# T&T trial: adding Testosterone to Tamoxifen in male breast cancer patients

Published: 04-04-2022 Last updated: 16-11-2024

Primary Objective: To assess the safety profile (AEs, SAEs) on combined treatment with tamoxifen and testosterone.Secondary Objectives:• AR to ER ratio on baseline FES- and FDHT-PET imaging (assessed per lesion and per patient by quantitative...

Ethical review	Approved WMO
Status	Completed
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

# Summary

#### ID

NL-OMON51371

**Source** ToetsingOnline

Brief title T&T trial

# Condition

• Breast neoplasms malignant and unspecified (incl nipple)

**Synonym** male breast cancer

**Research involving** Human

### **Sponsors and support**

**Primary sponsor:** Universitair Medisch Centrum Groningen **Source(s) of monetary or material Support:** Ministerie van OC&W

### Intervention

Keyword: male breast cancer, Tamoxifen, Testosterone

#### **Outcome measures**

#### **Primary outcome**

Safety profile, defined as the number of AEs and SAEs that occur while on tamoxifen and testosterone treatment.

#### Secondary outcome

• AR to ER ratio on baseline FES- and FDHT-PET imaging (assessed per lesion and

per patient by quantitative analysis using standardized uptake values (SUV))

and/or tumor tissue (assessed by percentage of ER and AR expression).

• Treatment response on 8 weeks FDG-PET/CT (assessed per lesion and per patient

by quantitative analysis using standardized uptake values (SUV).

• Relation between baseline imaging and tumor characteristics to treatment

response.

• Difference in adverse events between the two testosterone dosages.

# **Study description**

#### **Background summary**

Male breast cancer (BC) is rare and usually shows favorable characteristics with expression of the estrogen-, progesterone- and androgen receptor (ER, PR and AR), but not the human epidermal growth factor-2 receptor (HER2). In ER+ BC, contrary to triple negative BC, the AR appears to function as tumor suppressor. Recently, in preclinical ER+ BC models growth inhibition was shown when an androgen agonist was combined with standard ER modulator tamoxifen. Therefore, this could potentially be a rational treatment option for patients with ER+ BC as well. However, earlier studies in female BC patients showed considerable side effects due to virilization, and treatment with androgen agonists was subsequently abandoned. No data exist in male BC patients, but it is highly conceivable that virilization is not as concerning in male BC patients and could potentially even be considered as beneficial. Recent data suggest that the ratio of AR to ER in the tumor is relevant for response to AR and ER targeting treatments. Assessment in tumor tissue however can only reflect one part of one tumor lesion. Whole body ER and AR expression can be visualized using  $16\alpha$ -[18F]fluoro- $17\beta$ oestradiol (FES) positron emission tomography (PET) and [18F]fluoro-dihydrotestosterone (FDHT) PET. These scans potentially allow fine-tuning of combined treatment with an androgen agonist and tamoxifen. Ultimately, this could lead to a new, additional combined endocrine approach in the treatment of male BC patients. Particularly regarding the expected favorable (side) effects of this combination in men, this could contribute to improved quality of life in male BC patients.

### Study objective

Primary Objective: To assess the safety profile (AEs, SAEs) on combined treatment with tamoxifen and testosterone.

Secondary Objectives:

• AR to ER ratio on baseline FES- and FDHT-PET imaging (assessed per lesion and per patient by quantitative analysis using standardized uptake values (SUV) and/or tumor tissue (assessed by percentage of ER and AR expression).

• Treatment response on 8 weeks FDG-PET/CT.

• Relation between baseline imaging and tumor characteristics to treatment response.

• Difference in adverse events between the two testosterone dosages.

• Increase in free testosterone levels, related to treatment response and toxicity.

• Monitoring of blood hematocrite, related to testosterone treatment.

• CtDNA for ER mutation analysis and CTCs (for ER and AR expression) at baseline, prior to cycle 2 and 3, related to response and FES- and FDHT PET imaging.

### Study design

This is a concise single arm, feasibility study, which will be executed in the University Medical Center Groningen, The Netherlands. Male patients with metastatic BC (n=6) are eligible for this study after at least 1 line of conventional endocrine therapy.

### Intervention

After the baseline imaging with FES- and FDHT-PET is completed, tamoxifen 20mg 1dd1 (standard dosage) plus testosterone (Androgel®) will be started. The first 3 patients will receive 25mg testosterone once daily (half the standard starting dosage for male hypogonadism). If this is well tolerated after 3 weeks, the dosage will be increased to 50mg once daily. Out of precaution, the

safety profile of the 50mg dosage in the first 3 patients will be evaluated after all 3 patients have received 50mg testosterone for 8 weeks, prior to proceeding to the next 3 patients. Patients will be treated with tamoxifen and testosterone until disease progression or unacceptable toxicity.

#### Study burden and risks

At baseline two additional visits for FES- and FDHT PET imaging are required. FES- and FDHT PET imaging, with a standard 3 Mbq/kg injection dose, lead to an additional radiation exposure of 4.6 and 3.6 mSv respectively. This is comparable to a standard FDG PET for each scan. Further participation will be embedded in standard care, meaning no additional drawing of blood, site visits or physical examinations will be required in addition to those already required for standard care. Tamoxifen is part of the standard treatment strategy in male BC and is known to induce toxicity such as hot flashes and loss of libido. Testosterone is known to induce virilization. Based on the well-known safety profile of tamoxifen and testosterone separately in men, and the previous data of combined tamoxifen and AR agonists in female BC patients, showing no additional toxicity other than expected based on the separate compounds, no unexpected toxicity of the combination is expected in male BC patients. Furthermore, it is conceivable that the combined treatment is better tolerated (and possibly more effective) than standard tamoxifen alone in men with BC.

# Contacts

#### Public

Universitair Medisch Centrum Groningen

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# **Trial sites**

# **Listed location countries**

Netherlands

# **Eligibility criteria**

#### Age

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

# **Inclusion criteria**

1. Male

2. A history of proven ER+ (>10% of cells), AR+ (>10% of cells), and HER2-metastatic BC

3. Tumor progression after at least one line of conventional endocrine therapy (tamoxifen, AI, fulvestrant, CDK4/6, ±LHRH analogue).

- 4. Age >= 18 years
- 5. Adequate hematological, renal and liver function as follows:
- Absolute neutrophil count > 1.5 x 109/L
- Platelet count >100 x 109/L
- White blood cell count  $>3 \times 109/L$
- AST and ALT <2.5 or <5.0 in case of liver metastases x upper limit of normal (ULN)
- Creatinine clearance >50mL/min
- Prothrombin time, partial thromboplastin time and INR <1.5 x ULN
- 6. Written informed consent

# **Exclusion criteria**

- 1. History of prostate, testicular or liver cancer
- 2. Patients already using testosterone supplements
- 3. Patients using medication with anti-androgenic effects (e.g. spironolactone)
- 4. Elevated PSA (>4 $\mu$ g/L) or severe urinary tract problems (as defined with a

Prostate Symptom Score >19). Patients with known BRCA mutation and PSA \*3  $\mu$ g/L will be referred to the urologist for prostate cancer screening, and can participate if they have no signs of prostate cancer.

5. Hematocrit >50%

6. Patients with uncontrolled hypertension, diabetes mellitus or other significant cardiovascular morbidity.

7. Patients with recent history of coronary artery disease or trombo-embolic events within 6 months prior to screening

8. Severe concurrent disease, infection, co morbid condition that, in the

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judgment of the investigator would make the patient inappropriate for enrollment

9. Visceral crisis and/or rapid progression necessitating chemotherapy

- 10. Previous allergic reaction to androgen agonists
- 11. Contra-indication for PET imaging
- 12. Tamoxifen or fulvestrant treatment <5 weeks prior to FES-PET.

# Study design

# Design

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

# Recruitment

NL	
Recruitment status:	Completed
Start date (anticipated):	10-11-2022
Enrollment:	6
Туре:	Actual

### Medical products/devices used

Product type:	Medicine
Brand name:	Testosterone/Androgel
Generic name:	Testosterone/Androgel
Registration:	Yes - NL outside intended use

# **Ethics review**

Approved WMO	
Date:	04-04-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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Approved WMO	
Date:	20-10-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	
Date:	26-02-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

# **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	EUCTR2021-002170-72-NL
ССМО	NL79433.042.22
Other	volgt