1.0 Abstract

Title

The **CRYSTAL** Study: A **C**ross-sectional and retrospective chart review study for assessing psoR**I**asis severit**Y** by absolute PA**S**I score in modera**T**e to severe psoriatic p**A**tients routine**L**y treated with systemic treatment in Bulgaria, Estonia, Hungary, Latvia, Lithuania, Romania and Russia.

Keywords

moderate to severe psoriasis, biologics, non-biologics, tumor necrosis factor (TNF) inhibitors, interleukin (IL)-17 inhibitors, IL-12/23 inhibitors, IL-23 inhibitors, systemic treatment, conventional agents, psoriasis area and severity index (PASI), absolute PASI, health-related quality of life (HRQoL), Dermatology Life Quality Index (DLQI), work productivity loss and activity impairment, cross-sectional

Rationale and Background

Systemic treatment for patients with moderate to severe psoriasis includes conventional agents (such as methotrexate, cyclosporine and acitretin), biologics with different modes of action [tumor necrosis factor (TNF) inhibitors, interleukin (IL)-12/23 inhibitors, IL-17 inhibitors], and an oral small-molecule inhibitor of phosphodiesterase-4 (PDE4). However, despite this range of currently available therapies, real-world evidence indicates that a substantial percentage of patients do not achieve skin clearance and are possibly undertreated. At the same time, newer biologic treatment options have raised expectations for treatment success from PASI75 to PASI90 and even to PASI100. In clinical trial settings, PASI90 and PASI100 response rates with a new class of biologics that targets interleukin (IL)-23 (i.e., IL-23 inhibitors) are high, substantially lowering the percentage of patients with residual disease. Furthermore, several studies show that clear or almost clear skin translates to better HRQoL. In addition to treatment goals of PASI90 and PASI100, absolute PASI $\leq$5, $\leq$3 and $\leq$1 rates are being used in various clinical trials of newer biologics. This concept of 'absolute' PASI is especially useful in routine clinical settings, since baseline PASI is often difficult to obtain. Accumulating evidence suggests that treatment goals defined by absolute PASI targets may enable a more standardized quality of care in the future.

The new classes of biologics (such as the IL-23 inhibitors) recently introduced in routine clinical practice have altered the treatment armamentarium of psoriasis. The absence of a nationwide psoriasis patient registries, alongside the anticipated introduction of new biologic treatment modalities into the local markets in the near future, highlight the need for real-world evidence studies regarding psoriasis patient clinical management and quality of care. In light of the above, the present study aimed to fill this information gap, by characterizing the current state of moderate to severe psoriasis patients that have been on systemic treatments for at least 24 weeks, by assessing absolute PASI scores, measuring the burden of the disease in terms of HRQoL, work productivity loss and activity impairment and describing the systemic treatment patterns in the real-world clinical setting in Bulgaria, Estonia, Hungary, Latvia, Lithuania, Romania and Russia.

Research Question and Objectives

Primary objective:

- To characterize the current disease severity, by assessing the absolute PASI score of patients with moderate to severe psoriasis that have been under continuous systemic treatment (either as monotherapy or as combination regimens) for at least 24 weeks.

Secondary objectives:

- To assess the absolute PASI ≤1/≤3/≤5 response rates at enrollment, and to capture the duration of the current absolute PASI score, overall and by current systemic treatment option.
- To assess the absolute PASI >5 and >8 rates at enrollment, overall and by current systemic treatment option.
- To describe patient treatment history (i.e., all pharmacological and non-pharmacological treatments received from psoriasis diagnosis until enrollment).
- To describe current systemic treatment for psoriasis [i.e., chemical substance(s), starting dosage(s), treatment duration, any dosage intensification(s) that have occurred from the start of the current treatment until enrollment, and dosage at enrollment].
- To describe the demographic and clinical characteristics of patients with moderate to severe psoriasis routinely managed with systemic treatment, in the overall study population.
- To assess both dermatology-specific and generic HRQoL at enrollment, by the use of the DLQI and the EuroQol 5-Dimensions 5-Levels (EQ-5D-5L) questionnaire, overall and by current systemic treatment option.
- To evaluate the correlation of the dermatology-specific and generic HRQoL with the absolute PASI scores of the overall study population at enrollment.
- To assess the psoriasis-related work productivity loss and activity impairment at enrollment through the use of the Work Productivity and Activity Impairment Questionnaire:Psoriasis (WPAI:PSO) questionnaire in the overall study population and in the different groups of patients by current systemic treatment option and by absolute PASI at enrollment (i.e., PASI ≤1, ≤3, ≤5, and >5).
- To assess patient satisfaction with the overall control of psoriasis achieved with the current treatment, as measured at enrollment using a single-item 7-point Likert-type scale, overall and by current systemic treatment option.
- To identify potential patient parameters, treatment and disease characteristics of interest (including concurrent psoriatic arthritis [PsA]), that might be associated with absolute PASI score at enrollment.

Exploratory objective:

- To assess the absolute PASI score by current systemic treatment option.

Study Design

This was an epidemiological, multi-country, multicenter, cross-sectional and retrospective chart review study with a single-visit data collection schedule, which included a representative sample of patients diagnosed with chronic moderate to severe plaque-type psoriasis routinely treated by

hospital- and office-based dermatology specialists practicing in geographically diverse locations throughout Central and Eastern Europe.

Results

Patient disposition

Overall, 690 eligible patients were enrolled in the study (between 1-Sep-2020 and 11-Feb-2021), by dermatology specialists practicing in 29 hospital centers/clinics/healthcare institutions located across seven Central and Eastern European countries (Bulgaria, Estonia, Hungary, Latvia, Lithuania, Romania and Russia).

Demographic and clinical characteristics of the overall study population

Of the evaluable patients of the overall study population, 99.9% (688/689) were Caucasian, 64.9% (448/690) males, 75.2% (519/690) urban residents, 64.1% (442/690) employed, 74.4% (505/679) married, 22.8% (157/690) current smokers, and 46.0% (316/687) had ≥13 years of education.

The patients' median (Interquartile Range, IQR) age at onset of psoriasis signs/symptoms and diagnosis of plaque psoriasis was 26.0 (17.7-39.2) and 32.9 (20.8-46.6) years, respectively, whereas a median (IQR) of 11.8 (5.8-21.8) years had elapsed from psoriasis diagnosis to the study visit. At initial disease diagnosis, 29.1% (172/591) had mild, 42.3% (250/591) moderate, and 28.6% (169/591) severe psoriasis. A family history of psoriasis was reported by 31.8% (207/650) of the evaluable patients.

At the study visit, the patients' median (IQR) age was 49.7 (39.4-60.2) years. Among evaluable patients, the median (IQR) Body Mass Index (BMI) was 27.8 (24.7-31.6) kg/m^2, with 39.1% (268/685) classified as overweight and 33.9% (232/685) as obese. In addition, 31.5% (216/685) had a history of psoriatic arthritis, while 13.0% (89/682) had active psoriatic arthritis. Moreover, 4.9% (34/688) had dactylitis, 5.5% (38/687) spondylitis, 4.3% (29/681) enthesitis, and 27.5% (189/688) nail psoriasis, whereas 17.0% (117/690) reported severe itching/pruritus over the past 7 days. Of the patients, 80.1% (553/690) had psoriatic plaques (excluding nails), with the most common sites of disease localization being the upper extremities (72.5%), followed by lower extremities (67.8%), trunk (45.9%), head (41.6%), genitals/groin (4.7%) and intertriginous areas (4.5%). Of the patients 46.5% (321/690) had at least one past or ongoing clinically significant medical condition/disease/surgery, with 41.0% (283/690) having at least one comorbidity. The most common past or ongoing medical conditions/comorbidities reported at a frequency of ≥5% were hypertension (25.9%), and diabetes mellitus (9.1%).

Psoriasis treatment history from diagnosis until the study visit (including the current treatment)

From disease diagnosis until the study visit:

- All patients (100.0%) had received **systemic** treatment
  - 92.9% (641/690) had received **biologic** systemic treatment, of whom

- ✓ 70.7% (453/641) had received TNF inhibitors
- ✓ 32.8% (210/641) had received IL-17 inhibitors
- ✓ 17.9% (115/641) had received IL-12/23 inhibitors
- ✓ 3.0% (19/641) had received IL-23 inhibitors
- ✓ 0.3% (2/641) had received targeted T-cell modulators
- ✓ one patient (0.2%) had received biologic agent (in the context of a clinical trial) the active substance of which was recorded as 'unknown' by the physician

➢ 83.0% (573/690) had received **non-biologic** systemic treatment

- 95.9% (662/690) had received non-systemic treatment [topical or photo(chemo)therapy] treatment
  - ➢ 95.1% (656/690) had received at least one topical treatment
  - ➢ 64.5% (445/690) had received photo(chemo)therapy.

Treatment for psoriasis from disease diagnosis until the start of the current systemic therapy

Prior to the start of current systemic treatment, of the patients:

- 95.2% (657/690) had received at least one prior **pharmacological or non-pharmacological** treatment for psoriasis which had been discontinued at current systemic treatment initiation. In particular:
  - ➢ 80.0% (552/690) had received at least one prior **systemic** treatment
    - ✓ 27.1% (187/690) had received prior **biologic** agents [median (IQR) of 1.0 (1.0-1.0) course]
      - – 20.0% (138/690) had received TNF inhibitors
      - – 6.7% (46/690) had received IL-17 inhibitors
      - – 3.3% (23/690) had received IL-12/23 inhibitors
      - – 0.3% (2/690) had received targeted T-cell modulators
      - – one patient (0.1%) had received biologic agent (in the context of a clinical trial) the active substance of which was recorded as "unknown" by the physician
    - ✓ 73.9% (510/690) had received prior **non-biologic** systemic treatment
  - ➢ 90.6% (625/690) had received at least one prior **non-systemic** treatment [topical or photo(chemo)therapy]
    - ✓ 88.0% (607/690) of the patients had received prior **topical** treatment
    - ✓ 62.0% (428/690) had received **photo(chemo)therapy**.

Characteristics of current systemic treatment for psoriasis

At the study visit, current systemic treatment was received over a median (IQR) period of 27.7 (14.3-59.6) months and comprised the following treatment patterns:

➢ **Monotherapy** with **biologic** agent in 88.4% (610/690) (median treatment duration: 28.9 months)
- ✓ **TNF inhibitor** in 48.6% (335/690) (median treatment duration: 50.0 months)
- ✓ **IL-17 inhibitor** in 24.2% (167/690) (median treatment duration: 16.6 months)

- ✓ **IL-12/23 inhibitor** in 12.9% (89/690) (median treatment duration: 23.1 months)
- ✓ **IL-23 inhibitor** in 2.8% (19/690) (median treatment duration: 9.2 months)

- **Monotherapy** with **non-biologic (conventional) agent** in 7.2% (50/690) (median treatment duration: 16.0 months)
- **Combination therapy** in 4.3% (30/690) (median treatment duration: 57.4 months)
  - ✓ **TNF inhibitor + conventional agent** in 3.3% (23/690) (median treatment duration: 61.9 months)
  - ✓ **IL-12/23 inhibitor + conventional agent** in 0.6% (4/690) (median treatment duration: 67.4 months)
  - ✓ **IL-17 inhibitor + conventional agent** in 0.3% (2/690) (median treatment duration: 13.9 months)
  - ✓ **Folic acid and derivatives + conventional agent** in 0.1% (1/690) (treatment duration: 6.5 months)

Dose intensifications and reasons for intensifications of current systemic treatment

During the period from the start of current systemic treatment until the study visit, at least one dose intensification was reported in 5.5% (38/690) of the overall population due to insufficient response in the vast majority of the cases. In particular, at least one dose intensification was reported in:

- 3.1% (19/610) of the patients treated with **biologic monotherapy**
- 10.0% (5/50) of the patients treated with **non-biologic monotherapy**
- 46.7% (14/30) of the patients treated with **combination therapy**

Patient and disease characteristics at the start of current systemic treatment for psoriasis

At the start of current systemic treatment for psoriasis, the median (IQR) patient age, BMI and disease duration were 45.9 (35.9-56.6) years, 27.8 (24.4-31.4) kg/m^2, and 8.3 (2.0-19.1) years, respectively. The physician-reported disease severity was severe in 54.9% (379/690) and moderate in 45.1% (311/690) of the patients, while among evaluable patients, 60.4% (406/672) had severe itching/pruritus, 44.6% (303/679) nail psoriasis, 25.9% (177/684) active PsA, 11.7% (80/684) dactylitis, 10.6% (72/682) spondylitis, and 8.0% (54/674) enthesitis.

The median (IQR)/mean (SD) absolute PASI score was:

- 20.0 (14.0-25.0)/20.9 (9.2) in the **overall population**
- 20.0 (14.1-25.0)/21.0 (9.0) in patients treated with **biologic monotherapy**
  - ✓ 20.0 (14.2-25.0)/21.0 (8.9) in patients treated with TNF inhibitors
  - ✓ 20.8 (14.0-24.7)/21.3 (9.6) in patients treated with IL-17 inhibitors
  - ✓ 20.0 (14.2-24.4)/19.8 (7.7) in patients treated with IL-12/23 inhibitors
  - ✓ 23.0 (17.0-30.5)/24.9 (10.8) in patients treated with IL-23 inhibitors
- 17.4 (12.0-24.4)/17.7 (7.3) in patients treated with **non-biologic monotherapy**
  - ✓ 17.4 (12.0-24.4)/17.7 (7.3) in patients treated with conventional agents
- 19.4 (15.0-29.6)/24.2 (13.3) among patients treated with **combination therapy**
  - ✓ 21.6 (15.0-30.0)/25.0 (14.1) in patients treated with conventional systemic agents + TNF inhibitors

- ✓ 18.8 (17.3-32.4)/24.9 (14.0) in patients treated with conventional systemic agents + IL-12/23 inhibitors
- ✓ 19.5 (18.0-21.0)/19.5 (2.1) in patients treated with conventional systemic agents + IL-17 inhibitors
- ✓ 13.5 for the single patient treated with conventional systemic agents + folic acid

Absolute PASI score at the study visit

At the study visit, the median (IQR)/mean (SD) absolute PASI score was:

- 1.4 (0.4-4.2)/3.5 (5.7) in the **overall population**
- 1.2 (0.4-3.6)/3.1 (5.4) in patients treated with **biologic monotherapy**
  - ✓ 1.2 (0.4-3.0)/2.8 (5.5) in patients treated with TNF inhibitors
  - ✓ 1.2 (0.2-4.3)/3.1 (4.4) in patients treated with IL-17 inhibitors
  - ✓ 1.2 (0.0-5.6)/3.9 (6.4) in patients treated with IL-12/23 inhibitors
  - ✓ 1.5 (0.0-8.0)/4.2 (5.1) in patients treated with IL-23 inhibitors
- 6.1 (1.8-13.5)/8.8 (7.9) in patients treated with **non-biologic monotherapy**
- 1.6 (0.2-3.9)/3.0 (4.6) in patients treated with **combination therapy**
  - ✓ 1.5 (0.2-2.4)/2.1 (2.4) in patients treated with conventional systemic agents + TNF inhibitors
  - ✓ 8.3 (2.4-17.0)/9.7 (9.6) in patients treated with conventional systemic agents + IL-12/23 inhibitors
  - ✓ 1.1 (0.3-1.8)/1.1 (1.1) in patients treated with conventional systemic agents + IL-17 inhibitors
  - ✓ 0.0 for the single patient treated with conventional systemic agents + folic acid.

PASI ≤1/≤3/≤5 response rates and duration of current absolute PASI score at the study visit

The proportions of patients with absolute PASI score ≤1, ≤3 and ≤5, and the relevant median absolute PASI duration (presented in parentheses) at the study visit were:

- 42.3% (11.0 months), 69.1% (13.6 months) and 80.0% (15.5 months) in the **overall population**
- 44.1% (11.5 months), 72.0% (13.7 months) and 82.6% (15.7 months) in patients treated with **biologic monotherapy**
  - ✓ 42.4% (14.0 months), 75.8% (16.6 months) and 86.3% (22.8 months), in patients treated with TNF inhibitors
  - ✓ 47.3% (8.2 months), 69.5% (10.2 months) and 82.0% (9.9 months) in patients treated with IL-17 inhibitors
  - ✓ 43.8% (14.3 months), 66.3% (15.5 months) and 74.2% (19.1 months) in patients treated with IL-12/23 inhibitors
  - ✓ 47.4% (4.1 months), 52.6% (5.7 months) and 63.2% (5.7 months) in patients treated with IL-23 inhibitors

- 20.0% (3.2 months), 32.0% (6.3 months) and 48.0% (7.6 months) in patients treated with **non-biologic monotherapy**
- 43.3% (9.6 months), 73.3% (12.0 months) and 80.0% (25.5 months), in patients treated with **combination therapy**
  - ✓ 43.5% (9.6 months), 78.3% (14.6 months) and 82.6% (27.9 months), in patients receiving conventional systemic agents + TNF inhibitors
  - ✓ one of the four patients treated with conventional systemic agents + IL-12/23 inhibitors had absolute PASI score ≤1 (68.3 months), who was also the only one with absolute score ≤3 (68.3 months), while two patients (the aforementioned and one more) had absolute PASI score ≤5 (39.8 months).
  - ✓ one of the two patients receiving conventional systemic agents + IL-17 inhibitors had absolute PASI score ≤1 (0.0 months) and both of them had score ≤3 (0.1 months) and ≤5 (0.1 months).
  - ✓ the single patient receiving conventional systemic agents + folic acid had absolute PASI score ≤1 (duration was missing).

Absolute PASI >5 and >8 rates at the study visit

The proportions of patients with absolute PASI score >5 and >8 at the study visit, were:

- 20.0% (138/690) and 12.0% (83/690), in the **overall population**
- 17.4% (106/610) and 9.5% (58/610) in patients treated with **biologic monotherapy**
  - ✓ 13.7% (46/335) and 5.4% (18/335) in patients treated with TNF inhibitors
  - ✓ 18.0% (30/167) and 11.4% (19/167) in patients treated with IL-17 inhibitors
  - ✓ 25.8% (23/89) and 19.1% (17/89) in patients treated with IL-12/23 inhibitors
  - ✓ 36.8% (7/19) and 21.1% (4/19) in patients treated with IL-23 inhibitors
- 52.0% (26/50) and 46.0% (23/50) in patients treated with **non-biologic monotherapy**
- 20.0% (6/30) and 6.7% (2/30) in patients treated with **combination therapy**
  - ✓ 17.4% (4/23) of the patients receiving conventional systemic agent + TNF inhibitors had absolute PASI score >5, but none of the patients had PASI score >8
  - ✓ two of the four patients treated with conventional systemic agents + IL-12/23 inhibitors had absolute PASI score >5 and >8.
  - ✓ none of the two patients treated with conventional systemic agents + IL-17 inhibitors had absolute PASI score >5
  - ✓ the single patient treated with conventional systemic agents + folic acid did not have absolute PASI score >5.

Dermatology-specific and generic HRQoL at the study visit

DLQI at the study visit

At the study visit, the median (IQR) DLQI total score in the overall population was 1.0 (0.0-4.0); the DLQI domain with the highest median (IQR) score was 'symptoms and feelings' [1.0 (0.0-2.0)], while the median score in all other DLQI domains was 0.0.

Among patients receiving **biologic monotherapy**, the median (IQR) DLQI total score was 1.0 (0.0-4.0), while among those receiving **non-biologic monotherapy**, it was 4.5 (1.0-13.0).

Regarding specific monotherapy treatment options, the median (IQR) DLQI total score among patients treated with TNF inhibitors, IL-17 inhibitors, IL-12/23 inhibitors, IL-23 inhibitors and conventional systemic agents was 1.0 (0.0-4.0), 1.0 (0.0-4.0), 1.0 (0.0-4.0), 2.0 (0.0-5.0) and 4.5 (1.0-13.0), respectively.

Among patients receiving **combination therapy**, the median (IQR) total DLQI score was 2.0 (0.0-6.0), 8.0 (4.0-9.5), and 4.0 (2.0-6.0) in the subgroups of patients receiving conventional agent + TNF inhibitor, conventional agents + IL-12/23 inhibitors, and conventional agents + IL-17 inhibitors, respectively, while for the single patient receiving conventional agents + folic acid and derivatives the total DLQI score was 5.0. The most negatively affected domain in all treatment subgroups was 'symptoms and feelings'.

The respective proportions of patients with DLQI total score of 0-1 and ≤5 were:

- 54.5% (375/688) and 79.9% (550/688) in the **overall population**
- 57.6% (350/608) and 82.2% (500/608) in patients treated with **biologic monotherapy**
  - ✓ 58.6% (195/333) and 82.3% (274/333) in patients treated with TNF inhibitors
  - ✓ 59.3% (99/167) and 84.4% (141/167) in patients treated with IL-17 inhibitors
  - ✓ 52.8% (47/89) and 77.5% (69/89) in patients treated with IL-12/23 inhibitors
  - ✓ 47.4% (9/19) and 84.2% (16/19) in patients treated with IL-23 inhibitors
- 26.0% (13/50) and 60.0% (30/50) in patients treated with **non-biologic monotherapy**
- 40.0% (12/30) and 66.7% (20/30) in patients treated with **combination therapy**
  - ✓ 47.8% (11/23) and 73.9% (17/23) in patients treated with conventional systemic agent + TNF inhibitors
  - ✓ one of the four patients treated with conventional systemic agents + IL-12/23 inhibitors had DLQI ≤5 and 0-1
  - ✓ one of the two patients receiving conventional systemic agents + IL-17 inhibitors had DLQI ≤5 but not 0-1
  - ✓ the single patient treated with conventional systemic agents + folic acid had DLQI ≤5 but not 0-1.

EQ-5D-5L at the study visit

At the study visit, in the overall population, the most negatively affected EQ-5D dimension was 'pain/discomfort', with 37.2% (256/689) of patients with available data reporting problems in this dimension, followed by 'anxiety/depression' [29.3% (202/689) with problems], 'mobility' [25.7% (177/689) with problems], and 'usual activities' [20.0% (138/689) with problems], while the least affected dimension was 'self-care', with 15.2% (105/689) of the patients reporting problems.

The respective proportions of patients with available data reporting problems in the EQ-5D dimensions 'pain/discomfort', 'anxiety/depression', 'mobility', 'usual activities', and 'self-care' were:

- 34.2% (208/609), 27.9% (170/609), 24.3% (148/609), 17.6% (107/609), and 14.0% (85/609), in patients receiving **biologic monotherapy**
  - ✓ 36.5% (122/334), 29.3% (98/334), 23.7% (79/334), 17.7% (59/334), and 13.8% (46/334) in patients treated with **TNF inhibitors**
  - ✓ 28.1% (47/167), 23.4% (39/167), 23.4% (39/167), 15.6% (26/167), and 12.6% (21/167) in patients treated with **IL-17 inhibitors**
  - ✓ 38.2% (34/89), 33.7% (30/89), 28.1% (25/89), 19.1% (17/89), and 15.7% (14/89) in patients treated with **IL-12/23 inhibitors**
  - ✓ 26.3% (5/19), 15.8% (3/19), 26.3% (5/19), 26.3% (5/19), and 21.1% (4/19) in patients treated with **IL-23 inhibitors**
- 52.0% (26/50), 38.0% (19/50), 28.0% (14/50), 38.0% (19/50), and 22.0% (11/50) in patients receiving **non-biologic monotherapy**
- 73.3% (22/30), 43.3% (13/30), 30.0% (15/50), 40.0% (12/30), and 30.0% (9/30) in patients treated with **combination therapy**.

At the study visit, the respective median (IQR) EQ-5D-5L utility index and EuroQol Visual Analogue (EQ-VAS) scores were:

- 1.0 (0.8-1.0) and 85.0 (70.0-95.0) in the **overall population**
- 1.0 (0.8-1.0) and 88.0 (75.0-95.0) in patients treated with **biologic monotherapy**
  - ✓ 1.0 (0.8-1.0) and 85.0 (75.0-95.0) in patients treated with TNF inhibitors
  - ✓ 1.0 (0.8-1.0) and 90.0 (75.0-95.0) in patients treated with IL-17 inhibitors
  - ✓ 1.0 (0.8-1.0) and 85.0 (70.0-90.0) in patients treated with IL-12/23 inhibitors
  - ✓ 1.0 (0.7-1.0) and 88.0 (70.0-95.0) in patients treated with IL-23 inhibitors
- 0.8 (0.7-1.0) and 80.0 (60.0-90.0) in patients treated with **non-biologic monotherapy**
- 0.7 (0.6-0.9) and 80.0 (55.0-90.0) in the subpopulation treated with **combination therapy**
  - ✓ 0.8 (0.6-1.0) and 80.0 (60.0-90.0) in patients treated with conventional agents + TNF inhibitors
  - ✓ 0.7 (0.7-0.8) and 55.0 (50.0-72.5) in patients treated with conventional agents + IL-12/23 inhibitors
  - ✓ 0.6 (0.6-0.6) and 50.0 (50.0-50.0) in patients treated with conventional agents + IL-17 inhibitors
  - ✓ 0.6 and 80.0 in the single patient receiving conventional agents + folic acid.

Correlation of DLQI and EQ5D scores with absolute PASI score at the study visit

In the overall population:

- the correlation between the DLQI total score and the absolute PASI score at the study visit was moderate positive (Spearman rho = 0.591, $p<0.001$);

- the correlation between the EQ-VAS total score and the absolute PASI score at the study visit was negligible (Spearman rho = -0.282, p<0.001);
- the correlation between the EQ-5D utility index score and the absolute PASI score at the study visit was low negative (Spearman rho = -0.323, p<0.001).

Psoriasis-related work productivity loss and activity impairment at the study visit

At the study visit, 99.4% (686/690) of the patients completed the WPAI:PsO questionnaire, of whom 64.4 % (442/686) reported being currently employed (working for pay).

In the subpopulations with absolute PASI score ≤1, ≤3, ≤5, and >5 at the study visit, 68.4% (199/291), 66.5% (316/475), 66.4% (364/548), and 56.5% (78/138) of the patients who completed the WPAI:PsO, respectively, reported they were currently employed.

In the overall study population and in all subpopulations with absolute PASI score ≤1, ≤3 and ≤5, the median scores for the WPAI:PsO domains '*work productivity loss'* and *'activity impairment'* were 0.0, whereas in the subpopulation with absolute PASI score >5 the respective scores were 20.0, and 25.0.

In patients receiving **monotherapy**, in those receiving **biologic monotherapy** and in all biologic monotherapy treatment options (TNF inhibitors, IL-17 inhibitors, IL-12/23 inhibitors, IL-23 inhibitors) the median score for each of the WPAI:PsO domains at the study visit was 0.0. In patients receiving **non-biologic monotherapy,** the median scores for '*work productivity loss'* and '*activity impairment'* at the study visit were 10.0 and 20.0, respectively.

In the subpopulation of patients receiving **combination therapy** and in patients receiving conventional agent + TNF inhibitor, the median score for each of the WPAI:PsO domains at the study visit was 0.0. In the subpopulation of patients receiving conventional agent + IL12/23 inhibitor, the median scores for *'work productivity loss'* and *'activity impairment'* at the study visit were 25.0 and 20.0, respectively, while for the two patients receiving conventional agent + IL17 inhibitor who were not employed, the median score for 'activity impairment' was 75.0. The score for each of the WPAI:PsO domains for the patient receiving conventional agent + folic acid and derivatives was 0.0.

Patient satisfaction with control of psoriasis with current systemic treatment at the study visit

At the study visit, 99.4% (686/690) of the patients scored their satisfaction with the overall control of the disease achieved with their current systemic treatment on a single-item 7-point Likert-type scale. The respective proportions of patients who were satisfied (completely satisfied) and dissatisfied with their current treatment were:

- 90.8% (59.5%), and 5.8% in the **overall population**
- 92.4% (61.7%), and 4.8% in patients treated with **biologic monotherapy**
  - ✓ 91.9% (58.3%) and 5.1% in patients treated with TNF inhibitors
  - ✓ 94.5% (68.5%) and 4.2% in patients treated with IL-17 inhibitors

- ✓ 89.9% (60.7%) and 5.6% in patients treated with IL-12/23 inhibitors
- ✓ 94.7% (68.4%) and 0.0% in patients treated with IL-23 inhibitors

- 74.0% (30.0%) and 18.0% in patients treated with **non-biologic monotherapy**
- 86.7% (63.3%) and 6.7% in patients treated with **combination therapy**
  - ✓ 91.3% (65.2%) and 4.3% in patients treated with conventional systemic agent + TNF inhibitors
  - ✓ two of the four patients treated with conventional systemic agents + IL-12/23 were satisfied (both completely satisfied) and one patient was dissatisfied
  - ✓ both patients receiving conventional systemic agents + IL-17 inhibitors, one of which was completely satisfied
  - ✓ the single patient receiving conventional systemic agents + folic acid was completely satisfied.

Association of patient/treatment/disease characteristics with absolute PASI score at the study visit

Multivariable linear regression analysis indicated that the following factors have a statistically significant effect on the mean absolute PASI score at the study visit:

- **Absolute PASI score at the start of current systemic treatment (or most recent assessment):** Each one-unit increase in the absolute PASI score at the start of current treatment was found to be associated with a 0.09-unit increase in the absolute PASI score at the study visit (95% CI: 0.05, 0.14; p<0.001).
- **Current systemic treatment with biologics:** The estimated difference in the mean absolute PASI scores at the study visit between patients currently treated with biologics and those treated with non-biologics was -4.96 (95% CI: -6.58, -3.33; p<0.001) when all other factors are held constant.
- **Disease duration (years) at the start of current treatment:** Each one-year increase in the disease duration at the start of current treatment was found to be associated with a 0.06-unit decrease (-0.06) in the absolute PASI score at the study visit (95% CI: -0.09, -0.02; p=0.003) when all other factors are held constant.
- **Duration (months) of current systemic treatment:** Each one-month increase in the duration of current systemic treatment is associated with a 0.03-unit decrease (-0.03) in the absolute PASI score at the study visit (95% CI: -0.04, -0.02; p<0.001) when all other factors are held constant.
- **Patient age at the start of current treatment:** Each one-year increase in patient age at the start of current treatment is associated with a 0.05-unit increase in the absolute PASI score at the study visit (95% CI: 0.01, 0.08; p=0.005) when all other factors are held constant.

Discussion

Generalizability

The eligible study population was enrolled from 29 sites across 7 CEE countries. The study sites were located in cities, which, combined are home to ~4% (for Hungary) to 41% (for Estonia) of the population of each country. Patient enrollment from geographically diverse locations throughout

CEE as well as from different settings, such as public, private, state budgetary, and university hospitals, empowers generalizability of the study outcomes and helps depict variations in medical practice paradigms of moderate to severe chronic plaque psoriasis management across a broad spectrum of healthcare environments in real-world. This was also facilitated by enrollment of patients with a non-limiting set of clinical characteristics, as long as they fulfilled the criterion of diagnosis with chronic moderate to severe plaque-type psoriasis and had available absolute PASI score at the start of their current systemic treatment or within the period between 30 days prior to and 7 days after the start of treatment. In order to enhance the external validity of the study, a patient identification and enrollment log was utilized, in which all eligible patients who declined to participate were documented; no such case was reported. Nevertheless, it is noted that since the study sites were selected through non-probability sampling, the generalizability of the study results is indeterminate.

Conclusion

In the overall study population, after a 2.3-year median duration of current systemic treatment mainly comprising of biologic agents (in ~93%), approximately 58%, 31% and 20% of the patients had absolute PASI score >1, >3 and >5, respectively. In addition, almost half of the patients (~46%) had DLQI score >1, with one out of five (20%) having a DLQI score >5, and two out of five (~40%) not being completely satisfied with the overall disease control achieved with their current treatment. Considering that achievement of a PASI score lower than 3 indicates treatment success, while a score >5 suggests the need for treatment alteration, and a DLQI score >1 indicates impact of psoriasis on patients' disease-specific QoL (with scores >5 signifying at least moderately affected QoL), the results of the present study support that in the participating CEE countries, despite the wealth of currently available treatments, for a considerable proportion of patients with moderate to severe psoriasis there is still room for improvement in terms of achieving long-term treatment goals including skin clearance, improved QoL, and greater patients' satisfaction.