Clinical trial results:
A 52-Week, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of a 200-mcg Dose of IPP-201101 Plus Standard of Care in Patients With Systemic Lupus Erythematosus

Summary

EudraCT number	2015-003341-25
Trial protocol	HU DE FR GB IT
Global end of trial date	24 January 2018

Results information

Result version number	v1 (current)
This version publication date	09 February 2019
First version publication date	09 February 2019

Trial information

Trial identification

Sponsor protocol code	IPP-201101/005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02504645
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ImmuPharma France SA
Sponsor organisation address	5, rue du Rhône, 68100, France,
Public contact	Robert Zimmer, ImmuPharma SA, 00 33 (0)6 18 22 16 50, robert.zimmer@immupharma.com
Scientific contact	Robert Zimmer, ImmuPharma SA, 00 33 (0)6 18 22 16 50, robert.zimmer@immupharma.com

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	11 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 January 2018
Global end of trial reached?	Yes
Global end of trial date	24 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of a 200-mcg dose every 4 weeks for 48 weeks of IPP-201101 compared with placebo in patients with active systemic lupus erythematosus (SLE) as assessed by the SLE responder index (SRI) at week 52.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 32
Country: Number of subjects enrolled	Czech Republic: 15
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Hungary: 24
Country: Number of subjects enrolled	United States: 73
Country: Number of subjects enrolled	Mauritius: 49
Worldwide total number of subjects	204
EEA total number of subjects	82

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)	204
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants should fulfilled study eligibility criteria to be randomized.

Pre-assignment

Screening details:

303 participants were enrolled and 204 were randomized. 2 were randomized but not treated. The 99 who were not randomised did not meet study entry criteria.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard of care + 200 mcg SC IPP-201101

Arm description:

200 mcg SC IPP-201101 every 4 weeks

Arm type	Experimental
Investigational medicinal product name	IPP-201101
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

200 mcg administered subcutaneoulsy every 4 weeks.

Arm title	Standard of care + Placebo SC

Arm description:

Placebo was administered subcutaneously every 4 weeks

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was administered subcutaneously every 4 weeks

Number of subjects in period 1	Standard of care + 200 mcg SC IPP-201101	Standard of care + Placebo SC
Started	101	103
Completed	77	76
Not completed	24	27
Consent withdrawn by subject	6	6
Adverse event, non-fatal	6	3
Other	5	4
Pregnancy	1	2
Lost to follow-up	2	4
Protocol deviation	2	4
Lack of efficacy	2	4

Baseline characteristics

Reporting groups	
Reporting group title	Standard of care + 200 mcg SC IPP-201101
Reporting group description:	
200 mcg SC IPP-201101 every 4 weeks	
Reporting group title	Standard of care + Placebo SC
Reporting group description:	
Placebo was administered subcutaneously every 4 weeks	

Reporting group values	Standard of care + 200 mcg SC IPP-201101	Standard of care + Placebo SC	Total
Number of subjects	101	103	204
Age categorical Units: Subjects			
Adults (18-64 years)	101	103	204
Age continuous Units: years			
median	42.55	43.69	
standard deviation	± 11.86	± 11.49	-
Gender categorical Units: Subjects			
Female	96	94	190
Male	5	9	14
Race Units: Subjects			
White	59	66	125
Black or African American	14	10	24
Native Hawaiian or Other Pacific Islander	0	2	2
Asian	4	1	5
Other	24	24	48
American Indian or Alaska Native	0	0	0
Ethnicity Units: Subjects			
Not Hispanic or Latino	88	84	172
Hispanic or Latino	13	19	32

End points

End points reporting groups

Reporting group title	Standard of care + 200 mcg SC IPP-201101
Reporting group description: 200 mcg SC IPP-201101 every 4 weeks	
Reporting group title	Standard of care + Placebo SC
Reporting group description: Placebo was administered subcutaneously every 4 weeks	

Primary: Proportion of patients responders using the SRI at week 52

End point title	Proportion of patients responders using the SRI at week 52
End point description: A SRI response was defined as a reduction from baseline in the SLEDAI-2K score of at least 4 points, no worsening in PhGA (with worsening defined as an increase in PhGA of more than 0.30 point from baseline), no new BILAG A body system score, and no more than 1 new BILAG B body system score from baseline.	
End point type	Primary
End point timeframe: At week 52	

End point values	Standard of care + 200 mcg SC IPP-201101	Standard of care + Placebo SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	101		
Units: patients				
responders	53	45		

Statistical analyses

Statistical analysis title	Primary Analysis of SRI Response at Week 52
Comparison groups	Standard of care + Placebo SC v Standard of care + 200 mcg SC IPP-201101
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2631
Method	Chi-squared

Post-hoc: Proportion of reponders of EU patients having anti-dsDNA at randomization

End point title	Proportion of reponders of EU patients having anti-dsDNA at randomization

End point description:

End point type	Post-hoc

End point timeframe:

At week 52

End point values	Standard of care + 200 mcg SC IPP-201101	Standard of care + Placebo SC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	55		
Units: patient				
Responders	32	26		

Statistical analyses

Statistical analysis title	Post Hoc analysis
Comparison groups	Standard of care + Placebo SC v Standard of care + 200 mcg SC IPP-201101
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0218
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) and serious adverse events (SAEs) are reported from informed consent signature and up to 30 days post last dose.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Standard of care + IPP-201101 SC 200 mcg
Reporting group description: -	
Reporting group title	Standard of care + Placebo SC

Reporting group description: -

Serious adverse events	Standard of care + IPP-201101 SC 200 mcg	Standard of care + Placebo SC	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 101 (12.87%)	16 / 101 (15.84%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Mesothelioma malignant			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	0 / 101 (0.00%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	1 / 101 (0.99%)	3 / 101 (2.97%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Face Edema			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Pelvic fluid collection			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine Hemorrhage			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Subdural Hematoma			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular Accident			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoesthesia			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 101 (1.98%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Butterfly rash			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cutaneous lupus erythematosus			

subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hematuria			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			
subjects affected / exposed	1 / 101 (0.99%)	2 / 101 (1.98%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Respiratory Tract Infection			
subjects affected / exposed	1 / 101 (0.99%)	0 / 101 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 101 (0.00%)	1 / 101 (0.99%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Standard of care + IPP-201101 SC 200 mcg	Standard of care + Placebo SC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	94 / 101 (93.07%)	96 / 101 (95.05%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 101 (2.97%)	7 / 101 (6.93%)	
occurrences (all)	4	9	
Nervous system disorders			
Headache			

subjects affected / exposed	12 / 101 (11.88%)	17 / 101 (16.83%)	
occurrences (all)	18	31	
Migraine			
subjects affected / exposed	5 / 101 (4.95%)	1 / 101 (0.99%)	
occurrences (all)	5	1	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	8 / 101 (7.92%)	7 / 101 (6.93%)	
occurrences (all)	9	11	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	5 / 101 (4.95%)	0 / 101 (0.00%)	
occurrences (all)	21	0	
Mucosal ulceration			
subjects affected / exposed	4 / 101 (3.96%)	8 / 101 (7.92%)	
occurrences (all)	9	8	
Pyrexia			
subjects affected / exposed	5 / 101 (4.95%)	5 / 101 (4.95%)	
occurrences (all)	8	6	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	6 / 101 (5.94%)	7 / 101 (6.93%)	
occurrences (all)	8	11	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	6 / 101 (5.94%)	2 / 101 (1.98%)	
occurrences (all)	8	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 101 (2.97%)	6 / 101 (5.94%)	
occurrences (all)	3	6	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	12 / 101 (11.88%)	13 / 101 (12.87%)	
occurrences (all)	17	15	
Rash			

subjects affected / exposed	12 / 101 (11.88%)	8 / 101 (7.92%)	
occurrences (all)	14	13	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	3 / 101 (2.97%)	6 / 101 (5.94%)	
occurrences (all)	3	6	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	12 / 101 (11.88%)	13 / 101 (12.87%)	
occurrences (all)	13	19	
Arthritis			
subjects affected / exposed	15 / 101 (14.85%)	14 / 101 (13.86%)	
occurrences (all)	25	27	
Back pain			
subjects affected / exposed	9 / 101 (8.91%)	9 / 101 (8.91%)	
occurrences (all)	9	10	
Myalgia			
subjects affected / exposed	6 / 101 (5.94%)	1 / 101 (0.99%)	
occurrences (all)	7	1	
Systemic lupus erythematosus			
subjects affected / exposed	2 / 101 (1.98%)	10 / 101 (9.90%)	
occurrences (all)	2	11	
Infections and infestations			
Bronchitis			
subjects affected / exposed	7 / 101 (6.93%)	8 / 101 (7.92%)	
occurrences (all)	7	8	
Nasopharyngitis			
subjects affected / exposed	8 / 101 (7.92%)	7 / 101 (6.93%)	
occurrences (all)	14	8	
Pharyngitis			
subjects affected / exposed	2 / 101 (1.98%)	5 / 101 (4.95%)	
occurrences (all)	2	5	
Upper respiratory tract infection			
subjects affected / exposed	20 / 101 (19.80%)	28 / 101 (27.72%)	
occurrences (all)	25	32	
Urinary tract infection			

subjects affected / exposed occurrences (all)	23 / 101 (22.77%) 32	10 / 101 (9.90%) 19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 June 2016	Exclusion criteria "(e)" updated to clarify wash out period in case of use of B-cell depleting agent

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported