EVELO BIOSCIENCES

Understanding the Unmet Need in Psoriasis and Atopic Dermatitis and the Potential for EDP1815

October 22, 2020

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Agenda

Opening Remarks
Simba Gill, Ph.D., CEO, Evelo

Unmet Need in Psoriasis –Treatment Landscape and Patient Experience
Benjamin Ehst, M.D., Ph.D., Board-certified Dermatologist, Investigator and Clinical Associate Professor with the Oregon Medical Research Center

Brief Review of EDP1815 Clinical Data
Duncan McHale, M.B.B.S., Ph.D., CMO, Evelo

Q&A

EDP1815 in Atopic Dermatitis
Douglas Maslin, MPhil, MB BChir, Immunology Clinical Lead, Evelo, Doctor of Dermatology and Clinical Pharmacology, Addenbrooke's Hospital, Cambridge

Atopic Dermatitis Fireside Chat
Dr. Benjamin Ehst & Dr. Douglas Maslin

Q&A

Concluding Remarks
Simba Gill

Simba Gill, Ph.D.

Chief Executive Officer

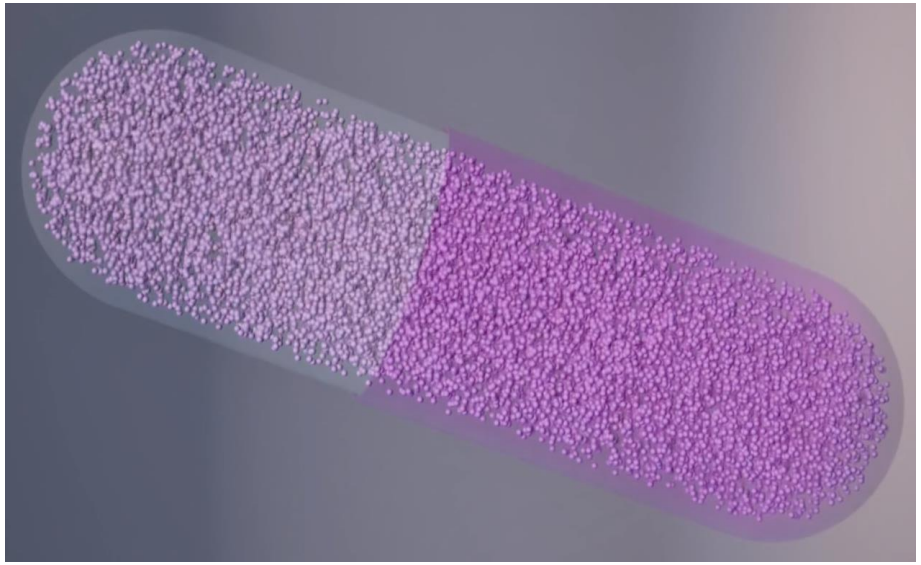
The Small Intestinal Axis: the motherboard of the immune system, can be harnessed to develop a new profile of medicine

SINTAX™ – The Small Intestinal Axis

- The small intestine relays messages from the external world throughout the body
- This is SINTAX, and it is central to human biology
- Selected single bacterial strains have specific interactions with the immune system
- Medicines that target SINTAX can induce inflammation resolution

EDP1815 has the potential to be an effective, well tolerated, convenient, and affordable broadly acting anti-inflammatory medicine

- EDP1815 is a pharmaceutical preparation of a single strain of the human commensal bacteria *Prevotella histicola*
- Non-living and non-colonizing, with no impact on the microbiome
- EDP1815 makes direct contact with immune cells in the small intestine, modulating systemic inflammation, without absorption
- EDP1815 has potent activity across multiple inflammatory pathways
- EDP1815 was well tolerated with no overall difference reported from placebo



Medicines targeting SINTAX have the potential to address unmet need for 40 million psoriasis patients globally

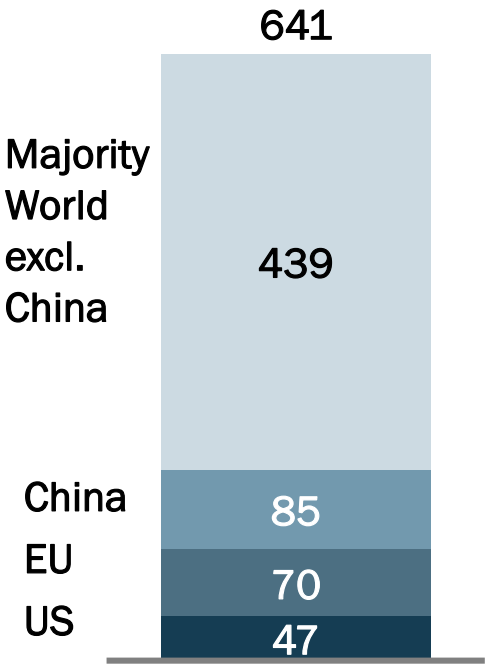
Addressing need across patient segment and geography	Psoriasis patient segments	Patient population[1]
1 Treatment for midline/ pre-biologic patients	Moderate psoriasis, pre-biologic (US+EU)[2]	~3.6M
2 Treatment for patients in fast-growing global markets	Moderate psoriasis (Majority World)[3]	~6.2M
3 Treatment for severe patients not effectively treated with existing therapies	Severe psoriasis (WW)[2,3]	0.4M US+EU 2M Majority World ~2.4M
4 Treatment for patients with mild disease seeking effective, safe, convenient affordable therapy	Mild psoriasis (WW)[2,3]	7 US+EU 20M Majority World ~27M
	Total treatable patients	~40M

SINTAX medicines have the potential to become the foundational treatment for over 600 million people

Requirement	Topical[1]	Small molecules[2]	Biologics[3]	Evelo product candidates, potentially
Safe	●			●
Efficacious		●	●	●
Convenient		●		●
Scalable	●	●		●
Affordable	●			●

Potential to create new market as mid-line therapy and defer use of injectable biologics / specialty drugs and expand to first-line treatment to become foundational therapy for patients globally

Global prevalence for select immune disorders[1] Millions



1 Includes psoriasis, psoriatic arthritis, axial spondyloarthropathy, rheumatoid arthritis, atopic dermatitis, asthma, IBD, MS, Parkinson's, and Alzheimer's

SOURCE: Websearch, DRG reports, IQVIA reports, Global Health Data Exchange

Bridging the Treatment Gap in Psoriasis

Benjamin Ehst, M.D., Ph.D., Lead Investigator
Oregon Medical Research Center, Portland, OR

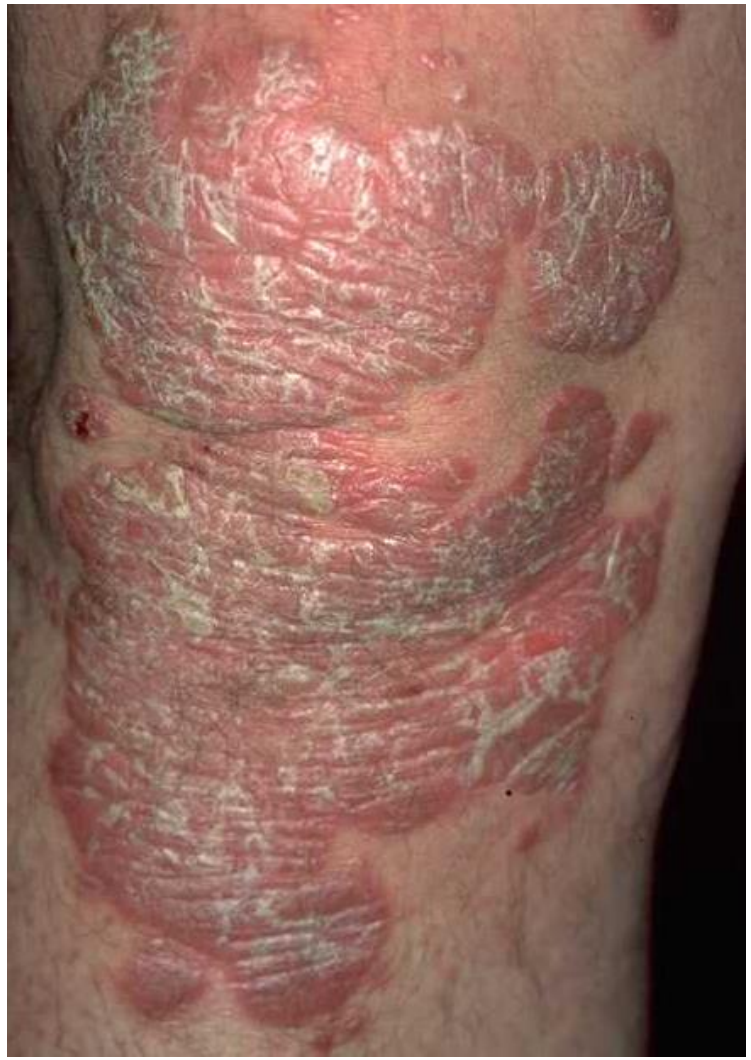
Psoriasis by the Numbers

- Psoriasis affects 2-3% of the world's population

  (156 million people)

- 80% of psoriasis is mild to moderate

  (125 million people)



"...the majority of recent innovation have been targeted to the moderate-to-severe patient population, with little new successful development for those psoriasis patients with mild and moderate disease."

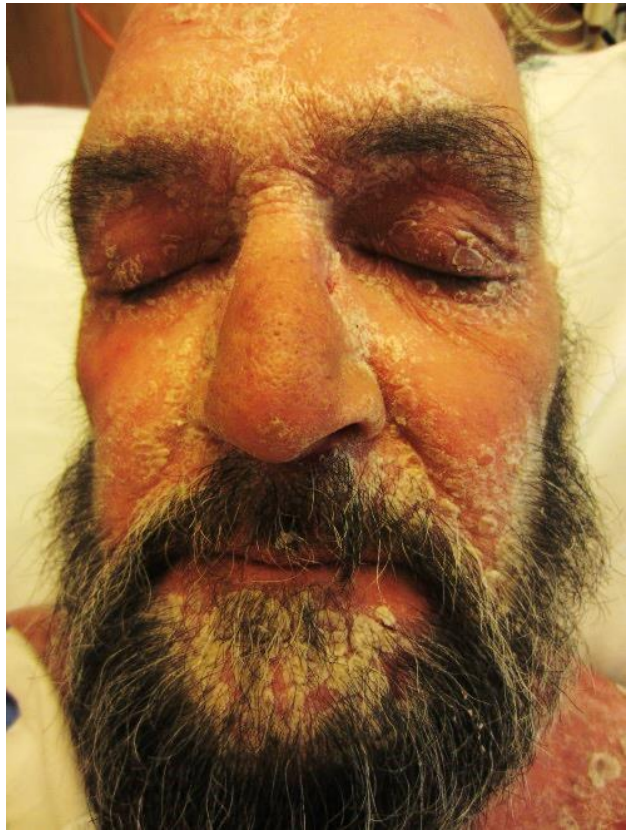
Statement from the International Psoriasis Council, 2019

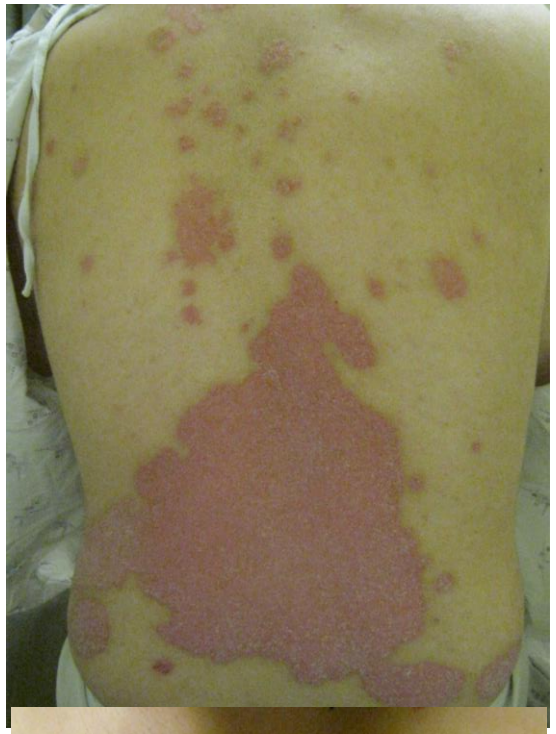
Strober et al. Dermatol Ther 2019;9:5-18

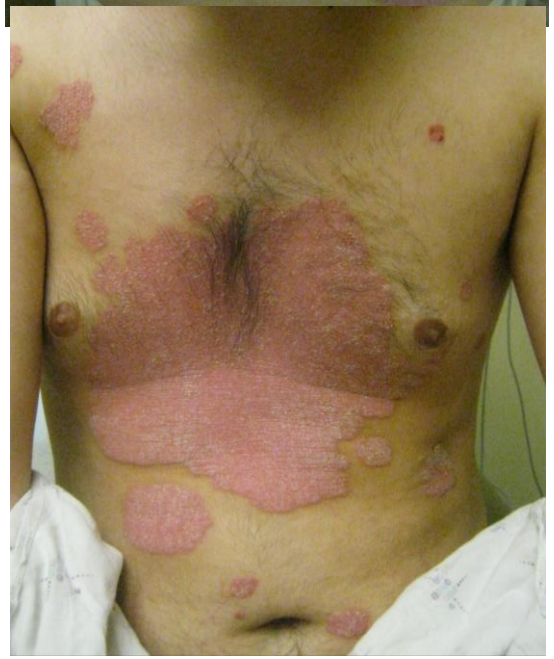
What is Mild to Moderate Psoriasis?

Current (old) definition:

- <5% Body surface area (mild)
- 5-10% BSA (moderate) and
- >10% BSA (severe)







Strober et al. J Amer Acad Dermatol; 2020;82(1):117-122

Who Should Receive What Therapy?

Older definition:

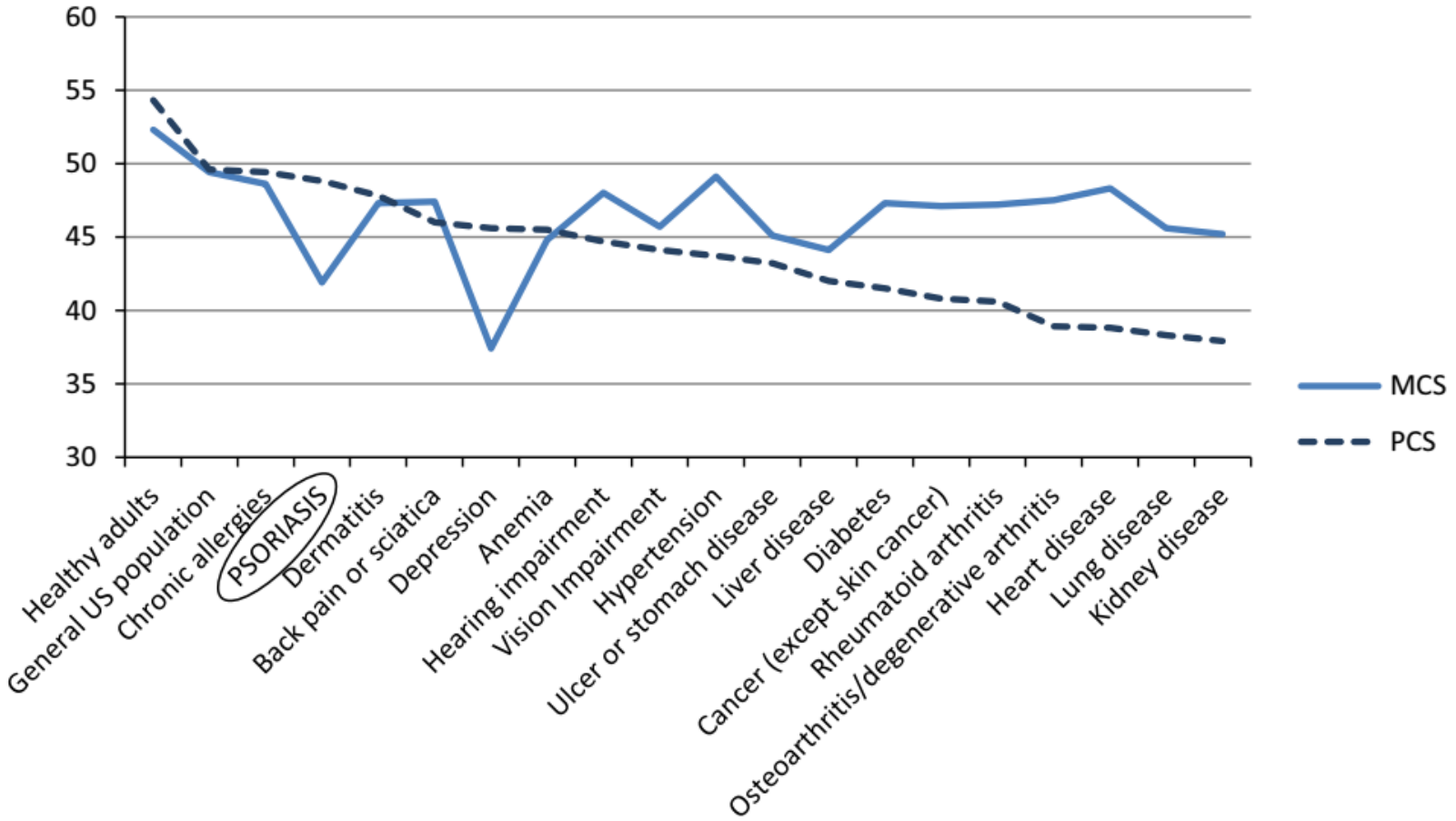
- <5% BSA (mild)
- 5-10% BSA (moderate) and
- >10% BSA (severe)

Emerging definition:

- Candidates for topical therapy
- Candidates for systemic therapy
  - >10% BSA
  - Disease involving special areas
  - Failure of topical therapy

Strober et al. J Amer Acad Dermatol; 2020;82(1):117-122

High Psychological Burden of Psoriasis (Not Just a Skin Disease)



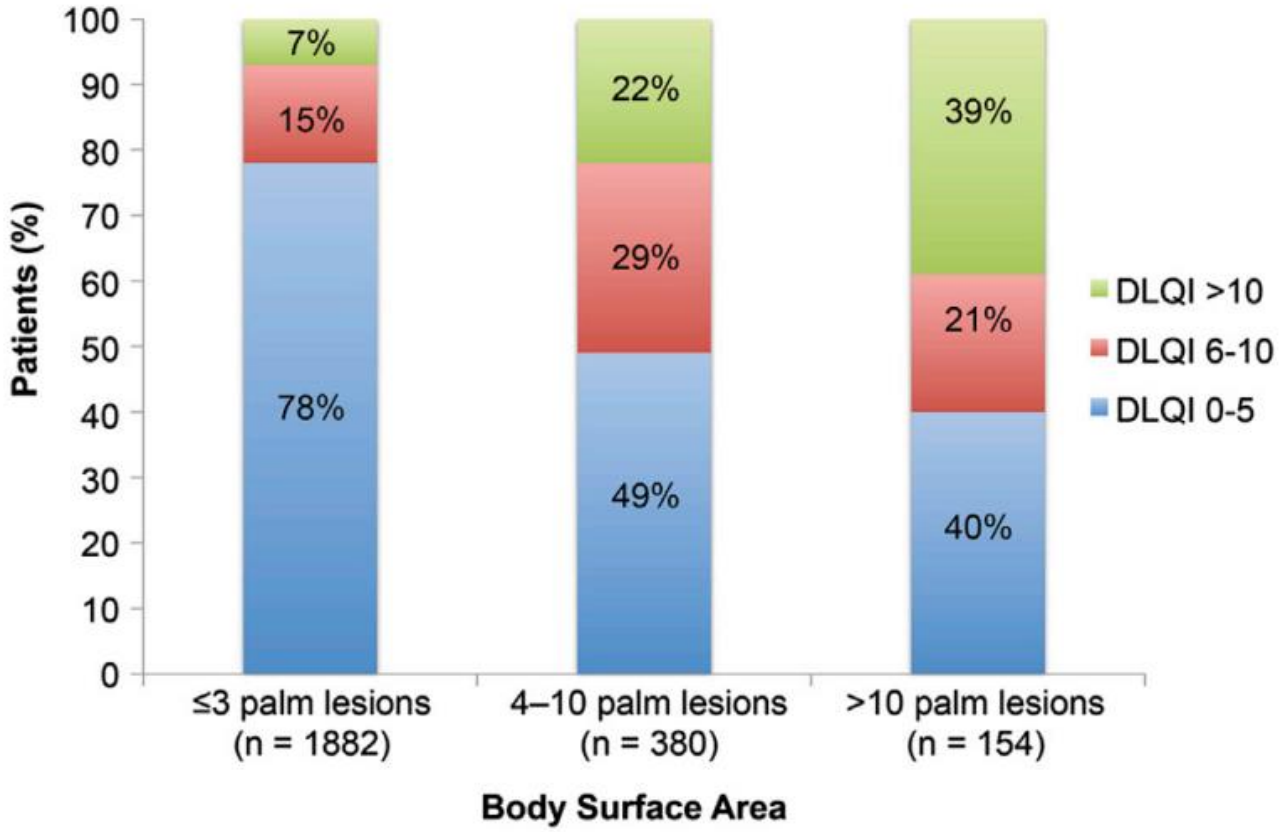
SF-12 survey in Italian outpatient derm clinics, ~1500 patients, 50% very mild or mild, and 40% moderate

Mental Component Scores did not correlate with Psoriasis Severity!

Sampogna et al. J Dermatol; 2019;46:1153-9

Quality of Life Is Affected By Mild PsO, And Worsens with PsO Severity

MAPP Survey 2012
n=3426 patients



Lebwohl et al. J Am Acad Dermatol; 2014;70(5):871-81

Current Treatment Options for Psoriasis

Topicals

Corticosteroids

Calcipotriene/Calcitriol

Tazarotene

Calcineurin inhibitors

Phototherapy

Systemic Non-biologics

Apremilast (FDA-approved 2014)

Cyclosporine (1997)

Acitretin (1997)

Methotrexate (1972)

Tofacitinib, Fumaric acid esters, Hydroxyurea, Mycophenolate mofetil, Azathioprine, Leflunomide, Tacrolimus, Thioguinine

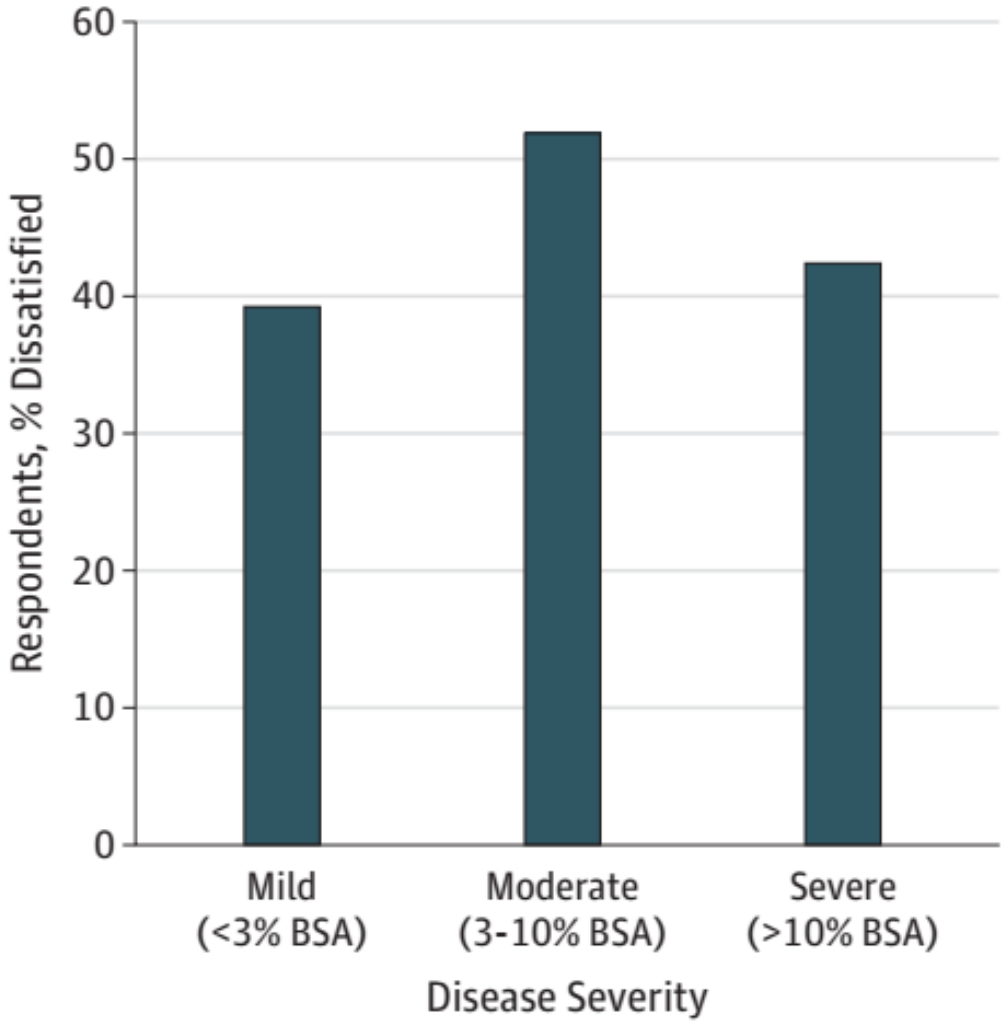
Biologics

Etanercept, Adalimumab, Infliximab, Certolizumab, Ustekinumab, Secukinumab, ixekizumab, Brodalumab, Guselkumab, Tildrakizumab, Risankizumab

Moderate-Severe PsO!

