Clinical trial results:
Open-label, multicenter, dose-escalating phase II study to investigate the safety, tolerability, and early signs of efficacy of subcutaneous administrations of Tadekinig alfa (IL-18BP) in patients with Adult -onset Still's Disease (AoSD) during 12 weeks

Summary

EudraCT number	2014-002500-24
Trial protocol	DE
Global end of trial date	28 July 2016

Results information

Result version number	v1 (current)
This version publication date	12 August 2017
First version publication date	12 August 2017

Trial information

Trial identification

Sponsor protocol code	AOSD.2014.001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AB2 Bio Ltd.
Sponsor organisation address	EPFL Innovation Park, Building B, 4th floor, Lausanne, Switzerland, CH-1015
Public contact	Eduardo Schiffrin, Medical Director, AB2 Bio Ltd., +41 21693 82 83, eduardo.schiffrin@ab2bio.com
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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	21 April 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safe use of Tadekinig alfa in AoSD patients

Protection of trial subjects:

In order to enhance patients' compliance, local skin treatment was proposed to the patients to mitigate local inflammatory reactions at the injection site.
The patient completed a daily diary recording daily symptoms at the injection site and other unusual remarkable symptom to continuously assess patient wellbeing and safety.
Finally, temporal treatment interruptions have been allowed in case of fever of any signs of undergoing infections unrelated to the treated condition.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 February 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Switzerland: 2
Worldwide total number of subjects	23
EEA total number of subjects	21

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)	20

From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

After the subject has agreed to participation by signing the consent, an inclusion/exclusion checklist will be completed by the physician.
Demographics and history
Physical examination, vital signs, and SDAI, assessment of 44 joints
Routine lab testing (ESR, CRP, hematology and clinical chemistry, urinalysis, TB testing, Serology)
Coagulation

Pre-assignment period milestones

Number of subjects started	33[1]
Number of subjects completed	23

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screening Failure: 10

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The worldwide number corresponds to the number of patients enrolled (23) and not to the number of patients screened (33).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 / 80 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Tadekinig alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients will receive the treatments three times a week (TIW). The 80mg cohort will receive 1ml of the study product. Patients of the 160mg dose cohort will receive 2 vials. The 320mg cohort, received 4 vials.

Arm title	Cohort 1 / 80-160 mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Tadekinig alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients will receive the treatments three times a week (TIW). The 80mg cohort will receive 1ml of the study product. Patients of the 160mg dose cohort will receive 2 vials. The 320mg cohort, received 4 vials.

Arm title	Cohort 2 / 160 mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Tadekinig alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients will receive the treatments three times a week (TIW). The 80mg cohort will receive 1ml of the study product. Patients of the 160mg dose cohort will receive 2 vials. The 320mg cohort, received 4 vials.

Arm title	Cohort 2 / 160-320 mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Tadekinig alfa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Patients will receive the treatments three times a week (TIW). The 80mg cohort will receive 1ml of the study product. Patients of the 160mg dose cohort will receive 2 vials. The 320mg cohort, received 4 vials.

Number of subjects in period 1	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg
Started	4	6	12
Completed	3	5	7
Not completed	1	1	5
Consent withdrawn by subject	-	-	1
Adverse event, non-fatal	1	1	3
Other	-	-	1

Number of subjects in period 1	Cohort 2 / 160-320 mg
Started	1
Completed	1
Not completed	0
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Other	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 / 80 mg
Reporting group description: -	
Reporting group title	Cohort 1 / 80-160 mg
Reporting group description: -	
Reporting group title	Cohort 2 / 160 mg
Reporting group description: -	
Reporting group title	Cohort 2 / 160-320 mg
Reporting group description: -	

Reporting group values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg
Number of subjects	4	6	12
Age categorical Units: Subjects			
Adults (18-64 years)	2	6	11
From 65-84 years	2	0	1
Age continuous Units: years			
arithmetic mean	55	41.7	41.9
full range (min-max)	31 to 65	24 to 58	21 to 77
Gender categorical Units: Subjects			
Female	3	3	9
Male	1	3	3

Reporting group values	Cohort 2 / 160-320 mg	Total	
Number of subjects	1	23	
Age categorical Units: Subjects			
Adults (18-64 years)	1	20	
From 65-84 years	0	3	
Age continuous Units: years			
arithmetic mean	30		
full range (min-max)	30 to 30	-	
Gender categorical Units: Subjects			
Female	1	16	
Male	0	7	

End points

End points reporting groups

Reporting group title	Cohort 1 / 80 mg
Reporting group description: -	
Reporting group title	Cohort 1 / 80-160 mg
Reporting group description: -	
Reporting group title	Cohort 2 / 160 mg
Reporting group description: -	
Reporting group title	Cohort 2 / 160-320 mg
Reporting group description: -	

Primary: Body temperature

End point title	Body temperature[1]
End point description:	
End point type	Primary
End point timeframe:	
At 12 weeks	

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: The analysis that have been performed are descriptive statistics.

