Clinical trial results:
An open-label proof-of-concept study with a double-masked, dose-ranging component to assess the effects of AIN457 in patients with noninfectious uveitis

Summary

EudraCT number	2011-001243-67
Trial protocol	DE
Global end of trial date	13 September 2013

Results information

Result version number	v1 (current)
This version publication date	13 July 2016
First version publication date	31 July 2015

Trial information

Trial identification

Sponsor protocol code	CAIN457A2208

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00685399
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	13 September 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 September 2013
Global end of trial reached?	Yes
Global end of trial date	13 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of intravenous AIN457 in patients with uveitis.

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	10 June 2008
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	United States: 72
Country: Number of subjects enrolled	Germany: 7
Worldwide total number of subjects	79
EEA total number of subjects	7

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)	75
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Cohort 4 was originally comprised of patients from all other core cohorts of this study whose uveitis was in remission at the end of study observation (Cohorts 1, 2, and 3).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Cohort 1-300mg s.c. bi-weekly (q2wks)

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

Dosage and administration details:

Cohort 1-300mg s.c. bi-weekly (q2wks)

Arm title	Cohort 2

Arm description:

(300mg s.c. bi-weekly (q2wks)), 3 patients from cohort 1 rolled into this cohort

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

Dosage and administration details:

(300mg s.c. bi-weekly (q2wks)), 3 patients from cohort 1 rolled into this cohort

Arm title	Cohort 3

Arm description:

10 mg/kg i.v. every 4 weeks (q4 wks)

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

Dosage and administration details: 10 mg/kg i.v. every 4 weeks (q4 wks)

Arm title	Cohort 5
Arm description: 30 mg/kg AIN457 IV q4 weeks	
Arm type	Experimental
Investigational medicinal product name	Sekukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 30 mg/kg AIN457 IV q4 weeks	
Arm title	Cohort 6 Arm 1
Arm description: 300mg sc q 2wks	
Arm type	Experimental
Investigational medicinal product name	Sekukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 300mg sc q 2wks	
Arm title	Cohort 6 Arm 2
Arm description: 10mg/kg i.v. q2wks	
Arm type	Experimental
Investigational medicinal product name	Sekukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 10mg/kg i.v. q2wks	
Arm title	Cohort 6 Arm 3
Arm description: 30mg/kg i.v. q4wks	
Arm type	Experimental
Investigational medicinal product name	Sekukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 30mg/kg i.v. q4wks	

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	16	17	5
Completed	10	3	2
Not completed	6	14	3
Consent withdrawn by subject	2	1	-
Adverse event, non-fatal	-	-	-
Administrative Problems	2	2	1
Protocol deviation	1	-	-
Lack of efficacy	1	11	2

Number of subjects in period 1	Cohort 5	Cohort 6 Arm 1	Cohort 6 Arm 2
Started	4	12	13
Completed	4	10	13
Not completed	0	2	0
Consent withdrawn by subject	-	-	-
Adverse event, non-fatal	-	1	-
Administrative Problems	-	-	-
Protocol deviation	-	-	-
Lack of efficacy	-	1	-

Number of subjects in period 1	Cohort 6 Arm 3
Started	12
Completed	10
Not completed	2
Consent withdrawn by subject	2
Adverse event, non-fatal	-
Administrative Problems	-
Protocol deviation	-
Lack of efficacy	-

Period 2	
Period 2 title	Extension
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Cohort 4

Arm description:

Extension- All patients are rollover patients from other cohorts. AIN457 10 mg/kg iv PRN no more than once per month. COHORT 4 not added to total mean as they are already included.

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

Dosage and administration details:

Extension- All patients are rollover patients from other cohorts. AIN457 10 mg/kg iv PRN no more than once per month. COHORT 4 not added to total mean as they are already included.

Number of subjects in period 2	Cohort 4
Started	28
Completed	21
Not completed	7
Consent withdrawn by subject	1
Adverse event, non-fatal	2
Administrative Issues	1
Protocol deviation	1
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
Cohort 1-300mg s.c. bi-weekly (q2wks)	
Reporting group title	Cohort 2
Reporting group description:	
(300mg s.c. bi-weekly (q2wks)), 3 patients from cohort 1 rolled into this cohort	
Reporting group title	Cohort 3
Reporting group description:	
10 mg/kg i.v. every 4 weeks (q4 wks)	
Reporting group title	Cohort 5
Reporting group description:	
30 mg/kg AIN457 IV q4 weeks	
Reporting group title	Cohort 6 Arm 1
Reporting group description:	
300mg sc q 2wks	
Reporting group title	Cohort 6 Arm 2
Reporting group description:	
10mg/kg i.v. q2wks	
Reporting group title	Cohort 6 Arm 3
Reporting group description:	
30mg/kg i.v. q4wks	

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	16	17	5
Age categorical Units: Subjects			
18y < 65y	15	16	5
65y < 85y	1	1	0
Gender, Male/Female Units: Participants			
male	4	5	2
Female	12	12	3

Reporting group values	Cohort 5	Cohort 6 Arm 1	Cohort 6 Arm 2
Number of subjects	4	12	13
Age categorical Units: Subjects			
18y < 65y	4	11	12
65y < 85y	0	1	1
Gender, Male/Female Units: Participants			
male	1	4	4
Female	3	8	9

Reporting group values	Cohort 6 Arm 3	Total	
Number of subjects	12	79	

Age categorical Units: Subjects			
18y < 65y	12	75	
65y < 85y	0	4	
Gender, Male/Female Units: Participants			
male	3	23	
Female	9	56	

Subject analysis sets

Subject analysis set title	Adverse Events
Subject analysis set type	Safety analysis
Subject analysis set description: Found in Adverse Event Section	
Subject analysis set title	Intermediate Uveitis
Subject analysis set type	Full analysis
Subject analysis set description: Intermediate uveitis is a form of uveitis localized to the vitreous and peripheral retina.	
Subject analysis set title	Posterior uveitis
Subject analysis set type	Full analysis
Subject analysis set description: Inflammation in the back of the eye is commonly characterized by: Floaters,Blurred vision,Photopsia or seeing flashing lights	
Subject analysis set title	Responders
Subject analysis set type	Full analysis
Subject analysis set description: Total number of responders	
Subject analysis set title	Pan Uveitis
Subject analysis set type	Full analysis
Subject analysis set description: Panuveitis is a generalized inflammation of not only the whole of the uveal tract but also involves the retina and vitreous humor	
Subject analysis set title	Anterior Uveitis
Subject analysis set type	Full analysis
Subject analysis set description: Anterior uveitis includes iridocyclitis and iritis. Iritis is the inflammation of the anterior chamber and iris. Iridocyclitis presents the same symptoms as iritis, but also includes inflammation in the vitreous cavity	
Subject analysis set title	Birdshot
Subject analysis set type	Full analysis
Subject analysis set description: Birdshot chorioretinopathy is a rare form of bilateral posterior uveitis affecting the eye. It causes severe, progressive inflammation of both the choroid and retina	
Subject analysis set title	Sympathetic Opthalmia
Subject analysis set type	Full analysis
Subject analysis set description: Sympathetic ophthalmia (SO) is a bilateral diffuse granulomatous uveitis (a kind of inflammation) of both eyes following trauma to one eye.	
Subject analysis set title	Multi-focal Choroiditis
Subject analysis set type	Full analysis
Subject analysis set description: MCP is a condition characterized by intraocular inflammation and multifocal choroidal lesions occurring in the absence of any known ocular or systemic disease	

Reporting group values	Adverse Events	Intermediate Uveitis	Posterior uveitis
Number of subjects	79	79	79
Age categorical Units: Subjects			
18y < 65y	75	75	75
65y < 85y	4	4	4
Gender, Male/Female Units: Participants			
male			
Female			

Reporting group values	Responders	Pan Uveitis	Anterior Uveitis
Number of subjects	79	79	79
Age categorical Units: Subjects			
18y < 65y	75	75	75
65y < 85y	4	4	4
Gender, Male/Female Units: Participants			
male			
Female			

Reporting group values	Birdshot	Sympathetic Opthalmia	Multi-focal Choroiditis
Number of subjects	79	79	79
Age categorical Units: Subjects			
18y < 65y	75	75	75
65y < 85y	4	4	4
Gender, Male/Female Units: Participants			
male			
Female			

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description: Cohort 1-300mg s.c. bi-weekly (q2wks)	
Reporting group title	Cohort 2
Reporting group description: (300mg s.c. bi-weekly (q2wks)), 3 patients from cohort 1 rolled into this cohort	
Reporting group title	Cohort 3
Reporting group description: 10 mg/kg i.v. every 4 weeks (q4 wks)	
Reporting group title	Cohort 5
Reporting group description: 30 mg/kg AIN457 IV q4 weeks	
Reporting group title	Cohort 6 Arm 1
Reporting group description: 300mg sc q 2wks	
Reporting group title	Cohort 6 Arm 2
Reporting group description: 10mg/kg i.v. q2wks	
Reporting group title	Cohort 6 Arm 3
Reporting group description: 30mg/kg i.v. q4wks	
Reporting group title	Cohort 4
Reporting group description: Extension- All patients are rollover patients from other cohorts. AIN457 10 mg/kg iv PRN no more than once per month. COHORT 4 not added to total mean as they are already included.	
Subject analysis set title	Adverse Events
Subject analysis set type	Safety analysis
Subject analysis set description: Found in Adverse Event Section	
Subject analysis set title	Intermediate Uveitis
Subject analysis set type	Full analysis
Subject analysis set description: Intermediate uveitis is a form of uveitis localized to the vitreous and peripheral retina.	
Subject analysis set title	Posterior uveitis
Subject analysis set type	Full analysis
Subject analysis set description: Inflammation in the back of the eye is commonly characterized by: Floaters,Blurred vision,Photopsia or seeing flashing lights	
Subject analysis set title	Responders
Subject analysis set type	Full analysis
Subject analysis set description: Total number of responders	
Subject analysis set title	Pan Uveitis
Subject analysis set type	Full analysis
Subject analysis set description: Panuveitis is a generalized inflammation of not only the whole of the uveal tract but also involves the retina and vitreous humor	
Subject analysis set title	Anterior Uveitis

Subject analysis set type	Full analysis

Subject analysis set description:

Anterior uveitis includes iridocyclitis and iritis. Iritis is the inflammation of the anterior chamber and iris. Iridocyclitis presents the same symptoms as iritis, but also includes inflammation in the vitreous cavity

Subject analysis set title	Birdshot
Subject analysis set type	Full analysis

Subject analysis set description:

Birdshot chorioretinopathy is a rare form of bilateral posterior uveitis affecting the eye. It causes severe, progressive inflammation of both the choroid and retina

Subject analysis set title	Sympathetic Opthalmia
Subject analysis set type	Full analysis

Subject analysis set description:

Sympathetic ophthalmia (SO) is a bilateral diffuse granulomatous uveitis (a kind of inflammation) of both eyes following trauma to one eye.

Subject analysis set title	Multi-focal Choroiditis
Subject analysis set type	Full analysis

Subject analysis set description:

MCP is a condition characterized by intraocular inflammation and multifocal choroidal lesions occurring in the absence of any known ocular or systemic disease

Primary: Number of participants with ocular examinations, physical examination, and adverse events

End point title	Number of participants with ocular examinations, physical examination, and adverse events[1]

End point description:

All safety measures are described in the adverse event section.

End point type	Primary

End point timeframe:

Baseline day through end of study

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: insufficient number of participants with events and so there were no statistics performed

End point values	Adverse Events			
Subject group type	Subject analysis set			
Number of subjects analysed	0[2]			
Units: participants				

Notes:

[2] - See Safety

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in ocular inflammation Responders at day 57

End point title	Reduction in ocular inflammation Responders at day 57

End point description:

Patients from cohorts 1 and 3 participated in an open-label, single sequence, proof-of-concept study to evaluate the effects of 2 intravenous doses of 10 mg/kg of AIN457. Patients from cohort 2 participated in a randomized, double-masked study to evaluate the effects of a single initial dose of 10 mg/kg of Sp2/0-derived AIN457, 3 mg/kg CHO-derived AIN457, or 1 mg/kg of CHO-derived AIN457, followed, if deemed necessary, by a second dose at 10 mg/kg 2 or 3 weeks after the initial dose. Cohort 5 was an open-label single-dose safety study of 30 mg/kg AIN457 delivered in a single 2 hour i.v. infusion. Cohort

6 patients received both subcutaneous and intravenous study drug administration in a double-masked, double dummy design. Patients who responded to AIN457 therapy while in cohorts 1, 2, 3, 5 or 6 and who passed the end of study visit in these cohorts could be enrolled into cohort 4 in which they could continue to receive AIN457 as needed

End point type	Secondary

End point timeframe:

One week through nine months

End point values	Responders	Intermediate Uveitis	Posterior uveitis	Pan Uveitis
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	79	79	79
Units: Participants				
Cohort 1 10mg/Kg Sp2/0	11	0	3	5
Cohort 2 10mg/Kg Sp2/0	1	0	0	1
Cohort 2 10mg/Kg CHO	5	1	0	3
Cohort 2 3mg/Kg CHO	0	0	0	0
Cohort 2 1mg/Kg CHO	0	0	0	0
Cohort 3 10mg/Kg CHO	3	0	0	0

End point values	Anterior Uveitis	Birdshot	Sympathetic Opthalmia	Multi-focal Choroiditis
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	79	79	79[3]
Units: Participants				
Cohort 1 10mg/Kg Sp2/0	3	0	0	0
Cohort 2 10mg/Kg Sp2/0	0	0	0	0
Cohort 2 10mg/Kg CHO	1	0	0	0
Cohort 2 3mg/Kg CHO	0	0	0	0
Cohort 2 1mg/Kg CHO	0	0	0	0
Cohort 3 10mg/Kg CHO	0	2	1	0

Notes:

[3] - insufficient number of participants with events

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in ocular inflammation Complete Responders at day 57

End point title	Reduction in ocular inflammation Complete Responders at day 57

End point description:

Patients from cohorts 1 and 3 participated in an open-label, single sequence, proof-of-concept study to evaluate the effects of 2 intravenous doses of 10 mg/kg of AIN457. Patients from cohort 2 participated in a randomized, double-masked study to evaluate the effects of a single initial dose of 10 mg/kg of Sp2/0-derived AIN457, 3 mg/kg CHO-derived AIN457, or 1 mg/kg of CHO-derived AIN457, followed, if deemed necessary, by a second dose at 10 mg/kg 2 or 3 weeks after the initial dose. Cohort 5 was an open-label single-dose safety study of 30 mg/kg AIN457 delivered in a single 2 hour i.v. infusion. Cohort 6 patients received both subcutaneous and intravenous study drug administration in a double-masked,

double dummy design. Patients who responded to AIN457 therapy while in cohorts 1, 2, 3, 5 or 6 and who passed the end of study visit in these cohorts could be enrolled into cohort 4 in which they could continue to receive AIN457 as needed

End point type	Secondary

End point timeframe:

One week through nine months

End point values	Responders	Intermediate Uveitis	Posterior uveitis	Pan Uveitis
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	79	79	79
Units: Participants				
Cohort 2 10mg/Kg Sp2/0	0	0	0	0
Cohort 2 10mg/Kg CHO	2	0	0	1
Cohort 2 3mg/Kg CHO	0	0	0	0
Cohort 2 1mg/Kg CHO	0	0	0	0
Cohort 3 10mg/Kg CHO	3	0	0	0
Cohort 6 300 mg SC	2	0	1	1
Cohort 6 10 mg/Kg iv	5	1	2	2
Cohort 6 30 mg/Kg iv	3	1	0	2

End point values	Anterior Uveitis	Birdshot	Sympathetic Opthalmia	Multi-focal Choroiditis
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	79	79	79	79
Units: Participants				
Cohort 2 10mg/Kg Sp2/0	0	0	0	0
Cohort 2 10mg/Kg CHO	1	0	0	0
Cohort 2 3mg/Kg CHO	0	0	0	0
Cohort 2 1mg/Kg CHO	0	0	0	0
Cohort 3 10mg/Kg CHO	0	2	1	0
Cohort 6 300 mg SC	0	0	0	0
Cohort 6 10 mg/Kg iv	0	0	0	0
Cohort 6 30 mg/Kg iv	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with ability to induce a remission in uveitis

End point title	Number of participants with ability to induce a remission in uveitis

End point description:

Not enough patients for analysis...only a few that are detailed by narrative in study report

End point type	Secondary

End point timeframe:
one week through nine months

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 5
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[4]	0[5]	0[6]	0[7]
Units: Participants				

Notes:
[4] - insufficient number of participants with events
[5] - insufficient number of participants with events
[6] - insufficient number of participants with events
[7] - insufficient number of participants with events

End point values	Cohort 6 Arm 1	Cohort 6 Arm 2	Cohort 6 Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[8]	0[9]	0[10]	
Units: Participants				

Notes:
[8] - insufficient number of participants with events
[9] - insufficient number of participants with events
[10] - insufficient number of participants with events

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Reduction in other immunosuppressant drugs

End point title	Number of participants with Reduction in other immunosuppressant drugs

End point description:

End point type	Secondary

End point timeframe:
One week through nine months

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 5
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[11]	0[12]	0[13]	0[14]
Units: participants				

Notes:
[11] - insufficient number of participants with events
[12] - insufficient number of participants with events
[13] - insufficient number of participants with events
[14] - insufficient number of participants with events

End point values	Cohort 6 Arm 1	Cohort 6 Arm 2	Cohort 6 Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[15]	0[16]	0[17]	
Units: participants				

Notes:

[15] - insufficient number of participants with events

[16] - insufficient number of participants with events

[17] - insufficient number of participants with events

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with remission in uveitis

End point title	Number of participants with remission in uveitis

End point description:

Not enough patients for analysis...only a few that are detailed by narrative in study report

End point type	Secondary

End point timeframe:

one week through nine months

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 5
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[18]	0[19]	0[20]	0[21]
Units: Participants				

Notes:

[18] - insufficient number of participants with events

[19] - insufficient number of participants with events

[20] - insufficient number of participants with events

[21] - insufficient number of participants with events

End point values	Cohort 6 Arm 1	Cohort 6 Arm 2	Cohort 6 Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[22]	0[23]	0[24]	
Units: Participants				

Notes:

[22] - insufficient number of participants with events

[23] - insufficient number of participants with events

[24] - insufficient number of participants with events

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants able to re-induce a remission if a flare-up occurs

End point title	Number of participants able to re-induce a remission if a flare-up occurs

End point description:

Not enough patients for analysis...only a few that are detailed by narrative in study report

End point type	Secondary

End point timeframe:

One week through nine months

End point values	Cohort 1	Cohort 2	Cohort 3	Cohort 5
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[25]	0[26]	0[27]	0[28]
Units: Participants				

Notes:

[25] - Not enough patients for analysis

[26] - Not enough patients for analysis

[27] - Not enough patients for analysis

[28] - Not enough patients for analysis

End point values	Cohort 6 Arm 1	Cohort 6 Arm 2	Cohort 6 Arm 3	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[29]	0[30]	0[31]	
Units: Participants				

Notes:

[29] - Not enough patients for analysis

[30] - Not enough patients for analysis

[31] - Not enough patients for analysis

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events are monitored from date of First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All other adverse events are monitored from First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

AE additional description

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Cohort 1 - AIN457 10mg/kg SP2/0 10mg/kg SP2/0

Reporting group description:

Cohort 1 - AIN457 10mg/kg SP2/0 10mg/kg SP2/0

Reporting group title	Cohort 2 - AIN457 10mg/kg SP2/0 10mg/kg SP2/0

Reporting group description:

Cohort 2 - AIN457 10mg/kg SP2/0 10mg/kg SP2/0

Reporting group title	Cohort 2 - AIN457 10mg/kg CHO 10mg/kg CHO

Reporting group description:

Cohort 2 - AIN457 10mg/kg CHO 10mg/kg CHO

Reporting group title	Cohort 2 - AIN457 3mg/kg CHO 10mg/kg CHO

Reporting group description:

Cohort 2 - AIN457 3mg/kg CHO 10mg/kg CHO

Reporting group title	Cohort 2 - AIN457 1mg/kg CHO None

Reporting group description:

Cohort 2 - AIN457 1mg/kg CHO None

Reporting group title	Cohort 2 - AIN457 1mg/kg CHO 10mg/kg CHO

Reporting group description:

Cohort 2 - AIN457 1mg/kg CHO 10mg/kg CHO

Reporting group title	Cohort 3 - AIN457 10mg/kg CHO 10mg/kg CHO

Reporting group description:

Cohort 3 - AIN457 10mg/kg CHO 10mg/kg CHO

Reporting group title	Cohort 5 - AIN457 30mg/kg i.v. q4wks

Reporting group description:

Cohort 5 - AIN457 30mg/kg i.v. q4wks

Reporting group title	Cohort 6 - AIN457 300mg sc q2wks

Reporting group description:

Cohort 6 - AIN457 300mg sc q2wks

Reporting group title	Cohort 6 - AIN457 10mg/kg i.v. q2wks

Reporting group description:

Cohort 6 - AIN457 10mg/kg i.v. q2wks

Reporting group title	Cohort 6 - AIN457 30mg/kg i.v. q4wks

Reporting group description:

Cohort 6 - AIN457 30mg/kg i.v. q4wks

Reporting group title	Cohort 4 (extension) - AIN457

Reporting group description:

Cohort 4 (extension) - AIN457

Serious adverse events	Cohort 1 - AIN457 10mg/kg SP2/0 10mg/kg SP2/0	Cohort 2 - AIN457 10mg/kg SP2/0 10mg/kg SP2/0	Cohort 2 - AIN457 10mg/kg CHO 10mg/kg CHO
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine cancer			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Tibia fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 2 - AIN457 3mg/kg CHO 10mg/kg CHO	Cohort 2 - AIN457 1mg/kg CHO None	Cohort 2 - AIN457 1mg/kg CHO 10mg/kg CHO
Total subjects affected by serious			

adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine cancer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Tibia fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 3 - AIN457 10mg/kg CHO 10mg/kg CHO	Cohort 5 - AIN457 30mg/kg i.v. q4wks	Cohort 6 - AIN457 300mg sc q2wks
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Uterine cancer			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Tibia fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 6 - AIN457 10mg/kg i.v. q2wks	Cohort 6 - AIN457 30mg/kg i.v. q4wks	Cohort 4 (extension) - AIN457
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine cancer			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural			

complications			
Tibia fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	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	Cohort 1 - AIN457 10mg/kg SP2/0 10mg/kg SP2/0	Cohort 2 - AIN457 10mg/kg SP2/0 10mg/kg SP2/0	Cohort 2 - AIN457 10mg/kg CHO 10mg/kg CHO
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	1 / 1 (100.00%)	4 / 5 (80.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	2 / 15 (13.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 15 (13.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Uterine spasm			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1

Oropharyngeal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Sinus congestion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vocal cord disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anxiety disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervousness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood bilirubin increased			

subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Blood pressure increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Blood urine present			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Intraocular pressure increased			
subjects affected / exposed	5 / 15 (33.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	5	0	0
Lipase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lymphocyte percentage decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neutrophil percentage increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Protein urine			

subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Back injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Laceration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Post procedural complication			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Radius fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Aphonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	3 / 15 (20.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	4	0	0
Headache			

subjects affected / exposed	10 / 15 (66.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	30	0	0
Hyperaesthesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Paraesthesia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Sinus headache			
subjects affected / exposed	2 / 15 (13.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Somnolence			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Tension headache			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Anterior chamber flare			

subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Chalazion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Colour blindness acquired			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Conjunctival hyperaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Corneal disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	3 / 15 (20.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	8	0	1
Eye pruritus			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Eye swelling			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			

subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Foreign body sensation in eyes			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Iridocyclitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Iris adhesions			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Iris bombe			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Keratoconjunctivitis sicca			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Macular fibrosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Macular oedema			
subjects affected / exposed	1 / 15 (6.67%)	1 / 1 (100.00%)	1 / 5 (20.00%)
occurrences (all)	1	1	1
Ocular hyperaemia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Papilloedema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Photophobia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Photopsia			

subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pupillary reflex impaired			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Retinal detachment			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Retinal tear			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Scleritis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Uveitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vision blurred			
subjects affected / exposed	3 / 15 (20.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	3	0	1
Visual acuity reduced			
subjects affected / exposed	2 / 15 (13.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Vitreous detachment			
subjects affected / exposed	0 / 15 (0.00%)	1 / 1 (100.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	3	0	1
Vitreous haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Abdominal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	3 / 15 (20.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	4	0	0
Constipation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Inguinal hernia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Tooth disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	2 / 15 (13.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	5	0	0
Hepatobiliary disorders			
Non-alcoholic steatohepatitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Dermatitis acneiform			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Madarosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	3	0	1
Rash pruritic			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin odour abnormal			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	3	0	1
Back pain			
subjects affected / exposed	2 / 15 (13.33%)	0 / 1 (0.00%)	1 / 5 (20.00%)
occurrences (all)	3	0	1
Exostosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Joint swelling			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Limb discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	2 / 15 (13.33%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Myalgia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Spondylitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lice infestation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			

subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vaginitis bacterial			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 15 (6.67%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Increased appetite			
subjects affected / exposed	0 / 15 (0.00%)	0 / 1 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 2 - AIN457 3mg/kg CHO 10mg/kg CHO	Cohort 2 - AIN457 1mg/kg CHO None	Cohort 2 - AIN457 1mg/kg CHO 10mg/kg CHO
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	2 / 2 (100.00%)	3 / 4 (75.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Fibroadenoma of breast			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infusion site extravasation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Uterine spasm			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vocal cord disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Anxiety disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervousness			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Intraocular pressure increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lymphocyte percentage decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neutrophil percentage increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Protein urine			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Back injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Post procedural complication			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Radius fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

Palpitations			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Aphonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	3 / 4 (75.00%)
occurrences (all)	1	0	4
Hyperaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinus headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tension headache			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Anterior chamber flare			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chalazion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Colour blindness acquired			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Corneal disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye irritation			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Eye pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Eyelid oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Foreign body sensation in eyes			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Iridocyclitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Iris adhesions			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Iris bombe			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Keratoconjunctivitis sicca			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Macular fibrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Macular oedema			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Papilloedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pupillary reflex impaired			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retinal detachment			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retinal tear			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Scleritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Vitreous detachment			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitreous haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Inguinal hernia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Mouth ulceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Tooth disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Non-alcoholic steatohepatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Madarosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Pruritus generalised			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psoriasis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin odour abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Exostosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Spondylitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Lice infestation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vaginitis bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Gout			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 3 - AIN457 10mg/kg CHO 10mg/kg CHO	Cohort 5 - AIN457 30mg/kg i.v. q4wks	Cohort 6 - AIN457 300mg sc q2wks
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	3 / 4 (75.00%)	9 / 12 (75.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Infusion site extravasation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	2 / 5 (40.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pyrexia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Uterine spasm			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Vocal cord disorder			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Anxiety disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Nervousness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood urine present			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Intraocular pressure increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lymphocyte percentage decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Neutrophil percentage increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Protein urine			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Back injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscle strain			

subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Post procedural complication			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Radius fracture			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Aphonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	3 / 5 (60.00%)	2 / 4 (50.00%)	5 / 12 (41.67%)
occurrences (all)	4	3	12
Hyperaesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sinus headache			

subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tension headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Anterior chamber flare			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Cataract			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Chalazion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Colour blindness acquired			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis allergic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Corneal disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Eye pruritus			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Eye swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Foreign body sensation in eyes			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Iridocyclitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Iris adhesions			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Iris bombe			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Keratoconjunctivitis sicca			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Macular fibrosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Macular oedema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Papilloedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pupillary reflex impaired			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Retinal detachment			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Retinal tear			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Scleritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Uveitis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Vision blurred			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Visual acuity reduced			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vitreous detachment			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	2 / 5 (40.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Vitreous haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Abdominal pain lower			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Inguinal hernia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tooth disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Non-alcoholic steatohepatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Alopecia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 5 (0.00%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Madarosis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pruritus generalised			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Psoriasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Rash pruritic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Skin odour abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Exostosis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Spondylitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	1 / 5 (20.00%)	1 / 4 (25.00%)	0 / 12 (0.00%)
occurrences (all)	1	1	0

Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Lice infestation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 4 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Oral herpes			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vaginitis bacterial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Viral upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 4 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 6 - AIN457 10mg/kg i.v. q2wks	Cohort 6 - AIN457 30mg/kg i.v. q4wks	Cohort 4 (extension) - AIN457
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 13 (76.92%)	12 / 12 (100.00%)	20 / 28 (71.43%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 13 (15.38%)	2 / 12 (16.67%)	1 / 28 (3.57%)
occurrences (all)	2	2	1
Infusion site extravasation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	2	0
Irritability			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Oedema peripheral			

subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	1 / 28 (3.57%)
occurrences (all)	0	1	1
Pyrexia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			
Uterine haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Uterine spasm			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Vocal cord disorder			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	3	0	0
Anxiety disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Nervousness			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			

subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Blood triglycerides increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Intraocular pressure increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	4
Lipase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Lymphocyte percentage decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Neutrophil percentage increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Protein urine			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Back injury			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Joint injury			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Muscle strain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Post procedural complication			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Radius fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Aphonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	3 / 13 (23.08%)	4 / 12 (33.33%)	1 / 28 (3.57%)
occurrences (all)	5	7	1
Hyperaesthesia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Migraine			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			

subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	2
Presyncope			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Sinus headache			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Tension headache			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	1 / 28 (3.57%)
occurrences (all)	1	1	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Anterior chamber flare			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Chalazion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Colour blindness acquired			

subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Conjunctival hyperaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	3 / 28 (10.71%)
occurrences (all)	0	0	3
Corneal disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	2	0	2
Eye irritation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Eye pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	3 / 28 (10.71%)
occurrences (all)	1	1	6
Eye pruritus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Eye swelling			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	2 / 28 (7.14%)
occurrences (all)	0	1	2
Foreign body sensation in eyes			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Iridocyclitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Iris adhesions			

subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Iris bombe			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Keratoconjunctivitis sicca			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Macular fibrosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	1	0	1
Macular oedema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Ocular hyperaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	3 / 28 (10.71%)
occurrences (all)	0	0	4
Papilloedema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	1	0	2
Photopsia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Pupillary reflex impaired			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Retinal detachment			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Retinal tear			

subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Scleritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Vision blurred			
subjects affected / exposed	0 / 13 (0.00%)	3 / 12 (25.00%)	1 / 28 (3.57%)
occurrences (all)	0	3	1
Visual acuity reduced			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Vitreous detachment			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	2
Vitreous floaters			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	4 / 28 (14.29%)
occurrences (all)	0	1	4
Vitreous haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0

Constipation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Mouth ulceration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Tooth disorder			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Non-alcoholic steatohepatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Dermatitis acneiform			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Madarosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	2 / 28 (7.14%)
occurrences (all)	3	1	2
Pruritus generalised			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Rash			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	1 / 28 (3.57%)
occurrences (all)	1	1	3
Rash pruritic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Skin odour abnormal			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Exostosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Spondylitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0

Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	2
Gastroenteritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Hordeolum			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Lice infestation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	3 / 12 (25.00%)	6 / 28 (21.43%)
occurrences (all)	2	3	14
Oral herpes			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			

subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	2 / 28 (7.14%)
occurrences (all)	0	0	2
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	1 / 28 (3.57%)
occurrences (all)	0	2	1
Vaginitis bacterial			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	0 / 28 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 13 (0.00%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 June 2008	Patients were randomized prior to this date. Amendment 1 modified key secondary efficacy outcomes and key efficacy variables, to use a 15-letter change in BCVA rather than a 10-letter change, as one of the criteria for declaring a patient as responding to therapy with AIN457, to use a 2- grade improvement in vitreous haze as an outcome criterion, and to delete the secondary efficacy variable "change in macular edema". The exclusion criteria were modified to add aqueous tap to ocular surgeries allowed in the study eye, to allow "up to every hour while awake" use of topical corticosteroids, and to allow patients to be on any dose of prednisone before baseline day. Additionally, it modified the section on Rescue medication so that clinical assessments continued after rescue.)
01 August 2008	This amendment was issued when 4 patients had been randomized, introduced the following change: removal of the weight inclusion criterion that specified a range of masses (45 –100 kg, or 99 to 220 pounds).
17 February 2009	This amendment introduced the following changes: Addition of two new cohorts of patients, designated cohort 2 and cohort 3. The study of cohort 2 had the following objectives: - determine if a single dose of AIN457 was sufficient to induce a remission of uveitis within 3 weeks, -determine if AIN457 produced from Sp2/0 cells was similar in efficacy to AIN457produced from CHO cells, -determine the time to flare-up once a remission was achieved, -determine if remission can be re-induced with AIN457 once a flare-up occurred, -determine if continued periodic doses of AIN457 maintain a remission. Cohort 3 was to determine whether AIN457 was efficacious in treating forms of uveitis that often progress to blindness with all currently available immunosuppressive therapies. The amendment also revised certain inclusion and exclusion criteria. For example, the 3-week washout period for oral low-molecular weight immunosuppressant drugs was eliminated. Patients with active uveitis were allowed to continue their oral immunosuppressant drugs throughout the interval between the screening visit and the baseline visit when the first dose of AIN457 was given, thereby improving the safety of enrolled patients as it minimized the deleterious effects of up to 3 weeks of untreated uveitis or the need to start corticosteroids during this interval. Another inclusion criterion that was revised was the requirement for visual acuity of 20/40 or less. Many eyes with active uveitis have visual acuity better than 20/40, and it was reasonable to determine how well AIN457 suppressed uveitis in these eyes. Finally, an exclusion criterion was added for patients whose disease had resolved between screening and baseline visits.
06 April 2009	This amendment was to clarify and emphasize that the patients and all assessing personnel (e.g., the investigators and clinical coordinators) would be masked to the treatment arm assigned to patients randomized to Cohort 2. Additionally, patients from Cohort 1 who proceeded to participate in Cohort 2 were randomized to only the 3 mg/kg and 1 mg/kg initial doses, not the 10 mg/kg dose that was given to cohort 1. The following changes were also introduced -physical examinations at screening and at various time points during the trial,-clarification on testing for tuberculosis required for patients, AIN457 doses of 10 mg/kg would not be given more frequently than every 4 weeks (lower doses of 3 mg/kg or 1 mg/kg could be given as frequently as every 3 weeks), mentions in the synopsis that AIN457 comes in 150-mg vials as well as 50-mg vials, reduction in the exclusion period after ocular surgery before enrollment to 4 months from 6 months , elimination of the contingency of dosing patients in cohort 2 with the Sp2/0-derived AIN457 in an unblinded manner prior to the availability of CHO-derived AIN457, and provides for emergency unblinding of treatment assignment in cohort 2.

