1 SYNOPTIC CLINICAL STUDY REPORT TITLE PAGE

This study was terminated early due to low recruitment and the availability of other treatment options as agreed with the Paediatric Committee (PDCO). The sponsor (LEO Pharma A/S) received a full product specific waiver (including all subsets of the paediatric population). As the study terminated early, the sponsor decided not to test the planned objectives and endpoints described in the protocol.

Study Title:	A Phase 3, Randomised, Double-Blind, Multi-Centre Trial to Evaluate the Efficacy, Safety, and Tolerability of Brodalumab Treatment Compared to Placebo (Blinded) and Ustekinumab (Open-Label) in Adolescent Subjects (12–17 Years of Age) with Moderate-to-Severe Plaque Psoriasis
Short Study Title:	Efficacy and Safety of Brodalumab in Adolescents from 12 to 17 Years of Age with Moderate-to-Severe Plaque Psoriasis; EMBRACE 1
Study Number:	LP0160-1396
Paediatric Investigation Plan:	EMEA-001089-PIP02-13
Regulatory Agency Identifier Numbers:	World Health Organization (WHO) universal trial number (UTN): U1111-1282-4459 European Union Drug Regulating Authorities Clinical Trials (EudraCT) number: 2019-001868-30 National Clinical Trial (NCT) number: NCT04305327
Sponsor:	LEO Pharma A/S Industriparken 55 DK-2750 Ballerup Denmark Phone: +45 44 94 58 88
Sponsor's Responsible Medical Officer:	[redacted]
Contract Research Organization:	[redacted]

Study Phase:	Phase 3
Test Product:	Brodalumab (trade name Kyntheum in Europe)
Indication:	Moderate-to-severe plaque psoriasis
Study Initiation Date (First Subject Enrolled):	07 Dec 2022
Study Early Termination Date:	05 May 2023
Report Version and Date:	18 Oct 2023, Version 1.0

This study was conducted in compliance with Good Clinical Practice (GCP), including the archiving of essential documents.

2 SYNOPSIS

Name of Sponsor/Company:
LEO Pharma A/S
Industriparken 55
DK-2750 Ballerup
Denmark

Name of Finished Investigational Medicinal Product: Brodalumab (trade name Kyntheum in Europe)

Name of Active Ingredient: Brodalumab

Indication: Moderate-to-severe plaque psoriasis

Study Number: LP0160-1396

Regulatory Agency Identifier Numbers:
World Health Organisation (WHO) universal trial number (UTN): U1111-1282-4459
European Union Drug Regulating Authorities Clinical Trials (EudraCT) number: 2019-001868-30
National Clinical Trial (NCT) number: NCT04305327

Paediatric Investigation Plan: EMEA-001089-PIP02-13

Study Title: A Phase 3, Randomised, Double-Blind, Multi-Centre Trial to Evaluate the Efficacy, Safety, and Tolerability of Brodalumab Treatment Compared to Placebo (Blinded) and Ustekinumab (Open-Label) in Adolescent Subjects (12–17 Years of Age) with Moderate-to-Severe Plaque Psoriasis

Short Study Title: Efficacy and Safety of Brodalumab in Adolescents from 12 to 17 Years of Age with Moderate-to-Severe Plaque Psoriasis; EMBRACE 1

Study Phase: Phase 3

Number of Study Sites and Countries: The study enrolled subjects from 9 investigative sites in Belgium, Germany, Hungary, Italy, Poland, and Spain

Signatory Investigator: [redacted]

Publication (References): None

Study Period:

Date of first subject enrolled 07 Dec 2022

Date of last subject completed 05 May 2023

Background and Rationale for the Study: At the time of study initiation, this trial was part of the paediatric investigational plan (PIP) agreed with the Paediatric Committee (PDCO) to investigate whether brodalumab was efficacious and safe in treated adolescents from 12 to 17 years of age with moderate-to-severe plaque psoriasis. The study was designed to determine the efficacy and safety of brodalumab as compared to the placebo and comparator ustekinumab. The pharmacokinetics data from this trial would have been used to determine an appropriate dose of brodalumab to be used in a future trial with subjects from 6 to 11 years of age. Since it is recommended that children follow a vaccination schedule, the trial was also designed to assess immunisation responses against a combined tetanus, diphtheria, and acellular pertussis (Tdap) or a combined tetanus and diphtheria (Td) vaccine.

The trial design included a placebo arm to decrease the sample size and reduce the number of children included in the clinical study. In addition, rescue treatment was permitted if the severity of plaque psoriasis worsened, and all subjects were planned to switch to active treatment at Week 12.

Planned Objectives and Endpoints

Table 1 Objectives and Endpoints

Objectives	**Endpoints supporting the objectives**
Primary objective	
To determine the efficacy of subcutaneous administration of brodalumab compared with placebo in treating adolescents with moderate-to-severe plaque psoriasis	*Primary endpoint:* • Having at least 75% improvement in Psoriasis Area and Severity Index (PASI) score from baseline (PASI 75 response), assessed at Week 12. *Key secondary endpoints:* • Static Physician's Global Assessment (sPGA) score of 0 or 1, assessed at Week 12. • sPGA score of 0, assessed at Week 12. • PASI 90 response, assessed at Week 12.

Table 1 Objectives and Endpoints

Objectives	**Endpoints supporting the objectives**
	• PASI 100 response, assessed at Week 12. • Children's Dermatology Life Quality Index (CDLQI) total score of 0 or 1, assessed at Week 12. *Secondary endpoint:* • Family Dermatology Life Quality Index (FDLQI) total scoreof 0 or 1, assessed at Week 12. *Other endpoints:* • Change from baseline in Adolescent Pruritus Numeric Rating Scale (NRS; weekly average), assessed at Week 12. • Improvement of at least 4 units in Adolescent Pruritus NRS (weekly average), assessed at Week 12. • Change from baseline in itch-related sleep NRS (weekly average), assessed at Week 12.
Secondary objectives	
To evaluate the efficacy of brodalumab compared with ustekinumab in treating adolescents with moderate-to-severe plaque psoriasis.	*Other endpoints:* • PASI 75 response, assessed separately at Week 12 and Week 52. • PASI 90 response, assessed separately at Week 12 and Week 52. • PASI 100 response, assessed separately at Week 12 and Week 52. • sPGA score of 0 or 1, assessed separately at Week 12 and Week 52. • sPGA score of 0, assessed separately at Week 12 and Week 52.

Table 1 Objectives and Endpoints

Objectives	Endpoints supporting the objectives
	• CDLQI total score of 0 or 1, assessed separately at Week 12 and Week 52. • FDLQI total score of 0 or 1, assessed separately at Week 12 and Week 52. • Change from baseline in Adolescent Pruritus NRS (weekly average), assessed at Week 12 and Week 52. • Improvement of at least 4 units in Adolescent Pruritus NRS (weekly average), assessed separately at Week 12 and Week 52. • Change from baseline in itch-related Sleep NRS (weekly average), assessed at Week 12 and Week 52.
To evaluate the safety of brodalumab compared with placebo (until Week 12) and ustekinumab (throughout the trial) in adolescents with moderate-to-severe plaque psoriasis.	*Secondary endpoints:* • Occurrence of adverse events (AEs) up to Week 60. • Presence of anti-drug antibodies (ADA), assessed at Weeks 4, 16, and 52. • Serum concentration of interleukin-17 (IL-17) and blood levels of T-cell subsets ($CD4^+$ and $CD8^+$), assessed at Weeks 8, 12, and 52. *Other endpoints:* • Laboratory toxicity, assessed at Weeks 4, 16, and 52. • Vital signs, assessed at Weeks 4, 16, and 52. • Blood levels of T-helper cells (Th1, Th17, and Th22), assessed at Weeks 8, 12, and 52.

Table 1 Objectives and Endpoints

Objectives	Endpoints supporting the objectives
	• Concentration of blood biomarkers, assessed at Weeks 8, 12, and 52. • Columbia-Suicide Severity Rating Scale (C-SSRS) score up to Week 60. • Patient Health Questionnaire-9 modified for adolescents without question number 9 (PHQ-A) score up to Week 60.
To evaluate the pharmacokinetics of brodalumab in adolescents with moderate-to-severe plaque psoriasis.	*Secondary endpoint:* • Serum concentrations of brodalumab, assessed at Weeks 4, 8, 10, 12, 16, 22, and 52. *Other endpoint:* • Area under the serum concentration-time curve at Weeks 10-12, derived using all available concentrations in Weeks 0-52.
To evaluate the immunogenicity of a tetanus toxoid (TT)-containing vaccine in adolescents with moderate-to-severe plaque psoriasis who are treated with brodalumab or placebo.	*Secondary endpoint:* • Anti-tetanus toxoid antibodies (aTTA) ≥0.1 IU/mL, assessed at Week 12 (post-vaccination). *Other endpoints:* • Change from baseline in lymphocyte subsets ($CD4^+$, $CD8^+$, and $CD19^+$), assessed at Week 12 (post-vaccination). • Change from baseline in aTTA, assessed at Week 12 (post-vaccination). • Booster response to TT-containing vaccine, defined as: ○ 3-fold increase of aTTA, assessed at Week 12, if subject has an aTTA ≤1.0 IU/mL at Week 0.

Table 1 Objectives and Endpoints

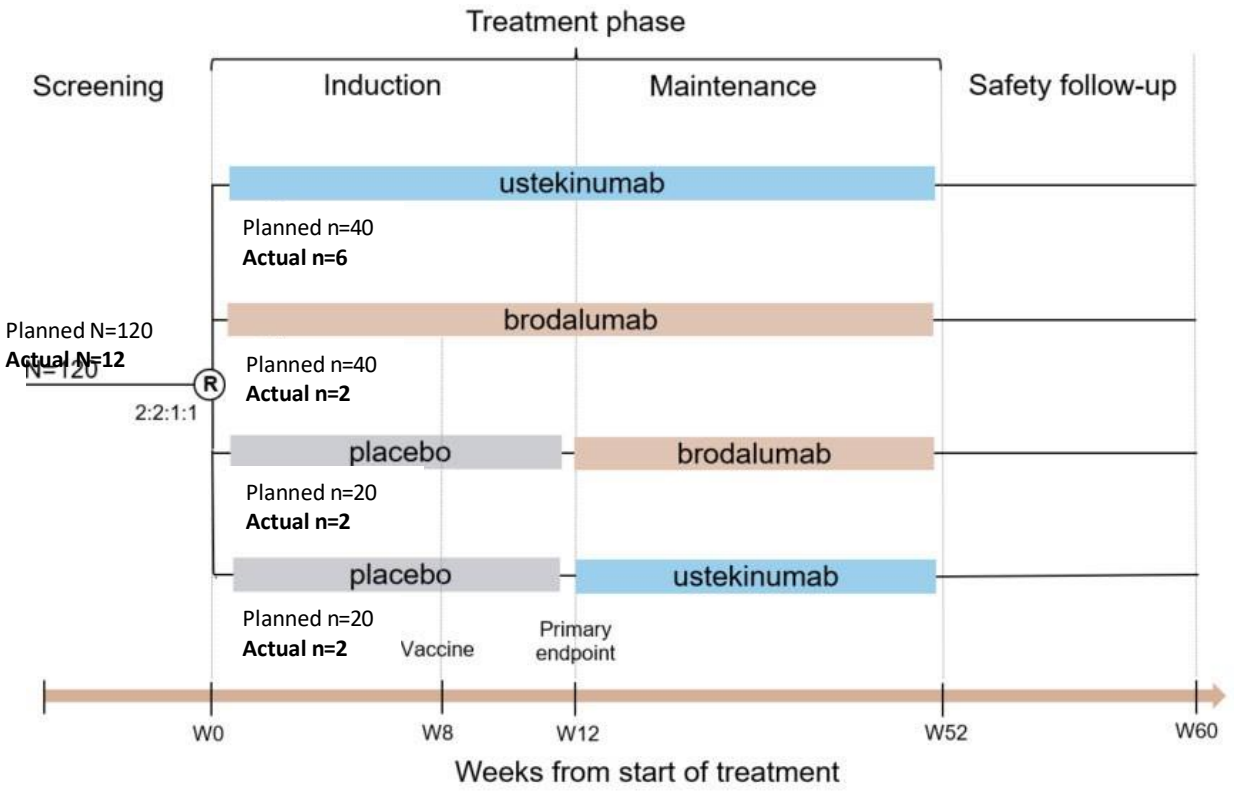
Objectives	Endpoints supporting the objectives
	○ ≥2.5 IU/mL increase of aTTA, assessed at Week 12, if subject has an aTTA >1.0 IU/mL at Week 0. • Change from baseline in aTTA, assessed at Week 8 (pre-vaccination).

Abbreviations: ADA, anti-drug antibodies; AEs, adverse events; aTTA, anti-tetanus toxoid antibodies; C-SSRS, Columbia-Suicide Severity Rating Scale; CDLQI, Children's Dermatology Life Quality Index; FDLQI, Family Dermatology Life Quality Index; IL-17, interleukin-17; NRS, numeric rating scale; PASI, Psoriasis Area Severity Index; PHQ-A, Patient Health Questionnaire-9 modified for adolescents without question number 9; sPGA, static Physician's Global Assessment; Th, T-helper; TT, tetanus toxoid.

Methodology: Initially, this study was designed as a clinical phase 3, multi-centre, randomised, placebo-controlled (double-blind until Week 12), and comparator-controlled (open-label ustekinumab) trial in which adolescents with moderate-to-severe plaque psoriasis were treated with brodalumab, ustekinumab, and placebo followed by brodalumab, or placebo followed by ustekinumab (Figure 1). This study was terminated early due to low recruitment and the availability of other treatment options as agreed with the PDCO. The sponsor received a full product specific waiver (including all subsets of the paediatric population). Refer to the protocol for the full planned study design.

It was planned for the study to consist of a screening period of 2 to 4 weeks (Week -4/-2 to Week 0), an induction period of 12 weeks (Week 0 to Week 12), a maintenance period of 40 weeks (Week 12 to Week 52), and a safety follow-up period of 8 weeks (Week 52 to Week 60). At the time of early termination, the longest a subject stayed in the study was until Week 20.

Figure 1 Planned Study Design Including Planned and Actual Number of Subjects



Abbreviations: N, total number of subjects in the trial; n, number of subjects in each treatment arm; R, randomisation; W, weeks.

Induction period from Week 0 to Week 12

Subjects randomised at Week 0 to brodalumab or any of the 2 placebo arms received injections at Weeks 0, 1, 2, 4, 6, 8, and 10. The dose was determined by the subject's body weight at Week 0 (Day 1):

- Subjects weighing 30 to <70 kg received 140 mg brodalumab (in a 1.0 mL syringe) or 1.0 mL brodalumab placebo.
- Subjects weighing ≥70 kg received 210 mg brodalumab (in a 1.5 mL syringe) or 1.5 mL brodalumab placebo.

Subjects randomised at Week 0 to ustekinumab received injections at Weeks 0 and 4. The ustekinumab dose was determined by the subject's body weight at each dosing visit:

- Subjects weighing 30 to <60 kg received 0.75 mg ustekinumab per kg body weight.
- Subjects weighing ≥60 and ≤100 kg received 45 mg ustekinumab.

- Subjects weighing >100 kg received 90 mg ustekinumab.

Vaccination

Subjects randomised at Week 0 to brodalumab or any of the 2 placebo arms received 1 dose of 0.5 mL of non-live T-cell-dependent tetanus toxoid (TT)- containing vaccine at Week 8. The vaccine response was evaluated at Week 12 and vaccine-related safety assessments were evaluated throughout the trial. Subjects randomised to ustekinumab only did not receive the vaccination.

Planned maintenance period from Week 12 to Week 52

Subjects randomised at Week 0 to either brodalumab or ustekinumab would have continued with the allocated treatment until Week 52:

- Subjects on brodalumab treatment were to receive injections every 2 weeks from Week 12 to Week 50 (applicable to 1 subject with last study visit before early termination at Week 13).

- Subjects on ustekinumab treatment were to receive injections at Weeks 16, 28, and 40 (applicable to 0 subjects as none had reached Week 16 at early termination).

Subjects randomised to placebo followed by ustekinumab were to switch to ustekinumab treatment during the maintenance period and were to receive ustekinumab injections at Weeks 12, 16, 28, and 40 (applicable to 1 subject with last study visit before early termination at Week 20). The ustekinumab dose was to be determined by the subject's body weight at each dosing visit:

- If the subject weighed between 30 to <60 kg, the subject was to receive 0.75 mg ustekinumab per kg body weight.

- If the subject weighed between ≥60 and ≤100 kg, the subject was to receive 45 mg ustekinumab.

- If the subject weighed between >100 kg, the subject was to receive 90 mg ustekinumab.

Rescue treatment

From Week 4 and after, rescue treatment with topical corticosteroids (class I to IV, according to the WHO classification of topical corticosteroids, as deemed appropriate by the investigator) was allowed in all 4 treatment arms in subjects with an increase of ≥25% in Psoriasis Area and Severity Index (PASI) score from baseline (Week 0).

Safety follow-up

When the study terminated early, subjects were asked to attend a safety follow-up visit 8 weeks after the last administration of investigational medicinal product (IMP).

Number of Subjects (Planned and Actual): It was anticipated that approximately 120 subjects at approximately 75 sites in Europe would be randomised in a 2:2:1:1 ratio. The actual number of subjects enrolled was 12 in Europe.

Table 2 Number of Subjects Enrolled by Country and Sex

Country	Number of Sites	Number of Subjects Enrolled	Sex
Belgium	2	2	1 Male, 1 Female
Germany	2	4	3 Male, 1 Female
Hungary	1	1	1 Female
Italy	1	1	1 Female
Poland	2	3	3 Female
Spain	1	1	1 Female

Diagnosis and Main Criteria for Inclusion and Exclusion

Main criteria for inclusion:

- Subject was diagnosed with chronic plaque psoriasis at least 6 months before randomisation.
- Subject had a diagnosis of moderate-to-severe plaque psoriasis as defined by PASI ≥12, static Physician's Global Assessment (sPGA) ≥3, and body surface area ≥10% at screening and at baseline.
- Subject, in whom topical therapy was not adequate, and who was a candidate for systemic therapy.
- Subject had no evidence of active or latent tuberculosis according to local standard of care for patients requiring initiation of a biologic treatment.

Main criteria for exclusion:

- Subject was diagnosed with erythrodermic psoriasis, pustular psoriasis, guttate psoriasis, medication-induced psoriasis, or other skin conditions (eg, eczema).
- Subject had been vaccinated with a TT-containing vaccine ≤18 months prior to first dose of IMP.

- Subject had been vaccinated with a TT-containing vaccine within 5 years prior to the first dose of IMP - applicable for countries in EU and UK.

- Subject had developed or experienced either Guillain-Barré syndrome, encephalopathy, Arthus-type hypersensitivity, or severe allergic reactions in connection with previous Tdap or Td vaccine.

- Subject with chronic or recurrent infections, or active infection, systemically treated within 4 weeks prior to first dose of IMP.

- Subject had a known history of Crohn's disease.

- Subject had any active malignancy or a history of any malignancy within 5 years.

- Subject had a history of suicidal behaviour and had suicidal ideation with some intent to act or specific plan and intent.

- Subject had a history of depressive disorder with severe episode(s) within the last 2 years.

- Subject had received anti-interleukin (IL)-12/23p40 for less than 12 months prior to the first dose of IMP or had previously no response to anti-IL-12/23p40 therapy.

- Subject had previously received anti-IL-17 therapy.

Investigational Medicinal Products, Dose, Mode of Administration, and Batch Numbers:

Table 3 Investigational Medicinal Products, Active Substance and Concentration, Dosage Form, Mode of Administration, and Batch Numbers

IMP	Description	Active substance and concentration	Dosage form	Mode of administration	Batch Numbers
Brodalumab	Recombinant fully human monoclonal immunoglobulin G (IgG)2 antibody that binds with high affinity to the human interleukin-17 receptor A (IL-17RA) and blocks the interaction with IL-17A, IL-17E, and IL-7F	Brodalumab, 140 mg/mL - BLINDED	Solution for injection	Subcutaneous	B4105, B3222
Placebo	Placebo solutions were similar to the active brodalumab solutions except they did not contain any active substance	N/A (matching placebo for 140 mg/mL) - BLINDED	Solution for injection	Subcutaneous	
Brodalumab	Recombinant fully human monoclonal IgG2 antibody that binds with high affinity to the human IL-17RA and blocks the interaction with IL-17A, IL-17E, and IL-7F	Brodalumab, 210 mg/1.5 mL - BLINDED	Solution for injection	Subcutaneous	B4264, B3223
Placebo	Placebo solutions were similar to the active brodalumab solutions except they did not contain any active substance	N/A (matching placebo for 210 mg/1.5 mL) - BLINDED	Solution for injection	Subcutaneous	

Table 3 Investigational Medicinal Products, Active Substance and Concentration, Dosage Form, Mode of Administration, and Batch Numbers

IMP	Description	Active substance and concentration	Dosage form	Mode of administration	Batch Numbers
Brodalumab	Recombinant fully human monoclonal IgG2 antibody that binds with high affinity to the human IL-17RA and blocks the interaction with IL-17A, IL-17E, and IL-7F	Brodalumab, 140 mg/mL - OPEN LABEL	Solution for injection	Subcutaneous	B4204, B4107, B3224
Brodalumab	Recombinant fully human monoclonal IgG2 antibody that binds with high affinity to the human IL-17RA and blocks the interaction with IL-17A, IL-17E, and IL-7F	Brodalumab, 210 mg/1.5 mL - OPEN LABEL	Solution for injection	Subcutaneous	B4108, B3225, B3978
Ustekinumab	Human IgG1κ monoclonal antibody against the p40 subunit of the IL-12 and IL-23 cytokines	Ustekinumab, 90 mg/mL	Solution for injection	Subcutaneous	B4096, B3227, B4036
Tdap; vaccine including pertussis	A combined TT, diphtheria toxoid, and acellular pertussis vaccine (adsorbed, reduced antigen content)	Each 0.5 mL dose was formulated to contain TT ≥20 IU, diphtheria toxoid ≥2 IU, pertussis toxoid 20 µg	Suspension for injection	Intramuscular	B4122, B3565

Table 3 Investigational Medicinal Products, Active Substance and Concentration, Dosage Form, Mode of Administration, and Batch Numbers

IMP	Description	Active substance and concentration	Dosage form	Mode of administration	Batch Numbers
Td; vaccine including pertussis	A combined TT and diphtheria toxoid vaccine (adsorbed, reduced antigen content)	Each 0.5 mL dose was formulated to contain TT ≥20 IU and diphtheria toxoid ≥2 IU	Suspension for injection	Intramuscular	B4121, B3566

Abbreviations: IgG, immunoglobulin G; IgG1κ, immunoglobulin G1 kappa; IL, interleukin; IL-17RA, interleukin-17 receptor A; IMP, investigational medicinal product; N/A, not applicable; Td, combined tetanus and diphtheria vaccine; Tdap, combined tetanus, diphtheria, and acellular pertussis vaccine; and TT, tetanus toxoid.

Planned and Actual Duration of Treatment: Planned duration was 52 weeks including a 12-week induction period and a 40-week maintenance period. At the time of early termination, the subject who had been in the study for the longest had reached the Week 20 visit.

Statistical Methods: At early termination, 12 subjects had been enrolled into the study. It had been planned to enrol approximately 120 subjects.

As the study terminated early, the sponsor decided not to test the objectives and related endpoints described in the protocol. Collected data was listed and summaries were provided for demographics and baseline characteristics, exposure to IMP, haematology and chemistry, vital signs, Columbia-Suicide Severity Rating Scale (C-SSRS), Patient Health Questionnaire-A (PHQ-A), and PASI. Adverse events (AEs) were tabulated by occurrence.

As no endpoints were tested, none of the estimand strategies described in protocol Section 14.3.5 were implemented. No inferential statistics are presented.

No tables, figures, or listings are provided for intercurrent events; it was assumed that 11/12 subjects discontinued due to early termination of the study (1 withdrawal by subject – the subject was randomised in error and discontinued per protocol), and that any rescue medications were shown in the concomitant medication listing. The statistical analysis plan (SAP) Section 12.0 contains details related to the scope of the analyses.

The following analyses had been planned, but were not analysed by the external vendors:

- Electrocardiogram
- Pharmacokinetics
- Anti-drug antibodies (ADA)

Subject Disposition: 22 subjects were screened and 12 subjects were randomised to the following 4 treatment arms: brodalumab (2 subjects), ustekinumab (6 subjects), placebo followed by brodalumab (2 subjects), and placebo followed by ustekinumab (2 subjects). All subjects received at least 1 dose of IMP and were included in both the safety analysis set (SAS) and full analysis set (FAS). Eleven of the 12 subjects enrolled discontinued the study due to early termination by the sponsor. One subject (ustekinumab arm) discontinued the study by subject withdrawal (subject was randomised in error and discontinued per protocol). This subject had important protocol deviations of missing the PHQ-A assessment at screening and receiving 1 dose of IMP (ustekinumab) in error.

Overall, there were 15 important protocol deviations for 6 subjects. The categories for the deviations were as follows: study assessments (10 deviations), selection criteria (3 deviations), study conduct/procedure (1 deviation), and other (1 deviation). In the opinion of the investigator, none of the protocol deviations had any impact on subject safety.

Demographic and Baseline Characteristics: The mean age of subjects was 14.7 years (range: 12 to 17 years); most subjects were female (8/12 subjects); most were White (10/12 subjects); and most were in the weight group <70 kg (9/12 subjects). Plaque psoriasis duration ranged from 3 years to 14 years; half of the subjects (6 subjects) had a duration of plaque psoriasis ≤5 years and the other half (6 subjects) had a duration of plaque psoriasis >5 years. Previous treatment for plaque psoriasis included topical treatment (7/12 subjects), systemic treatment or biologic (4/12 subjects), and photochemotherapeutical treatment (2/12 subjects). Four subjects had no previous treatment for plaque psoriasis. All subjects had no inflammatory disease diagnoses other than plaque psoriasis.

Efficacy Results: Due to early termination of the study, the only efficacy data available was a summary of PASI scores by treatment arm and time point from screening to Week 20 for the FAS (Table 4). The number of subjects included at each time point decreased from Week 0 to Week 20. Baseline mean PASI scores at Week 0 were as follows: brodalumab group (17.35 [std 0.919], 2 subjects), ustekinumab group (20.43 [std 9.645], 6 subjects), placebo-brodalumab group (18.25 [std 2.475], 2 subjects), and placebo-ustekinumab group (14.00 [std 1.131], 2 subjects). At Week 12, a total of 2 subjects were included in the analysis and mean PASI scores were as follows: brodalumab group (0.50, 1 subject) and placebo-ustekinumab (14.40, 1 subject). At early termination, mean PASI scores were lower than baseline for each treatment arm. Mean PASI scores at early termination were as follows: brodalumab group (0.10 [std 0.141],

2 subjects), ustekinumab group (11.90 [std 6.609], 5 subjects), placebo-brodalumab group (14.65 [std 2.192], 2 subjects), and placebo-ustekinumab group (11.05 [std 0.778], 2 subjects).

Table 4 Summary of PASI Score by Treatment Arm and Time Point (FAS)

Parameter Time Point	Brodalumab (N=2)	Ustekinumab (N=6)	Placebo-Brodalumab (N=2)	Placebo-Ustekinumab (N=2)
PASI Score				
Screening				
n	2	6	2	2
Mean (std)	15.20 (0.283)	20.28 (9.646)	17.35 (3.748)	13.45 (0.354)
Median	15.20	15.80	17.35	13.45
Q1, Q3	15.00, 15.40	13.50, 27.00	14.70, 20.00	13.20, 13.70
Min, Max	15.0, 15.4	12.8, 36.8	14.7, 20.0	13.2, 13.7
Week 0				
n	2	6	2	2
Mean (std)	17.35 (0.919)	20.43 (9.645)	18.25 (2.475)	14.00 (1.131)
Median	17.35	16.85	18.25	14.00
Q1, Q3	16.70, 18.00	14.00, 27.00	16.50, 20.00	13.20, 14.80
Min, Max	16.7, 18.0	11.1, 36.8	16.5, 20.0	13.2, 14.8
Week 12				
n	1	0	0	1
Mean (std)	0.50			14.40
Median	0.50			14.40
Q1, Q3	0.50, 0.50			14.40, 14.40
Min, Max	0.5, 0.5			14.4, 14.4
Week 20				
n	0	0	0	1
Mean (std)				9.60
Median				9.60
Q1, Q3				9.60, 9.60
Min, Max				9.6, 9.6
Early Termination				
n	2	5	2	2
Mean (std)	0.10 (0.141)*	11.90 (6.609)	14.65 (2.192)	11.05 (0.778)
Median	0.10	13.80	14.65	11.05
Q1, Q3	0.00, 0.20	5.40, 14.90	13.10, 16.20	10.50, 11.60
Min, Max	0.0, 0.2	5.0, 20.4	13.1, 16.2	10.5, 11.6

Abbreviations: BSA, body surface area; FAS, full analysis set; Max, maximum Min, minimum; N, total number of subjects; n, number of subjects; PASI, Psoriasis Area and Severity Index; Q1, lower quartile; Q3, upper quartile; sPGA, static Physician's Global Assessment; std, standard deviation.
*The 2 subjects in the brodalumab group (1001-01 and 1018-02) responded well to the treatment. The PASI scores at all visits were consistent with BSA and sPGA score.
Source: Table 14.2.1

Summary of Safety Results: Overall, over half the subjects (7/12 subjects) reported 12 treatment-emergent AEs (TEAEs; hereafter referred to as AEs). Five AEs were reported in the ustekinumab group (3/6 subjects); 4 AEs were reported in the brodalumab group (2/2 subjects); 3 AEs were reported in the placebo-ustekinumab group (2/2 subjects); and no AEs were reported in the placebo-brodalumab group. All AEs were mild or moderate in severity and lasted between 1 day and 14 days. None of the AEs led to IMP or study discontinuation. No severe AEs, serious adverse events, or deaths were reported in the study.

Half of the AEs were reported for the system organ class of infections and infestations (6 AEs, 6 subjects). The most common AE was nasopharyngitis (3 AEs, 3 subjects). The remaining AEs were single events.

No AEs considered probably related to IMP were reported. Two subjects reported 3 AEs considered possibly related to IMP and both subjects were in the ustekinumab group. One subject reported mild AEs of abdominal pain and dizziness; both AEs lasted for 2 days and were considered recovering/resolving at the time of reporting. The other subject reported a moderate AE of nasopharyngitis; the AE lasted for 14 days and was considered recovering/resolving at the time of reporting.

No clinically meaningful changes in C-SSRS, laboratory values, urinalysis, vital signs, or physical examinations were reported.

Overall Conclusions: Due to early termination of the study, the only efficacy data available was a summary of PASI scores by treatment arm and time point from screening to Week 20. The number of subjects included at each time point decreased from Week 0 to Week 20. Mean PASI scores decreased from baseline to early termination as follows: brodalumab group (from 17.35 [std 0.919] to 0.10 [std 0.141], 2 subjects); ustekinumab group (from 20.43 [std 9.645], 6 subjects to 11.90 [std 6.609], 5 subjects); placebo-brodalumab group (18.25 [std 2.475] to 14.65 [std 2.192], 2 subjects); and placebo-ustekinumab group (14.00 [std 1.131] to 11.05 [std 0.778], 2 subjects).

For this population, treatment with brodalumab for plaque psoriasis was well tolerated and no new safety concerns were identified as compared with the known safety profile of the drug.

2.1.1 Signatures of Lead Investigator and Sponsor's Responsible Medical Officer

CLINICAL STUDY REPORT APPROVAL

Sponsor: LEO Pharma A/S

Study Number: LP0160-1396

Study Title: A Phase 3, Randomised, Double-Blind, Multi-Centre Trial to Evaluate the Efficacy, Safety, and Tolerability of Brodalumab Treatment Compared to Placebo (Blinded) and Ustekinumab (Open-Label) in Adolescent Subjects (12–17 Years of Age) with Moderate-to-Severe Plaque Psoriasis

Approved by:

[redacted] **Date**

Lead Investigator

[redacted]

[redacted] **Date**

[redacted]

LEO Pharma A/S

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Date

Medical Lead

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Date

Biostatistics Lead, [redacted]

LEO Pharma A/S