Clinical trial results:
Significance of the FSH receptor polymorphism p.N680S for the efficacy of FSH therapy of idiopathic male infertility: a pharmacogenetic approach.

Summary

EudraCT number	2010-020240-35
Trial protocol	IT DE
Global end of trial date	14 April 2015

Results information

Result version number	v1 (current)
This version publication date	18 November 2021
First version publication date	18 November 2021
Summary attachment (see zip file)	Final Manuscript (Simoni_Hum Reprod_2016.pdf)

Trial information

Trial identification

Sponsor protocol code	2010-020240-35

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Modena and Reggio Emilia
Sponsor organisation address	Via Campi, Modena, Italy,
Public contact	Manuela SImoni, University of Modena and Reggio Emilia, +39 0593961815, manuela.simoni@unimore.it
Scientific contact	Manuela Simoni, University of Modena and Reggio Emilia, +39 0593961815, manuela.simoni@unimore.it

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	12 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 April 2015
Global end of trial reached?	Yes
Global end of trial date	14 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

In men with idiopathic infertility, the sperm DNA fragmentation index (DFI) within 12 weeks of FSH therapy and 12 weeks follow-up improves depending on the FSHR genotype as assessed by the non-synonymous SNP rs6166 (wild type or p.N680S).

Protection of trial subjects:

NA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2013
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	Germany: 20
Country: Number of subjects enrolled	Italy: 60
Worldwide total number of subjects	80
EEA total number of subjects	80

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)	80
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The population to be studied are adult men with:
- age 20-50 years
- idiopathic male factor infertility for at least one year;
- homozygous FSHR allele at codon 680 (wild type: Asn/Asn or Ser/Ser);
- sperm DFI > 15%;
- normal serum FSH levels (< 8 IU/L)
- normal serum LH, testosterone, prolactin and estradiol levels
- no female infertility

Pre-assignment

Screening details:

During the pre-assignement phase, inclusion and exclusion criteria were evaluated in all men attending the Andrological outpatients clinic for couple infertility

Pre-assignment period milestones

Number of subjects started	80
Number of subjects completed	80[1]

Notes:

[1] - The number of subjects reported to be in the pre-assignment period is not consistent with the number starting period 1. It is expected that the number completing the pre-assignment period are also present in the arms in period 1.
Justification: The number of patients is correctly reported

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

The subject and the investigators were blinded for the subjects' genotype

Arms

Are arms mutually exclusive?	No
Arm title	Group 1

Arm description:

Patients with FSHR p.680N>S N homozygous

Arm type	Experimental
Investigational medicinal product name	FSH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

150 IU every other day

Arm title	Group 2

Arm description:

Patients with FSHR p.680N>S S homozygous

Arm type	Experimental

Investigational medicinal product name	FSH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

150 IU every other day

Number of subjects in period 1	Group 1	Group 2
Started	40	40
Completed	33	33
Not completed	7	7
Physician decision	7	7

Period 2

Period 2 title	End of treatment phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

Patients with FSHR p.680N>S N homozygous

Arm type	Experimental
Investigational medicinal product name	FSH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

150 IU every other day

Arm title	Group 2

Arm description:

Patients with FSHR p.680N>S S homozygous

Arm type	Experimental
Investigational medicinal product name	FSH
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:
150 IU every other day

Number of subjects in period 2	Group 1	Group 2
Started	33	33
Completed	33	33

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	80	80	
Age categorical Units: Subjects			
Adult, higher than 18 years	80	80	
Gender categorical Units: Subjects			
Female	0	0	
Male	80	80	

End points

End points reporting groups	
Reporting group title	Group 1
Reporting group description: Patients with FSHR p.680N>S N homozygous	
Reporting group title	Group 2
Reporting group description: Patients with FSHR p.680N>S S homozygous	
Reporting group title	Group 1
Reporting group description: Patients with FSHR p.680N>S N homozygous	
Reporting group title	Group 2
Reporting group description: Patients with FSHR p.680N>S S homozygous	

Primary: Sperm DNA Fragmentation Index	
End point title	Sperm DNA Fragmentation Index
End point description: Sperm DNA Fragmentation Index	
End point type	Primary
End point timeframe: After treatment and follow-up phases	

End point values	Group 1	Group 2	Group 1	Group 2
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	33	33	33
Units: percent				
number (not applicable)	33	33	33	33

Statistical analyses

Statistical analysis title	Comparison between genotypes
Statistical analysis description: Patients were first divided according to the genotype of the rs6166 in the FSHR, forming two groups: homozygous FSHR p.N680S N and homozygous FSHR. Comparison of variables between different groups was performed by Mann-Whitney test.	
Comparison groups	Group 1 v Group 2

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mann-Whitney

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Potential adverse events were evaluated at each visit

Assessment type	Non-systematic

Dictionary used

Dictionary name	AIFA
Dictionary version	1

Reporting groups

Reporting group title	Group 1
Reporting group description: -	
Reporting group title	Group 2

Reporting group description: -

Serious adverse events	Group 1	Group 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (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: 0 %

Non-serious adverse events	Group 1	Group 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 33 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No adverse events were recorded, neither serious nor not-serious

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/27329968