South Beach Symposium
clinical + aesthetic dermatology
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Leon H. Kircik M.D.

Clinical Professor of Dermatology

Indiana University School of Medicine

Mount Sinai Medical Center, New York, NY

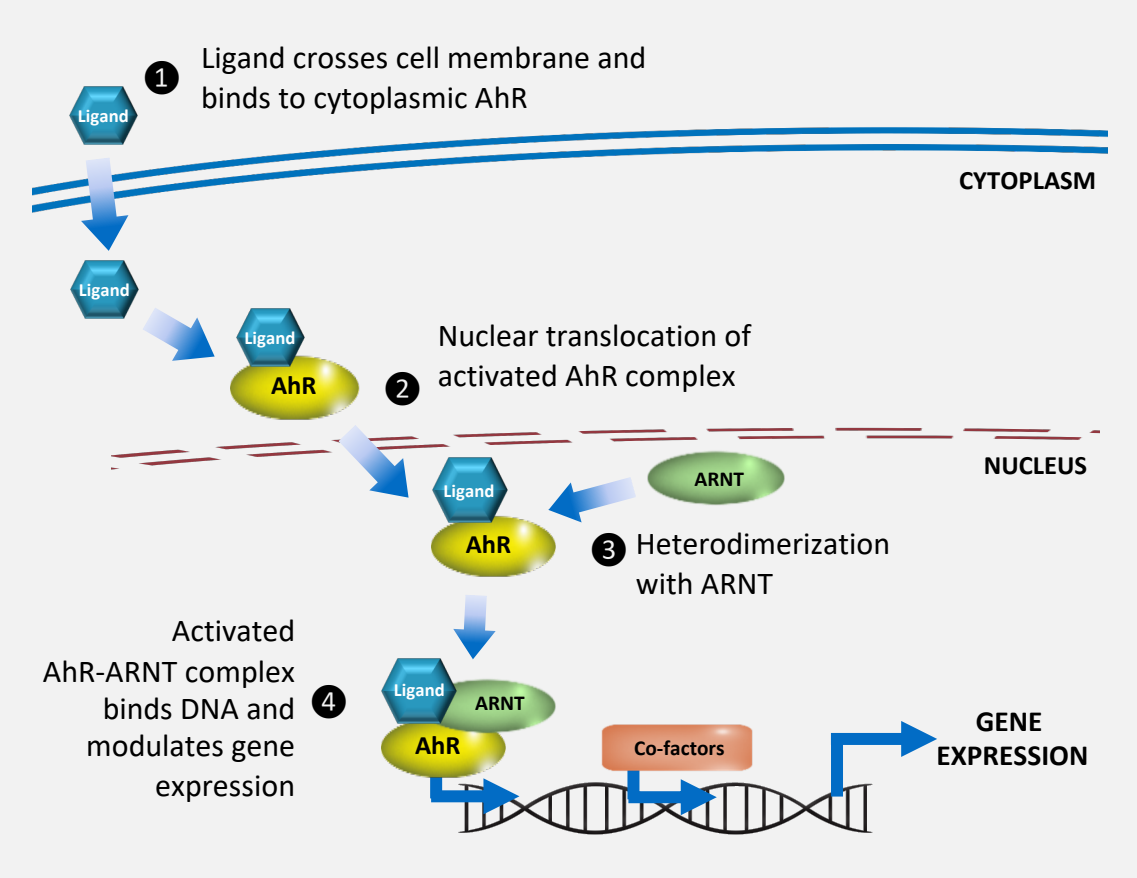
Physicians Skin Care, PLLC

Louisville, KY

Tapinarof: Therapeutic AhR Modulating Agent (TAMA)

- Tapinarof is a topical, small molecule TAMA that directly binds to and activates AhR transcription factor[1]
- AhR activation via tapinarof *in vitro* and animal models leads to:
  - Reduction of Th17 cytokine expression[1]
  - Reduction of Th2 cytokine expression[1,2]
  - Decreased oxidative stress[1]
  - Increased skin barrier proteins[1]

AhR pathway[3]



AhR, aryl hydrocarbon receptor; ARNT, aryl hydrocarbon receptor nuclear translocator; TAMA, therapeutic aryl hydrocarbon receptor modulating agent; Th, T helper cell.

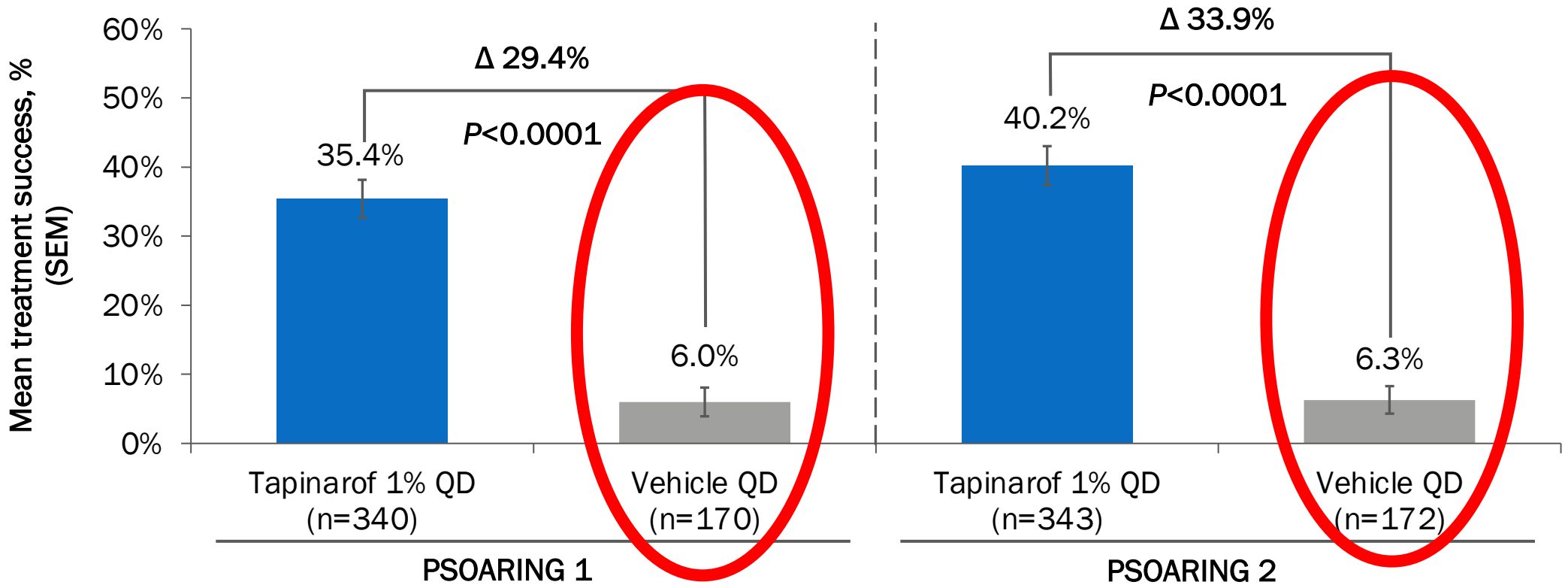
1. Smith SH et al. *J Inv Dermatol* 2017;137:2110–2119; 2. Negishi T et al. *J Immunol.*2005;175;7348–7356; 3. Furue M et al. *J Dermatological Sci*. 2015;80:83–88.

Tapinarof Cream 1% QD for the Treatment of Plaque Psoriasis: Efficacy and Safety in Two Pivotal Phase 3 Trials

Mark Lebwohl,[1] Linda Stein Gold,[2] Bruce Strober,[3] Kim Papp,[4] April Armstrong,[5] Jerry Bagel,[6] Leon Kircik,[1,7] Benjamin Ehst,[8] H Chih-ho Hong,[9] Jennifer Soung,[10] Jeff Fromowitz,[11] Scott Guenthner,[12] Stephen C Piscitelli,[13] David S Rubenstein,[13] Philip M Brown,[13] Anna M Tallman,[13] Robert Bissonnette[14]

[1]Icahn School of Medicine, Mount Sinai, New York, NY, USA; [2]Henry Ford Health System, Detroit, MI, USA; [3]Yale University, New Haven and Central Connecticut Dermatology Research, Cromwell, CT, USA; [4]Probity Medical Research, Waterloo, ON, Canada; [5]Keck School of Medicine University of Southern California, Los Angeles, CA, USA; [6]Psoriasis Treatment Center of Central New Jersey, NJ, USA; [7]Skin Sciences, PLLC, Louisville, KY, USA; [8]Oregon Medical Research Center, Portland, OR, USA; [9]University of British Columbia and Probity Medical Research, Surrey, BC, Canada; [10]Southern California Dermatology, Santa Ana, CA, USA; [11]Dermatology of Boca, Boca Raton, FL, USA; [12]The Indiana Clinical Trials Center, PC, Plainfield, IN, USA; [13]Dermavant Sciences, Inc., Durham, NC, USA; [14]Innovaderm Research Inc., Montreal, QC, Canada

