FRI0429

NON TOPICAL PHARMACOLOGICAL TREATMENT OF EARLY, UNTREATED (DMARD-NAÏVE, SYSTEMIC THERAPY-NAÏVE) PSORIATIC DISEASE: A SYSTEMATIC REVIEW

Gabriele De Marco^{1,2}, Anna Berekmeri^{1,2}, Laura C. Coates³, Sayam Dubash^{1,2}, Dafna D. Gladman⁴, Ennio Lubrano⁵, Dennis McGonagle^{1,2}, Farrouq Mahmood², Antonio Marchesoni⁶, Alexis Ogdie⁷, Miriam Wittmann^{1,2}, Helena Marzo-Ortega^{1,2}, Philip Helliwell^{1,2}. ¹University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom; ²NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom; ³University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom; ⁴University of Toronto, Toronto Western Hospital and Krembil Research Institute, Toronto, Ontario, Canada; ⁵Università degli Studi del Molise, Dipartimento di Medicina e Scienze della Salute "Vincenzo Tiberio", Campobasso, Italy; ⁶ASST Gaetano Pini-CTO, Rheumatology, Milan, Italy; ⁷Perelman School of Medicine, University of Pennsylvania, Philadelphia, United States of America

Background: Psoriatic disease (PsD) refers to a systemic condition, probably driven by chronic and complex inflammatory mechanisms. PsD patients experience a fickle mixture of cutaneous (nail dystrophy, psoriatic lesions spectrum) and musculoskeletal (MSK: arthritis, enthesitis, dactylitis, spondylitis) inflammatory features, variously associated with other co-morbidities (ocular or bowel inflammatory disease, increased cardiovascular risk and metabolic syndrome). Current evidence is limited in respect of the management of early, treatment-naïve PsD.

Objectives: To assess the literature with a focus on pharmacological interventions in early, treatment-naïve PsD.

Methods: Seven research questions were formulated according to the PICO approach: are interventions effective in obtaining control of overall PsD activity? Are interventions effective on peripheral arthritis? On dactylitis? On spondylitis? On enthesitis? On skin and nails? The search was designed as a systematic review of the literature. Early PsD was defined as disease duration ≤2 years, except for studies investigating outcomes restricted to the skin. Criteria for including records were: adult human participants; participants with cutaneous features of PsD; participants with MSK features of PsD; double blind, single blind and non-blinded RCT; well-designed prospective studies/series.

The search protocol was registered on PROSPERO [1], the search was performed between June 2018 and January 2019.

Results: Resources available were widely explored (4 databases, 5 trial registers, 5 conference archives; see figure). The search retrieved 156,348 references (publication range 1946–2019) of which 308 (0.2%) qualified for full-text-assessment (FTA, figure); 7 (0.0004%) fulfilled the selection criteria and only 4 underwent data extraction.

The search protocol was registered on PROSPERO [1], the search was performed between June 2018 and January 2019.

Results: Resources available were widely explored (4 databases, 5 trial registers, 5 conference archives; see figure). The search retrieved 156,348 references (publication range 1946–2019) of which 308 (0.2%) qualified for full-text-assessment (FTA, figure); 7 (0.0004%) fulfilled the selection criteria and only 4 underwent data extraction.

Ref. type	PsD feature targeted	Intervention (success)	Primary outcome
1 RCT	Skin	Secukinumab (yes) vs fumarates (no)	PASI75
2 cohort	MSK	MTX part of T2T (yes)	Unclear
3 RCT	MSK	MTX (partial)	Joint count
4 RCT	Skin	Apremilast (yes)	PGAxBSA

Meta-analysis was impossible due to data heterogeneity (disease classification criteria, outcome measures and intervention durations). Although no clinical study adopted comprehensive composite indexes as primary outcome measures, 40% of FTA references described more than one component of PsD (i.e.: cutaneous and MSK) at least within the baseline characteristics. A substantial proportion of FTA references did describe, among participants recruited, many who were early untreated PsD at baseline. Unfortunately, separate analyses were not possible due to unavailability of the original datasets. A subset (10%) of the FTA references did not report on the participants' exposure to previous treatment.

Conclusion: Few studies addressed early, treatment naïve PsD. The underrepresentation of such data may be related to trial-enrolment criteria. More studies are needed to investigate this identified unmet need.

REFERENCES:

- [1] http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018097366

Non topical pharmacological treatment of early, untreated (DMARD-naïve, systemic therapy-naïve) psoriatic disease: a systematic review

Figure

Acknowledgement: The authors wish to thank librarians J. Emmel and L. Mason for their support.

Disclosure of Interests: Gabriele De Marco: None declared, Anna Berekmeri: None declared, Laura C Coates Grant/research support from: AbbVie, Celgene, Lilly, Novartis and Pfizer, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead Sciences Inc., Janssen, Lilly, Novartis, Pfizer, Prothena Corp and UCB, Sayam Dubash: None declared, Dafna D Gladman Grant/research support from: AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB, Ennio Lubrano Consultant for: Consultancy fees as speaker from Abbvie, Celgene, Novartis and Pfizer, Dennis McGonagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB, Farrouq Mahmood: None declared, Antonio Marchesoni Consultant for: honoraria from Abbvie, BSM, Celgene, Janssen, MSD, Novartis, Pfizer, UCB, Alexis Ogdie Grant/research support from: (To my university) Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly and Company, Novartis, Pfizer, and Takeda, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly, Novartis, Pfizer Inc, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Miriam Wittmann Consultant for: consultancy honoraria from Abbvie, Celgene, Janssen, L'Oreal, Novartis and Pfizer, Helena Marzo-Ortega Grant/research support from: Janssen, Novartis and Pfizer, Consultant for: AbbVie, Celgene, Janssen, Eli-Lilly, Novartis and UCB, Speakers bureau: AbbVie, Celgene, Janssen, Eli-Lilly, Novartis and UCB, Philip Helliwell Grant/research support from: Paid to charity: from AbbVie, Janssen and Novartis, Consultant for: Paid to charity: from AbbVie, Amgen, Pfizer, and UCB and Celgene. Paid to self: from Celgene and Galapagos

DOI: 10.1136/annrheumdis-2019-eular.1837

FRI0430

IXEKIZUMAB IMPROVES THE SIGNS AND SYMPTOMS OF PSORIATIC ARTHRITIS REGARDLESS OF SEX, DURATION OF DISEASE, OR BODY MASS INDEX IN TWO RANDOMIZED, PHASE 3 CLINICAL TRIALS

Lili Eder¹, Satish Odhav², Mariusz Korkosz³, Aubrey Trevelin Sprabery⁴, Amanda M. Gellett⁴, Chen-Yen Lin⁴, So Young Park⁴, Clinton C. Bertram⁴, Alexis Ogdie⁵.

¹Women's College Hospital, Alberta, Canada; ²Arthritis Clinic, Jackson, United States of America; ³Jagiellonian University Medical College, Kraków, Poland; ⁴Eli Lilly and Company, Indianapolis, United States of America; ⁵Penn Medicine, Philadelphia, United States of America

Background: Ixekizumab (IXE) is a high-affinity monoclonal antibody that selectively targets interleukin-17A. During 24 weeks (wks) of treatment, IXE resulted in significantly greater improvements versus placebo (PBO) in the signs and symptoms of active psoriatic arthritis (PsA) in two randomized Phase 3 studies.^{1,2}

Objectives: To evaluate the consistency of clinical response with IXE in demographic subsets of patients (pts) with active PsA.

Methods: Clinical response to IXE was analyzed from an integrated database of 2 randomized, double-blind, Phase 3 studies in biologic Disease

Modifying Anti-Rheumatic Drug (bDMARD)-naïve (SPIRIT-P1) pts or in pts with prior inadequate response or intolerance to TNF inhibitors (SPIRIT-P2). Analyses were conducted on subgroups defined by sex, body mass index (BMI), and duration of disease (<5 or ≥5 years) at baseline for pts who were randomly assigned to either PBO or the approved dosing regimen of IXE (80 mg IXE every 4 wks [IXE Q4W] with a starting dose of 160-mg IXE). Efficacy in each subgroup was evaluated as the percentage of pts at Wk 24 achieving ≥20%, 50%, or 70% improvement from baseline in the American College of Rheumatology criteria (ACR20/50/70) or minimal disease activity. Missing data were imputed using nonresponder imputation (NRI).

	ACR20		ACR50		ACR70		MDA	
	PBO (N=224)	IXE Q4W (N=229)	PBO (N=224)	IXE Q4W (N=229)	PBO (N=224)	IXE Q4W (N=229)	PBO (N=224)	IXE Q4W (N=229)
Sex								
Male	23/104 (22)	67/108 (62)†	12/104 (12)	51/108 (47)†	3/104 (3)	31/108 (29)†	9/104 (9)	38/108 (35)†
Female	32/120 (27)	60/121 (50)†	10/120 (8)	35/121 (29)†	3/120 (3)	21/121 (17)†	11/120 (9)	28/121 (23)†
Time since symptom onset, years								
0 to <5	21/63 (33)	39/71 (55)*	11/63 (18)	28/71 (39)†	3/63 (5)	18/71 (25)†	11/63 (18)	24/71 (34)*
≥5	34/161 (21)	88/158 (56)†	11/161 (7)	58/158 (37)†	3/161 (2)	34/158 (22)†	9/161 (6)	42/158 (27)†
BMI category, (kg/m²)								
Underweight (<18.5)	0/0 (0)	0/3 (0)	0/0 (0)	0/3 (0)	0/0 (0)	0/3 (0)	0/0 (0)	1/3 (33)
Normal (≥18.5 and <25)	13/39 (33)	30/49 (61)*	6/39 (15)	20/49 (41)*	4/39 (10)	11/49 (22)	7/39 (18)	15/49 (31)
Overweight (≥25 and <30)	19/90 (21)	37/67 (55)†	10/90 (11)	29/67 (43)†	2/90 (2)	20/67 (30)†	9/90 (10)	25/67 (37)†
Obese (≥30 and <40)	18/74 (24)	47/84 (56)†	6/74 (8)	29/84 (35)†	0/74 (0)	18/84 (21)†	4/74 (5)	21/84 (25)†
Extreme Obese (≥40)	5/20 (25)	11/24 (46)	0/20 (0)	6/24 (25)*	0/20 (0)	2/24 (8)	0/20 (0)	3/24 (13)

Data are provided as n/Ns (%) where n=number of responders and N=number of patients in each subgroup
p-values from Fisher's exact test. *p<0.05, †p<0.01, ‡p<0.001
ACR20/50/70 = ≥20%, 50%, or 70% improvement from baseline in the American College of Rheumatology criteria; BMI = body mass index; IXE Q4W = 80 mg IXE every 4 wks; MDA = minimal disease activity; NRI = nonresponder imputation; PBO = Placebo

Results: Response rates at Wk 24 (Table) were significantly ($p<0.05$) greater in pts receiving IXE versus PBO across all endpoints assessed in subgroups defined by sex, disease duration, and in pts with overweight and obese BMI at baseline. Response rates were significantly greater with IXE compared to PBO for ACR20 and ACR50 in the normal BMI subgroup and for ACR50 in the extreme obese BMI subgroup. Assessment of superiority of IXE versus PBO in underweight and extreme obese subgroups was limited by small sample sizes; only three patients (all receiving IXE Q4W) had underweight BMI at baseline. For all endpoints assessed, numerically greater response rates were observed with IXE Q4W in male versus female pts.

Conclusion: IXE was superior to PBO in the treatment of pts with active PsA at Wk 24 regardless of sex or disease duration, as well as in normal, overweight, and obese BMI subgroups.

REFERENCES:

- [1] Mease, et al. Ann Rheum Dis. 2017
- [2] Nash, et al. Lancet. 2017

Disclosure of Interests: Eli Lilly and Company, Amgen, Celgene, UCB, Janssen, Novartis, and Pfizer, Consultant for: AbbVie, Eli Lilly and Company, Amgen, Celgene, UCB, Janssen, Novartis, and Pfizer, Satish Odhav Grant/research support from: AbbVie, Ardea Biosciences, AstraZeneca, BMS, Celgene Corporation, Centocor, Eli Lilly and Company, Galapagos, Genentech, GSK, Human Genome Sciences, Janssen, Merck, Mesoblast, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis, Takeda Pharmaceuticals, UCB, and Vertex Pharmaceuticals, Consultant for: AbbVie, Ardea Biosciences, AstraZeneca, BMS, Celgene Corporation, Centocor, Eli Lilly and Company, Galapagos, Genentech, GSK, Human Genome Sciences, Janssen, Merck, Mesoblast, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis, Takeda Pharmaceuticals, UCB, and Vertex Pharmaceuticals, Speakers bureau: AbbVie, Ardea Biosciences, AstraZeneca, BMS, Celgene Corporation, Centocor, Eli Lilly and Company, Galapagos, Genentech, GSK, Human Genome Sciences, Janssen, Merck, Mesoblast, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis, Takeda Pharmaceuticals, UCB, and Vertex Pharmaceuticals, Speakers bureau: AbbVie, Ardea Biosciences, AstraZeneca, BMS, Celgene Corporation, Centocor, Eli Lilly and Company, Galapagos, Genentech, GSK, Human Genome Sciences, Janssen, Merck, Mesoblast, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis, Takeda Pharmaceuticals, UCB, and Vertex Pharmaceuticals, Mariusz Korkosz Consultant for: Eli Lilly and Company, Novartis, Roche, MSD, UCB, and AbbVie, Speakers bureau: Eli Lilly and Company, Novartis, Roche, MSD, UCB, and AbbVie, Aubrey Trevelin Sprabery Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Amanda M. Gellett Shareholder of: Eli Lilly and Company,

Employee of: Eli Lilly and Company, Chen-Yen Lin Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, So Young Park Employee of: Eli Lilly and Company, Clinton C Bertram Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Alexis Ogdie Grant/research support from: (To my university) Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly and Company, Novartis, Pfizer, and Takeda, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly, Novartis, Pfizer Inc, Takeda, Consultant for: AbbVie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: AbbVie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda

DOI: 10.1136/annrheumdis-2019-eular.1474

FR10431

EFFECT OF PHOSPHODIESTERASE 4 INHIBITION WITH APREMILAST ON BODY WEIGHT AND VASCULAR FUNCTION IN PSORIATIC ARTHRITIS – INITIAL RESULTS FROM THE IMMUNE METABOLIC ASSOCIATIONS IN PSORIATIC ARTHRITIS (IMAPA) STUDY

Lyn D. Ferguson¹, Paul Welsh¹, Naveed Sattar¹, Iain McInnes², Stefan Siebert².

¹University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom; ²University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom

Background: Psoriatic arthritis (PsA) is associated with obesity and increased cardiometabolic risk. Weight loss is associated with improved disease activity and has been noted with the phosphodiesterase 4 (PDE4) inhibitor apremilast.

Objectives: To investigate the effects of PDE4 inhibition with apremilast on body weight, vascular function and disease activity in psoriatic disease.

Methods: The Immune Metabolic Associations in Psoriatic Arthritis (IMAPA) study is a prospective, open label study of adults receiving apremilast 30mg BD as part of routine care for psoriasis and/or PsA. Cardiometabolic, anthropometric, and disease activity assessments were performed at baseline, months 1, 3, and 6. A subgroup underwent endothelial function assessment by Endo-PAT at baseline and month 3. Repeated measures mixed models were used to compare changes in body weight, waist circumference, systolic & diastolic BP, reactive hyperaemia index (RHI), and disease activity markers with apremilast.

Results: 53 participants were recruited; mean age (SD) 52 (13) years, 64% female, mean disease duration (SD) 9.3 (8.1) years. To date, data available for n=47 at month 1, n=42 month 3, and n=29 at month 6. Mean weight loss after 6 months apremilast was -1.9kg (95% CI -2.8, -1.0); 13% (7/53) lost ≥5% body weight. Statistically significant improvements in 66/68 joint count, DAS28-ESR, PtGA, PGA, pain-VAS, LEI, and ESR were seen at month 6. There was no statistically significant change in RHI, SBP, or DBP (table 1). Weight change showed no statistically significant correlation with change in joint or skin disease activity markers.

Conclusion: Apremilast was associated with modest weight loss and reduced disease activity over 6 months. There did not appear to be any significant alteration in endothelial function, however this was assessed in relatively small numbers and many patients had baseline results within normal range. Improvements in disease activity with apremilast appear largely independent of weight change in this cohort.

Acknowledgement: Celgene; BHF (RE/13/50177).

Disclosure of Interests: Lyn D. Ferguson: None declared, Paul Welsh: None declared, Naveed Sattar Grant/research support from: Boehringer Ingelheim, Consultant for: Eli Lilly, Boehringer Ingelheim, Janssen, Novo Nordisk, Sanofi, Speakers bureau: Eli Lilly, Boehringer Ingelheim, Janssen, Novo Nordisk, Sanofi, Iain McInnes Grant/research support from: AstraZeneca, Celgene, Compugen, Novartis, Roche, UCB Pharma, Consultant for: AbbVie, Celgene, Galvani, Lilly, Novartis, Pfizer, UCB Pharma, Stefan Siebert Grant/research support from: AbbVie, Novartis, Pfizer, Janssen, BMS, Celgene, UCB, and Boehringer Ingelheim, Consultant for: AbbVie, UCB, Pfizer, Janssen, Boehringer Ingelheim, Celgene, and Novartis, Speakers bureau: AbbVie, UCB, Pfizer, Janssen, Boehringer Ingelheim, Celgene, and Novartis

DOI: 10.1136/annrheumdis-2019-eular.1204