EVELO

High Treatment Dissatisfaction Among PsO Patients – 2011 NPF Survey



Armstrong et al., JAMA Derm, 2013;149(10):1180-5

Limitations of Topical Therapy

Inconvenient

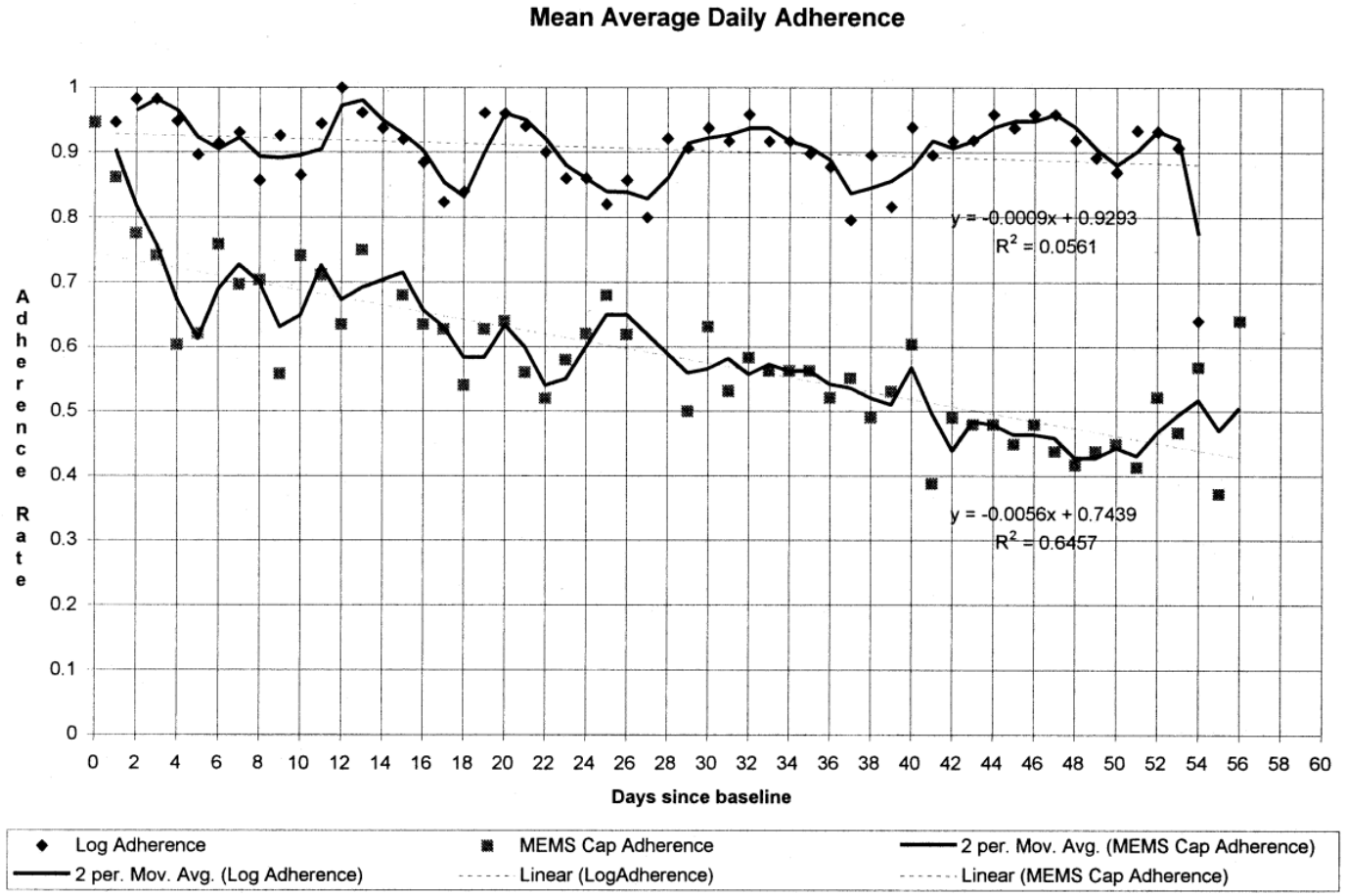
Poor adherence

Need for continued use

Side effects

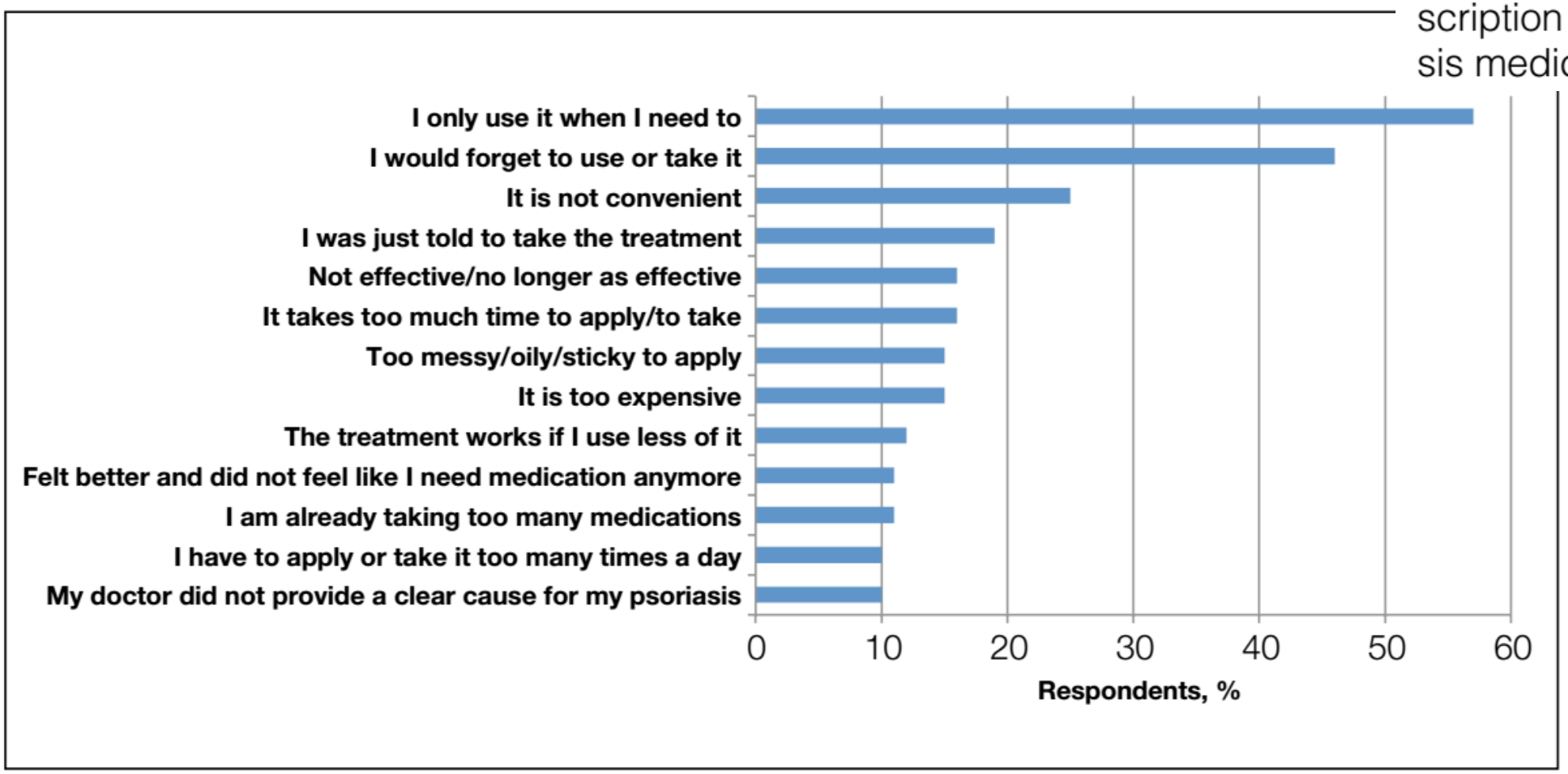
Don’t address systemic inflammation

Adherence to topical therapy decreases during the course of an 8-week psoriasis clinical trial: Commonly used methods of measuring adherence to topical therapy overestimate actual use



Carroll et al. JAAD, 2004:51(2)212-16

Figure 3. Reasons for nonadherence to prescription topical psoriasis medication (n=86).



US Respondents of Multi-National Survey of PsO

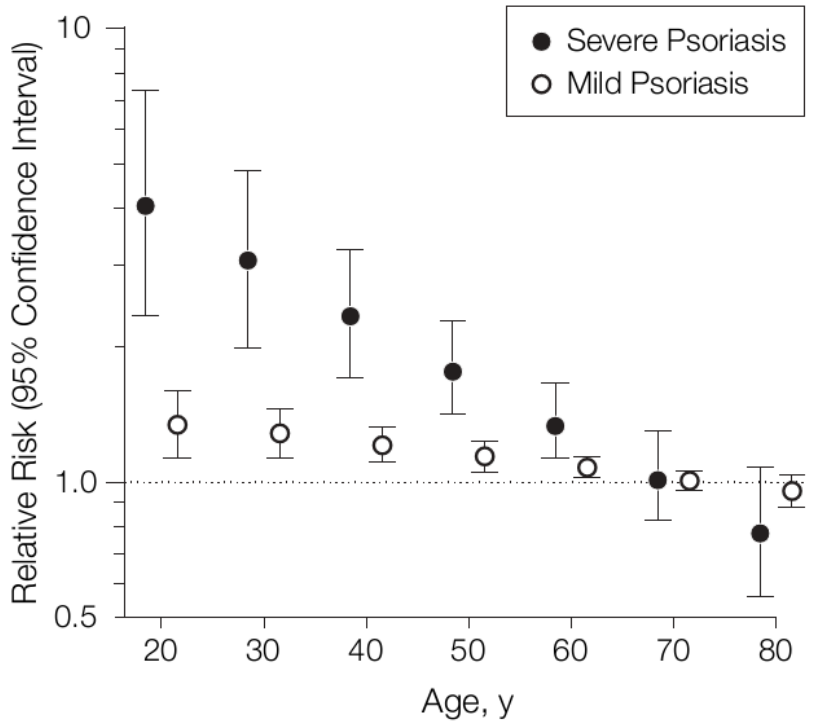
Feldman Cutis, 2013:92:258-63

High Relative Risk of MI in Young Severe Psoriatics

GPRD, mild PsO (127,139 patients), severe (3837 patients), and controls (556,995)

PsO confers independent risk of MI in mild (HR 1.54 [95% CI 1.24-1.91]) and severe cases (HR 7.08 [3.06-16.36]); models adjusted for risk factors for MI

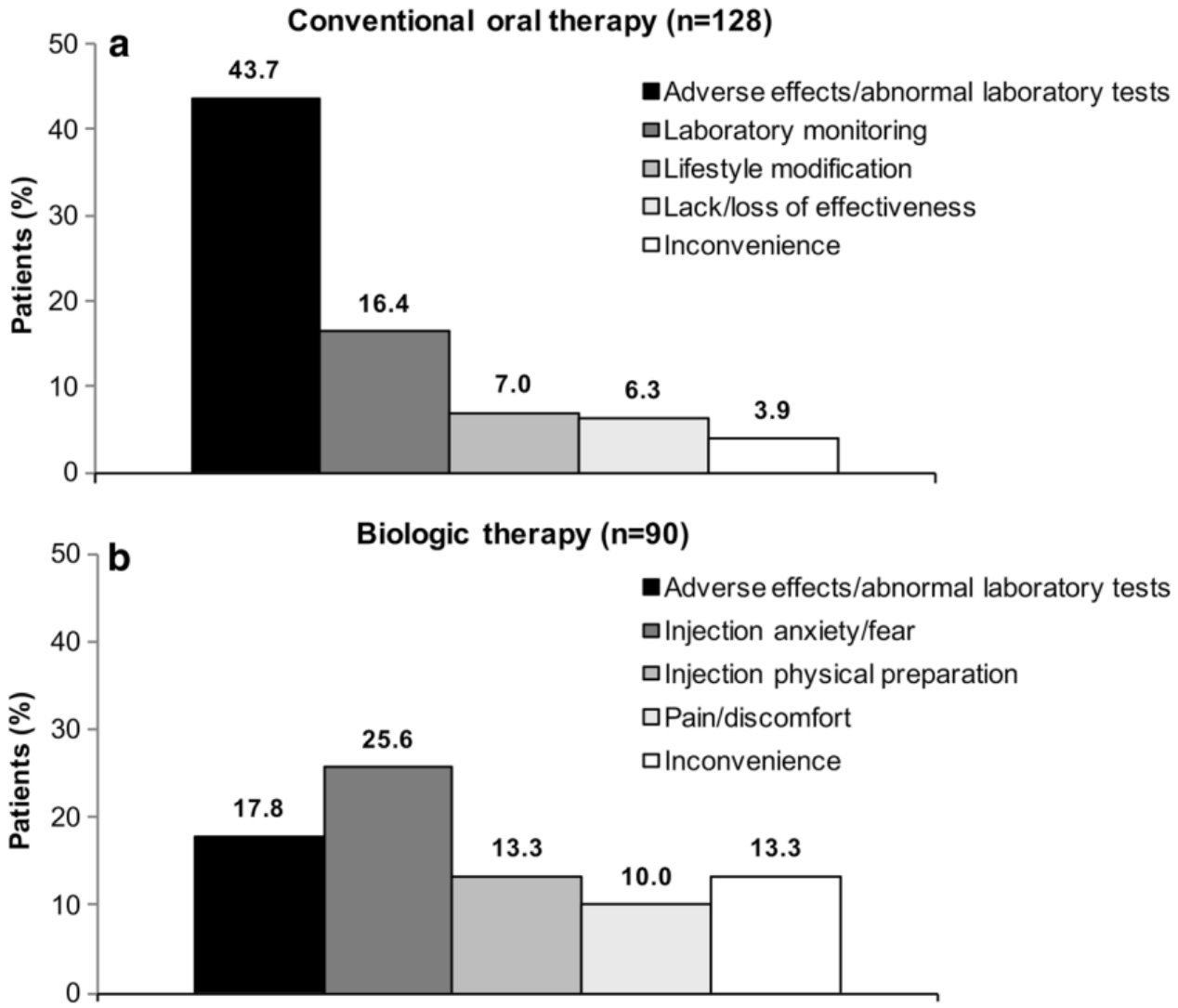
Figure. Adjusted Relative Risk of Myocardial Infarction in Patients With Psoriasis Based on Patient Age



Gelfand et al, JAMA, 2006;296(14):1735-41

Patients Find Current Systemic Meds Burdensome

US PsO patients in MAPP Survey



Lebwohl et al, Am J Clin Dermatolg 2016, 17:87-97

Physician Preferences for Psoriasis Therapy

Table 3 Top five attributes of an ideal therapy and greatest unmet therapeutic needs

Ideal therapy	Unmet therapeutic needs
Dermatologists psoriasis	**Dermatologists psoriasis**
No increased risk of serious infection or cancer (36.6%)	Improved efficacy (35.5%)
Manageable tolerability profile (17.4%)	Improved long-term safety (33.5%)
Provides clearance of at least 50% (18.4%)	A new mechanism of action (11.8%)
Improved access to therapy (11.0%)	Another oral option (11.5%)
Oral administration (12.0%)	Improved tolerability (7.4%)

MAPP Survey Results, n=391 dermatologists in N America and Europe

van der Kerkhof et al, JEADV 2015;29:2002-10

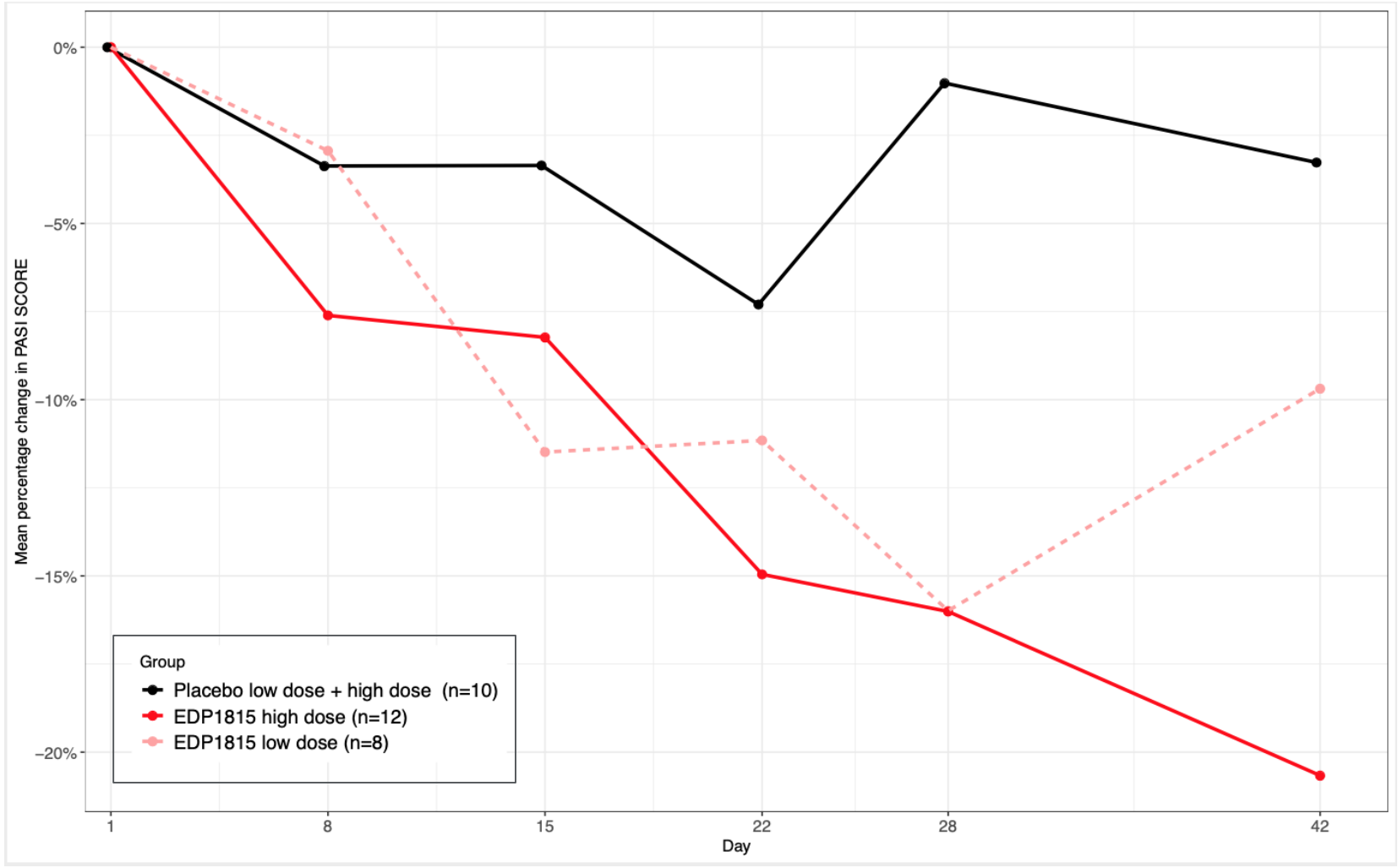
Duncan McHale, M.B.B.S., Ph.D.

Chief Medical Officer

Positive Phase 1b clinical data in psoriasis

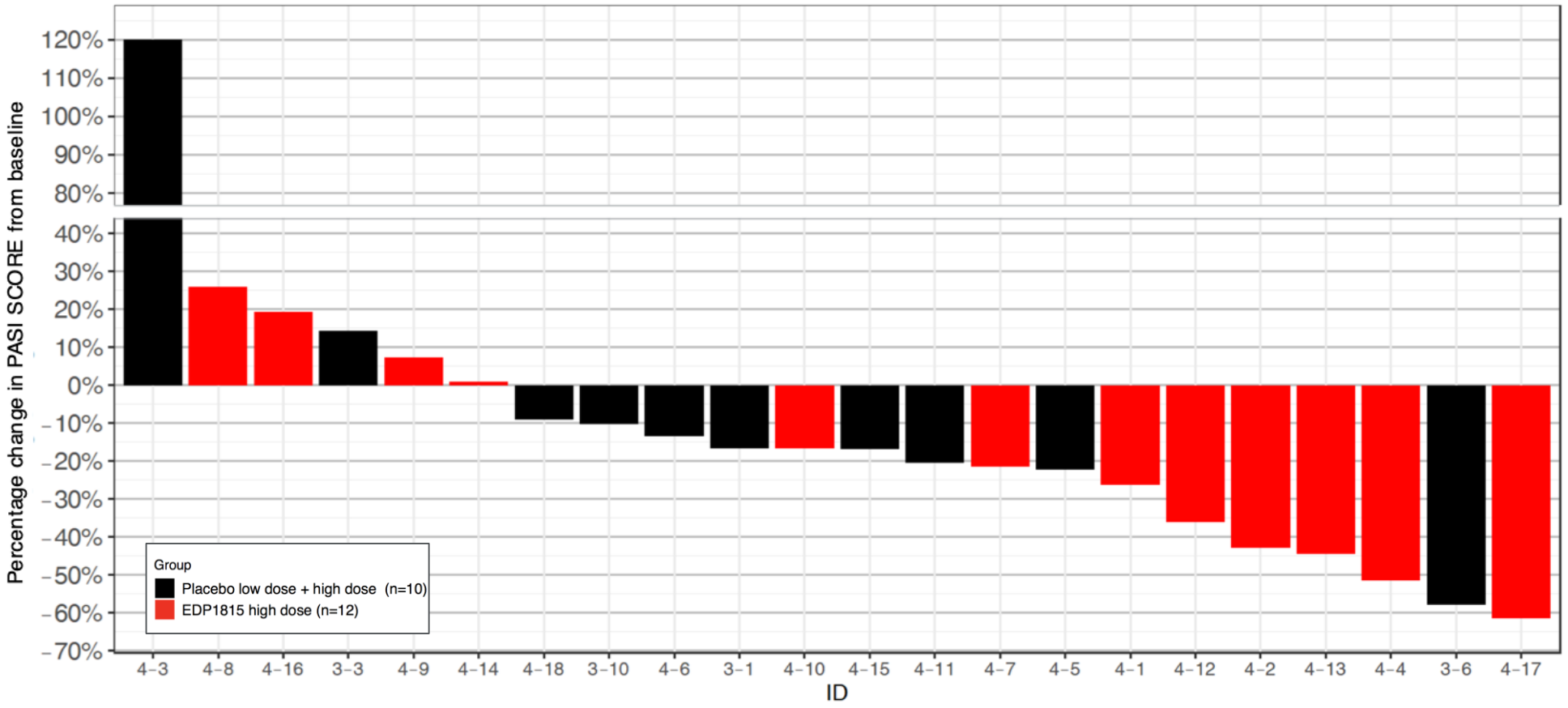
- Well tolerated with no overall difference reported from placebo
- Clinical effects observed in Phase 1b trial (two cohorts), including:
  - Reduction in mean PASI scores vs. placebo
  - Reduction in Lesion Severity Score in-line with PASI
- Continued reductions from baseline observed in high dose cohort at day 42 indicative of a sustained clinical effect
- Phase 1b data suggests potential for a superior profile to Otezla

Continued improvement in PASI score across the dosing period in both cohorts



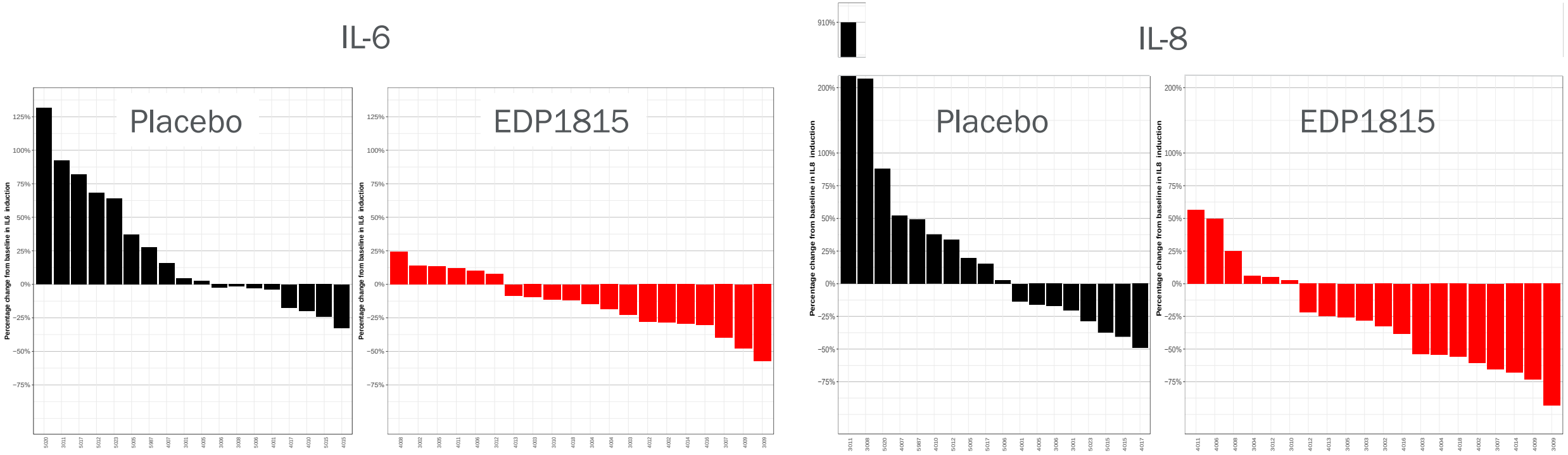
Dosing period

Individual reductions in PASI of up to 61% at day 42



- 50% of those dosed with EDP1815 achieved at least PASI 25 at Day 42 vs. 10% with placebo

EDP1815 reduces systemic inflammatory response



- High and low dose EDP1815 cohorts pooled.
- Each bar shows data from an individual patient. Similar trends for TNF and IL1β.
- IL-6 and IL-8 are key drivers of hyperinflammation in COVID-19.

EDP1815 Phase 2 dose-ranging trial in mild to moderate psoriasis

Trial Summary

- Double-blind, placebo-controlled, dose-ranging trial ~225 patients
- Evaluate three doses of enteric capsule formulation of EDP1815 vs. placebo
- Will include individuals with more active disease scores than Phase 1b (PASI score of 6-15)

Summary of Endpoints

- Primary endpoint: Mean reduction in PASI score at 16 weeks
- Key secondary endpoints:
  - PGA (Physician's Global Assessment)
  - BSA (Body Surface Area)
  - PGA x BSA
  - DLQI (Dermatology Life Quality Index)
  - Lesion Severity Score (LSS)

First subjects have been dosed and interim data expected by mid-2021

EDP1815 has potential to become foundational psoriasis treatment

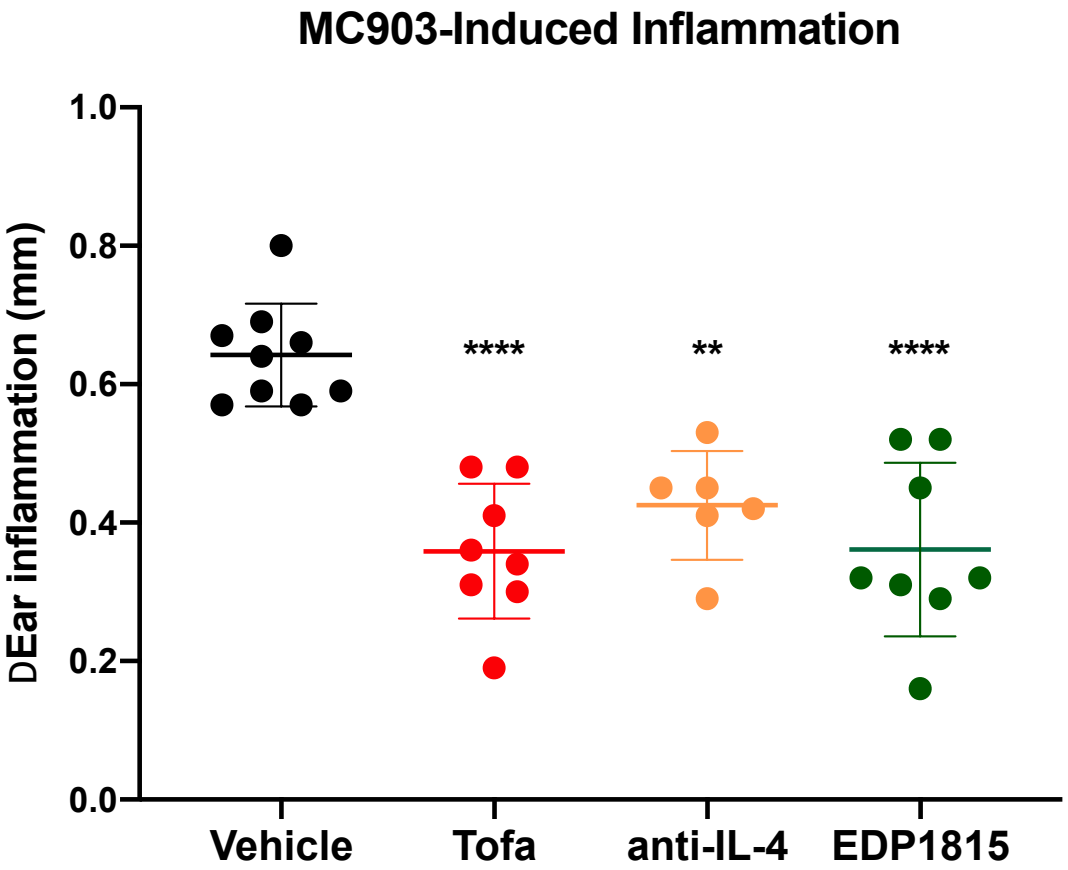
1. Positive clinical effects observed
2. Well tolerated with no difference reported from placebo
3. Convenient oral once a day dosing
4. Affordable

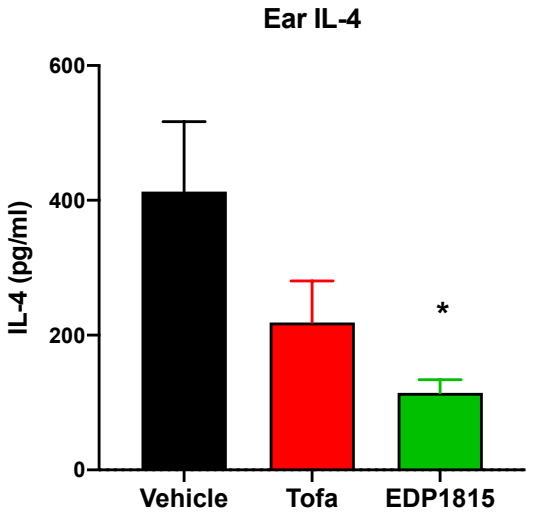
- Opportunity to address unmet medical need in patients inadequately treated with topical therapies and not severe enough / eligible for biologic therapies

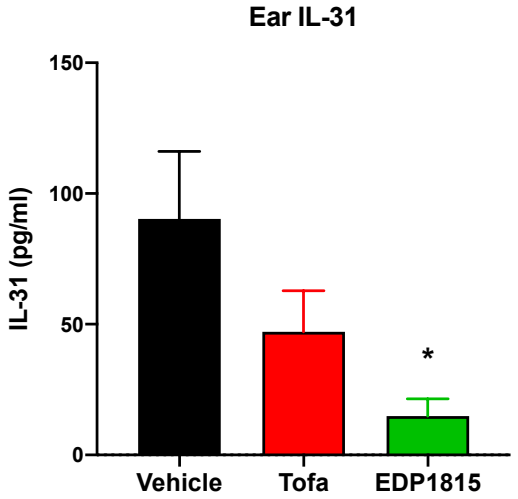
Douglas Maslin, MPhil, MB BChir

Immunology Clinical Lead

EDP1815 has striking effects in models of Th2 inflammation



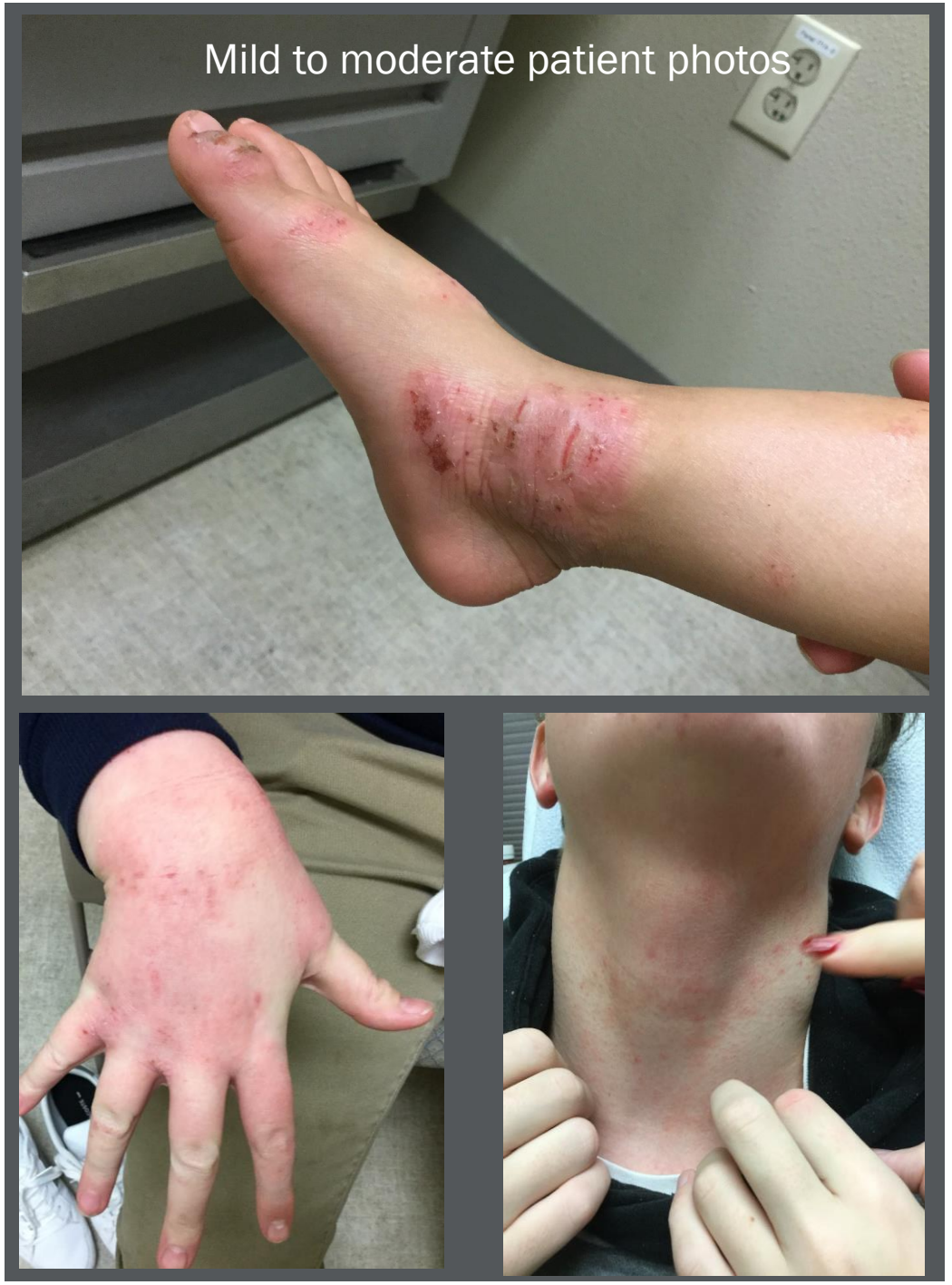




Patients with a therapeutic need

Score	Morphological Description
0 – Clear	No inflammatory signs of atopic dermatitis (no erythema, no induration/papulation, no lichenification, no oozing/crusting). Post-inflammatory hyperpigmentation and/or hypopigmentation may be present.
1 – Almost clear	Barely perceptible erythema, barely perceptible induration/papulation, and/or minimal lichenification. No oozing or crusting.
2 – Mild	Slight but definite erythema (pink), slight but definite induration/papulation, and/or slight but definite lichenification. No oozing or crusting.
3 – Moderate	Clearly perceptible erythema (dull red), clearly perceptible induration/papulation, and/or clearly perceptible lichenification. Oozing and crusting may be present.
4 – Severe	Marked erythema (deep or bright red), marked induration/papulation, and/or marked lichenification. Disease is widespread in extent. Oozing or crusting may be present.

& a BSA of 5 - 40 %



https://www.eczemacouncil.org/assets/docs/Validated-Investigator-Global-Assessment-Scale_vIGA-AD_2017.pdf

Phase 1b clinical trial design

Trial Summary

- Double-blind, placebo-controlled trial
- 24 patients with mild and moderate atopic dermatitis, randomized 2:1 (active : placebo)
- 56 days of once daily oral administration of enteric capsule formulation

Summary of Endpoints

- Primary endpoint: Safety and tolerability
- Key secondary endpoints: Established markers of clinical efficacy

Clinical Assessments	Patient Reported Outcomes
IGA	Dermatology Life Quality Index (DLQI)
BSA	Patient-Orientated Eczema Measure (POEM)
Eczema Area and Severity Index (EASI)	Pruritus-NRS
Scoring Atopic Dermatitis (SCORAD)	

Trial fully enrolled with data expected 1Q 2021

EDP1815 has the potential to meet the need for an effective, safe, oral, and affordable medicine in atopic dermatitis

- There is a vast unmet need in mild and moderate atopic dermatitis, beyond the currently available poorly tolerated topical treatments
- There are no licensed oral systemic therapies for this patient group
- Injectable biologics and oral JAK inhibitors are targeted for more severe patients

A clean safety profile with an IGA improvement of ≥ 10% relative to placebo would represent a positive result

Planning for success in atopic disease

- Results expected 1Q 2021: looking for signs of efficacy that meet the unmet need
- Progress directly to a Phase 2 or 2/3 study in atopic dermatitis
- Progress into pediatric atopic dermatitis
- Consider progressing forward in other Th2 diseases e.g. allergy and/or asthma

Pipeline is rich in anticipated near-term clinical catalysts

Candidate	Catalyst
EDP1815 – TACTIC-E COVID-19	**4Q 2020:** Phase 2/3 interim safety data and futility analysis
EDP1815-205 COVID-19	**4Q 2020:** Phase 2 data
EDP1815 Psoriasis	**Mid-2021:** Phase 2 interim data
EDP1815 Atopic dermatitis	**1Q 2021:** Phase 1b data
EDP1503 Oncology	**4Q 2020:** Phase 1/2 data in triple-negative breast cancer
EDP1867 Atopic dermatitis	**1Q 2021:** Phase 1b initiation **Mid-2021:** Phase 1b data