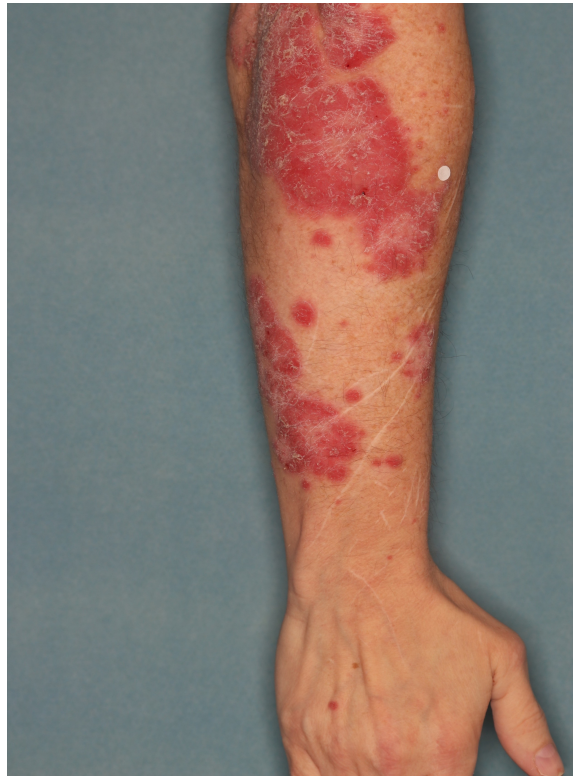
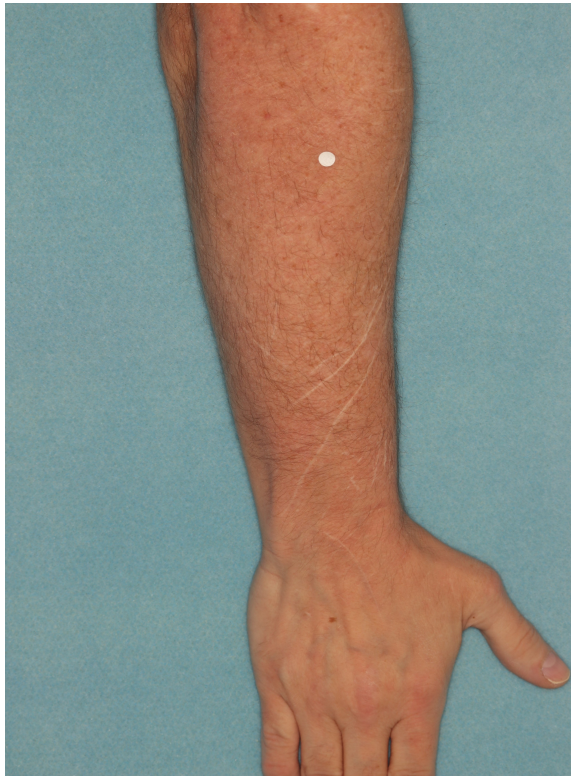
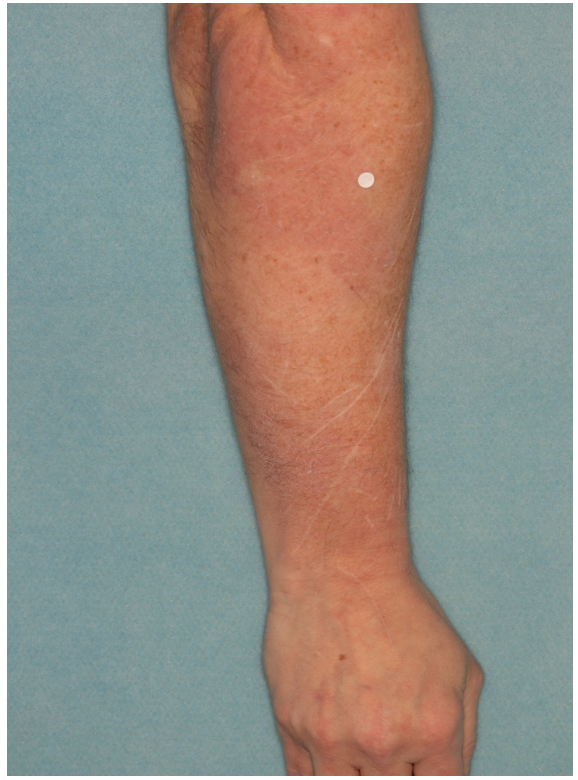
Tapinarof 1% QD: Primary Endpoint of PGA Response at Week 12 was Achieved in Both Studies



PGA response rate* was highly statistically significant in the tapinarof cream 1% QD group versus vehicle in both PSOARING 1 and 2: 35.4% vs 6.0% (*P*<0.0001) and 40.2% vs 6.3% (*P*<0.0001), respectively

*PGA of 0 or 1 and ≥2-grade improvement at Week 12.
ITT population. *P* value based upon Cochran-Mantel-Haenszel analysis stratified by baseline PGA score.
ITT, intent-to-treat; PGA, Physician Global Assessment; QD, once daily; SEM, standard error of mean

Tapinarof 1% QD Clinical Response of Patient with Plaque Psoriasis who Achieved Primary and Secondary Efficacy Endpoints at Week 12

Baseline	Week 4	Week 12
		
• PGA = 3 • PASI = 17.6	• PGA = 2 • PASI = 4	• PGA = 0 • PASI = 0

PGA and PASI are global efficacy assessments. Example of one representative target lesion of a patient treated with tapinarof 1% QD; individual results may vary. Photographs demonstrate improvement in PGA and PASI at Week 4 and 12.
PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily.

Tapinarof 1% QD AE Profile Consistent with Previous Studies[1,2]

