Clinical trial results:
Phase II, open label, international, multicentre clinical trial to investigate safety and efficacy of oral ITF 2357 in patients with active systemic onset juvenile idiopathic arthritis SOJIA

Summary

EudraCT number	2006-000089-35
Trial protocol	IT
Global end of trial date	25 August 2008

Results information

Result version number	v2 (current)
This version publication date	31 July 2019
First version publication date	25 May 2019
Version creation reason	• Correction of full data set Friendly description should be changed.

Trial information

Trial identification

Sponsor protocol code	DSC/05/2357/19

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00570661
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Italfarmaco S.p.A.
Sponsor organisation address	Via dei Lavoratori, 54, Milan, Italy, 20092
Public contact	Clinical Trial Transparency Manager, Italfarmaco S.p.A., Italfarmaco S.p.A., +39 02 66041503, info@italfarmaco.com
Scientific contact	Clinical Trial Transparency Manager, Italfarmaco S.p.A., Italfarmaco S.p.A., +39 02 66041503, info@italfarmaco.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000551-PIP01-09
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	25 August 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 August 2008
Global end of trial reached?	Yes
Global end of trial date	25 August 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the safety and tolerability of oral ITF2357 in patients with active SOJIA with inadequate response or intolerance to standard therapy with oral steroids and methotrexate, with or without previously used biologic agents.

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki and in accordance with the International Conference on Harmonization (ICH) Consolidated Guideline on Good Clinical Practice (GCP).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 September 2006
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	Romania: 5
Country: Number of subjects enrolled	Serbia: 12
Worldwide total number of subjects	17
EEA total number of subjects	5

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)	7
Adolescents (12-17 years)	8
Adults (18-64 years)	2
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Seventeen patients were screened and enrolled in the study.

Pre-assignment

Screening details:

Patients with SOJIA according to the International League against Rheumatism criteria, established before the age of 16 y and for at least 6 mo before the study entry, having active disease for at least 1 mo while receiving more than 0.2 mg/kg/day prednisolone or equivalent steroid with/without concurrent methotrexate therapy (≥ 10 mg/m2 weekly).

Period 1

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

Blinding implementation details:

Not applicable. The study was open label.

Arms

Arm title	ITF2357

Arm description:

ITF2357 hard gelatine capsules were administered orally, in fed conditions, at the cumulative daily dose of 1.5 mg/kg achieved by administration of 0.75 mg/kg at 12-hour interval for 4 weeks initially. The doses of 1.5 mg/kg/day were achieved by administration of an appropriate number of capsules of definite strength. Treatment was further prolonged up to 12 weeks in total if so suggested by the observed benefits and the lack of treatment-limiting toxicity.

Arm type	Experimental
Investigational medicinal product name	ITF2357
Investigational medicinal product code	
Other name	Givinostat, histone deacetylase inhibitor
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

ITF2357 hard gelatine capsule for oral administration supplied at the dose strengths of 7.5, 10, 12.5, 15, 20 mg and 50 mg. The investigational product was administered orally, in fed conditions, at the cumulative daily dose of 1.5 mg/kg achieved by administration of 0.75 mg/kg at 12-hour interval. Each patient received the same daily dose for the whole treatment period. ITF2357 was initially administered for 4 weeks. Treatment was further prolonged up to 12 weeks in total if so suggested by the observed benefits and the lack of treatment-limiting toxicity.

Number of subjects in period 1	ITF2357
Started	17
Completed	10
Not completed	7
Unmet crtierion of sufficient therapeutic response	1
Adverse event, non-fatal	1
Disease worsening	5

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	17	17	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	11.18		
standard deviation	± 5.39	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	11	11	

Subject analysis sets

Subject analysis set title	ITF2357 - ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All recruited patients who received study medication and for whom at least one safety or efficacy measurement was available.

Subject analysis set title	ITF2357 - PP population
Subject analysis set type	Per protocol

Subject analysis set description:

All patients who completed the study without any major deviations from the protocol procedures.

Reporting group values	ITF2357 - ITT population	ITF2357 - PP population	
Number of subjects	17	9	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	 11.18 ± 5.39	 ±	
Gender categorical Units: Subjects			
Female Male	6 11	1 8	

End points

End points reporting groups

Reporting group title	ITF2357

Reporting group description:

ITF2357 hard gelatine capsules were administered orally, in fed conditions, at the cumulative daily dose of 1.5 mg/kg achieved by administration of 0.75 mg/kg at 12-hour interval for 4 weeks initially. The doses of 1.5 mg/kg/day were achieved by administration of an appropriate number of capsules of definite strength. Treatment was further prolonged up to 12 weeks in total if so suggested by the observed benefits and the lack of treatment-limiting toxicity.

Subject analysis set title	ITF2357 - ITT population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All recruited patients who received study medication and for whom at least one safety or efficacy measurement was available.

Subject analysis set title	ITF2357 - PP population
Subject analysis set type	Per protocol

Subject analysis set description:

All patients who completed the study without any major deviations from the protocol procedures.

Primary: Number of patients completing week 12 of treatment

End point title	Number of patients completing week 12 of treatment[1]

End point description:

All patients in the study PP population (N=9) completed 12 weeks of treatment with ITF2357 according to the specifications of the protocol and thus reached the primary end-point of the study.
The asnalysis was repeated on the ITT population: 10 out of the 17 patients in the ITT population completed 12 weeks of treatment and reached the primary end-point of the study.

End point type	Primary

End point timeframe:

At week 12.

Notes:

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

End point values	ITF2357 - ITT population	ITF2357 - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	9		
Units: number of patients				
Completers	10	9		
Non completers	7	0		

Statistical analyses

No statistical analyses for this end point

Secondary: JIA Outcome Core Set Variables - Patient global assessment

End point title	JIA Outcome Core Set Variables - Patient global assessment

End point description:

Patient/parent global Visual Analogue Scale (VAS) (VAS) is from 0 to 100.

End point type	Secondary

End point timeframe:

At pretreatment visit, at weeks 2, 4, 6, 8, 10 and 12 (End of treatment), 1 month and 3 months follow up (FU1, FU3) in the PP and ITT populations respectively.

End point values	ITF2357 - ITT population	ITF2357 - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17[2]	9		
Units: score				
arithmetic mean (standard deviation)				
pre-treatment	47.71 (± 21.45)	48.00 (± 22.50)		
week 2	42.47 (± 21.30)	43.33 (± 21.15)		
week 4	28.88 (± 22.48)	21.22 (± 14.00)		
week 6	22.36 (± 18.33)	19.11 (± 15.00)		
week 8	18.00 (± 13.99)	17.22 (± 14.59)		
week 10	22.33 (± 19.58)	17.44 (± 13.28)		
week 12	24.21 (± 20.89)	19.11 (± 14.57)		
FU1	26.56 (± 18.02)	18.11 (± 15.53)		
FU3	22.71 (± 17.85)	15.38 (± 15.32)		

Notes:

[2] - n=16 at week 4 and FU1
n=14 at week 6, week 12 and FU3
n=12 at week 8 and week 10

Statistical analyses

No statistical analyses for this end point

Secondary: JIA Outcome Core Set Variables - Physician global assessment

End point title	JIA Outcome Core Set Variables - Physician global assessment

End point description:

Physician's global c (VAS) is from 0 to 100.

End point type	Secondary

End point timeframe:

At pretreatment visit, at weeks 2, 4, 6, 8, 10 and 12 (End of treatment), 1 month and 3 months follow up (FU1, FU3) in the PP and ITT populations respectively.

End point values	ITF2357 - ITT population	ITF2357 - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17[3]	9		
Units: score				
arithmetic mean (standard deviation)				
pre-treatment	56.12 (± 12.99)	50.44 (± 8.43)		
week 2	46.35 (± 22.08)	39.44 (± 22.72)		
week 4	37.19 (± 22.59)	37.67 (± 14.39)		
week 6	32.86 (± 22.94)	24.89 (± 18.45)		
week 8	25.50 (± 16.59)	22.44 (± 15.53)		
week 10	29.08 (± 22.58)	22.11 (± 16.99)		
week 12	31.64 (± 23.95)	21.22 (± 17.40)		
FU1	31.38 (± 22.36)	19.44 (± 19.02)		
FU3	29.87 (± 19.89)	23.44 (± 21.41)		

Notes:

[3] - n=16 at week 4 and FU1
n=15 at FU3
n=14 at week 6 and week 12
n=12 at week and week 10

Statistical analyses

No statistical analyses for this end point

Secondary: JIA Outcome Core Set Variables - Number of joints with active arthritis

End point title	JIA Outcome Core Set Variables - Number of joints with active arthritis

End point description:

Number of active joints is from 0 to 75.

End point type	Secondary

End point timeframe:

At pretreatment visit, at weeks 2, 4, 6, 8, 10 and 12 (End of treatment), 1 month and 3 months follow up (FU1, FU3) in the PP and ITT populations respectively.

End point values	ITF2357 - ITT population	ITF2357 - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17[4]	9		
Units: number				
arithmetic mean (standard deviation)				
pre-treatment	9.82 (± 9.11)	9.33 (± 8.70)		
week 2	8.41 (± 9.49)	7.11 (± 8.62)		
week 4	6.38 (± 9.26)	3.78 (± 5.47)		
week 6	3.57 (± 4.33)	3.44 (± 5.29)		

week 8	3.42 (± 4.29)	3.67 (± 4.85)		
week 10	2.75 (± 4.03)	2.89 (± 4.54)		
week 12	4.86 (± 4.74)	3.44 (± 4.59)		
FU1	3.88 (± 4.49)	3.00 (± 4.50)		
FU3	5.00 (± 6.05)	3.33 (± 4.58)		

Notes:

[4] - n=16 at week 4 and FU1
n=15 at FU3
n=14 at week 6 and week 12
n=12 at week and week 10

Statistical analyses

No statistical analyses for this end point

Secondary: JIA Outcome Core Set Variables - Number of joints with limitation

End point title	JIA Outcome Core Set Variables - Number of joints with limitation

End point description:

Number of joints with limited range of motion is from 0 to 75.

End point type	Secondary

End point timeframe:

At pretreatment visit, at weeks 2, 4, 6, 8, 10 and 12 (End of treatment), 1 month and 3 months follow up (FU1, FU3) in the PP and ITT populations respectively.

End point values	ITF2357 - ITT population	ITF2357 - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17[5]	9		
Units: number				
arithmetic mean (standard deviation)				
pre-treatment	11.59 (± 14.00)	10.00 (± 9.53)		
week 2	10.41 (± 14.42)	8.56 (± 9.76)		
week 4	7.44 (± 11.56)	6.44 (± 7.20)		
week 6	7.86 (± 11.91)	5.78 (± 7.17)		
week 8	4.67 (± 6.08)	5.78 (± 6.63)		
week 10	4.42 (± 5.65)	5.22 (± 6.32)		
week 12	8.79 (± 12.27)	4.78 (± 5.65)		
FU1	7.94 (± 12.22)	5.00 (± 5.92)		
FU3	7.20 (± 8.79)	5.22 (± 5.70)		

Notes:

[5] - n=16 at week 4 and FU1
n=15 at FU3
n=14 at week 6 and week 12
n=12 at week and week 10

Statistical analyses

No statistical analyses for this end point

Secondary: JIA Outcome Core Set Variables - CHAQ

End point title	JIA Outcome Core Set Variables - CHAQ

End point description:

The Childhood Health Assessment Questionnaire (CHAQ) is from 0 to 3

End point type	Secondary

End point timeframe:

At pretreatment visit, at weeks 2, 4, 6, 8, 10 and 12 (End of treatment), 1 month and 3 months follow up (FU1, FU3) in the PP and ITT populations respectively.

End point values	ITF2357 - ITT population	ITF2357 - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17[6]	9[7]		
Units: score				
arithmetic mean (standard deviation)				
pre-treatment	1.75 (± 0.74)	1.55 (± 0.54)		
week 2	1.39 (± 0.87)	1.13 (± 0.57)		
week 4	1.23 (± 0.88)	0.93 (± 0.55)		
week 6	1.02 (± 0.82)	0.75 (± 0.56)		
week 8	0.85 (± 0.82)	0.58 (± 0.50)		
week 10	0.85 (± 0.87)	0.55 (± 0.50)		
week 12	0.95 (± 0.82)	0.58 (± 0.41)		
FU1	1.02 (± 0.93)	0.56 (± 0.39)		
FU3	0.85 (± 0.78)	0.58 (± 0.51)		

Notes:

[6] - n=16 at week 4 and FU1
n=14 at week 6, week 12 and FU3
n=12 at week 8 and week 10
[7] - n=8 at FU3

Statistical analyses

No statistical analyses for this end point

Secondary: JIA Outcome Core Set Variables - ESR

End point title	JIA Outcome Core Set Variables - ESR

End point description:

Measurements of erythrocyte sedimentation rate (ESR) were performed at the local laboratory cooperating with each study site.

End point type	Secondary

End point timeframe:

At pretreatment visit, at weeks 2, 4, 6, 8, 10 and 12 (End of treatment), 1 month and 3 months follow up (FU1, FU3) in the PP and ITT populations respectively.

End point values	ITF2357 - ITT population	ITF2357 - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17[8]	9[9]		
Units: mm/h				
arithmetic mean (standard deviation)				
pre-treatment	62.71 (± 31.76)	65.22 (± 23.05)		
week 2	59.12 (± 30.90)	53.44 (± 26.54)		
week 4	59.50 (± 34.71)	52.67 (± 22.66)		
week 6	53.90 (± 22.35)	57.67 (± 20.66)		
week 8	49.92 (± 31.20)	49.33 (± 33.78)		
week 10	59.25 (± 23.35)	58.33 (± 23.40)		
week 12	54.14 (± 37.07)	56.44 (± 40.76)		
FU1	46.31 (± 28.30)	39.89 (± 28.32)		
FU3	41.00 (± 25.02)	44.57 (± 25.00)		

Notes:

[8] - n=16 at week 4 and FU1
n=14 at week 12
n=13 at FU3
n=12 at week 8
n=10 at week 6
n=8 at week 10
[9] - n=7 at FU3
n=6 at week 6 and week 10

Statistical analyses

No statistical analyses for this end point

Secondary: Overall SFS results - Sum of first five variables and sum of last five variables

End point title	Overall SFS results - Sum of first five variables and sum of last five variables

End point description:

Modified Systemic Feature Score (SFS) variables included:
- temperature, rash, lymph nodes, liver and spleen size, and clinical evidence of serositis (clinical variables)
- ESR, CRP, leukocyte count, haemoglobin, thrombocyte count (laboratory variables).

Items in both sets of variables were scored as present (1) or not present (0) based on predefined criteria, described in the attached chart.
SFS data were presented as the sum of the first 5 items and the sum of the last 5 items. Each sum could range from a minimum of 0 to a maximum of 5.

End point type	Secondary

End point timeframe:

At pretreatment visit, at weeks 2, 4, 6, 8, 10 and 12 (End of treatment), 1 month and 3 months follow up (FU1, FU3) in the PP and ITT populations respectively.

