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The effect of DSP-2230/placebo on renal function

Submission date	Recruitment status	[ ] Prospectively registered
07/10/2013	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
12/11/2013	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
30/10/2019	Nervous System Diseases	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
DSP-2230 (the study drug) is being developed as a possible treatment for a condition called neuropathic pain - a pain caused by damage to, or disease of, the nerves.
The aim of this study is to look at how the drug affects kidney function after a single dose of study drug on Day 1 and following multiple dosing of the study drug over about 2 weeks. Throughout the study you may be dosed with study drug or placebo (dummy). The safety and tolerability of the study drug will also be assessed. Throughout the study, at set times, you will receive intravenous infusions (injections into a vein) of iohexol and para-amino hippurate (PAH). These are marketed products (iohexol in the EU and PAH in the USA). They are not the study drug and will be used to assess kidney function only. These products are commonly used for this purpose.

Who can participate?
Healthy men aged 18 to 55 years.

What does the study involve?
The study will involve up to four visits to the Quotient unit. The screening visit will be either one longer visit of up to 4 hours or two shorter visits of up to 2 hours to check if you are suitable for the study. During the residential visit you will stay in the Unit for 22 days, during which time urine and blood samples will be collected, you will receive injections and intravenous infusion, and you will be randomly allocated to receive either the oral doses of the study drug or the placebo. The follow-up visit will be about 10 days after the last dose. This will be a 30-minute visit to check you are in the same condition as before you started the study. Your total participation in this study is expected to be about 7 weeks from the screening visit until the follow-up visit.

What are the possible benefits and risks of participating?
You will not receive any medical benefit from taking part in this study; however, the development of another treatment for peripheral neuropathic (nerve) pain may benefit the population as a whole. During the screening visit you will be tested for human immunodeficiency virus (HIV) and hepatitis B and C. During the study you will have frequent blood samples taken. This is a standard procedure which is unlikely to cause you any problems but can sometimes

cause discomfort. There is a risk of bruising, reddening and swelling of the vein, but this normally clears up with no further trouble. We prefer to take the blood samples using a cannula (plastic tube) placed in a vein in your arm and which stays there until we have finished taking the samples, so that we dont have to keep using needles on days when we need a lot of blood samples.

Where is the study run from?
Quotient Clinical Limited, UK.

When is the study starting and how long is it expected to run for?
The study started in October 2013 and will run until December 2013.

Who is funding the study?
Sunovion Europe Pharmaceuticals Ltd.

Who is the main contact?
Dr Phil Evans

Contact information

Type(s)
Scientific

Contact name
Dr Phil Evans

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Additional identifiers

Clinical Trials Information System (CTIS)
2013-002250-75

Integrated Research Application System (IRAS)
138354

Protocol serial number
D8450117, IRAS 138354

Study information

Scientific Title
A phase 1 study to investigate the effect of single and repeated doses of DSP-2230/placebo on renal function in healthy subjects

Study objectives
Primary objectives:
To assess the pharmacodynamics (PD) of DSP-2230 based on the glomerular filtration rate (GFR) after a single dose (400 mg DSP-2230/placebo) and after 13 days of dosing (80 mg DSP-2230 /placebo b.i.d. for 12 days followed by a single dose of 80 mg DSP-2230/placebo on the last day).

Secondary objectives:
To assess the following after a single dose (400 mg SP-2230/placebo) and after 13 days of dosing (80 mg DSPE/placebo b.i.d. for 12 days followed by a single dose of 80 mg DSP-2230 /placebo on the last day):
1. Further PD effects of DSP-2230 on renal plasma flow and tubular secretion of creatinine in healthy subjects
2. The safety and tolerability of DSP-2230
3. The pharmacokinetics (PK) of DSP-2230 and its major metabolite

Ethics approval required
Old ethics approval format

Ethics approval(s)
South-East Wales Research Ethics Committee, 20/09/2013, ref: 13/WA/0280

Study design
Single-centre double-blind randomised placebo-controlled study

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Peripheral Neuropathic Pain

Interventions
Up to 44 subjects will be enrolled and randomised to receive DSP-2230 or placebo in a 1:1 ratio.

Subjects randomised to DSP-2230: 400 mg DSP-2230 suspension (single dose on Day 1), 80 mg DSP-2230 suspension (multiple dosing Days 2-13; single dose Day 14)

Subjects randomised to placebo: Placebo suspension.

On days -1, 1 and 13, Para-Amino Hippurate (PAH) will be used to measure effective renal plasma flow and iohexol will be used to measure glomerular filtration rate (GFR)

Subjects will be given intravenous (i.v.) bolus loading dose injections into the injection catheter of Iohexol 20 µmol/kg body weight of Omnipaque 240 solution and PAH 8 mg/kg body weight over 2 minutes.

Thereafter, maintenance infusions of iohexol and PAH will be given at the following infusion rates: Iohexol 10 µmol iohexol/min (600 µmol/h) and PAH 12.5 mg/min (750 mg PAH/h). The

infusions will start 80 minutes before dosing with DSP-2230 or placebo and continue for 240 minutes post-dose.

The follow-up visit is a 30-minute check, undertaken approximately 10 days after the last dose.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
DSP-2230

Primary outcome(s)
To assess the PD of DSP-2230 using the GFR measured by iohexol plasma clearance. The primary PD endpoint is the glomerular filtration rate (GFR) measured by iohexol clearance on days -1 (baseline) and on day 1 (after a single dose of DSP2230 or placebo) and day 13 (after multiple dosing of DSP-2230 or placebo).

Key secondary outcome(s))
Pharmacodynamic endpoints:
The secondary PD endpoints comprise the following:
1. Renal plasma flow measured by para-amino hippurate (PAH) clearance
2. Urinary and plasma creatinine levels
3. Symmetrical dimethyl arginine (SDMA)
4. Cystatin-C

Pharmacokinetic endpoints:
The plasma concentration time profile and PK parameters of DSP-2230 will be determined from plasma samples collected on Day 1 (single dose) and Day 14 (multiple doses).

Safety endpoints:
Safety and tolerability will be assessed using the following endpoints:
1. Adverse events (AEs) and serious AEs (SAEs)
2. Vital signs
3. Electrocardiogram (ECG) and ECG time intervals
4. Clinical chemistry and haematology
5. Urinalysis including biomarkers of renal function

The secondary PD endpoint is the renal plasma flow measured by PAH clearance and the tubular secretion of creatinine on days -1 (baseline) and on day 1 (after a single dose of DSP-2230 or placebo) and day 13 (after multiple dosing of DSP-2230 or placebo). In addition, safety endpoints AEs, vital signs, ECG and ECG time intervals, clinical chemistry including serum creatinine, haematology and urinalysis including biomarkers of renal function, will be measured after single and 13 days multiple dosing of DSP-2230 or placebo.

Completion date
01/12/2013

Eligibility

Key inclusion criteria
1. All subjects (males) will be in good health aged ≥ 18 and ≤ 55 years with no evidence of systemic disease
2. Be able to comply with all aspects of the protocol
3. Able to give written informed consent to participate in the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Male

Key exclusion criteria
1. All subjects will not have, or have had a history of, clinically significant neurological, gastrointestinal, renal, hepatic, cardiovascular, psychological, pulmonary, metabolic, endocrine, haematological or other major disorders
2. They will not have, or have had a history of, drug or alcohol abuse
3. Will not have participated in a clinical study with an investigational medicinal product (IMP) within 3 months of randomisation into the current study
4. Will not have donated or lost >500 mL of blood or blood products in the 3 months preceding the start of dosing

Date of first enrolment
03/10/2013

Date of final enrolment
01/12/2013

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

Quotient Clinical Ltd
Nottingham
United Kingdom
NG11 6JS

Sponsor information

Organisation
Sunovion Pharmaceuticals Europe Ltd (UK)

ROR
https://ror.org/03sh4z743

Funder(s)

Funder type
Industry

Funder Name
Sunovion Pharmaceuticals Europe Ltd

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No