Proof-of-concept study on treating cognitive side-effects of Tamoxifen with guanfacine in postmenopausal women with E2/Pg receptor-positive breast cancer.

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Provide proof-of-concept for the hypothesis that guanfacine diminishes cognitive side-effects in ER+ BC patients treated with adjuvant hormonal therapy. Secondary, provide data for power calculations in later studies.

Ethical review	Approved WMO
Status	Pending
Health condition type	Cognitive and attention disorders and disturbances
Study type	Interventional

Summary

ID

NL-OMON43176

Source
ToetsingOnline

Brief title
A study on the effect of guanfacine of the side effects of Tamoxifen

Condition

- Cognitive and attention disorders and disturbances

Synonym
attentional deficit, Memory loss

Research involving
Human

Sponsors and support

Primary sponsor: Limoxifen BV
Source(s) of monetary or material Support: Limoxifen BV

Intervention

Keyword: Breast cancer, Guanfacine, Tamoxifen

Outcome measures

Primary outcome

Change in cognitive functions from placebo to guanfacine condition. Cognitive functions are assessed by standardized neuropsychological tasks and include executive functions, attention, memory, and processing speed.

Secondary outcome

Change in depression / anxiety and physical side-effects from placebo to guanfacine condition. Affect is measured by a standardized questionnaire (POMS). Physical side-effects recorded include those reported for tamoxifen and guanfacine. The most commonly reported side effects for tamoxifen (hot flushes, vaginal bleeding and secretions, pruritus vulvae) and guanfacine (sedation, headache, abdominal pains, signs and symptoms related to changes in blood pressure) are explicitly asked about during a weekly structured telephone interview.

Study description

Background summary

Following primary treatment, Estradiol Receptor positive (ER+) Breast Cancer (BC) is usually treated with adjuvant hormone therapy. The latter consists of Tamoxifen or Aromatase Inhibitors (AI). Apart from hormonal side-effects,

cognitive and affective side-effects are also reported, a finding that is supported by neuropsychological research. These effects probably stem from interactions with sex hormone receptors in the brain. Guanfacine is a noradrenergic alpha2A agonist, that has been shown to improve catecholaminergic Prefrontal Cortex (PFC) network connections. Therefore, it was hypothesized that guanfacine will have a positive effect on cognitive/affective side effects of adjuvant hormonal treatment.

Study objective

Provide proof-of-concept for the hypothesis that guanfacine diminishes cognitive side-effects in ER+ BC patients treated with adjuvant hormonal therapy. Secondary, provide data for power calculations in later studies.

Study design

Double-blind placebo-controlled cross-over

Intervention

Guanfacine, 0.03-047. mg/kg (2 or 3 mg) once daily, for four consecutive weeks, and placebo during four weeks. Note that all participants are on stable 20 mg daily Tamoxifen treatment, on inclusion, after completion and during all study conditions.

Study burden and risks

The burden associated with the study consists of a screening and baseline visit, including blood sampling and 1-hour cognitive testing. Blood sampling and cognitive testing are repeated on two other visits. Finally, a weekly telephone interview on physical side-effects. Risks are those associated with guanfacine intake, which are well-known and closely monitored.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• treated with adjuvant tamoxifen therapy for ER receptor-positive Breast Cancer
• on tamoxifen treatment for 3-18 months, 20 mg stable dosing for at least a month
• postmenopausal
• subjective complaints of cognitive side effects
• weight between 50 and 90 kg
• 20 <= BMI <= 27
• fluent in Dutch
• normal (or corrected-to-normal) vision
• normal dexterity

Exclusion criteria

• prior exposure to chemotherapy
• diagnosis of prior or existing cardiovascular, neurological or psychiatric disorder that may influence sensitivity to guanfacine or study endpoint(s)
• contraindications for guanfacine (hypotension, bradycardia, syncope, extended QT interval)
• (prior) diagnosis of ADHD
• use of clonidine or other anti-hypertensive agents
• use of drugs with a strong influence on CYP2D6, CYP3A4/5 (e.g., ketoconazole, carbamazepine)
• use of SSRIs and other antidepressants

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-03-2016
Enrollment:	15
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	22-03-2016
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	26-07-2016
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen

	(Wijchen)
Approved WMO Date:	22-02-2017
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	06-06-2017
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

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	EUCTR2016-000506-11-NL
CCMO	NL56785.072.16