1. ABSTRACT

- **Title**

APPRECIATE™ (APREmilast ClinIcAl Treatment Experience in psoriasis): A Multi-center, Retrospective Observational Study of Real-World Experience of Psoriasis Patients Treated with Apremilast in Clinical Dermatology Practice.

- **Keywords**

Psoriasis, Otezla, Apremilast, Real-World, Experience

- **Rationale and Background**

Psoriasis is a chronic disease that requires long-term treatment, ideally with effective agents that offer convenient dosing and a low incidence of adverse events (AEs). In the European Union (EU) and United States of America (USA), apremilast (Otezla®) is approved for the treatment of moderate to severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, methotrexate or psoralen and ultraviolet A light. This study was conducted to understand the real-world use of apremilast and the experience of both physicians prescribing apremilast and their psoriasis patients treated with apremilast.

- **Research Question and Objectives**

The primary objective was to describe the treatment patterns and outcomes among apremilast users in routine clinical dermatology practice, from the physician and patient perspective.

The secondary objectives were to describe

  - the characteristics of patients prescribed apremilast,
  - the use of apremilast within the treatment algorithm with respect to prior therapies,
  - reasons for initiation of apremilast,
  - physician's perceived effectiveness of apremilast,
  - reasons for discontinuation in patients who discontinued, and
  - physician and patient satisfaction with apremilast.

- **Study Design**

This cross-sectional study involved patients treated for psoriasis with apremilast and their physicians completing questionnaires at 6 (±1) months after initiation of apremilast. This study is primarily descriptive in nature, and no priori hypotheses were specified.

- **Setting**

This study was conducted at 111 sites in 10 European Union (EU) countries: Germany (27 sites), Sweden (15 sites), the UK and Ireland (16 sites), Austria (13 sites), Switzerland (16 sites), Spain (13 sites), the Central and Eastern European countries (CEE) countries (11 sites). The start of data collection began on 30 June 2016 and ended on 27 October 2021. The database lock was on 01 December 2021.

- **Subjects and Study Size, Including Dropouts**

Patients were eligible if they met the following criteria: (1) adult (≥ 18 years) patient with plaque psoriasis, treated per EU Summary of Product Characteristics (SmPC) with apremilast; (2) initiated treatment with apremilast 6 (±1) months prior to the survey

(patients may or may not have completed 6 months of apremilast treatment) and (3) provided informed consent.

A total of 616 patients were enrolled into the study: 126 patients in Germany, 77 patients in Sweden, 126 patients in the UK and Ireland, 72 patients in Austria, 83 patients in Switzerland, 82 patients in Spain and 50 patients in the CEE countries. Of 616 patients enrolled, 610 patients (99.03%) were evaluable for safety (i.e., included in the Safety Analysis Set [SAF]) and effectiveness (i.e., included in the Full Analysis Set [FAS]).

- **Variables and Data Sources**

Data was collected from patients and physicians via questionnaires completed at 6 (±1) months after initiation of apremilast. Patient questionnaires included the Patient Benefit Index [PBI] and Treatment Satisfaction Questionnaire for Medications, version 9 [TSQM-9]). Physician questionnaires explored the physician's pre-treatment expectations at the time of initiating treatment with apremilast, and their satisfaction with the treatment. Data on patient characteristics (including medical history), psoriasis clinical assessments and symptoms (including Dermatology Life Quality Index [DLQI] and Psoriasis Area and Severity Index [PASI]) were obtained from medical records when available.

- **Results**

In the 610 patients included in the study, at the apremilast initiation, the mean (±SD) total PASI and DLQI scores were 12.33 ± 8.159 and 13.3 ± 7.40, respectively. The majority of patients (80.16%) had visible (i.e., scalp, hands, feet) psoriatic lesions. Around two-thirds of patients (66.39%) suffered from pruritus. The most frequent comorbid condition was psoriatic arthritis which was documented for 24.10% of patients.

The majority of patients (90.00%) had received any prior systemic psoriasis therapy. No concomitant systemic therapies or phototherapy was reported for 527 patients (86.39%). The most frequent reason reported for stopping previous treatments was lack of efficacy (438 patients [71.80%]).

The most common reasons for considering apremilast were fewer side effects compared to other treatments (340 patients [55.74%]), followed by ease of use (oral) (336 patients [55.08%]), and previous treatment not being effective (335 patients [54.92%]). The main reason for starting apremilast was previous therapy ineffective (417 patients [68.36%]).

Physician's pre-treatment expectations[1] regarding the overall clearance of psoriasis plaques were that patient's "symptoms will be much better" (for 319 patients [52.3%]), "will improve moderately" (for 279 patients [45.7%]), or "will improve slightly" (7 patients [1.1%]). Post-treatment (6 ±1 months), physicians' expectations were achieved in nearly three-quarters (73.1%) of patients: partially for 128 patients (21.0%), successfully for 185 patients (30.3%), and exceeded for 133 patients (21.8%).

At 6 (±1) months after initiation with apremilast, 7 out of 10 patients (69.67%; 425 patients) were continuing their apremilast treatment; their mean (±SD) duration[2] of treatment with apremilast was 183.3 ± 25.65 days. Among these, 122 patients with ongoing apremilast treatment and with a DLQI of ≥ 5 at the apremilast initiation visit, an improvement of at least 5 points was observed in 89 patients (72.95%, 95% CI: 64.16%, 80.59%). For the

[1] Pre-treatment expectations have been documented in the eCRF once per site and allocated to each patient of that site for tabulation. Fulfillment of expectations for a symptom could only be documented if this symptom was present at apremilast initiation visit.

[2] For patients with treatment status ongoing duration of apremilast treatment is the time between Index date to date of follow-up status (6 [±1] months after the Index Date).

same group of patients, an improvement of at least 5 points of both DLQI and PASI50 was observed in 73 patients (59.84%, 95% CI: 50.58%, 68.61%).

At 6 (±1) months after initiation with apremilast, 185 patients (30.33%) had discontinued apremilast therapy; their mean (±SD) duration[3] of treatment with apremilast was 110.8 ± 58.68 days. Reasons for apremilast discontinuation were due to lack of efficacy (90 patients [14.75%]), safety/tolerability (77 patients [12.62%]) or reported as 'other' (18 patients [2.95%]) by the investigators. Overall, 72 patients (11.80%) stopped treatment due to an AE.

Overall, AEs were documented in 272 patients (44.59%), the most frequent being in the system organ class (SOC) gastrointestinal disorders (205 patients, 33.61%), followed by nervous system disorders (65 patients, 10.66%). Most commonly reported AEs at the preferred term (PT) level were diarrhoea (18.69%), followed by nausea (14.43%) and headache (8.52%). SAEs were reported for 7 patients (1.15%) and SADRs for 4 patients (0.66%).

Physician's perceived effectiveness of apremilast included improvements (i.e., assessments of 'slightly better', 'moderately better', and 'much better') in the majority of patients for all symptoms and for overall clearance of plaque psoriasis. More than half of physicians (> 58%) agreed or strongly agreed that apremilast provided a rapid response, notably reduced plaque psoriasis, a sustained response, clearance in specific areas, improved overall wellbeing, reduced itch, and reduced joint pain in patients with psoriatic arthritis.

For patients, the needs that ranked highest in importance (mean ≥ 3.5) were to get better skin quickly, to have confidence in the therapy, to regain control of the disease, and be healed from all skin defects. From their apremilast treatment, the most important benefits (highest scores; mean ≥ 2.4) experienced by patients were: finding a clear diagnosis and therapy, having confidence in the therapy, being free of itching, no longer having burning sensations on your skin, needing less time for daily treatment, getting better skin quickly, regaining control of disease, and being able to lead a normal everyday life. The mean (±SD) global PBI score was 2.4 ± 1.33 for all patients, and 2.8 ± 1.10 for patients continuing treatment.

More than half of the 610 patients stated that apremilast had helped their psoriasis ('agree' or 'strongly agree') with regard to clearance of specific areas, rapid response, reduced itch, and a sustained response. Patients' mean (±SD) treatment satisfaction based on the TSQM-9 subscales was 80.56 ± 18.87 for convenience, 59.04 ± 28.81 for treatment effectiveness, and 57.60 ± 30.85 for global satisfaction. The majority of patients (> 53%) reported that apremilast 'met expectations' or 'exceeded expectations': to reduce regular blood tests or other monitoring, to help the patient take it as prescribed (easy to use), to reduce the number of times the patient has to go to the hospital, and to reduce itch.

- **Discussion**

The APPRECIATE study provided insights into the expectations of physicians and patients with psoriasis treatment with apremilast, and their experience with apremilast. At 6 (±1) months after apremilast initiation, many patients (69.67%) had ongoing apremilast treatment, and half to three-quarters of these patients (50.34% to 72.95%) showed notable improvement in the treatment outcomes PASI and DLQI. Additionally, both physicians and patients reported satisfaction with apremilast, including to clearance of specific areas, rapid response, reduced itch, and a sustained response.

[3] For patients with treatment status discontinued duration of apremilast treatment is the time between Index date to date of discontinuation.

- **Marketing Authorization Holder(s)**

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