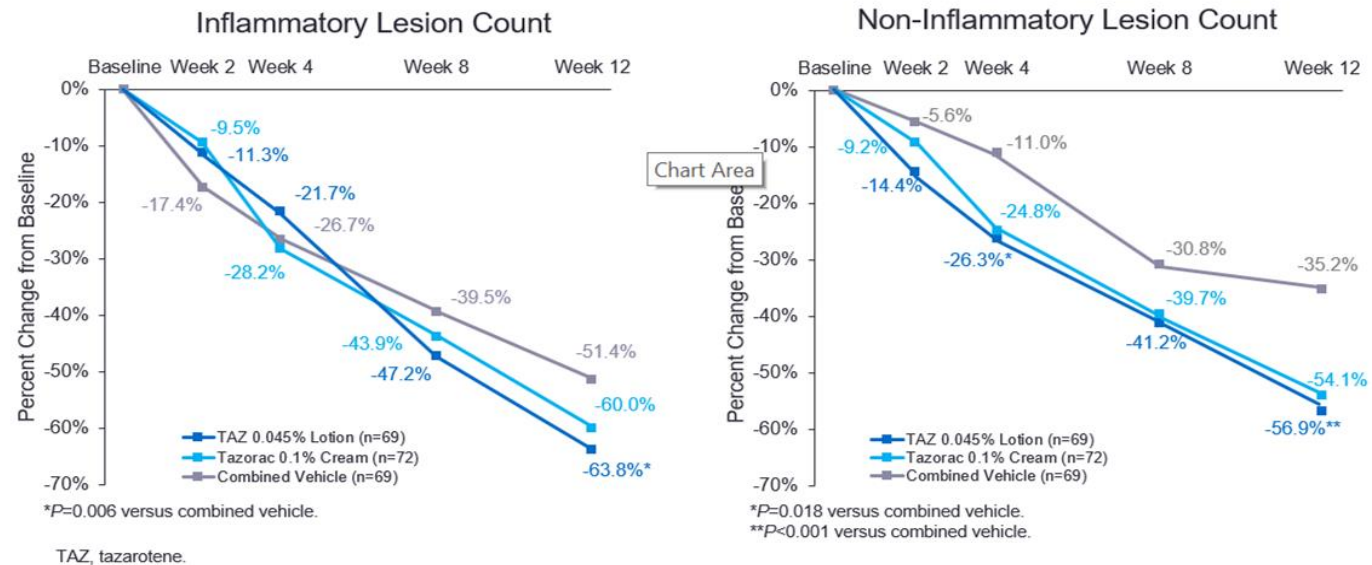
VS

TAZAROTENE 0.1%  
CREAM (n=72)

VS

VEHICLES (n=69)

