



Clinical trial results:

Karisma Pilot: A randomized, open pilot study to investigate the mammographic density reduction in healthy women ,within the Karma cohort, for two different doses of tamoxifen.

Summary

EudraCT number	2014-005005-20
Trial protocol	SE
Global end of trial date	03 February 2016

Results information

Result version number	v1 (current)
This version publication date	16 March 2023
First version publication date	16 March 2023

Trial information

Trial identification

Sponsor protocol code	2014-005005-20
-----------------------	----------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04079517
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Karolinska Institutet
Sponsor organisation address	Nobels väg 6, Solna, Sweden, 17177
Public contact	Per Hall, Södersjukhuset, Karma Study Center Karolinska Institutet, 0046 +4670750 2110, per.hall@ki.se
Scientific contact	Per Hall, Södersjukhuset, Karma Study Center Karolinska Institutet, 0046 +4670750 2110, per.hall@ki.se

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	29 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 February 2016
Global end of trial reached?	Yes
Global end of trial date	03 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective: To identify time to mammographic density change in healthy women using two different doses of tamoxifen.

Protection of trial subjects:

Side effects were reported in a structured questionnaire at baseline and months 3, 6, and 9.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 March 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	32
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 723 participants of the Karma cohort, a prospective screening cohort,⁸ were invited when they attended their biannual screening mammography.

Pre-assignment

Screening details:

Out of 723 invited 56 (7.7%) women were willing to participate, 14 did not fulfill exclusion/inclusion criteria and 42 (5.8%) were finally included.

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	10 mg of tamoxifen
------------------	--------------------

Arm description:

This arm studied the side effects, adherence and a possible difference in effect after exposure to 10 mg of tamoxifen.

Arm type	Experimental
Investigational medicinal product name	TAMOXIFEN
Investigational medicinal product code	SUB10825MIG
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Daily doses, 10 mg, of tamoxifen for 6 months.

Arm title	20 mg of tamoxifen
------------------	--------------------

Arm description:

This arm studied the side effects, adherence and a possible difference in effect after exposure to 20 mg of tamoxifen.

Arm type	Active comparator
Investigational medicinal product name	TAMOXIFEN
Investigational medicinal product code	SUB10825MIG
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Daily doses, 20 mg, of tamoxifen for 6 months.

Number of subjects in period 1	10 mg of tamoxifen	20 mg of tamoxifen
Started	23	19
Completed	18	15
Not completed	5	4
Adverse event, non-fatal	5	4

Baseline characteristics

Reporting groups

Reporting group title	10 mg of tamoxifen
Reporting group description: This arm studied the side effects, adherence and a possible difference in effect after exposure to 10 mg of tamoxifen.	
Reporting group title	20 mg of tamoxifen
Reporting group description: This arm studied the side effects, adherence and a possible difference in effect after exposure to 20 mg of tamoxifen.	

Reporting group values	10 mg of tamoxifen	20 mg of tamoxifen	Total
Number of subjects	23	19	42
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	59.74	62.32	
standard deviation	± 8.48	± 6.74	-
Gender categorical Units: Subjects			
Female	23	19	42
Postmenopausal			
Number of women who are premenopausal and postmenopausal.			
Units: Subjects			
Postmenopausal	16	15	31
Premonopausal	7	4	11

End points

End points reporting groups

Reporting group title	10 mg of tamoxifen
Reporting group description: This arm studied the side effects, adherence and a possible difference in effect after exposure to 10 mg of tamoxifen.	
Reporting group title	20 mg of tamoxifen
Reporting group description: This arm studied the side effects, adherence and a possible difference in effect after exposure to 20 mg of tamoxifen.	

Primary: Change in mammographic density at 3 months following start of two different doses of tamoxifen

End point title	Change in mammographic density at 3 months following start of two different doses of tamoxifen
End point description: Average changes of mammographic density at 3 months compared to baseline were calculated with 95% confidence intervals.	
End point type	Primary
End point timeframe: 3 months compared to baseline.	

End point values	10 mg of tamoxifen	20 mg of tamoxifen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	14		
Units: percent				
arithmetic mean (confidence interval 95%)	-2.1 (-4.2 to -0.1)	-1.3 (-3.7 to 1.1)		

Statistical analyses

Statistical analysis title	Changes in mammographic density at 3 months
Statistical analysis description: Average changes of mammographic density at 3 months, compared to baseline, were calculated with 95% confidence intervals.	
Comparison groups	10 mg of tamoxifen v 20 mg of tamoxifen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	> 0.05
Method	t-test, 2-sided

Primary: Change in mammographic density at 6 months, following start of two different doses of tamoxifen

End point title	Change in mammographic density at 6 months, following start of two different doses of tamoxifen
-----------------	---

End point description:

Average changes of mammographic density at 6 months, compared to baseline, were calculated with 95% confidence intervals.

End point type	Primary
----------------	---------

End point timeframe:

6 months compared to baseline.

End point values	10 mg of tamoxifen	20 mg of tamoxifen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	14		
Units: percent				
arithmetic mean (confidence interval 95%)	-3.1 (-5.7 to -0.5)	-1.0 (-4.1 to 2.0)		

Statistical analyses

Statistical analysis title	Changes in mammographic density at 6 months
----------------------------	---

Statistical analysis description:

Average changes of mammographic density at 6 months, compared to baseline, were calculated with 95% confidence intervals.

Comparison groups	10 mg of tamoxifen v 20 mg of tamoxifen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	> 0.05
Method	t-test, 2-sided

Primary: Change in mammographic density at 9 months, following start of two different doses of tamoxifen

End point title	Change in mammographic density at 9 months, following start of two different doses of tamoxifen
-----------------	---

End point description:

End point type	Primary
----------------	---------

End point timeframe:

9 months compared to baseline.

End point values	10 mg of tamoxifen	20 mg of tamoxifen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	14		
Units: percent				
arithmetic mean (confidence interval 95%)	-3.3 (-6.1 to -0.5)	-2.5 (-5.7 to 0.8)		

Statistical analyses

Statistical analysis title	Changes in mammographic density at 9 months
Statistical analysis description:	
Average changes of mammographic density at 9 months, compared to baseline, were calculated a with 95% confidence intervals.	
Comparison groups	10 mg of tamoxifen v 20 mg of tamoxifen
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	> 0.05
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During intake of IMP plus 1 month.

Adverse event reporting additional description:

A total of 911 symptom reports were registered but no serious adverse event was seen.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	18.0
--------------------	------

Reporting groups

Reporting group title	10 mg of tamoxifen
-----------------------	--------------------

Reporting group description:

This arm studied the side effects, adherence and a possible difference in effect after exposure to 10 mg of tamoxifen.

Reporting group title	20 mg of tamoxifen
-----------------------	--------------------

Reporting group description:

This arm studied the side effects, adherence and a possible difference in effect after exposure to 20 mg of tamoxifen.

Serious adverse events	10 mg of tamoxifen	20 mg of tamoxifen	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	0 / 19 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	10 mg of tamoxifen	20 mg of tamoxifen	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 23 (78.26%)	18 / 19 (94.74%)	
Nervous system disorders			
Numbness/tingling in the hands and feet			
subjects affected / exposed	3 / 23 (13.04%)	5 / 19 (26.32%)	
occurrences (all)	3	5	
Mood swings			
subjects affected / exposed	6 / 23 (26.09%)	6 / 19 (31.58%)	
occurrences (all)	6	6	

Headache			
subjects affected / exposed	10 / 23 (43.48%)	9 / 19 (47.37%)	
occurrences (all)	10	9	
Concentration ability impaired			
subjects affected / exposed	1 / 23 (4.35%)	2 / 19 (10.53%)	
occurrences (all)	1	2	
Feeling sad			
subjects affected / exposed	3 / 23 (13.04%)	5 / 19 (26.32%)	
occurrences (all)	3	5	
Irritability			
subjects affected / exposed	5 / 23 (21.74%)	7 / 19 (36.84%)	
occurrences (all)	5	7	
Lack of energy			
subjects affected / exposed	6 / 23 (26.09%)	7 / 19 (36.84%)	
occurrences (all)	6	7	
Worry			
subjects affected / exposed	7 / 23 (30.43%)	6 / 19 (31.58%)	
occurrences (all)	7	6	
Eyesight changes			
subjects affected / exposed	6 / 23 (26.09%)	8 / 19 (42.11%)	
occurrences (all)	6	8	
Difficulty sleeping			
subjects affected / exposed	11 / 23 (47.83%)	9 / 19 (47.37%)	
occurrences (all)	11	9	
Feel lightheaded (dizzy)			
subjects affected / exposed	4 / 23 (17.39%)	4 / 19 (21.05%)	
occurrences (all)	4	4	
Reproductive system and breast disorders			
Vaginal bleeding or spotting			
subjects affected / exposed	0 / 23 (0.00%)	2 / 19 (10.53%)	
occurrences (all)	0	2	
Vaginal discharge			
subjects affected / exposed	7 / 23 (30.43%)	11 / 19 (57.89%)	
occurrences (all)	7	11	
Sexual feeling decreased			

subjects affected / exposed	9 / 23 (39.13%)	10 / 19 (52.63%)	
occurrences (all)	9	10	
Vaginal itching/irritation			
subjects affected / exposed	3 / 23 (13.04%)	5 / 19 (26.32%)	
occurrences (all)	3	5	
Pain from breast tissue or breast skin			
subjects affected / exposed	4 / 23 (17.39%)	5 / 19 (26.32%)	
occurrences (all)	4	5	
Fragile mucous membranes/ Mucous membrane disorder			
subjects affected / exposed	7 / 23 (30.43%)	10 / 19 (52.63%)	
occurrences (all)	7	10	
Painful intercourse			
subjects affected / exposed	4 / 23 (17.39%)	5 / 19 (26.32%)	
occurrences (all)	4	5	
Dryness vaginal			
subjects affected / exposed	11 / 23 (47.83%)	14 / 19 (73.68%)	
occurrences (all)	11	14	
Skin and subcutaneous tissue disorders			
skin rashes			
subjects affected / exposed	6 / 23 (26.09%)	4 / 19 (21.05%)	
occurrences (all)	6	4	
Hair loss			
subjects affected / exposed	7 / 23 (30.43%)	7 / 19 (36.84%)	
occurrences (all)	7	7	
Itching			
subjects affected / exposed	3 / 23 (13.04%)	0 / 19 (0.00%)	
occurrences (all)	3	0	
Renal and urinary disorders			
Problems with urination			
subjects affected / exposed	2 / 23 (8.70%)	3 / 19 (15.79%)	
occurrences (all)	2	3	
Endocrine disorders			
Cold sweat			
subjects affected / exposed	8 / 23 (34.78%)	9 / 19 (47.37%)	
occurrences (all)	8	9	
Night sweats			

subjects affected / exposed occurrences (all)	15 / 23 (65.22%) 15	18 / 19 (94.74%) 18	
Menopausal hot flushes subjects affected / exposed occurrences (all)	14 / 23 (60.87%) 14	17 / 19 (89.47%) 17	
Musculoskeletal and connective tissue disorders			
muscle cramps (e.g. in legs) subjects affected / exposed occurrences (all)	14 / 23 (60.87%) 14	16 / 19 (84.21%) 16	
Pain in joints subjects affected / exposed occurrences (all)	12 / 23 (52.17%) 12	11 / 19 (57.89%) 11	
Metabolism and nutrition disorders			
Diarrhoea subjects affected / exposed occurrences (all)	6 / 23 (26.09%) 6	3 / 19 (15.79%) 3	
Constipation subjects affected / exposed occurrences (all)	4 / 23 (17.39%) 4	5 / 19 (26.32%) 5	
weight gain subjects affected / exposed occurrences (all)	12 / 23 (52.17%) 12	14 / 19 (73.68%) 14	
Nausea subjects affected / exposed occurrences (all)	7 / 23 (30.43%) 7	6 / 19 (31.58%) 6	
Vomiting subjects affected / exposed occurrences (all)	12 / 23 (52.17%) 12	13 / 19 (68.42%) 13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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/35605013>