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	9	1
Units: °C				
arithmetic mean (full range (min-max))	35.8 (35 to 37)	36.3 (36 to 37)	36.6 (36 to 38)	35.9 (35.9 to 35.9)

Statistical analyses

No statistical analyses for this end point

Primary: Heart rate

End point title	Heart rate[2]
End point description:	
End point type	Primary
End point timeframe:	
At 12 weeks	

Notes:

[2] - 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: The analysis that have been performed are descriptive statistics.

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	9	1
Units: bpm				
arithmetic mean (full range (min-max))	83 (73 to 90)	86.5 (71 to 100)	82.4 (69 to 101)	81 (81 to 81)

Statistical analyses

No statistical analyses for this end point

Primary: Systolic blood pressure

End point title	Systolic blood pressure[3]

End point description:

End point type	Primary

End point timeframe:

At 12 weeks

Notes:

[3] - 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: The analysis that have been performed are descriptive statistics.

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	9	1
Units: mmHg				
arithmetic mean (full range (min-max))	116 (106 to 134)	122.5 (108 to 150)	123.6 (99 to 148)	112 (112 to 112)

Statistical analyses

No statistical analyses for this end point

Primary: Diastolic blood pressure

End point title	Diastolic blood pressure[4]

End point description:

End point type	Primary

End point timeframe:

At 12 weeks

Notes:

[4] - 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: The analysis that have been performed are descriptive statistics.

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	9	1
Units: mmHg				
arithmetic mean (full range (min-max))	71.7 (62 to 90)	80.8 (69 to 100)	75 (51 to 100)	82 (82 to 82)

Statistical analyses

No statistical analyses for this end point

Primary: lymph node enlargement

End point title	lymph node enlargement[5]

End point description:

End point type	Primary

End point timeframe:

At 12 weeks

Notes:

[5] - 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: The analysis that have been performed are descriptive statistics.

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: Number of patients				
normal	3	6	8	1
abnormal	0	0	1	0
not done	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: liver and spleen

End point title	liver and spleen[6]

End point description:

End point type	Primary

End point timeframe:

At 12 weeks

Notes:

[6] - 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: The analysis that have been performed are descriptive statistics

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: Number of patients				
normal	3	6	8	1
abnormal	0	0	0	0
not done	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Primary: Immunogenicity - rfIL-18BP antibodies

End point title	Immunogenicity - rfIL-18BP antibodies[7]

End point description:

Number of patients with samples that screened positive in the ADA assay

End point type	Primary

End point timeframe:

Visit = V6 (Follow-up)

Notes:

[7] - 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: The analysis that have been performed are descriptive statistics.

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: Nb of patients with positive samples				
Yes	4	4	7	1
No	0	2	4	0

Statistical analyses

No statistical analyses for this end point

Primary: Injection site reaction - pain

End point title	Injection site reaction - pain[8]

End point description:

End point type	Primary

End point timeframe:

Visit = V6 (follow-up)

Notes:

[8] - 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: The analysis that have been performed are descriptive statistics.

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: Number of patients				
none	3	6	8	1
mild	1	0	0	0
moderate	0	0	0	0
severe	0	0	1	0
missing	0	0	2	0

Statistical analyses

No statistical analyses for this end point

Primary: 12-lead ECG : Performance of ECG

End point title	12-lead ECG : Performance of ECG[9]

End point description:

End point type	Primary

End point timeframe:

Visit = V5 (12 weeks)

Notes:

[9] - 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: The analysis that have been performed are descriptive statistics.

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: number of patients				
normal	2	5	8	1
abnormal, not clinically significant	1	1	1	0
abnormal, clinically significant	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Skin rash - Change compared to Baseline

End point title	Skin rash - Change compared to Baseline

End point description:

All subjects were analyzed but not all subjects had skin rash at baseline, 7/10 in Cohort 1 and 6/13 in Cohort 2.

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: Number of patients				
unchanged	1	1	6	1
slightly decreased	0	0	0	0
markedly decreased	0	0	1	0
slightly increased	0	0	0	0
markedly increased	0	1	1	0
resolved	2	4	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: 44 joint count assessment and possible findings - swelling, tenderness

End point title	44 joint count assessment and possible findings - swelling, tenderness

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: Number of patients				
no	3	0	1	1
yes	0	6	8	0

Statistical analyses

No statistical analyses for this end point

Secondary: Serum CRP - absolute change from baseline

End point title	Serum CRP - absolute change from baseline

End point description:

End point type	Secondary

End point timeframe:

At week 12

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: percent				
arithmetic mean (full range (min-max))	0.8 (-48 to 43)	3.2 (-121 to 137)	-25.4 (-72 to 2)	-21.7 (-21.7 to -21.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Serum amyloid - SAA assessment

End point title	Serum amyloid - SAA assessment

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: ng/ml				
arithmetic mean (full range (min-max))	539689.63 (5488.8 to 1570747.1)	440916.82 (10437.8 to 866008.4)	114679.1 (2668.1 to 692619.6)	15112.5 (15112.5 to 15112.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Ferritin - absolute change from baseline

End point title	Ferritin - absolute change from baseline

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: percent				
arithmetic mean (full range (min-max))	-230 (-487 to 22)	393.1 (-1000 to 3721)	-143 (-408 to -19)	-32.3 (-32.3 to -32.3)

Statistical analyses

No statistical analyses for this end point

Secondary: SDAI - absolute change from baseline

End point title	SDAI - absolute change from baseline

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: percent				
arithmetic mean (full range (min-max))	-8.1 (-22 to 0)	-7.2 (-37 to 20)	-13.2 (-24 to 10)	-12.7 (-12.7 to -12.7)

Statistical analyses

No statistical analyses for this end point

Secondary: SAA assessment: S100A8/A9

End point title	SAA assessment: S100A8/A9

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	8	1
Units: ng/ml				
arithmetic mean (full range (min-max))	3466.33 (1663 to 6113)	10544.4 (996 to 28381)	3905.75 (1385 to 6298)	2666 (2666 to 2666)

Statistical analyses

No statistical analyses for this end point

Secondary: SAA assessment: S100A12

End point title	SAA assessment: S100A12

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	8	1
Units: ng/ml				
arithmetic mean (full range (min-max))	42.5 (26.3 to 68.2)	204.5 (15.4 to 482.5)	70.98 (22.3 to 155.3)	29.3 (29.3 to 29.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Leucocytes

End point title	Leucocytes

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	8	1
Units: /nl				
arithmetic mean (full range (min-max))	7.63 (5 to 9.8)	10.07 (7 to 13)	9.29 (6.7 to 12.2)	9.3 (9.3 to 9.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Interleukin 18

End point title	Interleukin 18

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	8	1
Units: pg/ml				
arithmetic mean (full range (min-max))	450.33 (255 to 695)	4274.2 (481 to 15290)	957 (366 to 2358)	1992 (1992 to 1992)

Statistical analyses

No statistical analyses for this end point

Secondary: Interleukin 18 binding protein

End point title	Interleukin 18 binding protein

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	8	1
Units: pg/ml				
arithmetic mean (full range (min-max))	1281114.67 (1071971 to 1457679)	1178679.8 (126244 to 2760364)	2070073.63 (838155 to 4083179)	9371548 (9371548 to 9371548)

Statistical analyses

No statistical analyses for this end point

Secondary: Interleukin 18 free

End point title	Interleukin 18 free[10]

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No results are available for the other arm(s).

End point values	Cohort 1 / 80-160 mg			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: pg/ml				
arithmetic mean (full range (min-max))	35.7 (35.7 to 35.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Interleukin 1ra

End point title	Interleukin 1ra

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	8	1
Units: ng/l				
arithmetic mean (full range (min-max))	31.3 (20.1 to 41.9)	54.48 (49.5 to 66.2)	31.18 (17.6 to 43)	48 (48 to 48)

Statistical analyses

No statistical analyses for this end point

Secondary: Interleukin 6

End point title	Interleukin 6

End point description:

End point type	Secondary

End point timeframe:

At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	7	1
Units: pg/ml				
arithmetic mean (full range (min-max))	2.87 (1 to 4.5)	7.18 (1.3 to 21.4)	2.09 (0.4 to 6.1)	1.1 (1.1 to 1.1)

Statistical analyses

No statistical analyses for this end point

Secondary: TNF-alpha

End point title	TNF-alpha

End point description:

End point type	Secondary

End point timeframe:
At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	5	8	1
Units: pg/ml				
arithmetic mean (full range (min-max))	3.08 (2.87 to 3.38)	5.25 (1.9 to 14.93)	2.3 (1.16 to 3.67)	2.21 (2.21 to 2.21)

Statistical analyses

No statistical analyses for this end point

Secondary: Triglycerides

End point title	Triglycerides

End point description:

End point type	Secondary

End point timeframe:
At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	8	1
Units: mmol/l				
arithmetic mean (full range (min-max))	1.9 (1.22 to 3.19)	1.41 (0.64 to 2.83)	1.06 (0.54 to 1.89)	0.95 (0.95 to 0.95)

Statistical analyses

No statistical analyses for this end point

Secondary: Therapeutic response at V5 (week 12)

End point title	Therapeutic response at V5 (week 12)

End point description:

End point type	Secondary

End point timeframe:
At 12 weeks

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	Cohort 2 / 160-320 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	6	12	1
Units: number of patients				
No	2	5	7	0
Yes	2	1	2	1
Unknown	0	0	3	0

Statistical analyses

No statistical analyses for this end point

Secondary: Prednisone : Maximum dose during treatment

End point title	Prednisone : Maximum dose during treatment[11]

End point description:

End point type	Secondary

End point timeframe:

During treatment

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No results are available for the other arm(s).

End point values	Cohort 1 / 80 mg	Cohort 1 / 80-160 mg	Cohort 2 / 160 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	5	10	
Units: mg/day				
arithmetic mean (full range (min-max))	17.5 (15 to 22.5)	29.5 (7.5 to 80)	22 (5 to 60)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Throughout the study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Tadekinig alfa 80 mg
Reporting group description: -	
Reporting group title	Tadekinig alfa 160 mg
Reporting group description: -	
Reporting group title	Tadekinig alfa 320 mg
Reporting group description: -	

Serious adverse events	Tadekinig alfa 80 mg	Tadekinig alfa 160 mg	Tadekinig alfa 320 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 10 (20.00%)	1 / 19 (5.26%)	0 / 1 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0		
Eye disorders			
Toxic optic neuropathy			
subjects affected / exposed	0 / 10 (0.00%)	1 / 19 (5.26%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Spondylolisthesis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 19 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 19 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 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	Tadekinig alfa 80 mg	Tadekinig alfa 160 mg	Tadekinig alfa 320 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 10 (80.00%)	18 / 19 (94.74%)	1 / 1 (100.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 10 (10.00%)	2 / 19 (10.53%)	1 / 1 (100.00%)
occurrences (all)	155	155	155
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 10 (0.00%)	3 / 19 (15.79%)	0 / 1 (0.00%)
occurrences (all)	155	155	155
Condition aggravated			
subjects affected / exposed	0 / 10 (0.00%)	3 / 19 (15.79%)	0 / 1 (0.00%)
occurrences (all)	155	155	155
Injection site erythema			
subjects affected / exposed	1 / 10 (10.00%)	2 / 19 (10.53%)	0 / 1 (0.00%)
occurrences (all)	155	155	155
Injection site reaction			
subjects affected / exposed	1 / 10 (10.00%)	2 / 19 (10.53%)	0 / 1 (0.00%)
occurrences (all)	155	155	155
Fatigue			
subjects affected / exposed	2 / 10 (20.00%)	0 / 19 (0.00%)	0 / 1 (0.00%)
occurrences (all)	155	155	155
Pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 19 (10.53%)	0 / 1 (0.00%)
occurrences (all)	155	155	155
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 10 (0.00%)	2 / 19 (10.53%)	0 / 1 (0.00%)
occurrences (all)	155	155	155
Nausea			
subjects affected / exposed	0 / 10 (0.00%)	2 / 19 (10.53%)	1 / 1 (100.00%)
occurrences (all)	155	155	155
Vomiting			

subjects affected / exposed	0 / 10 (0.00%)	2 / 19 (10.53%)	0 / 1 (0.00%)
occurrences (all)	155	155	155
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 10 (0.00%)	1 / 19 (5.26%)	1 / 1 (100.00%)
occurrences (all)	155	155	155
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)	4 / 19 (21.05%)	1 / 1 (100.00%)
occurrences (all)	155	155	155
Juvenile idiopathic arthritis			
subjects affected / exposed	0 / 10 (0.00%)	2 / 19 (10.53%)	0 / 1 (0.00%)
occurrences (all)	155	155	155
Pain in extremity			
subjects affected / exposed	0 / 10 (0.00%)	1 / 19 (5.26%)	1 / 1 (100.00%)
occurrences (all)	155	155	155
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 19 (5.26%)	1 / 1 (100.00%)
occurrences (all)	155	155	155
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 19 (5.26%)	0 / 1 (0.00%)
occurrences (all)	155	155	155
Gastroenteritis			
subjects affected / exposed	1 / 10 (10.00%)	1 / 19 (5.26%)	0 / 1 (0.00%)
occurrences (all)	155	155	155
Oral herpes			
subjects affected / exposed	1 / 10 (10.00%)	1 / 19 (5.26%)	0 / 1 (0.00%)
occurrences (all)	155	155	155

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 February 2015	Protocol version 2.0 dated 25 February 2015
28 August 2015	Protocol version 3.0 dated 28 August 2015
27 January 2016	Protocol version 4.0 dated 27 January 2016 - As of January 2016, the dose 320mg is stopped. Before this protocol amendment, one patient was escalated from 160mg to 320mg. This patient will continue the study under this dose

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported