SYNOPSIS

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

Protocol No.: CNTO1275PSA3002

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 Including Those Previously Treated With Biologic Anti-TNFα Agent(s)

Study Name: PSUMMIT II

EudraCT Number: 2009-012265-60

NCT No.: NCT01077362

Clinical Registry No.: CR016483

Principal Investigator: Christopher T. Richlin, MD

Study Center(s): 71 sites

Publication (Reference): None

Study Period: Through Week 24

Phase of Development: 3

Objectives: The primary objectives of this study were to evaluate the efficacy of ustekinumab in subjects with active psoriatic arthritis (PsA), including those previously treated with biologic anti-tumor necrosis factor alpha (anti-TNFα) agent(s), 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 were 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 including those previously treated with biologic anti-TNFα agent(s). Approximately 300 subjects were planned to receive treatment with subcutaneous (SC) ustekinumab 45 mg, 90 mg, or placebo by a 1:1:1 randomization at Weeks 0 and 4 followed by every 12 weeks (q12w) dosing, with the last dose at Week 40. Subjects randomized to placebo were to be crossed over to receive ustekinumab 45 mg at Weeks 24 and 28 followed by q12w dosing, with the last dose at Week 40. The expected duration of exposure to ustekinumab for enrolled subjects is 52 weeks. Subjects are to be followed for efficacy through Week 52 and for safety through Week 60.

Number of Subjects (planned and analyzed): Approximately 300 subjects were planned to receive treatment with ustekinumab 45 mg, ustekinumab 90 mg, or placebo (100 subjects per treatment group). A total of 312 subjects were randomly assigned: 104 to the placebo group, 103 to the ustekinumab 45 mg group, and 105 to the ustekinumab 90 mg group.

Diagnosis and Main Criteria for Inclusion: Men and women aged 18 to 99 years of age with a diagnosis of PsA for at least 6 months before the first study agent administration and had active PsA despite current or previous disease-modifying antirheumatic drug (DMARD) and/or nonsteroidal anti-inflammatory drug (NSAID) therapy. Per protocol, at least 150 but not more than 180 subjects could have been previously treated with single or multiple biologic anti-TNFα agent(s). Subjects had to manifest 5 or more swollen and 5 or more tender joints at screening and at baseline. At screening, subjects had to have C-reactive protein (CRP) ≥0.3 mg/dL, and have at least 1 of the PsA subtypes and active plaque psoriasis or a documented history of plaque psoriasis. Subjects previously treated with anti-TNFα agent(s) must have received at least 8 weeks of therapy with etanercept, adalimumab, golimumab or certolizumab pegol or at least 14 weeks of therapy with infliximab; or documented intolerance of anti-TNFα therapy for shorter periods of exposure.

Test Product, Dose and Mode of Administration, Batch No.: Ustekinumab was supplied in a prefilled 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.

Reference Therapy, Dose and Mode of Administration, Batch No.: Placebo was also supplied in a 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 volumes (ie, 1 mL nominal volume or 0.5 mL nominal volume). Each 1 mL of placebo for ustekinumab solution contained L-histidine, L-histidine monohydrochloride monohydrate, sucrose, and polysorbate 80 at pH 6.0. No preservatives were present.

Duration of Treatment: A total of 312 subjects were randomized to 1 of the 3 groups and received treatment with ustekinumab 45 mg, 90 mg, or placebo SC at Weeks 0 and 4 followed by q12w dosing, with the last dose at Week 40. Subjects randomized to placebo were eligible for crossover to receive ustekinumab 45 mg at Weeks 24 and 28 followed by q12w dosing, with the last dose at Week 40. Expected duration of exposure to study agent is 52 weeks. Subjects will be followed for efficacy through Week 52 and for safety through Week 60. The database lock (DBL) occurred at Week 24. An additional DBL will occur at Week 60. The end of the study will occur after the last subject completes the Week 60 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, subject weight at baseline (≤100 kg vs >100 kg), and by prior anti-TNFα exposure (ie, previously experienced vs naive to biologic anti-TNFα agents). The relationship between serum ustekinumab concentrations and selected efficacy endpoints were also assessed. The results from the population PK analysis are not included in this report.

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 between antibodies to ustekinumab and serum ustekinumab concentrations and selected efficacy and safety measures were also assessed.

Efficacy: 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 Psoriatic Arthritis Response Criteria (PsARC), Bath Ankylosing

Spondylitis Disease Activity Index (BASDAI), and Functional Assessment of Chronic Illness Therapy−Fatigue (FACIT-F). Psoriasis evaluations included the Psoriasis Area and Severity Index (PASI) and the Dermatology Life Quality Index (DLQI). The potential pharmacoeconomic benefit of ustekinumab treatment was also assessed. Radiographic imaging evaluations of the hands and feet will be addressed in a subsequent DBL.

Safety: Safety evaluations for all subjects were monitored through Week 24 and included measurement of vital signs (heart rate and blood pressure), physical evaluations (waist circumference and weight), and assessment of adverse events (AEs), and injection-site reactions that may have occurred at or between each evaluation visit. 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. Multiplicity 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 312 subjects randomly assigned to treatment at Week 0, 104 were assigned to the placebo group, 103 to the ustekinumab 45 mg group, and 105 to the ustekinumab 90 mg group. All randomized subjects received their assigned treatment at Week 0, with the exception of 1 subject in the ustekinumab 90 mg group who withdrew consent at the baseline visit and did not receive any study agent.
  - Through Week 24, a total of 41 (13.1%) subjects discontinued across the randomized treatment groups, with a higher rate of discontinuation in the placebo group (23.1%) than in the ustekinumab 45 mg (5.8%) or 90 mg (10.5%) groups. This difference was primarily driven by the higher proportion of subjects in the placebo group who discontinued for efficacy-related reasons (ie, lack of efficacy or AEs of worsening of PsA and/or psoriasis). In all treatment groups, the majority of discontinuations occurred before Week 12.
- Subject demographic characteristics at baseline were generally comparable across treatment groups. The majority of subjects were white (98.4%) and female (52.6%); the median age was 49 years, median weight was 88.3 kg, and median body mass index (BMI) was 30.3 kg/m^2.
- Baseline clinical characteristics of PsA from the ACR core set of outcome measurements were indicative of a population of subjects with moderately to severely active PsA and were generally comparable across the treatment groups. The median numbers of swollen and tender joints were 11.0 and 22.0, respectively; median VAS of patient's assessment of pain was 6.80; median VAS of patient's global assessment of disease activity was 6.20; median VAS of physician's global assessment of disease activity was 7.10; median HAQ-DI score was 1.25; and median CRP level was 9.32 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 health-

related quality of life (HRQoL): median percentage of BSA psoriasis skin involvement, 12%; median PASI score, 8.30; and median DLQI score, 11.00.

- Of the 312 randomized subjects, 180 (57.7%) had prior anti-TNFα exposure and 132 (42.3%) were anti-TNFα naive.
- At baseline, 157 (50.3%) subjects were receiving MTX and 155 (49.7%) subjects were not receiving MTX.
- Through Week 24, subjects who were randomly assigned to ustekinumab received a median dose of 180 mg. Subjects randomized to placebo who entered early escape received approximately 2 ustekinumab injections, while subjects randomized to ustekinumab received an average of 3 ustekinumab injections.

CLINICAL PHARMACOLOGY

Pharmacokinetics:

- 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 below the lowest quantifiable concentration of the assay (<0.16880 µg/mL) was observed in the 45 mg group compared with the 90 mg group.
- No consistent impact of MTX use on serum ustekinumab concentrations was observed between subjects who were and were not receiving MTX at baseline.
- Subjects of higher weight (>100 kg) had generally lower mean serum ustekinumab concentrations compared with subjects of lower weight (≤100 kg). Notably, mean preinjection serum ustekinumab concentrations at Week 16 were generally comparable between subjects >100 kg in the 90 mg group and subjects ≤100 kg in the combined 45 mg group.
- Mean serum ustekinumab concentrations in subjects who were previously treated with biologic anti-TNFα agents appeared to be generally lower than those in subjects who were naive to biologic anti-TNFα agents.

Immunogenicity:

- Through Week 24, the combined incidence of antibodies to ustekinumab was 6.1% (n=14) across all treatment groups.
- The incidence of antibodies to ustekinumab was generally comparable between the combined ustekinumab 45 mg group (6.0%; n=6) and the 90 mg group (7.1%; n=7).
- The incidence of antibodies to ustekinumab was lower in subjects who were receiving MTX at baseline (4.5%, n=5) compared with subjects who were not receiving MTX at baseline (7.6%, n=9).
- The incidence of antibodies to ustekinumab was higher in subjects who were previously treated with biologic anti-TNFα agents (8.5%, n=11) compared with subjects who were naive to biologic anti-TNFα agents (3.1%, n=3), although fewer subjects with prior anti TNFα exposure were taking MTX at baseline.
- Subjects who were positive for antibodies to ustekinumab had lower mean serum ustekinumab concentrations than subjects who were negative for antibodies to ustekinumab.

EFFICACY

Primary Endpoint:

- A significantly greater proportion of subjects in the combined ustekinumab and ustekinumab 45 mg and 90 mg groups (43.8%, 43.7%, and 43.8%, respectively) achieved an ACR 20 response at Week 24 compared with subjects in the placebo group (20.2%; all $p<0.001$).

Major Secondary Endpoints:

- There was significantly greater improvement in HAQ-DI scores at Week 24 in subjects in the combined ustekinumab and ustekinumab 45 mg and 90 mg groups (median change from baseline of −0.25, −0.13, and −0.25, respectively) compared with subjects in the placebo group (median of 0.00; all $p\leq0.002$).
- A significantly larger proportion of subjects with ≥3% BSA involvement of psoriasis at baseline in the combined ustekinumab and ustekinumab 45 mg and 90 mg groups demonstrated PASI 75 response at Week 24 (53.4%, 51.3%, and 55.6%, respectively) compared with subjects in the placebo group (5%; all $p<0.001$).
- A significantly greater proportion of subjects in the combined ustekinumab and ustekinumab 45 mg and 90 mg groups achieved an ACR 50 response (20.2% [p=0.002], 17.5% [p=0.018], and 22.9% [p<0.001], respectively) at Week 24 compared with subjects in the placebo group (6.7%).
- Numerically but not statistically significantly higher proportions of subjects achieved an ACR 70 response in the combined ustekinumab and ustekinumab 45 mg and 90 mg groups (7.7%, 6.8%, and 8.6%, respectively) at Week 24 compared with subjects in the placebo group (2.9%).

Other Efficacy Analyses:

- ACR 20, ACR 50, and ACR 70 responses in both ustekinumab 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.
- Modified PsARC and DAS28 responses 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 Week 24.
- For subjects with dactylitis at baseline, numerically but not significantly greater percentage improvements in dactylitis score were observed at Week 24 in the combined ustekinumab group and the ustekinumab 90 mg group compared with the placebo group. The percentage improvement in dactylitis score was similar between the 45 mg group and the placebo group.
- For subjects with enthesitis at baseline, significantly greater percentage improvements in enthesitis score were observed at Week 24 for the combined ustekinumab group and the ustekinumab 90 mg group compared with the placebo group ($p<0.005$ for all comparisons). Numerically but not significantly higher percentage improvement in enthesitis score was observed in the 45 mg group compared with the placebo group.
- For subjects with spondylitis with peripheral joint involvement as their primary arthritic presentation of PsA, improvement in BASDAI scores was noted at Week 24 in subjects treated with ustekinumab compared with placebo.
- ACR 20 response rates and HAQ-DI improvements were generally comparable in subjects treated with ustekinumab who were receiving MTX versus those not receiving MTX, although the treatment effect (ie, the difference in response rates between the combined ustekinumab group and placebo) was modestly greater in subjects who were not receiving MTX at baseline because of the higher

response rate or improvement in the placebo group in subjects who were receiving MTX. Significance was not reached for ACR 20 for the 90 mg group or for the change in HAQ-DI score at Week 24 for either dose group compared with placebo.

- A significantly higher proportion of subjects achieved both ACR 20 and PASI 75 at Week 24 in the combined ustekinumab group and the ustekinumab 45 mg and 90 mg groups (34.2%, 30.0%, and 38.3%) compared with the placebo group (2.5%; all $p<0.001$).
- At Week 24, a significantly higher proportion of subjects had a DLQI score of 0 or 1 in the combined ustekinumab group and the ustekinumab 45 mg and 90 mg groups (39.0%, 35.6%, and 42.6%, respectively) compared with the placebo group (11.1%; all $p<0.001$).
- SF-36 physical component summary (PCS) score improvement was significantly greater in both ustekinumab groups as compared with the placebo group at both Week 16 ($p=0.023$ for 45 mg, and $p=0.040$ for 90 mg) and Week 24 ($p=0.005$ for 45 mg and $p=0.001$ for 90 mg).
- SF-36 mental component summary (MCS) score improvement was significantly greater in both ustekinumab 45 mg group ($p=0.037$) and 90 mg group ($p=0.003$) as compared with the placebo group at Week 16. Improvement in SF 36 MCS score was numerically greater for the both 45 mg ($p=0.153$) and 90 mg group ($p=0.086$) as compared with the placebo group at Week 24.
- A statistically significant change from baseline in FACIT-F scores was observed at Week 24 in the combined ustekinumab group and the ustekinumab 45 mg and 90 mg groups compared with the placebo group (all $p<0.007$).

Health Economics Assessments:

- At both Week 16 and Week 24, the impact of PsA on work productivity was significantly greater in the combined ustekinumab group and the ustekinumab 45 mg and 90 mg groups compared with the placebo group ($p<0.001$ for all except the 45 mg group at Week 16 [$p<0.002$]).
- Overall, there were no consistently significant differences in the ustekinumab treatment groups compared with the placebo group in measures of employability or time lost from work due to PsA at Week 16 and Week 24.

Impact of Prior Anti-TNFα Exposure on Efficacy:

- Numerically higher responses for ustekinumab compared with placebo for ACR 20, ACR 50, ACR 70, and PASI 75 responses at Week 24 and greater improvement in HAQ-DI scores at Week 24 were seen in subjects with and without prior anti-TNFα exposure, although the treatment effect was higher in subjects without prior anti-TNFα exposure.
  - At Week 24, subjects with prior anti-TNFα exposure who received ustekinumab demonstrated significantly higher rates of ACR 20 response and PASI 75 response versus placebo. Significantly greater improvement in HAQ-DI at Week 24 was also seen in the ustekinumab groups compared with placebo for subjects with prior anti-TNFα exposure.

Other Subgroup Analyses:

- Numerically higher ACR 20 response was observed at Week 24 in almost all subgroups examined for both the 45 mg and 90 mg groups, although some variability in treatment effect was observed in subgroups due to smaller sample size.
  - Significantly higher ACR 20 response was observed at Week 24for both the 45 mg and 90 mg groups compared with the placebo group among subjects with prior DMARD use.

Efficacy and Pharmacokinetics:

- Subjects with higher trough serum ustekinumab concentrations tended to have higher clinical efficacy. Clinical efficacy (ACR 20, ACR 50, and PASI 75 responses) at Week 24 appeared to be generally associated with trough serum ustekinumab levels ≥0.16880 μg/mL.

Efficacy and Antibodies to Ustekinumab:

- Although the number of subjects who were positive for antibodies to ustekinumab was small, subjects who were positive for antibodies to ustekinumab tended to have lower clinical efficacy compared with subjects who were negative for antibodies to ustekinumab; however, antibody positivity did not preclude a clinical response.

SAFETY

Adverse Events:

- Through Week 16, AE rates in each of the ustekinumab groups were slightly higher than those observed in the placebo group although there was no dose response. The proportions of subjects reporting AEs were 54.8%, 63.1%, and 60.6% in the placebo and ustekinumab 45 mg and 90 mg groups, respectively.
- The SOC with the most commonly reported AEs through Week 16 was Infections and infestations (23.1%, 28.2%, and 26.0% in the placebo and ustekinumab 45 mg and 90 mg groups, respectively), predominantly nasopharyngitis and upper respiratory tract infection.
- 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. AE rates and AE profiles were also similar between the treatment groups.
- Among subjects with prior anti-TNFα exposure, the proportions of subjects reporting AEs were comparable across treatment groups through Week 16. No disproportional increase was observed through Week 24 in AE rates among these subjects and the AE profile was similar with that observed through Week 16.
- AEs were not impacted by age, sex, baseline weight, or concomitant use of MTX, although a higher proportion of male subjects in the ustekinumab-treated groups reported AEs compared with the placebo group (primarily due to slightly higher rates of nasopharyngitis and arthralgia in these subjects).

Serious Adverse Events:

- No deaths were reported through Week 24.
- Through Week 16, serious adverse event (SAE) rates in the ustekinumab 45 mg and 90 mg groups were similar (0.0% and 1.0%) and were numerically lower than in the placebo group (4.8%). SAEs were single events in all the treatment groups without any particular pattern.
- Through Week 24, the proportion of subjects who had 1 or more SAEs remained low: 1.3% in the all ustekinumab group and 4.8% in the placebo group.
- Among subjects with prior anti-TNFα exposure, the proportion of subjects who had an SAE was low through Week 16 (3.2%, 0.0%, and 1.7% in the placebo and ustekinumab 45 mg and 90 mg groups) and remained low through Week 24 (3.2% in the placebo group and 0.8% in the all ustekinumab group).
- SAEs were not impacted by baseline weight or concomitant use of MTX.

Adverse Events Leading to Study Agent Discontinuation:

- Through Week 16, the proportions of subjects who discontinued study agent due to 1 or more AEs were higher in the placebo group compared with the ustekinumab groups: 7.7% in the placebo group and 1.9% each in the ustekinumab 45 mg and 90 mg groups.
- Through Week 24, the proportion of subjects who discontinued study agent due to 1 or more AEs remained low: 1.9% in the combined ustekinumab 45 mg group and 2.9% in the 90 mg group, and 2.1% in the all ustekinumab group and 10.6% in the placebo group.
- Among subjects with prior anti-TNFα exposure, the proportion of subjects who discontinued study agent due to an AE through Week 16 was higher in the placebo group (11.3%) than in the ustekinumab groups (0.0% and 1.7% in the 45 mg and 90 mg groups). Higher rates of discontinuation continued to be seen through Week 24 in the placebo group compared with the all ustekinumab group (16.1% vs 1.5%), mostly due to worsening arthropathy or psoriasis.

Infections:

- Through Week 16, infection rates and types of infections were generally comparable across the treatment groups: 24.0%, 29.1%, and 25.0% in the placebo and ustekinumab 45 mg and 90 mg groups, respectively. The most commonly reported infections were nasopharyngitis, upper respiratory tract infection, and sinusitis.
- Through Week 24, no disproportional increase was observed in infection rates, and the types of infections were similar to that observed through Week 16. Infection rates and types of infections were similar among the treatment groups.
- Among subjects with prior anti-TNFα exposure, infection rates through Week 16 were higher in the placebo group (32.3%) compared with the ustekinumab 45 mg and 90 mg groups (28.3% and 20.7%, respectively), but more comparable at Week 24 (33.6% and 37.1% in the all ustekinumab and placebo groups, respectively).
- Infections were not impacted by baseline weight or concomitant use of MTX.
- One serious infection was reported through Week 24 (interstitial lung disease in the placebo group).
- No opportunistic infections or cases of TB were reported.

Injection-site Reactions:

- Rates of injections with injection-site reactions through Week 24 were 0.6% for ustekinumab 45 mg injections and 1.6% for ustekinumab 90 mg injections, compared with 0.4% for placebo injections. All injection-site reactions were mild in intensity.
- No possible anaphylactic or possible serum sickness-like reactions to study agent were reported.
- None of the subjects who were positive for antibodies to ustekinumab had an injection-site reaction through Week 24. There was no apparent association between the development of antibodies to ustekinumab and the development of injection-site reactions.

Malignancies:

- One malignancy was reported through Week 24 (nonserious squamous cell carcinoma in the ustekinumab 90 mg group).

Cardiovascular Events:

- No investigator-reported major adverse cardiovascular events (MACE) were reported in any group through Week 24.

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, markedly abnormal changes in hematology and chemistry generally remained low. Concomitant use of MTX did not appear to affect 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.
- No clinically relevant shifts were noted for total cholesterol, HDL- or LDL-cholesterol between subjects in the ustekinumab and placebo 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 groups 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.
- Greater efficacy was observed in the ustekinumab 90 mg group for some endpoints compared with the 45 mg group.
- Efficacy was demonstrated in subjects who were and were not receiving MTX.
- Efficacy was demonstrated in subjects who had prior anti-TNFα exposure and in subjects who were anti-TNFα naive.
- 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.
  - Ustekinumab was well tolerated regardless of concomitant MTX use.
  - Ustekinumab was well tolerated regardless of prior anti-TNFα exposure.

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