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LETTER TO THE EDITOR

Improvements in patient-reported outcomes with oral roflumilast for psoriasis: Results from a randomized controlled trial (PSORRO)

Dear Editor,

Psoriasis is associated with both physical and psychological discomfort, and in recent years, patient-reported outcomes (PROs) have become widely used in clinical and scientific settings. Comprising reports of a patient's health condition or behaviour that come directly from the patient, PROs provide clinicians with important information that may influence disease management.[1] Oral roflumilast is a phosphodiesterase (PDE)-4 inhibitor approved for chronic obstructive pulmonary disease, but recent data have shown that the therapy is also efficacious and safe in psoriasis.[2] The objective of this paper was to describe PROs with oral roflumilast in patients with moderate-to-severe psoriasis.

Data were collected in the PSORRO study, an investigator-initiated, company-independent 24-week trial, where patients were allocated 1:1 to oral roflumilast 500 μg once-daily or placebo, followed by open-label active treatment in both arms (EudraCT 2020-000711-76; ClinicalTrials.gov NCT04549870). Detailed study design has been published previously.[2] Predefined endpoints included dermatology life quality index (DLQI) (range 0–30), Beck depression inventory (BDI) II (range 0–63) and numeric rating scale (NRS) for itch and skin pain (range 0–10). In addition, patient-reported treatment satisfaction was quantified using a composite NRS covering effect, tolerance and convenience (range 0–10).

Statistical analyses were performed in Python version 3.7.6 (Python Software Foundation) with outcomes based on intention-to-treat (ITT) and tested with Mann–Whitney *U* tests (numeric variables) or chi-squared test/Fischer's exact test (categorical variables). Missing data were handled with non-responder imputation (NRI) and last observation carried forward (LOCF), when appropriate.

Forty-six patients were randomized; of these, 42 and 38 completed week 12 (placebo-controlled period) and 24 (open-label, active period), respectively. Baseline data were generally proportionate between the two groups (Table 1). Median age was 38.5 years; 74% were men and median psoriasis and severity index (PASI) was 10.8. At 12 weeks, significant improvements in DLQI and NRS itch, pain and treatment satisfaction were achieved with oral roflumilast compared to placebo. Responses were maintained through week 24, where a corresponding catch-up was seen in patients initially allocated to placebo. In both treatment arms, median BDI II was in the bottom end of the normal range at baseline and decreased during the study period, however not statistically significant (Table 2).

In this company-independent trial, significant PRO improvements were observed with oral roflumilast in patients with psoriasis. These results correspond well with efficacy (PASI75 in 44% of patients at week 24) and safety data from the PSORRO trial.[2] Previously, only one small pilot study has reported PROs with oral roflumilast. Here, 12 weeks treatment improved DLQI by 75% compared to 64% with subcutaneous methotrexate.[3] Topical roflumilast was approved in the United States in 2022, and in the phase III trials, pruritus decreased with active therapy.[4] As with apremilast, another PDE-4 inhibitor, oral roflumilast has been associated with psychiatric events, although rare.[5,6] In accordance with previously published results,[2,7] no new safety concerns relating to psychological well-being were identified in the current data material. However, the association should be kept in mind, as patients with psoriasis are reported to have an increased risk of depression, suicidality and anxiety.[8] In addition to its novelty, the current study excels by the placebo-controlled design and the independency. Limitations include relatively low baseline values, small sample size and thereby risk of bias, and that PROs were secondary endpoints in the study. In addition, more comprehensive patient-centred data, for example concerning work productivity, would have been relevant.

To conclude, treatment with oral roflumilast in patients with psoriasis provided significant improvements in DLQI, itch and skin pain over 24 weeks, along with high levels of treatment satisfaction. These findings support oral roflumilast as an attractive off-label treatment for psoriasis.

TABLE 1 Baseline data.

	Roflumilast, *n* = 23	Placebo, *n* = 23	All, *n* = 46
Clinical characteristics			
Age [years], median (IQR)	38.0 (30.0; 43.0)	39.0 (32.5; 50.0)	38.5 (30.0; 46.2)
Men, *n* (%)	15 (65)	19 (83)	34 (74)
Caucasian, *n* (%)	23 (100)	23 (100)	46 (100)
PASI, median (IQR)	10.9 (8.5; 15.6)	10.6 (9.7; 15.1)	10.8 (9.1; 15.4)
Psychiatric co-morbidity			
Depression, *n* (%)	0 (0)	2 (9)	2 (9)
Anxiety, *n* (%)	0 (0)	2 (9)	2 (9)
Life quality assessments			
DLQI, median (IQR)	11.0 (7.5; 14.5)	8.0 (6.5; 12.5)	9.5 (7.0; 13.8)
BDI II, median (IQR)	4.0 (2.0; 8.0)	3.0 (0.0; 9.5)	5.0 (5.0; 5.0)
NRS itch, median (IQR)	7.0 (6.0; 8.0)	8.0 (4.8; 8.0)	7.0 (6.0; 8.0)
NRS pain, median (IQR)	3.0 (0.5; 6.0)	4.0 (2.0; 6.0)	4.0 (2.0; 6.0)

Note: Data are shown for all randomized patients. Categorical variables are presented in frequencies and percentages; numerical data in median and IQR (non-normally distributed).

Abbreviations: BDI, Beck depression inventory; DLQI, dermatology life quality index; IQR, interquartile range; NRS, numeric rating scale; PASI, psoriasis area and severity index.

TABLE 2 Patient-reported outcomes.

	Week 12 (placebo-controlled phase)			Week 24 (open-label phase)	
	Roflumilast, *n* = 23	Placebo, *n* = 23	*p*-values	Roflumilast until week 12, *n* = 23	Placebo until week 12, *n* = 23
DLQI					
Score, median (IQR)	1.0 (0.0; 2.0)	5.5 (4.0; 10.8)	**<0.001**	1.0 (0.0; 1.8)	1.0 (0.0; 2.5)
Score ≤ 1, *n* (%)	11 (48)	2 (9)	**0.003**	13 (57)	12 (52)
Change from baseline, median (IQR)	−6.5 (−11.0; −5.0)	−2.0 (−5.0; −1.0)	**0.012**	−7.0 (−11.0; −5.0)	−7.5 (−12.5; −1.8)
BDI II					
Score, median (IQR)	1.0 (0.0; 1.2)	1.5 (0.0; 3.0)	0.29	1.0 (0.0; 2.0)	1.0 (0.0; 5.2)
Score < 14, *n* (%)	19 (83)	20 (87)	1.0	17 (74)	19 (83)
Change from baseline, median (IQR)	−1.5 (−3.2; −0.8)	−2.0 (−4.0; 0.0)	0.65	−2.5 (−4.0; −1.0)	−2.5 (−5.0; 1.0)
NRS itch					
Score, median (IQR)	1.0 (0.0; 3.0)	5.0 (4.0; 7.0)	**<0.001**	1.0 (0.0; 1.8)	1.5 (0.0–4.0)
NRS > 4-point reduction, *n* (%)	12 (52)	4 (17)	**0.013**	12 (52)	10 (43)
NRS ≤ 1, *n* (%)	12 (52)	3 (13)	**0.005**	13 (57)	10 (43)
Change from baseline, median (IQR)	−5.8 (−7.0; −2.8)	0.0 (−3.8; 0.4)	**<0.001**	−6.0 (−7.0; −4.0)	−4.0 (−7.6; −0.8)
NRS pain					
Score, median (IQR)	0.0 (0.0; 0.0)	3.0 (0.0; 5.8)	**<0.001**	0.0 (0.0; 0.0)	0.0 (0.0; 1.5)
NRS > 4-point reduction, *n* (%)	5 (22)	5 (22)	1.0	3 (13)	10 (43)
NRS ≤ 1, *n* (%)	18 (78)	8 (35)	**0.003**	15 (65)	15 (65)
Change from baseline, median (IQR)	−2.5 (−4.5; 0.0)	0.0 (−3.5; 1.0)	0.091	−1.0 (−3.0–0.0)	−4.5 (−6.2; 0.0)
NRS treatment satisfaction					
Score, median (IQR)	9.0 (7.0; 10.0)	2.0 (1.0; 4.0)	**<0.001**	10.0 (8.3; 10.0)	9.0 (7.8; 10.0)

Note: Data are shown for all randomized patients. Categorical variables are presented in number and percentages; numerical data as median and IQR (non-normally distributed). NRS ranges from 0 (worst) to 10 (best). Bold indicates statistical significance *p*-values.

Abbreviations: BDI, Beck depression inventory; DLQI, dermatology life quality index; IQR, interquartile range; NRS, numeric rating scale.

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CONFLICT OF INTEREST STATEMENT

Mette Gyldenløve: Outside the submitted work: Speaker honoraria from Galderma Nordic AB. Jennifer A. Sørensen: None. Simon Francis Thomsen: Outside the submitted work: Has been a speaker or has served on advisory boards for AbbVie, Almirall, Eli Lilly, Galderma, Incyte, Janssen Pharmaceuticals, LEO Pharma, Novartis, Pfizer, Sanofi, UCB Pharma and Union Therapeutics and has received research support from AbbVie, Janssen Pharmaceuticals LEO Pharma, Novartis, Sanofi and UCB Pharma. Simon Fage: Outside the submitted work: Has participated in clinical trials sponsored by LEO Pharma, Galderma, Eli Lilly, AbbVie, Novartis, Almirall, Innovaderm Research Inc., Sanofi and UCB. Lars Iversen: Outside the submitted work: Has served as a consultant and/or paid speaker for and/or participated in clinical trials sponsored by AbbVie, Almirall, Amgen, Astra Zeneca, BMS, Boehringer Ingelheim, Celgene, Centocor, Eli Lilly, Janssen Cilag, Kyowa, Leo Pharma, MSD, Novartis, Pfizer, Regranion, Samsung, Union Therapeutics and UCB. LI is also employed by MC2 Therapeutics A/S. Lone Skov: Outside the submitted work: Research funding from Almirall, Bristol-Myers Squibb, AbbVie, Janssen Pharmaceuticals, the Danish Psoriasis Foundation, the LEO Foundation and the Kgl. Hofbundtmager Aage Bang Foundation. Honoraria as consultant and/or speaker for AbbVie, Eli Lilly, Novartis, Pfizer, LEO Pharma, Janssen Cilag, UCB, Almirall, Bristol-Myers Squibb, Boehringer Ingelheim, Galderma, Novo and Sanofi. Investigator for AbbVie, Pfizer, Sanofi, Janssen Cilag, Boehringer Ingelheim, Eli Lilly, Novartis, Galderma and LEO Pharma. Claus Zachariae: Outside the submitted work: Paid speaker for Eli Lilly, Novartis, CSL, UCB and LEO Pharma. Consultant and/or advisory board member for AbbVie, Janssen Cilag, Novartis, Eli Lilly, LEO Pharma, UCB, Almirall, Takeda, Amgen and CSL. Alexander Egeberg: Outside the submitted work: Research funding from the Danish Psoriasis Foundation, the Kgl. Hofbuntmager Aage Bang Foundation, the Simon Spies Foundation, Pfizer, Eli Lilly, Novartis, AbbVie and Janssen Pharmaceuticals. Consultant and/or speaker honoraria from AbbVie, Almirall, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Galderma, Galápagos NV, Horizon Therapeutics, Janssen Pharmaceuticals, LEO Pharma, Mylan, Novartis, Pfizer, Samsung Bioepis Co., Ltd., UCB and Union Therapeutics. Currently employed by LEO Pharma. Mia-Louise Nielsen: None.

DATA AVAILABILITY STATEMENT

The data that support the findings of this article are available from the corresponding author upon reasonable request.

ETHICAL APPROVAL

Regulatory approvals were obtained from The Scientific Ethics Committee of the Capital Region of Denmark (H-20013697), the Danish Medicine Agency and the Danish Data Protection Agency. The trial was registered at EudraCT (2020-000711-76) and conducted in accordance with national data protection acts and the Edinburgh, Scotland, amendment (2000) to the Declaration of Helsinki 1964.

ETHICS STATEMENT

Not applicable.

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