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A study to investigate the safety, tolerability and activity of IPP-201101 in healthy volunteers

Submission date
30/05/2023

Recruitment status
No longer recruiting

Registration date
26/09/2023

Overall study status
Completed

Last Edited
06/12/2023

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
The purpose of this study is to investigate the study drug IPP-201101.
The main objectives of this study are as follows:
1. To determine the safety and tolerability (the degree to which side effects of a drug can be tolerated) of IPP-201101 when it is administered as a subcutaneous injection (injection into the tissue layer between the skin and muscle) at different dose strengths on one occasion.
2. To investigate the concentration of IPP-201101 in the blood and urine, how this changes over a period of time and whether there are differences in the concentration profile between different dose strengths.
3. To evaluate and compare the bioavailability (the degree and rate at which a substance such as a drug is absorbed into the body or is made available at the site of its desired effect) of IPP-201101 when it is administered as a subcutaneous injection in comparison to administration as an intravenous injection (an injection directly into a vein).

Who can participate?
Healthy adult males aged between 18 and 55 years

What does the study involve?
The study is an open-label bioavailability study evaluating the safety, tolerability and concentration in the blood and urine of IPP-201101 when it is given at different dose strengths and by different routes of administration.
The study will consist of up to three groups of eight participants, each group investigating a different dose strength of IPP-201101. In this study, all participants will be given IPP-201101 in the form of a subcutaneous injection. Group 2 will also complete a second treatment period whereby IPP-201101 will be given in the form of an intravenous injection. Each cohort of the study will consist of a screening visit (between 28 and 2 days prior to the first dose), a minimum of one treatment period (consisting of a maximum of 3 days with 2 overnight stays) and a post-study follow-up visit within 4-7 days (study Days 5-8) of the last dose of IPP-201101. For Cohort 2, the second treatment period will commence a minimum of 14 days following the dose administration in treatment period 1.
Blood and urine samples will be taken at set timepoints throughout the study in order to measure the concentration profile of IPP-201101. The researchers will compare the results from

each of the groups to determine if there are any significant differences in the safety profile of IPP-201101, the concentration of IPP-201101 in the blood and urine, how this changes over time and whether there are any differences in these factors between different dose strengths and in comparison to when the drug is given as a subcutaneous injection versus as an intravenous injection.

What are the possible benefits and risks of participating?
Taking part in this study is not expected to provide any direct medical benefit. However, the information the researchers get from this study may help improve the treatment of lupus.
The procedure for blood collection may cause mild pain and bruising at the collection site. The placement of an indwelling catheter is proposed in order to minimise these effects for rapid sampling. Very rarely, a blockage of a vein or a small nerve injury can occur, resulting in numbness and pain. If this occurs, it will resolve with time.
The participants' blood pressure and pulse will be measured using an inflatable cuff which will be placed on the arm. They may experience mild discomfort in the arm whilst the cuff is inflated.
Small sticky pads will be placed on the participants' upper body before the ECG and an ECG machine will measure the electrical activity of the heart. Before the pads are applied, the skin needs to be cleaned. Trained staff may need to shave/clip small patches of the participant's hair in these areas. Like Elastoplast® these sticky pads may be uncomfortable to remove.
It is possible that administration of the drug via either the subcutaneous or intravenous injection may cause some mild pain, irritation and bruising at the site of the injections but this should be mild in nature and resolve within a couple of days.
Participants should also be aware of the risks of exposure to COVID-19. When participants attend the clinical unit at each visit, they may be asked to complete a self-declaration form and temperature check to confirm that they are not showing any early signs of COVID-19 infection and that they have not had any contact with individuals who are currently self-isolating or have tested positive (dependent on risk mitigation measures employed at the clinical unit at the time of clinical conduct).
Participants may also be required to have a negative COVID-19 test before admission to the clinical unit for any overnight stays as defined within the study protocol. This procedure may cause some mild discomfort in the nose or throat when the swab is being taken but this should resolve after the procedure has been completed.
Additionally, at the clinical unit, participants may be asked to wear a facemask during procedures where clinical staff cannot maintain a 2 m distance. It is noted that if participants have a medical exemption from wearing a face mask, they will not be required to do so. In any circumstance, to prevent the risk of transmission between staff and participants, all staff will be wearing appropriate personal protective equipment i.e., face masks, face shields etc during the course of the study.
Male participants of childbearing potential will be required to use a highly effective or two effective methods of contraception (including a condom) with their partner of childbearing potential during the trial from Day -1 and for at least 3 months following the last dose of IPP-201101.

Where is the study run from?
Simbec-Orion Clinical Pharmacology Unit (UK)

When is the study starting and how long is it expected to run for?
August 2021 to March 2023

Who is funding the study?
ImmuPharma S.A. (UK)

Who is the main contact?
Tim Franklin, tim.franklin@immupharma.com

Contact information

Type(s)
Public

Contact name
Mr Tim Franklin

Contact details
ImmuPharma S.A/PLC
One Bartholomew Close
London
United Kingdom
EC1A 7BL
+44 (0)7465217878
Tim.franklin@immupharma.com

Type(s)
Scientific

Contact name
Mr Tim Franklin

Contact details
ImmuPharma S.A/PLC
One Bartholomew Close
London
United Kingdom
EC1A 7BL
+44 (0)7465217878
Tim.franklin@immupharma.com

Type(s)
Principal Investigator

Contact name
Dr Annelize Koch

Contact details
Simbec-Orion Clinical Pharmacology
Merthyr Tydfil Industrial Park
Cardiff Road
Merthyr Tydfil
United Kingdom
CF48 4DR
+44 (0)1443 694313
annelize.koch@simbecorion.com

Additional identifiers

EudraCT/CTIS number
2021-004976-33

IRAS number
305901

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IPP-201101, IRAS 305901

Study information

Scientific Title
A Phase I, open-label, single-dose pharmacokinetic study of IPP-201101 after subcutaneous and intravenous administration in healthy male volunteers

Acronym
RD 704.35328

Study objectives
The primary objective of this study is:
1. To characterise the pharmacokinetics (PK) of single doses of IPP-201101 after subcutaneous (s.c.) administration in healthy male volunteers.

The secondary objectives of this study are:
1. To determine the absolute bioavailability of IPP-201101 after s.c. administration to that of IPP-201101 dosed via the intravenous (i.v.) route in healthy male volunteers.
2. To assess the safety and tolerability of single s.c. doses of IPP-201101 when administered to healthy male volunteers.

The exploratory objectives of this study are:
1. To determine the reactive and neutralizing immunogenicity of IPP-201101.
2. To investigate the metabolite profile of IPP-201101 following single-dose administration to healthy male volunteers.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 20/10/2021, Wales Research Ethics Committee 1 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 (0)292 2940931; Wales.REC1@wales.nhs.uk), ref: 21/WA/0327
2. Approved 13/10/2021, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, UK; +44 (0) 20 3080 6000; info@mhra.gov.uk), ref: CTA 55538/0001/001-0001

Study design

Open-label single-dose study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Systemic lupus erythematosus (SLE)

Interventions
The study is an open-label bioavailability study evaluating the safety, tolerability and concentration in the blood and urine of IPP-201101 when it is administered at different dose strengths and via different routes of administration.
The study is planned to be conducted in two cohorts, each investigating a single dose level of IPP-201101. An additional cohort, investigating a third dose level, may be enrolled if deemed appropriate following review of all available PK data.
Each cohort will enrol 8 volunteers; Cohort 1 will investigate a low dose level while Cohort 2 will investigate a higher dose level of IPP-201101. Optional Cohort 3 may investigate a third intermediate dose level in order to further characterise the PK profile of IPP-201101; a decision on whether to proceed with optional Cohort 3 will be taken following a review of all available PK data from Cohort 1 and 2. The absolute bioavailability of IPP-201101 will also be investigated in Cohort 2.

Cohort 1: Each subject received a single subcutaneous dose of 200 µg IPP-201101 in treatment period 1.
Cohort 2: Each subject received a single subcutaneous dose of 800 µg IPP-201101 in treatment period 1 and (in order to assess absolute bioavailability) a single intravenous dose of 800 µg IPP-201101 in treatment period 2. Each dose was separated by at least 14 days washout.
No dose was administered in Cohort 3 as this was not conducted.

The study will comprise a pre-study screen, followed by one or two treatment periods (1 and 2) and a post-study follow-up.

Screening (Day 28 to Day 2): Screening assessments will be carried out within 28 days before the first administration of IMP. Eligible volunteers will be asked to return for the treatment period (s). Continued eligibility will be confirmed pre-dose during each treatment period.

Treatment Period(s) (Day 1 to Day 2): Eligible volunteers will receive a single dose of IPP-201101 via s.c. administration (Cohort 1 and Period 1 of Cohort 2). Subjects in Cohort 2 will undergo a

second in-house treatment period (Treatment Period 2) of 2 overnight stays (Day -1 to Day 2) and will receive a single dose of IPP-201101 via the i.v. route. Each treatment period will be approximately 2 days duration, from the day before dosing (Day 1) until 24 hours (h) post-dose (Day 2). During any treatment period, volunteers will arrive at the Clinical Unit on Day 1, IMP will be administered on the morning of Day 1 fasted (after an overnight fast of at least 10 h) and volunteers will be discharged at least 24 h post-dose (Day 2). PK samples will be collected pre-dose and up to 24 h post-dose (Day 2) (17 samples) for the measurement of IPP-201101 in plasma. Safety will also be evaluated at specified times. Where volunteers in Cohort 2 are enrolled to a second treatment period, there will be at least 14 days between dose administrations.

Post-Study: Post-study assessments will be conducted 5 to 8 days after the last dose of IMP.

The study end is defined as the last subject last visit. The study will take place in the Clinical Unit of Simbec-Orion Clinical Pharmacology (Clinical Unit) under full medical and nursing supervision.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic

Phase
Phase I

Drug/device/biological/vaccine name(s)
IPP-201101

Primary outcome measure
Pharmacokinetic parameters derived from analysis of plasma and urine concentrations of IPP-201101. The following PK parameters will be derived from plasma IPP-201101 concentrations:
1. Cmax: observed maximum concentration
2. tmax: time of occurrence of Cmax
3. λz: apparent first-order terminal elimination rate constant
4. t1/2: apparent terminal elimination half-life
5. AUC0 t: area under the concentration time curve (AUC) from time of dosing to last measurable concentration
6. AUC0 inf: AUC extrapolated to infinity
7. AUC%extrap: extrapolated area under the curve from tlast to infinity, expressed as a percentage
8. Cl/F: apparent total body clearance
9. Vz/F: apparent volume of distribution

Plasma samples for PK evaluation of IPP-20101 will be taken at the following timepoints:
Day 1: pre-dose, 5, 10, 15, 20, 25, 30, 40, 50 min and 1, 1.5, 2, 3, 4, 6, 8, and 12 h post-Day 1 dose in each treatment period.

The following PK parameters will be derived from urine IPP-201101 concentrations:
1. Ae: cumulative amount of drug excreted in urine
2. Ae%: percentage of dose excreted in urine over each collection interval
3. CLR: renal clearance

Urine samples for PK evaluation of IPP-20101 will be taken at the following timepoints:
Day 1: pre-dose 0-8 h, 8 12 h, and 12-24 h post-Day 1 dose in each treatment period

Secondary outcome measures
Safety endpoints defined as follows:
1. Adverse events (AEs) including serious AEs (SAEs) and treatment-emergent AEs (TEAEs) will be recorded from the point of informed consent up to the final post-study follow-up visit
2. Laboratory safety testing at Screening, Day -1, Day 2 of each treatment period (as applicable) and post-study follow-up visit on Days 5-8
3. Vital signs at Screening and Day 1 at pre-dose and 12 h post-dose, on Day 2 at 24 hours post-dose of each treatment period (as applicable) and at post-study follow-up visit on Day 5-8
4. 12-lead ECG at Screening and Day 1 at pre-dose and 12 h post-dose, on Day 2 at 24 hours post-dose of each treatment period (as applicable) and at post-study follow-up visit on Day 5-8
5. Injection site reaction examinations will be performed on Day 1 (1 h, 6 h and 12 h post-dose), Day 2 (24 h post-dose) of each treatment period (as applicable) and at post-study follow-up visit on Day 5-8

Overall study start date
24/08/2021

Completion date
21/03/2023

Eligibility

Key inclusion criteria
1. Healthy male volunteer, between 18 and 55 years of age, inclusive
2. Male volunteer (and partner of childbearing potential) willing to use a highly effective method of contraception or two effective methods of contraception, if applicable (unless anatomically sterile or where abstaining from sexual intercourse is in line with the preferred and usual lifestyle of the volunteer) from first dose until 3 months after last dose of IMP.
3. Volunteer with a body mass index (BMI) of 18-32 kg/m². BMI = body weight (kg) / [height (m)]²
4. No clinically significant history of previous allergy/sensitivity to IPP 201101 or any of the excipients contained within the IMP
5. No clinically significant abnormal test results for serum biochemistry, haematology and/or urine analyses within 28 days before the first dose administration of the IMP
6. Volunteer with a negative urinary drugs of abuse (DOA) toxicology screen (including alcohol) test results, determined within 28 days before the first dose administration of the IMP (N.B. A positive test result may be repeated at the Investigator's discretion)
7. Volunteer with negative human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg) and hepatitis C virus antibody (HCV Ab) test results at Screening
8. No clinically significant abnormalities in 12-lead electrocardiogram (ECG) determined within 28 days before the first dose of IMP including a PR interval > 220ms or QT interval corrected using Fredericia's formula (QTcF) >450 ms
9. No clinically significant abnormalities in vital signs (blood pressure/heart rate, oral temperature) determined within 28 days before the first dose of IMP
10. Volunteer must be available to complete the study (including all follow-up visits)
11. Volunteer must satisfy an Investigator about his/her fitness to participate in the study
12. Volunteer must provide written informed consent to participate in the study
13. Participants with a negative coronavirus disease 2019 (COVID-19) test on admission (if required)

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Male

Target number of participants
24

Total final enrolment
16

Key exclusion criteria
1. Evidence of clinically significant renal, hepatic, central nervous system, respiratory, cardiovascular or metabolic dysfunction
2. Individual or family history of pre-existing autoimmune or antibody-mediated diseases
3. Use of prescription or non-prescription drugs, including vitamins, herbal and dietary supplements within 28 days or 5 half-lives (whichever is longer) prior to the first dose of IMP
4. Volunteers who have received any prophylactic vaccine (including COVID-19 vaccine) or immunisation within the last 28 days or use of corticosteroids or immunosuppressive drugs within 28 days of IMP administration
5. A clinically significant history of drug or alcohol abuse (defined as the consumption of more than 14 units of alcohol a week for male volunteers) within the past 2 years
6. Inability to communicate well with the Investigators (i.e., language problem, poor mental development or impaired cerebral function)
7. Participation in a New Chemical Entity (NCE) clinical study within the previous 3 months or five half-lives whichever is the longest, or a marketed drug clinical study within the 30 days or five half-lives whichever is the longest, before the first dose of IMP. (Washout period between studies is defined as the period of time elapsed between the last dose of the previous study and the first dose of the next study).
8. Donation of 450 millilitres (ml) or more blood within the 3 months before the first dose of IMP
9. Vegans, vegetarians or other dietary restrictions (e.g., restrictions for medical, religious or cultural reasons, etc)
10. Users of nicotine products i.e., current smokers or ex-smokers who have smoked within 3 months prior to first dose administration with the study medication or users of cigarette replacements (i.e., e-cigarettes, nicotine patches or gums)
11. Volunteers who do not have suitable veins for multiple venepunctures/cannulation
12. Volunteers who have any clinical condition or prior therapy which, in the opinion of the Investigator, could jeopardize the safety or rights of a volunteer participating in the trial or

would render them unable to comply with the protocol
13. Volunteers who are study site employees, or immediate family members of a study site or sponsor employee

Date of first enrolment
18/01/2022

Date of final enrolment
22/02/2022

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec Research Limited
Simbec House Merthyr Tydfil Industrial Park
Merthyr Tydfil Industrial Park
Pentrebach
Merthyr Tydfil
Mid Glamorgan
United Kingdom
CF48 4DR

Sponsor information

Organisation
ImmuPharma S.A

Sponsor details
ImmuPharma S.A/PLC
One Bartholomew Close
London
England
United Kingdom
EC1A 7BL
+44 (0)7465217878
Tim.franklin@immupharma.com

Sponsor type
Industry

Website

https://www.immupharma.co.uk/

Funder(s)

Funder type
Industry

Funder Name
ImmuPharma S.A

Results and Publications

Publication and dissemination plan
1. Internal report
2. Submission to regulatory authorities

Intention to publish date
31/12/2025

Individual participant data (IPD) sharing plan
The study data will be shared with relevant research groups and external stakeholders collaborating with the study sponsor to support the future development of the IMP within the boundaries of strict confidentiality agreements.

The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	version 1.0	04/12/2023	06/12/2023	No	No