MASTERS OF PEDIATRIC DERMATOLOGY

The Latest in PEDIATRIC DERMATOLOGY: FROM INFANTS TO ADOLESCENTS

New Medications for Preteen Acne

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Disclosures

Vyne pharmaceuticals (Speaker Bureau)

Almirall– A(H)

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Learning Objective:

Review New Therapies for Preteen Acne

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Outline

- New Oral Agents
- New Topical Agents
- Future

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Sarecycline

- New tetracycline class oral antibiotic
- Only narrow spectrum tetracycline antibiotic
- 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

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Sarecycline

- Initial studies from age 9-45 years of age
- Lesions
  - 20-50 inflammatory
  - ≤ noninflammatory
- Nodules≤2
- IGA score of 3(moderate) or 4 (severe)

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Sarecycline

- 2 studies done and presented in one paper
- Both had similar statistically significant results
- Side effect profile was low

- 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.

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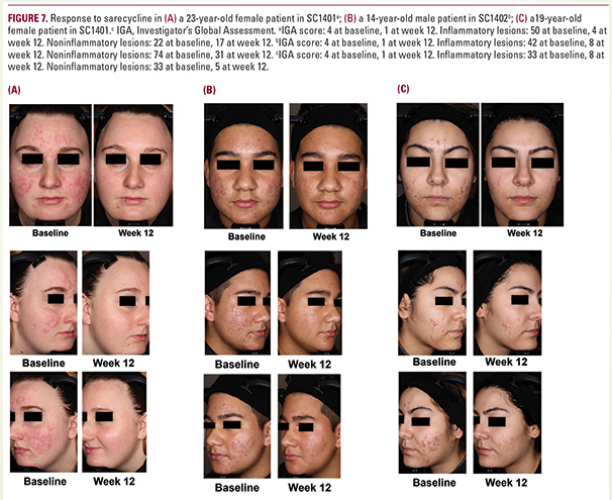
Sarecycline



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

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Sarecycline side effect profile

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[a]	3 (1.1)	0	1 (0.3)	0
Vulvovaginal mycotic infection[a]	2 (0.7)	0	3 (1.0)	0

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

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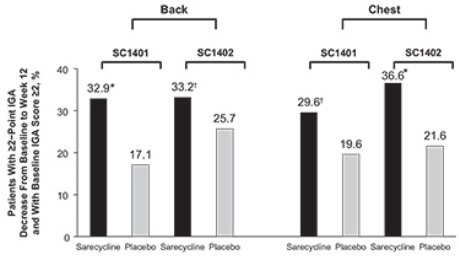
Sarecycline treating **truncal** acne

FIGURE 8. Percentage of patients with nonfacial IGA success at week 12 (ITT population). Nonfacial IGA success was defined as a ≥2-point decrease (improvement) in nonfacial IGA score from baseline and a score of clear/almost clear. In SC1401, 39.0% and 55.0% of the ITT population had baseline IGA scores ≥2 for chest and back acne, respectively. In SC1402, 47.7% and 62.1% of the ITT population had baseline IGA scores ≥2 for chest and back acne, respectively. IGA, Investigator's Global Assessment; ITT, intent-to-treat. *P<0.001 vs placebo; †P<0.05 vs placebo.



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

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New Topicals

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New retinoid – Trifarotene

- Trifarotene .0005% cream
- 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, Weglovska 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.

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New retinoid – Trifarotene

- Trifarotene .0005% cream
- The onset of effect was rapid versus vehicle:
  - significant reductions in both inflammatory and noninflammatory lesion counts seen 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, Weglovska 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.

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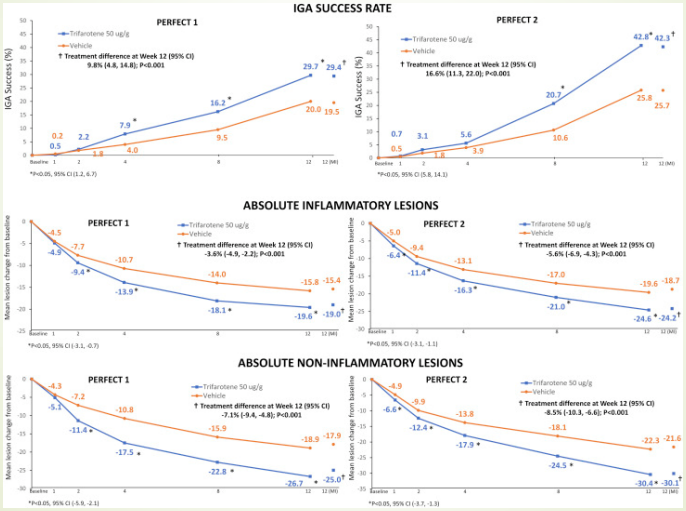
Trifarotene treatment responses



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New Retinoid formulations…. old retinoid

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

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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.

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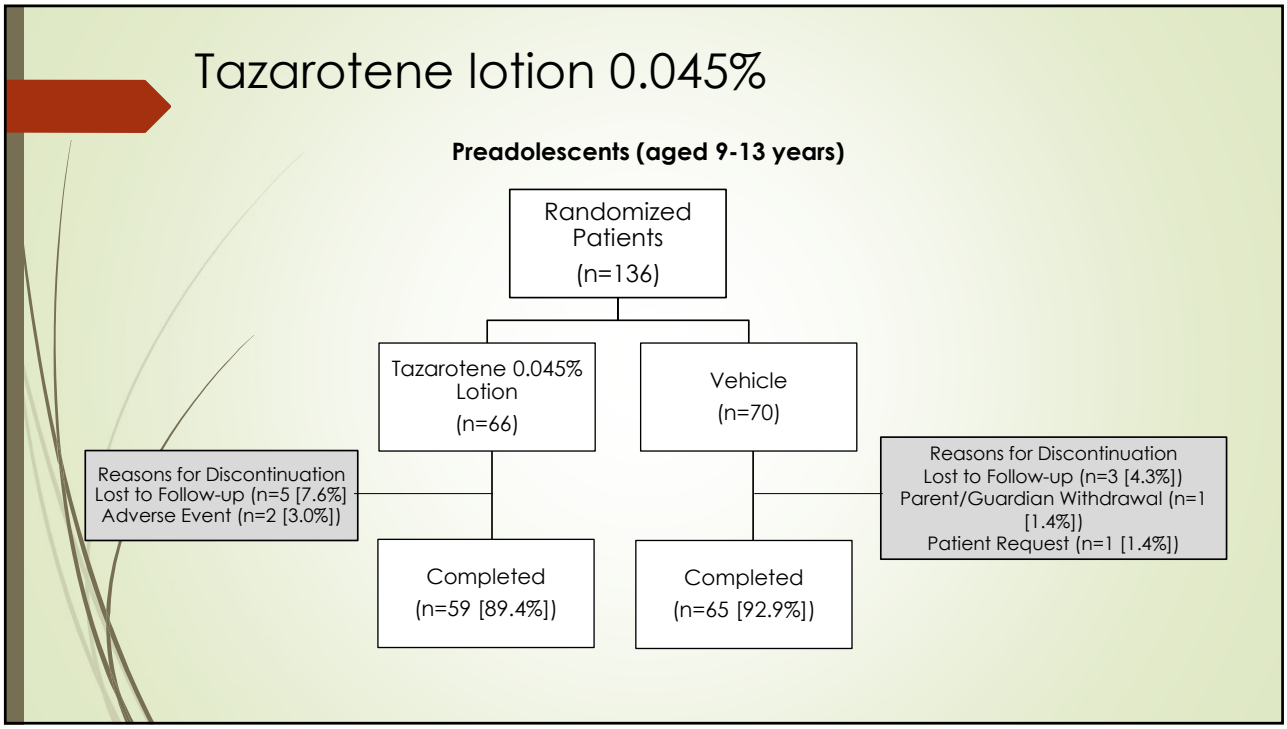
Tazarotene lotion 0.045%



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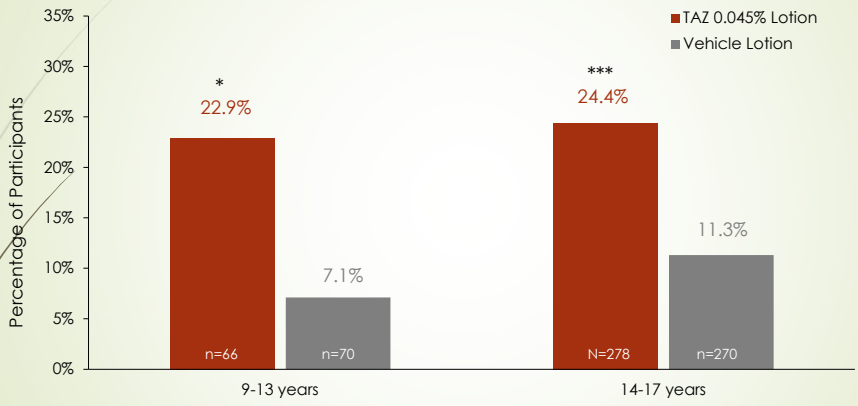
Tazarotene lotion .045%



*P<0.05 versus vehicle; ***P<0.001 versus vehicle
There was no significance difference between TAZ-treated age groups for treatment success.
Weeks 4 and 8 also assessed; no significant differences between treatment and vehicle for any age group at those weeks.
[a]At least a 2-grade improvement from baseline in EGSS and 'clear' or 'almost clear.'
EGSS, Evaluator's Global Severity Score.

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Figure 3. Percent Reduction in Inflammatory Lesion Count in Tazarotene lotion 0.045%

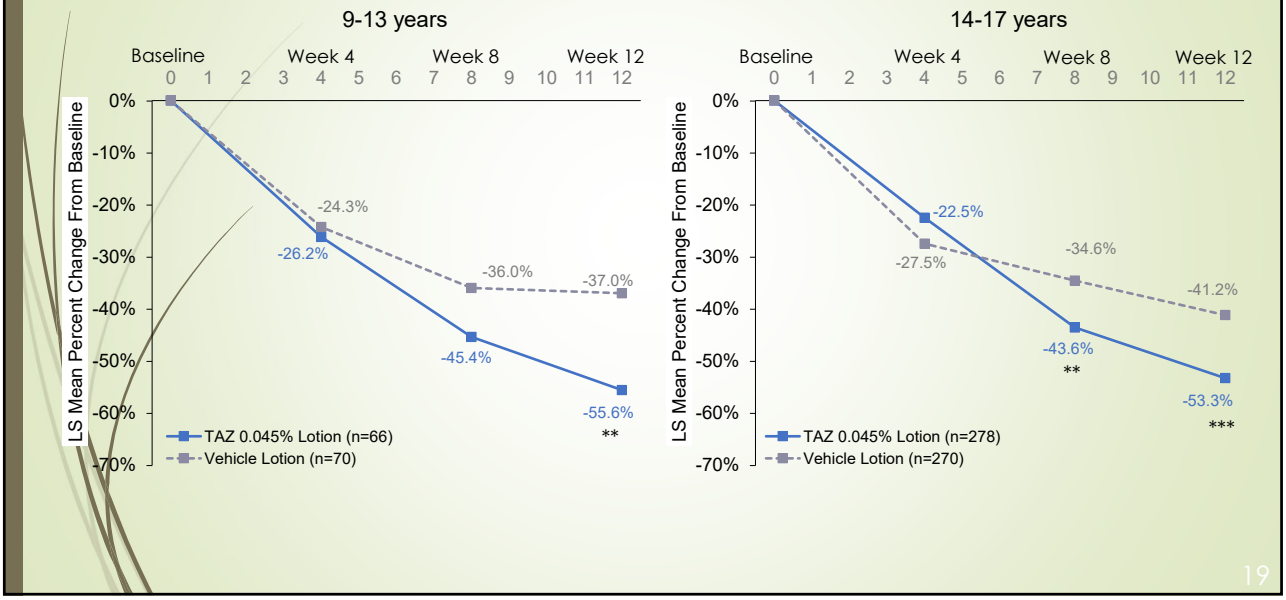

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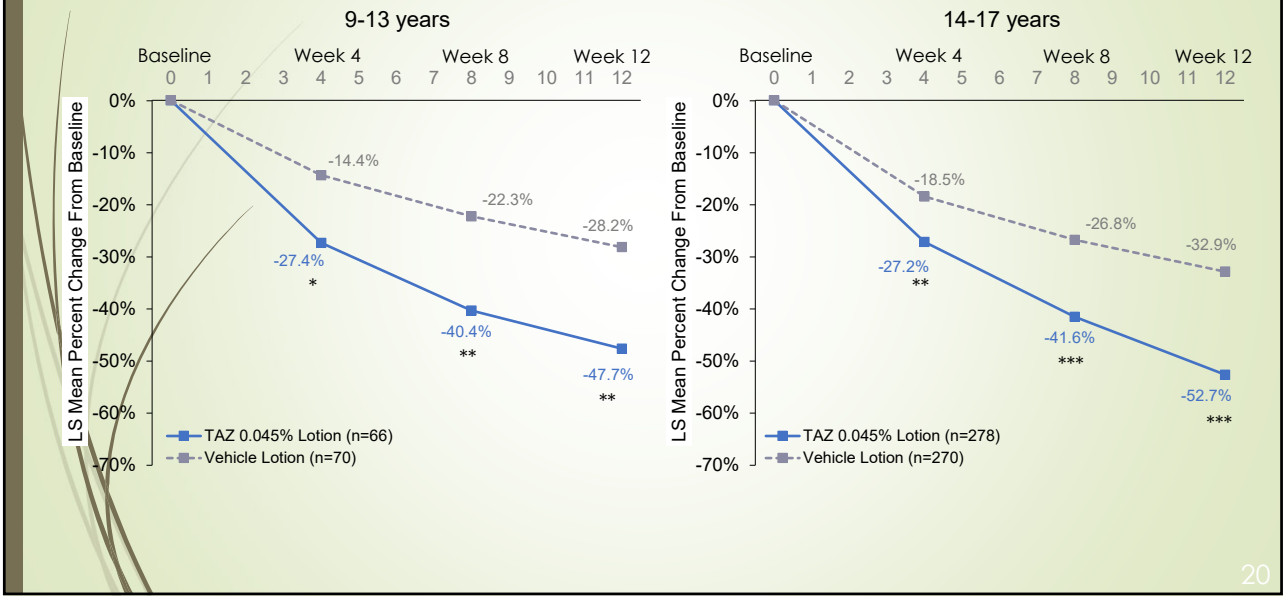
Figure 4. Percent Reduction in Noninflammatory Lesion Count in Tazarotene 0.045% lotion



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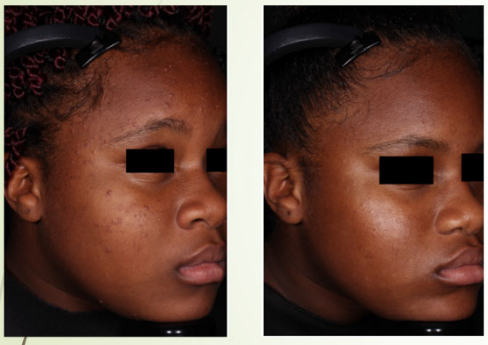
Before and After Pictures

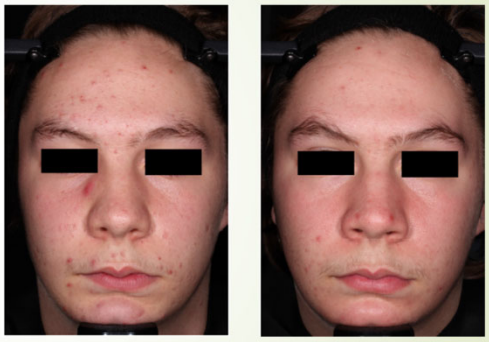
12-year-old TAZ 0.045%-treated female



Baseline
EGSS 3 (Moderate)

Week 12
EGSS 1 (Almost Clear)

14-year-old TAZ 0.045%- -treated male



Baseline
EGSS 3 (Moderate)

Week 12
EGSS 1 (Almost Clear)

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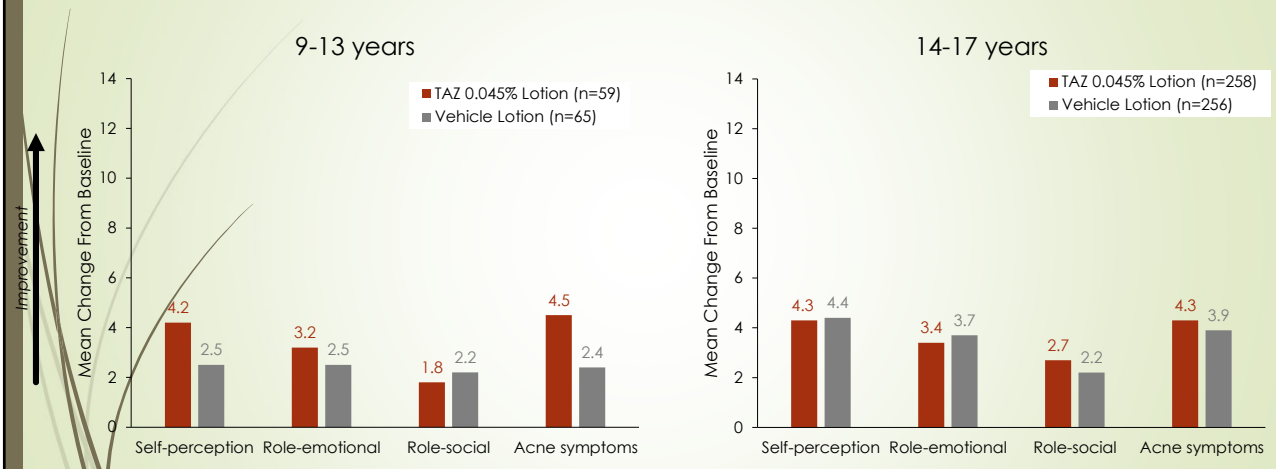
Figure 6. Change from Baseline at Week 12 in QoL Domains



Significant differences between treatment and vehicle were not assessed.
QoL, quality of life.

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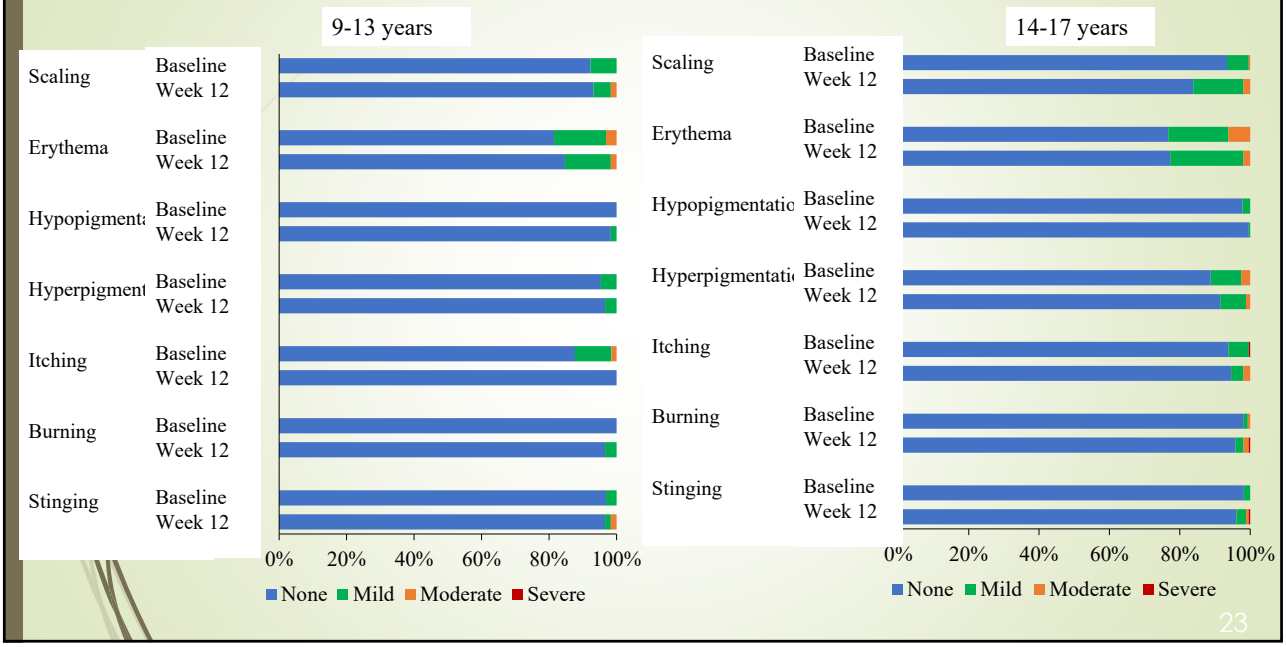
Figure 7. Cutaneous Safety and Tolerability



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Tretinoin 0.05% Lotion

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

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Figure 1: Patient Disposition Showing Percent Completion and Reasons for Discontinuation (ITT population pooled data): Comparison of Preadolescent and Adolescent Populations

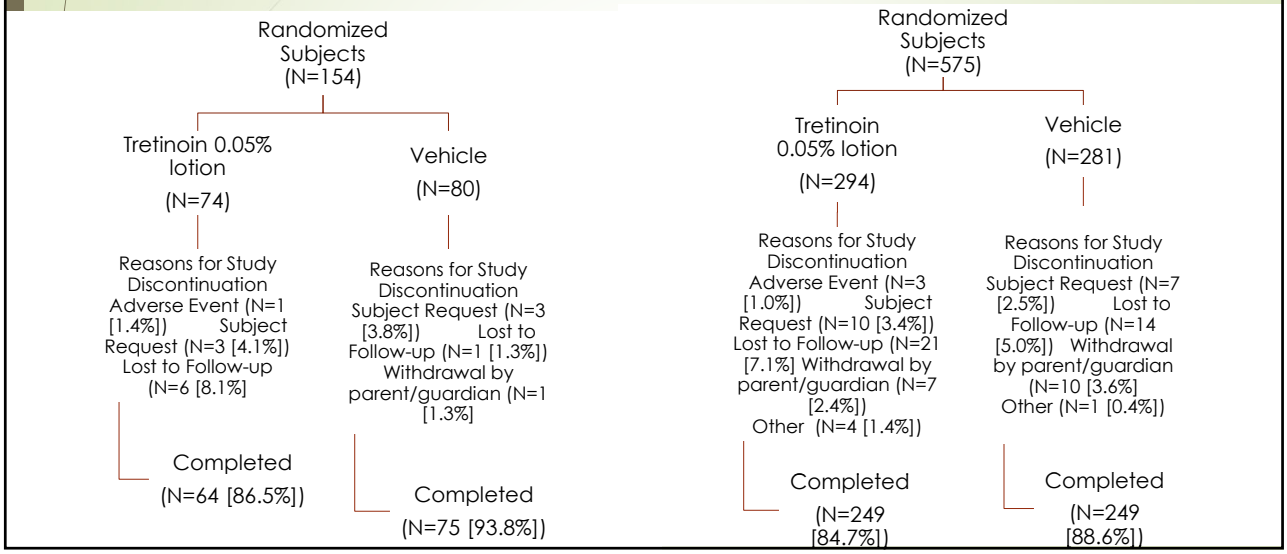

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Table 1: Demographics and Baseline Characteristics (ITT adolescent population, pooled data)

	Pooled data preadolescent population			Pooled data adolescent population		
	Tretinoin 0.05% (N=74)	Vehicle (N=80)	Total (N=154)	Tretinoin 0.05% (N=294)	Vehicle (N=281)	Total (N=154)
Age- Mean years (SD)	12.4 (0.97)	12.4 (0.92)	12.4 (0.94)	15.6 (1.08)	15.6 (1.07)	15.6 (1.08)
Range	9-13	9-13	9-13	14-17	14-17	14-17
Sex N (%)						
Male	31 (41.9%)	32 (40.0%)	63 (40.9%)	192 (65.3%)	172 (61.2%)	364 (63.3%)
Female	43 (58.1%)	48 (60.0%)	91 (59.1%)	102 (34.7%)	109 (38.8%)	211 (36.7%)
Ethnicity N (%)						
Hispanic or Latino	17 (23.0%)	24 (30.0%)	41 (26.6%)	114 (38.8%)	118 (42.0%)	232 (40.3%)
Not Hispanic or Latino	57 (77.0%)	56 (70.0%)	113 (73.4%)	180 (61.2%)	163 (58.0%)	343 (59.7%)
Race N (%)						
American Indian or Alaska Native	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.2%)
Asian	3 (4.1%)	2 (2.5%)	5 (3.2%)	15 (5.1%)	8 (2.8%)	23 (4.0%)
Black or African American	14 (18.9%)	15 (18.8%)	29 (18.8%)	39 (13.3%)	35 (12.5%)	74 (12.9%)
Native Hawaiian or Other Pacific Islander	0 (0.0%)	2 (2.5%)	2 (1.3%)	1 (0.3%)	1 (0.4%)	2 (0.3%)
Caucasian	55 (74.3%)	60 (75.0%)	115 (74.7%)	229 (77.9%)	229 (81.5%)	458 (79.7%)
Other	2 (2.7%)	1 (1.3%)	3 (1.9%)	9 (3.1%)	8 (2.8%)	17 (3.0%)
Evaluator's Global Severity Score N (%)						
3 – Moderate	72 (97.3%)	73 (91.3%)	145 (94.2%)	263 (89.5%)	247 (87.9%)	510 (88.7%)
4 - Severe	2 (2.7%)	7 (8.8%)	9 (5.8%)	31 (10.5%)	34 (12.1%)	65 (11.3%)
Inflammatory Lesion Count- Mean (SD)	26.2 (5.50)	27.2 (6.49)	26.7 (6.04)	27.0 (5.76)	26.9 (5.91)	27.0 (5.83)
Noninflammatory Lesion Count- Mean (SD)	48.3 (22.01)	52.1 (21.78)	50.3 (21.90)	45.8 (20.00)	47.2 (20.36)	46.5 (20.17)

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Figure 2: Percent Change in Inflammatory Lesions from Baseline to Week 12 (ITT population, pooled data, LS Mean)

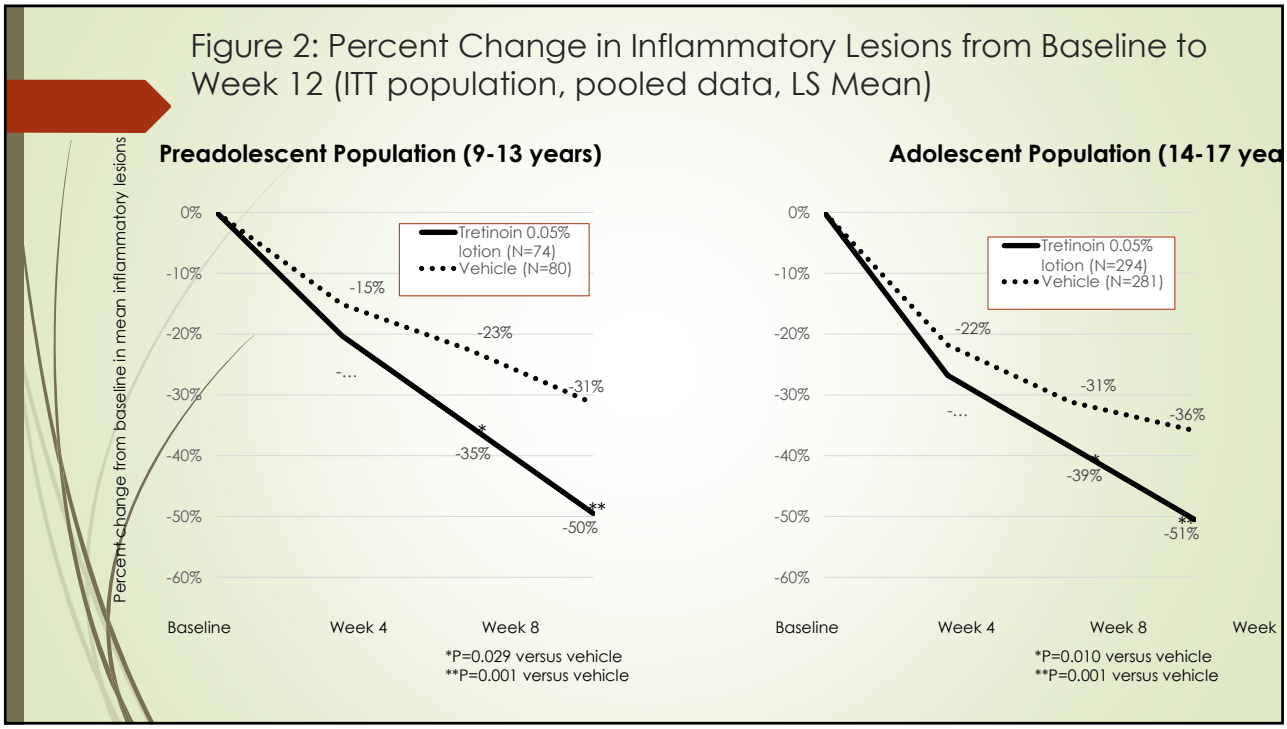

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Figure 3: Percent Change in Noninflammatory Lesions from Baseline to Week 12 (ITT population pooled data, LS Mean)

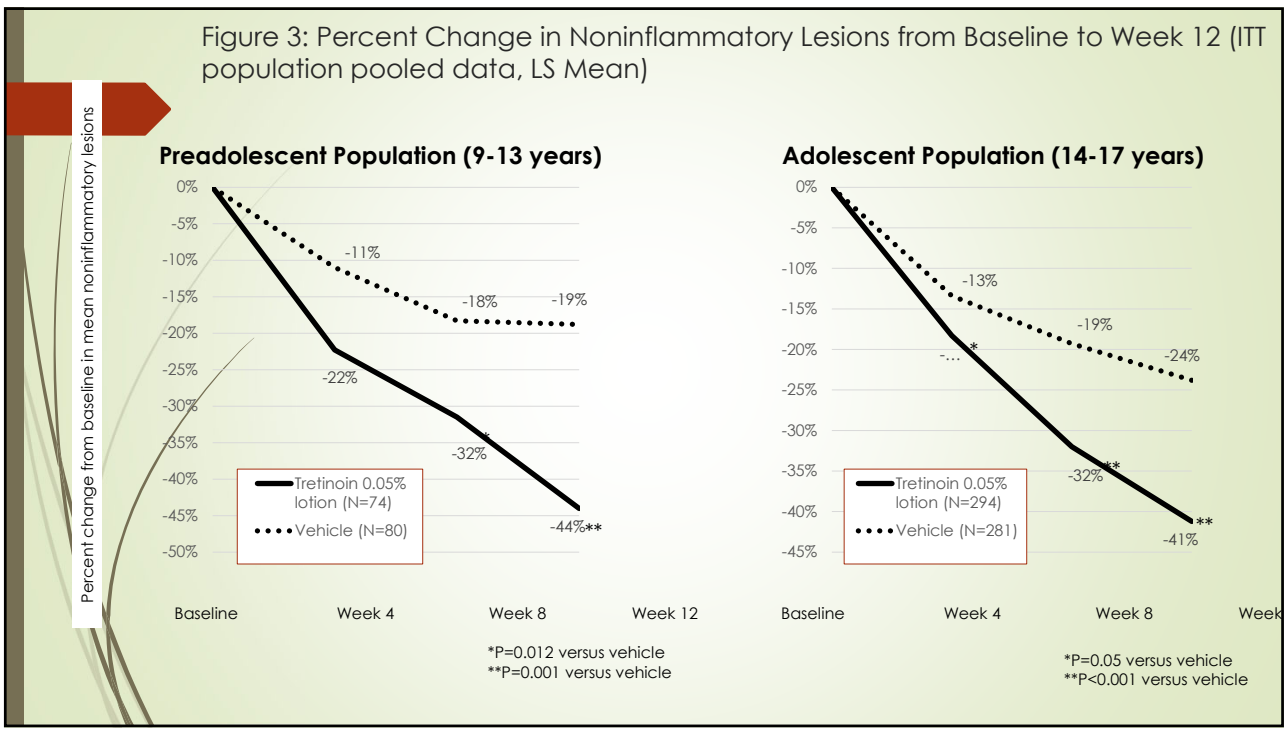

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Figure 4: Treatment Success. Subjects with at least a 2-grade improvement and 'clear' or 'almost clear at each study visit (ITT population pooled data)

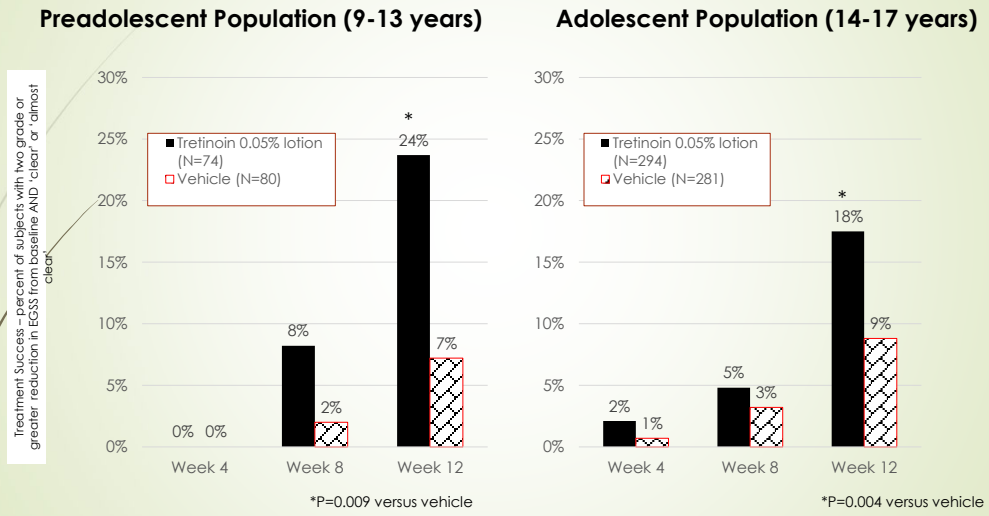

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Table 2: Treatment-Emergent and Related Adverse Event (AE) Characteristics through Week 12 (Safety population, pooled data)

	Preadolescent Population		Adolescent Population	
	Tretinoin 0.05% Lotion (N=72)	Vehicle Lotion (N=78)	Tretinoin 0.05% Lotion (N=281)	Vehicle Lotion (N=274)
Subjects reporting any TEAE	22 (30.6%)	18 (23.1%)	69 (24.6%)	46 (16.8%)
Subjects reporting any SAE	0 (0.0%)	0 (0.0%)	2 (0.7%)	0 (0.0%)
Subjects who died	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Subjects who discontinued due to TEAE	1 (1.4%)	0 (0.0%)	4 (1.4%)	0 (0.0%)
Severity of AEs reported				
Mild	11 (15.3%)	11 (14.1%)	35 (12.5%)	25 (9.1%)
Moderate	11 (15.3%)	4 (5.1%)	30 (10.7%)	21 (7.7%)
Severe	0 (0.0%)	3 (3.8%)	4 (1.4%)	0 (0.0%)
Relationship to study drug				
Related	7 (9.7%)	1 (1.3%)	22 (7.8%)	2 (0.7%)
Unrelated	15 (20.8%)	17 (21.8%)	47 (16.7%)	44 (16.1%)
Treatment Related AEs reported by ≥1% subjects				
Application site pain	4 (5.6%)	0 (0.0%)	9 (3.2%)	1 (0.4%)
Application site dryness	2 (2.8%)	0 (0.0%)	10 (3.6%)	0 (0.0%)
Application site erythema	0 (0.0%)	0 (0.0%)	5 (1.8%)	1 (1.3%)
Application site exfoliation	1(1.4%)	1 (1.3%)	1 (0.4%)	0 (0.0%)
Application site pruritus	1 (1.4%)	0 (0.0%)	1 (0.4%)	0 (0.0%)
Application site irritation	1 (1.4%)	0 (0.0%)	2 (0.7%)	1 (0.4%)

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Figure 5a: Cutaneous Safety and Tolerability Assessment from Baseline to Week 12 (Safety preadolescent population, pooled data)

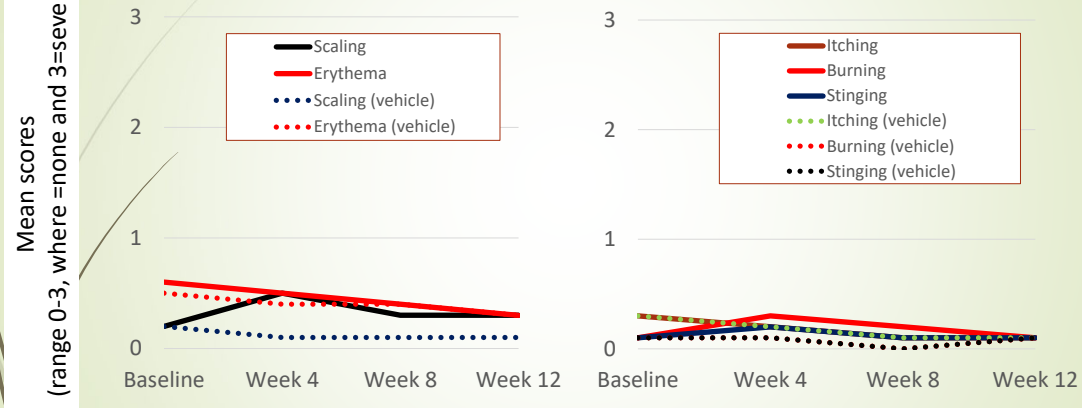

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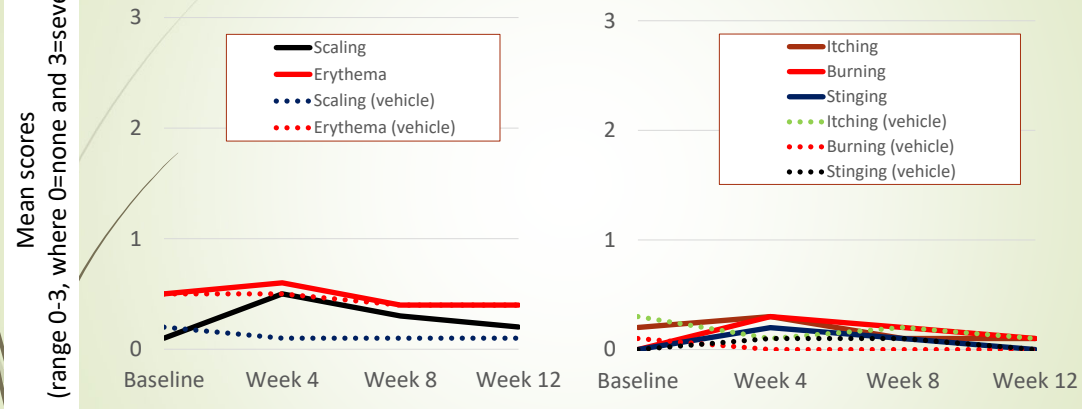
Figure 5b: Cutaneous Safety and Tolerability Assessment from Baseline to Week 12 (Safety adolescent population, pooled data)



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Tretinoin 0.05% Lotion

- Hispanics
- Asian

- Showed it worked well in specific populations

- Cook-Bolden FE, Weinkle SH, Guenin E, Bhatt V. Novel Tretinoin 0.05% Lotion for Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris in a **Hispanic** Population. J Drugs Dermatol. 2019 Jan 1;18(1):32-38

- Han G, Armstrong AW, Desai SR, Guenin E. Novel Tretinoin 0.05% Lotion for the Once-Daily Treatment of Moderate-to-Severe Acne Vulgaris in an **Asian** Population. J Drugs Dermatol. 2019 Sep 1;18(9):910-916

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Minocycline foam 4%

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

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

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New topical antiandrogen - clascoterone

- To what age?
  - 12 years and above
- Suppression of HPA axis?
  - By lab analysis there is suggestion this could happen
  - But clinically tolerated well
  - Should avoid using over large areas

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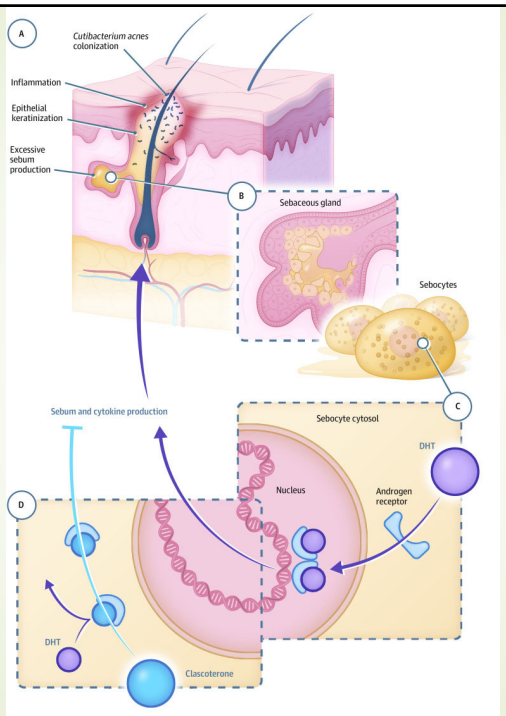

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Clascoterone Efficacy in 2 Phase 3 trials

- Both trials met the primary efficacy end points.
- Considerably more patients receiving clascoterone cream, 1%, vs vehicle achieved treatment success at week 12
- Clascoterone 18.4% (patients improved) vs Placebo 9.0%
- Clascoterone 20.3% vs Placebo 6.5%
- The absolute change from baseline in NILC and ILC at week 12 were also substantially greater with use of clascoterone cream, 1% vs vehicle.
- 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. 2020 Jun 1;156(6):621-630.

37

Clascoterone cream

- No systemic adverse effects were observed, which is consistent with the results of in vivo studies showing clascoterone has only local, not systemic, antiandrogenic activity.
- Side effect profile similar to placebo
- 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. 2020 Jun 1;156(6):621-630.

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New combination products in the pipeline

- Encapsulated benzoyl peroxide 3% / encapsulated tretinoin0.1%
- Encapsulated benzoyl peroxide 5%

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Remember the oldies but goodies, especially washes as these are easy to use.

- Benzoyl Peroxide
- Glycolic Acid
- Salicylic Acid

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