



## Clinical trial results:

**A Phase II, multicenter, randomized, double-blind, parallel group, placebo-controlled, adaptive dose-ranging study to evaluate the efficacy and safety of AIN457(secukinumab) in patients with relapsing multiple sclerosis**

### Summary

EudraCT number	2012-004019-29
Trial protocol	BE IT SE DE CZ FI ES PL
Global end of trial date	17 April 2014

### Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	18 July 2015

### Trial information

#### Trial identification

Sponsor protocol code	CAIN457B2203
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01874340
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

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	17 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 April 2014
Global end of trial reached?	Yes
Global end of trial date	17 April 2014
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was to evaluate the effect of three AIN457 doses (3, 7, and 15 mg/kg i.v.), compared to placebo, in reducing the cumulative number of new Gadolinium-enhancing T1-weighted lesions recorded on all available MRI scans at Months 3, 4, 5 and 6 in patients with RMS.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 2013
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	Japan: 1
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Turkey: 1
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Italy: 3
Worldwide total number of subjects	28
EEA total number of subjects	17

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)	28
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

patients were randomly assigned to treatment arms in a ratio of 1:1:1:1

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	AIN457 15 mg/kg
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Arm description:

AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.

<b>Arm title</b>	AIN457 7 mg/kg
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Arm description:

AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.

<b>Arm title</b>	AIN457 3 mg/kg
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Arm description:

AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.

<b>Arm title</b>	Placebo
Arm description: Matching placebo will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.	
Arm type	Placebo
Investigational medicinal product name	Matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.

<b>Number of subjects in period 1</b>	AIN457 15 mg/kg	AIN457 7 mg/kg	AIN457 3 mg/kg
Started	6	8	8
Completed	0	0	0
Not completed	6	8	8
Consent withdrawn by subject	-	-	-
Study terminated by Sponsor	6	8	8

<b>Number of subjects in period 1</b>	Placebo
Started	6
Completed	1
Not completed	5
Consent withdrawn by subject	1
Study terminated by Sponsor	4

## Baseline characteristics

### Reporting groups

Reporting group title	AIN457 15 mg/kg
Reporting group description:	
AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.	
Reporting group title	AIN457 7 mg/kg
Reporting group description:	
AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.	
Reporting group title	AIN457 3 mg/kg
Reporting group description:	
AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.	
Reporting group title	Placebo
Reporting group description:	
Matching placebo will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.	

Reporting group values	AIN457 15 mg/kg	AIN457 7 mg/kg	AIN457 3 mg/kg
Number of subjects	6	8	8
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	8	8
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	28.8	34.5	35.5
standard deviation	± 7.73	± 8.64	± 9.71
Gender, Male/Female			
Units: Participants			
Male	2	4	2
Female	4	4	6

Reporting group values	Placebo	Total	
Number of subjects	6	28	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	

Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	6	28	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous   Units: Years arithmetic mean standard deviation	34 ± 9.3	-	
Gender, Male/Female Units: Participants			
Male	2	10	
Female	4	18	

## End points

### End points reporting groups

Reporting group title	AIN457 15 mg/kg
Reporting group description: AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.	
Reporting group title	AIN457 7 mg/kg
Reporting group description: AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.	
Reporting group title	AIN457 3 mg/kg
Reporting group description: AIN457 will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.	
Reporting group title	Placebo
Reporting group description: Matching placebo will be administered intravenously at day1, Week 2, week 4 and every 4 weeks thereafter.	

### Primary: Cumulative number of new Gadolinium [Gd]-enhancing T1-weighted lesions

End point title	Cumulative number of new Gadolinium [Gd]-enhancing T1-weighted lesions <sup>[1]</sup>
End point description: Due to early termination this trial was not powered for efficacy no statistical analysis was performed	
End point type	Primary
End point timeframe: Months 3, 4, 5, 6	
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: Due to early termination, no statistical analysis was planned for this primary endpoint.	

End point values	AIN457 15 mg/kg	AIN457 7 mg/kg	AIN457 3 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 <sup>[2]</sup>	0 <sup>[3]</sup>	0 <sup>[4]</sup>	0 <sup>[5]</sup>
Units: T1 lesions				

Notes:

[2] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[3] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[4] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[5] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Annualized relapse rate

End point title	Annualized relapse rate
End point description: Due to early termination this trial was not powered for efficacy no statistical analysis was performed	



End point type	Secondary
End point timeframe:	
6 Months	

End point values	AIN457 15 mg/kg	AIN457 7 mg/kg	AIN457 3 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 <sup>[6]</sup>	0 <sup>[7]</sup>	0 <sup>[8]</sup>	0 <sup>[9]</sup>
Units: Number of Relapses				

Notes:

[6] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[7] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[8] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[9] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Combined unique active lesions (CUAL)

End point title	Combined unique active lesions (CUAL)
End point description:	
Due to early termination this trial was not powered for efficacy no statistical analysis was performed	
End point type	Secondary
End point timeframe:	
Months 3, 4, 5, 6	

End point values	AIN457 15 mg/kg	AIN457 7 mg/kg	AIN457 3 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 <sup>[10]</sup>	0 <sup>[11]</sup>	0 <sup>[12]</sup>	0 <sup>[13]</sup>
Units: Active Lesions				

Notes:

[10] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[11] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[12] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[13] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change in total volume of T2-weighted lesions

End point title	Change in total volume of T2-weighted lesions
End point description:	
Due to early termination this trial was not powered for efficacy no statistical analysis was performed	
End point type	Secondary

End point timeframe:

Baseline, Month 6

End point values	AIN457 15 mg/kg	AIN457 7 mg/kg	AIN457 3 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 <sup>[14]</sup>	0 <sup>[15]</sup>	0 <sup>[16]</sup>	0 <sup>[17]</sup>
Units: T2 Weighted Lesions				

Notes:

[14] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[15] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[16] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

[17] - No statistical analyses could be performed for the efficacy endpoints defined in the protocol.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of participants with Adverse events as a measure of safety and tolerability

End point title	Number of participants with Adverse events as a measure of safety and tolerability
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End point description:

Number of participants with Adverse events as a measure of safety and tolerability

End point type	Secondary
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End point timeframe:

6 months

End point values	AIN457 15 mg/kg	AIN457 7 mg/kg	AIN457 3 mg/kg	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	8	8	6
Units: Participants				
Adverse Events (AE)	1	3	3	2
Death	0	0	0	0
Non-Fatal Serious Adverse Event (SAE)	0	1	0	0

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

### Reporting groups

Reporting group title	AIN457 15 mg/kg
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Reporting group description:

AIN457 15 mg/kg

Reporting group title	AIN457 7 mg/kg
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Reporting group description:

AIN457 7 mg/kg

Reporting group title	Placebo
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Reporting group description:

Placebo

Reporting group title	AIN457 3 mg/kg
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Reporting group description:

AIN457 3 mg/kg

Serious adverse events	AIN457 15 mg/kg	AIN457 7 mg/kg	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
GASTRITIS			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	AIN457 3 mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Gastrointestinal disorders			
GASTRITIS			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	AIN457 15 mg/kg	AIN457 7 mg/kg	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	2 / 6 (33.33%)
Investigations			
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
WHITE BLOOD CELL COUNT INCREASED			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
NAUSEA			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
BACK PAIN			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1	0 / 6 (0.00%) 0
Infections and infestations BRONCHITIS subjects affected / exposed occurrences (all)  NASOPHARYNGITIS subjects affected / exposed occurrences (all)  TINEA VERSICOLOUR subjects affected / exposed occurrences (all)  PHARYNGITIS subjects affected / exposed occurrences (all)  VAGINAL INFECTION subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0  1 / 6 (16.67%) 1  0 / 6 (0.00%) 0  0 / 6 (0.00%) 0  0 / 6 (0.00%) 0  0 / 6 (0.00%) 0	1 / 8 (12.50%) 1  0 / 8 (0.00%) 0  0 / 8 (0.00%) 0  0 / 8 (0.00%) 0  0 / 8 (0.00%) 0	0 / 6 (0.00%) 0  0 / 6 (0.00%) 0  0 / 6 (0.00%) 0  1 / 6 (16.67%) 1  0 / 6 (0.00%) 0
Metabolism and nutrition disorders HYPERPHAGIA subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1	0 / 6 (0.00%) 0

<b>Non-serious adverse events</b>	AIN457 3 mg/kg		
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 8 (37.50%)		
Investigations C-REACTIVE PROTEIN INCREASED subjects affected / exposed occurrences (all)  WHITE BLOOD CELL COUNT INCREASED subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0  0 / 8 (0.00%) 0		
General disorders and administration site conditions PYREXIA			

subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Gastrointestinal disorders NAUSEA subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Skin and subcutaneous tissue disorders RASH subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all)  BACK PAIN subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0  0 / 8 (0.00%) 0		
Infections and infestations BRONCHITIS subjects affected / exposed occurrences (all)  NASOPHARYNGITIS subjects affected / exposed occurrences (all)  TINEA VERSICOLOUR subjects affected / exposed occurrences (all)  PHARYNGITIS subjects affected / exposed occurrences (all)  VAGINAL INFECTION subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0  1 / 8 (12.50%) 1  1 / 8 (12.50%) 1  0 / 8 (0.00%) 0  1 / 8 (12.50%) 1		
Metabolism and nutrition disorders HYPERPHAGIA			

subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 February 2013	The Amendment was issued prior to any patients enrolling in the study, introduced

Notes:

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### 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.

Study terminated early based upon development of another anti-IL17 fully human monoclonal antibody with better potential for treating MS patients. Due to early termination this trial was not powered for efficacy no statistical analysis was performed.

Notes: