Clinical trial results:
A prospective, randomised multi-centre phase II study evaluating the adjuvant, neoadjuvant or palliative treatment with tamoxifen +/- GnRH analogue versus aromatase inhibitor + GnRH analogue in male breast cancer patients.

Summary

EudraCT number	2009-015122-11
Trial protocol	DE
Global end of trial date	12 June 2018

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021
Summary attachment (see zip file)	MALE synopsis (GBG54_MALE_Clinical Study Report_Synopsis_2020-10-14.pdf)

Trial information

Trial identification

Sponsor protocol code	GBG54

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01638247
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GBG Forschungs GmbH
Sponsor organisation address	Martin-Behaim-Str. 12, Neu-Isenburg, Germany, 63263
Public contact	Medicine and Research, GBG Forschungs GmbH, +49 610274800, publications@gbg.de
Scientific contact	Medicine and Research, GBG Forschungs GmbH,, +49 610274800, publications@gbg.de

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 November 2017
Global end of trial reached?	Yes
Global end of trial date	12 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of estradiol suppression between the three treatment arms after three months by a standardized procedure for routine testing

Protection of trial subjects:

The trial protocol including amendments, the patient information and the informed consent were reviewed and approved from a properly constituted IRB/IEC for each site prior to the study start. The trial was in compliance with the International Conference on Harmonization (ICH) - Harmonized Tripartite Guideline for Good Clinical Practice (GCP) (E6), and the Commission Directives in the European Community as well as with the applicable German national laws and regulations, and with Declaration of Helsinki and its revisions in all aspects of preparation, monitoring, reporting, auditing, and archiving. IDMC was to ensure the ethical conduct of the trial and to protect patients' safety interests in this study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 October 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	10 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 52
Worldwide total number of subjects	52
EEA total number of subjects	52

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	31
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Approximately 55 months (Q-IV 2012 –Q-V 2017). 56 patients were randomized and 52 patients (17 in Tamoxifen arm, 17 in Tamoxifen + GnRH arm and 18 in Exemestane + GnRH arm) started therapy.

Pre-assignment

Screening details:

Male patients of at least 18 years of age with unilateral or bilateral breast cancer at primary diagnosis with estrogen receptor and/or
progesterone receptor positive tumor. Enrollment in the neoadjuvant, adjuvant (with adequate surgical treatment with histological complete resection including axillary lymph nodes) and metastatic setting possible.

Pre-assignment period milestones

Number of subjects started	52
Number of subjects completed	52

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tamoxifen

Arm description:

Tamoxifen 20 mg (standard therapy).

Arm type	Active comparator
Investigational medicinal product name	Exemestane (AROMASIN®)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg per os each day one tablet

Arm title	Tamoxifen + GnRH

Arm description:

Tamoxifen 20 mg + gonadotropin releasing hormone analogue (GnRH).

Arm type	Experimental
Investigational medicinal product name	Tamoxifen plus goserelin (ZOLADEX®) or leuprorelin (TRENANTONE®)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Implant
Routes of administration	Subcutaneous use

Dosage and administration details:

Tamoxifen 20mg, per os, each day one tablet,
GnRH: goserelin (ZOLADEX®) or leuprorelin (TRENANTONE®) used according to investigators choice, according to the manufacturer´s summary of product characteristics, once every three months (twice within the study) for six months or until progression, patient’s request or withdrawal from the study

(whatever comes first).

Arm title	Exemestane + GnRH
Arm description: Exemestane 25mg + gonadotropin releasing hormone analogue (GnRH).	
Arm type	Experimental
Investigational medicinal product name	Exemestane (AROMASIN®) plus GnRH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Exemestane (AROMASIN®), 25 mg, per os, each day one tablet
GnRH: goserelin (ZOLADEX®) or leuprorelin (TRENANTONE®) used according to investigators choice, according to the manufacturer´s summary of product characteristics, once every three months (twice within the study) for six months or until progression, patient's request or withdrawal from the study (whatever comes first).

Number of subjects in period 1	Tamoxifen	Tamoxifen + GnRH	Exemestane + GnRH
Started	17	17	18
Completed	16	16	17
Not completed	1	1	1
Patient`s wish	-	-	1
Adverse event, non-fatal	-	1	-
Progression	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Tamoxifen
Reporting group description:	
Tamoxifen 20 mg (standard therapy).	
Reporting group title	Tamoxifen + GnRH
Reporting group description:	
Tamoxifen 20 mg + gonadotropin releasing hormone analogue (GnRH).	
Reporting group title	Exemestane + GnRH
Reporting group description:	
Exemestane 25mg + gonadotropin releasing hormone analogue (GnRH).	

Reporting group values	Tamoxifen	Tamoxifen + GnRH	Exemestane + GnRH
Number of subjects	17	17	18
Age categorical Units: Subjects			
Age continuous			
patients evaluable at 3 months			
Units: years			
median	59	60	66
full range (min-max)	37 to 83	45 to 82	45 to 80
Gender categorical Units: Subjects			
Female	0	0	0
Male	17	17	18

Reporting group values	Total		
Number of subjects	52		
Age categorical Units: Subjects			
Age continuous			
patients evaluable at 3 months			
Units: years			
median			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	0		
Male	52		

Subject analysis sets	
Subject analysis set title	Tamoxifen
Subject analysis set type	Per protocol

Subject analysis set description:
all evaluable patients at 3 months

Subject analysis set title	Tamoxifen + GnRH
Subject analysis set type	Per protocol

Subject analysis set description:
all evaluable patients at 3 months

Subject analysis set title	Exemestane + GnRH
Subject analysis set type	Per protocol

Subject analysis set description:
all evaluable patients at 3 months

Reporting group values	Tamoxifen	Tamoxifen + GnRH	Exemestane + GnRH
Number of subjects	17	15	18
Age categorical Units: Subjects			
Age continuous			
patients evaluable at 3 months			
Units: years median full range (min-max)	 59.0 37.0 to 83.0	 60.0 45.0 to 82.0	 66.0 45.0 to 80.0
Gender categorical Units: Subjects			
Female	0	0	0
Male	17	15	18

End points

End points reporting groups

Reporting group title	Tamoxifen
Reporting group description: Tamoxifen 20 mg (standard therapy).	
Reporting group title	Tamoxifen + GnRH
Reporting group description: Tamoxifen 20 mg + gonadotropin releasing hormone analogue (GnRH).	
Reporting group title	Exemestane + GnRH
Reporting group description: Exemestane 25mg + gonadotropin releasing hormone analogue (GnRH).	
Subject analysis set title	Tamoxifen
Subject analysis set type	Per protocol
Subject analysis set description: all evaluable patients at 3 months	
Subject analysis set title	Tamoxifen + GnRH
Subject analysis set type	Per protocol
Subject analysis set description: all evaluable patients at 3 months	
Subject analysis set title	Exemestane + GnRH
Subject analysis set type	Per protocol
Subject analysis set description: all evaluable patients at 3 months	

Primary: changes in estradiol levels from baseline to 3 months

End point title	changes in estradiol levels from baseline to 3 months
End point description:	
End point type	Primary
End point timeframe: from baseline to 3 months	

End point values	Tamoxifen	Tamoxifen + GnRH	Exemestane + GnRH	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	17[1]	15[2]	18[3]	
Units: ng/L				
median (full range (min-max))	17 (-6 to 29)	-23 (-40 to 22)	-18.5 (-100 to 21)	

Notes:

[1] - patients evaluable at 3 months

[2] - patients evaluable at 3 months

[3] - patients evaluable at 3 months

Statistical analyses

Statistical analysis title	Change in estradiol level BL to 3 months 3 arms
Comparison groups	Tamoxifen v Tamoxifen + GnRH v Exemestane + GnRH
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [4]
Method	Kruskal-wallis

Notes:

[4] - Primarily, the Kruskal-Wallis test (due to the failed test of normality) was used to compare the decrease of estradiol level after three months study treatment between the three study arms.

Statistical analysis title	Change in estradiol level BL to 3 months B vs A
Statistical analysis description:	
Pairwise Wilcoxon tests arm B vs A	
Comparison groups	Tamoxifen + GnRH v Tamoxifen
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Change in estradiol level BL to 3 months C vs A
Comparison groups	Tamoxifen v Exemestane + GnRH
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Change in estradiol level BL to 3 months C vs B
Statistical analysis description:	
comparison of Arm C vs B was unplanned	
Comparison groups	Tamoxifen + GnRH v Exemestane + GnRH
Number of subjects included in analysis	33
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.587
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events occurring during the study treatment period were reported.

Adverse event reporting additional description:

Non-serious AEs are reported per patient; any grade (1-4) during the complete treatment duration for the overall safety Population are reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Tamoxifen
Reporting group description:	
Tamoxifen	
Reporting group title	Tamoxifen + GnRH
Reporting group description:	
Tamoxifen + GnRH	
Reporting group title	Exemestane + GnRH
Reporting group description:	
Exemestane + GnRH	

Serious adverse events	Tamoxifen	Tamoxifen + GnRH	Exemestane + GnRH
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 18 (16.67%)	1 / 16 (6.25%)	1 / 18 (5.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intestinal ischaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Groin abscess			

subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Tamoxifen	Tamoxifen + GnRH	Exemestane + GnRH
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 18 (88.89%)	16 / 16 (100.00%)	16 / 18 (88.89%)
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 18 (11.11%)	10 / 16 (62.50%)	12 / 18 (66.67%)
occurrences (all)	2	10	12
Vascular disorders			
subjects affected / exposed	2 / 18 (11.11%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 18 (27.78%)	5 / 16 (31.25%)	10 / 18 (55.56%)
occurrences (all)	5	5	10
Irritability			
subjects affected / exposed	0 / 18 (0.00%)	2 / 16 (12.50%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
General disorders and administrative site conditions			

subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 18 (5.56%)	8 / 16 (50.00%)	7 / 18 (38.89%)
occurrences (all)	1	8	7
Reproductive system disorders			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Psychiatric disorders			
Libido decreased			
subjects affected / exposed	3 / 18 (16.67%)	9 / 16 (56.25%)	10 / 18 (55.56%)
occurrences (all)	3	9	10
Sleep disorder			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	3 / 18 (16.67%)
occurrences (all)	0	1	3
Mental disorder	Additional description: Other psychiatric disorders, any grade		
subjects affected / exposed	1 / 18 (5.56%)	1 / 16 (6.25%)	2 / 18 (11.11%)
occurrences (all)	1	1	2
Investigations			
Total cholesterol increased			
subjects affected / exposed	3 / 18 (16.67%)	3 / 16 (18.75%)	9 / 18 (50.00%)
occurrences (all)	3	3	9
High density lipoprotein abnormal	Additional description: HDL cholesterol abnormal (decreased), any grade		
subjects affected / exposed	9 / 18 (50.00%)	7 / 16 (43.75%)	5 / 18 (27.78%)
occurrences (all)	9	7	5
Low density lipoprotein abnormal	Additional description: LDL cholesterol abnormal (increased), any grade		
subjects affected / exposed	2 / 18 (11.11%)	1 / 16 (6.25%)	4 / 18 (22.22%)
occurrences (all)	2	1	4
Prostatic specific antigen abnormal	Additional description: PSA abnormal (increased), any grade		
subjects affected / exposed	4 / 18 (22.22%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	4	0	1
Injury, poisoning and procedural complications			
Injury and poisoning, procedural complications			

subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	3 / 18 (16.67%)
occurrences (all)	0	0	3
Headache			
subjects affected / exposed	1 / 18 (5.56%)	1 / 16 (6.25%)	1 / 18 (5.56%)
occurrences (all)	1	1	1
Other neurological disorders			
subjects affected / exposed	1 / 18 (5.56%)	1 / 16 (6.25%)	1 / 18 (5.56%)
occurrences (all)	1	1	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Eye disorder			
subjects affected / exposed	2 / 18 (11.11%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	1
Gastrointestinal disorders			
Gastrointestinal disorder			
subjects affected / exposed	4 / 18 (22.22%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	4	0	1
Hepatobiliary disorders			
Hepatobilary disorders			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Renal and urinary disorders			

Renal and urinary disorders			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	3 / 18 (16.67%)	4 / 16 (25.00%)	2 / 18 (11.11%)
occurrences (all)	3	4	2
Bone pain			
subjects affected / exposed	3 / 18 (16.67%)	4 / 16 (25.00%)	5 / 18 (27.78%)
occurrences (all)	3	4	5
Arthralgia			
subjects affected / exposed	2 / 18 (11.11%)	0 / 16 (0.00%)	2 / 18 (11.11%)
occurrences (all)	2	0	2
Musculoskeletal disorder	Additional description: Other musculo-skeletal disorders, any grade		
subjects affected / exposed	1 / 18 (5.56%)	2 / 16 (12.50%)	1 / 18 (5.56%)
occurrences (all)	1	2	1
Infections and infestations			
Infection			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Metabolic disorder			
subjects affected / exposed	1 / 18 (5.56%)	1 / 16 (6.25%)	0 / 18 (0.00%)
occurrences (all)	1	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 July 2016	There was one protocol amendment with the following main changes: Patients with DCIS will not be enrolled due to potential overtherapy. Extension of staging and lab value period before randomization. Adaption of PSA, ASAT, ALAT and bilirubin values.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33538790