18 May 2009	This amendment was made to add exploratory pharmacogenetic studies with the objective of identifying genetic variants that may be associated with the etiology of uveitis that may predict the response to therapy with AIN457,susceptibility to interactions between AIN457 and other therapies and the risk for side effects. The logistics and consent processes of pharacogenetic data collection were detailed. These pharmacogenetic analyses are not part of this study report because they are planned to be combined with other studies of AIN457 to increase the number of patients and thereby the power of the analyses. The synopsis and assessment schedule were revised as well to change the current serum pregnancy test, conducted at study completion, to a urine pregnancy test. In addition, exclusion criteria were revised to increase the washout period to 12 months for two immunosuppressive agents, Raptiva and Rituxan, and to correct some minor clerical errors in language.
13 July 2009	This amendment introduced the following: AIN457 could be used as a rescue medication in patients whose uveitis responded after receiving two doses of 10 mg/kg while enrolled in Cohort 1 but whose uveitis did not subside for up to 8 weeks after a single dose of 1 or 3 mg/kg while enrolled in Cohort 2. Such patients, if their uveitis was active within 8-16 weeks after that single dose while in cohort 2, would be given one or two doses of 10 mg/kg iv. If their uveitis responded to these doses, then the patient would be provided periodic doses of AIN457 as specified in the protocol. Observing the efficacy of 10 mg/kg in comparison with 1 and 3 mg/kg AIN457 in the same patient would allow the selection of the optimal dose for the treatment of uveitis.
23 February 2010	This amendment allowed the continued treatment of study patients from Cohorts 1-3 who responded well with AIN457 and who preferred this therapy to any other uveitis therapy. These patients were enrolled into Cohort 4.
01 December 2010	This amendment was made to test for the first time in humans,a higher dose of AIN457, 30 mg/kg, given intravenously, and tested a subcutaneous route at adose of AIN457 (300 mg), and updated inclusion/exclusion criteria to be consistent with other uveitis studies.
13 May 2011	This amendment explained the retreatment sequence for patients in Safety Cohort 5. Although the critical data for patients in this cohort is the safety of a single 30 mg/kg iv infusion of AIN457, the protocol provided the opportunity for continued AIN457 treatment for these patients following confirmation of safety of this dose. Criteria for continued treatment were intended to be identical to those used for patients in Cohort 6. However, it was clearly stated in the protocol that no patient in this cohort was to receive a second dose of AIN457 30 mg/kg until all 4 patients in Cohort 5 had demonstrated that the dose was safe for a minimum of 29 days. As an unintended consequence of this stipulation, for all patients of this cohort, the second dose of study medication was delayed beyond Day 29. This amendment addressed the resultant changes in the visit and assessment schedule, as well as clarifying the institution of therapeutic intervention to maintain the patient's response until they could be re-treated. Cohort 4 was comprised of patients from all other cohorts of this study whose uveitis was in remission at the end of study observation. These patients are offered open-label access to AIN457 on a PRN basis. In this amendment Cohort 4 was extended to include open-label treatment for complete responders in Cohort 5 and Cohort 6 as well as to stipulate a firm end date for this open-label extension cohort as 1 year following last patient last visit date of Cohort 6. Cohort 4 efficacy assessment collections will be discontinued with safety being the key variable, after finalization of the current amendment. These amendments were not considered to have affected the interpretation of study results as they were minor and occurred prior to study unblinding.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported