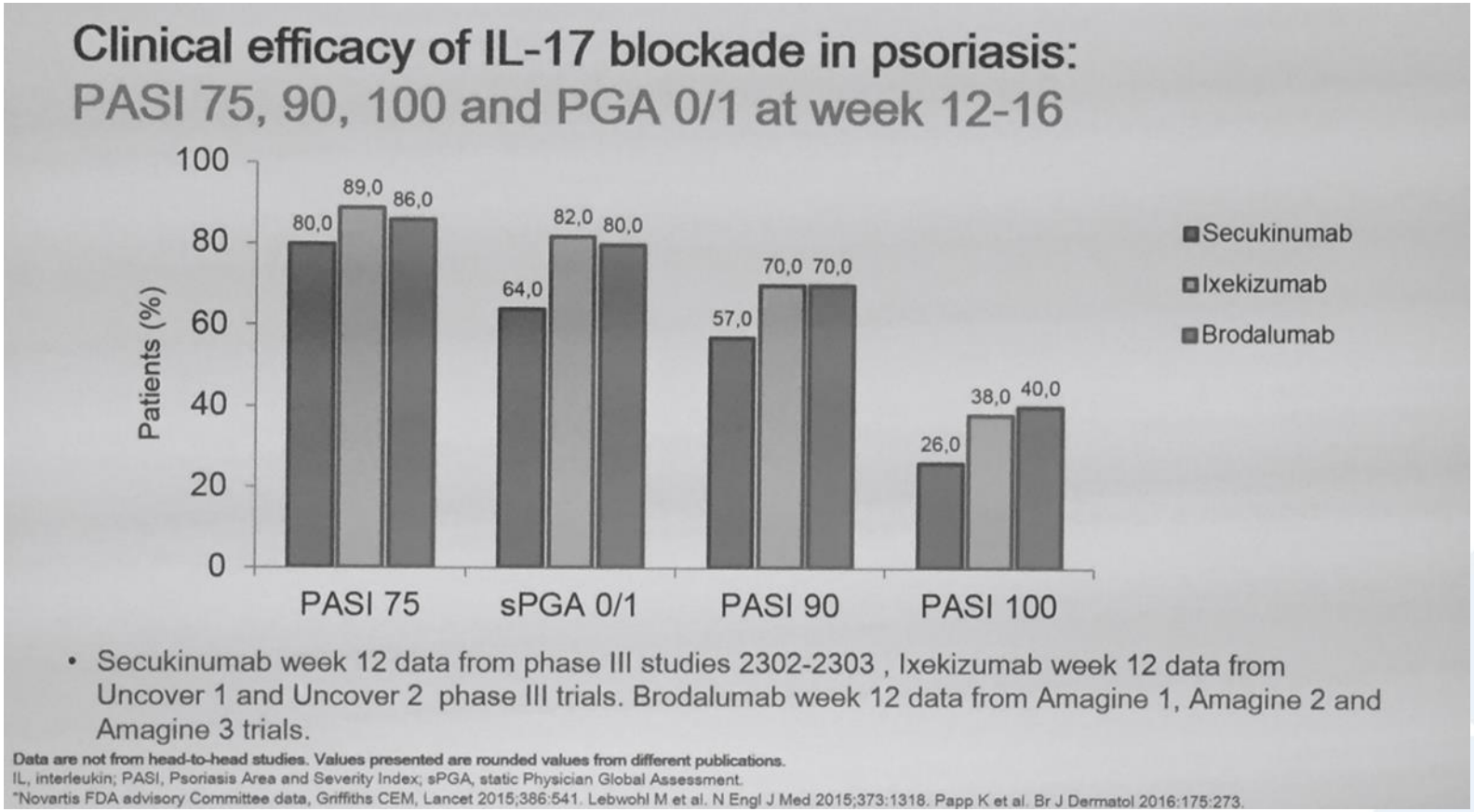
Viernes, 26 de Octubre

Noemí Eirís Salvado

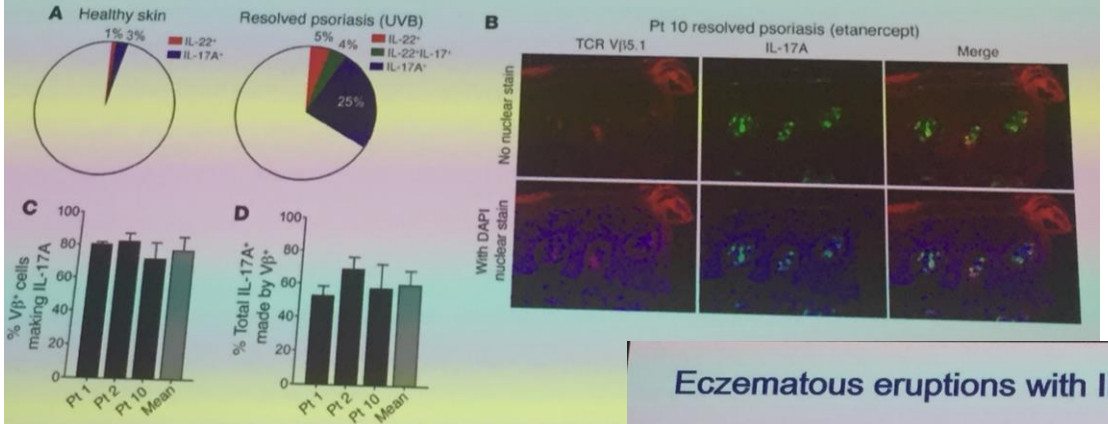
Complejo Asistencial Universitario de León

Iniciativa científica de:

DRUGS - ANTI IL17



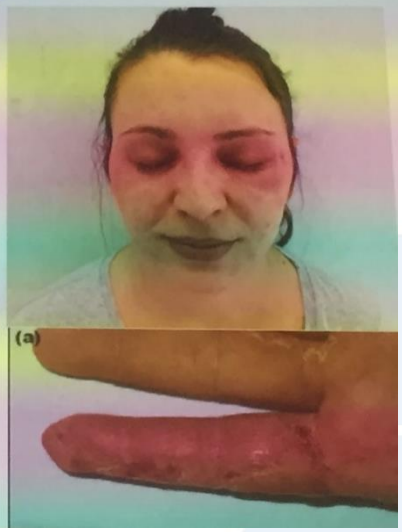
Resolved psoriasis lesions contain IL-17 producing T-cells



Magos T et al J Clin Inves.

Eczematous eruptions with IL-17 antagonists

- Occurs within weeks to months after starting IL-17 antagonists
- In patients with /without atopy
- May require withdrawal of the causative agent



Napolitano M et al Br J Dermatol 2019 (in press)
Munera-Campos M et al J Eur Acad Dermatol 2019 (in press)

DRUGS – ANTI P19

Impact of Mirikizumab Treatment on Psoriasis Disease Activity at Week 52 Based upon Prior Treatment with Biologic Therapy

Figure 4. PASI 90 Response Rates at Week 52 Among Exposure-Naïve and Prior-Exposure Patient Groups, NRI

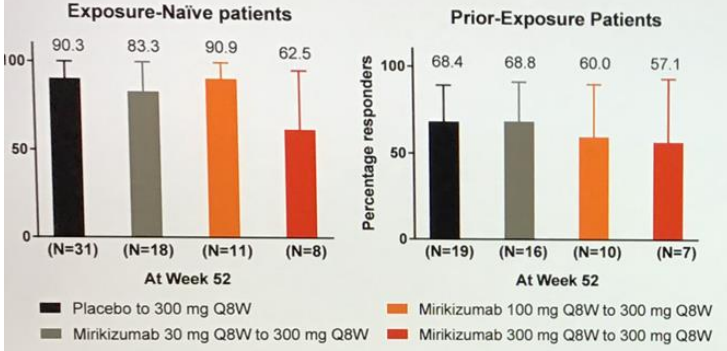
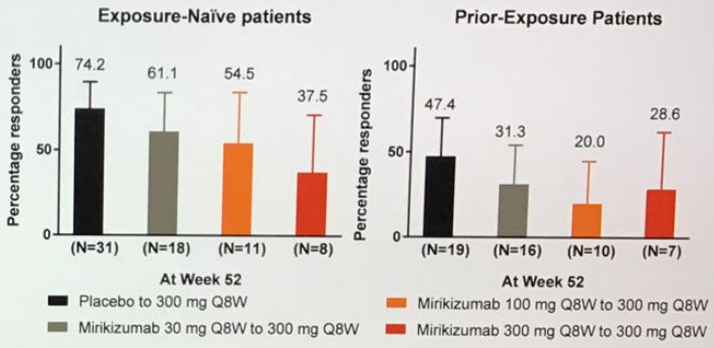


Figure 5. PASI 100 Response Rates at Week 52 Among Exposure-Naïve and Prior-Exposure Patient Groups, NRI



NRI=nonresponder imputation; PASI 90=≥90% improvement in Psoriasis Area and Severity Index; PASI 100=≥100% improvement in Psoriasis Area and Severity Index; Q8W=every 8 weeks

Conclusions:

- Long-term treatment (Weeks 16–52) with mirikizumab substantially improved disease activity in both exposure-naïve and prior-exposure-to-biologics patients with moderate-to-severe plaque psoriasis who did not achieve PASI 90 at Week 16.
- Results suggest that mirikizumab is effective in achieving high PASI 90 response among patients who received prior biologic therapy.

Disclosures:

- PR received Grant/research support from AbbVie, Allergan, Anacor Pharmaceuticals, Boehringer Ingelheim, Cassiopea SpA, Dermira, Eli Lilly and Company, Galderma Laboratories, Janssen-Ortho, Kadmon Corporation; Leo Pharma, Merck, Moberg Derma, Novartis, Pfizer, Ranbaxy Laboratories Limited, Sandoz, Viamet, Celicefix, and Cutanea; AI has received honoraria or fees for serving on advisory boards, as a speaker, as a consultant, and/or grants as an investigator from AbbVie, Celgene, Eli Lilly, Janssen, Kyowa Hakko Kirin, Maruho, and Novartis; DP, PK and JT are current employees and shareholders of Eli Lilly and Company; JL was an employee of Eli Lilly and Company; CM has been an advisory board member, investigator and/or speaker for: AbbVie, Amgen, Celgene, Eli Lilly and Company, Galderma, Leo Pharma, Merck, Novartis, and Tribute.
- This study was sponsored by Eli Lilly and Company. Medical writing assistance was provided by Lahari N A, a full time employee of Eli Lilly Services India Private Limited

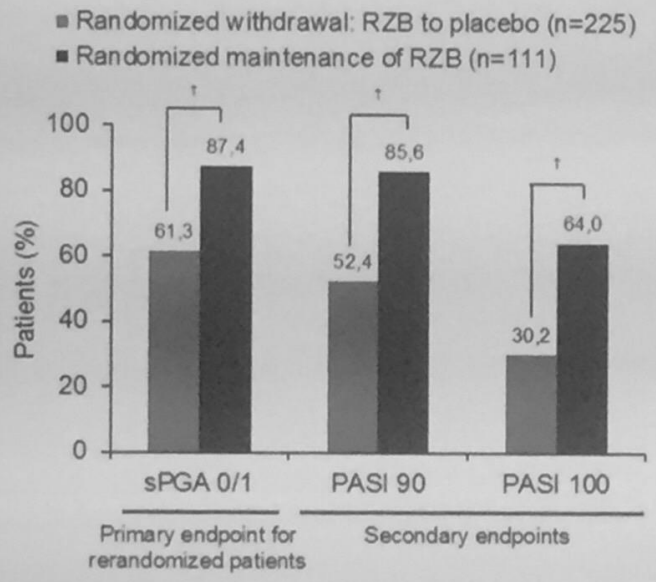
Reference:

1. Reich K, et al. *Br J Dermatol*. 2019 Feb 7. [Epub ahead of print]

SPIN 2019

IMMhance: Efficacy and safety of continuous 12-weekly risankizumab versus treatment withdrawal

Efficacy endpoints at Week 52 (NRI)

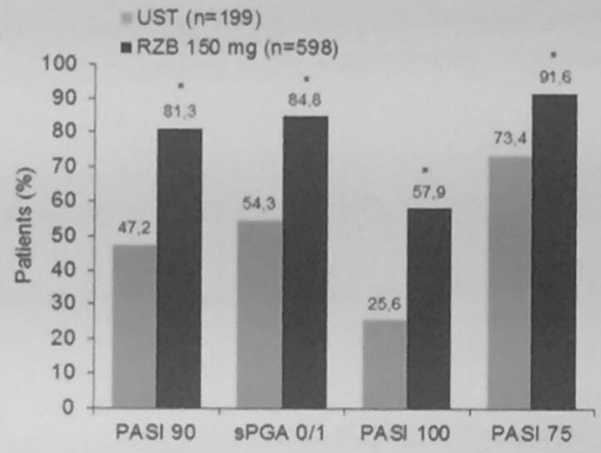


*P<0.01, †P<0.001 vs RZB/placebo

Langley R, et al. AAD 2019, P10093

598 patients receiving RZB and 199 receiving UST were included in this integrated analysis

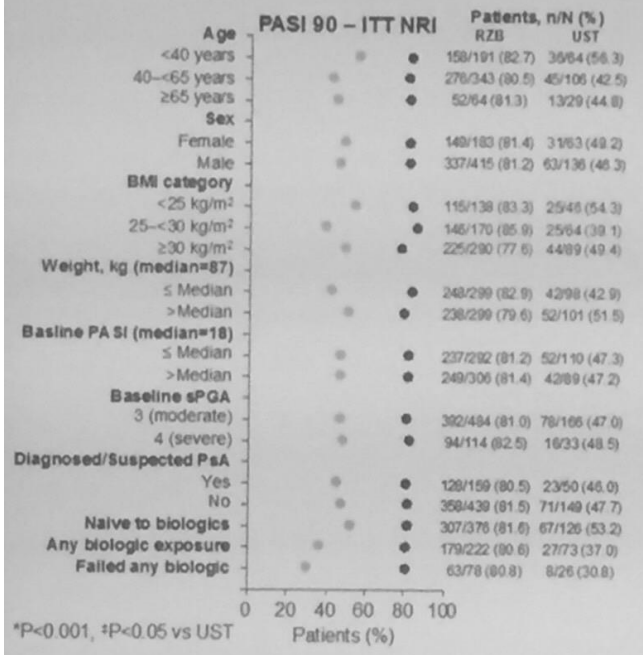
Efficacy outcomes at Week 52 (ITT NRI)

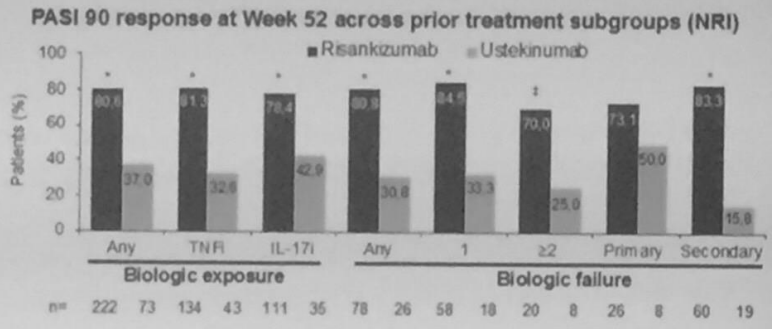


*P<0.001 vs ustekinumab

Lebwohl M, et al. AAD 2019, P8108 Sponsored by AbbVie Inc

ultIMMa-1 and ultIMMa-2: Durable efficacy of risankizumab compared with ustekinumab across subgroups of patients with psoriasis





Foley P, et al. AAD 2019, P9780 Sponsored by AbbVie Inc

Long-term safety of tildrakizumab in patients with moderate-to-severe psoriasis: pooled analysis through 148 weeks from two phase 3 trials

K Reich, D Thaçi, I Pau-Charles, A Igarashi, M Ohtsuki, MG Lebwohl, W Cantrell, S Rozzo, A Blauvelt, L Iversen

Table 1. Three-Year Cumulative EAIR of AEs

	TIL 100 mg N=872	TIL 200 mg N=928	PBO N=543	ETN N=313
SAE	118 (5.86)	112 (5.47)	13 (6.33)	20 (13.04)
Drug-related SAE	16 (0.79)	11 (0.54)	2 (0.97)	5 (3.26)
Discontinued due to SAE	19 (0.94)	16 (0.78)	1 (0.49)	5 (3.26)
Discontinued due to drug-related SAE	7 (0.35)	4 (0.20)	0 (0)	1 (0.65)
Severe infections	23 (1.14)	23 (1.12)	2 (0.97)	3 (1.96)
Malignancies (excluding NMSC)	11 (0.55)	8 (0.39)	0 (0)	2 (1.30)
NMSC	10 (0.50)	10 (0.49)	2 (0.97)	2 (1.30)
Confirmed MACE	8 (0.40)	11 (0.54)	1 (0.49)	1 (0.65)
Injection site reactions	39 (1.94)	47 (2.30)	11 (5.36)	62 (40.41)
Drug-related hypersensitivity reaction	6 (0.30)	3 (0.15)	1 (0.49)	0 (0)

Data are n (number of patients with event per 100 patient-years of exposure). AE: adverse event; EAIR: Exposure-Adjusted Incidence Rate; ETN: etanercept; MACE: Major adverse cardiovascular events; NMSC: non-melanoma skin cancer; PBO: placebo; SAE: serious adverse event.

Reich K, et al. Lancet 2017;390:276-88

6th Congress of the Skin Inflammation & Psoriasis International Network

SPIN 2019

25/27 APRIL 2019
CITÉ DES SCIENCES ET DE L'INDUSTRIE
PARIS - FRANCE

DEVELOPING A THERAPEUTIC WINDOW FOR SECUKINUMAB IN PSORIASIS: A STEP TOWARDS PERSONALIZED THERAPY

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2 Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Leuven, Belgium
3 Private practice Dermatology Maldegem, Belgium
4 Department of Dermatology, Maria Middelares Hospital, Ghent, Belgium

INTRODUCTION

A 'one size fits all' dosing regimen of secukinumab is currently applied in psoriasis patients which may lead to over- and undertreatment

OBJECTIVE

To define a therapeutic window of secukinumab that can be targeted in order to achieve optimal clinical response in psoriasis patients

MATERIALS AND METHODS

- 40 adult patients with psoriasis vulgaris
- Secukinumab 300 mg monthly (sc) for at least 24 weeks (maintenance)
- Single blood sampling at trough (before next administration)
- In-house developed secukinumab ELISA (KU Leuven)
- Clinical response evaluated with Psoriasis Area and Severity Index

TAKE HOME MESSAGE

Psoriatic patients with a suboptimal response and secukinumab trough concentrations below 33.2 µg/ml during maintenance are potentially undertreated and could benefit from dose intensification.

RESULTS

Secukinumab concentrations grouped based on absolute PASI

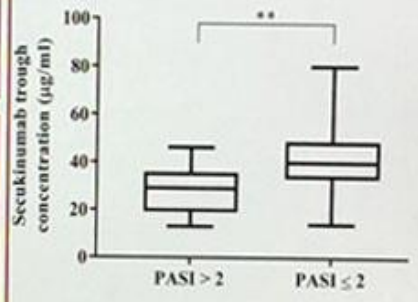


Figure 1. Secukinumab concentration (µg/ml) grouped based on absolute PASI score at trough.
Mann-Whitney U test, p = 0.004

Concentration effect curve of secukinumab for psoriasis cohort

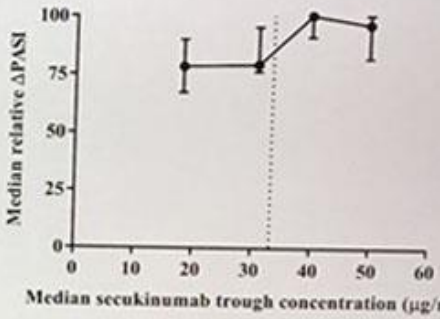


Figure 2. The dashed vertical line represents the pivotal secukinumab cutoff level of 33.2 µg/ml. Each black dot in the curve represents the median (IQR) secukinumab concentration, with correlating median ΔPASI score, for one group (4 equal-sized groups)

Funding: FWO-TBM (T003716N and T003218N)

KU LEUVEN SPIN GPs UZ

Contact:

Ustekinumab for the Treatment of Moderate-to-severe Plaque Psoriasis in Pediatric Patients (≥6 to <12 Years of Age): Results From CADMUS Jr

S. Philipp,[1] A. Menter,[2] A. Nikkels,[3] K. Barber,[4] M. Song,[5] B. Randazzo,[5] S. Li,[5] M.-C. Hsu,[5] A. Paller[6]

[1]Charite – Universitatsmedizin Berlin, Berlin, Germany; [2]Baylor Scott & White Health at Dallas, Dallas, TX, USA; [3]Centre Hospitalier Universitaire de Liege Domaine Universitaire du Sart Tilman, Liege, Belgium; [4]Kirk Barber Research, Inc., Calgary, Alberta, Canada; [5]Janssen Research & Development, LLC, Spring House, PA, USA; [6]Northwestern University Feinberg School of Medicine and Ann & Robert H Lurie Children's Hospital, Chicago, IL, USA

Author Disclosures: S. Philipp, A. Menter, A. Nikkels, K. Barber, and A. Paller are advisors, investigators, and/or speakers for Janssen. M. Song, B. Randazzo, S. Li, and M.-C. Hsu are employees of Janssen Research & Development, LLC.

Objective

- To evaluate the efficacy and safety of ustekinumab in pediatric patients with moderate-to-severe plaque psoriasis (PsO)

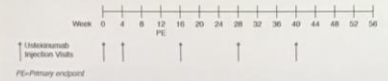
Methods

- CADMUS Jr is a phase 3, open-label, single-arm, multicenter (20 sites in 7 countries) study conducted to evaluate ustekinumab in pediatric patients (≥6 to <12 years of age) with moderate-to-severe plaque PsO
  - To be eligible for enrollment, patients had to have a:
    - Psoriasis Area and Severity Index (PASI) score ≥12
    - Physician's Global Assessment (PGA) score ≥3
    - Percent body surface area (BSA) involved with PsO ≥10%
    - And be candidates for phototherapy/systemic treatment or considered by the investigator to be poorly controlled with topical therapy
  - Patients received a weight-based standard dose of ustekinumab (Table 1) administered by subcutaneous (SC) injection at Weeks 0 and 4, followed by every 12 week dosing through Week 40 (Figure 1)
  - Primary Endpoint: PGA score of cleared (0) or minimal (1) (PGA 0/1) at Week 12
  - Major Secondary Endpoints:
    - PASI 75 response at Week 12
    - PASI 90 response at Week 12
    - Change from baseline in the Children's Dermatology Life Quality Index (CDLQI) at Week 12
  - Patients were considered non-responders after discontinuing treatment for lack of efficacy, an adverse event of PsO worsening, or use of a prohibited PsO treatment, zero improvement was assigned for these cases (treatment failure rules (TFR)). After applying TFR, no other imputation rules were applied except that patients with missing data at Week 12 were considered non-responders.
  - Safety was evaluated through Week 56

Table 1. Weight-based Dose of Ustekinumab

Weight	Ustekinumab Standard Dosage
<60 kg	0.75 mg/kg
≥60 to ≤100 kg	45 mg
>100 kg	90 mg

Figure 1. Study Design



PE=Primary endpoint

Results

- A total of 44 patients (age range, 6-11 years; mean age [± standard deviation (SD)], 8.9 [±1.74] years; mean weight, 38.4 (±14.68] kg) were enrolled and received at least one injection of ustekinumab (Table 2); most were white (90.9%) and female (61.4%)
- At baseline, the mean duration of PsO was 3.5 (±2.49) years. Patients had moderate-to-severe disease, as evidenced by the mean PASI score (17.9±7.73) and percent BSA (23.3±13.71); 65.9% and 34.1% of patients presented with PGA=3 (moderate) and PGA ≥4 (marked/severe) scores, respectively (Table 2). Mean CDLQI at baseline (8.1±5.69) indicated a moderately negative effect of PsO on health-related quality of life (HRQoL).
- Three patients (6.8%) discontinued study agent before Week 40

Table 2. Summary of Baseline Demographics, PsO Characteristics, and Previous PsO Medications and Therapies

	Ustekinumab
Patients enrolled and treated, N	44
Age [years], mean (SD)	8.9 (1.74)
Age range, years	(6, 11)
Female, n (%)	27 (61.4%)
Weight [kg], mean (SD)	38.4 (14.68)
Weight range, kg	(19, 99)
PsO Characteristics	
% BSA, mean (SD)	23.3 (13.71)
PASI score (0-72), mean (SD)	17.9 (7.73)
PGA score, n (%)	
Moderate (3)	29 (65.9%)
Marked (4)	14 (31.8%)
Severe (5)	1 (2.3%)
Previous PsO Medications and Therapies, n (%)	
Topical agents	43 (97.7%)
Phototherapy (PUVA or UVB)	15 (34.1%)
Non-biologic systemics	8 (18.2%)
Biologics	2 (4.5%)
Naïve to non-biologic systemics and biologics	34 (77.3%)
Naïve to non-biologic systemics and phototherapy	25 (56.8%)

PsO=Psoriasis; BSA=Body surface area; PASI=Psoriasis Area and Severity Index; PGA=Physician's Global Assessment; PUVA=Psoralen and Ultraviolet A; UVB=Ultraviolet B

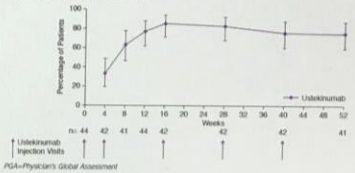
- At Week 12, 77.3% (95% confidence interval [CI]: 62.2%, 88.5%) of patients achieved a PGA 0/1 response, 84.1% (95% CI: 69.9%, 93.4%) achieved a PASI 75 response, and 63.6% (95% CI: 47.8%, 77.6%) achieved a PASI 90 response. The mean change from baseline in CDLQI was -6.3 (95% CI: -8.29, -4.28). (Table 3)

Table 3. Primary and Major Secondary Endpoints

Endpoints	Ustekinumab
Patients enrolled and treated, N	44
Primary Endpoint: PGA 0/1 at Week 12, n (%); (95% CI)	34 (77.3%); (62.2%, 88.5%)
Major Secondary Endpoints	
PASI 75 at Week 12, n (%); (95% CI)	37 (84.1%); (69.9%, 93.4%)
PASI 90 at Week 12, n (%); (95% CI)	28 (63.6%); (47.8%, 77.6%)
CDLQI mean change from baseline (SD); (95% CI)	-6.3 (6.43); (-8.29, -4.28)

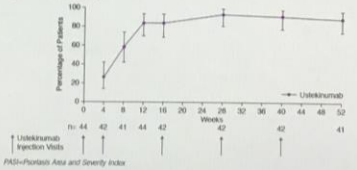
PGA=Physician's Global Assessment; CI=Confidence Interval; PASI=Psoriasis Area and Severity Index; CDLQI=Children's Dermatology Life Quality Index

Figure 2. PGA 0/1 Response Rate Over Time



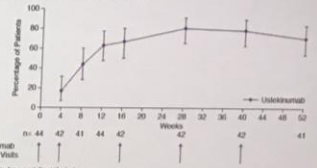
PGA=Physician's Global Assessment

Figure 3. PASI 75 Response Rate Over Time



PASI=Psoriasis Area and Severity Index

Figure 4. PASI 90 Response Rate Over Time



PASI=Psoriasis Area and Severity Index

- Overall, 34 patients (77.3%) had at least one adverse event and 3 patients (6.8%) each had one serious adverse event (mononucleosis, eyelid injury, and attention-deficit/hyperactivity disorder [ADHD]). One serious infection of mononucleosis was reported. Twenty-nine patients (65.9%) had infections (most commonly reported were nasopharyngitis, pharyngitis, and upper respiratory tract infection) and 12 (27.3%) had infections requiring treatment. (Table 4)
- All 16 injections with injection-site reactions were mild in intensity and resolved in less than 1 day. The most common injection-site reaction was injection site erythema. Of note, 5 of the 6 patients with injection-site reactions reported were from a single site.
- No malignancies, major adverse cardiovascular events, anaphylactic reactions, or serum sickness-like reactions were reported

Table 4. Overview of Safety Events Through Week 56

	Ustekinumab
Patients enrolled and treated, N	44
Average duration of follow-up (weeks)	53.15
Average exposure (number of administrations)	4.77
Patients who discontinued study agent because of ≥1 AE, n (%)	0
≥1 AE, n (%)	34 (77.3%)
≥1 SAE, n (%)	3 (6.8%)
Overall infections, n (%)	29 (65.9%)
Infections requiring treatment	12 (27.3%)
Serious infections	1 (2.3%)
Malignancy, n (%)	0
MACE*, n (%)	0
Anaphylactic reaction or serum sickness-like reaction, n (%)	0
Injection-site reaction, n (%)	6 (13.6%)
Total number of injections, n	210
Injections with injection-site reaction, n (%)	16 (7.6%)

AE=Adverse event; SAE=Serious adverse event; MACE=Major adverse cardiovascular event
*MACE: investigator reported nonfatal myocardial infarction (MI), nonfatal stroke or cardiovascular (CV) death

Conclusions

- Ustekinumab was highly effective in treating moderate-to-severe plaque PsO in patients 6-11 years of age, and no new safety concerns were identified in this pediatric population

Assessing The Differences Between Psoriasis Patients Who Are Aligned With Their Dermatologists On Their Current Disease Severity Versus Patients Who Are Misaligned

Neil Korman[1], Lisa Renda[2], Mwangi Murage[2], Orin Goldblum[2], Chen-Yen Lin[2], Steve Lobosco[3], James Lucas[3], Chloe Middleton[3] and Bill Malatestinic[2].

[1]University Hospitals Case Medical Center, Cleveland [2]Lilly USA, LLC, [3]Adelphi Real World, United Kingdom.

Introduction

Psoriasis (PsO) is a chronic inflammatory disease, typically characterized by red, thick and scaly plaques. Increased disease severity can have a negative impact on the quality of life of patients. Previous studies have indicated there is a disconnect between patients and dermatologists on disease severity.[1]

Objective

The aim of this analysis is to assess the differences in clinical burden and quality of life between patients who are aligned vs. misaligned with their dermatologist on their current disease severity.

Methods

Data were drawn from the Adelphi 2017 PsO Disease Specific Programme (DSP); a real world survey of PsO patients and their treating dermatologists in the US.

Dermatologists reported their assessment of the patient's current disease severity whilst patients independently reported their own subjective assessment of current disease severity as mild, moderate or severe. Patients were assigned to one of two groups ('aligned' or 'misaligned') based on agreement between patient self-reported and dermatologist reported severity.

Statistical analyses

Patient groups were compared using analysis of covariance continuous and multivariate logistic regression for categorical variabl Time since diagnosis, sex, current treatment with a biologic, a concurrent psoriatic arthritis were included as covariates.

Patient cohorts for analysis

Of the 219 patients included in the analysis, 164 were aligned and 5 were misaligned regarding reported disease severity (table 1).

Table 1: Dermatologist and patient reported disease severity

Base: n=219		Patient reported severity			
		Mild	Moderate	Severe	
Dermatologist reported severity	Mild	139	16	6	n=55 misaligned
	Moderate	21	19	7	
	Severe	3	2	6	n=164 aligned

1. C.E.M Griffiths, et al. Journal of the American Academy of Dermatology , Volume 76, Issue 6 , AB102 https://doi.org/10.1111/jdv.14937

Study was sponsored by Eli Lilly and Company

Assessing The Differences Between Psoriasis Patients Who Are Aligned With Their Dermatologists On Their Current Disease Severity Versus Patients Who Are Misaligned

- Demographically, patients who were misaligned were significantly older than aligned patients (51.0, vs. 45.5 years, p=0.005).
- Misaligned patients had a higher Body Surface Area (BSA) (10.08%, vs. 4.54%, p=0.002) (figure 1).
- On a scale of 0 (no itch) to 10 (worst possible itch), misaligned patients reported a higher intensity (4.21 vs. 2.67, p=<0.001) (figure 2) and greater odds of increased frequency of itching (OR: 3.655, p=<0.001) (figure 3).
- Misaligned patients also had higher odds of currently flaring (OR: 3.092, p=0.010) and lower odds of being satisfied with treatment control (OR: 0.390, p=0.006) (figure 3).

Figure 1: Current BSA%

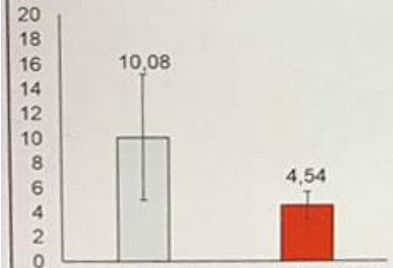


Figure 2: Intensity of Itching (0-10 scale)

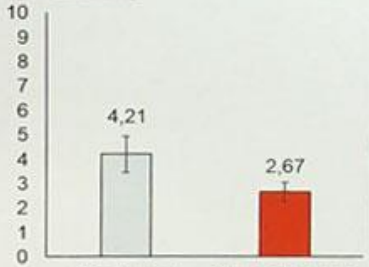
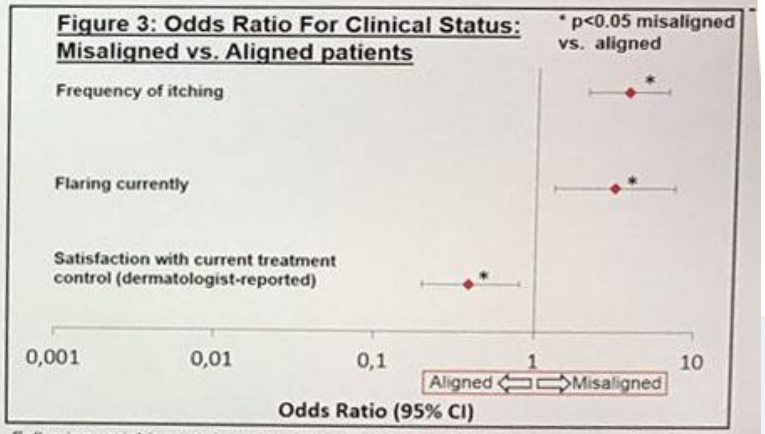


Figure 3: Odds Ratio For Clinical Status: Misaligned vs. Aligned patients



Following variables used as covariates; Time since diagnosis, sex, current treatment [illegible] logic, and concurrent psoriatic arthritis

Assessing The Differences Between Psoriasis Patients Who Are Aligned With Their Dermatologists On Their Current Disease Severity Versus Patients Who Are Misaligned

- Overall the mean DLQI score was significantly higher for misaligned patients (6.92 vs. 4.71, p=0.010) (figure 4).
- Misaligned patients had higher odds of reporting itchy/sore skin (OR: 3.232, p<0.001), being embarrassed with skin (OR: 2.355, p=0.004) and PsO influencing choice of clothes (OR: 2.642, p=0.002) (figure 5).
- Misaligned patients also had higher odds of reporting impaired sleep (OR: 2.486, p=0.003) (figure 5).

Figure 4: Dermatology Life Quality Index (DLQI) Score

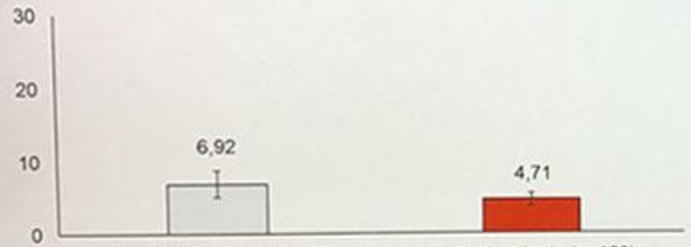
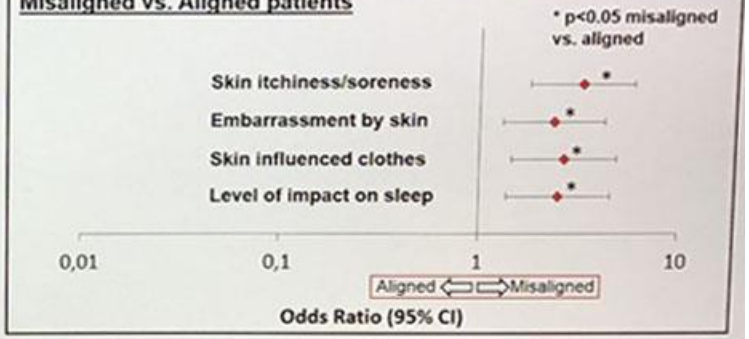


Figure 5: Dermatology Life Quality Index (DLQI) Domain Misaligned vs. Aligned patients



CONCLUSIONS

Patients who were misaligned with their dermatologist on the current level of their disease severity were more likely to report a higher clinical burden and lower levels of satisfaction with treatment control. They also had a higher likelihood of reporting a lower quality of life, greater intensity of itching and impaired sleep. These findings underscore the importance of alignment on severity between dermatologists and patients for optimal PsO control.

LIMITATIONS

Dermatologist inclusion is likely influenced by willingness to take part, and practical considerations of geographical location. The methodology relied on accurate reporting by physicians/patients.

Background

Chikungunya, dengue, and zika infections:

- Exacerbation of psoriasis J Dermatol. 2011;38:1033-4 J Clin Virol. 2014;61:442-3
- Relationship with the worsening of psoriasis?

Objectives

Does the arboviruses result in clinical modification of psoriasis in patients under biological therapy?

Methods

Retrospective (2016-2018, 53 consecutive patients):

- Psoriasis + biological therapy
- Active screening for arboviruses infections
- Demographic, clinical, therapeutic data
- Clinical outcomes:
  - No interference vs exacerbation of psoriasis
  - Need for biological suspension

Statistical analysis

- Independent t-test, chi-square test
- P<0.05 → significant

Results

- Age (52±14 years), Females (51%), BMI (±)
- Vulgar type (68%), since diagnosis (231±108 months)
- Biologic therapy (77±44months), adalimumab (37.5%)
- Arboviruses infection (11%)

Exacerbation of psoriasis (7%)

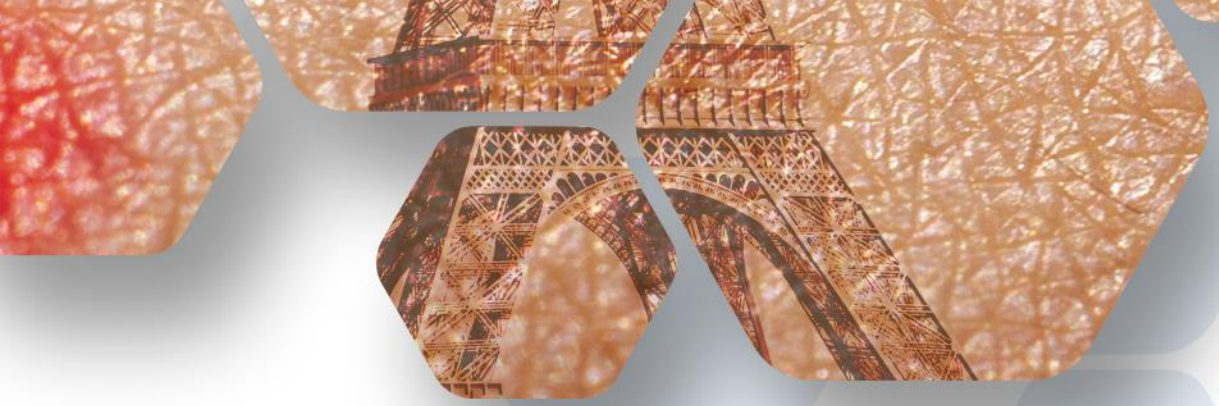
-Associated with presence of arboviruses infection (see Tabl

-83% successful management under biological therapy

Parameters	Psoriasis Worsening (No/Yes) n (%)	P-value
Arboviruses	50 (89.3) / 6 (10.7)	<0.01
Immunosup. therapy	24 (42.9) / 32 (57.1)	0.45
Comorbidity	24 (42.9) / 32 (57.1)	0.17
Alcoholism	52 (92.9) / 4 (7.1)	0.56
Familiar history	54 (96.4) / 2 (3.6)	0.69
Smoking	53 (94.6) / 3 (5.4)	0.07
Diagnosis/Biologic therapy	Variable by type	0.90

Conclusions

- Arboviruses infection was significantly associated with exacerbation of psoriasis.



Gracias por su atención

Iniciativa científica de: