Clinical trial results:
A Phase 3B, Randomized, Double-Blind Clinical Trial to Evaluate the Efficacy and Safety of Abatacept SC in Combination with Methotrexate Compared to Methotrexate Monotherapy in Achieving Clinical Remission in Adults with Early Rheumatoid Arthritis who are Methotrexate Naive

Summary

EudraCT number	2015-001275-50
Trial protocol	CZ AT DE GB HU SE FR FI ES NL RO IT
Global end of trial date	19 March 2020

Results information

Result version number	v1 (current)
This version publication date	04 April 2021
First version publication date	04 April 2021

Trial information

Trial identification

Sponsor protocol code	IM101-550

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, clinical.trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 January 2017
Global end of trial reached?	Yes
Global end of trial date	19 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective for this study is to compare the clinical efficacy of weekly abatacept in combination with MTX to MTX alone in achieving Remission, defined as SDAI ≤ 3.3, at Week 24.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 August 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 141
Country: Number of subjects enrolled	Australia: 23
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Brazil: 110
Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	Colombia: 66
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	France: 14
Country: Number of subjects enrolled	Hungary: 40
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Italy: 18
Country: Number of subjects enrolled	Korea, Republic of: 16
Country: Number of subjects enrolled	Monaco: 4
Country: Number of subjects enrolled	Mexico: 154
Country: Number of subjects enrolled	Peru: 59
Country: Number of subjects enrolled	Poland: 41
Country: Number of subjects enrolled	Qatar: 4
Country: Number of subjects enrolled	Romania: 1
Country: Number of subjects enrolled	Russian Federation: 40
Country: Number of subjects enrolled	Singapore: 4

Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	United States: 239
Country: Number of subjects enrolled	Chile: 70
Country: Number of subjects enrolled	Czechia: 39
Country: Number of subjects enrolled	Germany: 69
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	Japan: 124
Country: Number of subjects enrolled	Taiwan: 19
Country: Number of subjects enrolled	South Africa: 63
Worldwide total number of subjects	1458
EEA total number of subjects	261

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)	1254
From 65 to 84 years	202
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

994 treated in the induction period (IP). 184 from IP randomized and treated in De-Escalation (DeE), 685 treated in the Open Label (OL) and 120 treated in the Open Label Extension (OLE) period. Subjects (pt) in IP could move to the OL period after IP completion or through early IP escape. PT from DeE could transfer to OL or to OLE.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP)

Arm description:

Abatacept 125 mg subcutaneous injection once per week + Methotrexate at least 15mg per week tablet or capsule orally once per week

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

SC 125mg in 1ml pre-filled syringes

Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2.5 mg Tablet

Arm title	Placebo + Methotrexate (Cohort 1, IP)

Arm description:

Placebo of Abatacept 125 mg subcutaneous injection once per week + Methotrexate at least 15mg per week tablet or capsule orally once per week

Arm type	Placebo
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

SC placebo in 1ml pre-filled syringes

Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
2.5 mg Tablet

Arm title	Combination Therapy: Abatacept + Methotrexate (Cohort 2, IP)

Arm description:
Active abatacept SC (125 mg) weekly + methotrexate weekly

Arm type	Experimental
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
2.5 mg Tablet

Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:
SC 125mg in 1ml pre-filled syringes

Number of subjects in period 1[1]	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP)	Placebo + Methotrexate (Cohort 1, IP)	Combination Therapy: Abatacept + Methotrexate (Cohort 2, IP)
Started	451	301	242
Induction to Open Label (OL)	289 [2]	196 [3]	147 [4]
Early Escaped to Open Label	10 [5]	21 [6]	8 [7]
Induction to De-Escalation (DeE)	94 [8]	37 [9]	53 [10]
Completed	388	233	201
Not completed	63	68	41
Withdrawal of Consent	11	10	3
Adverse event, serious fatal	1	1	-
No Longer Meets Study Criteria	2	3	-
Poor/Non-Compliance	3	2	3
Not Disclosed	1	-	2
Adverse event, non-fatal	18	8	14
Pregnancy	2	-	-
Lost to follow-up	3	6	4
Subject Request to Discontinue	11	3	6

Lack of efficacy	11	35	9

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 994 subjects enrolled and treated

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This represents subjects who transitioned to DeEscalation or Open label periods

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This represents subjects who transitioned to DeEscalation or Open label periods

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This represents subjects who transitioned to DeEscalation or Open label periods

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This represents subjects who transitioned to DeEscalation or Open label periods

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This represents subjects who transitioned to DeEscalation or Open label periods

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This represents subjects who transitioned to DeEscalation or Open label periods

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This represents subjects who transitioned to DeEscalation or Open label periods

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This represents subjects who transitioned to DeEscalation or Open label periods

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This represents subjects who transitioned to DeEscalation or Open label periods

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description:	
Inclusive of all treatments, all periods	

Reporting group values	Overall Study	Total	
Number of subjects	994	994	
Age categorical Units: Subjects			
Adults (18-64 years)	865	865	
From 65-84 years	129	129	
Age Continuous Units: years			
arithmetic mean	49.1		
standard deviation	± 13.17	-	
Sex: Female, Male Units: Participants			
Female	781	781	
Male	213	213	
Race Units: Subjects			
WHITE	698	698	
BLACK/AFRICAN AMERICAN	43	43	
AMERICAN INDIAN/ALASKA NATIVE	4	4	
ASIAN	140	140	
RACE - OTHER/ NOT REPORTED	109	109	
Ethnicity Units: Subjects			
Hispanic or Latino	22	22	
Not Hispanic or Latino	112	112	
Ethnicity not reported	860	860	
MODIFIED SHARP/VAN DER HEIJDE TOTAL SCORE (mTSS)			
The Modified Total Sharp Score (mTSS) is calculated as the bilateral sum of erosion and Joint Space Narrowing (JSN) scores across all joints of the hands and feet.The score range for mTSS is 0-448. Higher scores indicate more joint damage.			
Units: Scores on a scale			
arithmetic mean	11.08		
standard deviation	± 17.839	-	
Tender Joints - 28			
number of painful joints from 28 joints			
Units: Joint Count			
arithmetic mean	13.4		
standard deviation	± 6.76	-	
Swollen Joints - 28			
number of swollen joints from 28 joints			
Units: Joint Count			
arithmetic mean	10.3		

standard deviation	± 5.77	-	
Subject global assessment of disease activity			
Subject’s global assessment of disease activity by using a Visual Analog Scale (VAS). The scale ranges from 0 mm to 100 mm, [0 mm=no pain to 100 mm=worst possible pain]			
Units: mm			
arithmetic mean	64.5		
standard deviation	± 23.28	-	
Physician global assessment of disease activity			
physician's global assessment of disease activity using a Visual Analog Scale (VAS). The scale ranges from 0 to 100 mm, [0=no arthritis activity to 100 =extremely active arthritis]			
Units: mm			
arithmetic mean	65.5		
standard deviation	± 18.99	-	
C-Reactive Protein (CRP)			
Units: mg/dL			
arithmetic mean	1.960		
standard deviation	± 2.5129	-	
DAS28-CRP			
The Disease Activity Score (DAS28-CRP) =0.56×sqrt(tender joints [count:1-28])+0.28×sqrt(swollen joints [count:1-28])+0.36×Ln(CRP level+1)+0.014×(patient’s disease assessment on 0-100 mm scale [100=most severe])+0.96. Range: 0.96 to no upper limit. Higher score=more severe disease.			
Units: Scores on a scale			
arithmetic mean	5.58		
standard deviation	± 1.049	-	
SDAI			
Simple Disease Activity Index is the numerical sum of five outcome parameters: tender joint count and swollen joint count based on a 28-joint assessment, patient global assessment and physician global assessment assessed on a visual analogue scale scale (range 0 to 10 cm), and C-reactive protein measured in mg/dL. SDAI total score range: 0 to 86. SDAI <= 3.3 indicates disease remission and SDAI >26 = high disease activity.			
Units: Scores on a scale			
arithmetic mean	38.69		
standard deviation	± 13.961	-	

End points

End points reporting groups

Reporting group title	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP)
Reporting group description:	
Abatacept 125 mg subcutaneous injection once per week + Methotrexate at least 15mg per week tablet or capsule orally once per week	
Reporting group title	Placebo + Methotrexate (Cohort 1, IP)
Reporting group description:	
Placebo of Abatacept 125 mg subcutaneous injection once per week + Methotrexate at least 15mg per week tablet or capsule orally once per week	
Reporting group title	Combination Therapy: Abatacept + Methotrexate (Cohort 2, IP)
Reporting group description:	
Active abatacept SC (125 mg) weekly + methotrexate weekly	

Primary: Percentage of participants in Simple Disease Activity Index (SDAI) remission at Week 24

End point title	Percentage of participants in Simple Disease Activity Index (SDAI) remission at Week 24
End point description:	
Simple Disease Activity Index (SDAI) is calculated using the following formula: TJC + SJC + PGA + MDGA + CRP (TJC = number of painful joints from 28 joints, SJC = number of swollen joints from 28 joints, PGA = patient global assessment on a visual analog scale 0-10 cm, MDGA = physician global assessment on a visual analog scale 0-10 cm, and CRP = c-reactive protein in mg/dL) SDAI Remission is defined as SDAI <= 3.3. Using a logistic regression model that includes treatment arm, randomization stratification factor, and baseline SDAI as continuous variable and point estimate of adjusted ORs, corresponding 95% CI and p-value was provided. SDAI total score range: 0 to 86. SDAI <= 3.3 indicates disease remission and SDAI >26 = high disease activity.	
End point type	Primary
End point timeframe:	
Week 24	

End point values	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP)	Placebo + Methotrexate (Cohort 1, IP)	Combination Therapy: Abatacept + Methotrexate (Cohort 2, IP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	225	150	0[1]	
Units: Percentage of participants				
number (confidence interval 95%)	21.3 (16.0 to 26.7)	16.0 (10.1 to 21.9)	(to)	

Notes:

[1] - Arm is not part of the Analysis population

Statistical analyses

Statistical analysis title	SDAI at 24 weeks
Comparison groups	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP) v Placebo + Methotrexate (Cohort 1, IP)

Number of subjects included in analysis	375
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2359
Method	Regression, Logistic

Secondary: Percentage of participants in Disease Activity Score (DAS)28 - c-reactive protein (CRP) remission at Week 24

End point title	Percentage of participants in Disease Activity Score (DAS)28 - c-reactive protein (CRP) remission at Week 24

End point description:

DAS28-CRP = Disease Activity Score 28 based on C-reactive protein DAS28-CRP Remission is defined as DAS28-CRP <= 2.6 Using a logistic regression model that includes treatment arm, stratification variable and baseline measure as continuous variable and point estimate of adjusted ORs, corresponding 95% CI and p-value was provided.

End point type	Secondary

End point timeframe:

Week 24

End point values	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP)	Placebo + Methotrexate (Cohort 1, IP)	Combination Therapy: Abatacept + Methotrexate (Cohort 2, IP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	225	150	0[2]	
Units: Percentage of Participants				
number (confidence interval 95%)	38.7 (32.3 to 45.0)	25.3 (18.4 to 32.3)	(to)	

Notes:

[2] - Arm is not part of the Analysis population

Statistical analyses

Statistical analysis title	DAS 28
Comparison groups	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP) v Placebo + Methotrexate (Cohort 1, IP)
Number of subjects included in analysis	375
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0112
Method	Regression, Logistic

Secondary: Percentage of participants in SDAI remission at Week 52

End point title	Percentage of participants in SDAI remission at Week 52

End point description:

Simple Disease Activity Index (SDAI) is calculated using the following formula: TJC + SJC + PGA + MDGA + CRP (TJC = number of painful joints from 28 joints, SJC = number of swollen joints from 28 joints, PGA = patient global assessment on a visual analog scale 0-10 cm, MDGA = physician global assessment on a visual analog scale 0-10 cm, and CRP = c-reactive protein in mg/dL) SDAI Remission is defined as SDAI <= 3.3. Using a logistic regression model that includes treatment arm, randomization stratification factor, and baseline SDAI as continuous variable and point estimate of adjusted ORs, corresponding 95% CI and p-value was provided. SDAI total score range: 0 to 86. SDAI <= 3.3 indicates disease remission and SDAI >26 = high disease activity.

End point type	Secondary

End point timeframe:

Week 52

End point values	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP)	Placebo + Methotrexate (Cohort 1, IP)	Combination Therapy: Abatacept + Methotrexate (Cohort 2, IP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	225	150	0[3]	
Units: Percentage of participants				
number (confidence interval 95%)	29.8 (23.8 to 35.8)	15.3 (9.6 to 21.1)	(to)	

Notes:

[3] - Arm is not part of the Analysis population

Statistical analyses

Statistical analysis title	SDAI at 52 weeks
Comparison groups	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP) v Placebo + Methotrexate (Cohort 1, IP)
Number of subjects included in analysis	375
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0021
Method	Regression, Logistic

Secondary: Mean change from baseline in radiographic progression of joint damage as measured by modified Sharp/van der Heijide Total Sharp scores (TSS) at Week 52

End point title	Mean change from baseline in radiographic progression of joint damage as measured by modified Sharp/van der Heijide Total Sharp scores (TSS) at Week 52

End point description:

The Modified Total Sharp Score (mTSS) is calculated as the bilateral sum of erosion and Joint Space Narrowing (JSN) scores across all joints of the hands and feet.The score range for mTSS is 0-448. Higher scores indicate more joint damage. The mean change from baseline in TSS using modified Sharp/van der Heijide scores was assessed using a rank-based nonparametric ANCOVA model.

End point type	Secondary

End point timeframe:

Week 52

End point values	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP)	Placebo + Methotrexate (Cohort 1, IP)	Combination Therapy: Abatacept + Methotrexate (Cohort 2, IP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	401	249	0[4]	
Units: Total Sharp Score				
arithmetic mean (standard deviation)	0.53 (± 2.279)	2.52 (± 6.205)	()	

Notes:

[4] - Arm is not part of the Analysis population

Statistical analyses

Statistical analysis title	TTS
Comparison groups	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP) v Placebo + Methotrexate (Cohort 1, IP)
Number of subjects included in analysis	650
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	rank-based ANCOVA

Secondary: Percentage of participants in Boolean remission at Week 52

End point title	Percentage of participants in Boolean remission at Week 52

End point description:

Boolean Remission is defined as Tender joint count less than 1, Swollen joint count less than 1, CRP less than 1 mg/dL, patient global assessment less than 1 (on 0 to 10 VAS scale). Logistic regression was used for this endpoint.

End point type	Secondary

End point timeframe:

Week 52

End point values	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP)	Placebo + Methotrexate (Cohort 1, IP)	Combination Therapy: Abatacept + Methotrexate (Cohort 2, IP)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	451	301	0[5]	
Units: Percentage of participants				
number (confidence interval 95%)	21.5 (17.7 to 25.3)	11.6 (8.0 to 15.2)	(to)	

Notes:
[5] - Arm is not part of the Analysis population

Statistical analyses

Statistical analysis title	Boolean Remission
Comparison groups	Combination Therapy: Abatacept + Methotrexate (Cohort 1, IP) v Placebo + Methotrexate (Cohort 1, IP)
Number of subjects included in analysis	752
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0006
Method	Regression, Logistic

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from start of treatment up to 56 days after last treatment.

Adverse event reporting additional description:

Randomization of DeE lead to 4 arms: Aba Weekly + MTX(50 subjects), Aba EoW + MTX (50 subjects), Aba Mono (47 subjects) , MTX alone (37 subjects) which had a total of 184 subjects.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Cohort 1:Aba + MTX

Reporting group description:

Subjects received abatacept 125 milligram (mg) subcutaneously (sc) with a combination of methotrexate of at least 15 mg tablet administered orally once per week (qw) up to week 24.

Reporting group title	Cohort 1:MTX Alone

Reporting group description:

Subjects received abatacept matching placebo 125 mg sc with a combination of methotrexate of at least 15 mg tablet administered orally qw up to week 24.

Reporting group title	Cohort 2:Aba + MTX

Reporting group description:

Subjects received abatacept 125 mg sc with a combination of methotrexate of at least 15 mg tablet administered orally qw up to week 56.

Reporting group title	Aba Weekly + MTX

Reporting group description:

Subjects who completed the 56 week Induction Period were randomized to this De-escalation Period received abatacept 125 mg sc with a combination of methotrexate of at least 15 mg tablet administered orally qw up to week 104.

Reporting group title	Aba EOW + MTX

Reporting group description:

Subjects who completed the 56 week Induction Period were randomized to this De-escalation Period received abatacept 125 mg sc every other week (EOW) alternating with a matching placebo of abatacept with a combination of methotrexate of at least 15 mg tablet administered orally weekly up to week 80.

Reporting group title	Aba Mono

Reporting group description:

Subjects who completed the 56 week Induction Period were randomized to this De-escalation Period received abatacept 125 mg sc with a combination of methotrexate matching placebo of at least 15 mg tablet administered orally weekly up to week 104.

Reporting group title	MTX Alone

Reporting group description:

Subjects who completed the 56 week Induction Period were randomized to this De-escalation Period received abatacept matching placebo 125 mg sc with a combination of methotrexate of at least 15 mg tablet administered orally weekly up to week 104.

Reporting group title	OL Aba + MTX

Reporting group description:

Subjects who completed the 104 week of treatment entered Open-Label Period received abatacept 125 mg sc with a combination of methotrexate matching placebo of at least 15 mg tablet administered orally qw up to week 104.

Reporting group title	OLE Aba

Reporting group description:

Subjects who completed the Induction Period and De-escalation Period with escape or remission entered 24 week optional Open Label Extension Period andreceived abatacept 125 mg sc qw up to week 128.

Serious adverse events	Cohort 1:Aba + MTX	Cohort 1:MTX Alone	Cohort 2:Aba + MTX
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 451 (7.10%)	9 / 301 (2.99%)	23 / 242 (9.50%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoid tumour of the gastrointestinal tract			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Benign ovarian tumour			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			

subjects affected / exposed	0 / 451 (0.00%)	1 / 301 (0.33%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lung			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Prostate cancer			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Renal cancer			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Squamous cell carcinoma			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Superficial spreading melanoma stage unspecified			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Vascular disorders			
Hypotension			

subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Knee operation			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Hydrometra			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metrorrhagia			

subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Ovarian cyst			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Vaginal polyp			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Bronchiectasis			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Pneumothorax			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary congestion			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Pulmonary embolism			

subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Investigations			
Oxygen saturation decreased			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Weight decreased			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	2 / 451 (0.44%)	0 / 301 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Femur fracture			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture displacement			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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

Humerus fracture			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Meniscus injury			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumoconiosis			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Radius fracture			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	1 / 451 (0.22%)	1 / 301 (0.33%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Atrial fibrillation			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Cardiac arrest			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure congestive			

subjects affected / exposed	0 / 451 (0.00%)	1 / 301 (0.33%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Angina pectoris			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Coronary artery occlusion			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Pericarditis			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Cerebrovascular accident			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Dysarthria			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar infarction			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Lacunar stroke			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Syncope			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxic-Ischaemic encephalopathy			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macular degeneration			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Macular hole			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Gastrointestinal disorders			
Gastritis erosive			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intestinal ischaemia			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Malocclusion			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Melaena			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	2 / 242 (0.83%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Cholelithiasis			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Renal and urinary disorders			
Bladder prolapse			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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

Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Intervertebral disc protrusion			
subjects affected / exposed	2 / 451 (0.44%)	0 / 301 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 451 (0.22%)	1 / 301 (0.33%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 451 (0.00%)	1 / 301 (0.33%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Spondylolisthesis			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Synovial cyst			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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

Exostosis			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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			
Appendicitis			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (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
Diverticulitis			
subjects affected / exposed	0 / 451 (0.00%)	1 / 301 (0.33%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 451 (0.44%)	2 / 301 (0.66%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	1 / 2	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 451 (0.00%)	1 / 301 (0.33%)	0 / 242 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 451 (0.44%)	1 / 301 (0.33%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess intestinal			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Cellulitis			

subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Haemophilus infection			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious mononucleosis			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Peritonsillar abscess			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Sepsis			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	0 / 242 (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
Tuberculosis			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
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			
Hyperglycaemia			

subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 451 (0.00%)	0 / 301 (0.00%)	1 / 242 (0.41%)
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	Aba Weekly + MTX	Aba EOW + MTX	Aba Mono
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 50 (6.00%)	3 / 50 (6.00%)	0 / 47 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoid tumour of the gastrointestinal tract			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Benign ovarian tumour			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Cervix carcinoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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

Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Metastases to lung			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Prostate cancer			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Renal cancer			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Squamous cell carcinoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Superficial spreading melanoma stage unspecified			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Uterine leiomyoma			

subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Surgical and medical procedures			
Knee operation			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 47 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 47 (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
Hydrometra			

subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Metrorrhagia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Ovarian cyst			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Vaginal polyp			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Bronchiectasis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pneumothorax			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary congestion			

subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pulmonary embolism			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Investigations			
Oxygen saturation decreased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Weight decreased			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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			
Overdose			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Subdural haematoma			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Femur fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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

Fracture displacement			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Humerus fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Meniscus injury			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pneumoconiosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Radius fracture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Skin laceration			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Atrial fibrillation			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Cardiac arrest			

subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Angina pectoris			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Coronary artery occlusion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Myocardial ischaemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pericarditis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Cerebrovascular accident			

subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Seizure			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Dysarthria			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Encephalopathy			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Epilepsy			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Lacunar infarction			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Lacunar stroke			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Syncope			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Hypoxic-Ischaemic encephalopathy			

subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Macular degeneration			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Macular hole			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Gastrointestinal disorders			
Gastritis erosive			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pancreatitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Intestinal ischaemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Malocclusion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Melaena			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pancreatitis acute			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Cholecystitis chronic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Cholelithiasis			

subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 47 (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
Renal and urinary disorders			
Bladder prolapse			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Osteoarthritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Rheumatoid arthritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Spinal pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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

Spondylolisthesis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Synovial cyst			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Exostosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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			
Appendicitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Diverticulitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Gastroenteritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Abscess intestinal			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Cellulitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Haemophilus infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Infectious mononucleosis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Sepsis			

subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Tuberculosis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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			
Hyperglycaemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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
Hyperkalaemia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (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	MTX Alone	OL Aba + MTX	OLE Aba
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 37 (0.00%)	40 / 685 (5.84%)	0 / 120 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoid tumour of the gastrointestinal tract			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Basal cell carcinoma			

subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign ovarian tumour			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Cervix carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Metastases to lung			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			

subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superficial spreading melanoma stage unspecified			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Surgical and medical procedures			
Knee operation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Hydrometra			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Metrorrhagia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal polyp			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchiectasis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Pulmonary congestion			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Oxygen saturation decreased			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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			
Overdose			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Femur fracture			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture displacement			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Meniscus injury			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Pneumoconiosis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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

Skin laceration			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Atrial fibrillation			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Coronary artery occlusion			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			

subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Seizure			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Dysarthria			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Encephalopathy			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Lacunar infarction			

subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lacunar stroke			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Hypoxic-Ischaemic encephalopathy			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 37 (0.00%)	2 / 685 (0.29%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Macular degeneration			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Macular hole			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis erosive			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Pancreatitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Intestinal ischaemia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malocclusion			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Pancreatitis acute			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Hepatobiliary disorders			

Cholecystitis acute			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Bladder prolapse			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Osteoarthritis			

subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Spinal pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Spondylolisthesis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Synovial cyst			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Exostosis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Pneumonia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 685 (0.29%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Abscess intestinal			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemophilus infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Infectious mononucleosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Peritonsillar abscess			

subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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			
Hyperglycaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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
Hyperkalaemia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 685 (0.00%)	0 / 120 (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:Aba + MTX	Cohort 1:MTX Alone	Cohort 2:Aba + MTX
Total subjects affected by non-serious adverse events			
subjects affected / exposed	237 / 451 (52.55%)	152 / 301 (50.50%)	123 / 242 (50.83%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	24 / 451 (5.32%)	15 / 301 (4.98%)	10 / 242 (4.13%)
occurrences (all)	33	20	11
Aspartate aminotransferase increased			
subjects affected / exposed	14 / 451 (3.10%)	10 / 301 (3.32%)	9 / 242 (3.72%)
occurrences (all)	16	14	11
Influenza a virus test positive			
subjects affected / exposed	1 / 451 (0.22%)	0 / 301 (0.00%)	0 / 242 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 451 (2.44%)	8 / 301 (2.66%)	5 / 242 (2.07%)
occurrences (all)	11	8	5
Nervous system disorders			
Headache			
subjects affected / exposed	31 / 451 (6.87%)	21 / 301 (6.98%)	8 / 242 (3.31%)
occurrences (all)	38	24	12
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	12 / 451 (2.66%)	18 / 301 (5.98%)	4 / 242 (1.65%)
occurrences (all)	12	22	5
General disorders and administration site conditions			
Drug intolerance			
subjects affected / exposed	7 / 451 (1.55%)	4 / 301 (1.33%)	0 / 242 (0.00%)
occurrences (all)	7	5	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	42 / 451 (9.31%)	24 / 301 (7.97%)	22 / 242 (9.09%)
occurrences (all)	56	27	25
Stomatitis			
subjects affected / exposed	27 / 451 (5.99%)	8 / 301 (2.66%)	1 / 242 (0.41%)
occurrences (all)	45	14	3
Abdominal pain upper			

subjects affected / exposed	12 / 451 (2.66%)	5 / 301 (1.66%)	14 / 242 (5.79%)
occurrences (all)	12	6	15
Diarrhoea			
subjects affected / exposed	17 / 451 (3.77%)	12 / 301 (3.99%)	13 / 242 (5.37%)
occurrences (all)	17	13	17
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	15 / 451 (3.33%)	16 / 301 (5.32%)	13 / 242 (5.37%)
occurrences (all)	16	17	13
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	63 / 451 (13.97%)	43 / 301 (14.29%)	36 / 242 (14.88%)
occurrences (all)	81	60	47
Pharyngitis			
subjects affected / exposed	22 / 451 (4.88%)	17 / 301 (5.65%)	14 / 242 (5.79%)
occurrences (all)	24	19	14
Upper respiratory tract infection			
subjects affected / exposed	24 / 451 (5.32%)	16 / 301 (5.32%)	18 / 242 (7.44%)
occurrences (all)	28	20	18
Bronchitis			
subjects affected / exposed	19 / 451 (4.21%)	12 / 301 (3.99%)	16 / 242 (6.61%)
occurrences (all)	20	12	20
Gastroenteritis			
subjects affected / exposed	13 / 451 (2.88%)	9 / 301 (2.99%)	10 / 242 (4.13%)
occurrences (all)	13	10	11
Herpes zoster			
subjects affected / exposed	3 / 451 (0.67%)	2 / 301 (0.66%)	1 / 242 (0.41%)
occurrences (all)	3	4	1
Urinary tract infection			
subjects affected / exposed	17 / 451 (3.77%)	9 / 301 (2.99%)	13 / 242 (5.37%)
occurrences (all)	20	13	18

Non-serious adverse events	Aba Weekly + MTX	Aba EOW + MTX	Aba Mono
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 50 (24.00%)	22 / 50 (44.00%)	10 / 47 (21.28%)
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	2 / 50 (4.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 50 (6.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	3	0	0
Influenza a virus test positive			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 50 (0.00%)	3 / 50 (6.00%)	0 / 47 (0.00%)
occurrences (all)	0	3	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
General disorders and administration site conditions			
Drug intolerance			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 50 (2.00%)	2 / 50 (4.00%)	0 / 47 (0.00%)
occurrences (all)	1	4	0
Stomatitis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	2 / 47 (4.26%)
occurrences (all)	0	1	9
Abdominal pain upper			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			

subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 50 (4.00%)	6 / 50 (12.00%)	4 / 47 (8.51%)
occurrences (all)	3	7	4
Pharyngitis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 50 (2.00%)	2 / 50 (4.00%)	1 / 47 (2.13%)
occurrences (all)	1	3	1
Bronchitis			
subjects affected / exposed	3 / 50 (6.00%)	6 / 50 (12.00%)	1 / 47 (2.13%)
occurrences (all)	3	6	1
Gastroenteritis			
subjects affected / exposed	0 / 50 (0.00%)	3 / 50 (6.00%)	1 / 47 (2.13%)
occurrences (all)	0	4	1
Herpes zoster			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	2 / 50 (4.00%)	1 / 50 (2.00%)	1 / 47 (2.13%)
occurrences (all)	2	1	1

Non-serious adverse events	MTX Alone	OL Aba + MTX	OLE Aba
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 37 (43.24%)	230 / 685 (33.58%)	15 / 120 (12.50%)
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 37 (0.00%)	20 / 685 (2.92%)	0 / 120 (0.00%)
occurrences (all)	0	23	0
Aspartate aminotransferase			

increased			
subjects affected / exposed	0 / 37 (0.00%)	11 / 685 (1.61%)	0 / 120 (0.00%)
occurrences (all)	0	11	0
Influenza a virus test positive			
subjects affected / exposed	2 / 37 (5.41%)	1 / 685 (0.15%)	0 / 120 (0.00%)
occurrences (all)	2	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 37 (0.00%)	4 / 685 (0.58%)	0 / 120 (0.00%)
occurrences (all)	0	4	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 37 (2.70%)	20 / 685 (2.92%)	0 / 120 (0.00%)
occurrences (all)	1	23	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 37 (2.70%)	10 / 685 (1.46%)	1 / 120 (0.83%)
occurrences (all)	1	11	1
General disorders and administration site conditions			
Drug intolerance			
subjects affected / exposed	2 / 37 (5.41%)	4 / 685 (0.58%)	0 / 120 (0.00%)
occurrences (all)	2	4	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 37 (2.70%)	23 / 685 (3.36%)	0 / 120 (0.00%)
occurrences (all)	1	24	0
Stomatitis			
subjects affected / exposed	2 / 37 (5.41%)	21 / 685 (3.07%)	2 / 120 (1.67%)
occurrences (all)	4	31	4
Abdominal pain upper			
subjects affected / exposed	0 / 37 (0.00%)	8 / 685 (1.17%)	1 / 120 (0.83%)
occurrences (all)	0	9	1
Diarrhoea			
subjects affected / exposed	1 / 37 (2.70%)	13 / 685 (1.90%)	1 / 120 (0.83%)
occurrences (all)	4	15	1
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 37 (2.70%)	11 / 685 (1.61%)	1 / 120 (0.83%)
occurrences (all)	1	11	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 37 (13.51%)	59 / 685 (8.61%)	6 / 120 (5.00%)
occurrences (all)	6	75	9
Pharyngitis			
subjects affected / exposed	2 / 37 (5.41%)	18 / 685 (2.63%)	0 / 120 (0.00%)
occurrences (all)	3	18	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 37 (8.11%)	28 / 685 (4.09%)	3 / 120 (2.50%)
occurrences (all)	3	31	4
Bronchitis			
subjects affected / exposed	0 / 37 (0.00%)	24 / 685 (3.50%)	1 / 120 (0.83%)
occurrences (all)	0	25	1
Gastroenteritis			
subjects affected / exposed	2 / 37 (5.41%)	13 / 685 (1.90%)	1 / 120 (0.83%)
occurrences (all)	2	13	1
Herpes zoster			
subjects affected / exposed	2 / 37 (5.41%)	7 / 685 (1.02%)	0 / 120 (0.00%)
occurrences (all)	2	7	0
Urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	26 / 685 (3.80%)	0 / 120 (0.00%)
occurrences (all)	0	34	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 September 2015	Incorporates changes in response to health authorities in countries participating in the Voluntary Harmonization Procedure (VHP)
22 February 2016	Provide clarifications of interpretation of the protocol and increase consistency in the protocol
27 November 2017	Added a new period (Optional Open Label Abatacept Extension for Subjects who Complete the DE Period); added a section 3.1.6.5 to describe the new period; added a sentence in Section 8.4.3, Safety analyses, to describe the analyses of those subjects. Updated the Medical Monitor Contact, added name of the Study Director, added abatacept/placebo and MTX reconciliation at Week 56 of IP, deleted BNP sample collection, added CRP collection at DE Week 64, added HAQ at Week 64, clarified corticosteroid rescue treatment to be for RA, corrected SAE reporting section.
08 January 2018	Corrected errors in Section 5.1, Table 5.1-6. Indicated the second phone call visit is at Week 112, deleted CRP testing at the office visits, added dosing of weekly SC abatacept, added diary cards will be collected at Week 116 and Week 128/ET, and indicated the office visit will be +/- 3 days of the target visit day.
26 April 2018	Updated the schematic in both the synopsis and body of the protocol to add the new optional open label SC abatacept period for DE completers. Added a paragraph in the synopsis to describe the optional open label SC abatacept period for DE completers. Modified the definition of serious breach. Two corrections made to Table 5.1-4 for procedures required at the ET or Final Visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported