STUDY REPORT SUMMARY (ABSTRACT)

A Prospective, Observational Study to Estimate the Proportion of Subjects with Plaque Psoriasis who Achieve Complete Clearance on Biologics

Background/Rationale:

Plaque psoriasis is a chronic skin disease that affects 1-3% of the United States (US) and European populations and severely impairs quality of life. Six biologics are authorized in Europe and in the US for treatment of subjects with moderate to severe psoriasis. These are the anti-tumor necrosis factor (TNF) drugs (etanercept, infliximab, and adalimumab), an interleukin (IL)-12/23 inhibitor (ustekinumab) and the IL-17A antagonists (secukinumab and ixekizumab). In addition, an anti-IL-17RA drug (brodalumab) is approved in the US. Complete skin clearance with these agents is achieved by a proportion ranging from 5% to 38% of subjects [Inzinger 2011; Lesiak 2010; Bardazzi 2010], and the treatment goal for biologics adopted by regulatory and reimbursement agencies is subject attainment of a 75% reduction from the baseline Psoriasis Area and Severity Index (PASI) score (i.e., PASI 75) or similarly, a (Static Physician's Global Assessment (sPGA) score of 0 or 1, or attainment of a 50% reduction in PASI score (PASI 50) from baseline with a Dermatology Quality of Life Index (DLQI)≤5 [Fredriksson 1978]. Specifically, the study's aim was to provide information on the effectiveness of approved biologics as they are used in clinical practice. This information is currently not consistently available from other sources, including existing psoriasis patient registries.

Objectives:

Primary objective: To estimate in each country, in subjects who are biologic treatment-naïve or biologic treatment-switching, the effectiveness of biologics in moderate to severe plaque psoriasis as measured by the proportion of subjects with total skin clearance (Static Psoriasis Area and Severity Index [sPASI]=0 or 100% improvement in PASI [PASI 100]) at 6 months after initiating a biologic.

Secondary objectives:

1. To evaluate maintenance of total skin clearance as measured by the proportion of subjects who were clear at month 6 and who maintained PASI 100 (or sPASI=0) at 12 months.
2. To evaluate total skin clearance as measured by the proportion of subjects with PASI 100 (or sPASI=0) at 12 months.
3. To describe the distribution of sPASI scores and percent PASI improvement from baseline at 6 months and 12 months.

4. For the sPGA, the Psoriasis Symptom Inventory (PSI), and the DLQI, respectively, to estimate the proportion of subjects with scores of 0 at 6 months among all subjects, at 12 months among all subjects, and separately at 12 months among the subjects with a score of 0 at 6 months.
5. For the sPGA, to estimate the proportion of subjects with a score of 0 or 1 at 6 months among all subjects, at 12 months among all subjects, and separately at 12 months among the subjects with a score of 0 or 1 at 6 months.
6. To estimate the proportion of subjects who were PSI responders (total PSI score ≤ 8, with no single item score > 1) at 6 months and 12 months.
7. To describe the distribution of scores for all patient-reported outcomes (PROs).
8. To evaluate the association between clinical measures (PASI, sPGA) and PROs (DLQI, PSI, Static Patient's Global Assessment [sPtGA], treatment satisfaction, global health status) at 6 and 12 months.

Exploratory objectives:

1. To characterize subjects initiating therapy, reasons for starting therapy or switching therapy at study entry, changes in therapy (initiation, discontinuation, dosing change) during the 12 months after initiating a biologic, and reasons for therapy changes.
2. To explore the relationship between PASI and sPGA during the 12 months after initiating a biologic, including the relationship between sPGA of 0 and PASI 100 (or sPASI=0).
3. To estimate the proportion of subjects with PASI 100 (or sPASI=0) and who did not use any additional psoriasis treatment other than the biologic.
4. To explore the association between clinical measures (PASI, sPGA) and use of concomitant skin medications (co-medications) during the 12 months after initiating a biologic.
5. To explore predictors of total skin clearance, including: demographics (age, sex, race/ethnicity), subject-reported behaviors (smoking, alcohol consumption), physical characteristics (weight, height), time since psoriasis diagnosis, selected co-morbidities (psoriatic arthritis, cardiovascular disease, kidney disease, liver disease, depression), prior biologic treatment (biologic treatment-naïve and biologic treatment-switching), prior use of non-biologic conventional systemic treatment, concomitant medications, PROs including treatment satisfaction and global health status, previous and current biologic class (anti-TNF, IL-12/23, IL-17).
6. To characterize the prevalence of selected co-morbid conditions and the use of selected non-psoriasis medications.

Methods:

Aim of the study: To estimate in each country the proportion of biologic treatment-naïve and biologic treatment-switching psoriasis subjects in the real-world context, having total clearance at 6 months after initiating a biologic.

Primary endpoint: Total skin clearance, defined as follows:

- PASI 100 or sPASI=0 at 6 months

Secondary and other endpoints:

- PASI 100 (or sPASI=0) at 12 months
- PASI 100 (or sPASI=0) at 6 months and 12 months
- % PASI improvement from baseline and sPASI scores at 6 months and 12 months
- sPGA=0 at 6 months and 12 months
- sPGA=0 or 1 at 6 months and 12 months
- PSI=0 at 6 months and 12 months
- PSI responders at 6 months and 12 months
- DLQI=0 at 6 months and 12 months
- sPtGA at 6 months and 12 months

Study design/type: A multinational, prospective observational cohort study of usual care for subjects initiating therapy for plaque psoriasis on approved biologic agents, conducted globally with subjects enrolled in the US and Europe. This was a non-interventional (NIS) study of usual care over the 12 months following initiation of biologic therapy.

Study population: Adults in 5 participating countries who were diagnosed by their physicians with moderate to severe plaque psoriasis, and were initiating biologic therapy (biologic treatment-naïve or biologic treatment-switching) for plaque psoriasis, were included (234 subjects in France, 67 subjects in Germany, 182 subjects in Italy, 95 subjects in the UK, 268 in the US).

Subject eligibility criteria:

- ≥ 18 years old, diagnosed with moderate to severe plaque psoriasis
- initiating a biologic approved for psoriasis (i.e., biologic treatment-naïve or biologic treatment-switching) at study entry
- able to fill out questionnaires
- provided written informed consent
- not participating in a clinical trial utilizing an investigational agent in the 3 months prior to the first biologic dose

Outcome variables:

- Skin clearance was the primary indicator of treatment effectiveness, and it was measured using the physician-reported PASI and sPGA.
- The secondary outcome variables were the PSI, the DLQI, the sPtGA, treatment satisfaction and global health status.

Exposure variables: Therapy discontinuations, switches, and dosing changes during follow-up, which were reported by the site and summarized for all subjects initiating biologic therapy at study entry.

Follow-up: Follow-up continued for approximately 12 months after the first dose or until the subject was lost to follow-up or withdrew from the study (for any reason including death), whichever came first. Data were obtained for each subject during scheduled visits at 6 months (± 6 weeks) and 12 months (± 6 weeks) after the first biologic dose, and at routine visits that occurred during the follow-up period. To the extent possible data were also collected at all other usual care visits that occurred during the follow-up.

Sample size: With a sample size goal of up to approximately 300 subjects per country and assuming a 10% drop-out rate, the 95% confidence interval (CI) for an expected proportion of 10% achieving total clearance (i.e., 27 of 270 subjects) at 6 months was 6.7% to 14.2%.

Statistical considerations: The full analysis set (FAS) included all enrolled subjects who satisfied the eligibility criteria. The primary endpoint was analyzed by country using this analysis set. Additionally, the primary endpoint was analyzed by country using a subset of subjects who completed PASI assessment at 6 months, who completed PASI assessments at 12 months, and who completed PASI assessments at both 6 and 12 months. Analyses to address the secondary and exploratory endpoints were performed using the FAS. Binominal exact 95% CIs indicated the precision of the estimated proportion of subjects with total skin clearance within each country. Descriptive statistics were used to describe all endpoints. The predictors of total skin clearance were explored using logistic regression. The outcomes in the in-text tables were presented as overall, by geographic region (Europe, US) and by prior biologic use (biologic treatment-naïve, biologic treatment-switching).

Results:

Baseline characteristics: There were 899 subjects screened, with 846 total moderate to severe plaque psoriasis subjects enrolled in the study (although they did not all complete assessments at 6 and 12 month visits). Of subjects in the full analysis set, 32% were from the US, 28% from France, 22% from Italy, 11% from UK and 8% from Germany. In addition, approximately 60% of subjects in the full analysis set were biologic treatment-naïve prior to study enrollment and the remaining 40% of subjects were switching to a different biologic agent at study entry. The mean age of subjects was 47.4 years (SD=13.76), 92% were White, and 63% were male.

The mean and median durations of psoriasis at baseline were 18.4 years (SD=13.2) and 15.5 years (interquartile range [IQR]: 8.3-26.0), respectively, with subjects reporting an average of 5.4 (SD=3.1) psoriasis plaque locations on the body, mainly on the legs (77%), the arms (75%), the scalp (61%), the back (58%) and the chest (56%). The mean and median durations of psoriasis in European subjects were, respectively 20.0 (SD=12.96) years and 17.2 (IQR: 10.3-28.8) years, whereas in the US, subjects reported a mean psoriasis duration of 15.2 (SD=13.1) years and a median of 11.6 (IQR: 4.9-21.2) years. In Europe, subjects reported an average of 5.5 (SD=3.1) psoriasis plaque locations on the body, mainly on the legs (77%), arms (77 %), scalp (64%), chest (61%), and back (60%). Subjects in the US reported an average of 5.2 (SD=3.0) psoriasis plaque locations on the body, most commonly on the legs (76%), arms (70%), scalp (55%), back (52%), and chest (45%). In subgroups by prior biologic use, the mean disease duration at baseline in biologic treatment-naïve subjects was 17.1 (SD=13.3) years; median of 14.4 (IQR: 6.2-25.3) years, and in biologic treatment-switching subjects the mean and median psoriasis duration were respectively 20.4 (SD=12.8) years and 17.6 (IQR: 10.9-28.2) years. Biologic treatment-naïve subjects reported an average of 5.5 (SD=3.0) psoriasis plaque locations on the body, with the legs (75%), arms (73%), scalp (65%), back (60%) and chest (57%) as the most frequent locations, while biologic treatment-switching subjects reported an average of 5.2 (SD=3.1) psoriasis plaque locations, mainly on the legs (80%), arms (77%), scalp (55%), back (55%) and chest (53%).

Nearly 64% of enrolled subjects reported at least one comorbidity at baseline, among which the most common was hypertension (52%), followed by hyperlipidemia, psoriatic arthritis, diabetes mellitus, and depression (reported in 33%, 28%, 22%, and 21% of subjects, respectively). Sixty percent of the European subjects and 72% of the US subjects reported at least one baseline comorbidity. Among those reporting comorbidities in Europe, the most common were hypertension (53%) and hyperlipidemia (29%), whereas diabetes mellitus, depression, and anxiety were respectively reported in 21, 18%, and 12% of subjects. In the US, hypertension and hyperlipidemia were also the most frequent conditions, reported in 51% and 39% of subjects (of those with comorbidities), while 24%, 28 % and 26% of subjects with comorbidities respectively reported diabetes, depression, and anxiety.

Psoriasis-related treatment patterns: Biologic use prior to baseline was reported in 40% of the full analysis set, including 35% of subjects in Europe and 51% of subjects in the US. Among those with prior biologic exposure, the prior treatments reported included etanercept (by 59%) and adalimumab (53%) (prior biologic use not mutually exclusive). Etanercept and adalimumab were the most reported prior treatments reported among those with prior biologic exposure both in Europe (56% and 49%, respectively) and in the US (63% and 59%, respectively). A total of 76% of the full analysis set reported prior conventional systemic treatment, and of those, the most common treatments were methotrexate (77%) and cyclosporine (45%) (prior conventional systemic treatment use not mutually exclusive). In Europe, 91% of subjects had prior conventional systemic treatment, compared with 43% in the US. By prior biologic use, 77% and 75% of the biologic treatment-naïve and biologic treatment-switching reported prior conventional systemic treatment, respectively. Furthermore, a small percentage of subjects overall (7.4%) were previously treated with phototherapy.

A total of 45% of subjects were prescribed a biologic agent at study enrollment because of prior conventional systemic treatment failure, 31% received a biologic due to failure of a prior biologic, and 17% received a biologic because of failure of prior topical treatment. Anti-TNF drugs were prescribed as the index study biologic for 61% of subjects (75% of biologic treatment-naïve subjects and 40% of biologic treatment-switching subjects). IL-12/23 inhibitors were administered to 30% of subjects at study entry, including 45% of biologic treatment-switching subjects and 20% of biologic treatment-naïve subjects. The remaining 9.0% of subjects received an IL-17 antagonist at study entry, prescribed to 15% of biologic treatment-switching subjects and 5% of biologic treatment-naïve subjects.

During the study period, 17% of subjects discontinued their initial biologic treatment, of whom 26% did so because of primary failure, whereas 13% of subjects who discontinued reported intolerance, 10% reported secondary failure, and 47% discontinued due to other reasons, with reasons including, but not limited to, an adverse event or drug reaction, dosing change, pregnancy, a change in insurance coverage, withdrawal of consent, or the subject being lost to follow-up. Of those who discontinued in Europe, 'other' reasons to discontinue were reported by 56% of subjects, and primary failure and intolerance were each reported by 17% of subjects, while in the US, the most commonly reported reasons were primary failure (41%), concerns about cost (15%), and 'other' reasons (31%). Biologic treatment-naïve patients mainly discontinued due to 'other' reasons (53%), primary failure (21%) and intolerance (16%), while biologic treatment-switching patients mainly discontinued due to 'other' reasons (42%), primary failure (30%) and secondary failure (19%).

Skin clearance following biologic treatment: The primary study endpoint of total skin clearance is defined as PASI 100 or sPASI=0.

6 months: At 6 months following the index date of biologic exposure, 599 (71%) subjects completed PASI assessments, of which 22.7% (95% CI: 19.4%, 26.3%) achieved total skin clearance, 35.6% (95% CI: 31.7%, 39.5%) achieved PASI 90, and 53.1% (95% CI: 49.0%, 57.1%) achieved PASI 75. In Europe, 73% of subjects were assessed with PASI scores, and of these, 22.5% (95% CI: 18.6%, 26.8%) achieved PASI 100 or sPASI=0. Sixty-eight percent of subjects completed a 6-month PASI assessment in the US, of which 23.2% (95% CI: 17.3%, 30.0%) achieved total skin clearance. Improvement to PASI 90 and PASI 75 were reported in 37.2% (95% CI: 32.6%, 42.1%) and 56.6% (n=237; 51.7%, 61.4%), respectively, of subjects assessed in Europe, while in the US, 31.7% (n=57; 95% CI: 24.9%, 39.0%) of subjects with completed PASI assessments achieved PASI 90 and 45.0% (n=81; 95% CI: 37.6%, 52.6%) achieved PASI 75. By prior biologic use, 70% and 73% of the biologic treatment-naïve and biologic treatment-switching subjects, respectively, completed PASI assessments, and of these subjects, 24.9% (n=89; 95% CI: 20.5%, 29.7%) of the biologic treatment-naïve subgroup and 19.6% (n=48; 95% CI: 14.8%, 25.1%) of the biologic treatment-switching subgroup achieved total skin clearance at month 6 (p=0.129). For subjects with available 6-month PASI scores, 39.2% (95% CI: 34.0%, 44.4%) of subjects in the biologic treatment-naïve subgroup and 30.3% (95% CI: 24.6%, 36.5%) of subjects in the biologic treatment-switching subgroup improved to PASI 90, and accordingly, 57.7% (95% CI: 52.4%, 62.9%) and 46.3% (95% CI: 39.9%, 52.8%) of subjects improved to PASI 75.

Further evaluating skin clearance by prior biologic use within each region showed that in the US, 27.4% (95% CI: 18.2%, 38.2%) of the biologic treatment-naïve subjects who completed a 6-month PASI assessment reported PASI 100, compared to 19.6% (95% CI: 12.2%, 28.9%) of the biologic treatment-switching subjects (p=0.215). In Europe, 24.1% (95% CI: 19.1%, 29.6%) and 19.6% (95% CI: 13.5%, 26.9%) of the treatment-naïve and treatment-switching subjects, respectively, improved from baseline to achieve total skin clearance at 6 months. The difference between both treatment groups was not statistically significant (p=0.292).

12 months: Twelve months following the index date of biologic treatment, there were 516 (61%) subjects assessed with PASI scores, with 26.1% (95% CI: 22.3%, 30.0%) of these subjects achieving total skin clearance (PASI 100 or sPASI=0). In addition, 42.2% (95% CI: 37.9%, 46.6%) of subjects with completed 12-month PASI assessments achieved PASI 90 and 64.1% (95% CI: 59.8%, 68.3%) achieved PASI 75. By geographic region, in Europe, 66% of subjects completed a 12-month PASI assessment, while 53% of those in the US completed 12-month PASI assessments, among which 27.6% (95% CI: 23.2%, 32.4%) and 21.8% (95% CI: 15.3%, 29.5%) of subjects in Europe and the US, respectively, achieved total skin clearance. PASI 90 and PASI 75 were achieved correspondingly in 45.5% (95% CI: 40.3%, 50.7%) and 66.6% (95% CI: 61.5%, 71.3%) of the subjects with available PASI scores in Europe, while in the US, 33.8% (95% CI: 26.1%, 42.2%) and 57.7% (95% CI: 49.2%, 66.0%) of subjects with non-missing data achieved PASI 90 and PASI 75, respectively. By prior biologic use, 61% (of the biologic treatment-naïve and 62% of the biologic treatment-switching subjects completed a PASI assessment, and among these subjects, 30.4% (95% CI: 25.4%, 35.9%) and 19.5% (95% CI: 14.4%, 25.5%), respectively achieved total skin clearance (p=0.005). Moreover, the subgroup of those naïve to biologics and who completed a 12-month assessment included 45.9% (95% CI: 40.3%, 51.7%) subjects who achieved PASI 90 and 68.7% (95% CI: 63.2%, 73.9%) who achieved PASI 75, and for subjects switching biologic treatment, 36.8% (95% CI: 30.3%, 43.8%) and 57.4% (95% CI: 50.4%, 64.2%) of subjects with available assessment data reported PASI 90 and PASI 75, respectively.

Sustained skin clearance: Among subjects who demonstrated total skin clearance at month 6 and who were assessed both at 6 and 12 months (n=105), 72% maintained total skin clearance (PASI 100 or sPASI=0) at month 12. Moreover, of subjects who failed to achieve PASI 100 or sPASI=0 at month 6 and who were assessed both at 6 and 12 months (n=343), 13% attained total skin clearance by month 12. The sustained total skin clearance from month 6 to month 12 was 75% in Europe and 64% in the US, while the proportion of subjects without PASI 100 or sPASI=0 at 6 months but attained total skin clearance by their 12-month visits was 14% in Europe and 12% in the US. By prior biologic use, of biologic treatment-naïve subjects who were assessed both at 6 and 12 months and who achieved total skin clearance at month 6 (n=89), 61% remained clear of plaque psoriasis at month 12, while among the biologic treatment-switching subjects who were assessed both at 6 and 12 months and who achieved total skin clearance at month 6 (n=48), 46% maintained total skin clearance at month 12 (p=0.095). Likewise, although not a significant difference (p=0.162), among those without PASI 100 or sPASI=0 at month 6 and who were assessed both at 6 and 12 months, 12% of subjects in the biologic treatment-naïve subgroup attained total skin clearance by month 12,

whereas subsequent total skin clearance occurred in 8% of biologic treatment-switching subjects who did not report a 6-month outcome of PASI 100 or sPASI=0.

sPGA: The sPGA scores measure the physician's assessment of the disease at a point in time or the global improvement from baseline, ranging from 0 "clear, no signs of psoriasis" to 5 "very severe disease", and sPGA of 0 or 1 is considered as a physician's impression of total skin clearance or nearly total skin clearance. At baseline, 833 (99%) subjects were assessed, and of those, less than 1% scored 0 points (clear, no signs of psoriasis), 2% scored 1 point (minimal disease), 13% scored 2 points (mild disease), 51% scored 3 points, (moderate disease), 28% scored 4 points (severe disease) and 6% scored 5 points (very severe disease). At 6 months, of the 604 (71%) subjects assessed, 23% achieved sPGA=0 and 56% achieved sPGA=1. At twelve months, of the 519 (61%) subjects assessed, 27% achieved sPGA=0 and 62% achieved sPGA=1. Among the 106 (24%) subjects who attained sPGA=0 at 6 months and were assessed both at 6 and 12 months, 72% maintained sPGA score of 0 at 12 months. In addition, among the 260 (58% of n=448 with non-missing 6-month sPGA) subjects who attained sPGA=0 or sPGA=1 at month 6 and were assessed both at 6 and 12 months, 81% obtained a sPGA score of 0 or 1 again at 12 months.

PASI vs. sPGA: With respect to the relationship between the two clinical measures of psoriasis severity, PASI and sPGA, 603 subjects at month 6 completed both scores. Among the 134 subjects with 6-month total skin clearance as measured by PASI 100, 99.2% (n=132) also reported sPGA=0. For subjects who achieved between PASI 90 but below PASI 100 (n=79), three (3.8%) subjects still reported total skin clearance as measured by sPGA=0, while the remaining 96.2% (n=76) of subjects had sPGA>0. In addition, all subjects who reported PASI 75 up to but not inclusive of PASI 90, also scored greater than 0 with sPGA (n=105). At month 6, there were 318 subjects in total who achieved PASI 75 through PASI 100, among which 42.7% (n=135) and 57.3% (n=181) reported sPGA=0 and sPGA>0, respectively.

Twelve months following biologic treatment initiation, 522 subjects had both PASI and sPGA scores available. This included 134 subjects who attained PASI 100, among which 100% also scored sPGA=0. In relation to the PASI result of PASI 90 to PASI 100 (non-inclusive) (n=84), 98.8% (n=81) of subjects had sPGA scores greater than 0, with one subject achieving sPGA=0. Of the 113 subjects with PASI 75 up to, but not including PASI 90, 108 (99.1%) subjects reported sPGA>0 and 1 (0.9%) subject scored sPGA=0. Lastly, there were 331 subjects who achieved between PASI 75 and PASI 100 at month 12, of which 41.8% (n=136) had a sPGA score of 0 and 58.2% (n=189) had a sPGA score greater than 0.

Concomitant psoriasis medication usage and skin clearance: Differences in sPGA scores were assessed between subgroups of subjects who received concomitant psoriasis medications and subjects who did not receive concomitant psoriasis medications at both 6 and 12 months post-initiation of biologic treatment. At month 6, there were 137 subjects and 463 subjects who did and did not use concomitant psoriasis medications, respectively, and also had available sPGA scores. Among subjects who did not use concomitant psoriasis medications, 25.1% (n=116) achieved total skin clearance as measured by sPGA=0, while in subjects who did use concomitant psoriasis medications, 16.1% (n=22) achieved sPGA=0, which was a statistically

significantly lower proportion (p<0.001). Twelve months following the initiation of biologic treatment, there were 118 subjects who received concomitant psoriasis medications and 397 subjects who did not receive concomitant psoriasis medications, all of whom had sPGA scores reported. Within the subgroup of those with concomitant psoriasis medication usage, 20.3% (n=24) of subjects achieved total skin clearance, while 28.7% (n=114) of those without concomitant psoriasis medication usage achieved sPGA=0 (p<0.001).

Skin clearance without additional psoriasis treatment: Evaluating the achievement of total skin clearance for the 660 enrolled subjects who did not use any psoriasis treatment in addition to biologics, there were 115 (17.4%; 95% CI: 14.6%, 20.5%) subjects at month 6 and 113 (17.1%; 95% CI: 14.3%, 20.2%) subjects at month 12 who achieved PASI 100 or sPASI=0. By geographic region, there were 444 subjects in Europe and 216 subjects in the US who did not use any additional psoriasis therapies outside of biologic treatment, among which total skin clearance was reported at month 6 for 18.0% (n=80; 95% CI: 14.6%, 21.9%) and 16.2% (n=35; 95% CI: 11.6%, 21.8%) of subjects in Europe and the US, respectively. At month 12, 19.6% (n=87; 95% CI: 16.0%, 23.6%) of those in Europe and 12.0% (n=26; 95% CI: 8.0%, 17.1%) of those in the US without additional psoriasis treatment attained total skin clearance. By prior biologic use, there were 407 biologic treatment-naïve subjects and 253 biologic treatment-switching subjects who did not use any psoriasis treatment in addition to biologic treatment. Total skin clearance was achieved at 6 months following biologic initiation in 18.7% (n=76; 95% CI: 15.0%, 22.8%) of the biologic treatment-naïve subjects and 15.4% (n=39; 95% CI: 11.2%, 20.5%) of the biologic treatment-switching subgroups, while at 12 months after starting biologic treatment, 18.9% (n=77; 95% CI: 15.2%, 23.1%) and 14.2% (n=36); 95% CI: 10.2%, 19.2%) of the biologic treatment-naïve and biologic treatment-switching subjects, respectively, achieved total skin clearance without the use of additional psoriasis treatment.

Predictors of total skin clearance: Univariate and multivariable logistic regression models were used to determine which sociodemographic and clinical factors, measured either at baseline or post-baseline, were predictors of 6-month and 12-month total skin clearance (PASI 100 or sPASI=0).

The baseline covariates included in the univariate logistic regression model as potential predictors of total skin clearance were: region, country, age, sex, race, weight, smoking status, alcohol consumption, time since psoriasis diagnosis, number of comorbidities, presence of psoriatic arthritis, prior biologic treatment (biologic treatment-switching vs. biologic treatment-naïve), number of prior non-biologic treatments, number of concomitant medications, and global health status. The post-baseline covariates included in the univariate logistic regression model were: drug class of the index biologic, dosing changes for the index biologic, and concomitant methotrexate usage.

