NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis

Generic Drug Name

secukinumab

Trial Indication(s)

Ankylosing spondylitis

Protocol Number

CAIN457K2340

Protocol Title

A randomized, partially-blinded study of secukinumab to demonstrate reduction of radiographic progression versus GP2017 (adalimumab biosimilar) at 104 weeks and to assess the long term safety, tolerability and efficacy up to 2 years in patients with active ankylosing spondylitis

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase III

Study Start/End Dates

Study Start Date: November 2017 (Actual)
Primary Completion Date: November 2021 (Actual)
Study Completion Date: November 2021 (Actual)

Reason for Termination (If applicable)

Study Design/Methodology

This was a Phase IIIb, multi-center, randomized, partially-blinded, active-controlled, parallel-group design in subjects with ankylosing spondylitis (AS). The study consisted of a screening period (up to 10 weeks before randomization), a treatment period (104 weeks), and two follow-up visits (Weeks 112 and 120).

Centers

171 centers in 30 countries: Spain(12), United Kingdom(14), United States(19), Germany(15), Canada(4), Denmark(2), Russia(15), Czech Republic(5), France(6), Finland(1), Slovakia (Slovak Republic)(5), Chile(4), Taiwan(5), Philippines(3), Australia(1), Poland(5), Israel(3), Netherlands(5), Peru(4), Japan(8), Portugal(6), Turkey(6), Belgium(2), Korea, Republic of(6), Mexico(5), Monaco(1), Greece(3), Romania(3), Colombia(2), Argentina(1)

Objectives:

The primary objective was to demonstrate the proportion of subjects on secukinumab (150 mg s.c. or 300 mg s.c.) with no radiographic progression as measured by modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) at Week 104 is superior to subjects on GP2017 (adalimumab biosimilar 40 mg s.c.).

Secondary objectives included change from baseline in modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) at Week 104, proportion of subjects with a syndesmophyte at baseline with no new syndesmophytes at Week 104, Berlin SI joint edema score at Week 104, ASspiMRI-a Berlin modification score at Week 104, Assessment of SpondyloArthritis International Society (ASAS) 20 response, ASAS 40 response, ASAS partial remission and Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease at Week 104, and overall safety and tolerability of secukinumab.

Test Product (s), Dose(s), and Mode(s) of Administration

Group 1: secukinumab 150 mg [1 x 1.0 mL s.c. plus placebo (1 x 1.0 mL s.c.)]
Group 2: secukinumab 300 mg (2 x 1.0 mL s.c.)
Group 3: GP2017 (adalimumab biosimilar) 40 mg (1 x 0.8 mL s.c.)

Subjects in both secukinumab dose groups received study treatment at baseline, Weeks 1, 2, 3 and 4 followed by treatment every 4 weeks through Week 100. Subjects in the GP2017 group received study treatment at baseline and every two weeks through Week 102. Subjects could self-administer all secukinumab / placebo and GP2017 doses at the study site or at home. Study treatment (secukinumab vs. GP2017) was provided in an open-label fashion. Subjects in the secukinumab groups were blinded to the dose (150 mg vs. 300 mg).

Statistical Methods

Primary endpoint

The primary efficacy objective was to demonstrate that the proportion of subjects on secukinumab (150 mg or 300 mg) with no radiographic progression was superior to GP2017 40 mg at Week 104. The analysis of the primary objective was based on the following estimand:

- Population – defined through appropriate inclusion/exclusion criteria to reflect the targeted AS population
- Variable – binary response variable indicating no radiographic progression, defined as a change from baseline in mSASSS at Week 104 of ≤ 0.5.
- Intercurrent event – regardless of adherence to randomized treatment
- Population-level summary – difference in proportions of responders between the secukinumab and GP2017 arms

The statistical hypothesis for no radiographic progression being tested was that there is no difference in the proportion of subjects with no radiographic progression at Week 104 in the secukinumab regimens versus GP2017 40 mg regimen. The primary analysis was conducted via logistic regression with treatment as factor and included baseline mSASSS as covariate. Difference in marginal response proportions with p-value and respective 95% confidence interval were estimated from the logistic regression model. Analysis was done on the FAS.

Secondary endpoints

Change from baseline in mSASSS was evaluated using ANCOVA model with treatment as a factor and baseline mSASSS as a covariate. The proportion of subjects with no new syndesmophyte was evaluated using a logistic regression model with treatment group as a factor and baseline mSASSS as a covariate..

Change from baseline to Week 104 in ASspiMRI-a Berlin modification score and Berlin SI joint edema score were evaluated using ANCOVA model with treatment as factor and baseline score as covariate. Pairwise comparison was performed for secukinumab (150 mg s.c. or 300 mg s.c.) versus GP2017. These were assessed and analyzed outside the testing strategy.

Response at Week 104 to ASAS 20, ASAS 40, ASAS partial remission and ASDAS inactive disease was evaluated using a logistic regression model with treatment group as a factor and baseline score (if appropriate) as a covariate. These were assessed and analyzed outside the testing strategy.

Handling of missing data for secondary variables included in the testing strategy was the same as for the primary variable. All analysis was done on the FAS.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
- Male or non-pregnant, non-nursing female patients at least 18 years of age
- Diagnosis of moderate to severe Ankylosing Spondylitis with radiologic evidence (centrally read X-ray) fulfilling the Modified New York criteria for AS despite previous or current NSAID/ nonbiologic DMARD therapy
- Active AS assessed by total BASDAI ≥ 4 on a scale of 0-10
- Spinal pain as measured by BASDAI question #2 ≥ 4 (0-10)
- Total back pain as measured by visual analog scale (VAS) ≥ 40 mm (0-100 mm)
- hsCRP ≥ 5 mg/L OR presence of at least 1 syndesmophyte on centrally read spinal X-ray

Exclusion Criteria:
- Patients with total ankylosis of the spine
- Pregnant or nursing (lactating) women
- Evidence of ongoing infectious or malignant process
- Previous exposure to any biologic immunomodulating agent, including those targeting IL-17, IL-17 receptor or TNFα
- Subjects taking high potency opioid analgesics
- Previous treatment with any cell-depleting therapies including but not limited to anti-CD20, investigational agents

Other protocol-defined inclusion/exclusion criteria may apply

Participant Flow Table

Overall Study

	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg	Total
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104	
Started	287	286	286	859
Completed	254	237	243	734
Not Completed	33	49	43	125
Adverse Event	9	12	8	29
Death	1	1	3	5
Lost to Follow-up	2	4	3	9
New Therapy For Study Indication	1	2	2	5
Physician Decision	4	12	10	26

Pregnancy	1	1	0	2
Progressive Disease	1	0	0	1
Protocol Deviation	1	1	3	5
Subject/Guardian Decision	13	16	14	43

Baseline Characteristics

	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg	Total
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104	
Number of Participants [units: participants]	287	286	286	859
Age Continuous (units: years) Mean ± Standard Deviation				
	42.1±11.99	42.2±12.47	41.9±12.68	42.1±12.37

Sex: Female, Male (units:) Count of Participants (Not Applicable)				
Female	57	63	65	185
Male	230	223	221	674
Race/Ethnicity, Customized (units: Participants)				
White	225	227	228	680
Black or African American	1	2	0	3
Asian	40	39	50	129
American Indian or Alaska Native	19	15	7	41
Other	1	0	0	1
Multiple	1	3	1	5
Modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) scores[1] (units: mSASSS scores) Mean ± Standard Deviation				
	17.602±21.3286	16.527±20.8153	15.695±19.4955	16.609±20.5506

[1] The modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) evaluates the outside corners of the vertebral spine for erosions, sclerosis, squaring, bony growths and spinal bridging. The mSASSS assesses the participant's spinal vertebrae for structural changes and scores each vertebrae from 0 (normal vertebrae) to 3 (bony growth that bridges one vertebrae to the neighboring vertebrae). A total of 24 vertebral corners are scored for a possible maximum grade of 72.

Primary Outcome Result(s)

Percentage of participants with no radiographic progression (estimate + 95% CI) at Week 104 (Multiple imputation) (Full analysis set)

(Time Frame: Baseline and at Week 104)

	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104
Number of Participants Analyzed [units: participants]	287	286	286
Percentage of participants with no radiographic progression (estimate + 95% CI) at Week 104 (Multiple imputation) (Full analysis set) (units: Percentage of participants)			
	66.1	66.9	65.6

Statistical Analysis

Groups	AIN457 150 mg/placebo, GP2017 40mg	
P Value	0.7164	Logistic regression model with treatment as a factor and baseline mSASSS

		score as a covariate using marginal standardization method.
Method	Regression, Logistic	
Other Marginal difference	1.51	
95 % Confidence Interval 2-Sided	-6.63 to 9.64	

Statistical Analysis

Groups	AIN457 300 mg, GP2017 40mg	
P Value	0.6925	
Method	Regression, Logistic	Logistic regression model with treatment as a factor and baseline mSASSS score as a covariate using marginal standardization method.
Other Marginal difference	1.67	
95 % Confidence Interval 2-Sided	-6.61 to 9.95	

Secondary Outcome Result(s)

Change from Baseline in mSASSS (estimate + 95% CI) at Week 104 (Multiple imputation) (Full analysis set)

(Time Frame: Baseline and at Week 104)

	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104
Number of Participants Analyzed [units: participants]	287	286	286
Change from Baseline in mSASSS (estimate + 95% CI) at Week 104 (Multiple imputation) (Full analysis set) (units: mSASSS scores) Least Squares Mean ± Standard Error			
	0.54 ± 0.175	0.55 ± 0.180	0.72 ± 0.177

Statistical Analysis

Groups	AIN457 150 mg/placebo, GP2017 40mg	
Non-Inferiority/Equivalence Test	Superiority	Due to the pre-defined hierarchical testing strategy, p values beyond the failed primary endpoint were not presented.
Other LS mean difference	-0.18	ANCOVA model with treatment as a factor and baseline mSASSS score as a covariate.
95 % Confidence Interval 2-Sided	-0.646 to 0.293	

Statistical Analysis

Groups	AIN457 300 mg, GP2017 40mg	
Non-Inferiority/Equivalence Test	Superiority	Due to the pre-defined hierarchical testing strategy, p values beyond the failed primary endpoint were not presented.
Other LS mean difference	-0.16	ANCOVA model with treatment as a factor and baseline mSASSS score as a covariate.
95 % Confidence Interval 2-Sided	-0.639 to 0.315	

Percentage of participants without new syndesmophytes by mSASSS (estimate + 95% CI) between baseline and Week 104 (Multiple imputation) (Syndesmophyte subset)

(Time Frame: Baseline and at Week 104)

	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104
Number of Participants Analyzed [units: participants]	211	204	212
Percentage of participants without new syndesmophytes by mSASSS (estimate + 95% CI) between baseline and Week 104 (Multiple imputation) (Syndesmophyte subset) (units: Percentage of participants)			
	56.9	53.8	53.3

Statistical Analysis

Groups	AIN457 150 mg/placebo, AIN457 300 mg	
Non-Inferiority/Equivalence Test	Superiority	Due to the pre-defined hierarchical testing

		strategy, p values beyond the failed primary endpoint were not presented.
Other Marginal difference	4.32	Logistic regression model with treatment as a factor and baseline count of vertebral corners with syndesmophyte as a covariate using marginal standardization method.
95 % Confidence Interval 2-Sided	-5.62 to 14.27	

Statistical Analysis

Groups	AIN457 300 mg, GP2017 40mg	
Non-Inferiority/Equivalence Test	Superiority	Due to the pre-defined hierarchical testing strategy, p values beyond the failed primary endpoint were not presented.
Other Marginal difference	1.09	Logistic regression model with treatment as a factor and baseline count of vertebral corners with syndesmophyte as a covariate using marginal standardization method.
95 % Confidence Interval 2-Sided	-9.13 to 11.31	

Change from Baseline in MRI Berlin SI joint edema score (estimate + 95% CI) ANCOVA up to Week 104 (Observed data) (MRI subset)

(Time Frame: Baseline and at Week 104)

	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104
Number of Participants Analyzed [units: participants]	137	137	144
Change from Baseline in MRI Berlin SI joint edema score (estimate + 95% CI) ANCOVA up to Week 104 (Observed data) (MRI subset) (units: Berlin SI joint edema scores) Least Squares Mean ± Standard Error			
Week 104 n=100, 93, 95	-1.527 ± 0.1057	-1.378 ± 0.1097	-1.710 ± 0.1087

Statistical Analysis

Groups	AIN457 150 mg/placebo, GP2017 40mg	Week 104 - 150 mg
Non-Inferiority/Equivalence Test	Other	Due to the pre-defined hierarchical testing

		strategy, p values beyond the failed primary endpoint were not presented.
Other LS Means	0.183	LS Means and 95% CI are from an ANCOVA model with treatment as a factor, baseline Berlin SI joint edema score as a covariate.
Standard Error of the mean	0.1517	
95 % Confidence Interval 2-Sided	-0.12 to 0.48	

Statistical Analysis

Groups	AIN457 300 mg, GP2017 40mg	Week 104 - 300 mg
Non-Inferiority/Equivalence Test	Other	Due to the pre-defined hierarchical testing strategy, p values beyond the failed primary endpoint were not presented.
Other LS Means	0.332	LS Means and 95% CI are from an ANCOVA model with treatment as a factor, baseline Berlin SI joint edema score as a covariate.
Standard Error of the mean	0.1545	
95 % Confidence Interval 2-Sided	0.03 to 0.64	

Change from Baseline in Berlin modification of ASspiMRI-a edema score (estimate + 95% CI) up to Week 104 (MRI subset)

(Time Frame: Baseline and at Week 104)

	AIN457 150 mg/placebo	AIN457 300 mg	GP2017 40mg
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104
Number of Participants Analyzed [units: participants]	137	137	144
Change from Baseline in Berlin modification of ASspiMRI-a edema score (estimate + 95% CI) up to Week 104 (MRI subset) (units: Berlin mod. of ASspiMRI-a edema scores) Least Squares Mean ± Standard Error			
Week 104 n=102, 96, 95	-1.224 ± 0.2306	-1.683 ± 0.2373	-2.101 ± 0.2378

Statistical Analysis

Groups	AIN457 150 mg/placebo, GP2017 40mg	Week 104 - 150 mg
Non-Inferiority/Equivalence Test	Other	Due to the pre-defined hierarchical testing

		strategy, p values beyond the failed primary endpoint were not presented.
Other LS Means	0.877	LS Means and 95% CI are from an ANCOVA model with treatment as a factor, baseline Berlin SI joint edema score as a covariate.
Standard Error of the mean	0.3316	
95 % Confidence Interval 2-Sided	0.22 to 1.53	

Statistical Analysis

Groups	AIN457 300 mg, GP2017 40mg	Week 104 - 300 mg
Non-Inferiority/Equivalence Test	Other	Due to the pre-defined hierarchical testing strategy, p values beyond the failed primary endpoint were not presented.
Other LS Means	0.419	LS Means and 95% CI are from an ANCOVA model with treatment as a factor, baseline Berlin SI joint edema score as a covariate.
Standard Error of the mean	0.3357	
95 % Confidence Interval 2-Sided	-0.24 to 1.08	

Percentage of responders for Assessment of SpondyloArthritis International Society 20 (ASAS20)

(Time Frame: Week 104)

	AIN457 150 mg/placebo	AIN457 300 mg
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104
Number of Participants Analyzed [units: participants]	287	286
Percentage of responders for Assessment of SpondyloArthritis International Society 20 (ASAS20) (units: Percentage participants with ASAS20) Number (95% Confidence Interval)		
Week 104	83.1 (77.8 to 87.4)	82.9 (77.3 to 87.4)

Statistical Analysis

Groups	AIN457 150 mg/placebo, AIN457 300 mg	
Non-Inferiority/Equivalence Test	Other	Due to the pre-defined hierarchical testing

		strategy, p values beyond the failed primary endpoint were not presented.
Other Marginal difference	1.54	Estimated mean, marginal difference and 95% confidence interval are from a logistic regression model with treatment as a factor using marginal standardization method
95 % Confidence Interval 2-Sided	-5.10 to 8.18	

Percentage of responders for Assessment of SpondyloArthritis International Society 40 (ASAS 40)

(Time Frame: Week 104)

	AIN457 150 mg/placebo	AIN457 300 mg
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104
Number of Participants Analyzed [units: participants]	287	286
Percentage of responders for Assessment of SpondyloArthritis		

International Society 40 (ASAS 40) (units: Percentage participants with ASAS40) Number (95% Confidence Interval)		
Week 104	69.9 (63.7 to 75.4)	73.5 (67.3 to 78.9)

Statistical Analysis

Groups	AIN457 150 mg/placebo, AIN457 300 mg	
Non-Inferiority/Equivalence Test	Other	Due to the pre-defined hierarchical testing strategy, p values beyond the failed primary endpoint were not presented.
Other Marginal difference	-2.34	Estimated mean, marginal difference and 95% confidence interval are from a logistic regression model with treatment as a factor using marginal standardization method.
95 % Confidence Interval 2-Sided	-10.18 to 5.51	

Percentage of responders for Assessment of SpondyloArthritis International Society with a partial remission response (Full analysis set)

(Time Frame: Week 104)

	AIN457 150 mg/placebo	**AIN457 300 mg**
Arm/Group Description	AIN457 150 mg and a matching placebo was	AIN457 300 mg (2 x 150 mg) was

	administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104
Number of Participants Analyzed [units: participants]	287	286
Percentage of responders for Assessment of SpondyloArthritis International Society with a partial remission response (Full analysis set) (units: Percentage participants) Number (95% Confidence Interval)		
Week 104	31.5 (25.9 to 37.7)	30.2 (24.5 to 36.6)

Statistical Analysis

Groups	AIN457 150 mg/placebo, AIN457 300 mg	
Non-Inferiority/Equivalence Test	Other	Due to the pre-defined hierarchical testing strategy, p values beyond the failed primary endpoint were not presented.

Method	Other Marginal difference	
Other Marginal difference	2.18	Estimated mean, marginal difference and 95% confidence interval are from a logistic regression model with treatment as a factor using marginal standardization method
95 % Confidence Interval 2-Sided	-5.34 to 9.69	

Percentage of participants with Assessment of SpondyloArthritis International Society for inactive disease response (Observed data) (Full analysis set)

(Time Frame: Week 104)

	AIN457 150 mg/placebo	**AIN457 300 mg**
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104
Number of Participants Analyzed [units: participants]	287	286
Percentage of participants with Assessment of SpondyloArthritis		

International Society for inactive disease response (Observed data) (Full analysis set) (units: Percentage of participants) Number (95% Confidence Interval)		
Week 104	31.1 (25.5 to 37.4)	31.7 (25.7 to 38.3)

Statistical Analysis

Groups	AIN457 150 mg/placebo, AIN457 300 mg	
P Value		Due to the pre-defined hierarchical testing strategy, p values beyond the failed primary endpoint were not presented.
Other Marginal difference	0.33	Estimated mean, marginal difference and 95% confidence interval are from a logistic regression model with treatment as a factor using marginal standardization method
95 % Confidence Interval 2-Sided	-7.08 to 7.74	

Safety Results

All-Cause Mortality

	AIN457 150 mg/placebo N = 286	AIN457 300 mg N = 285	GP2017 40 mg N = 285
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104
Total participants affected	1 (0.35%)	1 (0.35%)	3 (1.05%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse events were reported from first dose of study treatment until end of study treatment plus 84 days up to a maximum of 900 days for AIN 457 and 939 days for GP2017.
Source Vocabulary for Table Default	MedDRA (25.0)
Assessment Type for Table Default	Systematic Assessment

	AIN457 150 mg/placebo N = 286	AIN457 300 mg N = 285	GP2017 40 mg N = 285
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104
Total participants affected	40 (13.99%)	29 (10.18%)	32 (11.23%)
Cardiac disorders			
Cardiac failure	0 (0.00%)	0 (0.00%)	1 (0.35%)
Coronary artery disease	1 (0.35%)	0 (0.00%)	0 (0.00%)
Myocardial infarction	1 (0.35%)	0 (0.00%)	0 (0.00%)
Eye disorders			
Iridocyclitis	2 (0.70%)	1 (0.35%)	0 (0.00%)
Retinal detachment	0 (0.00%)	0 (0.00%)	1 (0.35%)
Retinal vein occlusion	0 (0.00%)	0 (0.00%)	1 (0.35%)
Gastrointestinal disorders			
Chronic gastrointestinal bleeding	0 (0.00%)	1 (0.35%)	0 (0.00%)

Colitis	3 (1.05%)	0 (0.00%)	0 (0.00%)
Colitis ulcerative	1 (0.35%)	0 (0.00%)	0 (0.00%)
Crohn's disease	2 (0.70%)	3 (1.05%)	0 (0.00%)
Diarrhoea	1 (0.35%)	0 (0.00%)	0 (0.00%)
Duodenal ulcer haemorrhage	0 (0.00%)	1 (0.35%)	0 (0.00%)
Gastroenteritis eosinophilic	0 (0.00%)	1 (0.35%)	0 (0.00%)
Gastrointestinal disorder	0 (0.00%)	1 (0.35%)	0 (0.00%)
Gastrooesophageal reflux disease	0 (0.00%)	0 (0.00%)	1 (0.35%)
Haemorrhoids	0 (0.00%)	0 (0.00%)	1 (0.35%)
Ileal ulcer	0 (0.00%)	1 (0.35%)	0 (0.00%)
Large intestine perforation	0 (0.00%)	1 (0.35%)	0 (0.00%)
Pancreatitis acute	1 (0.35%)	0 (0.00%)	2 (0.70%)
Umbilical hernia	0 (0.00%)	0 (0.00%)	1 (0.35%)
General disorders and administration site conditions			
Death	0 (0.00%)	1 (0.35%)	0 (0.00%)
Drug intolerance	1 (0.35%)	0 (0.00%)	0 (0.00%)
Medical device pain	1 (0.35%)	0 (0.00%)	0 (0.00%)
Non-cardiac chest pain	0 (0.00%)	0 (0.00%)	1 (0.35%)
Sudden death	0 (0.00%)	0 (0.00%)	1 (0.35%)
Hepatobiliary disorders			
Cholangitis	0 (0.00%)	0 (0.00%)	1 (0.35%)

Cholecystitis	1 (0.35%)	0 (0.00%)	0 (0.00%)
Cholelithiasis	0 (0.00%)	0 (0.00%)	1 (0.35%)
Cholestasis	1 (0.35%)	0 (0.00%)	0 (0.00%)
Immune system disorders			
Immunosuppression	0 (0.00%)	1 (0.35%)	0 (0.00%)
Infections and infestations			
Abscess intestinal	0 (0.00%)	1 (0.35%)	0 (0.00%)
Anal abscess	1 (0.35%)	0 (0.00%)	0 (0.00%)
Appendicitis	1 (0.35%)	1 (0.35%)	1 (0.35%)
Cellulitis	1 (0.35%)	0 (0.00%)	1 (0.35%)
COVID-19	1 (0.35%)	0 (0.00%)	1 (0.35%)
COVID-19 pneumonia	1 (0.35%)	0 (0.00%)	0 (0.00%)
Diverticulitis	0 (0.00%)	1 (0.35%)	0 (0.00%)
Epididymitis	1 (0.35%)	0 (0.00%)	0 (0.00%)
Erysipelas	1 (0.35%)	0 (0.00%)	0 (0.00%)
Myelitis	0 (0.00%)	1 (0.35%)	0 (0.00%)
Oral herpes	1 (0.35%)	0 (0.00%)	0 (0.00%)
Pneumonia	0 (0.00%)	1 (0.35%)	2 (0.70%)
Pulmonary tuberculosis	0 (0.00%)	0 (0.00%)	1 (0.35%)
Pyelonephritis	0 (0.00%)	2 (0.70%)	0 (0.00%)
Sepsis	0 (0.00%)	0 (0.00%)	1 (0.35%)
Septic shock	0 (0.00%)	0 (0.00%)	1 (0.35%)
Suspected COVID-19	0 (0.00%)	0 (0.00%)	1 (0.35%)
Urinary tract infection	0 (0.00%)	0 (0.00%)	2 (0.70%)

Injury, poisoning and procedural complications			
Exposure during pregnancy	0 (0.00%)	1 (0.35%)	0 (0.00%)
Femur fracture	1 (0.35%)	0 (0.00%)	0 (0.00%)
Hip fracture	0 (0.00%)	1 (0.35%)	1 (0.35%)
Joint injury	1 (0.35%)	0 (0.00%)	0 (0.00%)
Post procedural haemorrhage	0 (0.00%)	0 (0.00%)	1 (0.35%)
Tendon rupture	1 (0.35%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders			
Dehydration	0 (0.00%)	1 (0.35%)	0 (0.00%)
Hyperglycaemia	1 (0.35%)	0 (0.00%)	0 (0.00%)
Type 1 diabetes mellitus	0 (0.00%)	1 (0.35%)	0 (0.00%)
Musculoskeletal and connective tissue disorders			
Arthralgia	0 (0.00%)	1 (0.35%)	0 (0.00%)
Lumbar spinal stenosis	0 (0.00%)	1 (0.35%)	0 (0.00%)
Osteoarthritis	3 (1.05%)	1 (0.35%)	1 (0.35%)
Synovial cyst	0 (0.00%)	1 (0.35%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma	1 (0.35%)	1 (0.35%)	0 (0.00%)
Bladder neoplasm	1 (0.35%)	0 (0.00%)	0 (0.00%)

Chloroma	1 (0.35%)	0 (0.00%)	0 (0.00%)
Ovarian cancer	0 (0.00%)	0 (0.00%)	1 (0.35%)
Papillary thyroid cancer	1 (0.35%)	0 (0.00%)	0 (0.00%)
Nervous system disorders			
Brain hypoxia	0 (0.00%)	0 (0.00%)	1 (0.35%)
Facial paresis	1 (0.35%)	0 (0.00%)	0 (0.00%)
Guillain-Barre syndrome	0 (0.00%)	0 (0.00%)	1 (0.35%)
Lacunar stroke	1 (0.35%)	0 (0.00%)	0 (0.00%)
Parkinson's disease	0 (0.00%)	0 (0.00%)	1 (0.35%)
Subarachnoid haemorrhage	1 (0.35%)	0 (0.00%)	0 (0.00%)
Pregnancy, puerperium and perinatal conditions			
Abortion	1 (0.35%)	0 (0.00%)	0 (0.00%)
Product issues			
Device dislocation	0 (0.00%)	0 (0.00%)	1 (0.35%)
Device issue	0 (0.00%)	1 (0.35%)	0 (0.00%)
Psychiatric disorders			
Depression	1 (0.35%)	0 (0.00%)	1 (0.35%)
Depression suicidal	1 (0.35%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders			
Haematuria	0 (0.00%)	0 (0.00%)	1 (0.35%)
Hydronephrosis	1 (0.35%)	0 (0.00%)	1 (0.35%)
Micturition disorder	0 (0.00%)	0 (0.00%)	1 (0.35%)

Renal colic	0 (0.00%)	1 (0.35%)	0 (0.00%)
Ureterolithiasis	1 (0.35%)	0 (0.00%)	1 (0.35%)
Reproductive system and breast disorders			
Endometrial hyperplasia	0 (0.00%)	1 (0.35%)	0 (0.00%)
Ovarian cyst	1 (0.35%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	0 (0.00%)	0 (0.00%)	1 (0.35%)
Pleural effusion	1 (0.35%)	0 (0.00%)	1 (0.35%)
Pneumothorax spontaneous	0 (0.00%)	1 (0.35%)	0 (0.00%)
Skin and subcutaneous tissue disorders			
Eczema	0 (0.00%)	0 (0.00%)	1 (0.35%)
Purpura	1 (0.35%)	0 (0.00%)	0 (0.00%)
Vascular disorders			
Iliac artery occlusion	0 (0.00%)	1 (0.35%)	0 (0.00%)
Iliac artery stenosis	0 (0.00%)	1 (0.35%)	0 (0.00%)
Phlebitis	0 (0.00%)	1 (0.35%)	0 (0.00%)
Thrombosis	0 (0.00%)	0 (0.00%)	1 (0.35%)

Other Adverse Events by System Organ Class

Time Frame Adverse events were reported from first dose of study treatment until end of study treatment plus 84 days up to a maximum of 900 days for AIN 457 and 939 days for GP2017.

Source Vocabulary for Table Default	MedDRA (25.0)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	5%

	AIN457 150 mg/placebo N = 286	**AIN457 300 mg N = 285**	**GP2017 40 mg N = 285**
Arm/Group Description	AIN457 150 mg and a matching placebo was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	AIN457 300 mg (2 x 150 mg) was administered subcutaneously via pre-filled syringes at Baseline, Weeks 1, 2, 3 and 4, followed by dosing every 4 weeks until Week 104	GP2017 (adalimumab biosimilar) 40 mg was administered subcutaneously via pre-filled syringes at Baseline followed by dosing every 2 weeks until Week 104
Total participants affected	106 (37.06%)	107 (37.54%)	99 (34.74%)
Gastrointestinal disorders			
Diarrhoea	20 (6.99%)	22 (7.72%)	11 (3.86%)
Infections and infestations			
Nasopharyngitis	47 (16.43%)	40 (14.04%)	44 (15.44%)
Upper respiratory tract infection	17 (5.94%)	25 (8.77%)	18 (6.32%)
Musculoskeletal and connective tissue disorders			

Ankylosing spondylitis	11 (3.85%)	17 (5.96%)	12 (4.21%)
Arthralgia	16 (5.59%)	13 (4.56%)	12 (4.21%)
Nervous system disorders			
Headache	16 (5.59%)	17 (5.96%)	17 (5.96%)
Vascular disorders			
Hypertension	11 (3.85%)	11 (3.86%)	15 (5.26%)

Other Relevant Findings

Conclusion:

This trial helped researchers learn how well AIN457 works long-term and its safety in people with ankylosing spondylitis (AS). About the same percent of participants in each treatment group had no worsening of spinal damage after 2 years of treatment. The researchers concluded there was no meaningful difference between the 3 treatment groups. The researchers found no new safety concerns for the participants in this trial. The safety results were consistent with previous trials where participants with AS received AIN457 or GP2017.

Date of Clinical Trial Report

October 6, 2022