A Global, Multicenter, Single-arm, Matched External Control Study of Intrathecal SHP611 in Subjects with Late Infantile Metachromatic Leukodystrophy

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The primary objective of this study is to evaluate the effects of intrathecal (IT) administration of SHP611 (also known as TAK-611) on the time to loss of locomotion, as indicated by category 5 or higher in the Gross Motor Function Classification in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital and peripartum neurological conditions
Study type	Interventional

Summary

ID

NL-OMON52741

Source
ToetsingOnline

Brief title
EMBOLDEN

Condition

- Congenital and peripartum neurological conditions

Synonym
a rare inherited neurometabolic disorder affecting the brain, Arylsulfatase A Deficiency, Late Infantile Metachromatic Leukodystrophy, MLD

Research involving
Human

Sponsors and support

Primary sponsor: Shire
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: -intrathecal, -Late Infantile Metachromatic Leukodystrophy, -MLD, -SHP611

Outcome measures

Primary outcome

The primary efficacy endpoint is time to loss of locomotion, measured by progression to GMFC-MLD category 5 or higher, or death, whichever occurs first, up to Week 106, evaluated on subjects in Group A.

Secondary outcome

Secondary efficacy endpoint(s)

* Response in Group A, defined as maintenance of gross motor function at Week 106, evaluated as subjects who do not experience any even within Week 106, where event is defined as a decline in GMFC-MLD to category 5 or higher, or death
* Decline in gross motor function using GMFC-MLD:
o Change from baseline at Week 106and EOS in gross motor function, using the GMFC-MLD
o Subjects with unreversed decline from baseline in GMFC-MLD of more than 2 categories, defined as any decline of more than 2-categories that has not reverted to a 2-category decline (or better)at Week 106, evaluated on subjects in Group A

o Time to unreversed decline from baseline in GMFC-MLD of more than 2 categories, defined as any decline of more than 2-categories that has not reverted to a 2-category decline (or better) as of the last recorded observation

* Change from baseline at Week 106 and EOS in CSF sulfatides levels
* Response in Group A, defined as maintenance of gross motor function at Week 106, defined as a GMFM-88 total score >=40
* Decline in gross motor function using GMFM-88:
o Time to unreversed decline from baseline at Week 106 and EOS in GMFM-88 total score decrease of >20 points or unreversed decline to a score <40 points, whichever occurs firs to Change from baseline at Week 106 and EOS in gross motor function, using the GMFM-88 total score
o Subjects in Group A with GMFM-88 total score decrease of <=20 points from baseline and a total score that is >=40 at Week 106 and EOS
* Change from baseline at Week 106 and EOS in expressive language using the ELFC-MLD

Please refer to the study protocol for further details.

Study description

Background summary

Deficiency of the lysosomal enzyme arylsulfatase A in MLD leads to the accumulation of sulfated glycosphingolipids, known collectively as sulfatides. These accumulate in, and are toxic to, the cells which maintain the myelin insulation sheath of axons both centrally and peripherally. It is hypothesized

that IT administration of recombinant human arylsulfatase A (SHP611) would be sufficient to hydrolyze accumulated sulfatides in cells of the nervous system and could slow or prevent further accumulation, which should translate into motor system benefits. There are currently no approved therapies for MLD. Administration of SHP611 via an implanted intrathecal drug delivery device (IDDD) was well tolerated in Phase 1/2 studies in pediatric subjects with MLD and the device appeared to have an acceptable safety profile. In these studies, the higher dose appeared to show a signal of stabilized motor function in 4 of 12 subjects who received the 100 mg every-other-week (EOW) dose. This Phase 2b study will investigate the potential of IT SHP611 at a higher dose of 150 mg once weekly to stabilize or slow progression of motor dysfunction in pediatric subjects with late infantile MLD. The extension period of the study will evaluate long-term safety and efficacy outcomes of treatment with IT SHP611 in subjects who have participated in the study through Week 106.

Study objective

The primary objective of this study is to evaluate the effects of intrathecal (IT) administration of SHP611 (also known as TAK-611) on the time to loss of locomotion, as indicated by category 5 or higher in the Gross Motor Function Classification in Metachromatic Leukodystrophy (GMFC-MLD) compared with matched external control group data in children with late infantile MLD.

The key secondary objective of this study is to evaluate the effects of IT administration of SHP611 on gross motor function, using the Gross Motor Function Measure 88 (GMFM-88) total score compared with matched historical control data in children with MLD.

If suitable controls cannot be matched despite the sponsor's best efforts, change form baseline results of GMFC-MLD at week 106 will be compared with a prespecified objective threshold to evaluate primary efficacy for this study.

Study design

SHP611-201 is an a single-arm, matched external control, global, multicenter, Phase 2 trial. The study was planned to enroll up to 42 subjects with late infantile MLD who have an initial onset of neurological symptoms documented prior to 30 months of age (Groups A, B, C, and F), or who are minimally symptomatic and >=6 to <18 months of age (Group D), or who are early symptomatic and >=12 to <18 months of age (Group E). Minimally symptomatic is defined as being without clear symptoms of late infantile MLD or only showing mild symptoms (such as weakness) that do not meet the criteria for a GMFC-MLD category of >0. The rate and severity of disease progression is well documented in late infantile MLD. A distinguishing feature of the definition of late infantile MLD is the early age at disease symptom onset with a majority of patients with late infantile MLD showing first motor dysfunction before the age

of 18 months. Six subject groups are defined for this study based on age and motor dysfunction at screening:
• Group A (GMFC-MLD category 1 or 2): 18 to 48 months of age with a GMFC-MLD category of 1 or 2
• Group B (GMFC-MLD category 3): 18 to 72 months of age with a GMFC-MLD category of 3
• Group C (GMFC-MLD category 4): 18 to 72 months of age with a GMFC-MLD category of 4
• Group D (minimally symptomatic): >=6 to <18 months of age, with the same ASA allelic constitution as an older sibling with confirmed late infantile or juvenile onset MLD
• Group E (GMFC-MLD category 1 or 2): >=12 to <18 months of age, with documented diagnosis of MLD per inclusion criteria 1 and 2 with a history of achieving stable walking (defined as at least 1 month of independent walking) and a GMFC MLD category of 1 or 2
• Group F (GMFC-MLD category 5 or 6): 18 to 72 months of age with a GMFC-MLD category of 5 or 6
Subjects weighing >=7 kg (15.4 lbs) will receive 150 mg IT SHP611 weekly. It is anticipated that the majority of subjects will receive 150 mg IT weekly for a total treatment duration of 105 weeks; however, subjects weighing >=5 kg (11.0 lbs) to <7 kg (15.4 lbs) will receive 100 mg IT SHP611 weekly until they weigh >>=7 kg, at which time they will begin dosing with 150 mg IT SHP611 weekly.
The study will evaluate safety and efficacy of the treatment regimen on gross motor function using the GMFC MLD and GMFM-88 total score to measure disease progression (Groups A, B, C, E, and F). Subjects in Group D will be assessed with the Alberta Infant Motor Scale (AIMS) and the GMFM-88 until they are ambulating or 18 months of age, whichever comes first. Once the AIMS is no longer being used, the GMFC-MLD and GMFM-88 will be used to measure motor function in this group.
The primary efficacy endpoint is time to loss of locomotion, measured by progression to GMFC-MLD category 5 or higher, or death, whichever occurs first, up to Week 106, evaluated on subjects in Group A. A secondary efficacy endpoint is response in Group A, defined as maintenance of gross motor function at Week 106, evaluated as subjects who do not experience any event within Week 106, where event is defined as a decline in GMFC-MLD to category 5 or higher, or death.

The efficacy of SHP611 will be evaluated by comparison of SHP611-201 enrolled subjects in Group A with a matched external control group. The data from these untreated MLD subjects (ie, subjects who have received no investigational product or therapy) will come from the ongoing Global Leukodystrophy Initiative (GLIA MLD) natural history study.

The matched external control group must have data for at least baseline gross motor function evaluation. The filtering criteria for these external control subjects will be very similar to the inclusion/exclusion criteria for enrolled subjects in Group A of this present study.

Subjects will be implanted with the SOPH-A-PORT Mini S IDDD. Procedures for implantation are detailed in the device*s Instructions for Use (IFU) manual. Standard hospital procedures for surgery will be followed and the subject may be under anesthesia for this procedure. Prior to implantation, individual neurosurgeons may order additional imaging to estimate the canal size and spinal cord conus location in younger patients. After implantation, a leak test is performed by the neurosurgeon to ensure a sealed system is in place. X-rays may be performed as needed, particularly for younger subjects, throughout the study to confirm placement of the device and/or evaluate a nonworking catheter. In order to facilitate healing, subjects should remain under observation in the hospital setting until deemed clinically stable by the investigator and should limit activity for 24 hours after IDDD implantation. To allow for healing, a waiting period of 3 to 5 days after device implantation must be observed before the first administration of SHP611 may occur. If the device becomes nonfunctional at any time during the study, it may be removed, replaced, or revised as appropriate. After IDDD replacement or revision, a waiting period of 3-5 days must be observed before IT SHP611 dosing may resume. Examination of both the port and catheter track will be performed before each IT injection, which includes aspiration of CSF via the port.

During the treatment period, subjects will undergo assessments of gross motor function, brain imaging, and health-related quality of life. Initial assessment of gross motor function using the GMFC-MLD scale will be conducted by local, trained healthcare professionals and video-recorded. Videos of GMFC-MLD assessments will be evaluated by central video reviewers for primary scoring of gross motor function on the instrument.

Safety will be assessed by collection of adverse events, physical examinations, vital signs, concomitant medications, ECG, clinical laboratory testing, and monitoring of anti-SHP611 antibodies. Periodic assessments will be performed before and after SHP611 administration at specific study visits (eg, serum/CSF PK sampling and CSF, serum, and urine biomarkers sampling and testing).
The study will consist of a screening period of up to 28 days. Implantation of the SOPH-A-PORT Mini S IDDD may occur during a period of up to 10 days prior to the first administration of IT SHP611 to 28 days after the first administration of IT SHP611.IT SHP611 administrations that occur prior to implantation of the IDDD will be administered via LP.
Subjects will be assessed according to the following schedule:
• Screening (-28 to -1 days)
• Surgical implantation of IDDD (-10 to 28 days)
• Primary treatment period (Week 0 [baseline assessments prior to dosing] through Week 105)
• End of primary treatment period (Week 106)
• Extension treatment period (from Week 106 administration of SHP611)
• End of treatment (EOT) (last administration of SHP611)
• End of study (EOS) (1 week after EOT)
• Safety follow-up (2 weeks after EOS)

After the primary treatment period is completed at Week 106, subjects may participate in the extension period of the study where they may continue to receive treatment with SHP611 for an extended duration of time.
Subjects will receive weekly treatment until they or their parents/guardians decide to discontinue treatment; the sponsor discontinues the study; the subject is discontinued from the study due to medical or safety concerns; or the product becomes commercially available in the subject*s country of residence, whichever comes first. During the extension period, main site assessments will be scheduled every 6 months. These assessments may be skipped for a visit at the discretion of the investigator and upon discussion of the investigator with the Medical Monitor if it is determined that the subject is unable to perform the assessments. At the EOT visit, subjects will receive their last administration of SHP611 and comprehensive assessments will be completed at the EOS visit.
If a subject discontinues from the study earlier than EOS, every effort should be made to complete assessments for the EOS and the safety follow-up visits. Subjects are to have the IDDD removed when they discontinue from the study, unless the subject is continuing to receive treatment with SHP611 through another mechanism (eg, commercially available) or the investigator determines that the IDDD should not be removed from the subject based upon a safety assessment and the IDDD (full or partial) should remain in the subject.

Intervention

SHP611 (formerly designated as HGT-1110), recombinant human arylsulfatase A (rhASA).
Subjects weighing >=7 kg (15.4 lbs) will receive 150 mg IT SHP611 weekly for 105 weeks. Subjects weighing >=5 kg (11.0 lbs) to <7 kg will receive 100 mg IT SHP611 weekly; however, when the subjects weigh more than 7 kg they will begin dosing with 150 mg IT SHP611 weekly for the remainder of the study.
SHP611 administration will be via an implanted SOPH-A-PORT Mini S IDDD. If the device becomes nonfunctional at any time during the study, it will be removed and may be replaced or revised as appropriate. If use of the IDDD is not possible a lumbar puncture (LP) may be utilized to obtain CSF samples and/or to deliver investigational drug product. It is anticipated that LP may have to be performed with anesthesia support at the discretion of the investigator. After 12 consecutive LPs, the feasibility of further use of LPs for that subject will be determined at the discretion of the investigator and the Shire medical monitor and documented in a note to file.

Study burden and risks

This study requires that the patient will visit hospital 213 times over a period of 215 weeks. A visit will take 3 to about 4 hours. The patient will go through screening assessments. The child will receive the SOPH-A-PORT Mini S intrathecal drug delivery system (IDDD) via surgical implantation.

The child will receive once weekly injections of the study drug at 150 mg or 100mg depending on the weight of the patient, along with additional assessments conducted at each of the visits as written below :
- Physical examination - every visit
- Heart tracing (ECG) - at one visit
- Blood draws- a total of 15 times for testing purposes. The volume of blood that will be taken each time will vary from 1 mL to 16.5 mL. The total amount of blood drawn in this study will be about 162.5 mL.
- Questionnaires about about the child*s symptoms and well-being
- Anesthesia, as determined by the study doctor
- Vital signs (blood pressure, breathing rate, temperature, and heart rate) - every visit
- Height, weight and head circumference
- Hearing and vision
- The child*s overall motor functions,
- Urine sample
- Cerebrospinal fluid sample- every visit
- MRS (Magnetic Resonance Spectroscopy) and MRI (Magnetic Resonance Imaging)

Risks associated with the study drug
Pain and headache during or after the injection of study drug are possible. The injection procedure may be done incorrectly, including injecting study drug into the surrounding tissue, or using the wrong type of needle or improper technique while injecting medicine.
Injection of study drug, as with any protein, carries with it the risk of an infusion-related reaction. It is possible that the child will develop an allergic reaction or antibodies against the injected study drug.
Possible reactions to study drug may include a change in mental status or level of consciousness that are not caused by anesthesia or sedation medicine and may either occur immediately or develop post-injection over time, sudden behavior changes, seizure, rash, pruitis (itching), fever, feeling of warmth, respiratory (breathing) problems, change in blood pressure and heart rate, pain, stiffness and possible death. Other risks include headache, vomiting, nausea, dry mouth, loss of smell, and metallic taste. The child may also have a tingling or painful sensation to the lower legs.

Risks with Sedation or General Anesthesia
Serious side effects of anesthesia are uncommon but include: breathing problems, swallowing problems, an irregular heartbeat, increases or decreases in blood pressure, difficulty putting in or taking out a breathing tube, rapid changes in body temperature, allergic reactions, heart attack or stroke, a reaction to a medicine used in the anesthesia, or death from complications including changes in heartbeat, blood pressure, body temperature, or breathing.

Risks with the implanted study device
Implantation of the device involves risks similar to other procedures that involve direct access to the CSF in the spinal canal area. The risks associated

with the insertion and use of the implanted device (the port and tube) includes the following.

The component parts of the device may be mishandled before, during or after implantation of the device. During surgery, the access port may be placed or positioned incorrectly. The catheter (tube) may be positioned incorrectly. Potential complications from the surgery include infection, bleeding or bruising. Spinal cord or nerve damage resulting in nerve pain, inflammation of the tissues around the spinal cord, or paralysis may also occur during surgery.

After surgery, the port may break, fracture, invert (flip over) or rotate. The tube or port may become clogged or blocked, making injection of the study drug difficult or impossible. The tube may become kinked, disconnect from the port, or break. The port or tube may poke through the skin and scar tissue may form around the device. The child*s body may not respond well and may reject the implanted device. If these complications happen, the device will need to be repaired or replaced with surgery. The wound may not heal properly and may open along the suture line. The skin where the port is placed may become infected. Infection may also occur under the skin around the port site and/or along the catheter (tube). An infection may require treatment with medication and hospitalization. Fluid or blood collection or bruising around the port or catheter or at the incision sites may occur after surgery.
The device is made of artificial materials that contain various chemicals. For instance, the catheter contains Barium, which is a chemical that helps the doctor to see the catheter on X-rays. When the catheter comes into contact with fluids like cerebrospinal fluid, saline solution or study drug solution, it is possible that some of these chemicals may seep out of the catheter and into the fluids, which may then come into contact with the spinal canal, spinal cord and brain. At the moment, it is not completely known to what extent that happens, what chemicals might leach out of the device, and what might be the consequences. The potential risks associated with chemicals and materials used in the production of the device are not known

There are additional risks associated with direct access (directly into the spinal fluid), including spinal fluid leaks or spinal fluid collection beneath the skin. In clinical trials to date, patients have experienced spinal fluid effusions or leakage. Although CSF leakage/effusions are often mild, not requiring surgical intervention, there are cases where additional surgery including repair or replacement the device and anesthesia is required. Infection in the nervous system including meningitis (infection of the membranes covering the brain and spinal cord) or encephalitis (infection of the brain) may occur and could lead to brain injury or death.

If the surgeon experiences difficulty in implanting the catheter in the usual way via a hollow needle inserted between two vertebrae (bones of the spine), it may be necessary to remove a small piece of the bone of the vertebrae. This procedure is called a laminotomy (or laminectomy, if the entire back part of

the vertebra is removed). If such a procedure is necessary, the surgery will take longer than foreseen, and a longer hospital stay may be needed to allow for adequate pain control. Additional or increased risks include:
• Spinal instability and/or curvature of the spine
• Nerve damage - Damage can cause numbness, weakness, problems with urination or bowel movements, or persistent pain
• Spinal fluid leak
• Bleeding
• Infection

During and after the surgery to put in the device, the child will be properly monitored to make sure the risks are reduced as much as possible.
The device might fail to work properly at some point during the study. This would require additional surgery under general anesthesia, similar to what was done at the time of the initial device implantation. Depending on the nature of the problem with the device, the surgery may be limited to the port implant site (under the skin on the side of your child*s chest) or be a repeat of the entire implant procedure (implant of the port and catheter under the skin and reinsertion of the catheter in the spinal canal). The risks of surgery and general anesthesia at the time of device replacement are the same as those at the time of the initial implantation. In some patients, more than one revision will take place during the course of the study.

If the study doctor determines that the study device should not be removed from the subject based upon a safety assessment and the study device (full or partial) remains in the subject, then the subject will continue in the study under the safety follow-up period upon completion of their last study treatment period visit.The risks of partial removal (leaving a complete or a portion of the catheter in the spinal canal) include catheter migration and infection.

Risks of lumbar puncture
Lumbar puncture can cause a mild to severe headache which may last for several days. Other risks associated with the lumbar puncture include pain at the site where the needle entered the spinal canal, meningitis (an infection of the nervous system), bleeding, spinal fluid leakage, nerve damage and paralysis. It is also possible that an attempt to collect fluid will not yield any fluid. In order to decrease the risk of headache associated with lumbar punctures, the child will be asked to lie flat in a bed for about two hours after the procedure is completed and drink plenty of liquids. Medication may be used as well.

Risks of blood collection
The child may experience pain and discomfort at the site where the needle enters the skin. There is a slight risk of fainting, bruising, or swelling. On rare occasions, an infection may develop at the site where the needle enters the skin.

Risk of Magnetic Resonance Imaging (MRI)and Magnetic Resonance Spectroscopy (MRS)
For some people lying still inside this tube can bring out a fear of closed spaces. The MRI/MRS is also noisy. In order to limit movements and get a good picture, the child will be placed under general anesthesia.

Risk of X-rays
Once the intrathecal device has been surgically implanted, x-rays will be taken to make sure that device has been placed properly. X-rays expose the body to a small amount of radiation. X-rays may be performed as needed throughout the study to check if the device is still placed correctly and that the catheter is working as expected.

Risk of Electrocardiograms (ECG)
The sticky pads may cause a temporary skin reaction or skin irritation. In addition, these pads may cause some discomfort when they are removed, similar to the pulling sensation associated with the removal of a Band-Aid.

Risks associated with genetic testing
If your child*s genetic research data are shared with unauthorized users, your child may be at risk of loss of the privacy of his/her health data. This risk is minimized by protections described in the section below on protection of personal information.

Other Risks
The procedures in this study may have risks that are not known at this time.
*

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1. The subject must have a documented diagnosis of MLD (Groups A - F)
• Low ASA activity in leukocytes (compared to laboratory normal range)
AND
• Elevated sulfatides in urine
2. The subject must have a gait disorder due to spastic ataxia or weakness attributable to MLD by the investigator and documented by a primary care physician or a specialist physician by 30 months of age (Groups A-C, and F), or be minimally symptomatic and >=6 to <18 months of age (Group D); or be early symptomatic and >=12 to <18 months of age (Group E). Subjects in Group E must have neurological symptoms documented by either a primary care physician or a specialist physician.
3. The subject's age at the time of informed consent, must be:
• Group A: 18 to 48 months of age
• Group B: 18 to 72 months of age
• Group C: 18 to 72 months of age
• Group D: >=6 to <18 months of age
• Group E: >=12 to <18 months of age
• Group F: 18 to 72 months of age
4. The subject's GMFC-MLD level at screening must be:
• Group A: GMFC-MLD category of 1 or 2
• Group B: GMFC-MLD category of 3
• Group C: GMFC-MLD category of 4
• Group D: minimally symptomatic, and has the same ASA allelic constitution as an older sibling with confirmed late infantile or juvenile onset MLD
• Group E: early symptomatic, >=12 to <18 months of age with a GMFC-MLD category of 1 or 2, and with a history of achieving stable walking (defined as at least 1 month of independent walking)
• Group F: GMFC-MLD category of 5 or 6
5. The subject and his/her parent/representative(s) must have the ability to

comply with the clinical protocol.
6. Subject's parent or legally authorized representative(s) must provide written informed consent prior to performing any study-related activities. Study-related activities are any procedures that would not have been performed during normal management of the subject.
Inclusion and exclusion criteria for the matched historical controls will be provided in the Statistical Analysis Plan (SAP).

Exclusion criteria

1. Multiple sulfatase disorder as determined by abnormal activity of another lysosomal sulfatase (based upon the reference laboratory's normal range) or a known genetic disorder other than MLD
2. History of bone marrow transplant (BMT), hematopoietic stem cell transplantation (HSCT), or gene therapy or undergoes BMT, HSCT, or gene therapy at any point during the study
3. Primary presentation of MLD was behavioral or cognitive symptoms (per investigator's clinical judgment); behavioral symptoms that are secondary to motor deficits (eg: tantrums in response to loss of motor skills) are not exclusionary.
4. The subject has any known or suspected hypersensitivity to agents used for anesthesia or has history of difficult airway or potential for airway compromise
5. Any other medical condition or serious comorbid illness that in the opinion of the investigator would preclude participation in the study
6. Subjects with laboratory, ECG, or vital sign abnormalities reflecting intercurrent illness that may compromise their safety during the trial should not be enrolled. Abnormal laboratory, vital sign and ECG results at screening should be reviewed with the Takeda medical monitor.
7. The subject is enrolled in another clinical study that involves use of any investigational product (drug or device) within 30 days or 5 halflives (whichever is longer) prior to study enrollment or at any time during the study
8. The subject has had prior exposure to SHP611
9. The subject must weight > 11lbs (5kg)
10. The subject has a condition that is contraindicated as described in the SOPH-A-PORT Mini S IDDD Instructions for Use
a. The subject has had, or may have, an allergic reaction to the materials of construction
b. The subject has shown an intolerance to an implanted device
c. The subject's body size is too small to support the size of the SOPH-A-PORT Mini S Access Port
d. The subject's drug therapy requires substances known to be incompatible with the materials of construction
e. The subject has a known or suspected local or general infection
f. The subject is at risk of abnormal bleeding due to a medical condition or therapy

g. The subject has one or more spinal abnormalities that could complicate safe implantation or fixation
h. The subject has a functioning CSF shunt device gene therapy at any point during the study
3. Primary presentation of MLD was behavioral or cognitive symptoms (per investigator's clinical judgment); behavioral symptoms that are secondary to motor deficits (eg: tantrums in response to loss of motor skills) are not exclusionary.
4. The subject has any known or suspected hypersensitivity to agents used for anesthesia or has history of difficult airway or potential for airway compromise
5. Any other medical condition or serious comorbid illness that in the opinion of the investigator would preclude participation in the study
6. Subjects with laboratory, ECG, or vital sign abnormalities reflecting intercurrent illness that may compromise their safety during the trial should not be enrolled. Abnormal laboratory, vital sign and ECG results at screening should be reviewed with the Shire medical monitor.
7. The subject is enrolled in another clinical study that involves use of any investigational product (drug or device) within 30 days or 5 halflives (whichever is longer) prior to study enrollment or at any time during the study
8. The subject has had prior exposure to SHP611
9. The subject must weight > 11lbs (5kg)
10. The subject has a condition that is contraindicated as described in the SOPH-A-PORT Mini S IDDD Instructions for Use
a. The subject has had, or may have, an allergic reaction to the materials of construction
b. The subject has shown an intolerance to an implanted device
c. The subject's body size is too small to support the size of the SOPH-APORT Mini S Access Port
d. The subject's drug therapy requires substances known to be incompatible with the materials of construction
e. The subject has a known or suspected local or general infection
f. The subject is at risk of abnormal bleeding due to a medical condition or therapy
g. The subject has one or more spinal abnormalities that could complicate safe implantation or fixation
h. The subject has a functioning CSF shunt device
Filtering criteria for the selection of the matched external control group will be provided in the statistical analysis plan (SAP).

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2020
Enrollment:	2
Type:	Actual

Medical products/devices used

Generic name:	SOPH-A-PORT Mini s
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	SHP611
Generic name:	RECOMBINANT HUMAN ARYLSULFATASE A

Ethics review

Approved WMO Date:	10-04-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-10-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-02-2020
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-05-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-05-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-02-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-01-2023
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-03-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2018-003291-12-NL
ClinicalTrials.gov	NCT03771898
CCMO	NL68647.029.19