



## Clinical trial results:

### An Open Label Non-Randomized Study to Characterize the Steady State Pharmacokinetics of Sulfasalazine Delayed Release Tablets in Children With Juvenile Idiopathic Arthritis

#### Summary

EudraCT number	2017-000307-24
Trial protocol	Outside EU/EEA
Global end of trial date	21 January 2014

#### Results information

Result version number	v1 (current)
This version publication date	10 June 2022
First version publication date	10 June 2022

#### Trial information

##### Trial identification

Sponsor protocol code	A0031005
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00637780
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E42nd Street, New York, United States, NY 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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?	Yes

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 June 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 January 2014
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To characterise the steady state pharmacokinetics of sulfasalazine delayed release tablets in juvenile idiopathic arthritis subjects.

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 Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 June 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	United States: 1
Worldwide total number of subjects	2
EEA total number of subjects	0

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)	2
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The last subject enrolled in 2014 but the study was kept open for another 2 years and enrollment was not stopped. However, by 2016, no additional subjects were enrolled and thus the study was closed.

### Pre-assignment

Screening details:

A total of 2 subjects were screened and enrolled in this study at the time of study termination. Both subjects completed the study.

### Period 1

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

### Arms

<b>Arm title</b>	Sulfasalazine in Juvenile Idiopathic Arthritis
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Arm description:

All subjects received sulfasalazine 30-50 milligrams (mg) per kilograms (kg) per day, divided into twice daily (BID) doses, for 6 days. On Day 7, the morning dose was administered at the site in presence of site staff. Sulfasalazine was administered orally in the form of 500-milligram (mg) tablets.

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

Dosage and administration details:

Subjects received sulfasalazine at a dose of 30-50 mg per kg per day twice daily orally.

<b>Number of subjects in period 1</b>	Sulfasalazine in Juvenile Idiopathic Arthritis
Started	2
Completed	2

## Baseline characteristics

### Reporting groups

Reporting group title	Sulfasalazine in Juvenile Idiopathic Arthritis
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Reporting group description:

All subjects received sulfasalazine 30-50 milligrams (mg) per kilograms (kg) per day, divided into twice daily (BID) doses, for 6 days. On Day 7, the morning dose was administered at the site in presence of site staff. Sulfasalazine was administered orally in the form of 500-milligram (mg) tablets.

Reporting group values	Sulfasalazine in Juvenile Idiopathic Arthritis	Total	
Number of subjects	2	2	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	2	2	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	15.0		
standard deviation	± 1.4	-	
Sex: Female, Male			
Units: Subjects			
Female	1	1	
Male	1	1	

## End points

### End points reporting groups

Reporting group title	Sulfasalazine in Juvenile Idiopathic Arthritis
Reporting group description: All subjects received sulfasalazine 30-50 milligrams (mg) per kilograms (kg) per day, divided into twice daily (BID) doses, for 6 days. On Day 7, the morning dose was administered at the site in presence of site staff. Sulfasalazine was administered orally in the form of 500-milligram (mg) tablets.	

### Primary: Sulfasalazine Steady State Maximum Plasma Concentration (Cmax) and Predose Concentration (Cmin)

End point title	Sulfasalazine Steady State Maximum Plasma Concentration (Cmax) and Predose Concentration (Cmin) <sup>[1]</sup>
End point description: The 2 subjects who were enrolled and completed the study at the time of study termination were included in all analyses.	
End point type	Primary
End point timeframe: Day 7 predose, and 2, 4, 6, 10, and 12 hours postdose	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Only descriptive analysis was planned for this end point.	

End point values	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Micrograms per milliliter				
number (not applicable)				
Cmax - Value 1	17.6			
Cmax - Value 2	4.51			
Cmin - Value 1	4.28			
Cmin - Value 2	0.988			

### Statistical analyses

No statistical analyses for this end point

### Primary: Sulfasalazine Time for Cmax (Tmax) at Steady State

End point title	Sulfasalazine Time for Cmax (Tmax) at Steady State <sup>[2]</sup>
End point description: The 2 subjects who were enrolled and completed the study at the time of study termination were included in all analyses.	
End point type	Primary
End point timeframe: Day 7 predose, and 2, 4, 6, 10, and 12 hours postdose	

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive analysis was planned for this end point.

End point values	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: hours				
number (not applicable)				
Value 1	2.02			
Value 2	5.92			

### Statistical analyses

No statistical analyses for this end point

### Primary: Sulfasalazine Area Under the Concentration-time Profile From Time Zero to Time Tau, the Dosing Interval (AUCtau) at Steady State

End point title	Sulfasalazine Area Under the Concentration-time Profile From Time Zero to Time Tau, the Dosing Interval (AUCtau) at Steady State <sup>[3]</sup>
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End point description:

The 2 subjects who were enrolled and completed the study at the time of study termination were included in all analyses.

End point type	Primary
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End point timeframe:

Day 7 predose, and 2, 4, 6, 10, and 12 hours postdose

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive analysis was planned for this end point.

End point values	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Micrograms*hour per millilitre				
number (not applicable)				
Value 1	110			
Value 2	34.7			

### Statistical analyses

No statistical analyses for this end point

**Primary: Sulfapyridine Steady State Cmax and Cmin**

End point title	Sulfapyridine Steady State Cmax and Cmin <sup>[4]</sup>
End point description: Sulfapyridine and 5-aminosalicylic acid (5-ASA) are primary metabolites of sulfasalazine, the study drug. The 2 subjects who were enrolled and completed the study at the time of study termination were included in all analyses.	
End point type	Primary
End point timeframe: Day 7 predose, and 2, 4, 6, 10, and 12 hours postdose	
Notes: [4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Only descriptive analysis was planned for this end point.	

<b>End point values</b>	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Micrograms per milliliter				
number (not applicable)				
Cmax - Value 1	21.7			
Cmax - Value 2	7.68			
Cmin - Value 1	14.7			
Cmin - Value 2	4.79			

**Statistical analyses**

No statistical analyses for this end point

**Primary: Sulfapyridine Tmax at Steady State**

End point title	Sulfapyridine Tmax at Steady State <sup>[5]</sup>
End point description: Sulfapyridine and 5-ASA are primary metabolites of sulfasalazine, the study drug. The 2 subjects who were enrolled and completed the study at the time of study termination were included in all analyses.	
End point type	Primary
End point timeframe: Day 7 predose, and 2, 4, 6, 10, and 12 hours postdose	
Notes: [5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Only descriptive analysis was planned for this end point.	

<b>End point values</b>	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: hours				
number (not applicable)				

Value 1	4.00			
Value 2	11.9			

## Statistical analyses

No statistical analyses for this end point

### Primary: Sulfapyridine AUCtau at Steady State

End point title	Sulfapyridine AUCtau at Steady State <sup>[6]</sup>
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End point description:

Sulfapyridine and 5-ASA are primary metabolites of sulfasalazine, the study drug. The 2 subjects who were enrolled and completed the study at the time of study termination were included in all analyses.

End point type	Primary
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End point timeframe:

Day 7 predose, and 2, 4, 6, 10, and 12 hours postdose

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive analysis was planned for this end point.

<b>End point values</b>	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Micrograms*hour per millilitre				
number (not applicable)				
Value 1	232			
Value 2	67.3			

## Statistical analyses

No statistical analyses for this end point

### Primary: 5-aminosalicylic Acid (5-ASA) Steady State Cmax and Cmin

End point title	5-aminosalicylic Acid (5-ASA) Steady State Cmax and Cmin <sup>[7]</sup>
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End point description:

Sulfapyridine and 5-ASA are primary metabolites of sulfasalazine, the study drug. The 2 subjects who were enrolled and completed the study at the time of study termination were included in all analyses.

End point type	Primary
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End point timeframe:

Day 7 predose, and 2, 4, 6, 10, and 12 hours postdose

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive analysis was planned for this end point.



<b>End point values</b>	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Micrograms per milliliter				
number (not applicable)				
Cmax - Value 1	0.208			
Cmax - Value 2	0.0982			
Cmin - Value 1	0.0439			
Cmin - Value 2	0.0816			

## Statistical analyses

No statistical analyses for this end point

### Primary: 5-aminosalicylic Acid (5-ASA) Tmax at Steady State

End point title	5-aminosalicylic Acid (5-ASA) Tmax at Steady State <sup>[8]</sup>
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End point description:

Sulfapyridine and 5-ASA are primary metabolites of sulfasalazine, the study drug. The 2 subjects who were enrolled and completed the study at the time of study termination were included in all analyses.

End point type	Primary
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End point timeframe:

Day 7 predose, and 2, 4, 6, 10, and 12 hours postdose

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive analysis was planned for this end point.

<b>End point values</b>	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: hours				
number (not applicable)				
Value 1	0.000			
Value 2	11.9			

## Statistical analyses

No statistical analyses for this end point

### Primary: 5-aminosalicylic Acid (5-ASA) AUCtau at Steady State

End point title	5-aminosalicylic Acid (5-ASA) AUCtau at Steady State <sup>[9]</sup>
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End point description:

Sulfapyridine and 5-ASA are primary metabolites of sulfasalazine, the study drug. The 2 subjects who

were enrolled and completed the study at the time of study termination were included in all analyses.

End point type	Primary
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End point timeframe:

Day 7 predose, and 2, 4, 6, 10, and 12 hours postdose

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive analysis was planned for this end point.

<b>End point values</b>	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Micrograms*hour per milliliter				
number (not applicable)				
Value 1	1.63			
Value 2	1.04			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Withdrawals Due to TEAEs

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), and Withdrawals Due to TEAEs
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End point description:

An adverse event (AE) was any untoward medical occurrence attributed to study drug in a subject who received study drug. TEAEs are defined as newly occurring AEs or those worsening after first dose. AEs comprised both SAEs and non-SAEs. An SAE was an AE resulting in any of the following endpoints or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. The 2 subjects who were enrolled and completed the study at the time of study termination were included in all analyses.

End point type	Secondary
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End point timeframe:

28 Days post last dose (maximum up to Day 35)

<b>End point values</b>	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Subjects				
TEAEs	0			
SAEs	0			
Withdrawals due to TEAEs	0			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Laboratory Test Abnormalities

End point title	Number of Subjects With Laboratory Test Abnormalities
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End point description:

Number of subjects with laboratory test abnormalities without regard to baseline abnormality. Laboratory test parameters included hematology, coagulation, liver function, renal function, electrolytes, clinical chemistry, and urinalysis (dipstick and microscopy). The 2 subjects who were enrolled and completed the study at the time of study termination were included in all analyses.

End point type	Secondary
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End point timeframe:

Up to Day 7

End point values	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Subjects	1			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Vital Signs Values Meeting Categorical Summarization Criteria

End point title	Number of Subjects With Vital Signs Values Meeting Categorical Summarization Criteria
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End point description:

Vital sign values which met categorical summarisation criteria included: supine/sitting pulse rate less than (<) 40 or more than (>) 120 beats per minute (bpm); erect pulse rate <40 or >140 bpm; changes from baseline in same posture of systolic blood pressure (SBP) more than or equal to (>=) 30 millimeters of mercury (mm Hg) or diastolic blood pressure (DBP) >=20 mm Hg; SBP <90 mm Hg; and DBP <50 mm Hg. The 2 subjects who were enrolled and completed the study at the time of study termination were included in all analyses.

End point type	Secondary
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End point timeframe:

Up to Day 7

<b>End point values</b>	Sulfasalazine in Juvenile Idiopathic Arthritis			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Subjects	0			

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

28 Days post last dose (maximum up to Day 35)

Adverse event reporting additional description:

All treated subjects were analysed for AEs. The same event may appear as both an AE and an SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another participant, or one subject may have experienced both a serious and non-serious event during the study.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	NA
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Dictionary version	NA
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### Reporting groups

Reporting group title	Sulfasalazine in Juvenile Idiopathic Arthritis
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Reporting group description:

All subjects received sulfasalazine 30-50 mg per kg per day, divided into BID doses, for 6 days. On Day 7, the morning dose was administered at the site in presence of site staff. Sulfasalazine was administered orally in the form of 500-mg tablets.

Serious adverse events	Sulfasalazine in Juvenile Idiopathic Arthritis		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Sulfasalazine in Juvenile Idiopathic Arthritis		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There were no non-serious adverse events were reported in this study.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 May 2012	Subject selection, revised inclusion criteria #5 to indicate subjects must weigh at least 20 kg.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated prematurely and only 2 subjects were enrolled and completed the study.

Notes: