Clinical trial results:
Controlled randomized study on maintenance to low activity disease with low doses of SKA citokines compared with standard therapy (DMARDS)of arthritis management

Summary

EudraCT number	2011-003016-23
Trial protocol	IT
Global end of trial date	27 February 2015

Results information

Result version number	v1 (current)
This version publication date	08 January 2025
First version publication date	08 January 2025

Trial information

Trial identification

Sponsor protocol code	CIDAI

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GUNA S.p.a.
Sponsor organisation address	Via Palmanova, 71, Milan, Italy, 20132
Public contact	Segreteria ANTIAGE, ANTIAGE onlus, 39 0633585802, albertomigliore@terra.es
Scientific contact	Vincenzo Miranda, GUNA S.p.a., 39 0228018358, v.miranda@guna.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	27 February 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 February 2015
Global end of trial reached?	Yes
Global end of trial date	27 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Estimating that the proportion of patients who maintain the remission after the therapy of active branch is greater than or equal respect of patients in control branch.

Protection of trial subjects:

The use of celecoxib 200mg has been predicted as a pain killer in case of need.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2011
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	Italy: 39
Worldwide total number of subjects	39
EEA total number of subjects	39

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)	39
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at the Rheumatology Unit, San Pietro Hospital Fatebenefratelli, Rome, between July 2011 and March 2014. A total of 52 subjects were screened and 39 were enrolled and randomized as shown in the clinical trial flow diagram. In detail, five males and 34 females (mean age: 55.19) with RA, diagnosed according to ACR criteria, were

Pre-assignment

Screening details:

INCLUSION CRITERIA
- RA diagnosed according to ACR criteria
- Duration of disease <3 years
- Disease activity of 28 joints [DAS28] <3.2 after Biologic and/or DMARD therapy
- Patients who have reached the state of remission or LDA after treatment with Biologic or after one therapy with DMARDs
- Patients able to adhere to the procedures of the s

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

An active arm consisting of patients who had achieved a low level of activity or remission of the disease after biological therapy or conventional therapy with DMARDs (MTX, CyA, Leflunomide) who were treated with Guna-Anti IL1, Guna-Interleukin4, Guna-Interleukin10 formulated in a concentration of 10 fg/ml at a dose of 20 drops/day.

Arm type	Experimental
Investigational medicinal product name	Guna-Anti IL1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral drops, liquid
Routes of administration	Buccal use

Dosage and administration details:

20 drops/day.

Arm title	Group B

Arm description:

A control arm made up of patients who had achieved a low level of activity or remission of the disease after biological therapy or conventional therapy with DMARDs (MTX, CyA, Leflunomide) who were treated with traditional therapy alone (MTX, Steroids and NSAIDs)

Arm type	conventional therapy

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Group A	Group B
Started	19	20
Completed	19	20

Baseline characteristics

Reporting groups	
Reporting group title	Group A
Reporting group description:	
An active arm consisting of patients who had achieved a low level of activity or remission of the disease after biological therapy or conventional therapy with DMARDs (MTX, CyA, Leflunomide) who were treated with Guna-Anti IL1, Guna-Interleukin4, Guna-Interleukin10 formulated in a concentration of 10 fg/ml at a dose of 20 drops/day.	
Reporting group title	Group B
Reporting group description:	
A control arm made up of patients who had achieved a low level of activity or remission of the disease after biological therapy or conventional therapy with DMARDs (MTX, CyA, Leflunomide) who were treated with traditional therapy alone (MTX, Steroids and NSAIDs)	

Reporting group values	Group A	Group B	Total
Number of subjects	19	20	39
Age categorical			
Adults (18/84 years)			
Units: Subjects			

Age continuous			
Units: years			
median	47.08	63.3	
standard deviation	± 11.11	± 11.48	-
Gender categorical			
Units: Subjects			
Female	16	18	34
Male	3	2	5

End points

End points reporting groups

Reporting group title	Group A

Reporting group description:

An active arm consisting of patients who had achieved a low level of activity or remission of the disease after biological therapy or conventional therapy with DMARDs (MTX, CyA, Leflunomide) who were treated with Guna-Anti IL1, Guna-Interleukin4, Guna-Interleukin10 formulated in a concentration of 10 fg/ml at a dose of 20 drops/day.

Reporting group title	Group B

Reporting group description:

A control arm made up of patients who had achieved a low level of activity or remission of the disease after biological therapy or conventional therapy with DMARDs (MTX, CyA, Leflunomide) who were treated with traditional therapy alone (MTX, Steroids and NSAIDs)

Primary: Evaluate for how long the association of Guna-Anti IL 1, Guna-Interleukin 4, Guna-Interleukin 10, at low doses of 1fg/ml can maintain the low disease activity obtained after DMARDs or "Biologicals" in patients suffering from RA compared to treatment with

End point title	Evaluate for how long the association of Guna-Anti IL 1, Guna-Interleukin 4, Guna-Interleukin 10, at low doses of 1fg/ml can maintain the low disease activity obtained after DMARDs or "Biologicals" in patients suffering from RA compared to treatment with[1]

End point description:

The rate of maintenance of LDA at 12 months was superior in the group treated with low-dose cytokines compared with patients treated with DMARDs, 66.7% and 42.1%, respectively; however, the difference between the groups was not statistically significant.

End point type	Primary

End point timeframe:

From T0 to T12 month

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A descriptive analysis was performed for all the demographic variables and clinical features at baseline. Student’s t-test for paired data was conducted to evaluate the clinical efficacy parameters (DAS28) of treatment at 12 months, compared to baseline. In case of violation of the assumptions underlying the aforementioned parametric statistical tests, the analysis was performed with a nonparametric method, in particular, the Wilcoxon test. The McNemar test was used in each group of patients to

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	19		
Units: %				
median (standard deviation)	66.7 (± 0.00)	42.1 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

from T0 to T12

Adverse event reporting additional description:

Adverse events are monitored daily and possibly recorded via e-CRF

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Group A

Reporting group description: -

Reporting group title	Group B

Reporting group description: -

Serious adverse events	Group A	Group B	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (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 A	Group B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 20 (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: A total of 34 patients were exposed to treatments during 12 months. Respectively, 15 subjects in Group A, composed of patients who achieved an LDA or remission of the disease after biological therapy or conventional therapy with DMARDs, were treated with Guna-IL-4, Guna-IL-10, and Guna-Anti-IL-1 formulated concentration 10 fg/mL, and 19 patients in the Group B, who similarly achieved an LDA or remission of the disease after biological therapy or conventional therapy with DMARDs, were treated wit

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The results obtained do not reach the primary endpoint. It is important to underline that these results cannot be considered definitive as they emerged from an insufficiently representative sample and consequently (powerless than 80% due to the low n

Notes: