SYNOPSIS

Issue Date: 17 Jan 2013

Name of Sponsor/Company	Janssen Research & Development, Inc
Name of Finished Product	Ustekinumab
Name of Active Ingredient(s)	Ustekinumab

Protocol No.: CNTO1275PSA3001

Title of Study: A Phase 3 Multicenter, Randomized, Double-blind, Placebo-controlled Trial of Ustekinumab, a Fully Human Anti-IL-12/23p40 Monoclonal Antibody, Administered Subcutaneously, in Subjects with Active Psoriatic Arthritis.

Study Name: PSUMMIT I

EudraCT Number: 2009-012264-14

NCT No.: NCT01009086

Clinical Registry No.: CR016315

Principal Investigator: Iain B. McInnes, MD

Study Centers: 104 study sites

Publication (Reference): None

Study Period: Through Week 24

Phase of Development: Phase 3

Objectives: The primary objectives of this study are to evaluate the efficacy of ustekinumab in subjects with active psoriatic arthritis (PsA) by assessing the reduction in signs and symptoms of PsA and to evaluate the safety of ustekinumab in this population.

The secondary objectives of this study are to evaluate the efficacy of ustekinumab in:

- Improving physical function;
- Improving psoriatic skin lesions; and
- Inhibiting the progression of structural damage.

Methodology: This is a randomized, double-blind, placebo-controlled, parallel, multicenter 3-arm study (with early escape at Week 16) of ustekinumab in subjects with PsA. Six hundred and fifteen subjects were randomized to receive treatment with ustekinumab 45 mg (45 mg), ustekinumab 90 mg (90 mg), or placebo subcutaneous (SC) injections at Weeks 0 and 4, followed by every 12 week (q12w) dosing with the last dose at Week 88. Subjects randomized to placebo were eligible for crossover to receive ustekinumab at Weeks 24 and 28, followed by q12w dosing with the last dose at Week 88. Expected duration of exposure to study agent is 100 weeks. Subjects will be followed for efficacy through Week 100 and for safety through Week 108.

Number of Subjects (planned and analyzed): A target of 600 subjects was planned to be randomly assigned to treatment with 200 subjects each in the 45 mg, 90 mg, and or placebo groups, respectively.

A total of 615 subjects was randomly assigned across treatment groups with 205, 204, and 206 subjects in the 45 mg, 90 mg, and placebo groups, respectively.

Diagnosis and Main Criteria for Inclusion: Subjects were men or women between 18 and 99 years of age with the diagnosis of active PsA for at least 6 months prior to the first administration of study agent and had to have 5 or more swollen and tender joints at screening and at baseline. At screening, subjects had to have C-reactive protein (CRP) ≥0.3 mg/dL (modified to ≥0.3 mg/dL from ≥0.6 mg/dL with Protocol Amendment 3 dated 27 Oct 2010; upper limit of normal 1.0 mg/dL) and at least 1 of the PsA subsets, and/or active plaque psoriasis, or a documented history of plaque psoriasis.

Test Product, Dose and Mode of Administration, Batch No.: Ustekinumab was supplied in a pre-filled syringe (PFS) as a single-use, sterile solution in a BD Hypak™ 1 mL, type 1 glass syringe with a 27-gauge, 1/2-inch fixed needle. There were 2 dose strengths (ie, 90 mg in 1 mL nominal volume or 45 mg in 0.5 mL nominal volume). Each 1 mL of ustekinumab solution contained 90 mg ustekinumab, L-histidine, L-histidine monohydrochloride monohydrate, sucrose, and polysorbate 80 at pH 6.0. No preservatives were present. Five lots of ustekinumab (Batch No.: 08F011, 08F012, 09G041, 09G042, and 10C052) were used in the study.

Reference Therapy, Dose and Mode of Administration, Batch No.: The placebo was supplied in a PFS, a single-use, sterile solution in a BD Hypak™ 1 mL, type 1 glass syringe with a 27-gauge, 1/2-inch fixed needle. There were 2 dose volumes (ie, 1 mL nominal volume or 0.5 mL nominal volume). Each 1 mL of placebo solution contained L-histidine, L-histidine monohydrochloride monohydrate, sucrose, and polysorbate 80 at pH 6.0. No preservatives were present. Six lots of placebo (Batch No.: 08H021, 08H022, 09E021, 09E022, 10E011, and 10E012) were used in the study.

Duration of Treatment: Approximately 615 subjects were randomized in a 1:1:1 ratio to 1 of the 3 groups and received treatment with 45 mg, 90 mg, or placebo SC at Weeks 0 and 4 followed by q12w dose regimen with the last dose at Week 88. At Week 16, subjects with <5% improvement from baseline in both tender and swollen joint counts in the 45 mg and placebo groups were eligible for early escape and begin to receive ustekinumab 90 mg and 45 mg, respectively. Subjects randomized to placebo who did not qualify for early escape were to crossover to receive ustekinumab 45 mg at Weeks 24 and 28 followed by q12w dosing with the last dose at Week 88. The expected duration of exposure to study agent is 100 weeks. Subjects will be followed for efficacy through Week 100 and for safety through Week 108. The first database lock (DBL) occurred at Week 24. The 24-week DBL includes all pharmacokinetic (PK), efficacy, and safety data through Week 24 with the exception of the radiographic data for all randomized subjects. In addition, subject disposition and safety data (including laboratory data) through Week 52 for subjects randomized prior to 26 Oct 2010 who were supposed to have completed Week 52 visit by the time of the 24 week DBL (either terminated the study or completed through Week 52), and referred thereafter as "the Week 52 safety subset", were also included. Additional database locks will occur at Week 52 and Week 108. The end of the study will occur after the last subject completes the Week 108 visit.

Criteria for Evaluation:

Pharmacokinetics*:* Serum ustekinumab concentrations were summarized by ustekinumab treatment group and visit through Week 24. Serum ustekinumab concentrations were also summarized by methotrexate (MTX) use at baseline and subjects weight at baseline (≤100 kg versus >100 kg). The population PK modeling is not included in this report. The relationship of serum ustekinumab concentrations and selected efficacy was also assessed.

Immunogenicity: The incidence of antibodies to ustekinumab during the study was summarized for all subjects who had appropriate serum samples for antibody detection. The relationships of antibodies to ustekinumab with serum ustekinumab concentrations and selected efficacy and safety measures were also assessed.

Efficacy: The efficacy evaluations included PsA response evaluations and psoriasis response evaluations. PsA response evaluations included joint assessments, American College of Rheumatology (ACR) responses, Disease Activity Index Score 28 using CRP (DAS28), patient and physician global assessments of disease activity, dactylitis assessment, enthesitis assessment, Visual Analogue Scale (VAS) for pain assessment, Disability Index of the Health Assessment Questionnaire (HAQ-DI), 36-item short form health survey (SF-36), modified PsA response criteria (PsARC) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Psoriasis evaluations included psoriasis area and severity index (PASI) and dermatology life quality index (DLQI). The potential pharmacoeconomic benefit of ustekinumab treatment was also assessed. Radiographic imaging evaluations of the hands and feet through Week 24 will be addressed in the 52-Week Clinical Study Report.

Safety*:* Safety evaluations for all subjects were monitored and included measurement of vital signs (heart rate and blood pressure), physical evaluations (waist circumference and weight), assessment of adverse events (AEs), and injection site reactions that may have occurred between each of the evaluation visits. Tuberculosis evaluations, including QuantiFERON®-TB Gold Test and Mantoux tuberculin skin test (in countries where QuantiFERON®-TB Gold Testing was not licensed), were performed. Samples for routine laboratory analyses were collected.

Statistical Methods: Binary data (eg, the proportion of subjects with an ACR 20 response) were analyzed using the chi-square test or the Cochran-Mantel-Haenszel (CMH) test adjusted for baseline MTX usage (yes/no). Continuous data was analyzed using an analysis of covariance (ANCOVA) test on van der Waerden normal scores adjusted for baseline MTX usage (yes/no). Re-randomization tests were used as the primary statistical testing method to determine p-values for the analyses of the primary and the major secondary endpoints. All efficacy analyses were based on the intent-to-treat principle; thus, subjects were included in the efficacy analyses according to their assigned treatment group regardless of whether or not they received the assigned treatment. Multiplicty adjustments were made for the analyses of the primary and the major secondary endpoints. All statistical testing was performed 2-sided at an alpha level of 0.05.

RESULTS:

STUDY POPULATION:

- Of the 615 subjects randomly assigned to treatment at Week 0, 206 were assigned to the placebo group, 205 were assigned to the 45 mg group, and 204 were assigned the 90 mg group. All randomized subjects received their assigned treatment at Week 0 with the exception of 1 subject in the placebo group who withdrew consent and was never treated.
  - Through Week 24, a total of 30 subjects discontinued across the randomized treatment groups with a higher rate of discontinuation in the placebo group (7.3%) than either in the 45 mg (3.9%) or the 90 mg (3.4%) groups. The most common reason for discontinuation of study agent across all study groups was due to an AE. The higher proportion of subjects discontinuing study agent in the placebo group compared with the individual ustekinumab groups was primarily due to efficacy related reasons (ie, lack of efficacy and worsening of disease).
- For the Week 52 safety subset, which included 356 subjects randomized prior to 26 Oct 2010 who completed the Week 52 visit by the time of the 24-week DBL, the subject disposition was assessed.
  - Through Week 52, 41 subjects out of 356 discontinued study agent. The proportion of subjects was comparable in the placebo (13.6%) and 45 mg (12.5%) groups, but lower in the 90 mg group (8.5%). The most common reason for discontinuation was lack of efficacy (45 mg group), withdrawal of consent (90 mg group), and due to an adverse event (placebo group).
- Demographic characteristics of subjects at baseline were generally well balanced across treatment groups:
  - the majority of subjects were men (53.7%)
  - most subjects were Caucasian (96.6%)
  - the median age was 48.0 years
  - the median weight was 86.0 kg
- Baseline clinical characteristics of PsA from the ACR core set of outcome measurements were indicative of subjects with PsA of moderate to severe activity and generally comparable across the treatment groups.
  - Median number of swollen joints (10.00)
  - Median number of tender joints (20.00)
  - Median VAS of Patient's assessment of pain (6.60 cm)
  - Median VAS of Physician's Global Assessment of disease activity (6.50 cm)
  - Median HAQ-DI score was the same in all the treatment groups (1.25)
  - Median CRP level (10.30 mg/L)

- Baseline disease characteristics of psoriasis measurements for subjects with ≥3% body surface area (BSA) involvement with psoriasis were generally comparable across the treatment groups and were indicative of significant psoriatic skin involvement with a substantial negative impact on quality of life.
  - Median percent BSA (11.00)
  - Median PASI score (8.00)
  - Median DLQI score (10.00)
- Through Week 24, subjects in the study randomized to ustekinumab received a median dose of 180 mg. The placebo subjects who entered early escape received an average of approximately 2 ustekinumab injections while subjects randomized to the ustekinumab group received an average of approximately 3 ustekinumab injections.

CLINICAL PHARMACOLOGY SUMMARY

Pharmacokinetics Summary

- Dose proportionality in serum ustekinumab concentration was observed when comparing mean serum ustekinumab concentrations between the 45 mg and 90 mg groups.
- There was no evidence of accumulation in serum ustekinumab concentrations over time.
- A higher proportion of subjects with trough serum ustekinumab concentrations <0.16880 µg/mL was observed in the 45 mg group compared with the 90 mg group.
- Subjects who underwent early escape had relatively lower serum ustekinumab levels compared with subjects who did not early escape, as suggested by lower mean serum ustekinumab concentrations through Week 16 and a higher proportion of subjects with trough serum ustekinumab concentrations <0.16880 µg/mL at Week 16. However, subjects in the 45 mg group who underwent early escape had their serum ustekinumab concentrations increased after receiving the 90 mg dose at Week 16.
- Within each treatment group, mean serum ustekinumab concentrations in subjects who received MTX at baseline was slightly higher compared with subjects who did not receive MTX at baseline.
- Subjects of higher weight (>100 kg) had lower mean serum ustekinumab concentrations compared with subjects of lower weight (≤100 kg). Notably, mean serum ustekinumab concentrations at Weeks 4, 12, and 16 in subjects >100 kg in the 90 mg group were generally comparable to those observed in subjects ≤100 kg in the combined 45 mg group, and mean serum ustekinumab concentrations at Weeks 20 and 24 in subjects >100 kg in the 90 mg group were generally comparable to those observed in subjects ≤100 kg in the 45 mg group who did not early escape at Week 16.

Immunogenicity Summary

- Through Week 24, the combined incidence of antibodies to ustekinumab was 5.8% (n=26) across all treatment groups.
- The incidence of antibodies to ustekinumab was generally comparable between the combined 45 mg group (7.1%; n=14) and the 90 mg group (6.2%; n=12).
- The incidence of antibodies to ustekinumab was lower in subjects receiving MTX at baseline (3.3%) compared with subjects not receiving MTX at baseline (8.1%).

- Subjects who were positive for antibodies to ustekinumab had lower mean serum ustekinumab concentrations than subjects who were negative for antibodies to ustekinumab.

EFFICACY RESULTS:

Primary Endpoint

- A significantly greater proportion of subjects in the combined ustekinumab, 45 mg, and 90 mg groups (46.0%, 42.4%, and 49.5%, respectively) achieved an ACR 20 response at Week 24 compared with subjects in the placebo group (22.8%; $p<0.001$ for all comparisons).

Major Secondary Endpoints

- There was significantly greater improvement in HAQ-DI scores at Week 24 in subjects in the combined ustekinumab, 45 mg, and 90 mg groups (all with a median change from baseline of -0.25) compared with subjects in the placebo group (median of 0.00; $p<0.001$ for all comparisons).

- A significantly greater proportion of subjects with ≥3% BSA psoriasis skin involvement at baseline in the combined ustekinumab, 45 mg, and 90 mg groups demonstrated PASI 75 response at Week 24 (59.9%, 57.2%, and 62.4%, respectively) compared with subjects in the placebo group (11.0%; $p<0.001$ for all comparisons).

- A significantly greater proportion of subjects in the combined ustekinumab, 45 mg and 90 mg groups achieved an ACR 50 response (26.4%, 24.9%, 27.9% respectively) and an ACR 70 response (13.2%, 12.2%, 14.2% respectively) at Week 24 compared with subjects in the placebo group (ACR 50: 8.7%, ACR 70: 2.4%; $p<0.001$ for all comparisons).

Other Efficacy Analyses

- ACR 20, 50, and 70 responses in both the 45 mg and 90 mg groups were notably higher than in the placebo group beginning at Week 8. The maximum improvement based upon ACR 20, 50, 70 responses for both the 45 mg and 90 mg groups occurred at Week 20 or Week 24, 4 to 8 weeks after the Week 16 dose. There appeared to be decreases in response rates at Week 16 in the 45 mg group for ACR 20 response and ACR 50 response which were not observed in the 90 mg group.

- PsARC and DAS28 response were achieved in a significantly greater proportion of subjects in the combined ustekinumab group (and in each ustekinumab dose group) than in the placebo group at both Week 12 and a Week 24 ($p<0.001$ for all comparisons).

- For subjects with dactylitis at baseline, significantly greater improvement in dactylitis score at Week 24 was observed in both the 45 mg, 90 mg, and combined ustekinumab groups as compared with the placebo group ($p<0.001$ for all comparisons).

- For subjects with enthesitis at baseline, significantly greater improvement in enthesitis score at Week 24 was observed for both ustekinumab dose groups as compared with the placebo group ($p=0.002$ in the 45 mg group and $p<0.001$ in the 90 mg group).

- For subjects with the spondylitis with peripheral arthritis subset of PsA, a significantly higher proportion of subjects achieved at least 20% or at least 70% improvement in BASDAI score at Week 12 and Week 24 in both ustekinumab groups as compared with the placebo group.
  - The proportion of subjects achieving at least 50% improvement in BASDAI at Week 12 and Week 24 was numerically higher in both ustekinumab groups as compared with the placebo group.

- A significantly higher proportion of subjects achieved the ACR 20 at Week 24 in both ustekinumab groups as compared with the placebo group for both subjects receiving MTX (p=0.011 in the 45 mg group and p<0.001 in the 90 mg group) and those not receiving MTX at baseline (p=0.004 in the 45 mg group and p<0.001 in the 90 mg group).

- A significantly higher proportion of subjects achieved both ACR 20 and PASI 75 at Week 24 in both the 45 mg group (27.6%) and 90 mg group (41.6%) as compared with the placebo group (p<0.001 for all comparisons).

- At Week 24, there was a significantly higher proportion of subjects with a DLQI score of 0 or 1 in the combined ustekinumab group (45.2%), in the 45 mg group (37.2%), and in the 90 mg group (53.0%) compared with 8.3% in the placebo group (p<0.001 for all comparisons).

- A significantly greater improvement in SF-36 physical component summary (PCS) score was observed in both ustekinumab groups as compared with the placebo group at both Week 16 and Week 24 (p<0.001 for all comparisons).

- A significantly greater improvement in SF-36 mental component summary (MCS) score was observed in both the ustekinumab 45 mg group (p=0.005) and 90 mg group (p=0.018) as compared with the placebo group at Week 16. A significantly greater improvement in SF 36 MCS score was observed for the 90 mg group (p<0.001) as compared with the placebo group at Week 24.

- The proportion of subjects who achieved ACR 20, ACR 50 and PASI 75 responses at Week 24 was higher in subjects with preinjection serum ustekinumab levels ≥0.16880 μg/mL when compared with subjects with preinjection serum ustekinumab levels <0.16880 μg/mL.

- Subjects who were positive for antibodies to ustekinumab tended to have lower clinical efficacy when compared with subjects who were negative for antibodies to ustekinumab. However, antibody positivity to ustekinumab did not preclude a clinical response.

- Consistently and significantly higher proportions of subjects achieved ACR 20 at Week 24 in almost all the subgroups examined in the 90 mg group as compared with the placebo group. However, more variability was observed in the subgroups examined for the comparisons between the 45 mg group and the placebo group.

  - Statistically significant higher ACR 20 response was observed for both the 45 mg and 90 mg groups as compared with the placebo group among subjects with prior disease modifying antirheumatic drug use.

- There was no statistically significant difference in the time lost from work (days) between the ustekinumab treatment groups and placebo group at Week 16 and Week 24 for subjects <65 years old and employed full-time at baseline.

- Overall, there were no consistent statistically significant differences in the ustekinumab treatment groups compared with the placebo group in the measure of employability due to PsA at Week 16 and Week 24.

- At both Week 16 and Week 24, the impact of PsA on work productivity was significantly greater in the combined ustekinumab group (p<0.001), the 45 mg group (p=0.002), and the 90 mg group (p<0.001) compared with the placebo group.

SAFETY RESULTS:

Treatment emergent AEs and laboratory analyte values were also presented and summarized through Week 16 (the placebo-controlled period), and Week 24 for all subjects and through Week 52 for the Week 52 safety subset. Vital sign measurements (heart rate and blood pressure) and physical evaluation

(waist circumference and weight) are presented and summarized through Week 24. The Week 52 safety subset included 356 subjects randomized prior to 26 Oct 2010 who completed the Week 52 visit by the time 24-week DBL occurred.

Adverse Events

- Through Week 16, AE rate, and AE profiles in each of the 2 ustekinumab groups were comparable to those observed in the placebo group. The proportion of subjects reporting AEs was 39.5%, 43.1% and 43.4% in the 45 mg, 90 mg and placebo groups, respectively. The most commonly reported system organ class of AEs was Infections and Infestations (16.6%, 20.1%, and 20.5% in the 45 mg, 90 mg and placebo groups, respectively), and the most frequently reported AEs were predominantly nasopharyngitis and upper respiratory tract infection (URTI).

- Through Week 24, no disproportional increase from Week 16 was observed in AE rates, and the AE profile was similar to that observed through Week 16. Additionally, the AE rate and profile were similar between the treatment groups.

- Through Week 52, in the Week 52 safety subset, no disproportional increase from Week 24 was observed in AE rates, and the AE profile was similar to that observed through Week 24. Additionally, AE rates and AE profile were similar between the subjects initially randomized and treated with 45 mg and those with 90 mg.

- Safety profiles were not impacted by concomitant use of MTX, age, gender, and weight.

Serious Adverse Events

- No deaths were reported.

- Through Week 16, the proportion of subjects reporting one or more serious adverse events (SAEs) was similar across all 3 treatment groups (2.0%, 1.5% and 2.0% in 45 mg, 90 mg and placebo groups, respectively). SAEs were single events in all the treatment groups without any particular pattern.

- Through Week 24, the proportion of subjects experiencing 1 or more SAEs was 2.9% in the combined 45 mg and 1.5% in the 90 mg group. SAEs occurred in 2.1% of all ustekinumab-treated subjects and 2.4% of placebo-treated subjects.

- The proportion of subjects reporting one or more SAEs continued to be low among the Week 52 safety subset, 5.8% and 2.5% in the combined 45 mg and 90 mg group, respectively. No particular pattern was observed.

- SAEs were not impacted by concomitant use of MTX or weight.

Adverse Events Leading to Study Agent Discontinuation

- Through Week 16, the proportion of subjects who discontinued study agent due to 1 or more AEs were similar in the placebo group (1.5%) compared with the 45 mg (0.5%) or the 90 mg group (1.0%).

- Through Week 24, the proportion of subjects who discontinued study agent due to 1 or more AEs continued to be low (1.5% in the combined 45 mg group and 1.5% in the 90 mg group; 1.3% of all ustekinumab-treated subjects and 3.4% of placebo-treated subjects).

- The proportion of subjects who discontinued study agent due to 1 or more AEs among the Week 52 safety subset was 3.3% and 0.8% in the combined 45 mg group and 90 mg group, respectively.

Infections

- Through Week 16, infection rates and types of infections in both the 45 mg and 90 mg groups were comparable to those observed in the placebo group. The proportion of subjects reporting infections was 16.6%, 19.6% and 21.0% in the 45 mg, 90 mg, and placebo groups, respectively. The most commonly reported infections were nasopharyngitis and URTI.
- Through Week 24, no disproportional increase was observed in infection rates, and the types of infections were similar to that observed through Week 16. Additionally, infection rates and types of infections were similar between the treatment groups.
- Through Week 52, no disproportional increase was observed in infection rates, and the types of infections were similar to that observed through Week 24. Additionally, infection rates and types of infections were similar between the treatment groups.
- Infections were not impacted by concomitant use of MTX and weight.
- Serious Infections:
  - Through Week 24, no serious infections were reported.
  - Through Week 52, there were 4 serious infections: pharyngolaryngeal abscess, salpingitis, and 2 events of acute cholecystitis.

Injection-site Reactions

- Rates of injections with injection site reactions were 0.6% for the 45 mg injections and 0.8% for the 90 mg injections compared with 0.4% in the placebo injections. All injection-site reactions were mild.
- No possible anaphylactic or possible serum sickness-like reactions to study agent were reported. There was no apparent association between development of antibodies to ustekinumab and the development of injection-site reactions.

Malignancies

- No malignancies were reported.

Cardiovascular Events

- No major adverse cardiovascular event (MACE) was reported through Week 16 in any of the treatment groups.
- One subject randomized to the 45 mg group who did not enter early escape had a stroke between Weeks 16 and 24.
- In the Week 52 safety subset, 1 additional MACE (myocardial infarction reported in a placebo crossover subject) was reported approximately 6 months after the subject initiated treatment with ustekinumab.

Laboratory Test Results

- Through Week 16, markedly abnormal changes in hematology and chemistry were generally low and similar between placebo-treated and ustekinumab-treated subjects. Through Week 24 and Week 52, markedly abnormal changes in hematology and chemistry generally remained low. Concomitant use of MTX did not appear to impact the hematology and chemistry values.

- At Week 24, shifts in fasting glucose and change from baseline in fasting glucose were similar among the placebo and ustekinumab groups. At Week 24, the analyses of shifts combined with the change from baseline indicated that ustekinumab did not impact fasting glucose.

- Ustekinumab-treated subjects had slightly higher increases in fasting total cholesterol (TC), low density lipoprotein, high-density lipoprotein (HDL), and triglyceride than placebo-treated subjects; however, the change in the TC/HDL ratio was similar across all 3 treatment groups.

Vital Signs and Physical Measurements

- Heart rate, blood pressure, weight and waist circumference were similar across all treatment groups at baseline and Week 24.

STUDY LIMITATIONS:

The short placebo-controlled period (through Week 16) and the early escape for subjects in the 45 mg group to the 90 mg group might have affected the ability to assess the safety and efficacy between the ustekinumab groups and the placebo group as well as between the 45 mg and 90 mg group beyond Week 16.

CONCLUSIONS:

- Ustekinumab 45 mg or 90 mg administered at Week 0 and 4, followed by a q12w dose regimen demonstrated consistent efficacy across various endpoints evaluating joint signs and symptoms, soft tissue disease, skin disease, and health-related quality of life in subjects with active PsA.

- Dose proportionality in serum ustekinumab concentration was observed when comparing mean serum ustekinumab concentrations between the 45 mg and 90 mg groups.

- Greater efficacy was observed in the 90 mg dose group compared with the 45 mg dose group across multiple endpoints, and most notably in the primary endpoint of ACR 20 responses, and the secondary endpoints of ACR 50, ACR 70, PASI 75, enthesitis scores, and the combined ACR 20 and PASI 75 responses.

- Efficacy was demonstrated in both subjects receiving MTX and subject not receiving MTX.

- Ustekinumab was generally well tolerated in the PsA population at both doses tested, without any clinically meaningful differences in safety between the 45 mg and 90 mg dose groups.

- The safety profiles are similar for subjects receiving MTX and not receiving MTX.

- The overall safety profile was consistent with that reported for ustekinumab-treated subjects with psoriasis.

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