Based on the univariate logistic regression of 6-month data, the number of comorbidities at baseline, baseline global health status, and concomitant psoriatic arthritis were the factors found to be statistically significant (at the p≤0.05 level) predictors of total skin clearance. In relation to subjects with zero comorbidities at baseline, subjects with one, two, and three or

more comorbidities at baseline were respectively, 0.6 (95% CI: 0.3, 0.9, p=0.0166), 0.5 (95% CI: 0.3, 1.0, p=0.0410), and 0.4 (95% CI: 0.3, 0.8, p=0.0035) times less likely to achieve total skin clearance at month 6. Regarding baseline global health status, subjects who reported excellent health were 3.3 (95% CI: 1.1, 9.4, p=0.0268) times more likely than subjects who reported good health to achieve 6-month total skin clearance. Subjects with concomitant psoriatic arthritis had 0.6 (95% CI: 0.4, 1.0, p=0.0355) times the odds as those without psoriatic arthritis of achieving total skin clearance. In addition, though statistically significant (p=0.0059), an odds ratio (OR) of 1.0 for age suggested that it was not a predictor of total skin clearance at 6 months after biologic treatment initiation.

The univariate analysis of 12-month data showed that prior biologic treatment, country, baseline weight, and number of comorbidities at baseline were statistically significant (at the $p \leq 0.05$ level) predictors of total skin clearance at 12 months after starting biologic treatment. Biologic treatment-switching subjects were 0.6 (95% CI: 0.4, 0.8, p=0.0058) times less likely to achieve total skin clearance than biologic treatment-naïve subjects. Country was a statistically significant predictor for the comparison of the US to Italy, where subjects in the US were 0.6 (95% CI: 0.3, 1.0; p=0.0350) times less likely to achieve 12-month total skin clearance. Subjects greater than 100kg had 0.5 (95% CI: 0.3, 0.9; p=0.0229) times the odds of achieving total skin clearance in comparison to subjects who weighed 100kg or less. In comparison to subjects with zero concomitant medications at baseline, subjects with two and three or more concomitant medications were respectively, 0.3 (95% CI: 0.1, 0.7; p=0.0078) and 0.4 (95% CI: 0.2, 0.9; p=0.0282) times less likely to achieve total skin clearance. Similarly, subjects with two comorbidities at baseline had 0.5 (95% CI: 0.3, 1.0; p=0.0457) times the odds of achieving total skin clearance at month 12 than subjects with zero baseline comorbidities.

A backward stepwise multivariable logistic regression model was also used to identify predictors of total skin clearance. The baseline covariates included in the multivariable logistic regression model as potential predictors of total skin clearance were: region, age, sex, race, weight, smoking status, alcohol consumption, time since psoriasis diagnosis, number of comorbidities, presence of psoriatic arthritis, prior biologic treatment (biologic treatment-switching vs. biologic treatment-naïve), number of prior non-biologic treatments, number of concomitant medications, and global health status. The post-baseline covariates included in the multivariable logistic regression model were: drug class of the index biologic, dosing changes for the index biologic, and concomitant topical psoriasis medication usage.

Based on the multivariable logistic regression model, prior biologic treatment at baseline and drug class of the index biologic were found to be statistically significant predictors of skin clearance ($p<0.05$ level) at month 6. Biologic treatment-switching subjects were 0.6 (95% CI: 0.4, 0.9, p=0.0276) times less likely to achieve total skin clearance than biologic treatment-naïve subjects. Relative to those who were administered an anti-TNF drug as their index biologic, subjects who received an IL-12/23 inhibitor had 1.8 (95% CI: 1.2, 2.9; p=0.0096) times the odds of exhibiting total skin clearance. Although the relationship of age with skin clearance at month 6 was statistically significant (p=0.0080), a very small negative estimated coefficient for age (-0.02) with an OR of 1.0 suggested that age was not a predictor of total

skin clearance. At month 12, prior biologic treatment at baseline and the number of concomitant medications at baseline were found to be statistically significant predictors of total skin clearance. Biologic treatment-switching subjects were again 0.6 (95% CI: 0.4, 0.9, p=0.0079) times less likely to achieve total skin clearance than biologic treatment-naïve subjects. Subjects with two concomitant medications at baseline, compared to those with zero concomitant medications, were 0.3 (95% CI: 0.2, 0.8; p=0.0131) times less likely to demonstrate 12-month total skin clearance.

Patient-reported outcomes: The specific PROs collected from subjects in the full analysis set at their scheduled 6-month and 12-month follow-up visits included the PSI and sPtGA as measures of psoriasis severity, DLQI to understand psoriasis-related QoL, global health status, and treatment satisfaction. The association between the clinical (PASI, sPGA) and patient-reported measures (DLQI, PSI, sPtGA, treatment satisfaction, global health status) of plaque psoriasis severity was evaluated with Spearman correlation coefficients, inclusive of enrolled subjects with available PRO data at the 6-month and/or 12-month follow-up visits.

DLQI: Dermatological disease-related QoL was evaluated through the DLQI, where lower scores indicate a lesser degree of functional disability, a DLQI score of 0 corresponds to no impairment in a patient's psoriasis-related QoL, and a score of 30 corresponds to the maximum impairment of psoriasis on health-related quality of life (HRQoL). The mean total DLQI score in the full analysis set was 12.4 at baseline, which corresponds to a large effect on a patient's psoriasis-related QoL. With the average DLQI score decreasing by 8.4 points to 4.0, an improvement in HRQoL was observed at 6 months following the initiation of biologic treatment. Of the 603 (71%) subjects assessed at month 6, 31% reported zero psoriasis-related functional disability, and there was also a fraction of subjects who reported a clinically meaningful decline in psoriasis-related QoL (5%), as indicated by an increase in DLQI score of at least 4. Twelve months after initiation of biologic treatment, the average DLQI score decreased by 0.3 points to 3.7, though not a clinically meaningful decrease. However, improvement in HRQoL, as measured by an increase in the percentage of subjects achieving DLQI=0, was observed overall as among the 508 (60%) subjects assessed, 34% scored DLQI=0. The fraction of subjects with a clinically meaningful regression in HRQoL (i.e., an increase of 4 or more in DLQI score) was 4.0% of those with available DLQI score. At month 6, a moderate positive association was observed between DLQI and PASI scores (ρ=0.58), as well as between DLQI and sPGA scores (ρ=0.57), such that improvement in PASI and sPGA scores was associated with improvement in DLQI scores, and both correlations were statistically significant ($p<0.0001$). The relationship between DLQI and the two clinical outcomes was slightly stronger at month 12, when the correlations with PASI scores and sPGA scores were respectively ρ=0.63 and ρ=0.62 ($p<0.0001$ for both).

PSI: PSI scores quantify patient perception of eight specified psoriasis symptoms, where the severity of each symptom is scored from 0 (not at all) to 4 (very severe), and possible scores range from 0 to 32. A PSI responder, defined as a subject whose total PSI score is a maximum of 8 with no individual symptom score more than 1, represents a clinically meaningful outcome signifying minor or negligible symptom severity. At baseline, of the 834 (99%) subjects with available data, 6% did not perceive their psoriasis symptoms as being severe, but

by 6 months following biologic treatment initiation, of the 603 (71%) subjects with available data, 59% were PSI responders. This included 23% of subjects with information available who reported a 6-month PSI score of 0, representing that symptoms were "not at all" severe. Twelve months after the index dose of biologic treatment, 26% of subjects attained PSI=0 and 66% were designated as PSI responders. Among subjects in the full analysis set who reported "not at all" severe symptoms (PSI=0) at month 6, nearly 60% remained asymptomatic, scoring PSI=0 at month 12. Regarding the relationship between PSI and the clinical measures of psoriasis severity, PSI had a strong statistically significant positive association ($p<0.0001$) with PASI and sPGA (month 6: $\rho=0.64$ and $\rho=0.65$, respectively; month 12: $\rho=0.68$ and $\rho=0.69$, respectively), such that subjects experiencing total skin clearance (PASI 100 or sPGA=0) primarily reported "not at all" severe plaque psoriasis symptoms, with reductions in PSI and PASI occurring in parallel.

sPtGA: As a measure of patient-perceived plaque psoriasis severity, sPtGA is a PRO with possible subcategories ranging from "No psoriasis symptoms" to "Very severe psoriasis". At baseline, of the 837 (99%) subjects assessed, less than 1% reported no psoriasis symptoms and 3% presented very mild disease. At 6 months, 602 (71%) subjects were assessed, among which no psoriasis symptoms were reported by 15% of subjects and very mild disease was reported in 34% of subjects. At 12 months, 508 (60%) subjects were assessed, which included 17% of subjects with no psoriasis symptoms and 39% of subjects with very mild disease. In regards to the relationship of sPtGA with PASI and sPGA, sPtGA score had a strong and statistically significant correlation with clinical psoriasis severity as indicated by sPGA ($\rho=0.66$, $p<0.0001$). Per this positive association, increases in physician-reported sPGA scores were simultaneous to worsening subject-perceived psoriasis symptoms.

Global health status: An alternative and broader measure of subject-perceived health was global health status, which has five subcategories that range from 'poor' to 'excellent'. At baseline, 98% of the full analysis set had global health status available, among which 3% of subjects reported 'excellent' overall health, 15% reported 'very good' health, 48% of subjects had 'good' health, then 26% and 9% of subjects, respectively, reported 'fair' and 'poor' health. At the 6-month study time point, among the 71% of subjects with non-missing data, 46% of patients reported 'good' health, while the percentage of subjects with 'fair' health status decreased by 8% to 18%, and 4% of subjects still perceived themselves as having 'poor' health. After 12 months of biologic treatment, 60% of subjects had completed the global health assessment, of which 16% and 3% of subjects specified 'fair' or 'poor' health, respectively, with 46% still perceiving 'good' overall health. Given that global health status is a non-specific measure of subjects' general health perception, for which subjects may rate their health independently from their psoriasis, the association between global health status and clinically-assessed psoriasis severity was weak (month 6: $\rho=0.32$ with PASI score and $\rho=0.31$ with sPGA score; month 12: $\rho=0.28$ with PASI and $\rho=0.25$ with sPGA), though statistically significant ($p<0.0001$ for all correlations). Accordingly, global health status was most commonly 'good', irrespective of the clinical severity of plaque psoriasis indicated by the sPGA score.

Treatment satisfaction: The remaining PRO was regarding treatment satisfaction, where five possible responses ranged from 'very dissatisfied' to 'very satisfied'. Six months following treatment initiation, among the 600 (71%) subjects assessed, 13% of subjects reported dissatisfaction or extreme dissatisfaction with biologic treatment. After 12 months of follow-up, among the 505 (60%) subjects assessed, 11% reported being dissatisfied or very dissatisfied with their treatment. Approximately 73% of the assessed subjects were satisfied or very satisfied with their biologic treatment at both 6 and 12 months after treatment initiation. A moderate negative association was observed between treatment satisfaction with PASI scores (ρ= -0.47) and treatment satisfaction with sPGA scores (ρ= -0.50) at month 6, such that decreases in PASI and sPGA (i.e., improvement in clinical severity of psoriasis) were moderately related to increases in treatment satisfaction, with both correlations statistically significant ($p<0.0001$). At month 12, a moderate association between treatment satisfaction and the two clinical outcomes was also observed, when the correlations with PASI scores and sPGA scores were respectively ρ= -0.48 and ρ= -0.49 ($p<0.0001$ for both).

Discussion:

There were 846 total moderate to severe plaque psoriasis subjects enrolled in the study, with 60% of subjects biologic treatment-naive and 40% biologic treatment-switching prior to study enrollment. The US had a somewhat lower proportion of subjects (57.1%) who were biologic treatment-naïve than Europe (73.7%). Based on the characteristics observed in enrolled subjects, those included in this study are expected to represent patients with moderate and severe plaque psoriasis treated with biologics in real-world clinical practice in the studied countries. Observational studies on the effectiveness of biologic treatments in a real-world settings are scarce, and those previously conducted [Inzinger, 2011; Bardazzi, 2010; Cassano, 2004; van Lumig, 2013; Baskan, 2009; and Kalb, 2005] differ from this current study as they had a relatively short period of follow-up (12 to 24 weeks) and a small number of subjects (ranging from 12 to 85 subjects).

Skin clearance following biologic treatment: Only 23% of enrolled subjects with available data achieved total skin clearance at 6 months following the index date of biologic treatment. About 30% of those with available data reported improvement of PASI 90 and 50% at PASI 75 by month 6. Complete skin clearance at 6 months was comparable between Europe (22%) and the US (23%), while biologic treatment-naïve subjects were somewhat more likely than biologic treatment-switching subjects to obtain total skin clearance after six months on biologic treatment (25% compared to 20%, respectively), however this difference was not statistically significant.

These low rates of complete skin clearance seem to be comparable to other observational studies conducted on biologic treatments, even though the studies included outcomes from only 12 to 81 subjects, the total skin clearance rates as defined by different measures, was obtained after 6 to 24 weeks of follow-up in other observational studies ranges from 5% to 34.8% [Inzinger, 2011; Bardazzi, 2010; Cassano, 2004; van Lumig, 2013; Baskan, 2009; and Kalb, 2005].

Comparing biologic treatment-switching and biologic treatment-naïve subjects showed a consistently lower rate of PASI 100 total skin clearance, as well as incomplete skin clearance as measured by PASI 90 and PASI 75, for subjects in the biologic treatment-switching group than in biologic treatment-naïve subjects. Several reasons could be postulated for such differences, but one is that some patients in the biologic treatment-switching group might have more severe disease difficult to treat.

Total skin clearance at 12 months following the index date of biologic treatment shows a similar pattern as that at 6 months, and the proportion of subjects with PASI 90 and PASI 75 were also similar to the improvement observed at month 6. Subjects in Europe more commonly demonstrated total skin clearance, as well as PASI 90 and PASI 75, than in the US. Only 26% of subjects achieved total skin clearance after 12 months of treatment, which is a low treatment success rate. At the 12-month follow-up visit, the dissimilarities between the subgroups by prior biologic use widened, such that PASI 100 or sPASI=0 was reported for 30% of the biologic treatment-naïve subjects, and were thus statistically significantly more likely than biologic treatment-switching subjects to obtain total skin clearance at month 12. This trend was also seen for PASI 90 and PASI 75. The differences could again be due to several factors, including subjects in the biologic treatment-switching subgroup have more severe disease that is difficult to treat.

Persistence of total skin clearance: Among subjects who completed both 6-month and 12-month PASI assessments and demonstrated total skin clearance at month 6, 72% maintained total skin clearance at month 12. The rate of persistence of total skin clearance to month 12 of follow-up was greater in Europe than in the US. Moreover, of subjects who failed to achieve PASI 100 or sPASI=0 at month 6, 13% achieved total skin clearance by month 12. This finding was similar in Europe and the US. Prolonged skin clearance was more frequent in biologic treatment-naïve than in biologic treatment-switching subjects, which was statistically significant. Of subjects who failed to achieve PASI 100 at month 6, more subjects in the biologic treatment-naïve subgroup achieved PASI 100 by month 12 than in the biologic treatment-switching subgroup, but this difference was not statistically significant.

Total skin clearance using the sPGA: An additional measure of skin clearance, the sPGA, was used to assess skin clearance, with similar results as those reported with PASI. Six months after starting biologic treatment, 23% of subjects achieved total skin clearance as per sPGA=0, with 56% obtaining scores of sPGA=0/1 (total or substantial skin clearance). Similar proportions of subjects received scores of sPGA=0/1 in Europe and the US, and biologic treatment-naïve subjects were more likely than biologic treatment-switching subjects to report considerable improvement at 6 months following treatment initiation. Twelve-month sPGA scores revealed a slight increase in the subjects (62%) attaining either sPGA=0 or sPGA=1 than observed at month 6. The percentage of subjects progressing to sPGA=0/1 12 months post-treatment initiation remained comparable between the region-specific subgroups and more subjects in the biologic treatment-naïve than in the biologic treatment-switching subgroups was observed.

Regarding the maintenance of skin clearance via sPGA scores, 72% of subjects maintained a sPGA of 0 at 12 months of biologic treatment, and this percentage was slightly higher (81%) for subjects with a sPGA of 0 or 1. Sustained skin clearance was more common in Europe than in the US, while biologic treatment-naïve subjects more commonly maintained prolonged skin clearance (sPGA=0/1) than biologic treatment-switching subjects.

Patient-reported outcomes: At baseline, 6% of subjects were identified as PSI responders, which is a clinically meaningful outcome signifying minor or negligible symptom severity, and by six months following biologic treatment initiation, almost 60% of subjects were PSI responders. There was no discernable difference in PSI scores by region, while the biologic treatment-naïve subgroup had a greater percentage of subjects who progressed to PSI=0 and subjects who were PSI responders than the biologic treatment-switching subgroup. At month 12, there was a minor reduction in plaque psoriasis symptoms, as measured by the greater proportion of patients achieving PSI=0 and the classification of PSI responder. The proportion of PSI responders was similar between the regions, and the percentage of subjects achieving PSI=0 and PSI responder status improved more in the biologic treatment-naïve subgroup than in the biologic treatment-switching subgroup. PSI had a positive, high and statistically significant positive association with sPGA/PASI, which is to be expected as higher scores on both indicate more severity or less skin clearance. The fact that patient-reports of severity correlate highly with physician score confirms that subjects evaluating their psoriasis' severity can do so as reliably as physician-reported (sPGA) assessments of plaque psoriasis severity or when assessed with a clinical instrument such as the PASI.

Another measure of subject-perceived plaque psoriasis severity, sPtGA also statistically significantly correlated with clinical psoriasis severity as measured by physician-reported assessment of psoriasis severity (sPGA), and this correlation was high and positive, again emphasizing that subjects are reliable assessors of their personal psoriasis disease severity. The score distributions of the sPGA seem to support an improvement of those reporting severe symptoms by month 6 which did not change by month 12. There were no differences by regions or prior biologic exposure subgroups.

Psoriasis-related HRQoL was assessed by the DLQI, where a substantial improvement in HRQoL was observed at 6 months following the initiation of biologic treatment, with 31% of subjects reporting zero psoriasis-related functional disability at month 6, and results comparable by region and greater improvement observed in the biologic treatment-naïve subgroup than in the biologic treatment-switching subgroup. Most changes in HRQoL at 12 months remained similar to those at 6 months, with again no differences among regions, and a slightly greater improvement in biologic treatment-naïve than in biologic treatment-switching subjects. Subject-reported DLQI scores correlated highly and positively to clinician-reported sPGA and PASI. Subjects with total or nearly total skin clearance did not have significant impairment of psoriasis-related QoL, with an increasing proportion of subjects reporting DLQI=0 concurrent to reductions in PASI score. As a result, this study supports the use of the PASI scoring to gain insights on the impact of therapeutic interventions on subjects' HRQoL. The lower correlation strength of the DLQI with sPGA and PASI than with PSI or sPtGA further supports that subjects are a reliable source of assessment for their personal disease

severity and HRQoL, even more so than clinical and physician-reported measures of disease severity. DLQI instead measures psoriasis-related HRQoL, which encompasses more life areas than skin-related symptoms and clearance, and is not always discussed in routine clinical encounter with a physician.

Regarding global health status, 26% and 9% of subjects reported ‘fair’ or ‘poor’ health, respectively at baseline. A decrease in global health status seemed to be observed in the distribution of responses by 6 months, which did not differ by regions or biologic treatment groups. Given that global health status is a non-specific measure of subjects’ general health perception, for which subjects may rate their health independently from their psoriasis, the association between global health status and clinically-assessed psoriasis severity, though statistically significant, was weak.

Treatment satisfaction was also subject-reported, and at 6 months following treatment initiation, the majority of subjects were either satisfied or very satisfied A slightly higher percentage of subjects in the US specified that they were dissatisfied or very dissatisfied with their treatment than in Europe, as well as a higher percentage of biologic treatment-switching subjects in comparison to biologic treatment-naïve subjects. After 12 months of follow-up, a small reduction in the percentage of dissatisfied or very dissatisfied subjects was observed, and again a greater percentage of subjects in the US and biologic treatment-switching subgroup reported dissatisfaction with their treatment. Despite the differences observed between the regions and treatment groups, roughly three-quarters of the subjects were satisfied with their biologic treatment at both six and 12 months after treatment initiation. As expected, there was a negative, moderate and statistically significant correlation between treatment satisfaction and PASI and sPGA, where subject-reported treatment satisfaction improved in parallel with reductions in sPGA and PASI score, indicating that the clinical severity of plaque psoriasis is an important component for subjects when evaluating their treatment. However, subjects were not asked about potential adverse side effects, which could have been a contributing factor in treatment satisfaction, and would also support the finding that most subjects discontinued their biologic treatment for reasons other than treatment failure.

Psoriasis-related treatment patterns: Regarding initial biologic treatment patterns upon study enrollment, almost half of subjects were prescribed a biologic agent as a result of conventional systemic treatment failure, followed by those who initiated biologic treatment because of prior biologic and topical treatment failure. In the US failure of a prior biologic or topical treatment were the main causes for biologic treatment initiation, however in Europe failure of a conventional systemic treatment was the main cause. Anti-TNF drugs were prescribed as the index biologic for 61% of subjects, and were more frequently initiated in biologic treatment-naïve subjects. IL-12/23 inhibitors were initiated to 30% of subjects overall, and the remaining 9.0% of subjects were given an IL-17 antagonist at study entry. The most frequent biologic agent used in biologic treatment-switching subjects was IL-12/23.During the study period, 17% of subjects discontinued their initial biologic treatment, and the greatest proportion discontinued due to ‘other reasons’, which ranged from an adverse event or drug reaction, to a dosing change, pregnancy, a change in insurance coverage, withdrawal of consent, or the subject being lost to follow-up.

PASI vs. sPGA: Among subjects with available scores, almost all subjects with PASI 100 at 6 months also had a sPGA=0, while those with PASI 90 at 6 months had sPGA of above 0 except for 3 subjects. Those with PASI 75 also had sPGA>0. The pattern of scores remained at 12 months, indicative that total skin clearance is measured consistently when using PASI 100 and the sPGA.

Total skin clearance by concomitant psoriasis medication usage: About 17% of subjects both at month 6 and 12 who achieved PASI 100 at 6 months and did not use any additional psoriasis treatment other than the biologic treatment. There were no major difference across regions and there was a slight increase in those numbers in biologic treatment-naïve subjects than biologic treatment-switching ones.

Differences in sPGA scores were assessed between subgroups of subjects who received concomitant psoriasis medications and subjects who did not receive concomitant psoriasis medications at both 6 and 12 months post-initiation of biologic treatment. At month 6, among those with available data, more subjects reached sPGA=0 among those who did not use concomitant psoriasis medication than those who did, a statistically significant difference ($p<0.001$). The same finding applied to sPGA=1, and again the difference was statistically significant. The same findings were seen for sPGA=0 at month 12, but was not statistically significant for sPGA=1. This interesting finding supports the notion that patients, when prescribed biologic treatments, should perhaps not use concomitant psoriasis medication for improved effectiveness.

Predictors of skin clearance: Exploring predictors of total skin clearance using a backward stepwise multivariable logistic regression model, prior biologic treatment at baseline and drug class of the index biologic were found to be statistically significant predictors of total skin clearance at month 6. Biologic treatment-switching subjects were 0.6 times less likely to exhibit total skin clearance at month 6 than biologic treatment-naïve subjects, Subjects whose index biologic was an IL-12/23 inhibitor had 1.8 times the odds of 6-month progression to PASI 100 or sPASI=0. Twelve months following biologic treatment initiation, multivariable analysis using the backward elimination approach identified prior biologic treatment at baseline and the number of concomitant medications at baseline as statistically significant predictors of 12-month total skin clearance. Treatment switching subjects were again 0.6 times less likely to achieve PASI 100 or sPASI=0 than treatment naïve subjects at month 12. Subjects with two concomitant medications at baseline, compared to those with zero concomitant medications, were 0.3 times less likely to demonstrate 12-month total skin clearance. A limitation of this analysis is that the factors considered as potential predictors of total skin clearance were primarily those measured at baseline, which could have changed during the follow-up period.

Conclusion:

This study observed subjects under routine clinical practice over the 12 months following initiation of biologic treatment and aimed at estimating the real-world effectiveness of biologics as measured by the proportion of subjects achieving total skin clearance at 6 and 12 months following treatment initiation.

About 20% of enrolled subjects with available data achieved total skin clearance at six months following the index date of biologic exposure, and more than 70% of these subjects maintained skin clearance by 12 months. An additional 13% of subjects who had not achieved total skin clearance at 6 months did progress to total skin clearance at 12 months. Maintained skin clearance was more likely to be achieved in biologic treatment-naïve subjects than in biologic treatment-switching patients.

A clinical score of skin clearance, the PASI, correlated with patient-reported measures of disease severity (PtGA, PSI), and with physician-reported measured of disease severity (PGA). Patient-reported HRQoL (DLQI), global health status, and treatment satisfaction also improved with improving total skin clearance and perceived disease severity.

Results were generally comparable across the US and EU. Biologic treatment-naïve subjects typically showed statistically significant improved skin clearance, perceived disease severity, and subject-reported HRQoL as compared to biologic treatment-switching subjects. This could be due to more severe subjects not being as responsive to treatment and being treated with several treatment options. Subjects treated with IL-12/23 inhibitors seemed to more commonly achieve total skin clearance, which was reflected in a statistically significant greater percentage with total skin clearance at 6 months in these subjects as compared to those prescribed anti-TNF agents, but at 12 months these differences dissipated.

The findings suggest that overall, biologic treatments seems to be a promising treatment option for subjects with moderate to severe psoriasis, however complete skin clearance is generally not achieved for the majority of subjects, which emphasizes the need for additional treatment options or guidance on when to try a different biologic treatment to achieve total skin clearance. Subjects are also taking biologic treatment for long periods of time (up to 12 months) without total skin clearance. Additional data is needed to support the evidence and need of biologic treatment guidelines in terms of the period of time when patients should remain on a biologic treatment when total skin clearance is not achieved within 6 months, as improvements at 12 months will be unlikely. An important proportion of subjects discontinued biologics for reasons other than treatment failure, such as an adverse event or drug reaction, dosing change, pregnancy, or a change in insurance coverage. Therefore close monitoring of these factors should be recommended during biologic treatment prescription to ensure compliance and increase the chances of an effective treatment. Further investigations would need to determine predictors and potential factors that distinguish subjects who are more likely to respond well to a biologic treatment than others. Additional guidelines are also to be provided regarding dose adjustment and combinations with conventional systemic or topical therapies to improve or maintain effectiveness. When different types of treatments are combined, efficacy goals can often be met using lower doses of each drug, potentially resulting in less treatment-associated toxicity.