



## Clinical trial results:

**An open label extension study to evaluate the safety, tolerability and efficacy of**

**AIN457 in patients with relapsing-remitting multiple sclerosis.**

### Summary

EudraCT number	2011-001629-25
Trial protocol	CZ
Global end of trial date	02 June 2014

### Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	24 July 2015

### Trial information

#### Trial identification

Sponsor protocol code	CAIN457B2201E1
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01433250
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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	02 June 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 June 2014
Global end of trial reached?	Yes
Global end of trial date	02 June 2014
Was the trial ended prematurely?	Yes

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the long term safety and tolerability of secukinumab in patients with RRMS who participated in the core CAIN457B2201 phase II PoC study.

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	28 February 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Czech Republic: 8
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Ukraine: 11
Worldwide total number of subjects	39
EEA total number of subjects	8

Notes:

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**Subjects enrolled per age group**

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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: -

### Pre-assignment

Screening details:

This was a multicenter, open-label, non-randomized, non-controlled trial that aimed at providing access to active treatment for at least 1 year to patients who had completed the core CAIN457B2201 study (24 weeks), in order to collect long-term safety data

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	AIN/AIN

Arm description:

AIN core 24 weeks/AIN extension 1 year

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intramuscular and intravenous use

Dosage and administration details:

10 mg/kg i.v. at the start of Week 1 and then

<b>Arm title</b>	PBO/AIN
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Arm description:

placebo first 24 weeks/ AIN extension for 52 weeks

Arm type	Placebo
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intramuscular and intravenous use

Dosage and administration details:

10 mg/kg i.v. at the start of Week 1 and then

<b>Number of subjects in period 1</b>	AIN/AIN	PBO/AIN
Started	22	17
Completed	19	14
Not completed	3	3
Consent withdrawn by subject	3	2
Protocol deviation	-	1



## Baseline characteristics

### Reporting groups

Reporting group title	AIN/AIN
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Reporting group description:

AIN core 24 weeks/AIN extension 1 year

Reporting group title	PBO/AIN
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Reporting group description:

placebo first 24 weeks/ AIN extension for 52 weeks

Reporting group values	AIN/AIN	PBO/AIN	Total
Number of subjects	22	17	39
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)	22	17	39
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous   Units: Years			
arithmetic mean	36.1	34.2	
standard deviation	± 10	± 8.71	-
Gender, Male/Female Units: Participants			
Female	12	12	24
Male	10	5	15
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	20	16	36
Unknown or Not Reported	1	1	2

## End points

### End points reporting groups

Reporting group title	AIN/AIN
Reporting group description: AIN core 24 weeks/AIN extension 1 year	
Reporting group title	PBO/AIN
Reporting group description: placebo first 24 weeks/ AIN extension for 52 weeks	

### Primary: Measure: number of subjects with adverse events, number of abnormalities in safety assessments

End point title	Measure: number of subjects with adverse events, number of abnormalities in safety assessments <sup>[1]</sup>
End point description: Safety outcomes will be described in Adverse events section as there was not an efficacy primary outcome	
End point type	Primary
End point timeframe: up to 97 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: No prespecified analysis were planned for this outcome measure

End point values	AIN/AIN	PBO/AIN		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22 <sup>[2]</sup>	17		
Units: participants	0	0		

Notes:

[2] - No prespecified statistical analysis was planned for this outcome measure

### Statistical analyses

No statistical analyses for this end point

### Secondary: Distribution of patients with relapses to end of study (EOS) (all subjects)

End point title	Distribution of patients with relapses to end of study (EOS) (all subjects)
End point description: Description: number of relapses based on neurological assessments and EDSS	
End point type	Secondary
End point timeframe: up to 97 weeks	

End point values	AIN/AIN	PBO/AIN		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17		
Units: Participants	9	5		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number lesions measured in the brain by magnetic resonance imaging. T1 Weighted MRI

End point title	Number lesions measured in the brain by magnetic resonance imaging. T1 Weighted MRI
End point description:	
Measures of absolute number of gadolinium [Gd]-enhancing lesions on T1-weighted scans	
End point type	Secondary
End point timeframe:	
up to 97 weeks	

End point values	AIN/AIN	PBO/AIN		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17		
Units: lesions				
arithmetic mean (full range (min-max))				
week 13 T1 (n=22, 16)	0.8 (0 to 4)	2 (0 to 15)		
week 25 T1 (n=22, 16)	0.6 (0 to 5)	1.9 (0 to 20)		
week 37 T1 (n=22, 15)	1 (0 to 5)	0.8 (0 to 4)		
week 53 T1 (n=14, 6)	0.3 (0 to 3)	0.3 (0 to 1)		
wk 73 T1 (n=11,9)	0.6 (0 to 3)	0.2 (0 to 1)		
EOT (n=15,13)	0.7 (0 to 5)	0.5 (0 to 3)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number lesions measured in the brain by magnetic resonance imaging. T2 Weighted MRI

End point title	Number lesions measured in the brain by magnetic resonance imaging. T2 Weighted MRI
End point description:	
Measures of absolute number of gadolinium [Gd]-enhancing lesions on T2-weighted lesions	
End point type	Secondary
End point timeframe:	
upto 97 weeks	



End point values	AIN/AIN	PBO/AIN		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17		
Units: lesions				
arithmetic mean (full range (min-max))				
week 13 T2 (n=22, 16)	1.3 (0 to 7)	2.2 (0 to 12)		
week 25 T2 (n=22, 16)	0.8 (0 to 6)	2.4 (0 to 21)		
week 37 T2 (n=22, 15)	1.3 (0 to 5)	1.3 (0 to 6)		
week 53 T2 (n=14, 6)	0.4 (0 to 4)	0.7 (0 to 3)		
wk 73 T2 (n=11,9)	1.3 (0 to 5)	0.9 (0 to 5)		
EOT T2 (n=15,13)	1.1 (0 to 4)	0.07 (0 to 3)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change in Brain Volume at end of study.

End point title	Change in Brain Volume at end of study.
End point description:	
Change in volume from start to end of study	
End point type	Secondary
End point timeframe:	
up to 97 weeks	

End point values	AIN/AIN	PBO/AIN		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17		
Units: ml				
arithmetic mean (standard deviation)	-14.8968 ( $\pm$ 63.73027)	-30.4346 ( $\pm$ 31.218)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Measure of disability: Expanded Disability Status Scale (EDSS).

End point title	Measure of disability: Expanded Disability Status Scale (EDSS).
End point description:	
The EDSS is a scale for assessing neurological impairment in MS (Kurtzke 1983) including (1) a series of scores in each of eight functional systems, and (2) the EDSS steps (ranging from 0 (normal) to 10	

(death due to MS). The functional systems are Visual, Brain Stem, Pyramidal, Cerebellar, Sensory, Bowel and Bladder, Cerebral and Other functions.

End point type	Secondary
End point timeframe:	
Baseline to End of Study	

End point values	AIN/AIN	PBO/AIN		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	17		
Units: participants				
Baseline score 0	1	0		
Baseline score 1.0	0	2		
Baseline score 1.5	5	5		
Baseline score 2.0	5	2		
Baseline score 2.5	1	1		
Baseline score 3.0	2	4		
Baseline score 3.5	2	0		
Baseline score 4.0	1	1		
Baseline score 4.5	2	2		
Baseline score 5.0	1	0		
Baseline score 6.0	1	0		
WK25 score 0	2	0		
WK25 score 1	1	2		
WK25 score 1.5	4	5		
WK25 score 2.0	4	1		
WK25 score 2.5	2	1		
WK25 score 3.0	2	4		
WK25 score 4.0	1	1		
WK25 score 4.5	3	1		
WK25 score 5.0	1	0		
WK25 score 5.5	0	1		
WK25 score 6.0	1	0		
WK25 score 6.5	1	0		
Safety Week 53 score 0	1	0		
Safety Week 53 score 1.0	1	1		
Safety Week 53 score 1.5	3	3		
Safety Week 53 score 2.0	4	0		
Safety Week 53 score 3.0	1	1		
Safety Week 53 score 3.5	1	0		
Safety Week 53 score 4.0	0	1		
Safety Week 53 score 5.0	1	0		
Safety Week 53 score 5.5	2	0		
Safety Week 53 score 6.0	1	0		
WK73 score 0	1	1		
WK73 score 1.0	2	1		
WK73 score 1.5	1	5		
WK73 score 2.0	2	0		
WK73 score 3.0	0	1		
WK73 score 4.0	1	0		

WK73 score 5.5	1	0		
WK73 score 6.0	1	0		
End of treatment score 0	1	1		
End of treatment score 1.0	2	1		
End of treatment score 1.5	2	5		
End of treatment score 2.0	2	1		
End of treatment score 2.5	2	1		
End of treatment score 3.0	0	3		
End of treatment score 3.5	1	0		
End of treatment score 4.0	2	0		
End of treatment score 4.5	0	1		
End of treatment score 5.5	0	1		
End of treatment score 6.0	1	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 are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

### Reporting groups

Reporting group title	PBO/AIN
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Reporting group description:

PBO/AIN

Reporting group title	AIN/AIN
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Reporting group description:

AIN/AIN

Serious adverse events	PBO/AIN	AIN/AIN	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	2 / 22 (9.09%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	0 / 17 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteochondrosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	PBO/AIN	AIN/AIN	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 17 (47.06%)	7 / 22 (31.82%)	
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Varicose vein			
subjects affected / exposed	0 / 17 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Cardiomyopathy			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Migraine			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Uterine cervical erosion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	2 / 22 (9.09%) 2	
Psychiatric disorders Anxiety disorder subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	2 / 22 (9.09%) 2	
Infections and infestations Cystitis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 22 (0.00%) 0	
Laryngitis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 22 (0.00%) 0	
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2	1 / 22 (4.55%) 1	
Pharyngitis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	2 / 22 (9.09%) 3	
Respiratory tract infection viral subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2	2 / 22 (9.09%) 3	
Rhinitis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 22 (0.00%) 0	
Metabolism and nutrition disorders Overweight subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 22 (0.00%) 0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 February 2013	This amendment was issued in order to prolong access to active treatment to all patients enrolled in the current CAIN457B2201E1 study until they could participate in another extension study. For this purpose additional treatment visits were scheduled and described. All patients continued to receive only active treatment throughout the study course. In addition this amendment included an adjustment of the frequency at which some assessments were scheduled in order to align with the ongoing secukinumab program. These changes were not expected to have an impact on the safety of the intended study population, analysis of results and the scientific value of the trial.

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.

Further development of secukinumab in MS is not being pursued and the extension study in MS, CAIN457B2201E1, was terminated. Termination of this study was not related to the safety or tolerability concerns observed in the study.

Notes: