Clinical trial results:
An international prospective, double-blind, placebo-controlled phase III RCT in which patients with moderate to severe psoriasis vulgaris are treated with s.c. methotrexate using an optimized treatment schedule

Summary

EudraCT number	2012-002716-10
Trial protocol	DE GB NL
Global end of trial date	07 April 2016

Results information

Result version number	v1 (current)
This version publication date	24 June 2022
First version publication date	24 June 2022

Trial information

Trial identification

Sponsor protocol code	165-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dermatologikum Hamburg
Sponsor organisation address	Stephansplatz 5, Hamburg, Germany, 20354
Public contact	Prof. Dr. med. Kristian Reich, Dermatologikum Hamburg, +49 4035107579,
Scientific contact	Prof. Dr. med. Kristian Reich, Dermatologikum Hamburg, +49 4035107579,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 May 2015
Global end of trial reached?	Yes
Global end of trial date	07 April 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to evaluate the efficacy of subcutaneous application of MTX in patients with moderate to severe psoriasis compared to placebo as determined by the number of patients reaching the primary endpoint PASI 75 after a 16 week treatment phase in the two study arms.

Protection of trial subjects:

Informed consent of subject was obtained in accordance with § 40 I 3 No. 3 Lit. b), II 1 AMG and § 40 I 3 No. 3 Lit. c). IIa 1&2 AMG by each investigator prior to inclusion of each patient to the study.
The nature, objective and importance of the study, the possible benefits and disadvantages or risks, and the study procedures were explained to each subject orally and in writing. The subjects were informed that their participation was voluntary, that they were free to withdraw from the study at any time, and that choosing not to participate would not impact on the subject’s care or future treatment.
Subjects were also informed that, by signing the ICF, they explicitly permitted authorised representatives of the sponsor and regulatory authorities to access study-related personal data to the extent permitted by the applicable law(s) and/or regulations without violating the confidentiality of the subject. Subjects were also informed that their consent to access their data could not be revoked.
Each subject was given sufficient time to read and discuss the ICF with the investigator prior to giving his/her written consent. Prior to study entry and any study-related examination, informed consent was documented by the subject’s dated signature. The subject was then given a copy of the information sheet and his/her signed ICF. The ICF was retained by the investigator as part of the study records. The terms and date of consent were also documented in the Case Report Form (CRF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 February 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Germany: 108
Worldwide total number of subjects	120
EEA total number of subjects	109

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	112
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 142 subjects were screened at 13 sites; 120 subjects were eligible and were randomized (13 sites: 11 in Germany, 0 in France, 1 in the Netherlands and 1 in the United Kingdom) to receive MTX/MTX or placebo/MTX. Study started on 22-FEB-2013 with the first subject randomization and was completed on 13-MAY-2015 with the last patient visit.

Pre-assignment

Screening details:

A total of 142 subjects were screened; 22 of them did not meet inclusion/exclusion criteria, requested consent withdrawal or were lost to follow-up. Main inclusion criteria: Adult patients; MTX naïve; moderate to severe plaques psoriasis for at least 6 months with or without psoriatic arthritis; use of highly effective contraception methods.

Period 1

Period 1 title	Double-blind treatment phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The trial was performed in a double-blind manner up to week 16. All study medication was supplied in identical packages. From week 16 commercial product was handed out to the patients with an additional label “for clinical study use only”. Patients of both arms remained blind to the identity of treatment from the time of randomisation until an interim database lock up to and including week 16 of their treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	MTX/MTX group

Arm description:

From week 0 to week 16:
The starting dose and regular maintenance dose was 17.5 mg MTX /0.35 mL NaCl (0.9%) solution (placebo) administered once weekly (every 7 days). However, if PASI 50 was not reached at week 8 the dosage was increased to 22.5 mg MTX per week or 0.45 mL placebo. The primary endpoint was assessed after 16 weeks of treatment.
If a patient showed a decrease of leukocytes, lymphocytes, erythrocytes or platelet counts of 30% at Day 5 after the first administration of MTX compared with baseline, the patient was to be withdrawn from treatment.

Arm type	Active comparator
Investigational medicinal product name	Methotrexate (MTX)
Investigational medicinal product code	
Other name	metex®, Metoject®
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Methotrexate (metex®/Metoject®) subcutaneously (s.c.) injected into the abdomen once weekly. The starting and regular maintenance dose was 17.5 mg per week. If PASI 50 was not reached at week 16, the dose was to be increased to 22.5 mg per week.

Arm title	Placebo/MTX group

Arm description:

From week 0 to week 16:
The starting dose and regular maintenance dose was 17.5 mg MTX /0.35 mL NaCl (0.9%) solution (placebo) administered once weekly (every 7 days). However, if PASI 50 was not reached at week 8 the dosage was increased to 22.5 mg MTX per week or 0.45 mL placebo. The primary endpoint was assessed after 16 weeks of treatment.

If a patient showed a decrease of leukocytes, lymphocytes, erythrocytes or platelet counts of 30% at Day 5 after the first administration of MTX compared with baseline, the patient was to be withdrawn from treatment.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching placebo (0.9% NaCl solution) s.c. injected into the abdomen once weekly (until week 16).

Number of subjects in period 1	MTX/MTX group	Placebo/MTX group
Started	91	29
Completed	77	22
Not completed	14	7
Consent withdrawn by subject	-	2
Adverse event, non-fatal	10	4
Lost to follow-up	2	-
discovery of patient ineligibility	1	-
Lack of efficacy	1	1

Period 2

Period 2 title	Open-label treatment phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The trial was performed in a double-blind manner up to week 16. All study medication was supplied in identical packages. From week 16 commercial product was handed out to the patients with an additional label "for clinical study use only". Patients of both arms remained blind to the identity of treatment from the time of randomization until an interim database lock up to and including week 16 of their treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	MTX/MTX group

Arm description:

From week 16 to week 52:
MTX/MTX: Patients stayed on their dose in the MTX/MTX. However, if at week 24 patients were receiving 17.5 mg MTX but PASI 75 was not yet reached the dosage was increased to 22.5 mg MTX per week. If patients had already been dosed with 22.5 mg MTX per week at week 24 and PASI 50 was not yet reached, patients were excluded from treatment.

Arm type	Active comparator

Investigational medicinal product name	Methotrexate (MTX)
Investigational medicinal product code	
Other name	metex®, Metoject®
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Commercial product was used. Patients stayed on their dose. If PASI 75 was not reached in patients receiving 17.5 mg at week 24, the dose was to be increased to 22.5 mg per week.

Arm title	Placebo/MTX group

Arm description:

From week 16 to week 52:
Placebo/MTX: From week 16 to week 52, patients received MTX according to the fixed dose schedule of the MTX/MTX (starting dose 17.5 mg with the possibility of up-titration after 8 weeks, i.e., at week 24). However, patients who reached PASI 75 under placebotreatment after 16 weeks were dosed with neither placebo nor MTX until relapse. After relapse, patients received a starting dose of 17.5 mg MTX as described above.

Arm type	Placebo
Investigational medicinal product name	Methotrexate (MTX)
Investigational medicinal product code	
Other name	metex®, Metoject®
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Commercial product was used. Patients stayed on their dose. If PASI 75 was not reached in patients receiving 17.5 mg at week 24, the dose was to be increased to 22.5 mg per week.

Number of subjects in period 2	MTX/MTX group	Placebo/MTX group
Started	77	22
Completed	56	15
Not completed	21	7
Consent withdrawn by subject	2	1
Adverse event, non-fatal	9	4
Lost to follow-up	1	2
discovery of patient ineligibility	2	-
Lack of efficacy	7	-

Baseline characteristics

Reporting groups

Reporting group title	MTX/MTX group

Reporting group description:

From week 0 to week 16:
The starting dose and regular maintenance dose was 17.5 mg MTX /0.35 mL NaCl (0.9%) solution (placebo) administered once weekly (every 7 days). However, if PASI 50 was not reached at week 8 the dosage was increased to 22.5 mg MTX per week or 0.45 mL placebo. The primary endpoint was assessed after 16 weeks of treatment.
If a patient showed a decrease of leukocytes, lymphocytes, erythrocytes or platelet counts of 30% at Day 5 after the first administration of MTX compared with baseline, the patient was to be withdrawn from treatment.

Reporting group title	Placebo/MTX group

Reporting group description:

From week 0 to week 16:
The starting dose and regular maintenance dose was 17.5 mg MTX /0.35 mL NaCl (0.9%) solution (placebo) administered once weekly (every 7 days). However, if PASI 50 was not reached at week 8 the dosage was increased to 22.5 mg MTX per week or 0.45 mL placebo. The primary endpoint was assessed after 16 weeks of treatment.
If a patient showed a decrease of leukocytes, lymphocytes, erythrocytes or platelet counts of 30% at Day 5 after the first administration of MTX compared with baseline, the patient was to be withdrawn from treatment.

Reporting group values	MTX/MTX group	Placebo/MTX group	Total
Number of subjects	91	29	120
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	84	28	112
85 years and over	7	1	8
Age continuous Units: years			
arithmetic mean	45.9	44.4	
standard deviation	± 12.9	± 10.8	-
Gender categorical Units: Subjects			
Female	26	4	30
Male	65	25	90
Race Units: Subjects			
White	89	28	117
Asian	2	0	2
Other	0	1	1
Employment status			

Units: Subjects			
Full-time employee	51	22	73
Part-time employee	13	0	13
Retired	10	2	12
Student	2	1	3
Other	15	4	19
Health insurance Units: Subjects			
Compulsory	75	27	102
Private	8	0	8
Other	8	2	10
Vascular disorders Units: Subjects			
Hypertension	27	7	34
Arteriosclerosis	1	0	1
Deep vein thrombosis	1	0	1
Varicose vein	1	0	1
None	61	22	83
Metabolism and nutrition disorders Units: Subjects			
Hypercholesterolaemia	2	4	6
Hyperlipidaemia	2	3	5
Obesity	2	1	3
Type 2 diabetes mellitus	2	1	3
Diabetes mellitus	2	0	2
Dyslipidaemia	1	0	1
Fructose intolerance	1	0	1
Glucose tolerance impaired	0	1	1
Gout	0	1	1
Hyperuricaemia	1	0	1
Iron deficiency	1	0	1
Lactose intolerance	1	0	1
None	76	18	94
Nervous system disorders Units: Subjects			
Migraine	9	1	10
Headache	5	1	6
Cerebrovascular accident	2	0	2
Cerebral ischaemia	0	1	1
Narcolepsy	1	0	1
Sciatica	1	0	1
Tension headache	0	1	1
VIIth nerve paralysis	1	0	1
None	72	25	97
Psychiatric disorders Units: Subjects			
Depression	9	3	12
Attention deficit/hyperactivity disorder	1	0	1
Panic disorder	0	1	1
Sleep disorder	1	0	1
None	80	25	105

Respiratory, thoracic and mediastinal disorders Units: Subjects			
Asthma	4	3	7
Chronic obstructive pulmonary disease	1	1	2
Emphysema	1	0	1
Pharyngeal erythema	1	0	1
Pulmonary sarcoidosis	0	1	1
Rhinitis allergic	1	0	1
Sleep apnoea syndrome	1	0	1
None	82	24	106
Cardiac disorders Units: Subjects			
Myocardial infarction	1	3	4
Coronary artery disease	1	1	2
Atrial fibrillation	1	0	1
Extrasystoles	0	1	1
Tachycardia	0	1	1
None	88	23	111
Prior medication: antipsoriatics Units: Subjects			
Antipsoriatics for topical use	37	9	46
Antipsoriatics for systemic use	27	8	35
None	27	12	39
Prior medication: corticosteroids Units: Subjects			
Corticosteroids	33	14	47
None	58	15	73
Concomitant medication: antiinflammatory and antirheumatic products Units: Subjects			
Antiinflammatory and antirheumatic products	37	8	45
None	54	21	75
Concomitant medication: analgesics Units: Subjects			
Other analgesics and antipyretics	24	11	35
Antimigraine preparations	3	0	3
Opioids	2	0	2
None	62	18	80
Concomitant medication: agents acting on the renin-angiotensin system Units: Subjects			
ACE Inhibitors, plain	9	8	17
Angiotensin II antagonists, plain	14	0	14
ACE inhibitors, combinations	1	1	2
None	67	20	87
Concomitant medication: antibacterials for systemic use Units: Subjects			
Macrolides, lincosamides and streptogramins	7	6	13

Beta-lactam antibacterials, penicillins	8	2	10
Other beta-lactam antibacterials	2	2	4
Quinolone antibacterials	3	1	4
Tetracyclines	4	0	4
None	67	18	85
Concomitant medication: drugs for acid related disorders Units: Subjects			
Drugs for peptic ulcer / gastro-oesophageal reflux	7	7	14
Antacids	1	1	2
None	83	21	104
Concomitant medication: lipid modifying agents Units: Subjects			
Lipid modifying agents, plain	4	6	10
Lipid modifying agents, combinations	1	0	1
None	86	23	109
Baseline PGA Units: Subjects			
Mild	6	0	6
Mild to moderate	11	7	18
Moderate	39	12	51
Moderate to severe	24	9	33
Severe	11	1	12
Psoriatic nail Units: Subjects			
Yes	62	22	84
No	29	6	35
Missing	0	1	1
Patients suffering from psoriatic arthritis (PsA) Units: Subjects			
Yes	11	2	13
No	80	27	107
PsA type (multiple choice) Units: Subjects			
Spinal involvement	1	0	1
Multiple small joints affected	7	1	8
Dactylitis	4	1	5
Enthesitis	0	0	0
Arthritis mutilans	0	0	0
None	79	27	106
PsA severity rating Units: Subjects			
Mild	4	1	5
Moderate	7	1	8
None	80	27	107
Height (cm) Units: centimetre			
arithmetic mean	175.0	178.4	

standard deviation	± 9.5	± 9.0	-
Weight (kg)			
Units: kilogram(s)			
arithmetic mean	92.0	96.7	
standard deviation	± 18.6	± 20.9	-
BMI (kg/m2)			
Units: kilogram(s)/square metre			
arithmetic mean	30.0	30.2	
standard deviation	± 6.1	± 6.1	-
Baseline median PASI			
Units: percent			
arithmetic mean	15.4	15.4	
standard deviation	± 5.9	± 5.3	-
Baseline BSA			
Units: square metre			
arithmetic mean	20.0	19.6	
standard deviation	± 11.8	± 12.5	-

Subject analysis sets

Subject analysis set title	Modified intent-to-treat (mITT) set (MTX/MTX)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The modified intent-to-treat (mITT) set comprises all patients who received the study treatment (MTX or placebo) at least once. Patients were analysed according to the treatment they were assigned to at randomisation. A non-responder imputation (NRI) was done for the primary efficacy parameter.

Subject analysis set title	Modified intent-to-treat (mITT) set (Placebo/MTX)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The modified intent-to-treat (mITT) set comprises all patients who received the study treatment (MTX or placebo) at least once. Patients were analysed according to the treatment they were assigned to at randomisation. A non-responder imputation (NRI) was done for the primary efficacy parameter.

Reporting group values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)	
Number of subjects	91	29	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	84	28	
85 years and over	7	1	
Age continuous			
Units: years			
arithmetic mean	45.9	44.4	
standard deviation	± 12.9	± 10.8	

Gender categorical Units: Subjects			
Female	26	4	
Male	65	25	
Race Units: Subjects			
White	89	28	
Asian	2	0	
Other	0	1	
Employment status Units: Subjects			
Full-time employee	51	22	
Part-time employee	13	0	
Retired	10	2	
Student	2	1	
Other	15	4	
Health insurance Units: Subjects			
Compulsory	75	27	
Private	8	0	
Other	8	2	
Vascular disorders Units: Subjects			
Hypertension	27	7	
Arteriosclerosis	1	0	
Deep vein thrombosis	1	0	
Varicose vein	1	0	
None	61	22	
Metabolism and nutrition disorders Units: Subjects			
Hypercholesterolaemia	2	4	
Hyperlipidaemia	2	3	
Obesity	2	1	
Type 2 diabetes mellitus	2	1	
Diabetes mellitus	2	0	
Dyslipidaemia	1	0	
Fructose intolerance	1	0	
Glucose tolerance impaired	0	1	
Gout	0	1	
Hyperuricaemia	1	0	
Iron deficiency	1	0	
Lactose intolerance	1	0	
None	76	18	
Nervous system disorders Units: Subjects			
Migraine	9	1	
Headache	5	1	
Cerebrovascular accident	2	0	
Cerebral ischaemia	0	1	
Narcolepsy	1	0	
Sciatica	1	0	

Tension headache	0	1	
VIIth nerve paralysis	1	0	
None	72	25	
Psychiatric disorders Units: Subjects			
Depression	9	3	
Attention deficit/hyperactivity disorder	1	0	
Panic disorder	0	1	
Sleep disorder	1	0	
None	80	25	
Respiratory, thoracic and mediastinal disorders Units: Subjects			
Asthma	4	3	
Chronic obstructive pulmonary disease	1	1	
Emphysema	1	0	
Pharyngeal erythema	1	0	
Pulmonary sarcoidosis	0	1	
Rhinitis allergic	1	0	
Sleep apnoea syndrome	1	0	
None	82	24	
Cardiac disorders Units: Subjects			
Myocardial infarction	1	3	
Coronary artery disease	1	1	
Atrial fibrillation	1	0	
Extrasystoles	0	1	
Tachycardia	0	1	
None	88	23	
Prior medication: antipsoriatics Units: Subjects			
Antipsoriatics for topical use	37	9	
Antipsoriatics for systemic use	27	8	
None	27	12	
Prior medication: corticosteroids Units: Subjects			
Corticosteroids	33	14	
None	58	15	
Concomitant medication: antiinflammatory and antirheumatic products Units: Subjects			
Antiinflammatory and antirheumatic products	37	8	
None	54	21	
Concomitant medication: analgesics Units: Subjects			
Other analgesics and antipyretics	24	11	
Antimigraine preparations	3	0	
Opioids	2	0	
None	62	18	

Concomitant medication: agents acting on the renin-angiotensin system Units: Subjects			
ACE Inhibitors, plain	9	8	
Angiotensin II antagonists, plain	14	0	
ACE inhibitors, combinations	1	1	
None	67	20	
Concomitant medication: antibacterials for systemic use Units: Subjects			
Macrolides, lincosamides and streptogramins	7	6	
Beta-lactam antibacterials, penicillins	8	2	
Other beta-lactam antibacterials	2	2	
Quinolone antibacterials	3	1	
Tetracyclines	4	0	
None	67	18	
Concomitant medication: drugs for acid related disorders Units: Subjects			
Drugs for peptic ulcer / gastro-oesophageal reflux	7	7	
Antacids	1	1	
None	83	21	
Concomitant medication: lipid modifying agents Units: Subjects			
Lipid modifying agents, plain	4	6	
Lipid modifying agents, combinations	1	0	
None	86	23	
Baseline PGA Units: Subjects			
Mild	6	0	
Mild to moderate	11	7	
Moderate	39	12	
Moderate to severe	24	9	
Severe	11	1	
Psoriatic nail Units: Subjects			
Yes	62	22	
No	29	6	
Missing	0	1	
Patients suffering from psoriatic arthritis (PsA) Units: Subjects			
Yes	11	2	
No	80	27	
PsA type (multiple choice) Units: Subjects			
Spinal involvement	1	0	
Multiple small joints affected	7	1	
Dactylitis	4	1	

Enthesitis	0	0	
Arthritis mutilans	0	0	
None	79	27	
PsA severity rating Units: Subjects			
Mild	4	1	
Moderate	7	1	
None	80	27	
Height (cm) Units: centimetre			
arithmetic mean	175.0	178.4	
standard deviation	± 9.5	± 9.0	
Weight (kg) Units: kilogram(s)			
arithmetic mean	92.0	96.7	
standard deviation	± 18.6	± 20.9	
BMI (kg/m2) Units: kilogram(s)/square metre			
arithmetic mean	30.0	30.2	
standard deviation	± 6.1	± 6.1	
Baseline median PASI Units: percent			
arithmetic mean	15.4	15.4	
standard deviation	± 5.9	± 5.3	
Baseline BSA Units: square metre			
arithmetic mean	20.0	19.6	
standard deviation	± 11.8	± 12.5	

End points

End points reporting groups

Reporting group title	MTX/MTX group

Reporting group description:

From week 0 to week 16:
The starting dose and regular maintenance dose was 17.5 mg MTX /0.35 mL NaCl (0.9%) solution (placebo) administered once weekly (every 7 days). However, if PASI 50 was not reached at week 8 the dosage was increased to 22.5 mg MTX per week or 0.45 mL placebo. The primary endpoint was assessed after 16 weeks of treatment.
If a patient showed a decrease of leukocytes, lymphocytes, erythrocytes or platelet counts of 30% at Day 5 after the first administration of MTX compared with baseline, the patient was to be withdrawn from treatment.

Reporting group title	Placebo/MTX group

Reporting group description:

From week 0 to week 16:
The starting dose and regular maintenance dose was 17.5 mg MTX /0.35 mL NaCl (0.9%) solution (placebo) administered once weekly (every 7 days). However, if PASI 50 was not reached at week 8 the dosage was increased to 22.5 mg MTX per week or 0.45 mL placebo. The primary endpoint was assessed after 16 weeks of treatment.
If a patient showed a decrease of leukocytes, lymphocytes, erythrocytes or platelet counts of 30% at Day 5 after the first administration of MTX compared with baseline, the patient was to be withdrawn from treatment.

Reporting group title	MTX/MTX group

Reporting group description:

From week 16 to week 52:
MTX/MTX: Patients stayed on their dose in the MTX/MTX. However, if at week 24 patients were receiving 17.5 mg MTX but PASI 75 was not yet reached the dosage was increased to 22.5 mg MTX per week. If patients had already been dosed with 22.5 mg MTX per week at week 24 and PASI 50 was not yet reached, patients were excluded from treatment.

Reporting group title	Placebo/MTX group

Reporting group description:

From week 16 to week 52:
Placebo/MTX: From week 16 to week 52, patients received MTX according to the fixed dose schedule of the MTX/MTX (starting dose 17.5 mg with the possibility of up-titration after 8 weeks, i.e., at week 24). However, patients who reached PASI 75 under placebotreatment after 16 weeks were dosed with neither placebo nor MTX until relapse. After relapse, patients received a starting dose of 17.5 mg MTX as described above.

Subject analysis set title	Modified intent-to-treat (mITT) set (MTX/MTX)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The modified intent-to-treat (mITT) set comprises all patients who received the study treatment (MTX or placebo) at least once. Patients were analysed according to the treatment they were assigned to at randomisation. A non-responder imputation (NRI) was done for the primary efficacy parameter.

Subject analysis set title	Modified intent-to-treat (mITT) set (Placebo/MTX)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The modified intent-to-treat (mITT) set comprises all patients who received the study treatment (MTX or placebo) at least once. Patients were analysed according to the treatment they were assigned to at randomisation. A non-responder imputation (NRI) was done for the primary efficacy parameter.

Primary: Primary endpoint: PASI 75 Response Rate at Week 16

End point title	Primary endpoint: PASI 75 Response Rate at Week 16

End point description:

The primary efficacy analysis evaluated the proportions (%) of patients achieving a PASI 75 response at week 16. The null hypothesis stated that the difference between the proportions equals zero. The proportions in each treatment arm were provided for the mITT together with 95% CIs according to Clopper and Pearson. The P value of the chi-square test (5% level of significance, two-sided) was

presented. The difference between proportions was provided for the mITT together with a 95% Wald CI.

End point type	Primary

End point timeframe:

Difference between treatments in PASI 75 (reduction of Psoriasis Area and Severity Index by ≥75% of baseline value) responder rate after week 16

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Number of subjects with success	37	3		

Statistical analyses

Statistical analysis title	chi-square test (5% significance level) (mITT set)
Comparison groups	Modified intent-to-treat (mITT) set (MTX/MTX) v Modified intent-to-treat (mITT) set (Placebo/MTX)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0026
Method	Chi-squared

Secondary: PASI 50 Responder Rate at Week 16

End point title	PASI 50 Responder Rate at Week 16

End point description:

End point type	Secondary

End point timeframe:

PASI 50 Responder Rate at Week 16.

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Number of subjects with success	60	9		

Statistical analyses

Statistical analysis title	chi-square test (5% significance level) (mITT set)
Comparison groups	Modified intent-to-treat (mITT) set (MTX/MTX) v Modified intent-to-treat (mITT) set (Placebo/MTX)
Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0009
Method	Chi-squared

Secondary: PASI 90 Response Rates at week 16

End point title	PASI 90 Response Rates at week 16
End point description:	
End point type	Secondary
End point timeframe:	
PASI 90 Response Rates at week 16.	

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Number of subjects with success	16	0		

Statistical analyses

Statistical analysis title	chi-square test (5% significance level) (mITT set)
Comparison groups	Modified intent-to-treat (mITT) set (MTX/MTX) v Modified intent-to-treat (mITT) set (Placebo/MTX)

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0153
Method	Chi-squared

Secondary: Physician’s Global Assessment (PGA) at week 16

End point title	Physician’s Global Assessment (PGA) at week 16

End point description:

End point type	Secondary

End point timeframe:

Physician’s Global Assessment (PGA) at week 16.

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: percent				
number (not applicable)				
PGA 0/1 Responder Rate	25	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Physician’s Global Assessment (PGA) at week 52

End point title	Physician’s Global Assessment (PGA) at week 52

End point description:

End point type	Secondary

End point timeframe:

Physician’s Global Assessment (PGA) at week 52

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: percent				
number (not applicable)				
PGA 0/1 Responder Rate	36	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Body Surface Area (BSA) at week 16

End point title	Body Surface Area (BSA) at week 16

End point description:

End point type	Secondary

End point timeframe:

Body Surface Area (BSA) at week 16

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	77	22		
Units: square metre				
arithmetic mean (standard deviation)	7.6 (± 7.4)	14.1 (± 9.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Body Surface Area (BSA) at week 52

End point title	Body Surface Area (BSA) at week 52

End point description:

End point type	Secondary

End point timeframe:

Affected Body Surface Area at week 52

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	56	15		
Units: square metre				
arithmetic mean (standard deviation)	3.3 (± 4.5)	3.2 (± 5.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Nail Psoriasis Severity Index (NAPSI) at week 16

End point title	Nail Psoriasis Severity Index (NAPSI) at week 16

End point description:

End point type	Secondary

End point timeframe:

Patients With at Least One Psoriatic Nail (NAPSI) at week 16

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Patients With at Least One Psoriatic Nail	55	16		
Patients Without Psoriatic Nail	22	6		
Missing	14	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Nail Psoriasis Severity Index (NAPSI) at week 52

End point title	Nail Psoriasis Severity Index (NAPSI) at week 52

End point description:

End point type	Secondary

End point timeframe:

Patients With at Least One Psoriatic Nail (NAPSI) at week 52.

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Patients With at Least One Psoriatic Nail	35	9		
Patients Without Psoriatic Nail	19	6		
Missing	37	14		

Statistical analyses

No statistical analyses for this end point

Secondary: NAPSI (Short Version) Total Score at week 16

End point title	NAPSI (Short Version) Total Score at week 16

End point description:

End point type	Secondary

End point timeframe:

NAPSI (Short Version) Total Score at week 16

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	77	22		
Units: severity index				
arithmetic mean (standard deviation)	3.7 (± 3.7)	5.0 (± 4.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: NAPSI (Short Version) Total Score at week 52

End point title	NAPSI (Short Version) Total Score at week 52

End point description:

End point type	Secondary

End point timeframe:
NAPSI (Short Version) Total Score at week 52

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	53	15		
Units: severity index				
arithmetic mean (standard deviation)	2.1 (± 3.0)	2.5 (± 3.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Psoriatic Arthritis Rating at week 16

End point title	Psoriatic Arthritis Rating at week 16

End point description:

End point type	Secondary

End point timeframe:
Psoriatic Arthritis Rating at week 16

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Slightly improved	1	1		
Improved	1	0		
Highly improved	6	0		
Missing	83	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Psoriatic Arthritis Rating at week 52

End point title	Psoriatic Arthritis Rating at week 52

End point description:

End point type	Secondary

End point timeframe:

Psoriatic Arthritis Rating at week 52

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Worsened	1	0		
Improved	2	0		
Highly improved	3	1		
Missing	85	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Dermatology Life Quality Index (DLQI) at week 16

End point title	Dermatology Life Quality Index (DLQI) at week 16

End point description:

End point type	Secondary

End point timeframe:

Dermatology Life Quality Index (DLQI) at week 16

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	77	21		
Units: score				
arithmetic mean (standard deviation)	3.9 (± 4.9)	8.7 (± 8.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dermatology Life Quality Index (DLQI) at week 52

End point title	Dermatology Life Quality Index (DLQI) at week 52

End point description:

End point type	Secondary

End point timeframe:

Dermatology Life Quality Index (DLQI) at week 52

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	56	15		
Units: score				
arithmetic mean (standard deviation)	1.8 (± 3.3)	3.1 (± 7.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D Pain/Discomfort at week 16

End point title	EQ-5D Pain/Discomfort at week 16

End point description:

End point type	Secondary

End point timeframe:

EQ-5D Pain/Discomfort at week 16

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
I have no pain or discomfort	46	8		
I have slight pain or discomfort	24	6		
I have moderate pain or discomfort	7	5		
I have severe pain or discomfort	0	3		
Missing	14	7		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D Pain/Discomfort at week 52

End point title	EQ-5D Pain/Discomfort at week 52

End point description:

End point type	Secondary

End point timeframe:

EQ-5D Pain/Discomfort at week 52

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
I have no pain or discomfort	37	11		
I have slight pain or discomfort	15	2		
I have moderate pain or discomfort	2	2		
I have severe pain or discomfort	1	0		
I have extreme pain or discomfort	1	0		
Missing	35	14		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D Anxiety/Depression at week 16

End point title	EQ-5D Anxiety/Depression at week 16

End point description:

End point type	Secondary

End point timeframe:

EQ-5D Anxiety/Depression at week 16

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				

I am not anxious or depressed	55	13		
I am slightly anxious or depressed	14	6		
I am moderately anxious or depressed	6	1		
I am severely anxious or depressed	2	2		
Missing	14	7		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D Anxiety/Depression at week 52

End point title	EQ-5D Anxiety/Depression at week 52

End point description:

End point type	Secondary

End point timeframe:

EQ-5D Anxiety/Depression at week 52

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
I am not anxious or depressed	46	12		
I am slightly anxious or depressed	10	2		
I am moderately anxious or depressed	0	1		
Missing	35	14		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ Visual Analogue Scale at week 16

End point title	EQ Visual Analogue Scale at week 16

End point description:

End point type	Secondary

End point timeframe:

EQ Visual Analogue Scale at week 16

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	77	22		
Units: score				
arithmetic mean (standard deviation)	78.5 (± 19.8)	65.7 (± 26.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ Visual Analogue Scale at week 52

End point title	EQ Visual Analogue Scale at week 52

End point description:

End point type	Secondary

End point timeframe:

EQ Visual Analogue Scale at week 52

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	56	15		
Units: score				
arithmetic mean (standard deviation)	83.3 (± 17.6)	82.6 (± 22.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: PASI 75 Responder Rate at week 52

End point title	PASI 75 Responder Rate at week 52

End point description:

End point type	Secondary

End point timeframe:

PASI 75 Responder Rate at week 52

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects	41	10		

Statistical analyses

No statistical analyses for this end point

Secondary: PASI 75 Response Rate at Week 32

End point title	PASI 75 Response Rate at Week 32

End point description:

End point type	Secondary

End point timeframe:

PASI 75 Response Rate at Week 32

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects	46	7		

Statistical analyses

No statistical analyses for this end point

Secondary: PASI 50 Responder Rate at Week 52

End point title	PASI 50 Responder Rate at Week 52

End point description:

End point type	Secondary

End point timeframe:

PASI 50 Responder Rate at Week 52

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects	53	10		

Statistical analyses

No statistical analyses for this end point

Secondary: PASI 90 Response Rates at week 52

End point title	PASI 90 Response Rates at week 52

End point description:

End point type	Secondary

End point timeframe:

PASI 90 Response Rates at week 52

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects	25	8		

Statistical analyses

No statistical analyses for this end point

Secondary: PSAT metex® Benefit at week 16

End point title	PSAT metex® Benefit at week 16

End point description:

The “Patient’s Satisfaction with metex® pre-filled syringe” (PSAT metex®) questionnaire (Benefit, Practicality, Satisfaction) was developed exclusively for this study to assess patient’s overall experience with s.c. self-injection. This questionnaire has not yet been validated.
PSAT metex® Benefit Items:
1. The treatment led to a rapid improvement in my skin symptoms.
2. I can easily handle my condition with this treatment.
3. With this treatment my skin no longer itches.
4. My skin is no longer painful with this treatment.
5. The time expenditure for the daily treatment is acceptable.
6. The treatment does not limit my general well-being.
7. As a result of the treatment, I am not worried that my skin condition will get worse.
8. I consider the improvement in the condition of my skin to be acceptable.
9. The treatment has met my expectations.
10. The side effects of the treatment were acceptable.

11. The positive aspects of the treatment outweigh the negative ones.

End point type	Secondary

End point timeframe:

PSAT metex® was assessed at V1, V5 and V0. The PSAT metex® score collected after 16 and 52 weeks of treatment (V5 and V10) was considered as secondary efficacy endpoint.

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Item 1: 2 – Agree	21	4		
Item 1: 3 – Strongly agree	50	5		
Item 2: 2 – Agree	19	7		
Item 2: 3 – Strongly agree	50	5		
Item 3: 2 – Agree	27	3		
Item 3: 3 – Strongly agree	38	3		
Item 4: 2 – Agree	16	4		
Item 4: 3 – Strongly agree	50	7		
Item 5: 2 – Agree	4	5		
Item 5: 3 – Strongly agree	71	12		
Item 6: 2 – Agree	12	4		
Item 6: 3 – Strongly agree	62	10		
Item 7: 2 – Agree	19	7		
Item 7: 3 – Strongly agree	55	6		
Item 8: 2 – Agree	27	4		
Item 8: 3 – Strongly agree	31	1		
Item 9: 2 – Agree	27	3		
Item 9: 3 – Strongly agree	40	3		
Item 10: 2 – Agree	18	4		
Item 10: 3 – Strongly agree	54	12		
Item 11: 2 – Agree	13	6		
Item 11: 3 – Strongly agree	61	7		

Statistical analyses

No statistical analyses for this end point

Secondary: PSAT metex® Benefit at week 52

End point title	PSAT metex® Benefit at week 52

End point description:

The “Patient’s Satisfaction with metex® pre-filled syringe” (PSAT metex®) questionnaire (Benefit, Practicality, Satisfaction) was developed exclusively for this study to assess patient’s overall experience with s.c. self-injection. This questionnaire has not yet been validated.
PSAT metex® Benefit Items:
1. The treatment led to a rapid improvement in my skin symptoms.
2. I can easily handle my condition with this treatment.

3. With this treatment my skin no longer itches.
4. My skin is no longer painful with this treatment.
5. The time expenditure for the daily treatment is acceptable.
6. The treatment does not limit my general well-being.
7. As a result of the treatment, I am not worried that my skin condition will get worse.
8. I consider the improvement in the condition of my skin to be acceptable.
9. The treatment has met my expectations.
10. The side effects of the treatment were acceptable.
11. The positive aspects of the treatment outweigh the negative ones.

End point type	Secondary

End point timeframe:

PSAT metex® was assessed at V1, V5 and V0. The PSAT metex® score collected after 16 and 52 weeks of treatment (V5 and V10) was considered as secondary efficacy endpoint.

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Item 1: 2 – Agree	10	4		
Item 1: 3 – Strongly agree	40	11		
Item 2: 2 – Agree	11	2		
Item 2: 3 – Strongly agree	40	12		
Item 3: 2 – Agree	24	3		
Item 3: 3 – Strongly agree	26	11		
Item 4: 2 – Agree	12	3		
Item 4: 3 – Strongly agree	37	11		
Item 5: 2 – Agree	3	1		
Item 5: 3 – Strongly agree	50	14		
Item 6: 2 – Agree	9	2		
Item 6: 3 – Strongly agree	43	11		
Item 7: 2 – Agree	12	3		
Item 7: 3 – Strongly agree	41	11		
Item 8: 2 – Agree	13	3		
Item 8: 3 – Strongly agree	35	10		
Item 9: 2 – Agree	9	4		
Item 9: 3 – Strongly agree	40	10		
Item 10: 2 – Agree	10	2		
Item 10: 3 – Strongly agree	39	11		
Item 11: 2 – Agree	7	2		
Item 11: 3 – Strongly agree	45	12		

Statistical analyses

No statistical analyses for this end point

Secondary: PSAT metex® Practicality at week 16

End point title	PSAT metex® Practicality at week 16

End point description:

The "Patient's Satisfaction with metex® pre-filled syringe" (PSAT metex®) questionnaire (Benefit, Practicality, Satisfaction) was developed exclusively for this study to assess patient's overall experience with s.c. self-injection. This questionnaire has not yet been validated.
PSAT metex® Practicality Items:
12. I do not feel afraid before being treated with needles or syringes.
13. I am certain that I perform the injection correctly.
14. I am not concerned about the pain when the needle pierces the skin.
15. I am concerned about redenning/swelling at the point of injection.
16. The general handling of the syringe is not difficult for me.
17. The injection can be performed easily when travelling.

End point type	Secondary

End point timeframe:

PSAT metex® was assessed at V1, V5 and V0. The PSAT metex® score collected after 16 and 52 weeks of treatment (V5 and V10) was considered as secondary efficacy endpoint.

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Item 12: 2 – Agree	13	2		
Item 12: 3 – Strongly agree	58	17		
Item 13: 2 – Agree	3	1		
Item 13: 3 – Strongly agree	72	21		
Item 14: 2 – Agree	9	2		
Item 14: 3 – Strongly agree	61	19		
Item 15: 0 – Strongly disagree	41	5		
Item 15: 1 – Disagree	12	5		
Item 16: 2 – Agree	7	1		
Item 16: 3 – Strongly agree	67	15		
Item 17: 2 – Agree	7	3		
Item 17: 3 – Strongly agree	56	15		

Statistical analyses

No statistical analyses for this end point

Secondary: PSAT metex® Practicality at week 52

End point title	PSAT metex® Practicality at week 52

End point description:

The "Patient's Satisfaction with metex® pre-filled syringe" (PSAT metex®) questionnaire (Benefit, Practicality, Satisfaction) was developed exclusively for this study to assess patient's overall experience with s.c. self-injection. This questionnaire has not yet been validated.
PSAT metex® Practicality Items:
12. I do not feel afraid before being treated with needles or syringes.
13. I am certain that I perform the injection correctly.
14. I am not concerned about the pain when the needle pierces the skin.
15. I am concerned about redenning/swelling at the point of injection.

16. The general handling of the syringe is not difficult for me.
17. The injection can be performed easily when travelling.

End point type	Secondary

End point timeframe:

PSAT metex® was assessed at V1, V5 and V0. The PSAT metex® score collected after 16 and 52 weeks of treatment (V5 and V10) was considered as secondary efficacy endpoint.

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Item 12: 2 – Agree	14	3		
Item 12: 3 – Strongly agree	35	9		
Item 13: 2 – Agree	4	2		
Item 13: 3 – Strongly agree	51	13		
Item 14: 2 – Agree	13	4		
Item 14: 3 – Strongly agree	39	10		
Item 15: 0 – Strongly disagree	28	4		
Item 15: 1 – Disagree	11	4		
Item 16: 2 – Agree	8	1		
Item 16: 3 – Strongly agree	45	13		
Item 17: 2 – Agree	9	1		
Item 17: 3 – Strongly agree	42	13		

Statistical analyses

No statistical analyses for this end point

Secondary: PSAT metex® Satisfaction at week 16

End point title	PSAT metex® Satisfaction at week 16

End point description:

The “Patient’s Satisfaction with metex® pre-filled syringe” (PSAT metex®) questionnaire (Benefit, Practicality, Satisfaction) was developed exclusively for this study to assess patient’s overall experience with s.c. self-injection. This questionnaire has not yet been validated.
PSAT metex® Satisfaction Items:
18. I am satisfied with the speed at which the treatment takes effect.
19. I am satisfied with the efficacy of the treatment.
20. I am satisfied with the tolerability of the treatment.
21. I am happy with the way the preparation can be handled, and its storage and application.
22. I would recommend the treatment to other patients.
23. I would repeat/continue with the treatment.
24. I have confidence in the treatment.

End point type	Secondary

End point timeframe:

PSAT metex® was assessed at V1, V5 and V0. The PSAT metex® score collected after 16 and 52 weeks of treatment (V5 and V10) was considered as secondary efficacy endpoint.

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Item 18: 2 – Agree	24	6		
Item 18: 3 – Strongly agree	47	3		
Item 19: 2 – Agree	17	5		
Item 19: 3 – Strongly agree	52	4		
Item 20: 2 – Agree	19	3		
Item 20: 3 – Strongly agree	55	13		
Item 21: 2 – Agree	7	6		
Item 21: 3 – Strongly agree	69	16		
Item 22: 2 – Agree	8	4		
Item 22: 3 – Strongly agree	65	13		
Item 23: 2 – Agree	7	2		
Item 23: 3 – Strongly agree	67	16		
Item 24: 2 – Agree	11	3		
Item 24: 3 – Strongly agree	64	16		

Statistical analyses

No statistical analyses for this end point

Secondary: PSAT metex® Satisfaction at week 52

End point title	PSAT metex® Satisfaction at week 52

End point description:

The "Patient's Satisfaction with metex® pre-filled syringe" (PSAT metex®) questionnaire (Benefit, Practicality, Satisfaction) was developed exclusively for this study to assess patient's overall experience with s.c. self-injection. This questionnaire has not yet been validated.
PSAT metex® Satisfaction Items:
18. I am satisfied with the speed at which the treatment takes effect.
19. I am satisfied with the efficacy of the treatment.
20. I am satisfied with the tolerability of the treatment.
21. I am happy with the way the preparation can be handled, and its storage and application.
22. I would recommend the treatment to other patients.
23. I would repeat/continue with the treatment.
24. I have confidence in the treatment.

End point type	Secondary

End point timeframe:

PSAT metex® was assessed at V1, V5 and V0. The PSAT metex® score collected after 16 and 52 weeks of treatment (V5 and V10) was considered as secondary efficacy endpoint.

End point values	Modified intent-to-treat (mITT) set (MTX/MTX)	Modified intent-to-treat (mITT) set (Placebo/MTX)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	91	29		
Units: Subjects				
Item 18: 2 – Agree	13	3		
Item 18: 3 – Strongly agree	39	11		
Item 19: 2 – Agree	8	3		
Item 19: 3 – Strongly agree	42	12		
Item 20: 2 – Agree	13	4		
Item 20: 3 – Strongly agree	40	11		
Item 21: 2 – Agree	8	3		
Item 21: 3 – Strongly agree	46	12		
Item 22: 2 – Agree	6	2		
Item 22: 3 – Strongly agree	48	13		
Item 23: 2 – Agree	6	0		
Item 23: 3 – Strongly agree	45	15		
Item 24: 2 – Agree	10	0		
Item 24: 3 – Strongly agree	44	15		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Adverse events were monitored throughout the course of the study from 1st injection of IMP (each sign/symptom that occurred between signing informed consent and 1st injection of IMP were recorded as part of the medical history).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	MTX/MTX group (Double-Blind Treatment Phase)

Reporting group description:

From week 0 to week 16:
The starting dose and regular maintenance dose was 17.5 mg MTX /0.35 mL NaCl (0.9%) solution (placebo) administered once weekly (every 7 days). However, if PASI 50 was not reached at week 8 the dosage was increased to 22.5 mg MTX per week or 0.45 mL placebo. The primary endpoint was assessed after 16 weeks of treatment.
If a patient showed a decrease of leukocytes, lymphocytes, erythrocytes or platelet counts of 30% at Day 5 after the first administration of MTX compared with baseline, the patient was to be withdrawn from treatment.

Reporting group title	Placebo/MTX group (Double-Blind Treatment Phase)

Reporting group description:

From week 0 to week 16:
The starting dose and regular maintenance dose was 17.5 mg MTX /0.35 mL NaCl (0.9%) solution (placebo) administered once weekly (every 7 days). However, if PASI 50 was not reached at week 8 the dosage was increased to 22.5 mg MTX per week or 0.45 mL placebo. The primary endpoint was assessed after 16 weeks of treatment.
If a patient showed a decrease of leukocytes, lymphocytes, erythrocytes or platelet counts of 30% at Day 5 after the first administration of MTX compared with baseline, the patient was to be withdrawn from treatment.

Reporting group title	MTX/MTX group (Open-Label Treatment Phase)

Reporting group description:

From week 16 to week 52:
MTX/MTX: Patients stayed on their dose in the MTX/MTX. However, if at week 24 patients were receiving 17.5 mg MTX but PASI 75 was not yet reached the dosage was increased to 22.5 mg MTX per week. If patients had already been dosed with 22.5 mg MTX per week at week 24 and PASI 50 was not yet reached, patients were excluded from treatment.

Reporting group title	Placebo/MTX group (Open-Label Treatment Phase)

Reporting group description:

From week 16 to week 52:
Placebo/MTX: From week 16 to week 52, patients received MTX according to the fixed dose schedule of the MTX/MTX (starting dose 17.5 mg with the possibility of up-titration after 8 weeks, i.e., at week 24). However, patients who reached PASI 75 under placebotreatment after 16 weeks were dosed with neither placebo nor MTX until relapse. After relapse, patients received a starting dose of 17.5 mg MTX as described above.

Serious adverse events	MTX/MTX group (Double-Blind Treatment Phase)	Placebo/MTX group (Double-Blind Treatment Phase)	MTX/MTX group (Open-Label Treatment Phase)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 91 (1.10%)	4 / 29 (13.79%)	2 / 76 (2.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign salivary gland neoplasm			
subjects affected / exposed	0 / 91 (0.00%)	0 / 29 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Inguinal hernia repair			
subjects affected / exposed	1 / 91 (1.10%)	0 / 29 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial stent insertion			
subjects affected / exposed	0 / 91 (0.00%)	1 / 29 (3.45%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroidectomy			
subjects affected / exposed	0 / 91 (0.00%)	0 / 29 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 91 (0.00%)	0 / 29 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Multiple sclerosis			
subjects affected / exposed	0 / 91 (0.00%)	1 / 29 (3.45%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	0 / 91 (0.00%)	1 / 29 (3.45%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Psoriasis			
subjects affected / exposed	0 / 91 (0.00%)	1 / 29 (3.45%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo/MTX group (Open-Label Treatment Phase)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign salivary gland neoplasm			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Inguinal hernia repair			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arterial stent insertion			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thyroidectomy			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Multiple sclerosis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastric ulcer			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	MTX/MTX group (Double-Blind Treatment Phase)	Placebo/MTX group (Double-Blind Treatment Phase)	MTX/MTX group (Open-Label Treatment Phase)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	75 / 91 (82.42%)	27 / 29 (93.10%)	59 / 76 (77.63%)
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	7 / 91 (7.69%)	2 / 29 (6.90%)	7 / 76 (9.21%)
occurrences (all)	7	2	7
Alanine aminotransferase increased			
subjects affected / exposed	4 / 91 (4.40%)	0 / 29 (0.00%)	2 / 76 (2.63%)
occurrences (all)	4	0	3
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 91 (0.00%)	0 / 29 (0.00%)	2 / 76 (2.63%)
occurrences (all)	0	0	3
Mean cell volume increased			
subjects affected / exposed	2 / 91 (2.20%)	0 / 29 (0.00%)	4 / 76 (5.26%)
occurrences (all)	2	0	5
Vascular disorders			

Hypertension			
subjects affected / exposed	3 / 91 (3.30%)	0 / 29 (0.00%)	3 / 76 (3.95%)
occurrences (all)	3	0	4
Nervous system disorders			
Headache			
subjects affected / exposed	12 / 91 (13.19%)	5 / 29 (17.24%)	5 / 76 (6.58%)
occurrences (all)	15	6	6
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 91 (8.79%)	1 / 29 (3.45%)	0 / 76 (0.00%)
occurrences (all)	11	1	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	2 / 91 (2.20%)	0 / 29 (0.00%)	3 / 76 (3.95%)
occurrences (all)	2	0	3
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	12 / 91 (13.19%)	0 / 29 (0.00%)	7 / 76 (9.21%)
occurrences (all)	17	0	7
Diarrhoea			
subjects affected / exposed	3 / 91 (3.30%)	1 / 29 (3.45%)	4 / 76 (5.26%)
occurrences (all)	4	1	4
Gastric ulcer			
subjects affected / exposed	0 / 91 (0.00%)	1 / 29 (3.45%)	0 / 76 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 91 (5.49%)	1 / 29 (3.45%)	2 / 76 (2.63%)
occurrences (all)	5	1	2
Oropharyngeal pain			
subjects affected / exposed	1 / 91 (1.10%)	2 / 29 (6.90%)	0 / 76 (0.00%)
occurrences (all)	1	2	0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	1 / 91 (1.10%)	4 / 29 (13.79%)	0 / 76 (0.00%)
occurrences (all)	1	4	0
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	6 / 91 (6.59%)	3 / 29 (10.34%)	7 / 76 (9.21%)
occurrences (all)	7	3	11
Arthralgia			
subjects affected / exposed	2 / 91 (2.20%)	0 / 29 (0.00%)	3 / 76 (3.95%)
occurrences (all)	3	0	5
Osteoarthritis			
subjects affected / exposed	0 / 91 (0.00%)	0 / 29 (0.00%)	2 / 76 (2.63%)
occurrences (all)	0	0	2
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	24 / 91 (26.37%)	7 / 29 (24.14%)	18 / 76 (23.68%)
occurrences (all)	28	7	24
Bronchitis			
subjects affected / exposed	3 / 91 (3.30%)	0 / 29 (0.00%)	3 / 76 (3.95%)
occurrences (all)	3	0	4
Influenza			
subjects affected / exposed	1 / 91 (1.10%)	1 / 29 (3.45%)	4 / 76 (5.26%)
occurrences (all)	1	1	5

Non-serious adverse events	Placebo/MTX group (Open-Label Treatment Phase)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 22 (77.27%)		
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	4 / 22 (18.18%)		
occurrences (all)	4		
Alanine aminotransferase increased			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Mean cell volume increased			

subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 2		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	 2 / 22 (9.09%) 2		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 1 / 22 (4.55%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	 2 / 22 (9.09%) 2		
Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all)	 1 / 22 (4.55%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Gastric ulcer subjects affected / exposed occurrences (all)	 3 / 22 (13.64%) 3 3 / 22 (13.64%) 3 0 / 22 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	 0 / 22 (0.00%) 0 1 / 22 (4.55%) 1		
Skin and subcutaneous tissue disorders			

Psoriasis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Osteoarthritis			
subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	5		
Bronchitis			
subjects affected / exposed	0 / 22 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	5 / 22 (22.73%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28012564