Treating Leg Symptoms in Women with X-linked Adrenoleukodystrophy: A Key to Improving Sleep and Gait Performance

Published: 15-08-2022
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This study has been transitioned to CTIS with ID 2024-518989-27-00 check the CTIS register for the current data. Objective: Primary Aim (PHASE 1):To determine the prevalence of RLS in women with ALD.Secondary Aim (PHASE 2):To determine whether in a...

Ethical review	Approved WMO
Status	Pending
Health condition type	Neurological disorders congenital
Study type	Interventional

Summary

ID

NL-OMON52216

Source
ToetsingOnline

Brief title
Treating Leg Symptoms in Woman with X-ALD

Condition

- Neurological disorders congenital
- Peripheral neuropathies

Synonym
restless legs syndrome, x-gebonden adrenoleukodystrofie

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ELA

Intervention

Keyword: Restless legs syndrome, X-ALD

Outcome measures

Primary outcome

Main study parameters/endpoints:

IRLS Score - The International Restless Legs Severity Scale (IRLS) is a severity rating scale developed by the International Restless Legs Syndrome Study Group. This scale consists of 10 items that evaluate RLS symptoms, sleep disturbance from RLS, impact of RLS on daily activities, and mood disturbance resulting from RLS symptoms. The scores for the 10 items are summed to produce a total score, which ranges from 0 (no severity) to 40 (most severe).

Secondary outcome

Exploratory Aims (PHASE 2):

- To determine whether pramipexole will have improved self-reported and objective sleep metrics (e.g., quality, disturbance, sleep latency and duration, and periodic limb movements of sleep) in women with ALD.

- To determine whether pramipexole will improve measures of walking and motor performance (25 feet walk test as well as the timed up and go test).

Study description

Background summary

X-linked adrenoleukodystrophy (ALD) is a neurodegenerative disease that affects both men and women (Moser et al, 2001). As ALD is an X-linked disease, women were previously considered asymptomatic carriers. It is now known that even though adrenal insufficiency and cerebral disease occur in less than 1% of

women, more than 80% eventually develop progressive spinal cord disease [Engelen et al 2014, Habekost et al 2014]. Although both men and women develop spinal cord disease, there are differences. Our longitudinal study of the myelopathy in women revealed that the rate of progression over close to 8 years was small and generally not perceived as clinically relevant (Huffnagel et al, 2019), prompting a search for alternative approaches to improve quality of life in women with ALD. Recently was observed that women are more frequently affected by movement disorders independent of the demyelinating brain disease seen in men. In a pilot study performed by Eichler telephone interviews with 20 female adults with ALD and found that 8/20 had evidence of Restless Leg Syndrome (RLS). Restless Legs Syndrome (RLS) is a movement disorder characterized by a powerful urge to move the legs, usually accompanied by unpleasant dysesthesias, that is precipitated by rest, relieved by movement, and most pronounced in the evening or at night (Trenkwalder et al., 2018). These symptoms contribute to the primary morbidity of RLS which is severe sleep disturbance, interfering with both falling and staying asleep as well as overall sleep quality due to RLS sensory-motor symptoms and the presence of periodic limb movements of sleep (PLMS) (Winkelman et al., 2009; Fulda, 2015). The severe restlessness and sleep disturbance produce substantial acute psychological distress. Both idiopathic and secondary RLS are independently associated with substantial long-term detrimental effects on health, cognition, quality of life, psychiatric morbidity and all-cause mortality (Winkelman et al., 2009, Li et al., 2013, 2018, Kendzerska et al., 2017; Zhuang et al., 2019).

Study objective

This study has been transitioned to CTIS with ID 2024-518989-27-00 check the CTIS register for the current data.

Objective:
Primary Aim (PHASE 1):
To determine the prevalence of RLS in women with ALD.
Secondary Aim (PHASE 2):
To determine whether in a blinded crossover study a 8-week pramipexole treatment course will significantly reduce RLS symptoms compared to placebo by self-report (IRLS) and objective leg movement activity using the Suggested Immobilization Test (SIT) in women with ALD.

Study design

Study design:
Phase 1: observational study
Phase 2: cross-over placebo controlled intervention study

Intervention

Intervention (if applicable): Study medication: pramipexole or placebo capsules, 0.125 mg
Day 0-7: 0.125 mg, QD
Day 7-14: 0.125 mg, QD or BID
Day 14-60: 0.125 mg QD, 0.125 mg BID or 0.125mg QID

Study burden and risks

Pramipexole may be effective in restless legs syndrome.
Pramipexole is a well-known drug and adverse events are well characterized.

The burden of participation includes:
Phase 1:
- Remote: pre-screening visit (V1)
- Remote: RLS diagnostic visit (V2)
- Remote: RLS severity visit (V3)
Phase 2, part 1:
- In person: Initation of blined placeco-controled crossover study (V4)
- Remote: Follow-up visits (V5-V7)
Phase 2, part 2:
- In person: Switch-over visit (V8)
neurological assessments, polysomnography, questionnaires
- Remote: Follow-up visits (V9-V11)
- In person: Final study visit (V12)

Patients also have complete an online sleep diary and for the last 7 days of the study period actigraphy will be recorded in the home setting.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

PHASE 1 (PREVALENCE STUDY)
Inclusion Criteria:
- Women of any ethnic origin.
- Ability to provide verbal consent
- A willingness and ability to comply with study procedures.
- Age 18-75 years
- Metabolically or genetically confirmed diagnosis of ALD

PHASE 2 (CROSS-OVER STUDY)
Inclusion Criteria:
- Participation in Phase 1
- Ability to provide written informed consent
- Women with ALD who have Restless Leg Syndrome (IRLS > 15)

Exclusion criteria

1. Pregnant. Research staff perform pregnancy tests upon visit to center.
2. Participants with active or unstable major psychiatric disorder other than ALD, who, in the investigators* judgement, require further treatment
3. Use of dopaminergic agonists or antagonists within the last 30 days
4. Alcohol use disorder within the last 30 days
5. History of being treated for restless legs syndrome, specifically with dopamine agonist medications
6. Methamphetamine or benzodiazepine dependence in the last 30 days
7. Neurological disorder or cardiovascular disease raising safety concerns about use of pramipexole and/or judged to interfere with ability to assess efficacy of the treatment
8. Medical instability considered to interfere with study procedures

9. Renal disease judged to interfere with drug metabolism and excretion
10. Patients who are deemed a fall risk as determined by the PI

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	30-06-2022
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Pramipexole
Generic name:	Pramipexole
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	15-08-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	28-09-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-12-2022
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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
EU-CTR	CTIS2024-518989-27-00
EU-CTR	CTIS2024-518989-27-01
EudraCT	EUCTR2022-001203-40-NL
CCMO	NL78835.018.22