## Percent Change in Inflammatory & Non-Inflammatory Lesion Count



### WEEK 12

Mean % Reduction Inflammatory Lesions

63.8% TAZ 0.045% LOTION vs 60% TAZ 0.1% CREAM

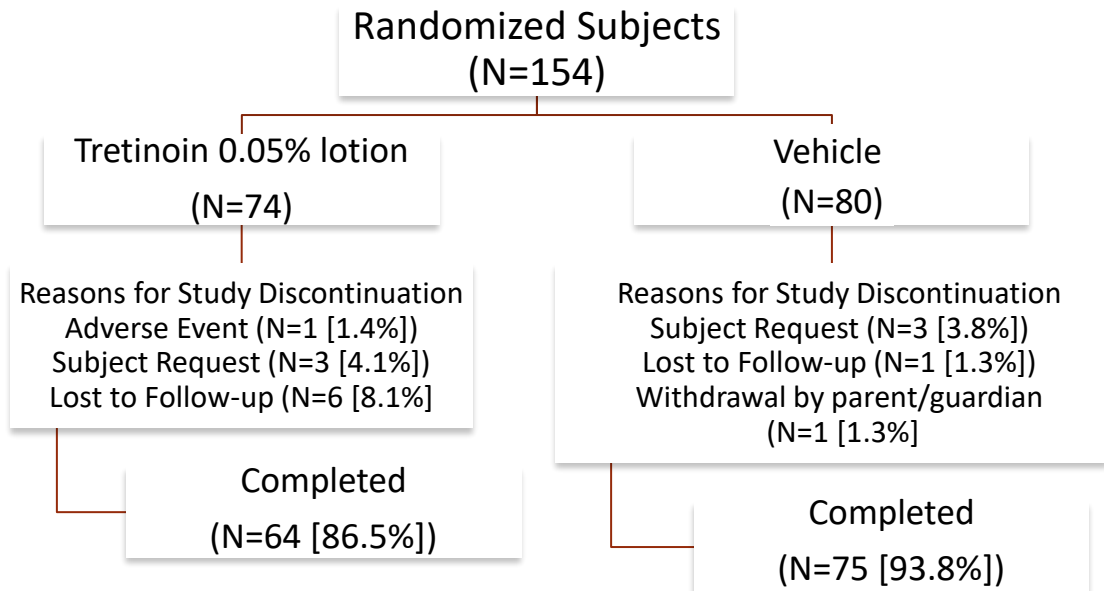
Mean % Reduction Comedonal Lesions

56.9% TAZ 0.045% LOTION 54.1% TAZ 0.1% CREAM

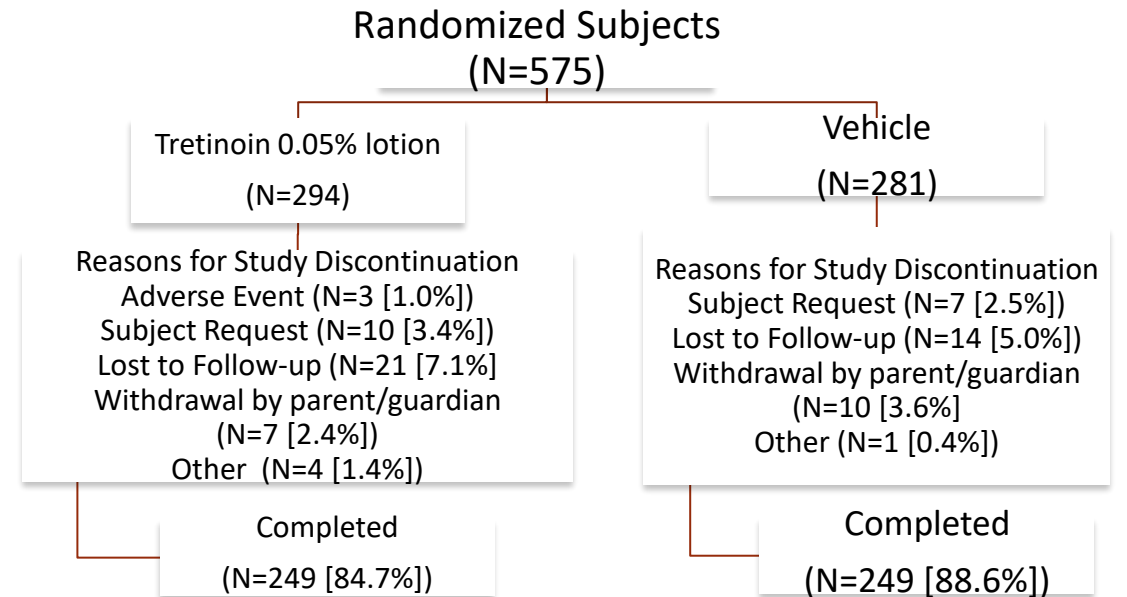
Dr. James Del Rosso

# Tretinoin, 0.05%

## Preadolescent Population (9-13 years)



## Adolescent Population (14-17 years)



- Tretinoin 0.05% lotion with polymeric emulsion technology
- FDA-approved in 2018 for acne vulgaris in ages 9+
- Low side effect profile

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.

# Why are formulations important?

Formulation	Creams	Gels	Lotions/Solutions	Foams
Contents	Oil in water emulsion	Semisolid emulsion in an alcohol base	Powder in water (some oil in water)	Water, stabilizing agents, surfactants, drug of choice, gas foaming agent
Relative potency	Moderate	Strong	Low	Moderate to High
Hydrating/drying properties	Some hydration	Drying	Drying (variable)	Drying (variable)
Generic variability	Potentially significant	Potentially significant	Potentially significant	Potentially significant
Sensitization Risk	Significant	Significant	Significant	Moderate
Irritation Risk	Very low	Relatively high	Moderate	Moderate
Body sites most useful	Virtually all sites	Oral, scalp	Scalp, intertriginous	Scalp
Body sites to avoid	Sites with maceration	Fissures, erosion, macerated sites	Fissures, erosion	Fissures, erosion
Patient preference	High rate of acceptance	Variable	Variable	Variable

Dr. Lawrence Schachner



# New Therapies in Pediatrics

- New FDA-approved oral and topical antibiotics specifically for acne vulgaris
- Sarecycline: systemic 2018 – 9 years and above
- Minocycline 4% foam: topical 2019 – 9 years and above
- Clascoterone 1% Cream: topical 2020 – 12 years and above
- Trifarotene 0.005% Cream: topical 2019 – 9 years and above

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# Considerations for the Diverse Patient

- Post-inflammatory hyperpigmentation
  - Patients with skin of color often experience more severe post-inflammatory hyperpigmentation than their Caucasian counterparts
  - Leading chief complaint in acne patients with skin of color
- Tips for communicating with patients and parents:
  - Communicate that you see the hyperpigmentation
  - Communicate *why* you are taking each step towards treating **both hyperpigmentation and acne**
  - Set expectations for their treatment journey

Dr. Candrice Heath