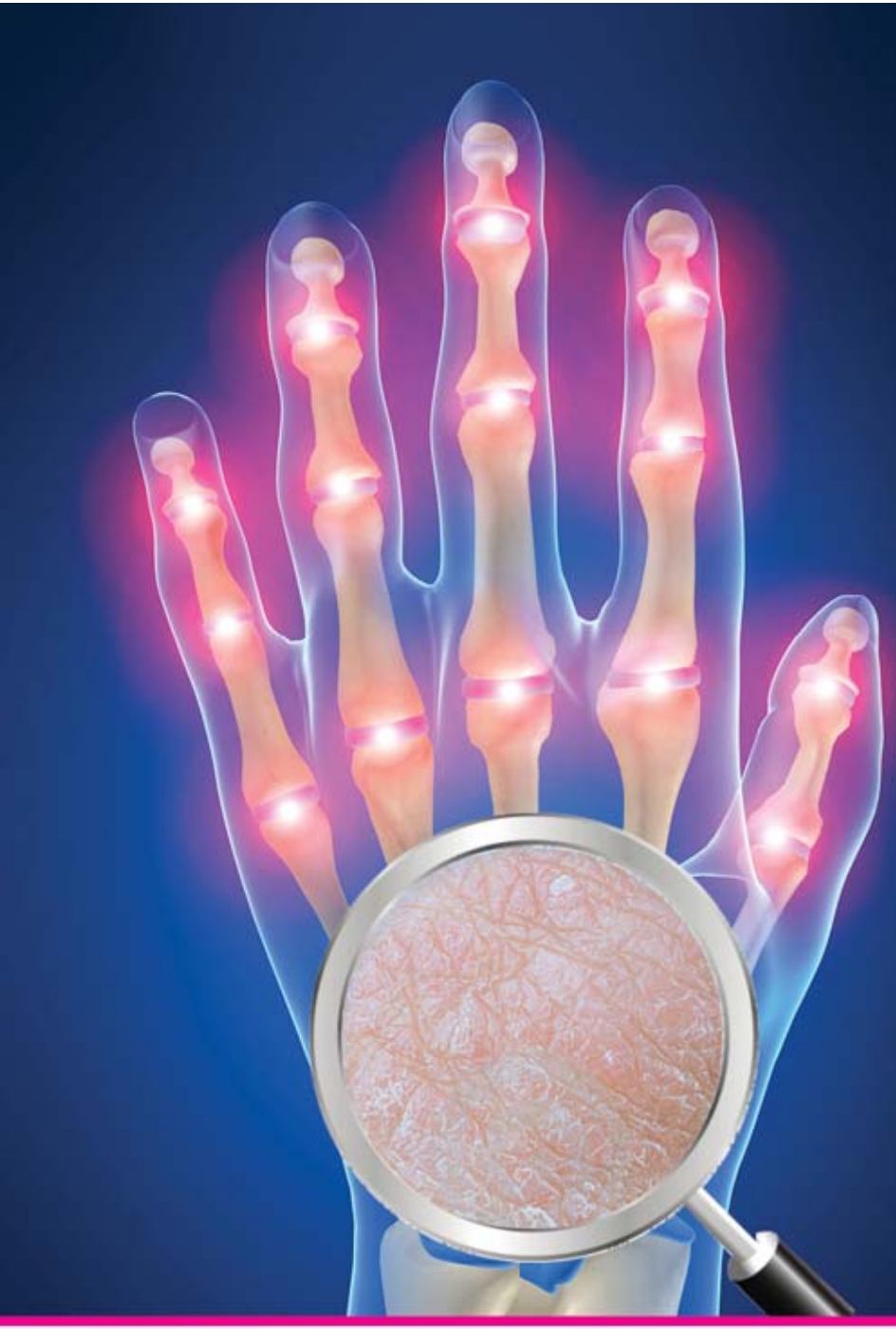


Examining the Latest Clinical Findings for Psoriasis and Psoriatic Arthritis to Enhance Managed Care Decision-Making

Jointly provided by Annenberg Center for Health Sciences at Eisenhower and Impact Education, LLC in collaboration with Postgraduate Institute for Medicine

Annenberg Center For Health Sciences at Eisenhower

Impact Education, LLC

PIM Postgraduate Institute for Medicine

This activity is supported by independent educational grants from Celgene Corporation, Janssen Biotech, Inc., and Novartis Pharmaceuticals Corporation.

Faculty Disclosure

- The ***faculty*** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

Jeffrey Dunn, PharmD, MBA

- *Consulting Fees*: Amgen, Pfizer, Inc.

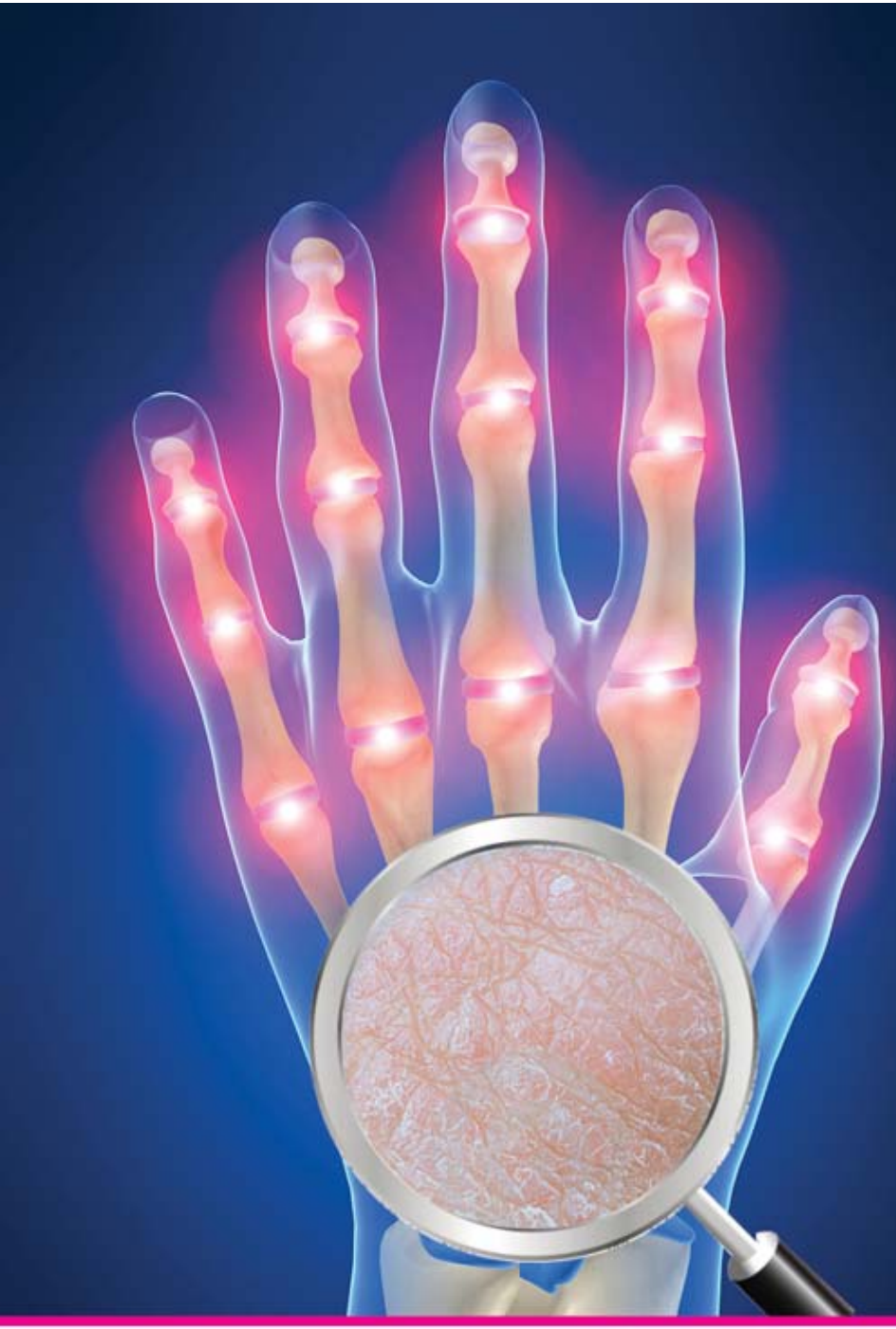
Agenda

7:05 AM – 7:25 AM	Assessing the Clinical Benefits of Current and Evolving Therapies for the Treatment of Psoriasis in a Managed Care Setting *Alan Menter, MD*
7:25 AM – 7:45 AM	Assessing the Clinical Benefits of Current and Evolving Therapies for the Treatment of Psoriatic Arthritis in a Managed Care Setting *Neal Birnbaum, MD*
7:45 AM – 8:00 AM	Applying Comparative Effectiveness Research (CER) as a Decision-Support Tool *Jeffrey D. Dunn, PharmD, MBA*
8:00 AM – 8:15 AM	Best Practice Tips and Tools to Implement New Care Models *Jeffrey D. Dunn, PharmD, MBA*
8:15 AM – 8:30 AM	Faculty Discussion/Question & Answer Session

Educational Objectives

After completing this activity, the participant should be better able to:

- Analyze the available evidence-base for the treatment of psoriasis and PsA in a true CER framework
- Assess current and emerging therapies for the treatment of psoriasis and PsA and cite their clinical trial data
- Address nonadherence factors associated with various therapies for psoriasis and PsA
- Integrate interventions to coordinate health plan and affiliated providers efforts in the health care reform era that will lead to better outcomes for patients with psoriasis and PsA
- Provide accurate and appropriate counsel as part of the managed care treatment team



Examining the Latest Clinical Findings for Psoriasis and Psoriatic Arthritis to Enhance Managed Care Decision-Making

Jointly provided by Annenberg Center for Health Sciences at Eisenhower and Impact Education, LLC in collaboration with Postgraduate Institute for Medicine

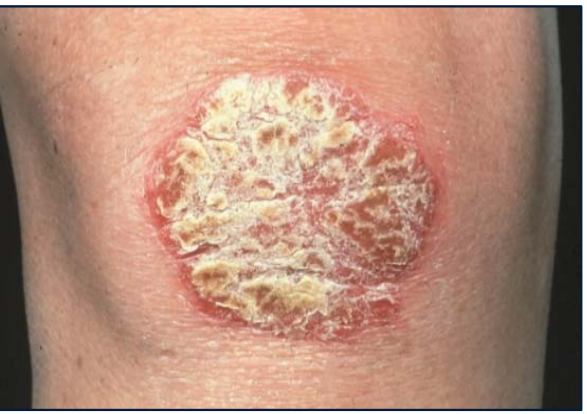
Annenberg Center For Health Sciences at Eisenhower

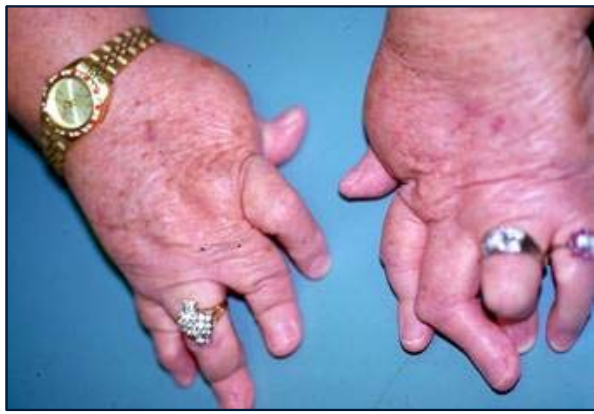
Impact Education, LLC

PIM Postgraduate Institute for Medicine

This activity is supported by independent educational grants from Celgene Corporation, Janssen Biotech, Inc., and Novartis Pharmaceuticals Corporation.

Assessing the Clinical Benefits of Current and Evolving Therapies for the Treatment of Psoriasis in a Managed Care Setting





Alan Menter, MD
Chief, Division of Dermatology
Baylor University Medical Center
Chair, Psoriasis Guidelines Committee
American Academy of Dermatology

Faculty Disclosure

- The ***faculty*** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

Alan Menter, MD

- *Advisory Board*: AbbVie, Inc., Allergan, Inc., Amgen, Boehringer Ingelheim Pharmaceuticals, Inc., Eli Lilly and Company, Genentech, Inc., Janssen Biotech, Inc., LEO Pharma Inc., Pfizer, Inc.
- *Consulting Fees*: AbbVie, Inc., Allergan, Inc., Amgen, Convoy Therapeutics, Inc., Eli Lilly and Company, Janssen Biotech, Inc., LEO Pharma Inc., Novartis Pharmaceuticals Corporation, Pfizer, Inc., Syntrix Biosystems, Inc., XenoPort, Inc.

Faculty Disclosure (continued)

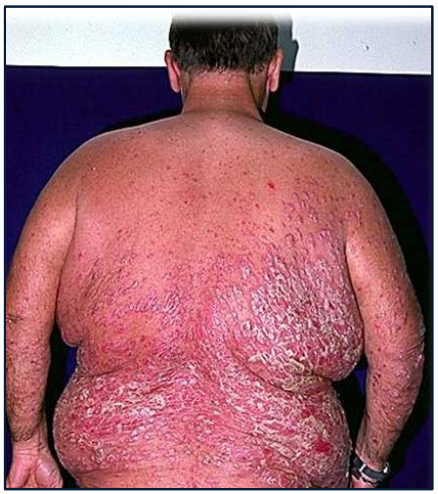
Alan Menter, MD

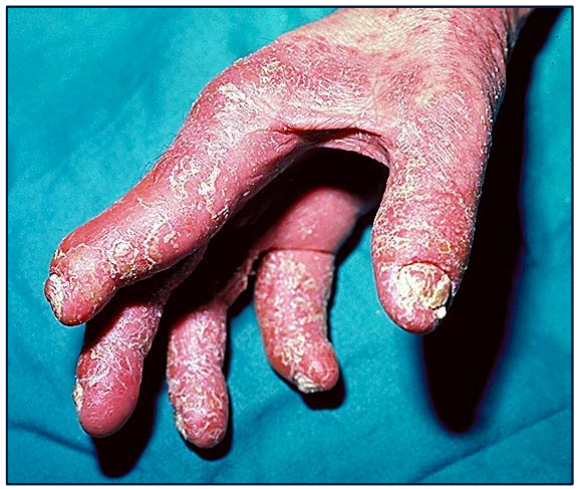
- *Investigator*: AbbVie, Inc., Allergan, Inc., Amgen, Boehringer Ingelheim Pharmaceuticals, Inc., Celgene Corporation, Eli Lilly and Company, Genentech, Inc., Janssen Biotech, Inc., LEO Pharma Inc., Merck & Co., Inc., Novartis Pharmaceuticals Corporation, Pfizer, Inc., Symbio/Maruho, Syntrix Biosystems, Inc.
- *Speaker*: AbbVie, Inc., Amgen, Janssen Biotech, Inc., LEO Pharma Inc., Pfizer, Inc.
- *Grant*: AbbVie, Inc., Allergan, Inc., Amgen, Boehringer Ingelheim Pharmaceuticals, Inc., Celgene Corporation, Genentech, Inc., Janssen Biotech, Inc., LEO Pharma Inc., Merck & Co., Inc., Novartis Pharmaceuticals Corporation, Pfizer, Inc., Symbio/Maruho, Syntrix Biosystems, Inc.
- *Honoraria*: AbbVie, Inc., Allergan, Inc., Amgen, Boehringer Ingelheim Pharmaceuticals, Inc., Convoy Therapeutics, Inc., Genentech, Inc., Janssen Biotech, Inc., LEO Pharma Inc., Novartis Pharmaceuticals Corporation, Pfizer, Inc., Syntrix Biosystems, Inc., XenoPort

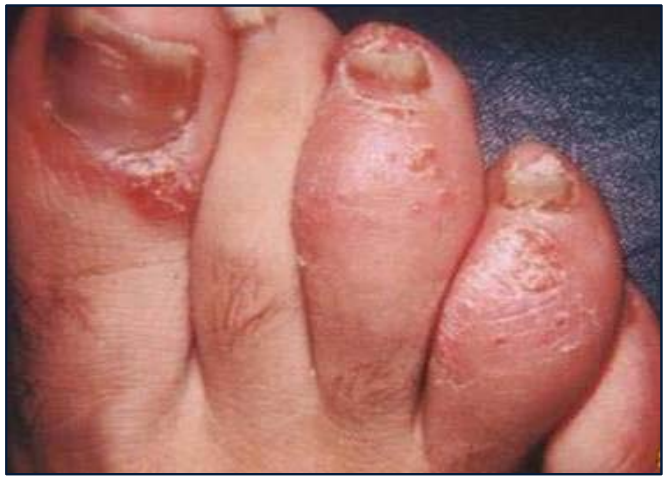
Agenda

- Unmet needs in the treatment of moderate to severe chronic plaque psoriasis
- Comorbidities in psoriasis
- Update on the efficacy and safety of recently approved medications in late-phase development for the treatment of moderate to severe plaque psoriasis
- Review of factors influencing a therapeutic success
- Multidisciplinary management of patients with psoriasis and associated psoriatic arthritis
- Summary

Unmet Needs in the Treatment of Moderate to Severe Chronic Plaque Psoriasis







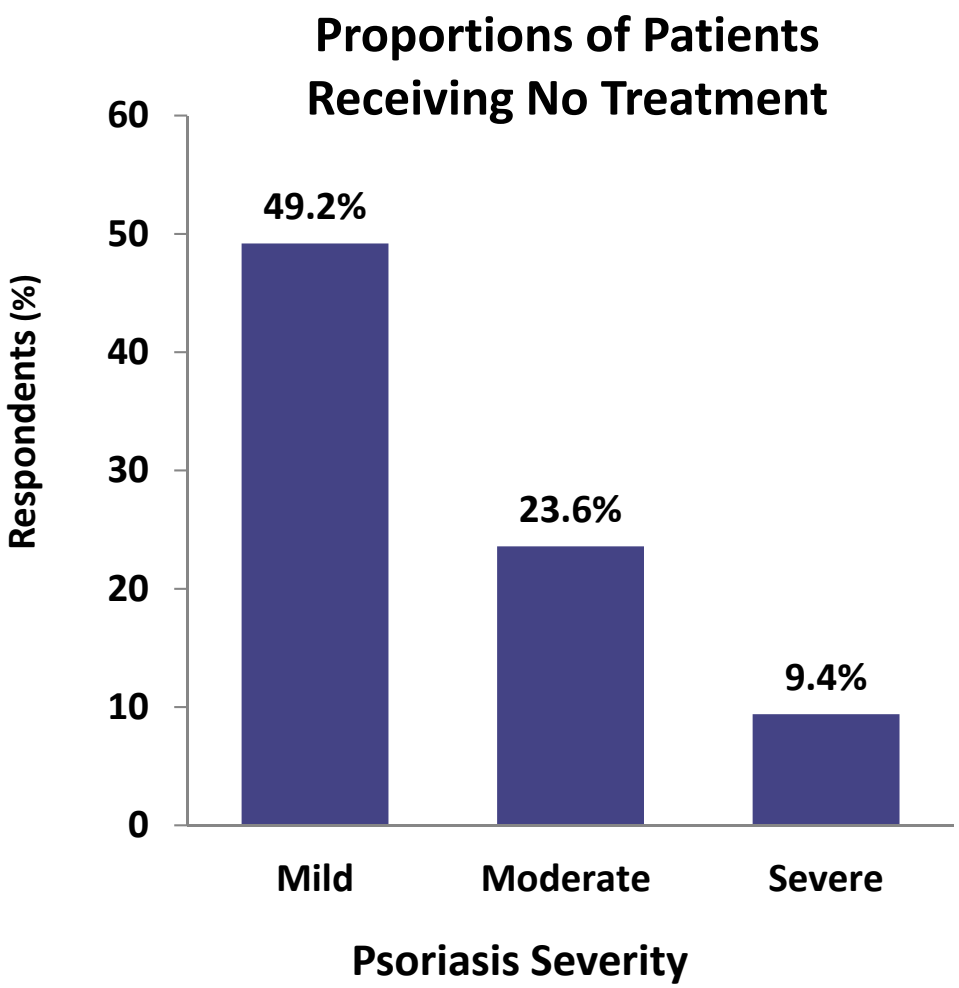
Psoriasis is the Most Prevalent Immune-Mediated Disease in the US

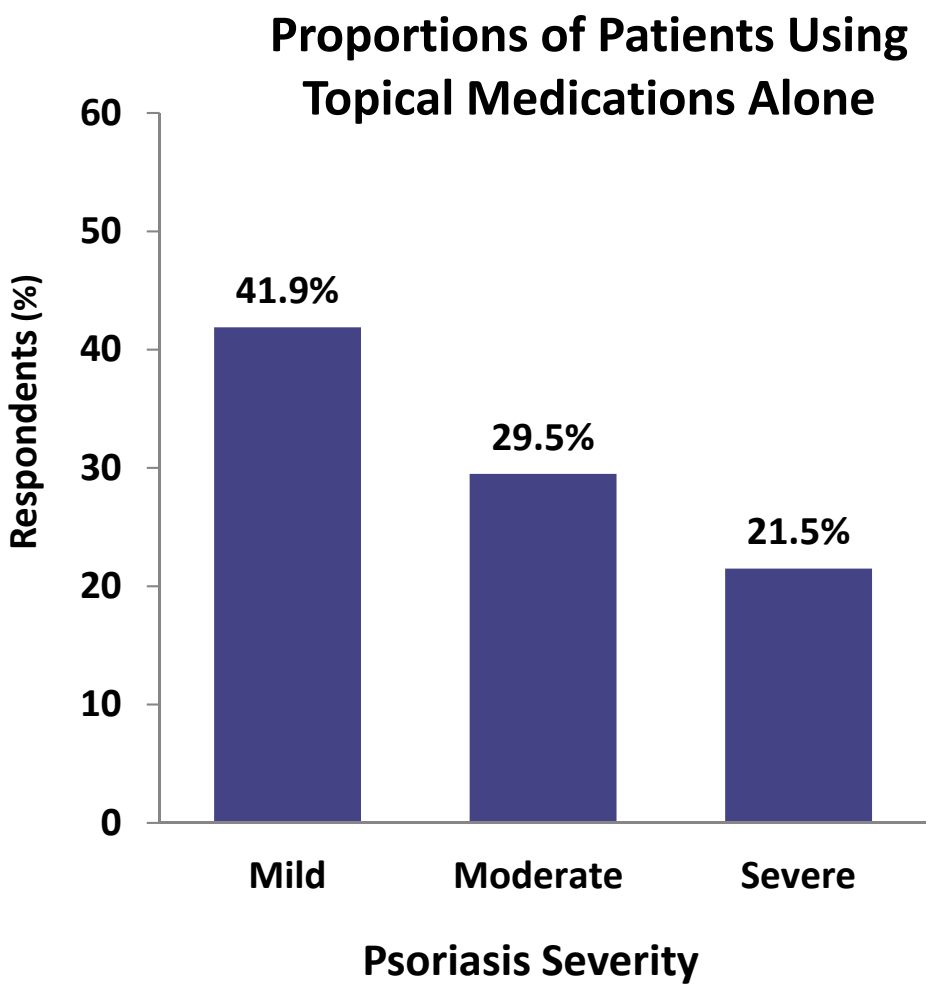
- ~ 7.5 million Americans (2.2% of the population) have psoriasis[1]
- Up to 30% of individuals with psoriasis also develop psoriatic arthritis[1]
- Onset occurs before the age of 40 in the majority of patients[1]
- 25% of cases are considered moderate to severe (eg, lesions that affect 10% of the body surface) [1]
- Systematic review of 22 studies indicated the total direct and indirect health care costs of psoriasis are $135 billion in the US[2]
- ~$26,000 per person including[1,2]
  - Cost of treatment interventions
  - Doctor visits
  - Lost productivity at work/school

1. National Psoriasis Foundation. http://www.psoriasis.org/research/science-of-psoriasis/statistics. Accessed February 20, 2015.
2. Brezinski EA, et al. *JAMA*. 2015 Jan 7. doi: 10.1001/jamadermatol.2014.3593. [Epub ahead of print]

Psoriasis Remains Significantly Undertreated

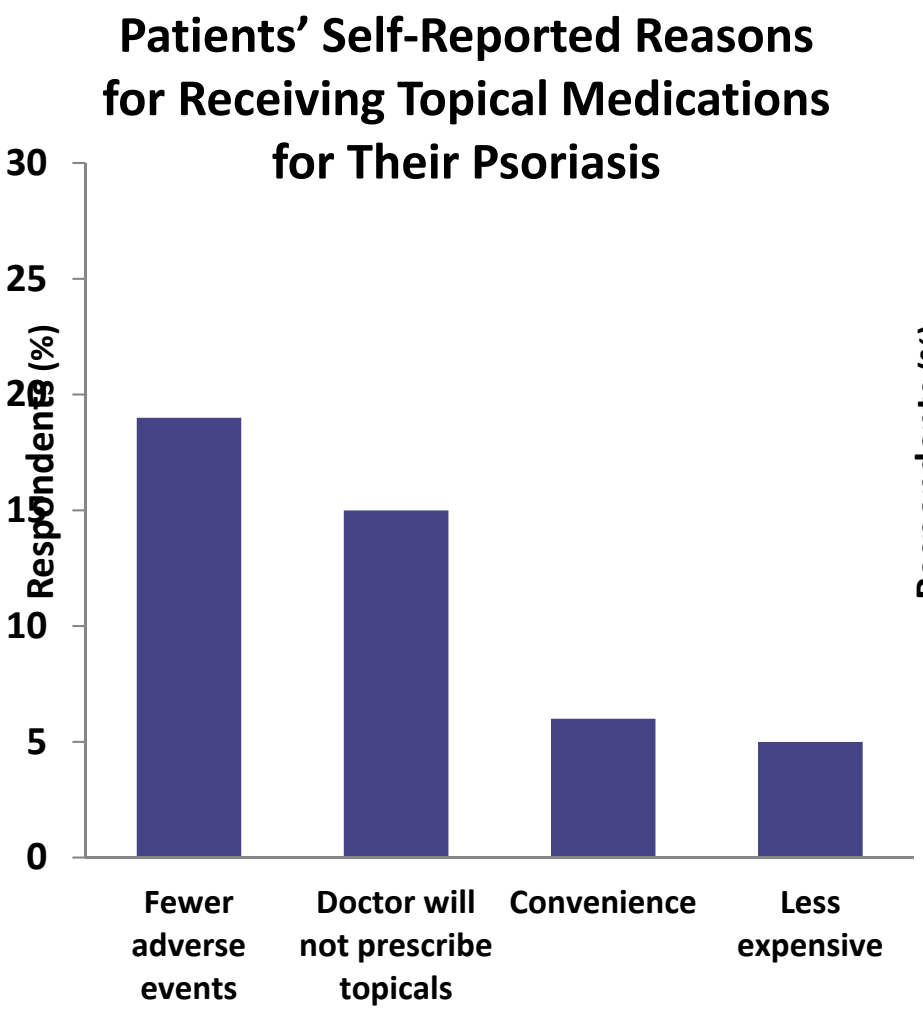
Data from the National Psoriasis Foundation National Survey

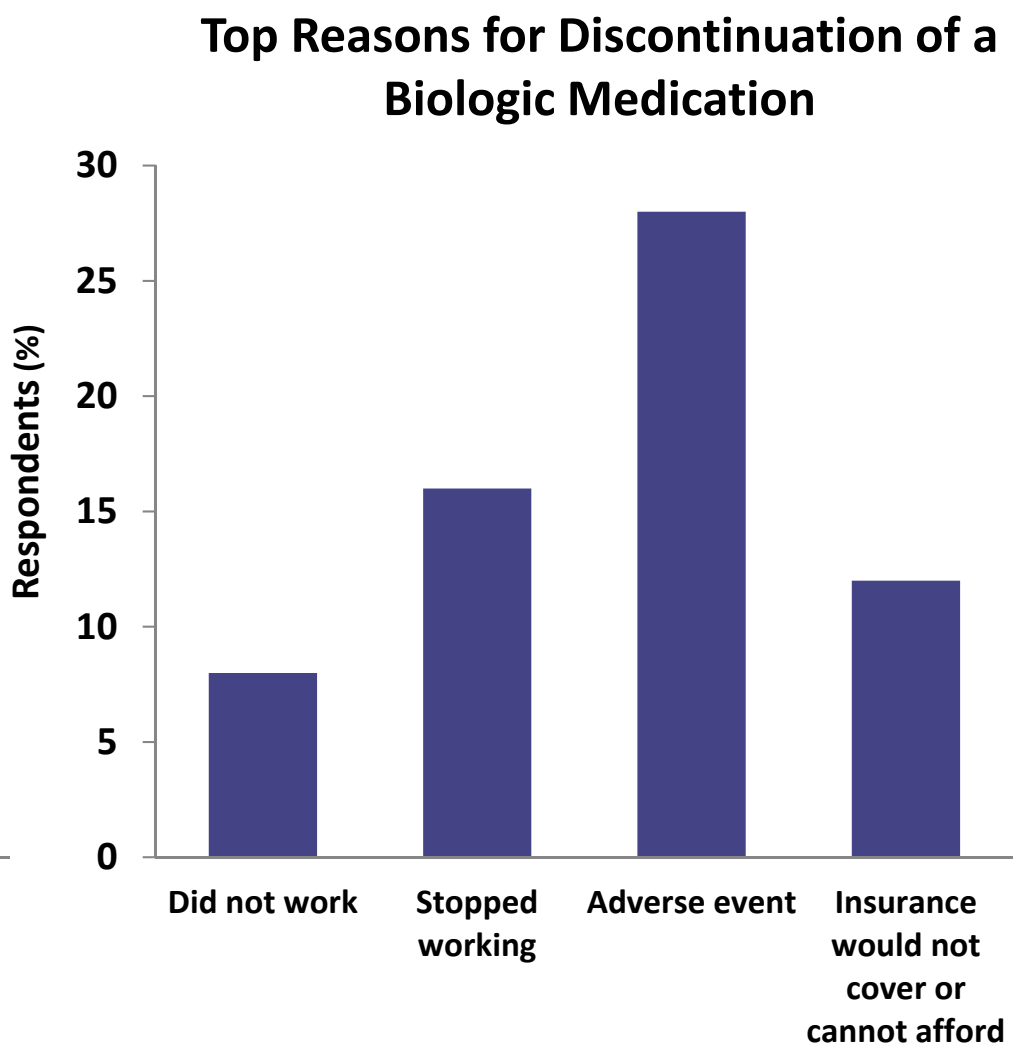




Armstrong AW, et al. *JAMA Dermatol*. 2013;149:1180-1185.

Psoriasis Remains Significantly Undertreated (continued)

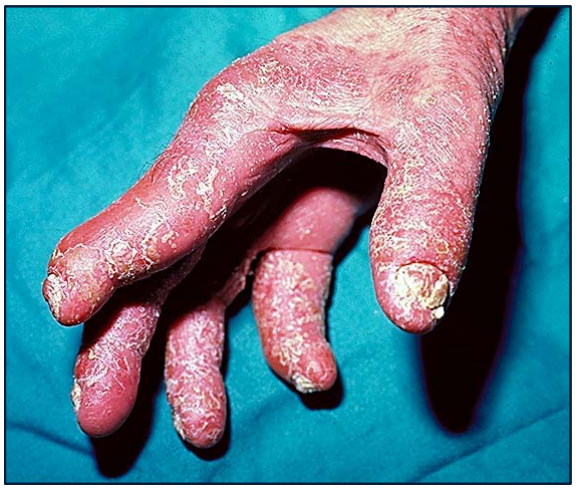




Armstrong AW, et al. *JAMA Dermatol*. 2013;149:1180-1185.

Slide 1: Comorbidities Associated with Psoriasis

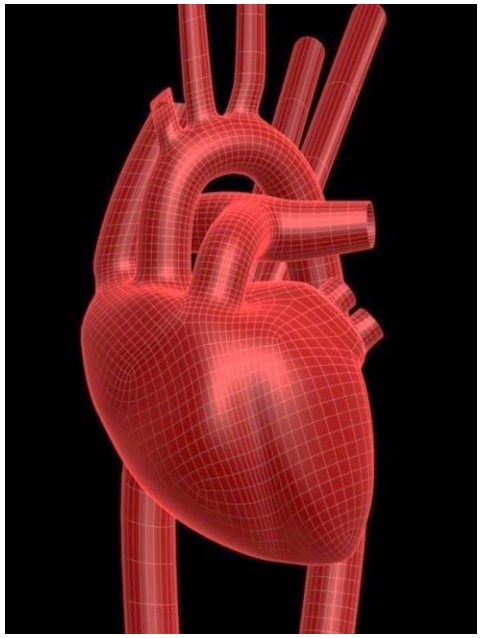
1. Obesity/metabolic syndrome
2. Psoriatic arthritis
3. Autoimmune diseases
4. Psychiatric diseases
5. Cardiovascular disease
6. Sleep apnea



All statistically validated

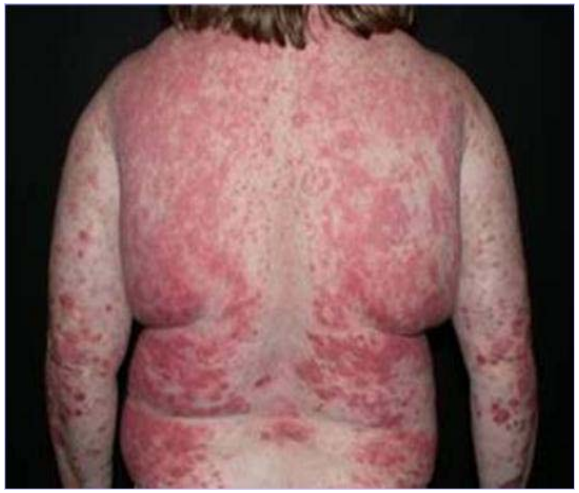
Slide 2: Comorbidities Associated with Psoriasis

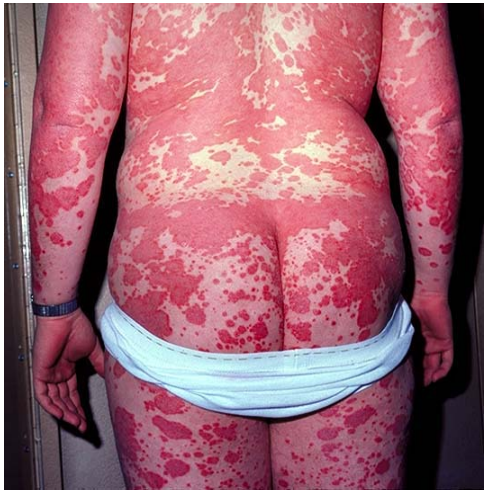
7. Renal disease
8. Personal behaviors, e.g. smoking
9. Cancer / Lymphoma
10. Nonalcoholic steatohepatitis (NASH)
11. Chronic obstructive pulmonary disease (COPD)
12. Increased mortality

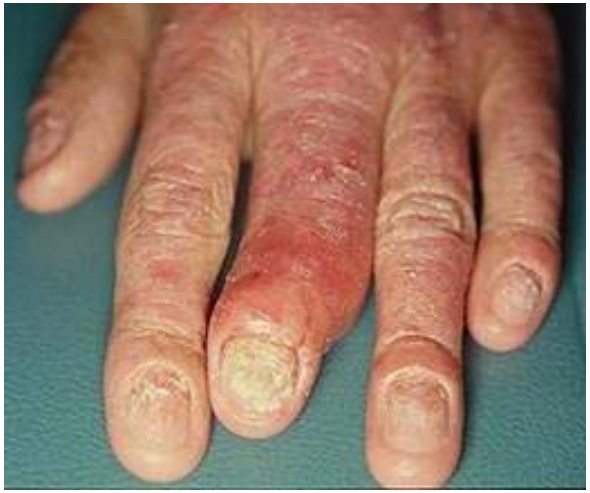


All statistically validated

Efficacy and Safety of Recently Approved Medications in Late-Phase Development for Psoriasis and Psoriatic Arthritis







Slide 1: Newly Approved Drugs and Agents in Late-Phase Development for Psoriasis

Drug	MOA	Dosing and Administration	Status
Apremilast (Otezla®)/Celgene[1]	Small molecule inhibitor of phosphodiesterase 4 (PDE-4)	Oral administration BID dosing	Approved September 2014
Secukinumab (Cosentyx®)/ Novartis[2]	Human (mAb) that selectively binds to IL-17A and inhibits its interaction with the IL-17 receptor	Subcutaneous (SC) injection at Weeks 0, 1, 2, 3, and 4 followed by every 4 weeks	Approved January 2015
Ixekizumab/Lilly[3]	Humanized IgG4 mAb that targets the IL-17A cytokine	SC injection every two or four weeks	Phase 3 (NDA submission expected in early 2015

1. Otezla® [package insert]. Summit, NJ: Celgene Corporation; 2014. 2. Cosentyx® [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp.; January 2015. 3. Eli Lilly and Company. Press release. August 21, 2014.

Slide 2: Newly Approved Drugs and Agents in Late-Phase Development for Psoriasis

Drug	MOA	Dosing and Administration	Status
Brodalumab/ Amgen & AstraZeneca[1]	IL-17 receptor antagonist; inhibits inflammatory signaling by blocking IL-17 cytokines	SC injection every two weeks	Phase 3
Tofacitinib (Xeljanz®)/Pfizer[2]	Small molecule JAK inhibitor	Oral (BID dosing) and topical administration	Phase 3

1. AstraZeneca , LP. Press release. November 25, 2014. 2. Pfizer Inc. Press release. May 23, 2014.

Apremilast Pivotal Trials

- Evaluated in 2 multicenter, randomized, double-blind, placebo-controlled trials
- Patients ≥18 years of age (n=1257) with moderate to severe plaque psoriasis
- Randomized to oral apremilast twice daily (n=419) or placebo (n=836)

Criteria and Endpoints

Selected inclusion criteria
- Body surface area (BSA) involvement ≥10%
- Static Physician's Global Assessment (sPGA) ≥3 (moderate or severe disease)
- Psoriasis Area Severity Index (PASI) ≥12
- Candidate for photo or systemic therapy

Selected secondary endpoints
- Proportion of patients achieving sPGA score of clear (0) or almost clear (1) at Week 16
- Change from baseline in pruritus Visual Analogue Scale (VAS) at Week 16

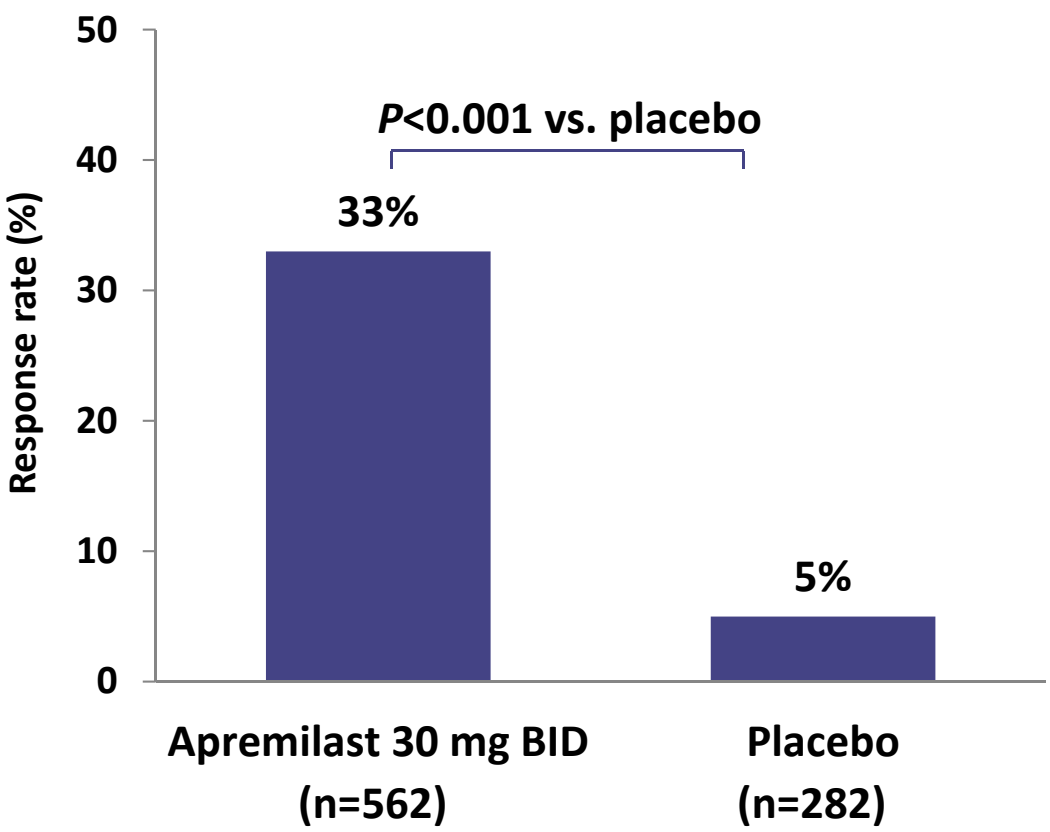
Selected exclusion criteria
- Active or incompletely treated tuberculosis (TB)
- Hepatitis B or C positive at screening
- History of HIV

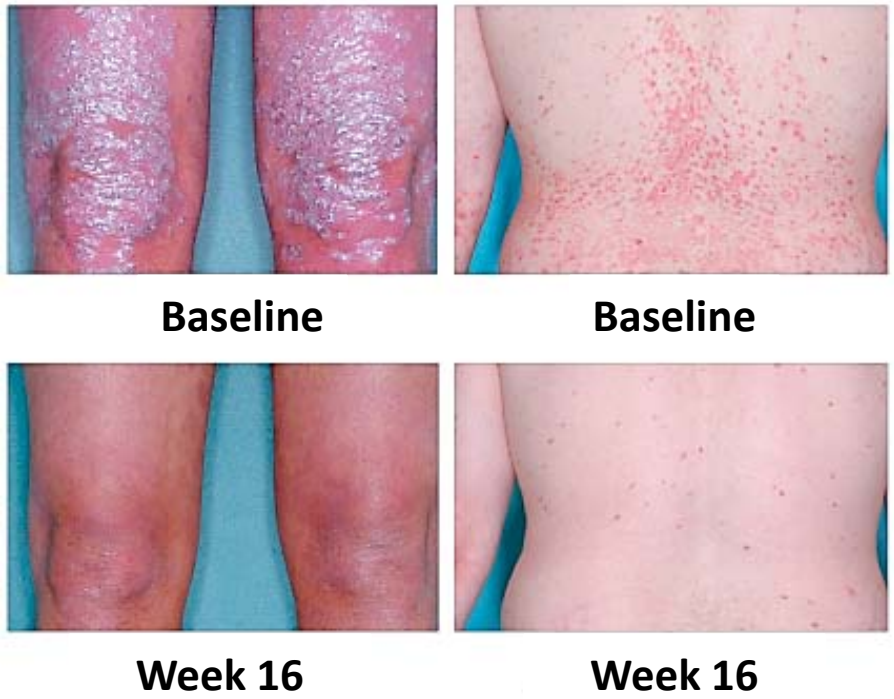
Selected exploratory endpoints
- Percent change from baseline in Nail Psoriasis Severity Index (NAPSI) score at Week 16 for patients with baseline nail psoriasis
- Proportion of patients with scalp psoriasis with improvement of Scalp Physician's Global Assessment (ScPGA) scores of clear (0) and minimal (1) at Week 16

Primary endpoint
- Proportion of patients achieving PASI 75 at Week 16

Reich K, et al. Apremilast, an Oral Phosphodiesterase 4 Inhibitor, in Patients With Moderate to Severe Psoriasis: 16-Week Results of a Phase 3, Randomized, Controlled Trial (ESTEEM 1). Late-breaking abstract. Presented at the 71st annual meeting of the American Academy of Dermatology. Miami, FL. March 1-5, 2013. Otezla® [package insert]. Summit, NJ: Celgene Corporation; 2014.

Apremilast Primary Efficacy Endpoint: PASI-75 at Week 16 (Study 1*)





*Results were consistent between Study 1 and Study 2.

Reich K, et al. Apremilast, an Oral Phosphodiesterase 4 Inhibitor, in Patients With Moderate to Severe Psoriasis: 16-Week Results of a Phase 3, Randomized, Controlled Trial (ESTEEM 1). Late-breaking abstract. Presented at the 71st Annual Meeting of the American Academy of Dermatology. Miami, FL. March 1-5, 2013. Otezla® [package insert]. Summit, NJ: Celgene Corporation; 2014.

Apremilast Safety: Adverse Reactions in ≥1% of Patients Up to Week 16

	Placebo (n=506) N (%)	Otezla® 30 mg BID (n=920) N (%)
Diarrhea	32 (6)	160 (17)
Nausea	35 (7)	155 (17)
Upper respiratory tract infection	31 (6)	84 (9)
Tension headache	21 (4)	75 (8)
Headache	19 (4)	55 (6)
Abdominal pain	11 (2)	39 (4)
Vomiting	8 (2)	35 (4)
Fatigue	9 (2)	29 (3)
Dyspepsia	6 (1)	29 (3)
Decreased appetite	5 (1)	26 (3)
Insomnia	4 (1)	21 (2)
Back pain	4 (1)	20 (20)
Migraine	5 (1)	19 (2)
Frequent bowel movements	1 (0)	17 (2)
Depression	2 (0)	12 (1)
Bronchitis	2 (0)	12 (1)
Tooth abscess	0 (0)	10 (1)
Folliculitis	0 (0)	9 (1)
Sinus headache	0 (0)	9 (1)

Discontinuation Rates Due to AEs

- Discontinuation due to any adverse reaction was 6.1% for apremilast vs. 4.1% for placebo
- Most common adverse reactions leading to discontinuation for apremilast were nausea (1.6%), diarrhea (1.0%), and headache (0.8%)
- 17% of patients had GI issues predominantly in first 2-4 weeks

Reich K, et al. Late-breaking abstract. Presented at the 71st Annual Meeting of the American Academy of Dermatology. Miami, FL. March 1-5, 2013.
Otezla® [package insert]. Summit, NJ: Celgene Corporation; 2014.

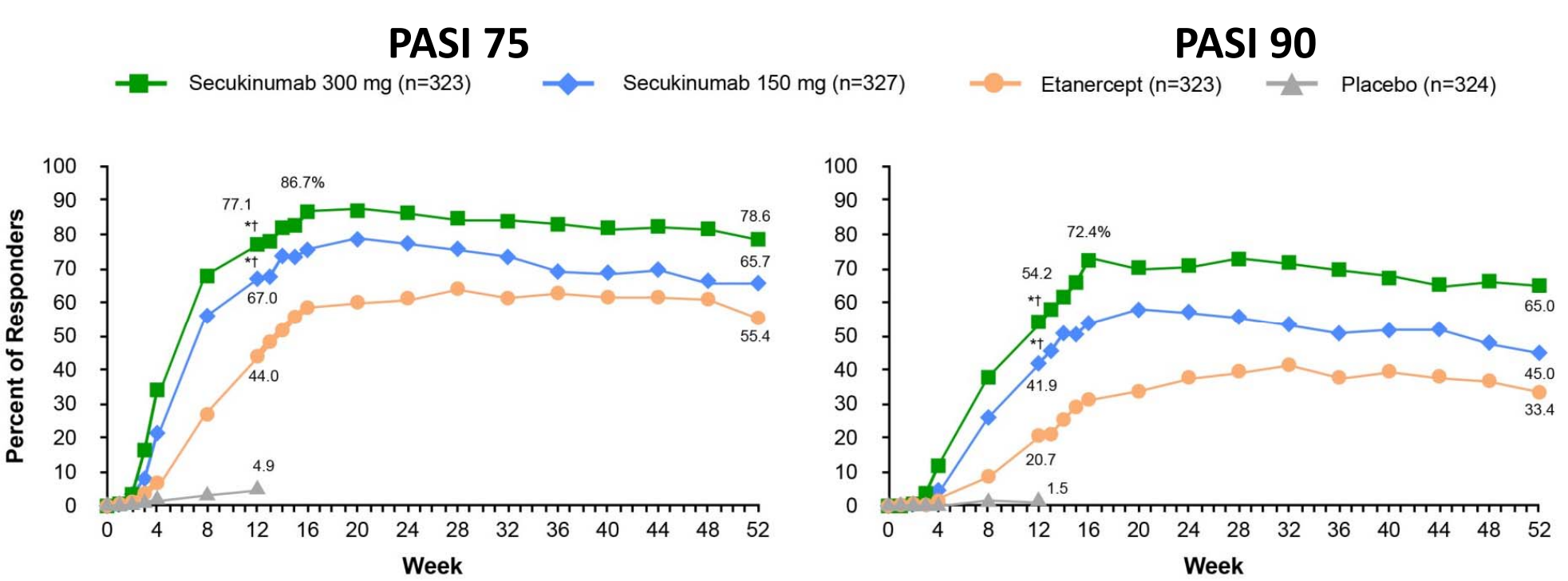
Secukinumab Pivotal Trials: Baseline Characteristics Were Well Balanced Across Studies

	ERASURE			FIXTURE			
	Secukinumab 300 mg (n=245)	Secukinumab 150 mg (n=245)	Placebo (n=248)	Secukinumab 300 mg (n=327)	Secukinumab 150 mg (n=327)	Etanercept (n=326)	Placebo (n=326)
Age (yr)	44.9	44.9	45.4	45.4	45.4	43.8	44.1
Male (%)	69.0	68.6	69.4	68.5	72.2	71.2	72.7
Weight (kg)	88.8	87.1	89.7	83.0	83.6	84.6	82.0
BMI	30.3	29.8	30.3	28.4	28.4	28.7	27.9
PASI	22.5	22.3	21.4	23.9	23.7	23.2	24.1
BSA	32.8	33.3	29.7	34.3	34.5	33.6	35.2
Any previous systemic therapy	66.5	63.7	58.9	63.0	64.8	65.6	62.6
Any previous biologic agent	28.6	29.8	29.4	11.6	13.8	13.8	10.7

BMI=Body Mass Index; PASI=Psoriasis Area Severity Index; BSA=Body Surface Area.

Langley RG, et al. *N Engl J Med*. 2014;371:326-338.

Secukinumab: Phase 3 FIXTURE Trial PASI 75/ PASI 90 Results (non-responder imputation)



*P < 0.0001 vs. placebo at Week 12; ↑P < 0.0001 vs. etanercept at Week 12.

Missing values were imputed as non-response. Non-responder imputation (NRI) is a conservative methodology for handling missing data in long-term clinical trials. NRI assumes that study dropouts are non-responders, regardless of whether or not the patient was responding to treatment at time of discontinuation. NRI may thus underestimate efficacy.

- Percentage of PASI 75/90 responders continued to increase after Week 12
- At Week 16, response rates were 86.7% (secukinumab 300 mg), 75.5% (150 mg), and 58.5% (etanercept) for PASI 75 and 72.4% (300 mg), 53.8% (150 mg), and 31.3% (etanercept) for PASI 90

PASI=Psoriasis Area Severity Index

Rich P, et al. *Br J Dermatol*. 2013;168:402-411.

Secukinumab: Adverse Reactions

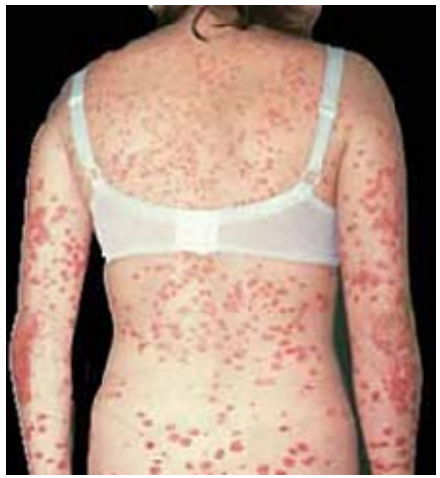
	Secukinumab		Placebo
	300 mg (n=691) N (%)	150 mg (n=692) N (%)	(n=694) N (%)
Nasopharyngitis	79 (11.4)	85 (12.3)	60 (8.6)
Diarrhea	28 (4.1)	18 (2.6)	10 (1.4)
Upper respiratory tract infection	17 (2.5)	22 (3.2)	5 (0.7)
Rhinitis	10 (1.4)	10 (1.4)	5 (0.7)
Oral herpes	9 (1.3)	1 (0.1)	2 (0.3)
Pharyngitis	8 (1.2)	7 (1.0)	0 (0)
Urticaria	4 (0.6)	8 (1.2)	1 (.01)
Rhinorrhea	8 (1.2)	2 (0.3)	1 (.01)

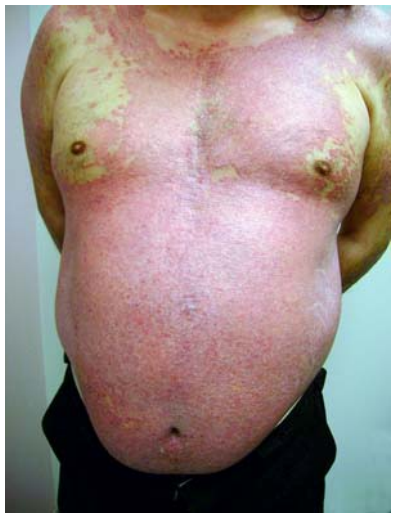
- Patients with **Crohn's disease** should be monitored closely when treated with secukinumab, as their condition may worsen.
- Phase 3 data showed an increasing trend for some types of infection with increasing serum concentration of secukinumab including Candida infections, herpes viral infections, and staphylococcal skin infections.

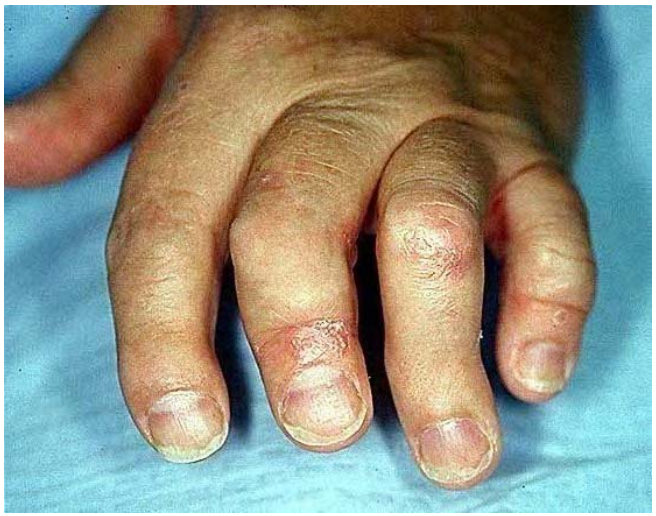
Cosentyx® [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp.; January 2015.

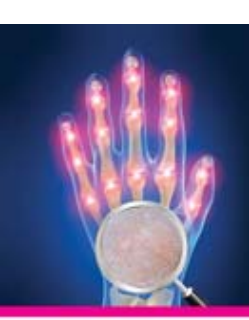
Factors Influencing Therapeutic Success

- Establishing treatment goals
- Considering patient preference when selecting a therapy







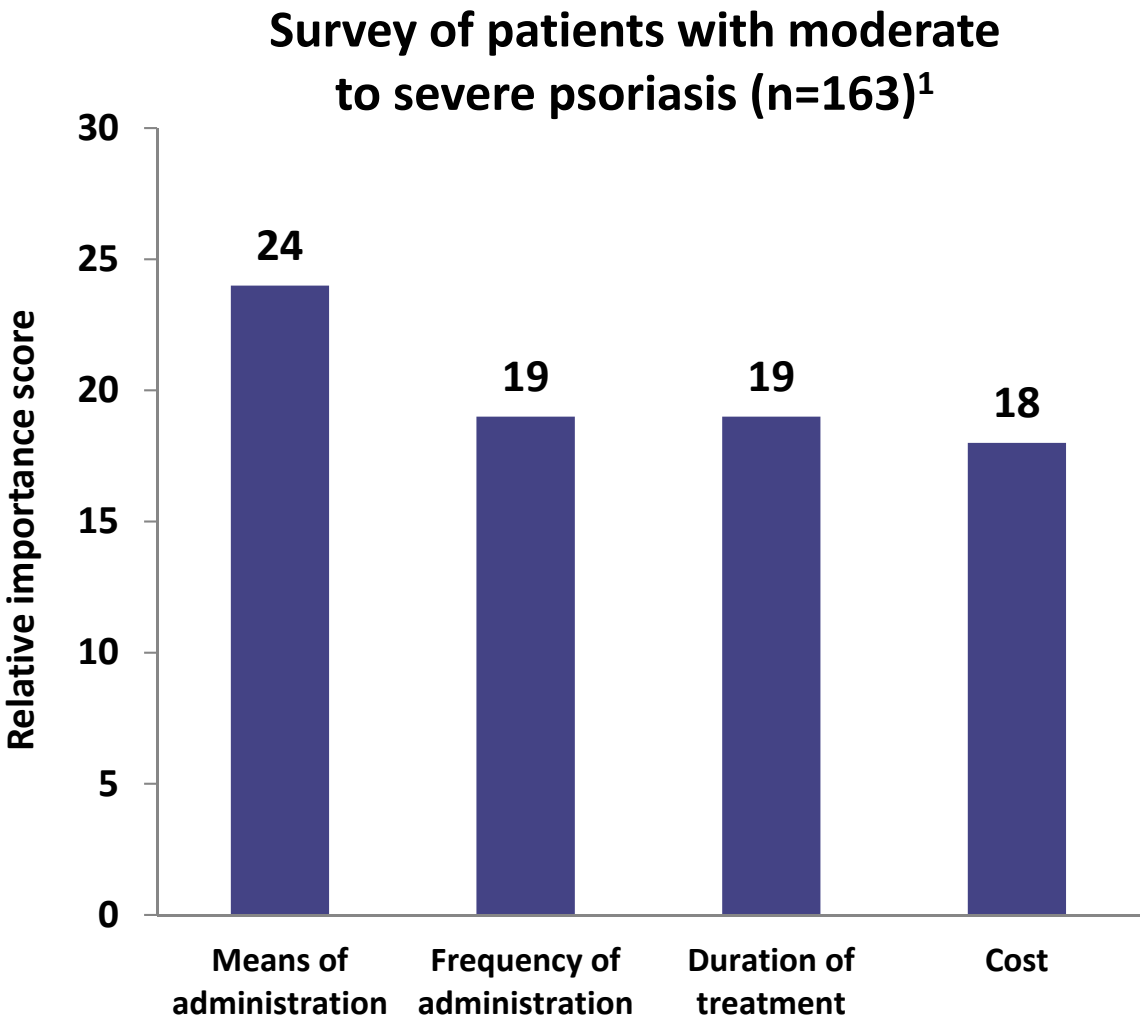


Establishing Treatment Goals is Important to Achieve and Maintain Treatment Success

- Clinical goal of psoriasis treatment: find the most efficient treatment, associated with the fewest possible AEs at a reasonable cost[1]
- Goal-oriented treatment strategies include:
  - Establishing clear treatment goals during the initial discussion of psoriasis therapy[2]
  - Regularly evaluating treatment response[2]
  - Modifying therapy when the results are insufficient[2]
- Patients should be included in the decision-making process to emphasize their responsibility in their own care and to improve adherence to medications[2]
- Patient preferences need to be considered when recommending an individualized treatment plan[1,2]

1. Schaarschmidt ML, et al. *Arch Dermatol*. 2011;147:1285-1294.
2. Brezinski E, Armstrong AW. *Semin Cutan Med Surg*. 2014;33:91-97.

Importance of Patient Preference When Selecting a Psoriasis Therapy

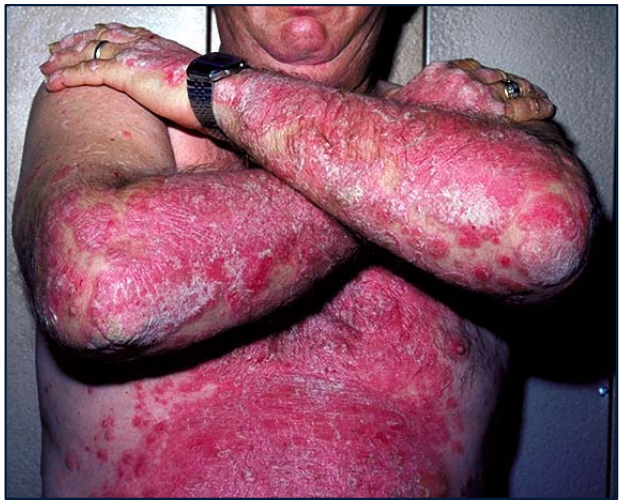


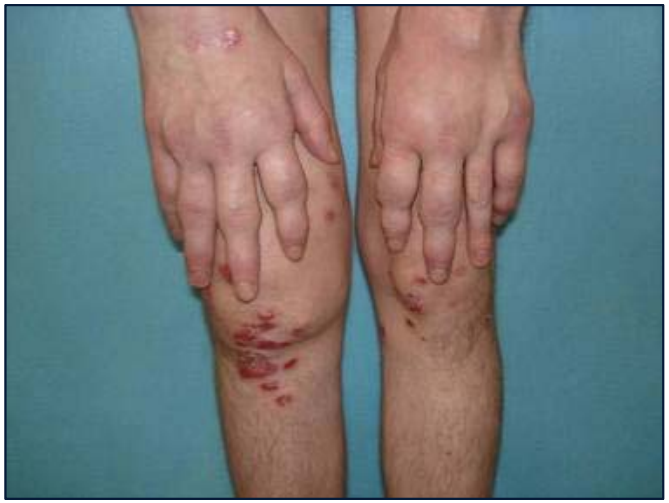
- 2 out of every 5 psoriasis patients may be nonadherent with their prescription medications[2]
- Poor fit of a recommended treatment into a patient's lifestyle may contribute to poor adherence[1]
- Medications with a convenient means of administration (eg, oral medication) can favorably impact adherence[3] and may reduce health care utilization[4]

1. Schaarschmidt ML, et al. *Arch Dermatol*. 2011;147:1285-1294.
2. Brezinski E, Armstrong AW. *Semin Cutan Med Surg*. 2014;33:91-97.
3. Jin J, et al. *Ther Clin Risk Manag*. 2008;4:269-286.
4. Bhosle MJ, et al. *J Dermatol Treat*. 2006;17:294-301.

Multidisciplinary Management of Patients with Psoriasis and Psoriatic Arthritis

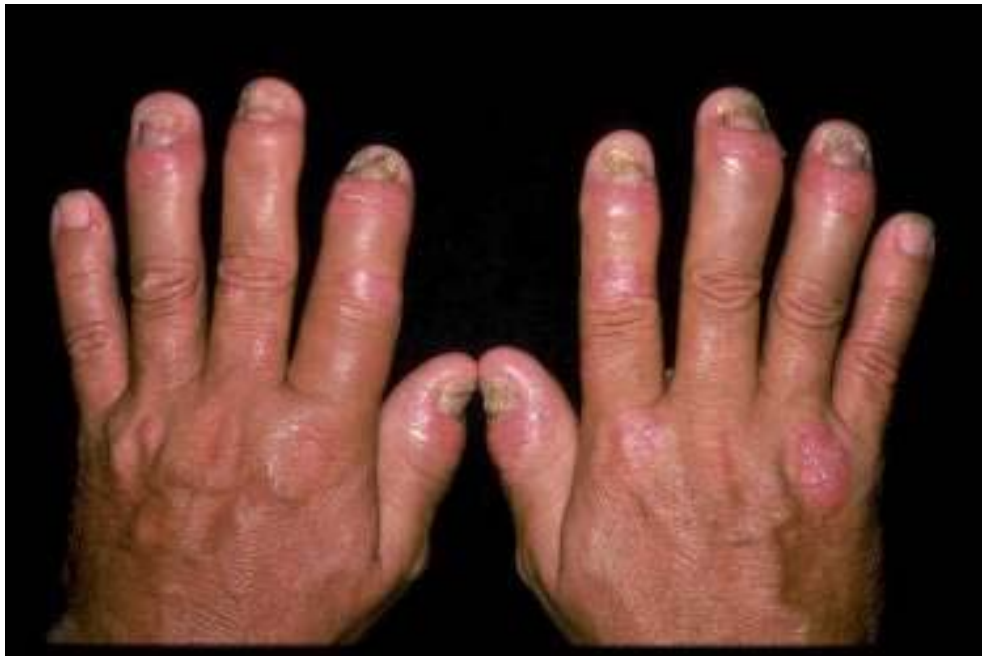
- Early detection and appropriate treatment reduce long-term consequences of psoriatic disease
- Both Dermatologists and Rheumatologists play an important role in screening for skin and joint manifestations of psoriatic disease



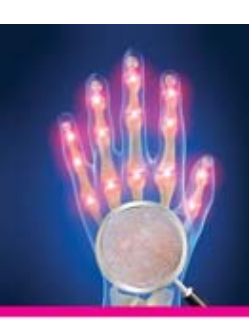


Skin Disease Precedes Joint Involvement in Patients with Psoriasis by Up to 10 Years

- An estimated 30% of patients with psoriasis are likely to develop psoriatic arthritis (PsA)
- In 84% of patients, skin disease preceded joint disease
- The severity of skin disease and the severity and course of arthritis usually do not correlate with each other
- Therapies that are effective for psoriasis may not be effective for PsA



Mease PJ, Armstrong AW. *Drugs.* 2014;74:423–441.
Gottlieb A, et al. *J Am Acad Dermatol*. 2008;58:851-864.



Because Psoriasis and Psoriatic Arthritis Share Common Pathologic Mechanisms, the Ideal Intervention Should Control Both Skin and Joint Signs and Symptoms

Cutaneous Psoriasis

- **Estimated prevalence:**
  - **1% to 2%**
  - **Up to 30% have joint lesions**
  - **35% to 70% have nail changes**
- **Transcription factors:**
  - **TNF-α →NF-κB or MAPK**
- **Genetic susceptibility loci:**
  - **40+ genes including HLA-C alleles**
- **Cytokine and other mediators:**
  - **TNF-α**
  - **IL-17**
  - **IL-12B/IL-23r**

Psoriatic Arthritis

- **Estimated prevalence:**
  - **0.25%**
  - **90% have skin lesions**
  - **80% have nail changes**
- **Transcription factors:**
  - **NF-κB→NF-κB or MAPK**
- **Genetic susceptibility loci:**
  - **< 5 loci; HLA-B alleles (B*27 & B*39:01)**
- **Cytokine and other mediators:**
  - **IL-12/IL-23, TNF-α, IL-17**
- **Inflammatory and cartilage markers**
  - **hsCRP, OPG, MMP-3, and the CPII:C2C ratio**
  - **RANK+ perivascular mononuclear cells; osteoclast precursors**

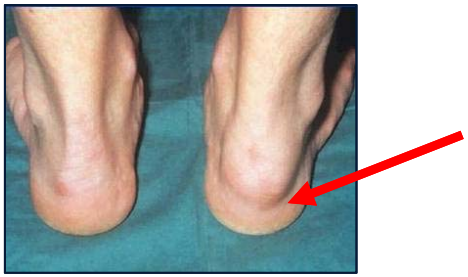
Shared Attributes

- **1:1 (male:female) prevalence**
- **Family or personal history of plaque psoriasis**
- **Cellular pathway:**
  - **T-cells**
  - **pDCs**
- **Transcription factors**
  - **Decreased AP-1**
- **Genetic susceptibility loci:**
  - **CARD15/PSORAS1/NOD2**
  - **TNF gene polymorphism**
- **Cytokine and other mediators:**
  - **TNF-α**
  - **Type 1 IFN**
  - **Amphiregulin**

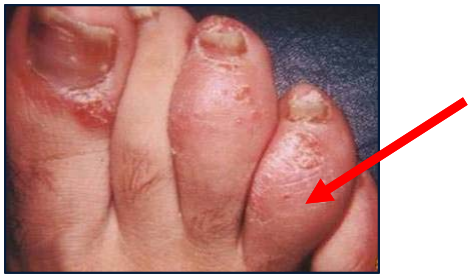
Mease PJ, Armstrong AW. *Drugs.* 2014;74:423–441.

Role of the Dermatologist in the Management of Joint Disease in Patients with Psoriasis

- Early detection and appropriate treatment of PsA will reduce long-term disability and minimize the need for health care resources
- Dermatologists play an important role in screening and diagnosing patients with early PsA
  - Conduct routine screening for PsA in their psoriasis patients
  - Assess severity and risk of progression
  - Initiate treatment that controls both skin and joint disease
- For patients with more severe or complicated symptoms, dermatologists and rheumatologists must collaborate to adequately manage both skin and joint psoriatic involvement over the long term



Enthesitis

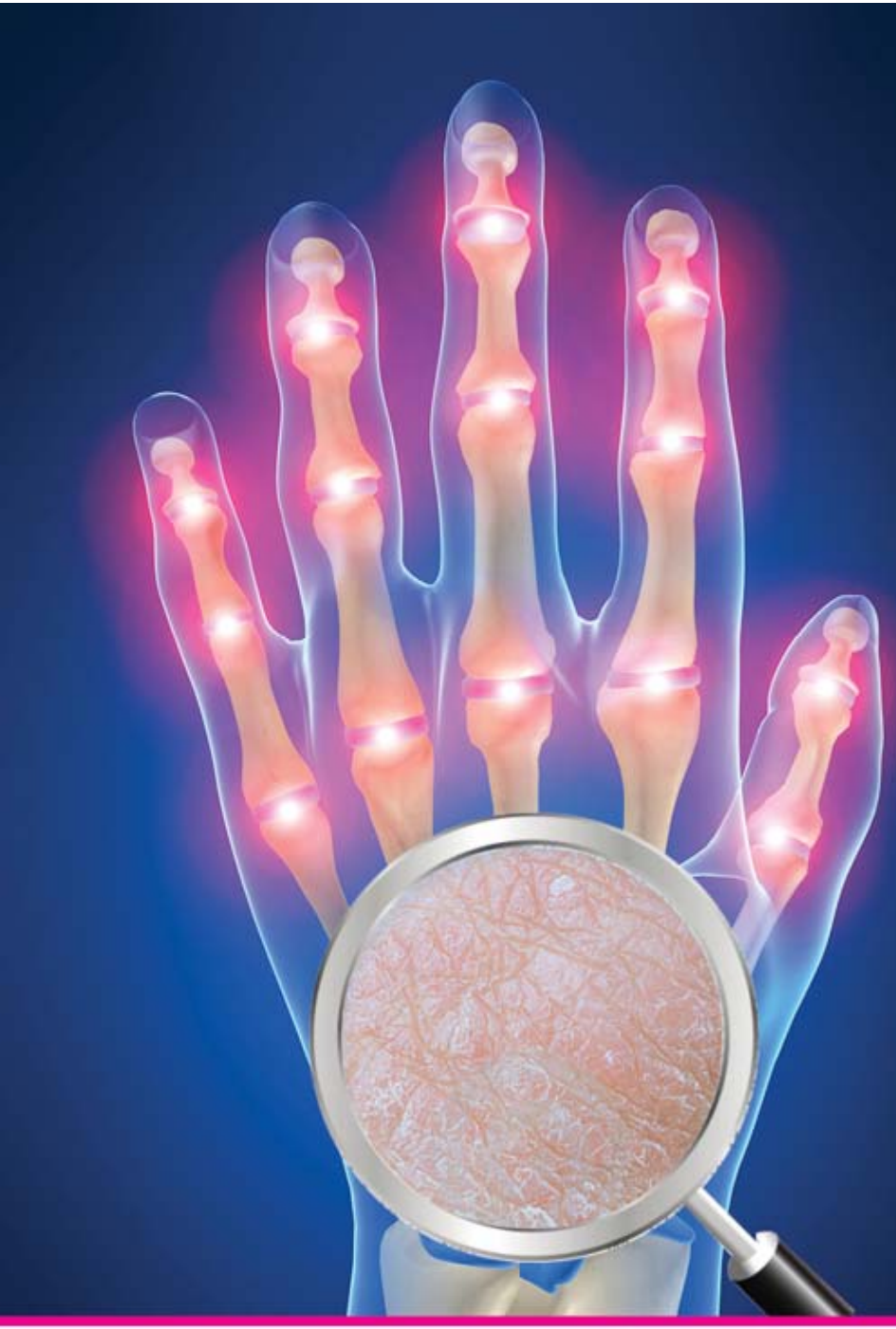


Dactylitis

Mease PJ, Armstrong AW. *Drugs.* 2014;74:423–441.

Summary

- Chronic moderate to severe plaque psoriasis remains undertreated
- Comorbidities must be recognized and appropriately managed.
- Apremilast (oral) and secukinumab (subcutaneous) were recently approved for the treatment of moderate to severe plaque psoriasis
  - Ixekizumab, brodalumab, and tofacitinib are currently in Phase 3 development
- Multiple disease and patient factors influence the degree of success realized by patients receiving psoriasis treatment
- Convenient and easy-to-use therapies will improve adherence
- Early detection and appropriate treatment of PsA will reduce long-term disability and utilization of health care resources
- Dermatologists should screen for PsA in their psoriasis patients and collaborate with rheumatologists to adequately manage both skin and joint involvement over the long term



Examining the Latest Clinical Findings for Psoriasis and Psoriatic Arthritis to Enhance Managed Care Decision-Making

Jointly provided by Annenberg Center for Health Sciences at Eisenhower and Impact Education, LLC in collaboration with Postgraduate Institute for Medicine

Annenberg Center For Health Sciences at Eisenhower

Impact Education, LLC

PIM Postgraduate Institute for Medicine

This activity is supported by independent educational grants from Celgene Corporation, Janssen Biotech, Inc., and Novartis Pharmaceuticals Corporation.

Assessing the Clinical Benefits of Current and Evolving Therapies for the Treatment of Psoriatic Arthritis in a Managed Care Setting

Neal Birnbaum, MD
Director, Division of Rheumatology
California Pacific Medical Center
Clinical Professor of Medicine
University of California, San Francisco

Faculty Disclosure

- The ***faculty*** reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME activity:

Neal Birnbaum, MD

- *Consulting Fees*: Pfizer, Inc.
- *Fees for Non-CME/CE Services*: AbbVie, Inc., Amgen, Janssen, Pfizer, Inc.

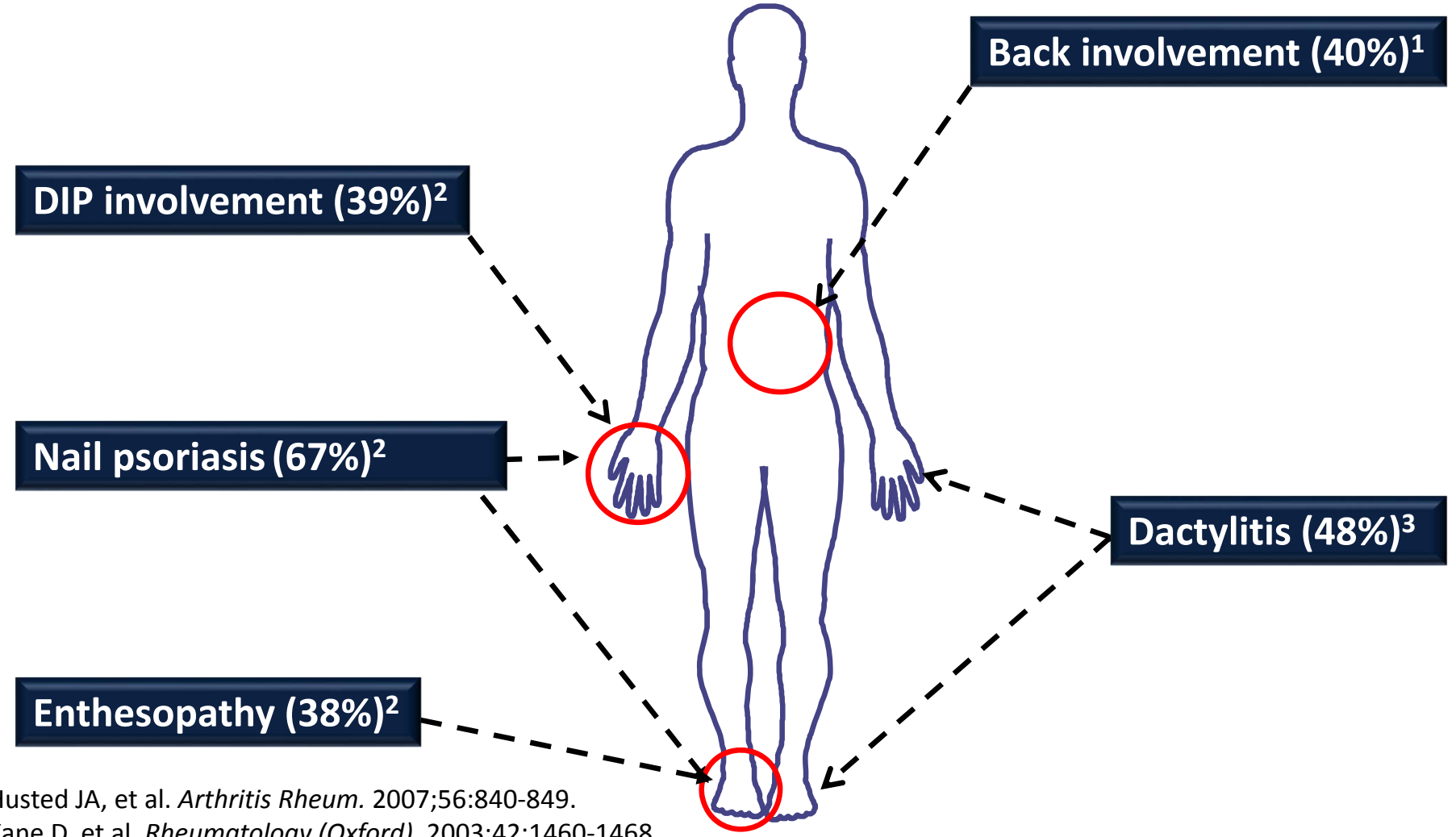
Agenda

- Overview of psoriatic arthritis
- Burden and unmet needs in the management of psoriatic arthritis
- Treatment recommendations
- Efficacy and safety of drugs recently approved for the treatment of psoriatic arthritis
- Multidisciplinary management of patients with psoriatic disease
- Summary

Overview of Psoriatic Arthritis

Psoriatic Arthritis is a Complex and Disabling Disease

- Psoriatic arthritis is characterized by stiffness, pain, swelling, and tenderness of the joints and surrounding ligaments and tendons

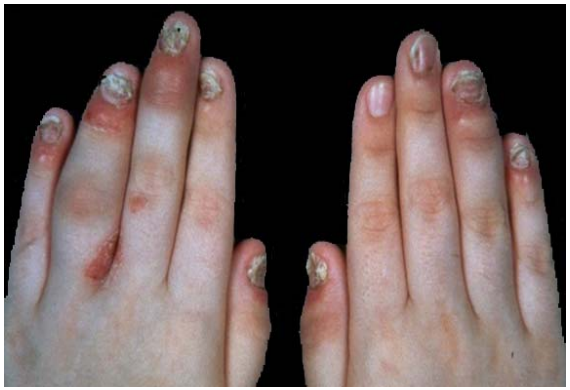


1. Husted JA, et al. *Arthritis Rheum.* 2007;56:840-849.
2. Kane D, et al. *Rheumatology (Oxford).* 2003;42:1460-1468.
3. Brockbank JE, et al. *Ann Rheum Dis.* 2005;64:188-190.

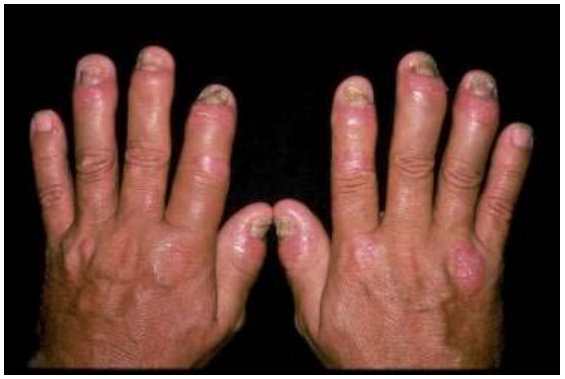
DIP=distal interphalangeal predominant

Psoriatic Arthritis Has a Diverse Clinical Presentation

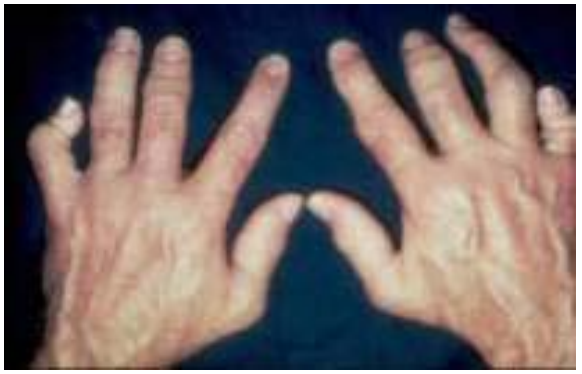
Asymmetric Oligoarthritis



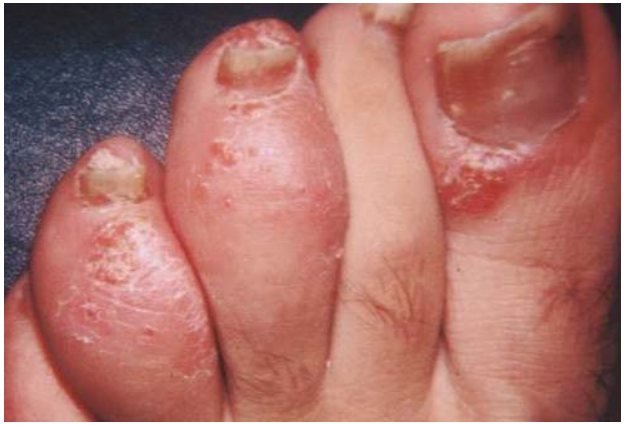
DIP Synovitis



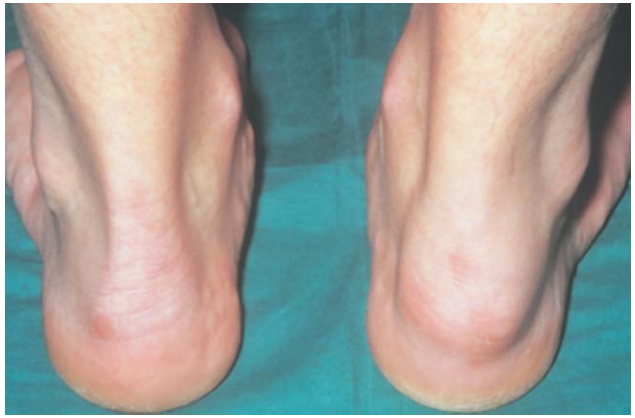
PIP Synovitis



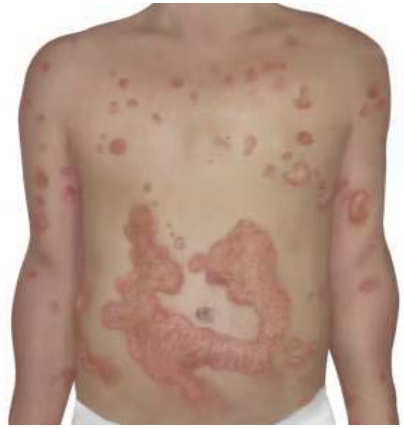
Dactylitis



Enthesitis



Psoriasis Plaques



DIP=distal interphalangeal predominant;
PIP=proximal interphalangeal joint

Differentiating Psoriatic Arthritis From Other Joint-Related Diseases

	Psoriatic Arthritis	Rheumatoid Arthritis	Osteoarthritis	Ankylosing Spondylitis
Peripheral disease	Asymmetric	Symmetric	Asymmetric	No
Sacroliitis	Asymmetric	No	No	Symmetric
Stiffness	Morning and/or with immobility	Morning and/or with immobility	With activity	Yes
Male:Female ratio	1:1	3:1	Hand/foot more common in females	1:3
Enthesitis	Yes	No	No	No
High titer RF	No	Yes	No	No
HLA association	CW6; B27	DR4	No	B27
Nail lesions	Yes	No	No	No
Psoriasis	Yes	Uncommon	Uncommon	Uncommon

Gottlieb A, et al. *J Am Acad Dermatol.* 2008;58:851-864.

RF=rheumatoid factor; HLA=human leukocyte antigen.

Psoriatic Arthritis: Burden and Unmet Needs

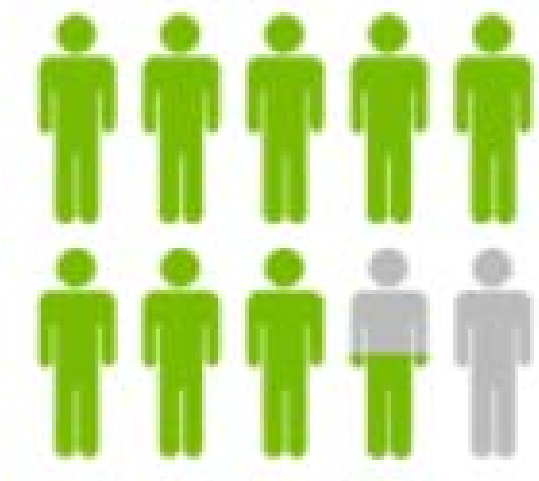
Prevalence of Psoriatic Arthritis in the US

Psoriatic Arthritis Affects an Estimated[1]

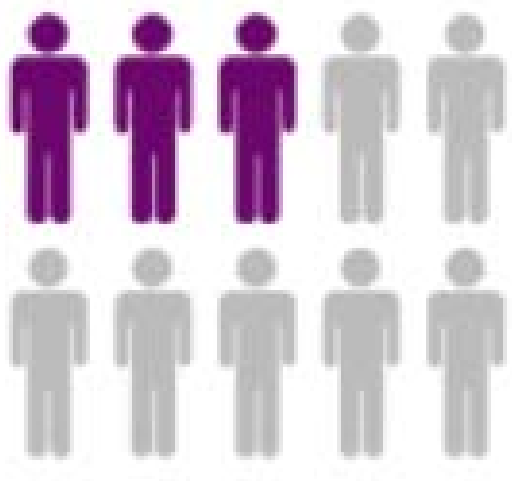
- Psoriatic arthritis usually appears about 5 to 12 years after psoriasis begins[2]
- Equally common in men and women[2]
- Most people develop it between 30 and 50 years of age, but it can begin at any age[2]

1. Wilson FC, et al. *J Rheumatol*. 2009;36:361–367.
2. American College of Rheumatology. https://www.rheumatology.org/Practice/Clinical/Patients/Diseases_And_Conditions/Psoriatic_Arthritis. Accessed February 23, 2015.

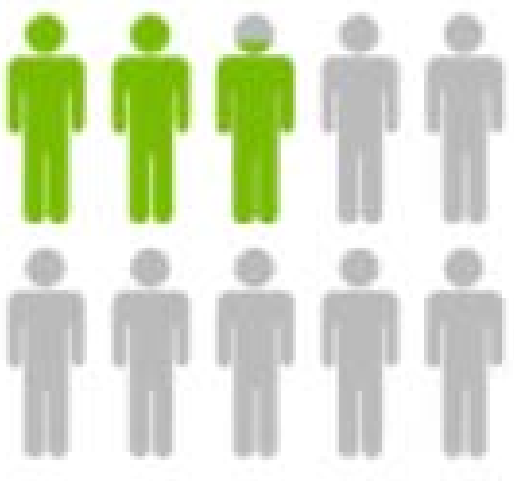
Psoriatic Arthritis May Occur With or Without Skin Involvement



~85% of patients with psoriatic arthritis were first diagnosed with psoriasis[1]



Psoriatic arthritis may develop in up to 30% of patients with psoriasis[2]



Undiagnosed psoriatic arthritis was reported in 29% of psoriasis patients seen in a single-center study[3]

1. Gottlieb AB, et al. *J Am Acad Dermatol*. 2008;58:851-864.
2. National Psoriasis Foundation. About psoriatic arthritis. https://www.psoriasis.org/about-psoriatic-arthritis. Accessed February 25, 2015.
3. Haroon M, et al. *Ann Rheum Dis.* 2013;72:736–740.

Psoriatic Arthritis Poses a Significant Clinical and Economic Burden

- Historically considered to be a "mild" disease[1]
  - However, 40%-60% of patients develop joint complications
- Joint damage contributes to[1]
  - Reduced articular function
  - Higher mortality
  - Impaired ability to work and form/maintain social relationships
  - Poor quality of life
- Average annual direct and indirect cost associated with psoriatic arthritis ranged from ~$8,367 to $18,110[2]
  - Hospitalizations accounted for almost 60% of direct costs
  - Disability and lost productivity accounted for the majority of indirect costs

1. Slobodin G, et al. *Isr Med Assoc J*. 2009;11:430-434.
2. Lee S, et al. *P&T.* 2010;35:680-689.

Unmet Needs in Psoriatic Arthritis

Awareness/Diagnosis Gaps	Treatment Gaps
• Minimal awareness among physicians – Patients fall in a gap between psoriasis and arthritis	• Available treatment algorithms have not been validated
• Frequently undiagnosed or misdiagnosed	• No standardized remission criteria
• Need for validated screening to identify patients at highest risk for disabling disease	• No available validated composite index combining physician- and patient-oriented outcomes
• Rheumatologist referral criteria are unclear	• Need for easy to use treatments with convenient means of administration

Helliwell P, et al. *Arthritis Care Res*. 2014;66:1759-1766.

Treatment Recommendations

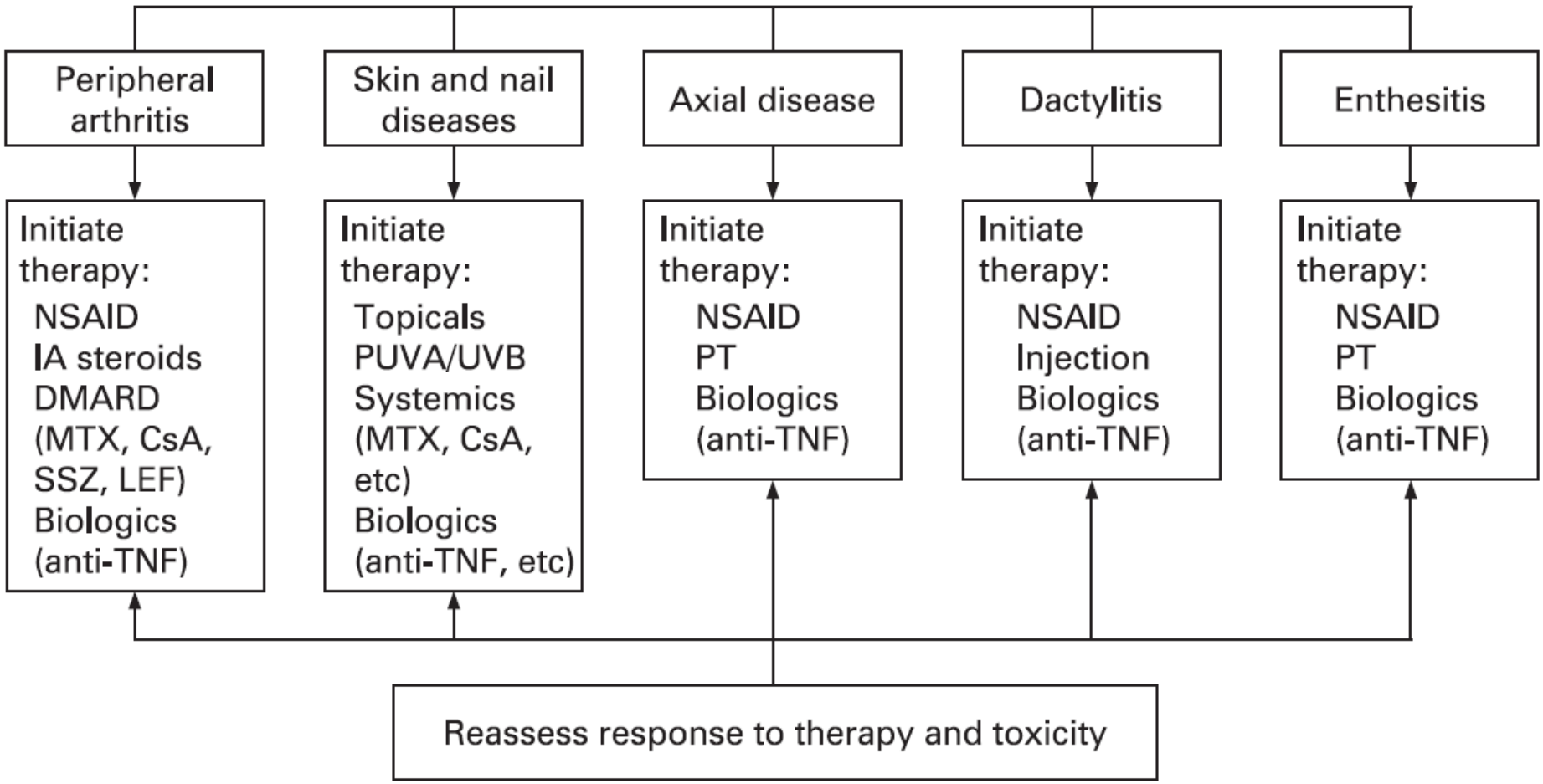
Goals of Treatment

- Goals of treatment[1]
  - Relieve or reduce joint pain
  - Reduce joint inflammation
  - Reduce swelling and tenderness
  - Prevent or delay joint damage
  - Improve function in daily activities
- Early diagnosis and treatment is associated with remission of symptoms[1]
- Early and sustained remission in 405 adults with psoriatic arthritis resulted in long-term improvements in physical function, health-related quality of life, work productivity, and reduction in health care utilization[2]

1. Smolen JS, et al. *Ann Rheum Dis*. 2014;73:6-16.
2. Kavanaugh A, et al. *Ann Rheum Dis*. 2011;70(Suppl3):238.

GRAPPA Treatment Recommendations for Psoriatic Arthritis

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) Treatment Guidelines



NSAID=nonsteroidal anti-inflammatory drugs; IA steroids=intra-articular corticosteroids; DMARD=disease-modifying antirheumatic drugs; MTX=methotrexate; CsA=cyclosporin A; SSZ=sulfasalazine; LEF=leflunomide; anti-TNF=anti-tumor necrosis factor; PUVA/UVB= psoralen + ultraviolet A/ultraviolet B; PT=physical therapy.

Richlin CT, et al. *Ann Rheum Dis*. 2009;68:1387-1394.

Efficacy and Safety of Recently Approved Drugs and Agents in Late-Phase Development

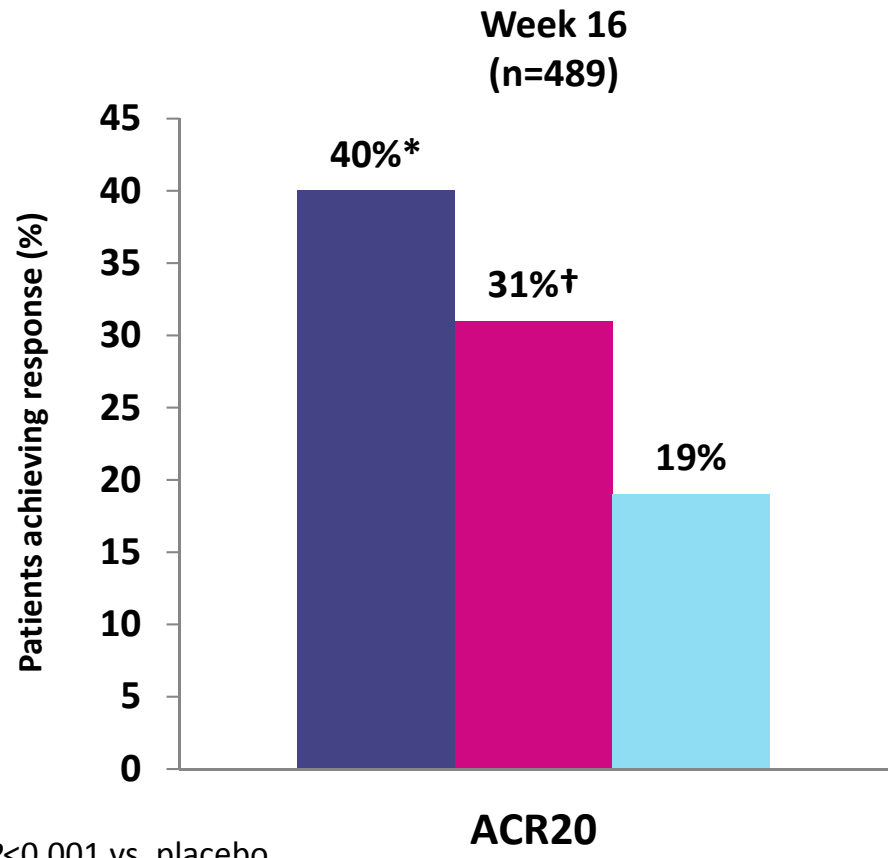
Newly Approved Drugs and Agents in Late-Phase Development for Psoriatic Arthritis

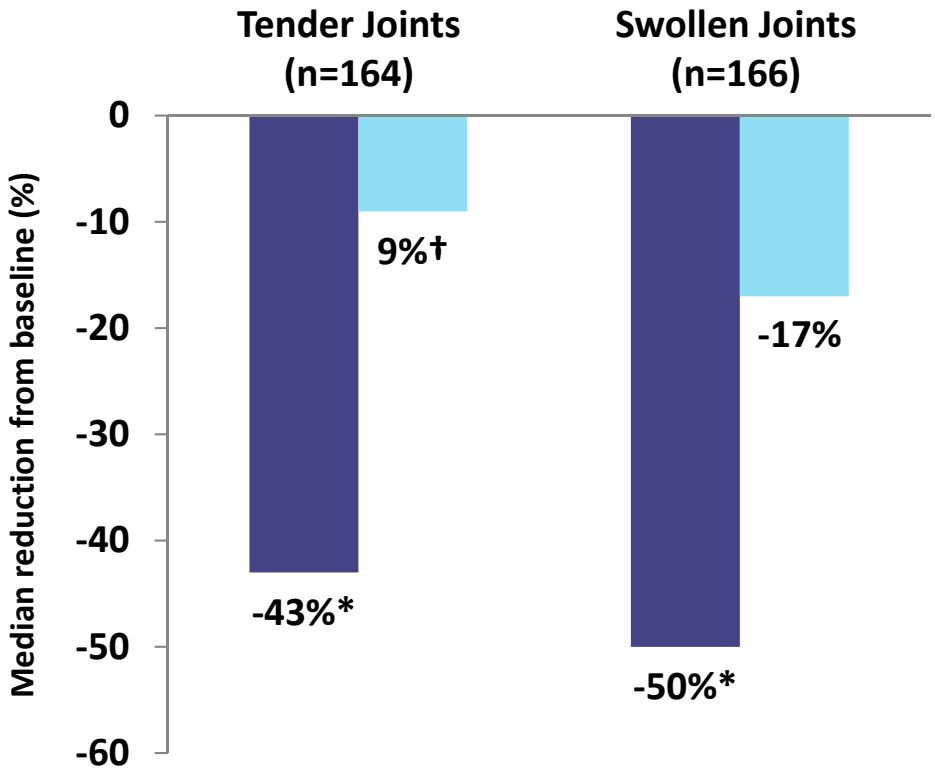
Drug	Mechanism of Action	Dosing & Administration	Status
Apremilast (Otezla®)/Celgene[1]	Small molecule inhibitor of phosphodiesterase 4	Oral administration BID dosing	Approved September 2014
Ustekinumab (Stelara®)/Janssen[2]	Inhibits IL-12 and IL-23 cytokines	SC injection; 45 mg initially, and 4 weeks later, followed by 45 mg every 12 weeks	Approved September 2013
Secukinumab (Cosentyx®)/ Novartis[3]	Selectively binds to IL-17A and inhibits its interaction with the IL-17 receptor	Subcutaneous (SC) injection at Weeks 0, 1, 2, 3, and 4 followed by 300 mg every 4 weeks	Approved for cutaneous psoriasis January 2015; Phase 3 for PsA
Brodalumab/ Amgen & AstraZeneca[4]	IL-17 receptor antagonist	SC injection every two weeks	Phase 3
Ixekizumab/Lilly[5]	IL-17A antagonist	SC injection every two or four weeks	Phase 3
Tofacitinib(Xeljanz®)/ Pfizer[6]	Janus kinase (JAK) inhibitor	Oral administration BID dosing	Phase 3

1. Otezla® [package insert]. Summit, NJ: Celgene Corporation; 2014. 2. Stelara® [package insert]. Horsham, PA: Janssen Biotech, Inc.; September 2013. 3. Cosentyx® [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp.; January 2015. 4. AstraZeneca, LP. Press release. November 25, 2014. 5. Eli Lilly and Company. Press release. August 21, 2014. 6. Pfizer Inc. Press release. May 23, 2014.

Apremilast Improved ACR20 and Joint Symptoms in Psoriatic Arthritis

Randomized, Double-blind, Placebo-controlled Trial Stratified for DMARD Use: Data from the PALACE 1 Trial





*P<0.001 vs. placebo
†P<0.02 vs. placebo

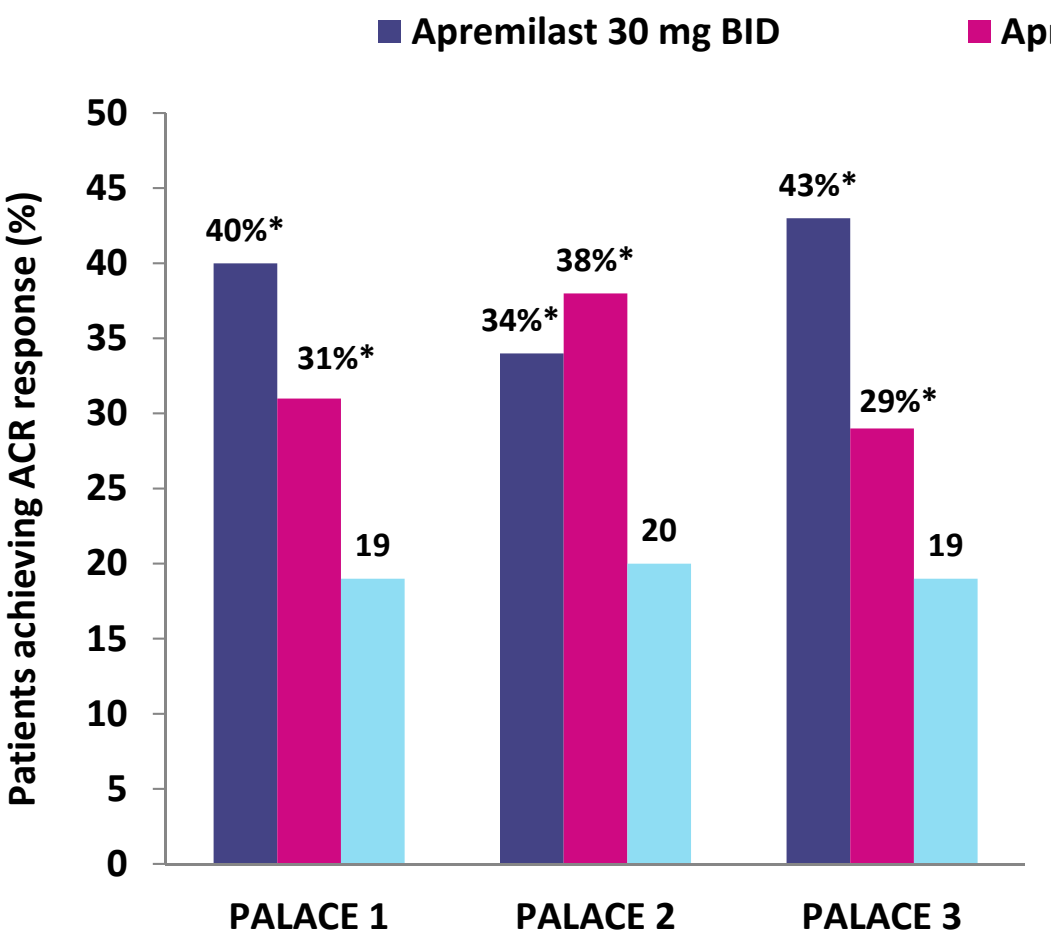
*p<0.0001 vs. placebo.

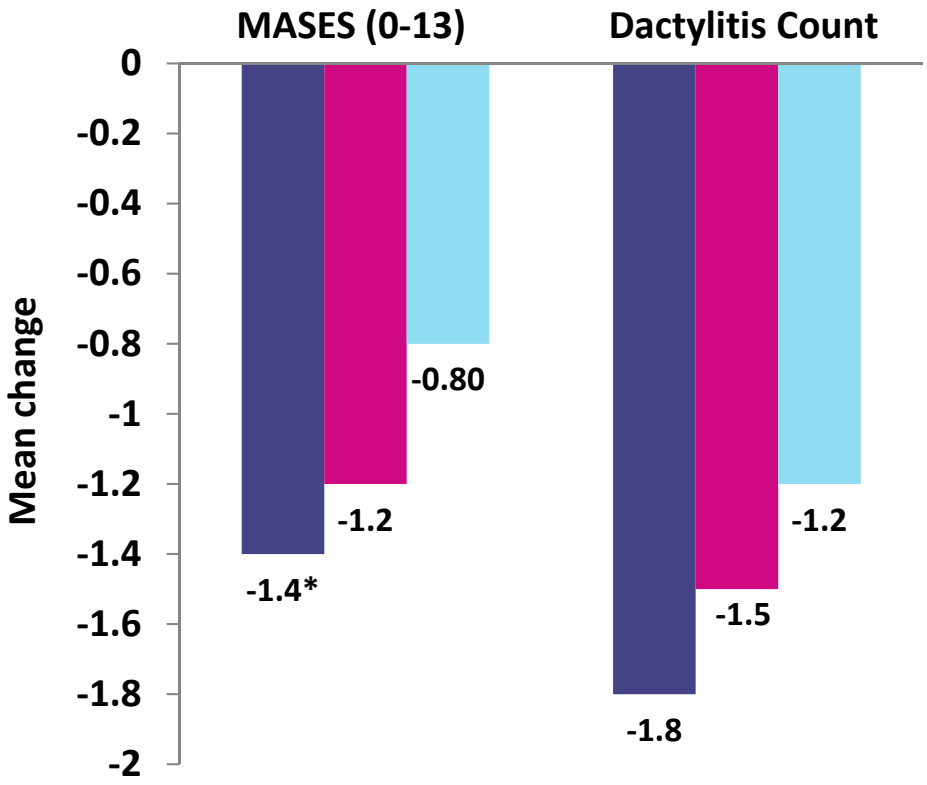
Apremilast 30 mg BID Apremilast 20 mg BID Placebo

Kavanaugh A, et al. *Ann Rheum Dis*. 2014;73:1020-1026.

ACR20=American College of Rheumatology 20% improvement criteria; DMARD=disease-modifying anti-rheumatic drug; PALACE= Psoriatic Arthritis Long-term Assessment of Clinical Efficacy 1.

Apremilast Improved Enthesitis and Dactylitis





*$P<0.02$ vs. placebo.

Gladman D, et al. *Arthritis Rheum*. 2013;65(suppl 10):816.
Kavanaugh A, et al. *Ann Rheum Dis*. 2014;73:1020-1026.

Apremilast Safety: Most Common Adverse Reactions

AEs Reported in ≥2% of Patients Receiving Apremilast 30 mg BID and ≥1% in Those Receiving Placebo

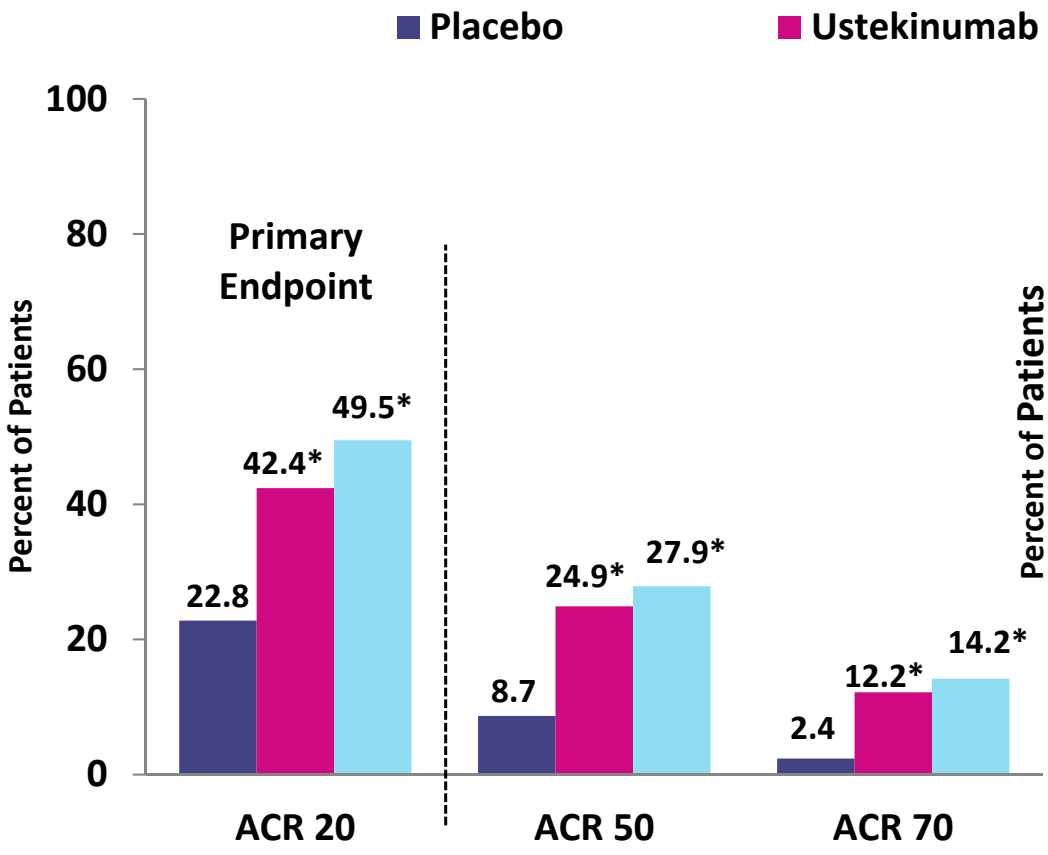
Adverse reaction	Apremilast 30 mg BID		Placebo	
	Day 1-5 (n=497) n (%)	Day 6-112 (n=493) n (%)	Day 1-5 (n=495) n (%)	Day 6-112 (n=490) n (%)
Diarrhea	46 (9.3)	38 (7.7)	6 (1.2)	8 (1.6)
Nausea	37 (7.4)	44 (8.9)	7 (1.4)	15 (3.1)
Headache	24 (4.8)	29 (5.9)	9 (1.8)	11 (2.2)
Upper respiratory tract infection	3 (0.6)	19 (3.9)	3 (0.6)	9 (1.8)
Vomiting	4 (0.8)	16 (3.2)	2 (0.4)	2 (0.4)
Nasopharyngitis	1 (0.2)	13 (2.6)	1 (0.2)	8 (1.6)
Abdominal pain	3 (0.6)	10 (2.0)	0 (0.0)	1 (0.2)

- Reports of the most common adverse reactions occurred within the first 2 weeks
- These events tended to resolve over time with continued dosing
- Most common adverse reactions leading to discontinuation: nausea (1.8%), diarrhea (1.8%), and headache (1.2%)

Kavanaugh A, et al. *Ann Rheum Dis*. 2014;73:1020-1026.
Otezla® [package insert]. Summit, NJ: Celgene Corporation; 2014.

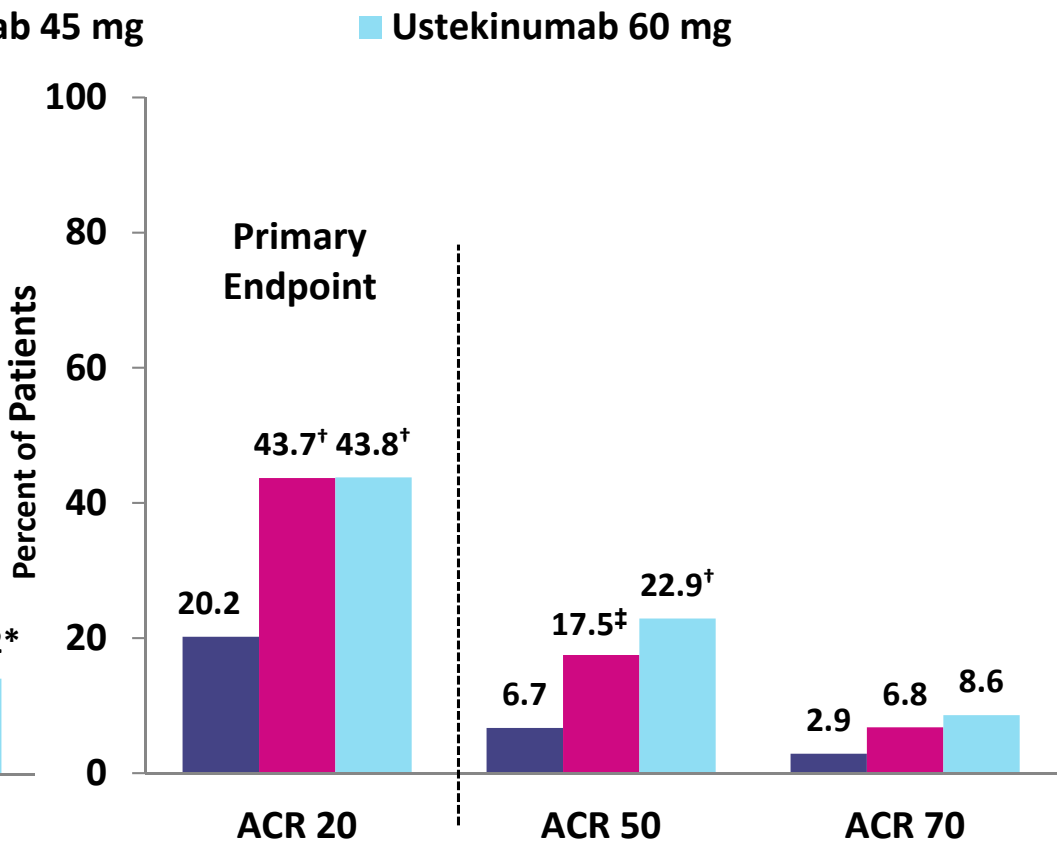
Ustekinumab In Psoriatic Arthritis: ACR 20/50/70 Responders at Week 24

PSUMMIT I Trial[1] (n=615)



*P<0.0001 vs. placebo

PSUMMIT II Trial[2] (n=312)



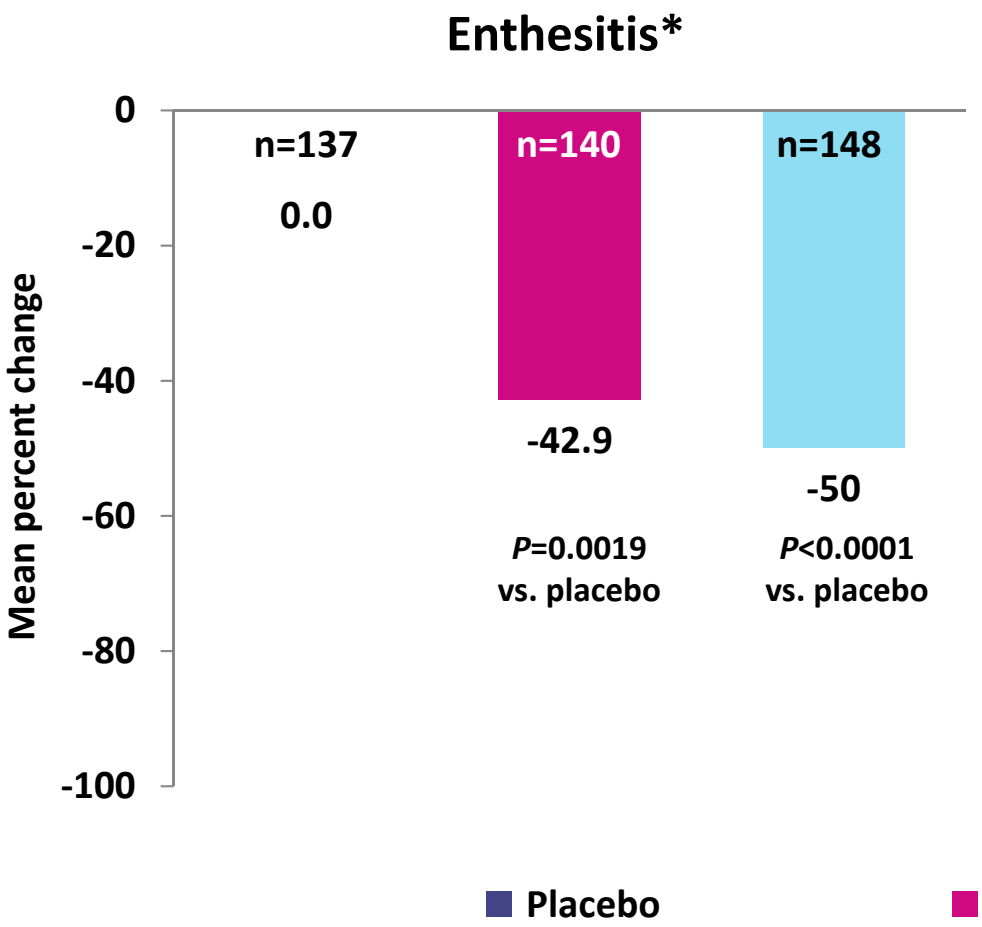
- Patients previously treated with 1 prior anti-TNF agent: 81 (45%)
- Patients previously treated with 2 prior anti-TNF agents: 54 (30%)
- Patients previously treated with ≥3 prior anti-TNF agents: 45 (25%)

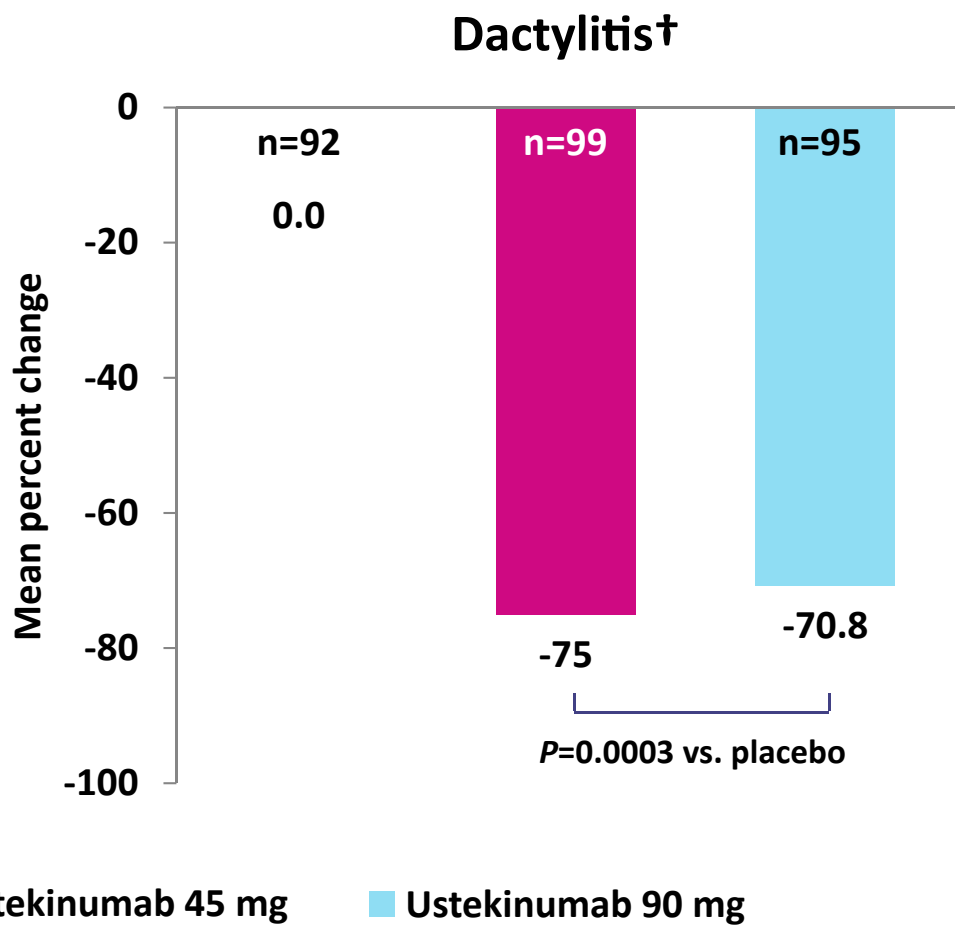
†P<0.001 vs. placebo; ‡P=0.018 vs. placebo.

1. McInnes IB, et al. *Lancet.* 2013;382:780-789.
2. Ritchlin C, et al. *Ann Rheum Dis*. 2014;73:990-999.

Ustekinumab In Psoriatic Arthritis: Change in Enthesitis and Dactylitis Scores at Week 24

Data from the PSUMMIT I Trial





Placebo Ustekinumab 45 mg Ustekinumab 90 mg

*$P<0.001$ vs. placebo; †$P=0.018$ vs. placebo.

McInnes IB, et al. *Lancet.* 2013;382:780-789.

Pooled Ustekinumab Safety During the Placebo-Controlled Period of PSUMMIT I & II

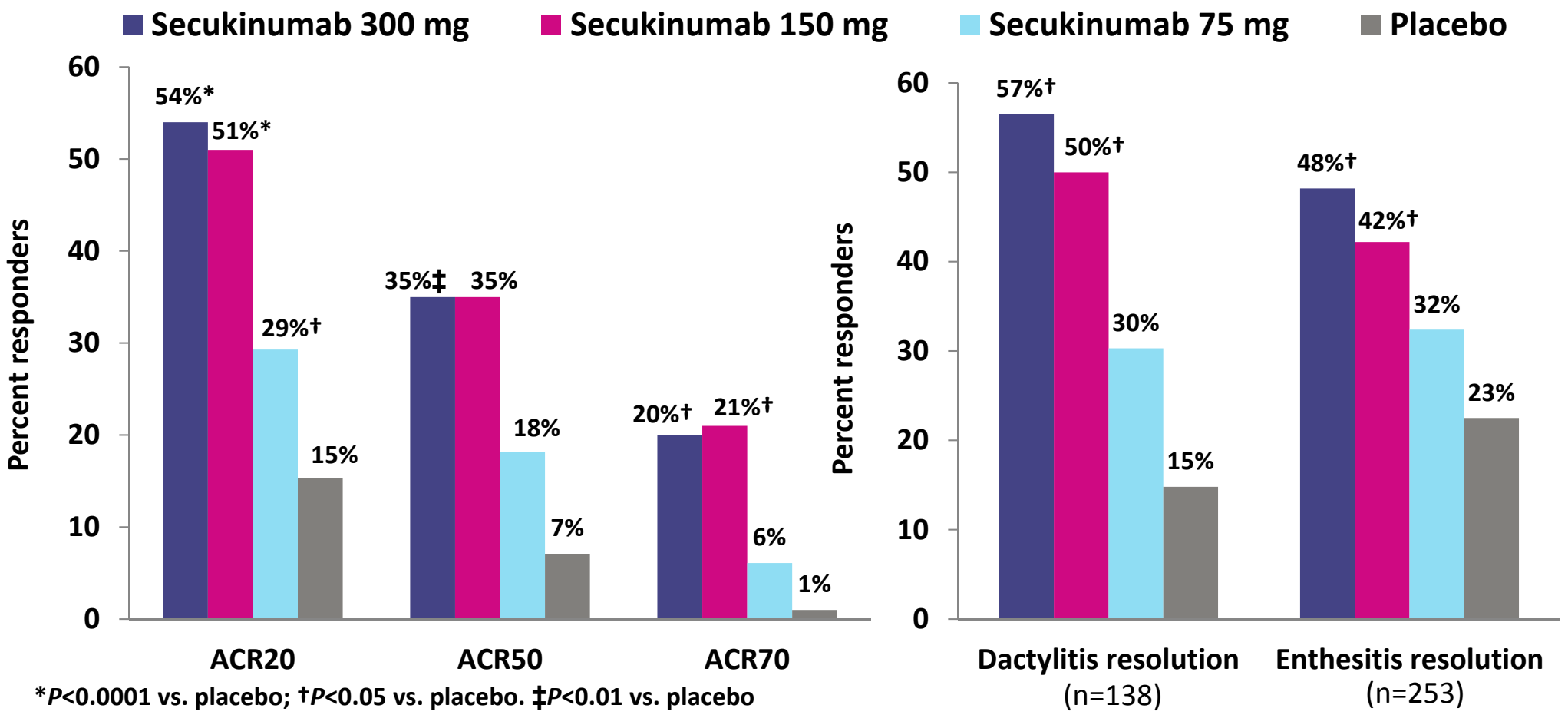
- Through Week 16, no cases of tuberculosis or opportunistic infections were reported
- Through Week 24, injection-site reactions occurred in 14 (1.5%) PBO patients, 6 (1.5%) ustekinumab 45 mg-treated patients, and 8 (2.2%) ustekinumab 90 mg-treated patients

	Placebo (n=309)	Ustekinumab 45 mg (n=308)	Ustekinumab 90 mg (n=308)
Average duration of f/u, weeks	15.79	16.15	16.01
Average exposure, no. of administrations	1.96	1.99	1.97
Adverse events (AEs)	148 (47.9)	149 (48.4%)	152 (49.4%)
Most common AEs (occurring in ≥3% of patients)			
Nasopharyngitis	13 (4.2%)	16 (5.2%)	21 (6.8%)
Headache	6 (1.9%)	15 (4.9%)	9 (2.9%)
Upper respiratory tract infection	14 (4.5%)	10 (3.2%)	12 (3.9%)
Arthralgia	4 (1.3%)	9 (2.9%)	10 (3.2%)
Serious AEs	9 (2.9%)	4 (1.3%)	4 (1.3%)
Infections	68 (22.0%)	64 (20.8%)	66 (21.4%)
Serious infections	1 (0.3%)	0	0
Infections requiring treatment	38 (12.3%)	28 (9.1%)	30 (9.7%)
AEs leading to discontinuation	11 (3.6%)	3 (1.0%)	4 (1.3%)
Malignancies	0	0	1 (0.3%)

McInnes IB, et al. *Lancet.* 2013;382:780-789.; Ritchlin C, et al. *Ann Rheum Dis*. 2014;73:990-999.; Stelara® [package insert]. Horsham, PA: Janssen Biotech, Inc.; 2014.

Treatment of Psoriatic Arthritis with Secukinumab: Summary of Select 24-Week Efficacy Results

Data from the FUTURE 2 Trial



*P<0.0001 vs. placebo; †P<0.05 vs. placebo. ‡P<0.01 vs. placebo

- **Adults (n=397) with active PsA stratified according to prior anti-TNF therapy**
- **Primary endpoint: ACR20 response at Week 24**

FUTURE 2=Efficacy at 24 Weeks With Long-Term Safety, Tolerability and Efficacy up to 5 Years of Secukinumab in Patients of Active Psoriatic Arthritis

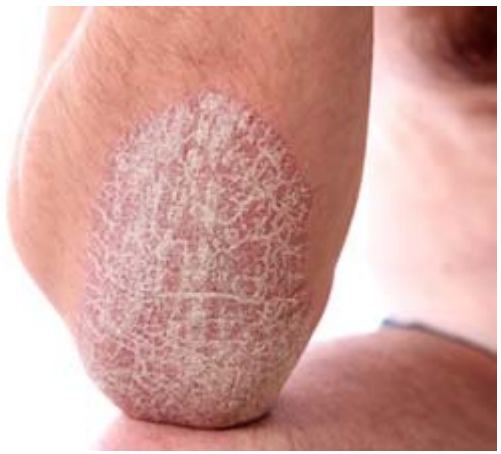
McInness IB, et al. Presented at the American College of Rheumatology Annual Meeting. November 18, 2014. Late breaking abstract #536.

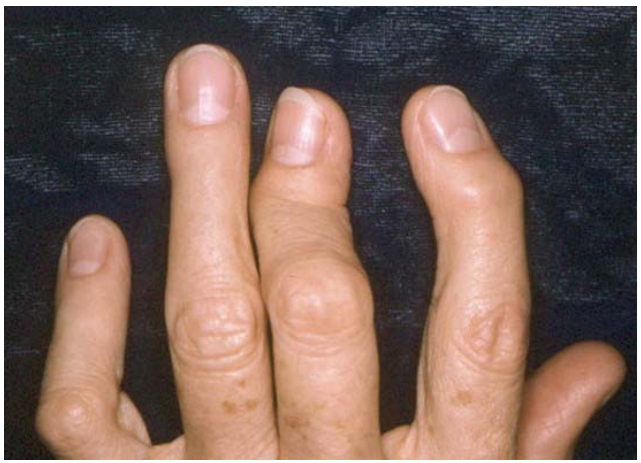
Secukinumab Safety: No New or Unexpected Safety Events Observed

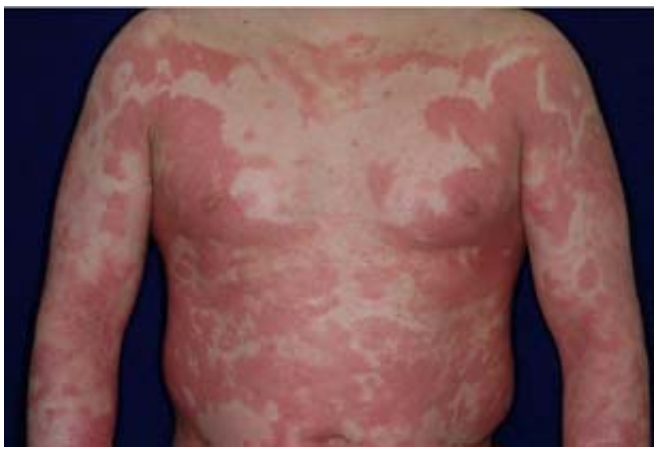
- No safety signals were noted; adverse events were few and comparable to placebo
- Overall incidence of AEs up to Week 16 was similar across secukinumab dose groups and placebo
  - 53.8% of subjects treated with secukinumab
  - 58.2% of subjects receiving placebo
- Serious AEs reported in 3.3% of secukinumab-treated patients and 2.0% of subjects receiving placebo

McInness IB, et al. Presented at the American College of Rheumatology Annual Meeting. November 18, 2014. Late breaking abstract #536.

Multidisciplinary Management of Patients with Psoriatic Disease







Role of the Rheumatologist in the Management of Psoriasis Arthritis

- Management of psoriatic joint disease often requires the expertise of a rheumatologist in conjunction with dermatology[1]
- Multidisciplinary care may facilitate the diagnosis of joint disease and offers a more comprehensive treatment approach for patients with both psoriasis and psoriatic arthritis[1]

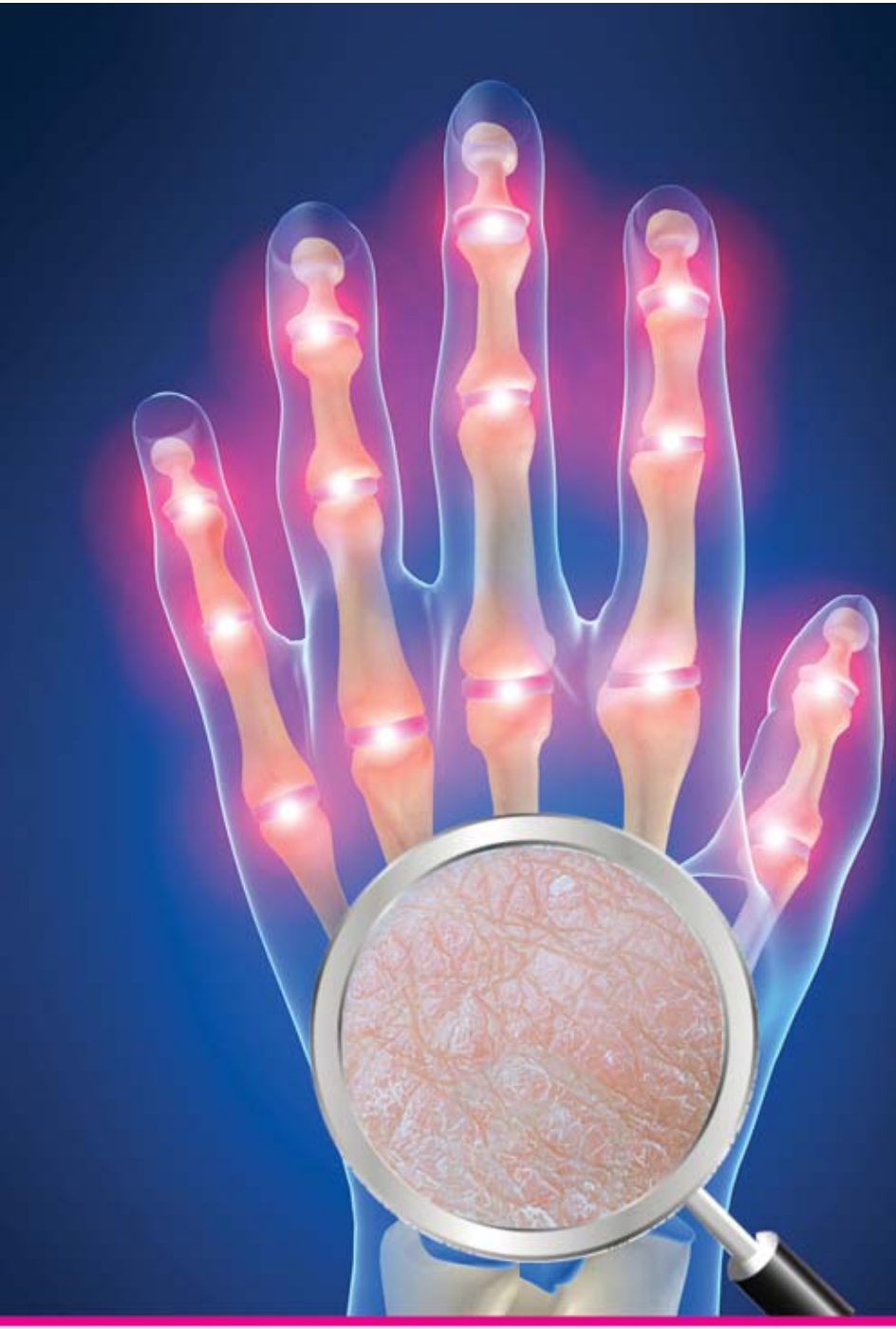
Sample Referral Criteria for Patients with Psoriatic Disease[2]

From Dermatology	From Rheumatology
• Peripheral arthritis • Dactyilitis • PIP/DIP synovitis • Enthesitis • Inflammatory low back pain • Unspecified joint pain • Asymmetrical oligoarthritis	• Patients with suspected arthritis and psoriasis • Patients with poor skin and PsA evolution • Patients with PsA and severe skin psoriasis (PASI) • Suspected skin complications associated with treatment

1. Velez NF, et al. *Arch Dermatol Res*. 2012;304:7-13.
2. Luelmo J, et al. *Rheumatol Clin*. 2014;10:141–146.

Summary

- Psoriatic arthritis is characterized by stiffness, pain, swelling, and tenderness of the joints and surrounding ligaments and tendons and may develop in up to 30% of patients with psoriasis
- Despite being considered a “mild disease”, more than half of all patients develop joint complications
- Early diagnosis and treatment can lead to remission of symptoms and reduction in utilization of health care resources
- Several new agents have been introduced with novel mechanisms of action, including the first oral therapy approved for psoriatic arthritis (apremilast)
- Multidisciplinary care may facilitate the diagnosis of joint disease and offers a more comprehensive treatment approach for patients with psoriatic disease



Examining the Latest Clinical Findings for Psoriasis and Psoriatic Arthritis to Enhance Managed Care Decision-Making

Jointly provided by Annenberg Center for Health Sciences at Eisenhower and Impact Education, LLC in collaboration with Postgraduate Institute for Medicine

Annenberg Center For Health Sciences at Eisenhower

Impact Education, LLC

PIM Postgraduate Institute for Medicine

This activity is supported by independent educational grants from Celgene Corporation, Janssen Biotech, Inc., and Novartis Pharmaceuticals Corporation.

Applying Comparative Effectiveness Research (CER) as a Decision-Support Tool

Jeffrey Dunn, PharmD, MBA

Senior Vice President

Chief Clinical Officer

VRx Pharmacy Services, LLC

Agenda

- Psoriatic disease management challenges
- Potential value of comparative effectiveness research (CER) in supporting benefit design decisions
- Challenges associated with CER in psoriatic disease
- Implementation of CER into psoriatic disease pharmacy benefit design decision making
- Summary

Psoriatic Disease Is Costly to Manage

- Drug costs
  - Acquisition
    - Pipeline burgeoning with novel biologic agents
- Administrative burden
  - Elusiveness of data to determine total costs due to lack of transparency driven by medical/pharmacy benefit designs
  - Patient education/health management programs
  - Management of safety monitoring
- Total costs need to be evaluated
  - Direct and indirect
  - Contract implications of indications
  - Role of Patient Assistance Programs

Management of Psoriatic Disease Can Challenge Provider Relations

- Fee schedules and reimbursement
  - Misaligned incentives
- Location/place of therapy
- Route of administration
- Support for mandated clinical pathways
- Delivery channels and other provider network issues

Psoriatic Disease and Benefit Design Challenges

- Impact of drug-formulary or benefit design decisions on health outcomes generally not measured
  - Medical vs. pharmacy
  - Reassessments of drugs for inclusion, exclusion, or change in formulary positioning
  - Evaluation of the real-world ability of drugs to improve outcomes
- Motivation for implementing benefit design changes
  - Driven by cost
  - Delivery channel complexity
  - Copay vs. coinsurance
  - Specialty tiers
  - Introduction of oral biologics
  - Anticipation of biosimilars

Biskupiak JE, et al. *J Manag Care Pharm*. 2012;18:S19-S28.

Decision Making in Psoriatic Disease is Challenged by Lack of Comparative Trials

- Lack of head-to-head trials comparing individual agents
- Large comparison trials are expensive and time consuming
- Difficult to conduct cross-trial comparisons due to differences in
  - Trial design
  - Sample size
  - Patient characteristics
  - Disease severity
  - Statistical analysis plan
  - Endpoints

1. Williams HC, Delavalle RP. *J Invest Dermatol*. 2012;132:1008-1172.
2. Nambudiri VE, Qureshi A. *J Invest Dermatol*. 2013; 133, e5. doi:10.1038/jid.2012.497.

Why Comparative Effectiveness Research?

- Pharmacists, physicians, payers, policy makers, and patients must often rely on incomplete data when making health care decisions
- Lack of head-to-head comparisons of competing treatment alternatives can lead to a “trial and error” approach to decision making
- If effectively designed and conducted, Comparative Effectiveness Research (CER) can help fill data gaps
  - Used to compare drug therapies in the absence of head-to-head data
  - Applicable to a wide variety of practice settings and diversity of patients

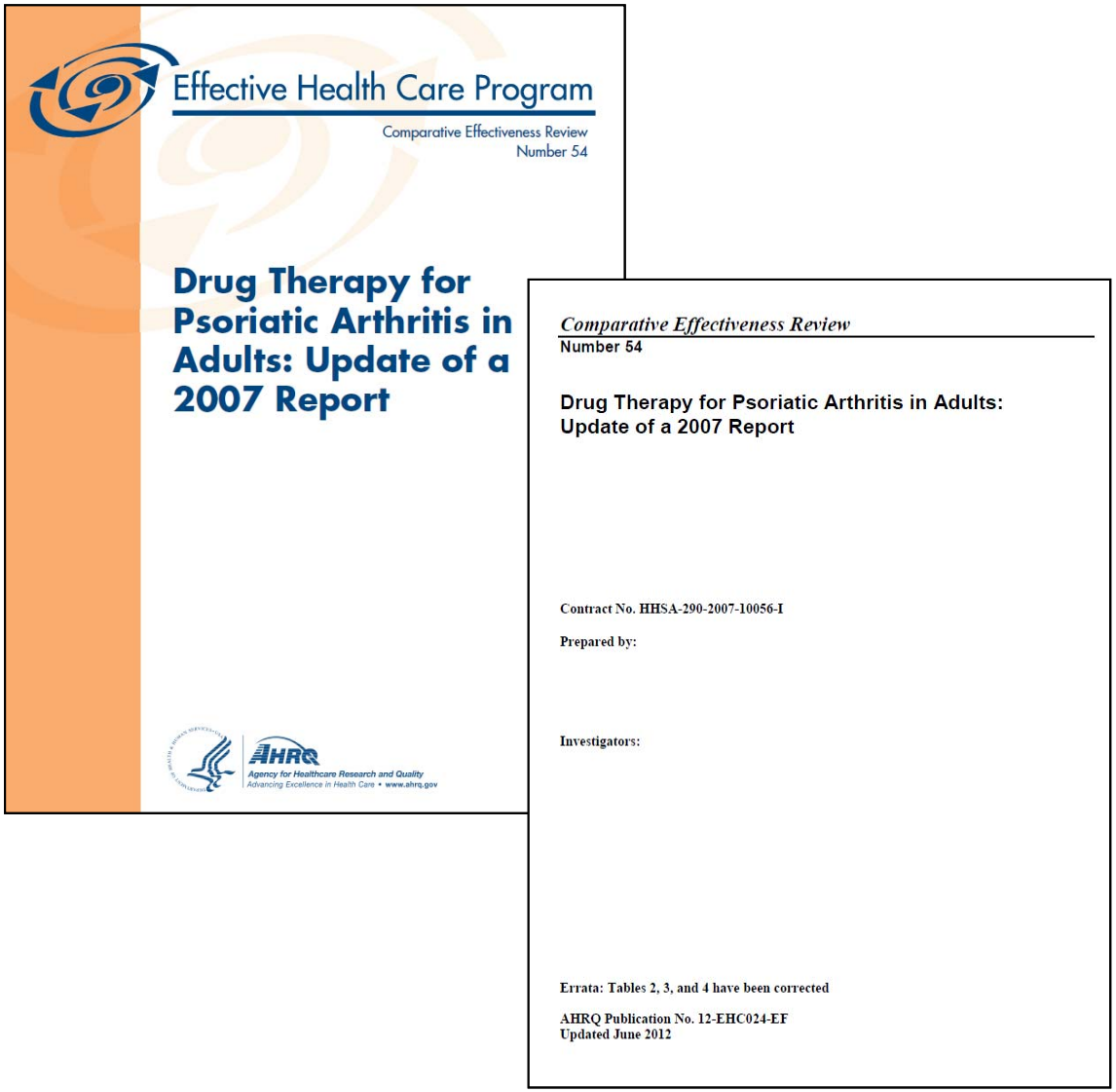
Brixner DI, Oderda G. *J Manag Care Pharm*. 2012;18(Suppl. 4-a):S3-S4.

What is Comparative Effectiveness Research?

- Comparative effectiveness research (CER) aims to inform health care decision making[1]
- Involves research that compares therapeutics, devices, diagnostic tests, interventions against each other[1]
- Weighs evidence on clinical effectiveness, benefits, and harms of different diagnostic and treatment options[2]

1. Agency for Healthcare Research and Quality. What Is Comparative Effectiveness Research. Available at: http://effectivehealthcare.ahrq.gov/index.cfm/what-is-comparative-effectiveness-research1/. Accessed February 17, 2015.
2. Nambudiri VE, Qureshi A. *J Invest Dermatol*. 2013;133, e5. doi:10.1038/jid.2012.497.

Application of CER to Psoriatic Disease



- CER analyses of therapies for psoriatic disease are limited
- Decision makers often extrapolate results of CER analyses of rheumatoid arthritis therapies to psoriasis and psoriatic arthritis

Donahue KE, et al. Comparative Effectiveness Review No. 54. http://www.effectivehealthcare.ahrq.gov/ehc/products/464/1045/CER54_PsoriaticArthritisDrugTherapies_FinalReport_20120601.pdf. Accessed February 27, 2015.

Example of CER for Psoriatic Arthritis: Summary of Findings for Traditional DMARDs

Comparisons	Efficacy, Effectiveness, and Harms
Leflunomide	• No head-to-head studies; current evidence limited to placebo controlled trials • Unable to draw conclusions on the comparative efficacy or harms of leflunomide vs. other treatments (Evidence Grade: Insufficient) • Single study reported statistical, but not clinical, improvement in health-related QoL, disease activity, and functional capacity (Evidence Grade: Low)
Methotrexate	• No head-to-head studies; current evidence limited to placebo controlled trials • Unable to draw conclusions on the comparative efficacy or harms of methotrexate (MTX) vs. other treatments (Evidence Grade: Insufficient) • Compared with placebo in one study, MTX resulted in greater improvement in physician assessment of disease activity vs. placebo (Evidence Grade: Low)
Sulfasalazine	• No head-to-head studies; current evidence limited to placebo controlled trials • Unable to draw conclusions on the comparative efficacy of sulfasalazine vs. other treatments (Evidence Grade: Insufficient) • Systematic review reported that sulfasalazine reduced disease activity (Evidence Grade: Moderate)

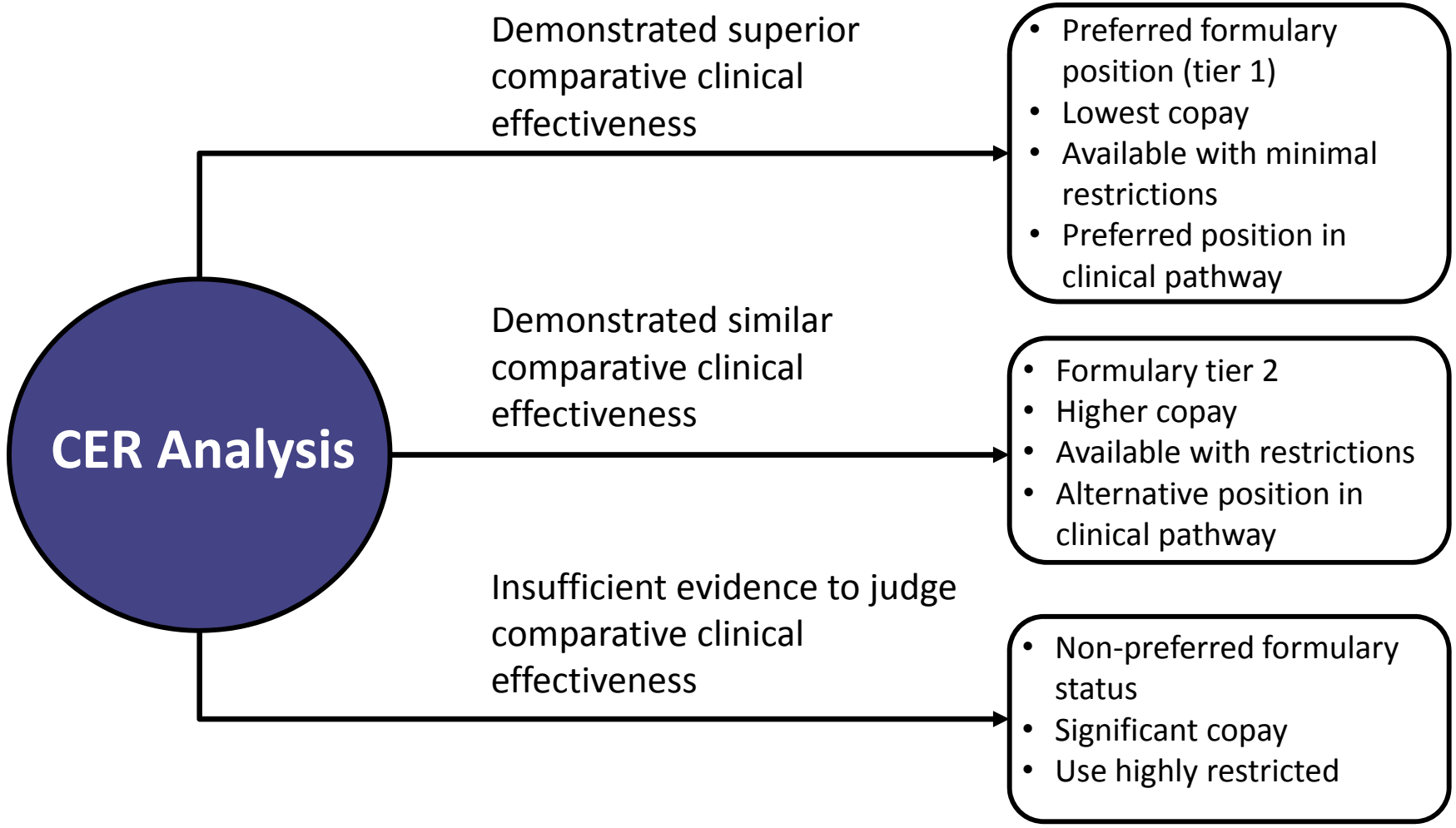
Donahue KE, et al. Comparative Effectiveness Review No. 54. http://www.effectivehealthcare.ahrq.gov/ehc/products/464/1045/CER54_PsoriaticArthritisDrugTherapies_FinalReport_20120601.pdf. Accessed February 27, 2015.

Example of CER for Psoriatic Arthritis: Summary of Findings for Biologic Agents

Comparisons	Efficacy, Effectiveness, and Harms
Biologic DMARD + Oral DMARD vs. Biologic DMARD or Oral DMARD	• Compared to anti-TNF monotherapy (adalimumab, etanercept, or infliximab), MTX + anti-TNF produced similar disease activity response rates (Evidence Grade: Low) • Unable to draw conclusions on the comparative harms of biologic DMARD + oral DMARD and other treatments (Evidence Grade: Insufficient) • Systematic review reported that both TNF inhibitors and sulfasalazine are effective, but did not achieve a minimal clinically important difference (Evidence Grade: Insufficient)
Biologic	• No head-to-head studies • Unable to draw conclusions on the comparative efficacy of biologics vs. other treatments (Evidence Grade: Insufficient) • Compared with placebo, adalimumab, etanercept, golimumab, and infliximab led to greater improvement in disease activity, functional capacity and health-related quality of life (Evidence Grade: Low to Moderate) • Etanercept had a lower rate of withdrawals due to AEs vs. in a prospective cohort study (Evidence Grade: Low) • Evidence of harm limited to placebo-controlled trials, where AEs are not the primary outcome; overall AE profiles appeared to be similar for biologic DMARDs and placebo (Evidence Grade: Low)

Donahue KE, et al. Comparative Effectiveness Review No. 54. http://www.effectivehealthcare.ahrq.gov/ehc/products/464/1045/CER54_PsoriaticArthritisDrugTherapies_FinalReport_20120601.pdf. Accessed February 27, 2015.

Using CER to Support Benefit Design Decisions



Biskupiak JE, et al. *J Manag Care Pharm*. 2012;18:S19-S28.

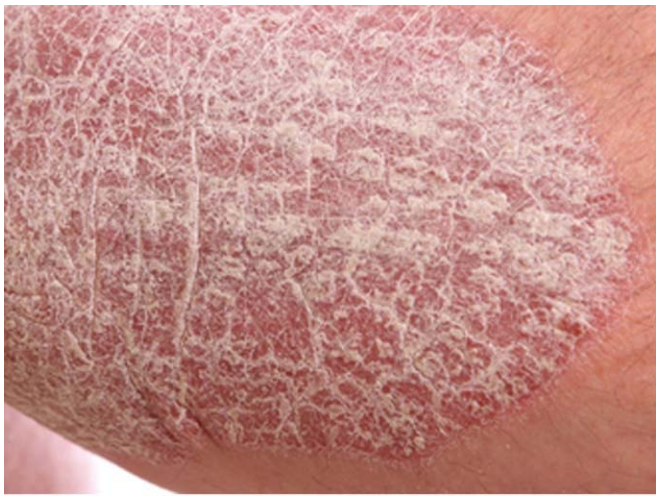
Using CER to Change Practice

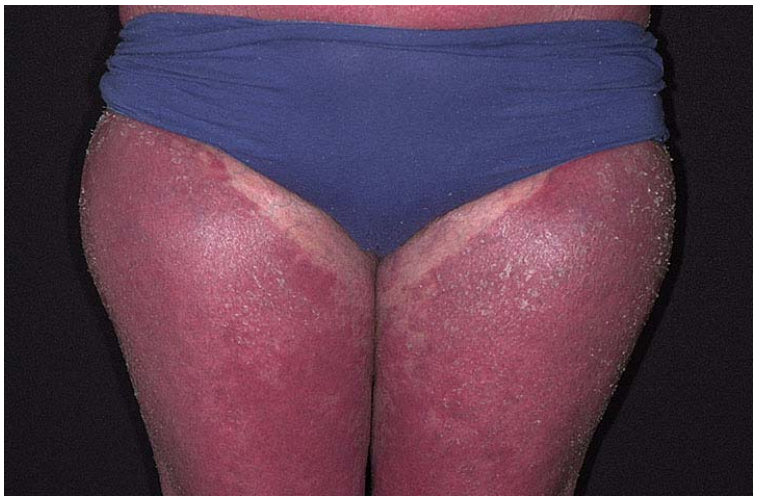
- Establishing parameters to measure improvements
  - Outcomes
  - Reduction in costs
  - Increase in value
- Determining threshold of positive effect to alter current behavior
  - Patients
  - Providers
  - Payers

Zwelling L. Comparative effectiveness research: how can it change practice? http://healthaffairs.org/blog/2011/04/18/comparative-effectiveness-research-how-can-it-change-practice/. April 18, 2011. Accessed February 17, 2015.

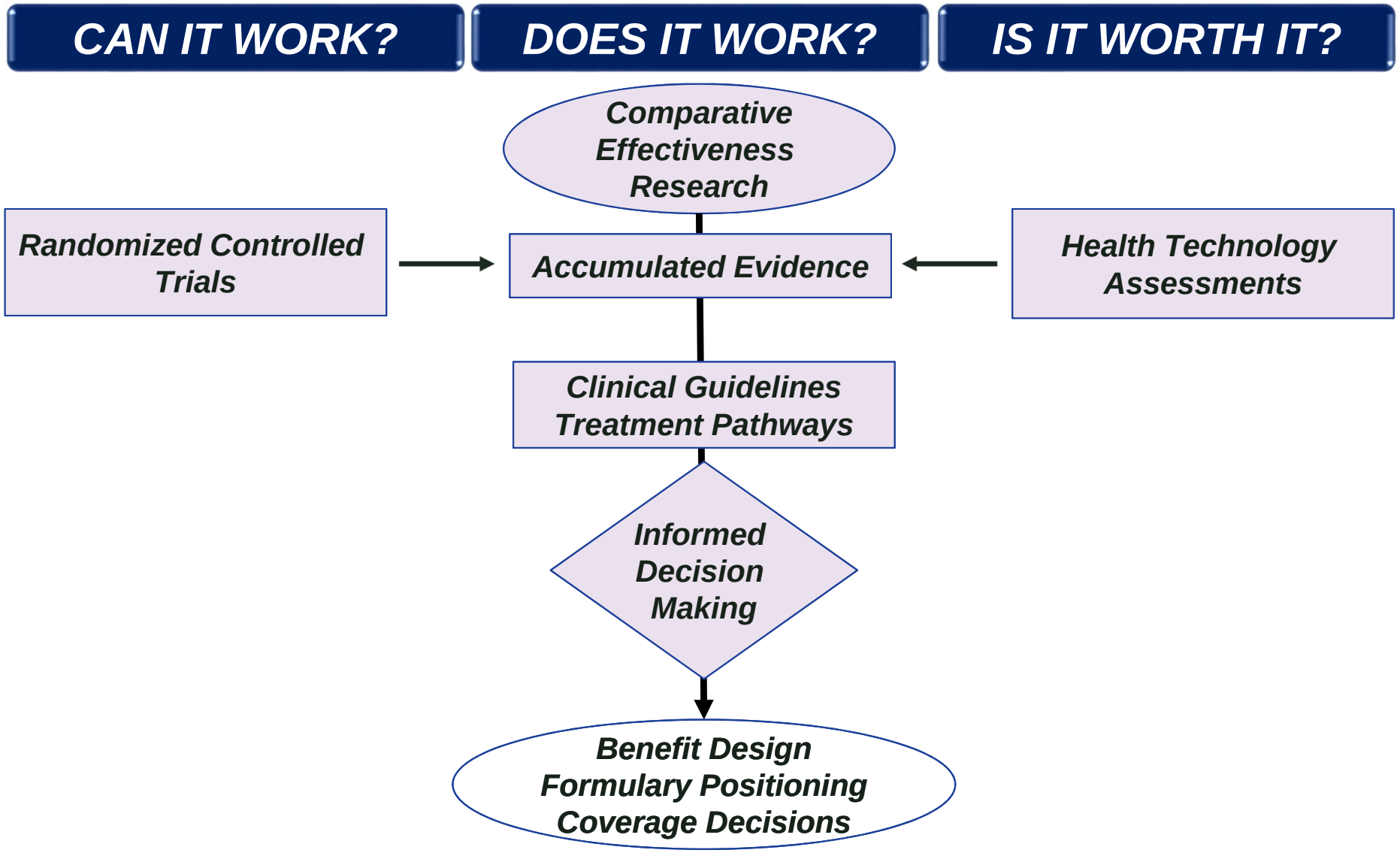
Using CER to Support Clinical Decision Making

- Guideline concordant care
  - Reduces variability in outcomes
  - Reduces variability in costs
  - Invests in patients' health and improves health outcomes
  - Reduces wasteful spending by using evidence to optimize efficacy and minimize toxicity





Using CER to Differentiate Treatment Alternatives



Drummond MF, et al. *Int J Technol Assess Health Care*. 2008;24:244-258.

Using CER to Evaluate Treatment Alternatives Without Head-to-Head Trials

- Identify and target key trials with similar patient characteristics, outcome measures, inclusion/exclusion criteria, etc.
- Evaluate drug benefit minus placebo benefit over defined time frame of defined and appropriate outcome measure(s)
- Determine appropriate costs over same time period
- Divide cost into drug benefit
- Compare cost to achieve predefined response
  - "How much do we pay for an outcome with all of the drugs"
- Have to hold industry accountable

Psoriasis Literature CER

Real-world comparison (Dermatology Clinical Effectiveness Research Network sites)

- Population**:**
  - N=203 on systemic monotherapy (acitretin, cyclosporine, infliximab) or common combination therapy (adalimumab, etanercept, infliximab, MTX)
  - N=168 on MTX
- Results:
  - All drugs/combinations more likely to produce clear/almost clear skin vs. MTX
  - No differences when defined by Health-Related Quality of Life
- Conclusions:
  - Clinical trials may overestimate effectiveness
  - Physician-reported response rates were different, but no absolute differences and no differences in Patient Reported Outcomes

Takeshita, et al. *J Am Acad Dermatol.* 2014;71:1167-1175.

Psoriasis Literature CER

- 14 studies (4 ustekinumab, 3 adalimumab, 3 infliximab, 4 etanercept)
  - Etanercept as reference drug
  - PASI 75 as primary outcome
- Conclusions:
  - Ustekinumab, adalimumab, and infliximab statistically superior to etanercept but…
    - 95% confidence interval does not achieve clinical relevance
    - Choice depends on safety, individual contraindications, and cost

Galvan-Banqueri, et al. *J Clin Pharm Ther.* 2013;38:121-130.

Inflammatory Disease

	Actemra®[1]	Simponi®[2]	Cimzia®[3]	Rituxan®[4]*	Orencia®[5]	Humira®[6]	Enbrel®[7]	Remicade®[8]	Stelara®[9]	Otezla®[10]
MOA	Anti-IL-6ra	Anti-TNF	Anti-TNF	Anti-B Cells	Anti-T Cell	Anti-TNF	Anti-TNF	Anti-TNF	IL-12 and 23ra	PDE4 Inhibitor
					Indications					
RA	x	x	x	x	x	x	x	x		
Juvenile RA	x				x	x	x			
Psoriatic Arthritis		x	x			x	x	x	x	x
Ankylosing Spondylitis		x	x			x	x	x		
Crohn's			x			x		x		
Plaque Psoriasis						x	x	x	x	x
Ulcerative Colitis		x				x		x		

* Rituxan® also indicated for cancer

1. Actemra® [package insert]. South San Francisco, CA: Genentech, Inc.; November 2014; 2. Simponi® [package insert]. Horsham, PA: Janssen Biotech, Inc.; December 2014; 3. Cimzia® [package insert]. Smyrna, GA: UCB, Inc.; October 2013; 4. Rituxan® [package insert]. South San Francisco, CA: Genentech, Inc.; August 2014; 5. Orencia® [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; December 2014; 6. Humira® [package insert]. North Chicago, IL: AbbVie Inc.; December 2014; 7. Enbrel® [package insert]. Thousand Oaks, CA: Immunex Corporation; November 2013; 8. Remicade® [package insert]. Horsham, PA: Janssen Biotech, Inc.; January 2015; 9. Stelara® [package insert]. Horsham, PA: Janssen Biotech, Inc.; September 2013; 10. Otezla® [package insert]. Summit, NJ: Celgene Corporation; 2014.

Summary of Clinical Trials: Plaque Psoriasis

Parameter	Amevive®[1] (alefacept)	Humira®[2] (adalimumab)	Enbrel®[3] (etanercept)		Remicade®[4] (infliximab)	Stelara®[5] (ustekinumab)		Otezla®[6] (apremilast)
Dose	15 mg IM q week	40 mg SQ eow	25 mg SQ 2x/wk	50 mg SQ each wk	3-5 mg/kg IV q 8 w	45 mg SQ q 12 w	90 mg SQ q 12 w	30 mg po bid
PASI 75 Score (3 months)	14-21% (4-5%)		32% (4%)	47% (4%)	70-75% (2%)	73% (4%)	49% (3%)	29-33%
PASI 75 Score (6 months)	NR	71% (7%)	41% (NA)	54% (NA)	36-54% (NA)	NR	NR	NR

1. Amevive®[package insert]. Deerfield, IL: Astellas Pharma US, Inc.; May 2011; 2. Humira® [package insert]. North Chicago, IL: AbbVie Inc.; December 2014; 3. Enbrel® [package insert]. Thousand Oaks, CA: Immunex Corporation; November 2013; 4. Remicade® [package insert]. Horsham, PA: Janssen Biotech, Inc.; January 2015; 5. Stelara® [package insert]. Horsham, PA: Janssen Biotech, Inc.; September 2013; 6. Otezla® [package insert]. Summit, NJ: Celgene Corporation; 2014.

Cost-Effectiveness: 12 Months

Drug*	PASI 75 3 months (- Placebo)	PASI 75 6 months (- Placebo)	Annual $	$/PASI 75
Alefacept[1]	16%	NR	Off market	NA
Adalimumab[2]	NR	64%	37,877	59,183
Etanercept[3]	43%	54% (placebo NR)	38,657	77,314
Infliximab[4] (average dose)	73%	54% (placebo NR)	29,704	55,007
Ustekinumab[5]	69%	NR	30,645-61,289	44,413-88,825
Apremilast[6]	33%	NR	22,813	69,130
Methotrexate[7]			40.32	

Internal pricing. Clinical data at 6 months.

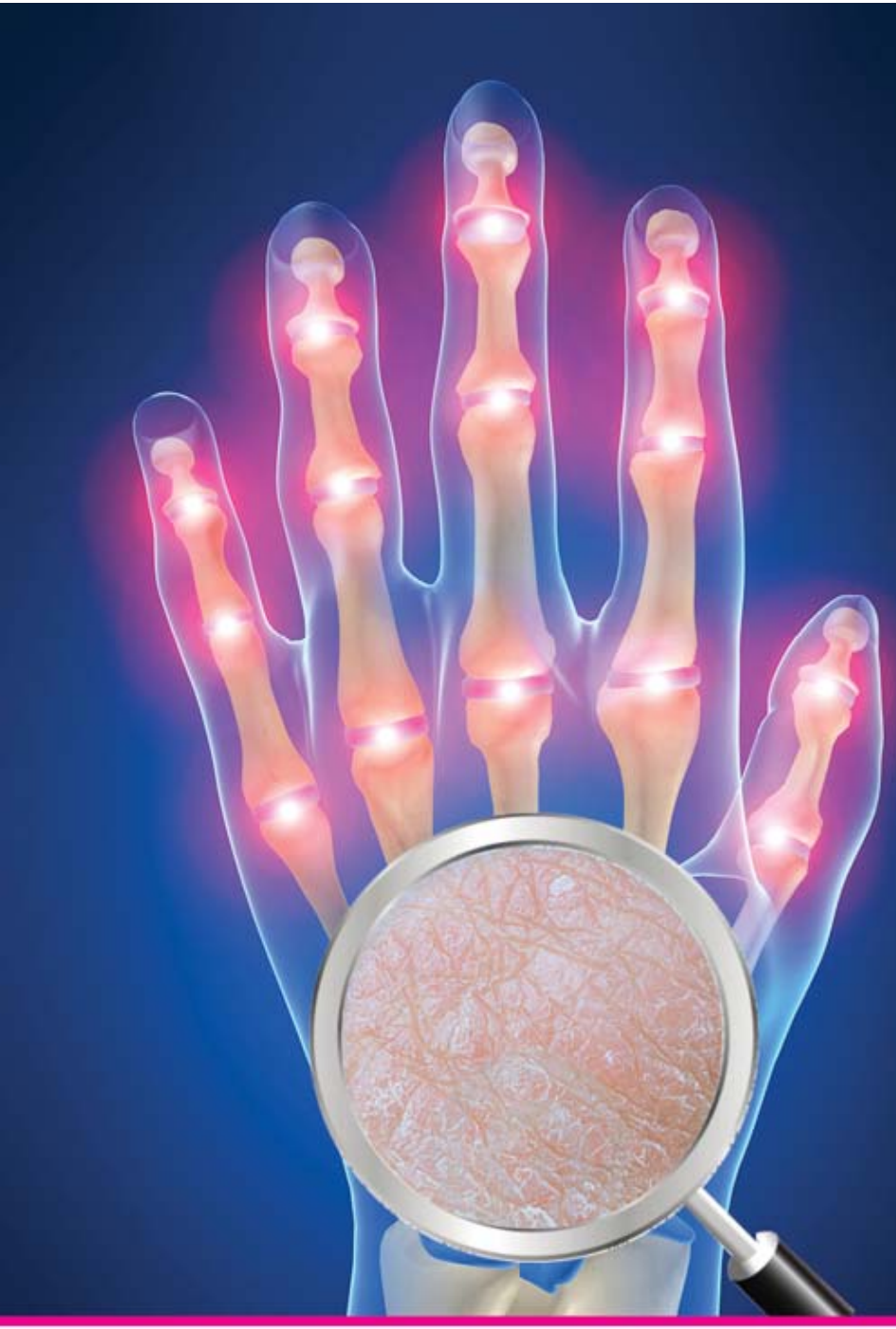
1. Amevive®[package insert]. Deerfield, IL: Astellas Pharma US, Inc.; May 2011; 2. Humira® [package insert]. North Chicago, IL: AbbVie Inc.; December 2014; 3. Enbrel® [package insert]. Thousand Oaks, CA: Immunex Corporation; November 2013; 4. Remicade® [package insert]. Horsham, PA: Janssen Biotech, Inc.; January 2015; 5. Stelara® [package insert]. Horsham, PA: Janssen Biotech, Inc.; September 2013; 6. Otezla® [package insert]. Summit, NJ: Celgene Corporation; 2014. 7. Methotrexate [package insert]. Bedford, OH: Bedford Laboratories™; April 2012.

Revisit: Internal CER Implications

- Annual cost
  - Rebates
  - Dosing
- Study design
  - Placebo data
- Benefits
  - Medical vs. pharmacy
    - Fee schedules
    - Out-of-pocket limits
  - Copay vs. coinsurance
- Use of retrospective real-world data

Summary

- Providers, patients, and payers are challenged to identify the most effective allocation of agents for optimal psoriatic disease management
  - Little data exists to guide individualization of therapy
- CER provides evidence to compare the effectiveness and safety of psoriasis/psoriatic arthritis therapies when head-to-head data is lacking
- Results are used to support clinical decision making
  - Designed to reflect ‘real world’ settings typical of day-to-day patients care
- Primary stakeholders include patients, physicians, managed care organizations, industry, and payers



Examining the Latest Clinical Findings for Psoriasis and Psoriatic Arthritis to Enhance Managed Care Decision-Making

Jointly provided by Annenberg Center for Health Sciences at Eisenhower and Impact Education, LLC in collaboration with Postgraduate Institute for Medicine

Annenberg Center For Health Sciences at Eisenhower

Impact Education, LLC

PIM Postgraduate Institute for Medicine

This activity is supported by independent educational grants from Celgene Corporation, Janssen Biotech, Inc., and Novartis Pharmaceuticals Corporation.

Best Practice Tips and Tools to Implement New Care Models

Jeffrey Dunn, PharmD, MBA
Senior Vice President
Chief Clinical Officer
VRx Pharmacy Services, LLC

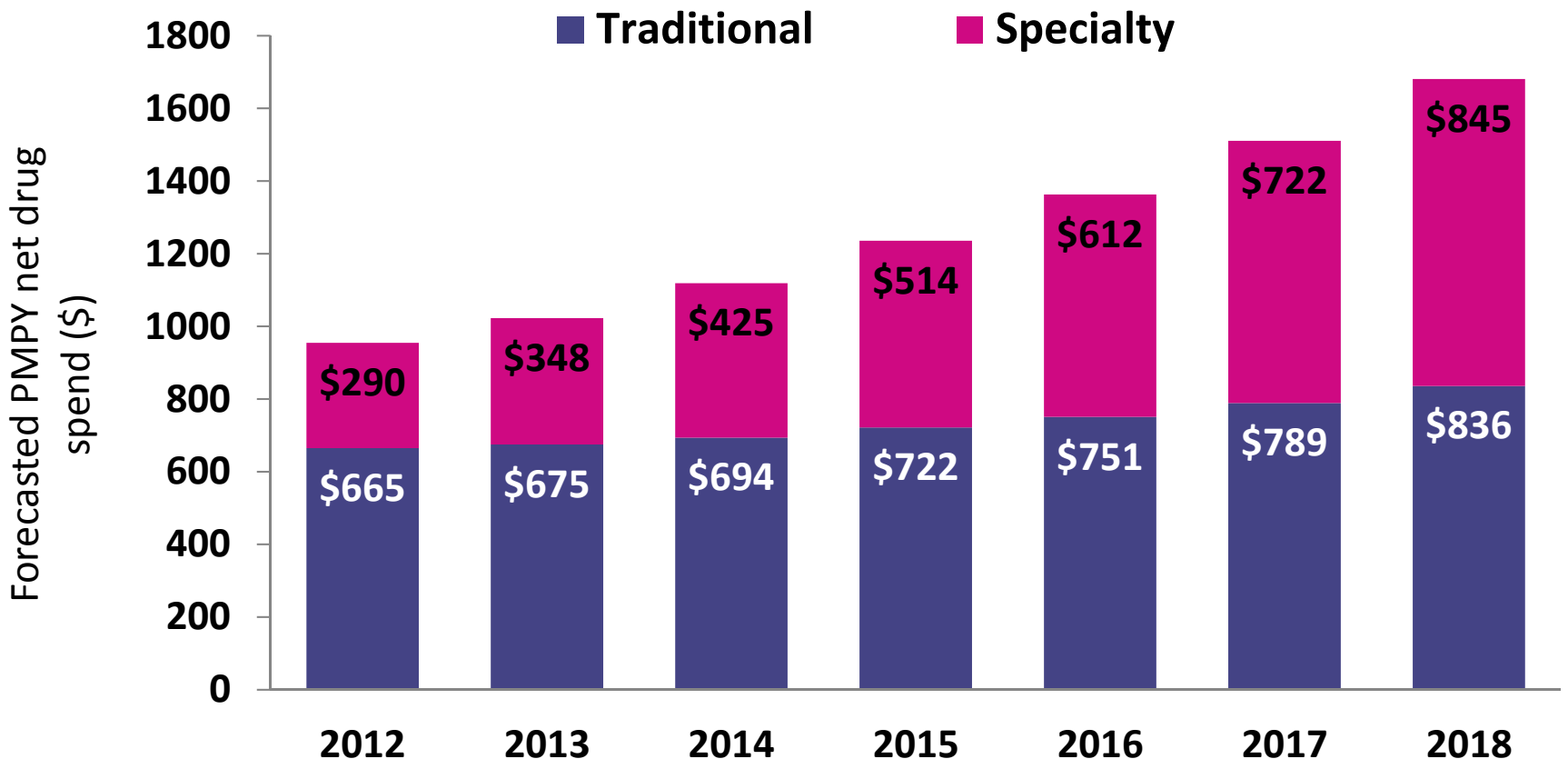
Agenda

- Current trends and challenges
- Psoriatic disease benefit design
- Overview of care models that integrate and coordinate care of patients with psoriatic disease
- Summary

Current Trends and Challenges

Pharmacy Spending on Specialty Drugs Expected to Grow as Coverage Shifts From the Medical Benefit

Spending on Specialty Drugs Projected to Surpass Sales of Traditional Agents by 2018

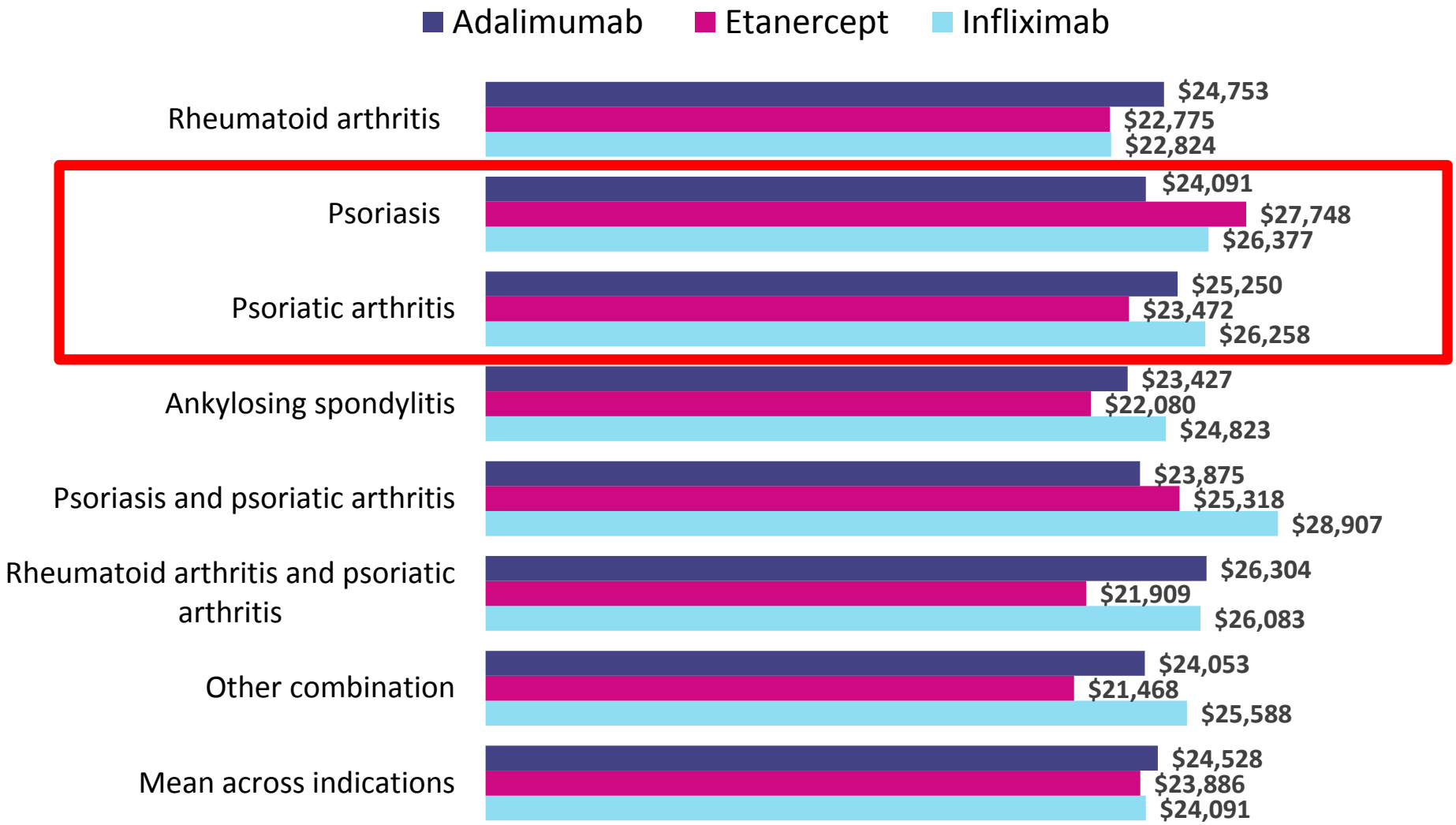


PMPY=per member per year

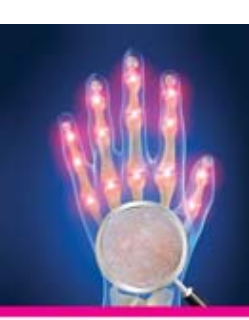
Artemetrx. Specialty drug trends across the pharmacy and specialty benefit. 2013. Available at: http://www.artemetrx.com/docs/ARTEMETRX_Specialty_Trend_Rpt.pdf. Accessed February 19, 2013.

Mean Annual Cost of Biologics for Treatment of Psoriatic Disease is ~$25,500 per Patient

Analysis of a PBM Claims Database for 8,306 Privately Insured Patients Conducted January 2008 and August 2011



Wu N, et al. *Clin Ther*. 2014;36:1231-1241.



Costs Shifting and Patient Adherence: A Tricky Balancing Act

Member Decision Factors

- **Cost**
- **Adherence**
- **Efficacy & tolerability**

Benefit Design Factors

- **Medical vs. Pharmacy**
- **Copay vs. coinsurance**
- **Specialty tiers**

Psoriatic Disease Benefit Design

Basic Tenets of Benefit Plan Design

Manage costs by restricting resource (eg, drug) utilization

Medical and pharmacy designs are usually independent

Cost sharing is used to influence patterns of utilization

Patient cost-share related to acquisition cost of the drug	Assumes an inelastic demand or willingness to pay

Willey VJ, et al. *Am J Manag Care*. 2008;14:S252-S263.

Common Components of Psoriatic Disease Benefit Design

Incentive Programs

Member | Physician: Differential reimbursement; P4P

↓

Specialty Pharmacy Integration

↓

Coordination/Collaboration

Data Management/Greater Use of Information Technology

↓

Case Management

Patient-focused Efforts to Increase Involvement in Their Own Disease Management

↓

Patient Support Programs

Mandatory? | Use of Manufacturer-Provider Programs?

Psoriatic Disease Pharmacy: Benefit Design Considerations

Benefit Design

Tiers	Biosimiliars
Evaluation of out-of-pocket expenses and distribution	First follow-on biologics are in late-stage development

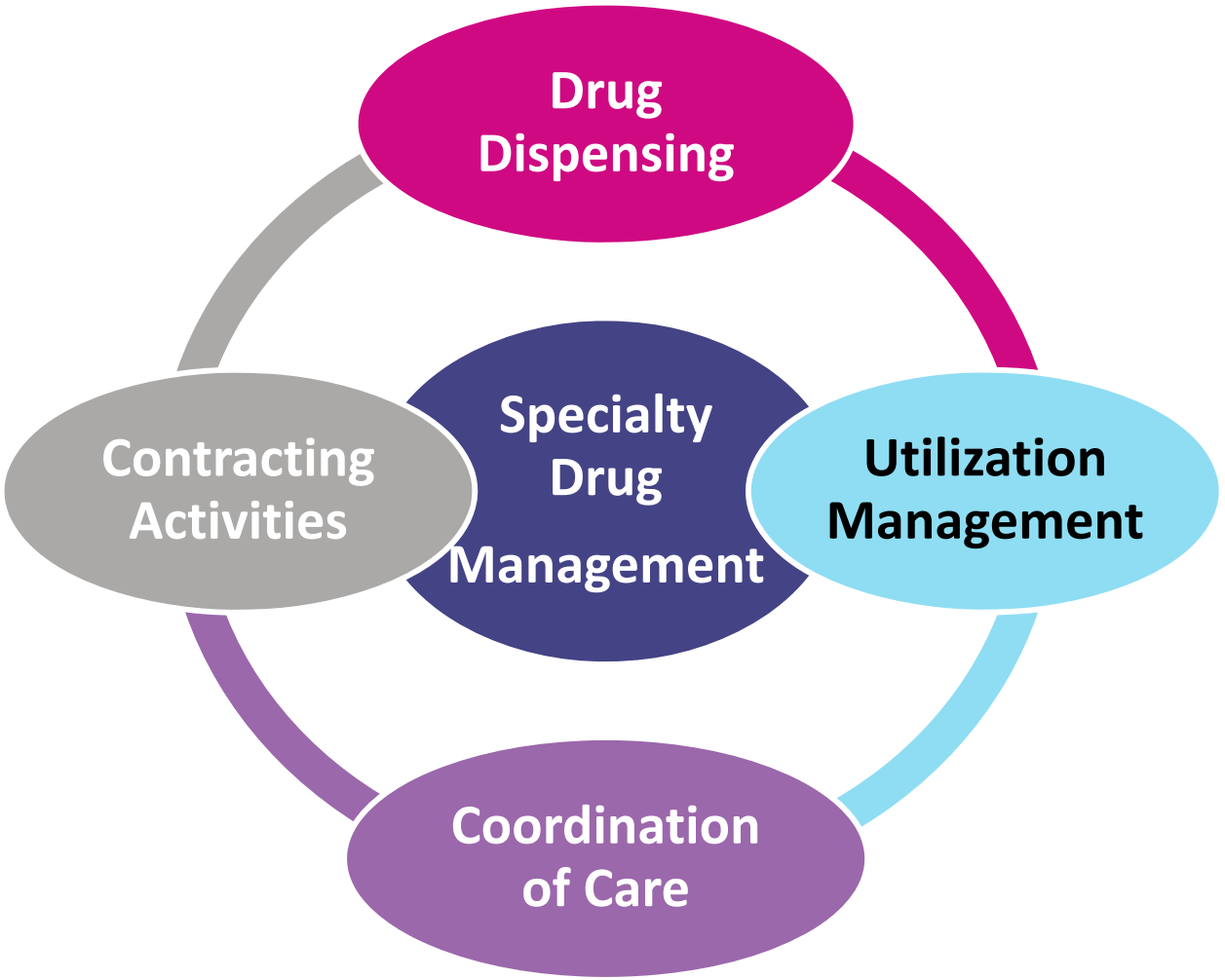
Application of Guidelines/Algorithms/Disease Management

Biosimilar Issues

- Rating/interchangeability
- Data extrapolation/indications
- Safety
- Manufacturing
- Cost
- Formulary Limitations/Restraints:
  - Tier one: Generics
  - Tier two: Preferred brand
  - Tier three: Non-preferred brand
  - Tier four: Specialty pharmaceuticals (often biologicals)
    - Biosimilars?

New Care Models

The Equation



+

Benefit Design (Cost Share) & Formulary

Psoriatic Disease Pharmacy: Integrating the Patient into the Care Model

Disease and Treatment Variables	Health Care Delivery Variables
Presence of asymptomatic disease	Patient education
Tolerability/drug interactions	Strengthening provider-patient relationship
Treatment efficacy	Patient empowerment
Patient adherence	Medication therapy management
Presence of comorbidities	Medication reminders
	Routine monitoring and adjustment of therapy
	Open and integrated communication channels between health care providers involved in the management of the patient

Psoriatic Disease Pharmacy: Formulary Management

More Formulary Control			
Need for data/ use of CER	Levels of evidence for prior authorization	Quantity limits	Start/stop rules

Contracts	
Work with manufacturers; outcomes based contracts	Net effective pricing

Health Care Reform is Stimulating a Move Away From Volume and Toward Value

Emphasis on Rewarding Value Not Volume

Value-based purchasing, shared savings, gain-sharing, bundled payments, capitation, etc.

Use of Incentives to Drive Coordination of Care

CMS 5-Star Rating System: Plans with >4 Stars receive bonuses and higher rebates

New Structures are Promoting Actual and Virtual integration

Accountable Care Organizations (ACOs), Medical Homes, Home-based chronic care management, community health teams, health care innovation zones

New Models of Care Delivery Share Themes Consistent With Current Efforts

Models and Tactics Used by Accountable Care Organizations to Drive Value

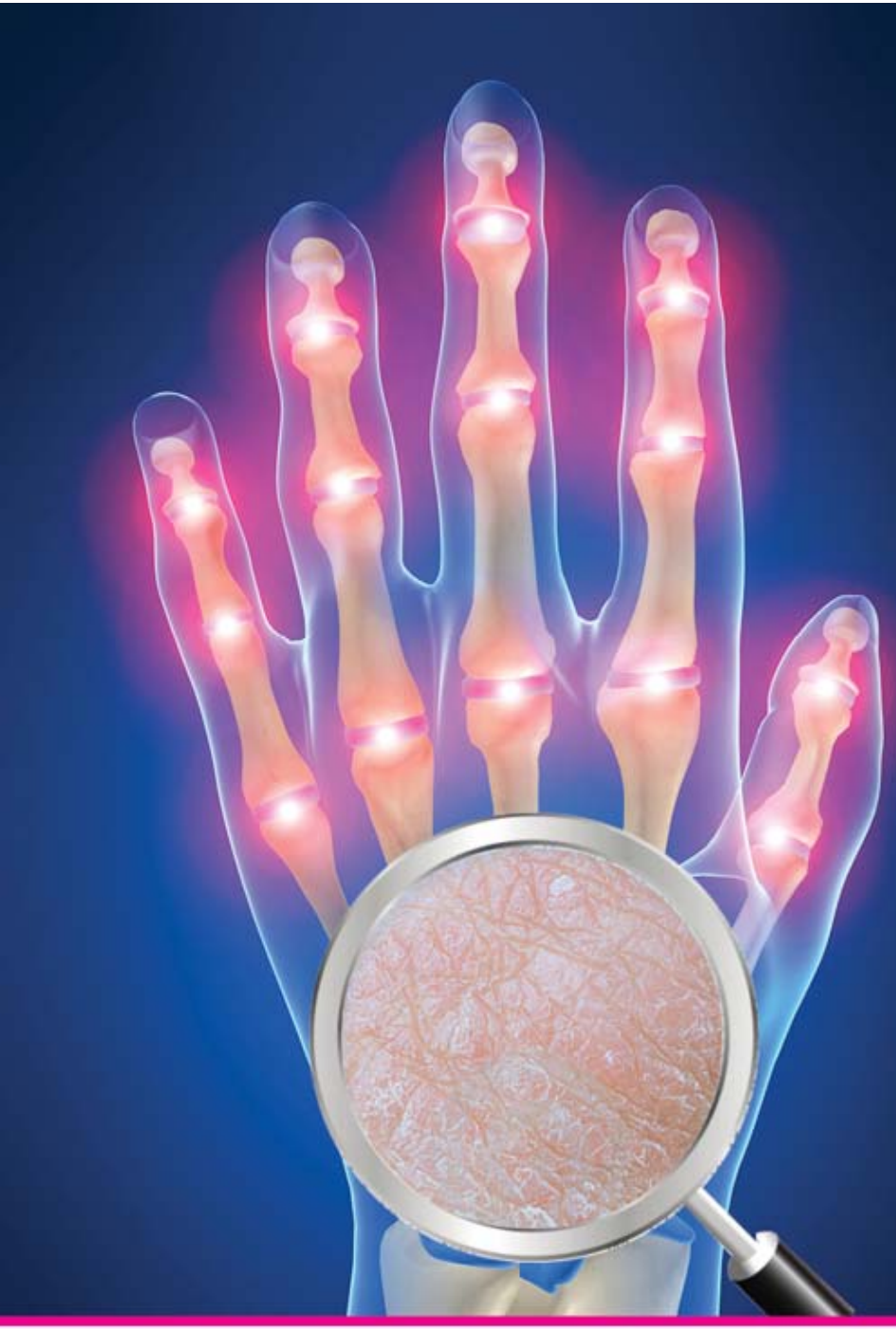
- Patient-Centered Medical Homes (advance primary care)
  - An organizational structure that supports health promotion, patient-centered care, and clinical integration
- Payment mechanisms focused on "fee-for-value" rather than "fee-for-volume":
  - Quality incentives for improved processes and outcomes
  - Incremental roll out to improve probability of success
    - Fee-for-service: per case/at risk quality payment (bundled/capitated)

Looking Forward: Specialty Care Management

Program	Actions
• Specialty Pharmacy Medication Therapy Management (MTM) – Integration with Care Management – Coordinate site of care – Ensure appropriate dosing – Adherence – Patient education – Expectation management	• Design workflow and integration with Care Management • Analyze drug utilization patterns to select targeted drugs/disease • Train personnel – Specialty diseases – Medications – Site of care logistics

Summary

- The number of novel agents approved to treat psoriatic disease continues to increase
- While the increasing number of treatment options benefits patients, providers, and payers, these same stakeholders are challenged by the acquisition cost of these therapies
- New plan designs and care models that emphasize value over volume of care are being implemented to ensure patients continue to have access to these innovative psoriatic disease therapies



Examining the Latest Clinical Findings for Psoriasis and Psoriatic Arthritis to Enhance Managed Care Decision-Making

Jointly provided by Annenberg Center for Health Sciences at Eisenhower and Impact Education, LLC in collaboration with Postgraduate Institute for Medicine

Annenberg Center For Health Sciences at Eisenhower

Impact Education, LLC

PIM Postgraduate Institute for Medicine

This activity is supported by independent educational grants from Celgene Corporation, Janssen Biotech, Inc., and Novartis Pharmaceuticals Corporation.