Clinical trial results:
A DOUBLE-BLIND, RANDOMISED, PLACEBO-CONTROLLED CLINICAL TRIAL OF THE SAFETY AND EFFICACY OF ANAKINRA IN PATIENTS WITH HIDRADENITIS SUPPURATIVA (PROTOCOL: HIDRA03)

Summary

EudraCT number	2011-005145-12
Trial protocol	GR
Global end of trial date	01 August 2014

Results information

Result version number	v1 (current)
This version publication date	07 January 2023
First version publication date	07 January 2023

Trial information

Trial identification

Sponsor protocol code	HIDRA03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01558375
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Athens, Medical School
Sponsor organisation address	Rimini 1, Chaidari, Athens, Greece,
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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	30 September 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 August 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The safety and efficacy of anakinra in patients with HS of Hurley II and III stage disease.

Protection of trial subjects:

No specific measures taken.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 April 2012
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	Greece: 20
Worldwide total number of subjects	20
EEA total number of subjects	20

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)	19
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at the Outpatient Department of Immunology of Infectious Diseases of Attikon University Hospital, Greece. The first patient was recruited on 3rd April 2012 and the last patient was recruited on 31st January 2014. A total of 20 patients were enrolled.

Pre-assignment

Screening details:

Inclusion criteria: 1) written informed consent provided by the patient, 2) age 18 years or older, 3) diagnosis of HS, and 4) Hurley stage II or III HS.
Screening: history/physical examination; skin tuberculin test; chest radiograph; serology for HIV and hepatitis virus B and C; white blood cell count, serum creatinine level, liver biochemistry

Period 1

Period 1 title	Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The randomized sequence was generated by an independent biostatistician. Anakinra was provided in single-use, prefilled glass syringes with 27-gauge needles. The syringes contained 100mg of anakinra in a volume of 0.67 mL. Identical placebo syringes contained 0.67 mL of sterile water for injection. The placebo and anakinra syringes were identical in appearance to ensure masking.

Arms

Are arms mutually exclusive?	Yes
Arm title	Anakinra arm

Arm description:

A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomised to receive anakinra.

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

Dosage and administration details:

Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Anakinra was provided in single use, prefilled glass syringes with 27-gauge needles. The syringes contained 100mg of anakinra in a volume of 0.67 mL.

Arm title	Placebo arm

Arm description:

A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomised to receive placebo.

Arm type	Placebo
Investigational medicinal product name	Sterile water for injection
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled injector
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Placebo was provided in single use, prefilled glass syringes with 27-gauge needles. The syringes contained sterile water for injection in a volume of 0.67 mL.

Number of subjects in period 1	Anakinra arm	Placebo arm
Started	10	10
Completed	10	10

Period 2

Period 2 title	Follow-up Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Anakinra arm

Arm description:

A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomized to receive anakinra. After treatment, patients were followed up from week 13 to week 24. The patients and investigators were masked to the administered treatment.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Placebo arm

Arm description:

A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomized to receive placebo. After treatment, patients were followed up from week 13 to week 24. The patients and investigators were masked to the administered treatment.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Anakinra arm	Placebo arm
Started	10	10
Completed	9	10
Not completed	1	0
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Anakinra arm
Reporting group description:	
A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomised to receive anakinra.	
Reporting group title	Placebo arm
Reporting group description:	
A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomised to receive placebo.	

Reporting group values	Anakinra arm	Placebo arm	Total
Number of subjects	10	10	20
Age categorical Units: Subjects			
Adults (18-64 years)	8	10	18
From 65-84 years	1	0	1
Not recorded	1	0	1
Age continuous Units: years			
arithmetic mean	42.8	36.0	
standard deviation	± 13.8	± 11.3	-
Gender categorical Units: Subjects			
Female	4	5	9
Male	5	5	10
Not recorded	1	0	1
Family history of HS Units: Subjects			
Yes	3	5	8
No	6	5	11
Not recorded	1	0	1
Smoking Units: Subjects			
Yes	8	8	16
No	1	2	3
Not recorded	1	0	1
Staphylococcus aureus nasal carriage Units: Subjects			
Yes	0	0	0
No	9	10	19
Not recorded	1	0	1
Hypothyrodism Units: Subjects			
Yes	2	2	4
No	7	8	15
Not recorded	1	0	1

Past treatment for HS: Incision and drainage Units: Subjects			
Yes	3	3	6
No	6	7	13
Not recorded	1	0	1
Past treatment for HS: Debridement Units: Subjects			
Yes	1	1	2
No	8	9	17
Not recorded	1	0	1
Past treatment for HS: Antibiotic Units: Subjects			
Yes	6	9	15
No	3	1	4
Not recorded	1	0	1
Past treatment for HS: Anti-tumor necrosis factor Units: Subjects			
Yes	4	3	7
No	5	7	12
Not recorded	1	0	1
Affected skin area: Axillae Units: Subjects			
Yes	5	7	12
No	4	3	7
Not recorded	1	0	1
Affected skin area: Submammary or inframammary fold Units: Subjects			
Yes	2	2	4
No	7	8	15
Not recorded	1	0	1
Affected skin area: Inguinal and crural fold Units: Subjects			
Yes	9	7	16
No	0	3	3
Not recorded	1	0	1
Affected skin area: Perianal Units: Subjects			
Yes	2	2	4
No	7	8	15
Not recorded	1	0	1
Affected skin area: Gluteal Units: Subjects			
Yes	4	4	8
No	5	6	11
Not recorded	1	0	1
Affected skin area: Scrotum Units: Subjects			
Yes	1	2	3

No	8	8	16
Not recorded	1	0	1
Affected skin area: Pubic Units: Subjects			
Yes	3	1	4
No	6	9	15
Not recorded	1	0	1
Hurley stage of HS Units: Subjects			
II	6	4	10
III	3	6	9
Not recorded	1	0	1
Time since HS onset Units: years			
arithmetic mean	12.3	11.1	
standard deviation	± 6.7	± 6.8	-
Body mass index, mean Units: kilogram(s)/square meter			
arithmetic mean	27.8	27.9	
standard deviation	± 5.1	± 6.8	-
Exacerbations per month Units: number			
median	2	2	
full range (min-max)	1 to 10	1 to 16	-
HS severity: DLQI Units: number			
arithmetic mean	20.7	14.3	
standard deviation	± 5.9	± 8.4	-
HS severity: VAS score Units: number			
arithmetic mean	67.0	55.0	
standard deviation	± 19.8	± 20.3	-
HS severity: VAS score for pain Units: number			
arithmetic mean	54.4	60.5	
standard deviation	± 22.9	± 21.7	-
HS severity: Disease activity score Units: number			
arithmetic mean	186.9	113.4	
standard deviation	± 112.9	± 94.9	-
HS severity: Sartorius score Units: number			
arithmetic mean	104.6	82.0	
standard deviation	± 54.2	± 58.9	-
Lesion count: Inflammatory nodule Units: Number of lesion per subject			
median	6	4	
full range (min-max)	4 to 23	3 to 30	-
Lesion count: Noninflammatory nodule Units: Number of lesion per subject			
median	1	3	

full range (min-max)	0 to 23	0 to 13	-
Lesion count: Draining fistula			
Units: Number of lesion per subject			
median	3	2	
full range (min-max)	1 to 40	0 to 23	-
Lesion count: Nondraining fistula			
Units: Number of lesion per subject			
median	0	0	
full range (min-max)	0 to 7	0 to 1	-
Lesion count: Scar			
Units: Number of lesion per subject			
median	0	6	
full range (min-max)	0 to 19	0 to 102	-

End points

End points reporting groups

Reporting group title	Anakinra arm
Reporting group description:	
A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomised to receive anakinra.	

Reporting group title	Placebo arm
Reporting group description:	
A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomised to receive placebo.	

Reporting group title	Anakinra arm
Reporting group description:	
A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomized to receive anakinra. After treatment, patients were followed up from week 13 to week 24. The patients and investigators were masked to the administered treatment.	

Reporting group title	Placebo arm
Reporting group description:	
A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomized to receive placebo. After treatment, patients were followed up from week 13 to week 24. The patients and investigators were masked to the administered treatment.	

Primary: The decrease of disease activity scores from the baseline visit to the end of treatment

End point title	The decrease of disease activity scores from the baseline visit to the end of treatment
End point description:	
The primary end point was the safety and efficacy of anakinra in patients with Hurley stage II or III HS based on decreased disease activity scores from the baseline visit to the end of treatment. Furthermore, the 2 study arms were compared regarding their DLQI, VAS score, development of serious adverse events, and HS severity (disease activity score, Sartorius score, and HiSCR) over the course of their visits.	

End point type	Primary
End point timeframe:	
From the baseline to week 12 (end of treatment).	

End point values	Anakinra arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: number of patients	7	2		

Attachments (see zip file)	Decrease of disease activity scores (Baseline-EOT)/Decrease of

Statistical analyses

Statistical analysis title	Fisher 2-sided test
Comparison groups	Anakinra arm v Placebo arm
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	Fisher 2-sided

Secondary: Change of the DLQI score at weeks 12 and 24 from baseline visit

End point title	Change of the DLQI score at weeks 12 and 24 from baseline visit

End point description:

The primary end point was the safety and efficacy of anakinra in patients with Hurley stage II or III HS based on decreased disease activity scores from the baseline visit to the end of treatment. Furthermore, the 2 study arms were compared regarding their DLQI, VAS score, development of serious adverse events, and HS severity (disease activity score, Sartorius score, and HiSCR) over the course of their visits.

End point type	Secondary

End point timeframe:

Weeks 12 and 24.

End point values	Anakinra arm	Placebo arm	Anakinra arm	Placebo arm
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	9	10
Units: 100% percentage				
arithmetic mean (standard error)				
Question 1	-30.5 (± 12.19)	-33.3 (± 16.33)	0 (± 15.8)	-35.71 (± 17.97)
Question 2	-22.2 (± 10.24)	-4.16 (± 10.24)	0 (± 27.38)	-38.09 (± 15.3)
Question 3	-23.81 (± 17.56)	33.33 (± 39.4)	-25 (± 25)	9.32 (± 32.9)
Question 4	-28.57 (± 21.42)	0 (± 0)	-16.6 (± 21.08)	-2.08 (± 18.69)
Question 5	-19.04 (± 17.97)	39.58 (± 35.62)	-2.77 (± 19.97)	-2.38 (± 18.69)
Question 6	-33.33 (± 17.81)	25 (± 41.18)	-8.33 (± 7.33)	26.19 (± 36.27)
Question 7	-41.67 (± 20.09)	7.4 (± 12.17)	10 (± 12)	-4.16 (± 16.88)
Question 8	-8.33 (± 7.33)	18.75 (± 23.02)	-8.33 (± 7.33)	2.38 (± 23.69)
Question 9	-7.14 (± 3.14)	50 (± 26.72)	-25 (± 17.07)	28.57 (± 27)
Question 10	21.42 (± 28.57)	-7.14 (± 22.92)	8.33 (± 15.36)	19.44 (± 30.9)

Attachments (see zip file)	Change of the DLQI score at weeks 12 and 24 from baseline

Statistical analyses

Statistical analysis title	Mann-Whitney test
Comparison groups	Placebo arm v Anakinra arm v Anakinra arm v Placebo arm
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Change of the VAS score at weeks 12 and 24 from baseline visit

End point title	Change of the VAS score at weeks 12 and 24 from baseline visit

End point description:

The primary end point was the safety and efficacy of anakinra in patients with Hurley stage II or III HS based on decreased disease activity scores from the baseline visit to the end of treatment. Furthermore, the 2 study arms were compared regarding their DLQI, VAS score, development of serious adverse events, and HS severity (disease activity score, Sartorius score, and HiSCR) over the course of their visits.

End point type	Secondary

End point timeframe:

Weeks 0, 12 and 24

End point values	Anakinra arm	Placebo arm	Anakinra arm	Placebo arm
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	9	10
Units: 100% percentage of change				
arithmetic mean (standard error)	-12.4608 (± 13.05674)	-16.1107 (± 15.89520)	-5.2618 (± 16.26598)	-18.2353 (± 17.48042)

Attachments (see zip file)	Change of the VAS score at weeks 12 and 24 from baseline

Statistical analyses

Statistical analysis title	Wilcoxon (Mann-Whitney)
Comparison groups	Anakinra arm v Placebo arm v Placebo arm v Anakinra arm
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Development of serious adverse events over the course of the study visits

End point title	Development of serious adverse events over the course of the study visits

End point description:

The primary end point was the safety and efficacy of anakinra in patients with Hurley stage II or III HS based on decreased disease activity scores from the baseline visit to the end of treatment. Furthermore, the 2 study arms were compared regarding their DLQI, VAS score, development of serious adverse events, and HS severity (disease activity score, Sartorius score, and HiSCR) over the course of their visits.

End point type	Secondary

End point timeframe:

Weeks 0, 12 and 24.

End point values	Anakinra arm	Placebo arm	Anakinra arm	Placebo arm
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	9	10
Units: number	0	0	0	0

Statistical analyses

Statistical analysis title	Mann-Whitney test
Comparison groups	Anakinra arm v Placebo arm v Anakinra arm v Placebo arm
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Wilcoxon (Mann-Whitney)

Secondary: Change of the Sartorius score at weeks 12 and 24 from baseline visit

End point title	Change of the Sartorius score at weeks 12 and 24 from baseline visit

End point description:

The primary end point was the safety and efficacy of anakinra in patients with Hurley stage II or III HS based on decreased disease activity scores from the baseline visit to the end of treatment. Furthermore, the 2 study arms were compared regarding their DLQI, VAS score, development of serious adverse events, and HS severity (disease activity score, Sartorius score, and HiSCR) over the course of their visits.

End point type	Secondary

End point timeframe:

Weeks 0, 12 and 24.

End point values	Anakinra arm	Placebo arm	Anakinra arm	Placebo arm
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	9	10
Units: 100% percentage				
arithmetic mean (standard error)	0.7658 (± 6.14684)	-0.1335 (± 2.67418)	5.3007 (± 9.68679)	4.2435 (± 1.90589)

Attachments (see zip file)	Change of the Sartorius score at weeks 12 and 24 from

Statistical analyses

Statistical analysis title	Mann-Whitney test
Comparison groups	Anakinra arm v Placebo arm v Anakinra arm v Placebo arm
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: The effects of anakinra on the time to a new exacerbation of HS

End point title	The effects of anakinra on the time to a new exacerbation of HS

End point description:

Secondary end points were the effects of anakinra on the time to a new exacerbation of HS and on the ex vivo function of PBMCs. This latter effect was defined by the difference in cytokine production by PBMCs between the 2 study arms over the course of the study visits.

End point type	Secondary

End point timeframe:

Weeks 0,12 and 24.

End point values	Anakinra arm	Placebo arm	Anakinra arm	Placebo arm
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	9	10
Units: cumulative % of patients				
number (not applicable)	11.1	77.8	33.3	88.9

Attachments (see zip file)	The effects of anakinra on the time to a new exacerbation of

Statistical analyses

Statistical analysis title	Log-rank test
Comparison groups	Anakinra arm v Placebo arm
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Logrank

Secondary: The effects of anakinra on the ex vivo function of PBMCs

End point title	The effects of anakinra on the ex vivo function of PBMCs

End point description:

Secondary end points were the effects of anakinra on the time to a new exacerbation of HS and on the ex vivo function of PBMCs. This latter effect was defined by the difference in cytokine production by PBMCs between the 2 study arms over the course of the study visits.
Peripheral blood mononuclear cells of patients randomized to placebo (n = 10) and to anakinra (n = 9) were isolated and stimulated with bacterial lipopolysaccharide (LPS), phytohemagglutin (PHA), and heat-killed isolates of Candida albicans (C albicans) and of Staphylococcus aureus (S aureus). Depicted here as concentrations at week 0 (baseline), week 12 (the end of treatment), and week 24 (the end of follow-up).

End point type	Secondary

End point timeframe:

Weeks 0, 12 and 24

End point values	Anakinra arm	Placebo arm	Anakinra arm	Placebo arm
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	9	10
Units: picogram(s)/millilitre(s)				
arithmetic mean (standard error)				
TNFα stimulated with bacterial lipopolysaccharide	285.1 (± 90.1)	2068.7 (± 1173.1)	1300.3 (± 904.5)	1528.5 (± 557.8)
TNFα stimulated with Candida albicans	13280.3 (± 9299.1)	15341.2 (± 4314.8)	11093.8 (± 2829.2)	19694 (± 6504.9)
TNFα stimulated with Staphylococcus aureus	737 (± 492.3)	1187.9 (± 408.8)	2788.5 (± 2010)	7128.3 (± 2477.2)
IL-1β stimulated with bacterial lipopolysaccharide	6573.3 (± 3149.5)	4438.8 (± 694.3)	4080.5 (± 1124)	4656.5 (± 1278.3)
IL-1β stimulated with Candida albicans	6935 (± 3961.2)	3017.5 (± 1313.2)	5840 (± 1690.7)	7028.2 (± 2372)
IL-1β stimulated with Staphylococcus aureus	2046.6 (± 957.1)	793.8 (± 149.6)	2137 (± 1275.9)	1838.3 (± 995.2)
IL-6 stimulated with bacterial lipopolysaccharide	31583.2 (± 8663)	40506.2 (± 10995.3)	20438.8 (± 5964.4)	31339 (± 10886.8)
IL-6 stimulated with Candida albicans	16541.6 (± 7214.6)	19518.8 (± 4543.5)	11836.7 (± 3194.2)	17075 (± 2844.7)
IL-6 stimulated with Staphylococcus aureus	9800 (± 1501.3)	20725 (± 5116.7)	11657.3 (± 3282.5)	20333.3 (± 4287.9)

IL-10 stimulated with phytohemagglutin	398 (± 132)	316.5 (± 156.2)	304.3 (± 65.9)	219.14 (± 94)
IL-10 stimulated with Candida albicans	220.8 (± 140.2)	329.1 (± 153.1)	92.3 (± 39.5)	186.8 (± 78.6)
IL-10 stimulated with Staphylococcus aureus	101.6 (± 32.5)	249.9 (± 92.1)	101.14 (± 38.7)	134.8 (± 63.6)
IL-17 stimulated with phytohemagglutin	2415.8 (± 636.5)	3602.8 (± 1340.5)	3122.8 (± 649.7)	2133.5 (± 392.3)
IL-17 stimulated with Candida albicans	1025.1 (± 513.1)	701.5 (± 242)	894.3 (± 247.8)	767.1 (± 164.7)
IL-17 stimulated with Staphylococcus aureus	589.1 (± 129.5)	1457.1 (± 660.1)	1327.1 (± 501.7)	1395.7 (± 394.7)
IL-22 stimulated with phytohemagglutin	5726.7 (± 1018.2)	3744.3 (± 1316.3)	6897.8 (± 1124)	2665.7 (± 561.8)
IL-22 stimulated with Candida albicans	7784.2 (± 2500.2)	5598.5 (± 1648.9)	5409.3 (± 1300)	8184.3 (± 2138.5)
IL-22 stimulated with Staphylococcus aureus	4025 (± 2207.5)	2446.4 (± 764.6)	3288.3 (± 859.6)	3130.7 (± 821.5)
INFγ stimulated with phytohemagglutin	1309 (± 458.9)	1326.1 (± 181.6)	5229.7 (± 3872.2)	1704 (± 654.1)
INFγ stimulated with Candida albicans	2338.7 (± 1805.7)	31641.8 (± 10994.8)	16145 (± 10967)	36377.1 (± 8229)
INFγ stimulated with Staphylococcus aureus	4420.8 (± 3845.5)	483.4 (± 316.4)	11521 (± 11375)	1672 (± 995)

Attachments (see zip file)	The difference in Interferon γ production by PBMCs over the The difference in Interleukin 1β production by PBMCs over the The difference in Interleukin 6 production by PBMCs over the The difference in Interleukin 10 production by PBMCs over the The difference in Interleukin 17 production by PBMCs over the The difference in Interleukin 22 production by PBMCs over the The difference in TNF production by PBMCs over the course of

Statistical analyses

Statistical analysis title	Mann-Whitney test
Comparison groups	Anakinra arm v Placebo arm v Anakinra arm v Placebo arm
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05 [1]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - TNFα(S aureus) wk.24 -placebo: P= .03 vs baseline
IL-6(LPS) wk.12 -anakinra: P= .046 vs baseline
IL-22(PHA) wk.24 -anakinra: P= .02 vs placebo
IFNγ(C albicans) wk.12 -placebo: P= .04 vs placebo
IFNγ(C albicans) wk.12 -anakinra: P= .02 vs baseline

Secondary: Change of the VAS score for pain at weeks 12 and 24 from baseline visit

End point title	Change of the VAS score for pain at weeks 12 and 24 from baseline visit

End point description:

The primary end point was the safety and efficacy of anakinra in patients with Hurley stage II or III HS based on decreased disease activity scores from the baseline visit to the end of treatment. Furthermore, the 2 study arms were compared regarding their DLQI, VAS score, development of serious adverse events, and HS severity (disease activity score, Sartorius score, and HiSCR) over the course of their visits.

End point type	Secondary

End point timeframe:

Weeks 0, 12 and 24.

End point values	Anakinra arm	Placebo arm	Anakinra arm	Placebo arm
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	9	10
Units: 100% percentage				
arithmetic mean (standard error)	-8.1406 (± 16.81452)	-2.3979 (± 21.06458)	-34.8280 (± 22.11349)	-18.6642 (± 17.00527)

Attachments (see zip file)	Change of the VAS score for pain at weeks 12 and 24 from

Statistical analyses

Statistical analysis title	Mann-Whitney test
Comparison groups	Anakinra arm v Placebo arm v Anakinra arm v Placebo arm
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Post-hoc: Change of the HiSCR score at weeks 12 and 24 from baseline visit

End point title	Change of the HiSCR score at weeks 12 and 24 from baseline visit

End point description:

The primary end point was the safety and efficacy of anakinra in patients with Hurley stage II or III HS based on decreased disease activity scores from the baseline visit to the end of treatment. Furthermore, the 2 study arms were compared regarding their DLQI, VAS score, development of serious adverse events, and HS severity (disease activity score, Sartorius score, and HiSCR) over the course of their visits.

End point type	Post-hoc

End point timeframe:

Weeks 0, 12 and 24.

End point values	Anakinra arm	Placebo arm	Anakinra arm	Placebo arm
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	9	10
Units: number	7	3	3	1

Attachments (see zip file)	Change of the HiSQR score at weeks 12 and 24 from baseline

Statistical analyses

Statistical analysis title	Fisher 2-sided test
Comparison groups	Anakinra arm v Placebo arm v Anakinra arm v Placebo arm
Number of subjects included in analysis	38
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.037
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Weeks 4, 8, 12, 16, 20 and 24	
Assessment type	Systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	5.0

Reporting groups	
Reporting group title	Anakinra arm
Reporting group description: A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomised to receive anakinra.	
Reporting group title	Placebo arm
Reporting group description: A total of 20 patients were enrolled in the study. Patients selected for enrollment were randomized at a 1:1 ratio to receive placebo or anakinra subcutaneously once daily for 12 weeks. Therefore, 10 patients were randomised to receive placebo.	

Serious adverse events	Anakinra arm	Placebo arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (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: 5 %

Non-serious adverse events	Anakinra arm	Placebo arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)	1 / 10 (10.00%)	
General disorders and administration site conditions			
Swelling at the injection site			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Diarrhea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Vaginal candidiasis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	

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 main limitation of the study was the few patients involved owing to the fact that this was a pilot study to validate the effect of an anti-IL strategy in HS. Despite the few enrolled patients, the results of anakinra use to treat HS are promising

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/26579854