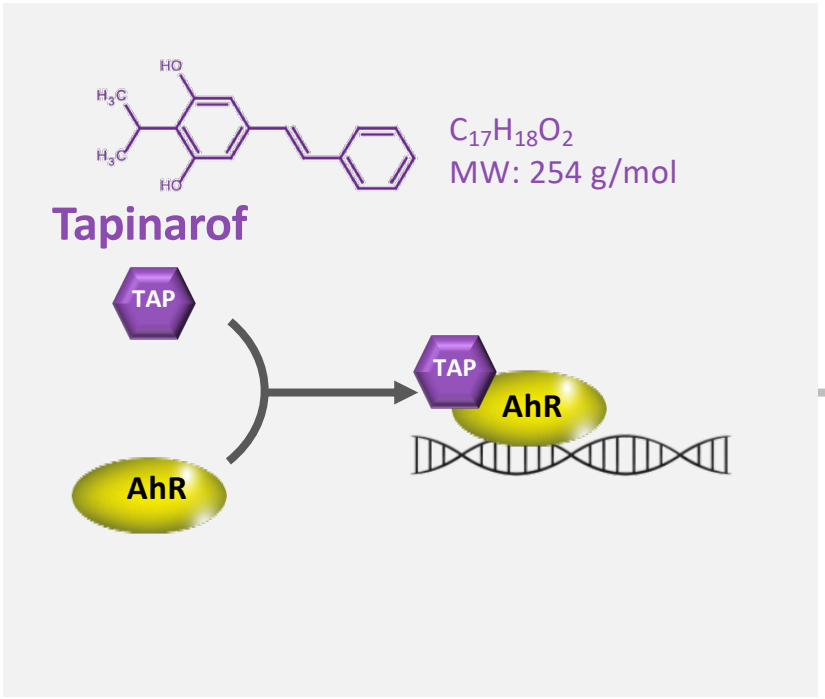
Patients, n (%)	PSOARING 1		PSOARING 2	
	Tapinarof 1% QD (n=340)	Vehicle QD (n=170)	Tapinarof 1% QD (n=343)	Vehicle QD (n=172)
Most common treatment-related TEAEs (≥1% in any group)				
Folliculitis	70 (20.6)	2 (1.2)	54 (15.7)	1 (0.6)
Contact dermatitis	13 (3.8)	2 (1.2)	16 (4.7)	0 (0.0)
Headache	5 (1.5)	1 (0.6)	1 (0.3)	0 (0.0)
Pruritus	4 (1.2)	0 (0.0)	2 (0.6)	0 (0.0)
Dermatitis	1 (0.3)	0 (0.0)	4 (1.2)	0 (0.0)
Study discontinuation due to AESI				
Folliculitis	6 (1.8)	0 (0.0)	3 (0.9)	0 (0.0)
Contact dermatitis	5 (1.5)	0 (0.0)	7 (2.0)	0 (0.0)
Headache	1 (0.3)	0 (0.0)	2 (0.6)	0 (0.0)
Severity of folliculitis, n (%) among subset of patients with AESI of folliculitis				
Mild	51 (63.8)	1 (50.0)	44 (72.1)	0 (0.0)
Moderate	28 (35.0)	1 (50.0)	17 (27.9)	1 (100.0)
Severe	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)

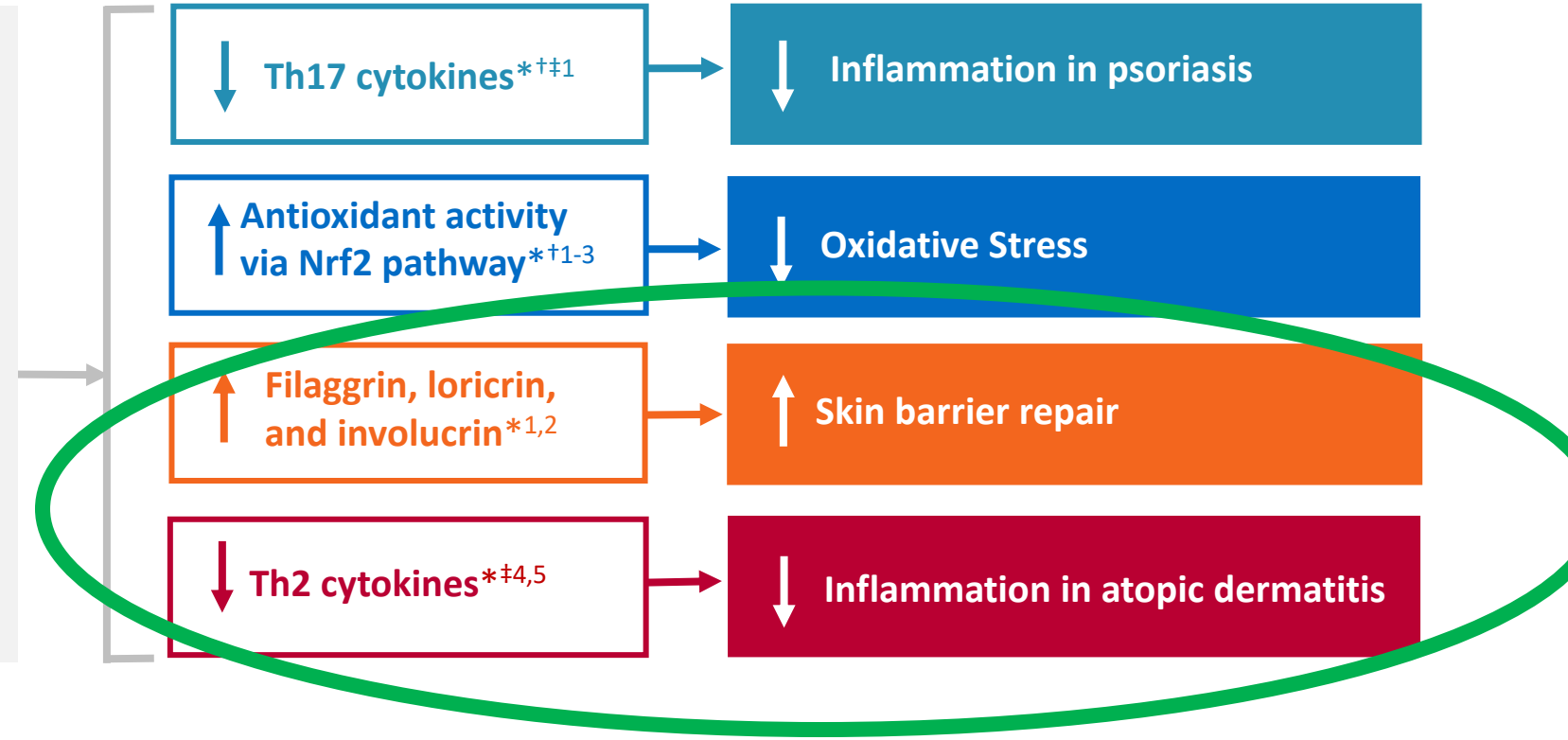
- The most common (≥1% in any group) treatment-related TEAEs were folliculitis, contact dermatitis, headache, pruritus, and dermatitis
- Folliculitis was mostly mild or moderate in severity in both studies and study discontinuation due to folliculitis was low: 1.8% (6/340) vs 0.0% (0/170) and 0.9% (3/343) vs 0.0% (0/172) in PSOARING 1 and 2, respectively

A patient is counted once only for each MedDRA preferred term. Safety population. TEAE defined as an AE that starts on or after the date of first dose of study drug.
AE, adverse event; AESI, adverse event of special interest; MedDRA, Medical Dictionary for Regulatory Activities; QD, once daily; TEAE, treatment-emergent adverse event.
1. Robbins K, et al. *J Am Acad Dermatol.* 2019;80:714–721; 2. Stein Gold L, et al. *J Am Acad Dermatol*. 2020; doi: 10.1016/j.jaad.2020.04.181.

Biologic Effects of Tapinarof

- Tapinarof is a small molecule therapeutic AhR modulating agent (TAMA) that uniquely activates the AhR pathway to decrease pro-inflammatory cytokines, decrease oxidative stress, increase skin barrier proteins and re-establish skin homeostasis[1]





*Demonstrated *in vitro*. †Demonstrated *ex vivo*. ‡Demonstrated in mice models. AhR, aryl hydrocarbon receptor; Nrf2, nuclear factor erythroid 2-related factor 2; TAMA, therapeutic AhR modulating agent; Th, T helper cell. **1**. Smith SH et al. *J Inv Dermatol* 2017;137:2110–2119. **2**. Furue M et al. *J Dermatological Sci*. 2015;80:83–88. **3**. Tsuji G et al. *J Invest Dermatol.* 2012;132:59–68. **4**. Dermavant DOF [DMVT-505 Th2 Polarization; Apr 2015]. **5**. Dermavant DOF [DMVT-505 AD Mouse Model; Oct 2016].

Roflumilast cream (ARQ-151) is a potent, selective PDE-4 inhibitor

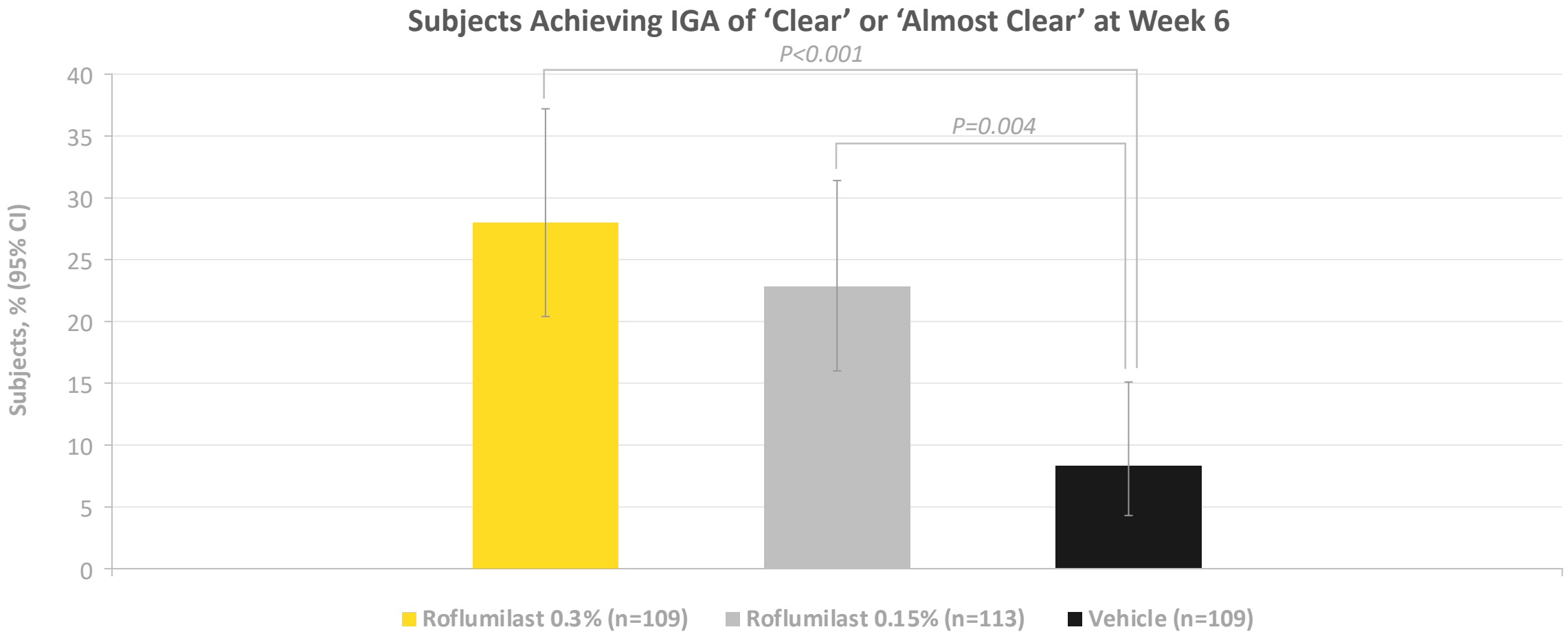
Demonstrates ~25- to >300-fold higher potency than currently available PDE-4 inhibitors[3]

ARQ-151, Roflumilast Cream, Improved Chronic Plaque Psoriasis in Phase 2b Study

Mark G. Lebwohl[1], Kim A. Papp[2], Linda Stein Gold[3], Melinda J. Gooderham[4], Leon H. Kircik[5], Zoe D. Draelos[6], Steven E. Kempers[7], Mathew Zirwas[8], Kathleen Smith[9], David W. Osborne[9], Marie-Louise Trotman[10], Lynn Navale[9], Charlotte Merritt[9], David R. Berk[9], Howard Welgus[9]

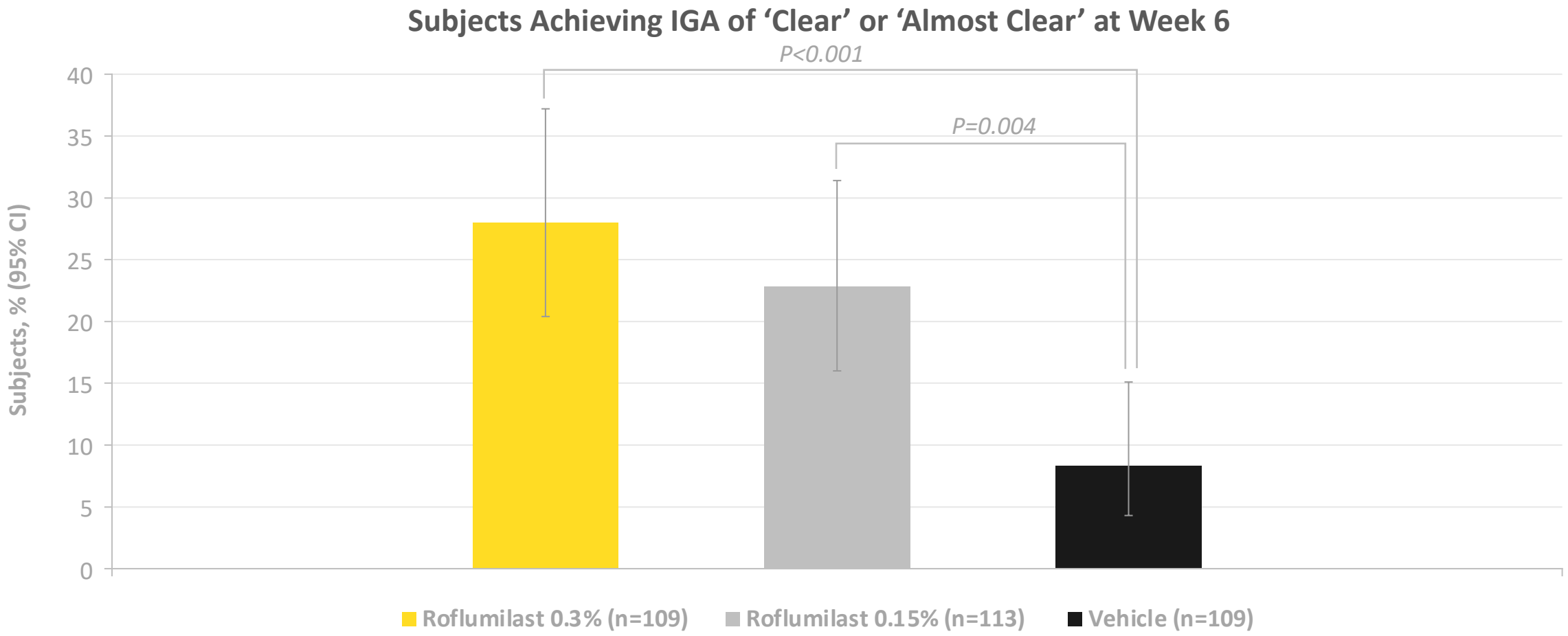
[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Probity Medical Research and K Papp Clinical Research, Waterloo, ON, Canada; [3]Henry Ford Medical Center, Detroit, MI, USA; [4]SkiN Centre for Dermatology, Probity Medical Research and Queen's University, Peterborough, ON, Canada; [5]Icahn School of Medicine, Mount Sinai, New York, NY, and Skin Sciences, Louisville, KY, USA; [6]Dermatology Consulting Services, High Point, NC, USA; [7]Minnesota Clinical Study Center, Fridley, MN, USA; [8]Probity Medical Research and Dermatologists of the Central States, Bexley, OH, USA; [9]Arcutis, Inc., Westlake Village, CA, USA; [10]ML Trotman Consulting, LLC, Newbury Park, CA, USA.

Primary Endpoint of IGA ‘Clear’ or ‘Almost Clear’ at Week 6 Was Met for Both Roflumilast Cream Doses



Data are presented for intent-to-treat population. CI: confidence interval; IGA: Investigator Global Assessment.

Primary Endpoint of IGA ‘Clear’ or ‘Almost Clear’ at Week 6 Was Met for Both Roflumilast Cream Doses



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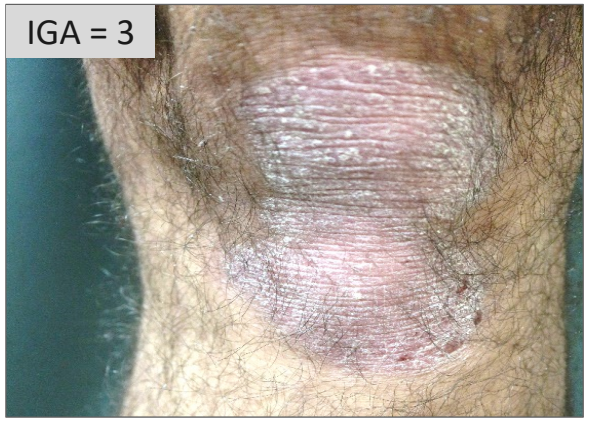
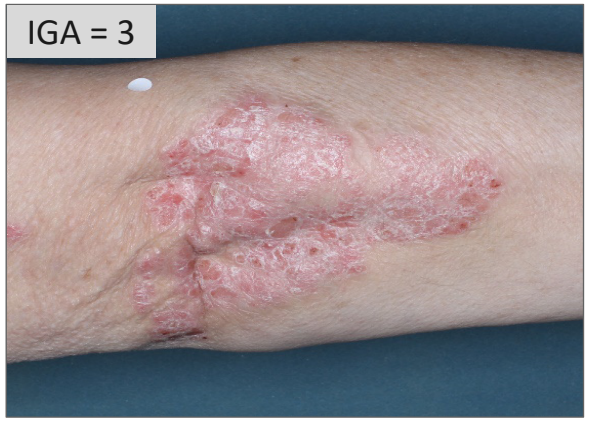
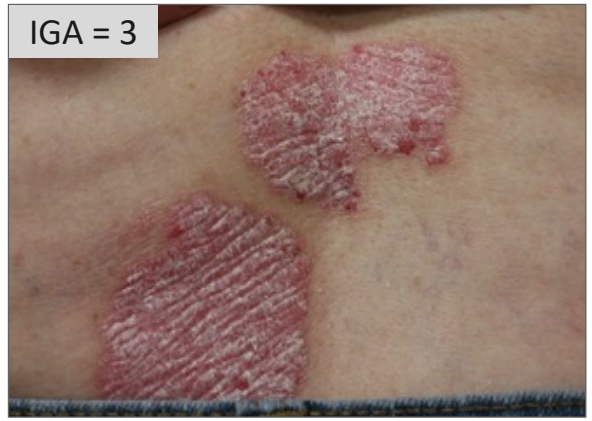
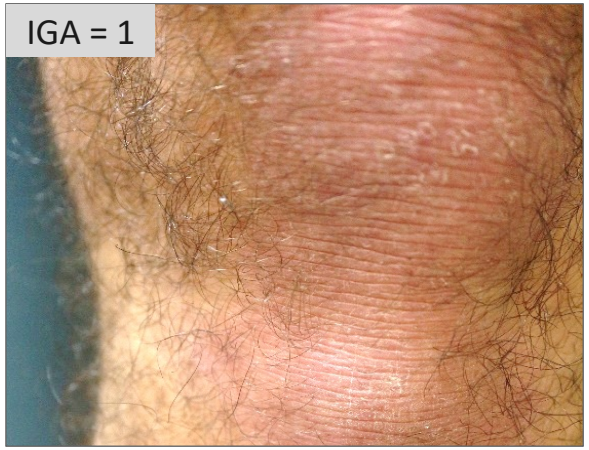
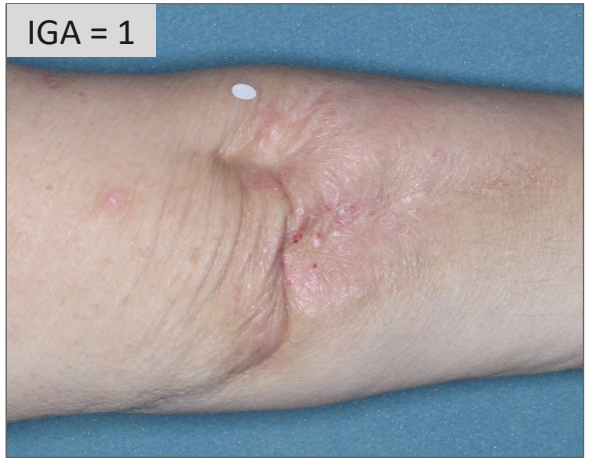
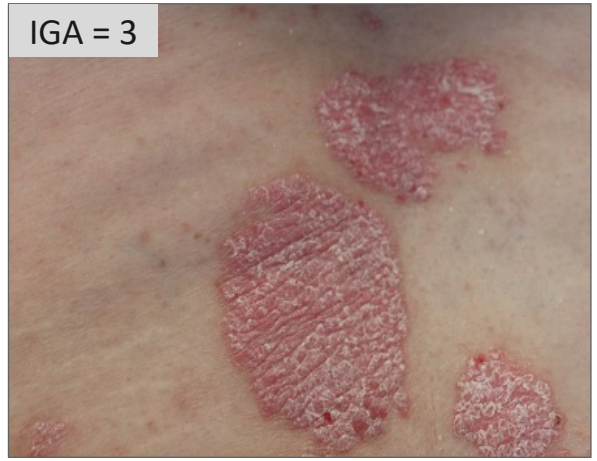
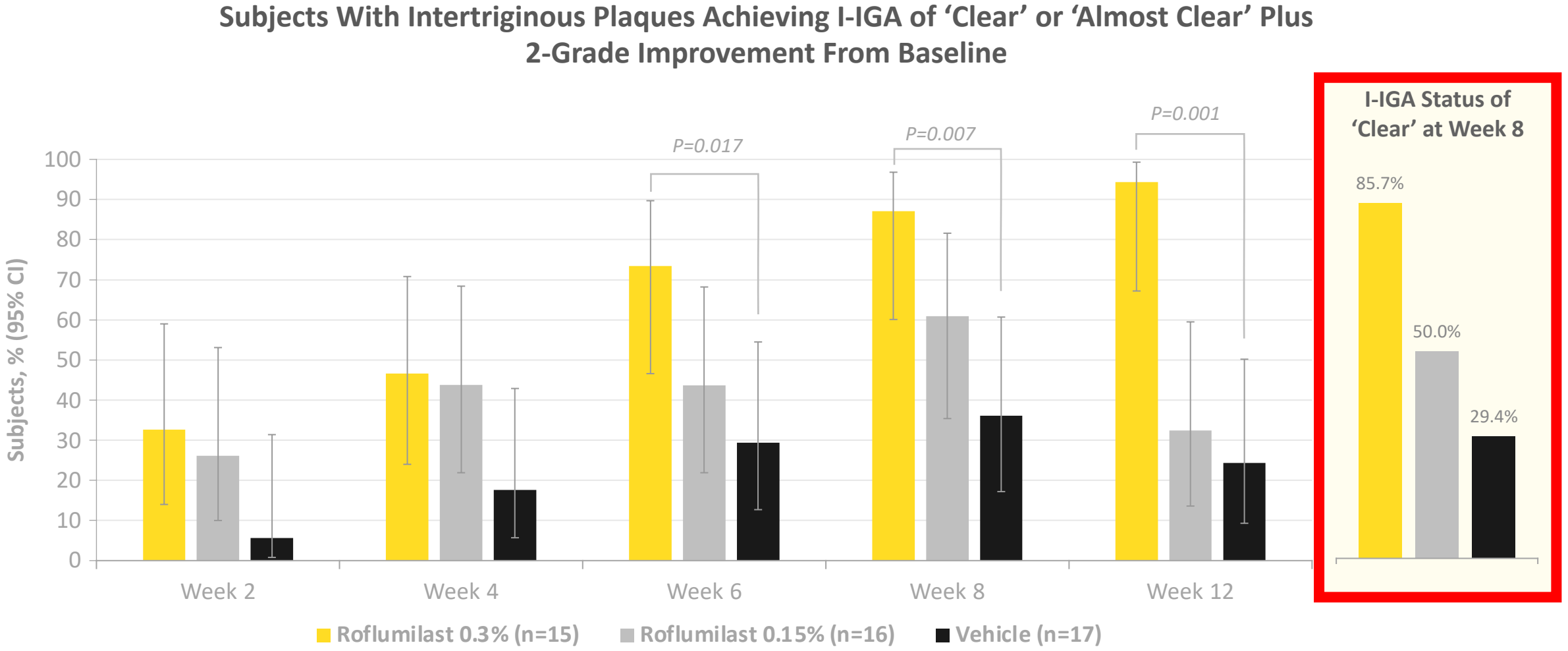
Roflumilast Cream Improved Severity of Plaque Psoriasis

	Roflumilast 0.3%	Roflumilast 0.15%	Vehicle
Baseline			
Week 8			

IGA: Investigator Global Assessment.

Most Subjects With Intertriginous Plaques Treated With Roflumilast Cream Achieved I-IGA Success by Week 6 With Continued Improvement Through Week 12



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