End point values	ITF2357 - ITT population	ITF2357 - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17[10]	9		
Units: score				
arithmetic mean (standard deviation)				
sum of clinical variables - pre-treatment	0.94 (± 0.75)	1.33 (± 0.71)		
sum of clinical variables - week 2	0.35 (± 0.61)	0.44 (± 0.73)		
sum of clinical variables - week 4	0.31 (± 0.48)	0.11 (± 0.33)		
sum of clinical variables - week 6	0.14 (± 0.36)	0.11 (± 0.33)		
sum of clinical variables - week 8	0.17 (± 0.39)	0.11 (± 0.33)		
sum of clinical variables - week 10	0.33 (± 0.65)	0.11 (± 0.33)		
sum of clinical variables - week 12	0.29 (± 0.47)	0.22 (± 0.44)		
sum of clinical variables - FU1	0.20 (± 0.41)	0.22 (± 0.44)		
sum of laboratory variables - pre-treatment	4.24 (± 1.15)	4.33 (± 1.00)		
sum of laboratory variables - week 2	2.65 (± 1.17)	2.44 (± 1.42)		
sum of laboratory variables - week 4	2.25 (± 1.18)	2.11 (± 0.93)		
sum of laboratory variables - week 6	1.93 (± 1.21)	1.56 (± 1.33)		
sum of laboratory variables - week 8	1.92 (± 1.44)	2.00 (± 1.66)		
sum of laboratory variables - week 10	2.08 (± 1.38)	2.00 (± 1.58)		
sum of laboratory variables - week 12	2.07 (± 1.27)	1.89 (± 1.45)		
sum of laboratory variables - FU1	2.56 (± 1.67)	2.22 (± 1.92)		

Notes:

[10] - n=16 at wk 4 (clin) & FU1 (lab)
n=14 at wk 6 & wk 12
n=12 at wk 8 & wk 10
n=15 at FU1 (clin)

Attachments (see zip file)	Overall SFS_PP and ITT populations/Overall SFS_PP and ITT Description/Description of criteria for SFS results.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: N. and % of pts with presence or absence of each item for SFS

End point title	N. and % of pts with presence or absence of each item for SFS

End point description:

Description of criteria for SFS results is attached.

End point type	Secondary

End point timeframe:

At pretreatment visit, at weeks 4, 8, 12 (End of treatment) and 1 month follow up (FU1) in the ITT and PP respectively. See the two tables attached.

End point values	ITF2357 - ITT population	ITF2357 - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	9		
Units: number and % of patients	0	0		

Attachments (see zip file)	ITT population/N. and % of pts with presence or absence of PP population/N. and % of pts with presence or absence of Description/Description of criteria for SFS results.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: N. and % of pts with sufficient therapeutic response at week 4 to continue treatment

End point title	N. and % of pts with sufficient therapeutic response at week 4 to continue treatment

End point description:

Therapeutic response at week 4 was considered sufficient by the Investigator if a decrease in Systemic Feature Score of 2 (at least one of the first five variables) and/or JIA30 response (or above: 50 or 70) was obtained.
Number of patients are reported here. For number and percentage of patients, see attached tables.

End point type	Secondary

End point timeframe:

At week 4.

End point values	ITF2357 - ITT population	ITF2357 - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	9		
Units: number of patients				
Therapeutic response	11	8		
Absence of therapeutic response	6	1		

Attachments (see zip file)	ITT population/N. and % of pts with sufficient therapeutic PP population/N. and % of pts with sufficient therapeutic

Statistical analyses

No statistical analyses for this end point

Secondary: N. and % of pts with JIA plus SFS clinical improvement

End point title	N. and % of pts with JIA plus SFS clinical improvement

End point description:

Clinical improvement at week 2, 4, 6, 8, 10 and 12 was evaluated on the basis of JIA30, JIA50 and JIA70 plus SFS (two points decrease in SFS) as per protocol.
Patients were considered as improved and with positive therapeutic response if 3 or more JIA Core Set Variables improved by 30% and no more than one worsened by 30%. JIA50 and JIA70 were defined as an improvement of 3 or more JIA Core Set Variables by 50% and 70%, respectively, and no more than 1 worsened by 30%. Additionally two points decrease in Systemic Feature Score were considered as disease improvement.
Number of patients at week 12 are reported here. For number and percentage of patients at all timepoints, see attached tables.

End point type	Secondary

End point timeframe:

At weeks 2, 4, 6, 8, 10 and 12.

End point values	ITF2357 - ITT population	ITF2357 - PP population		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	9		
Units: number of patients				
JIA30 plus SFS - Clinical improvement	10	8		
JIA30 plus SFS - Absence of clinical improvement	7	1		
JIA50 plus SFS - Clinical improvement	9	8		
JIA50 plus SFS - Absence of clinical improvement	8	1		
JIA70 plus SFS - Clinical improvement	9	8		
JIA70 plus SFS - Absence of clinical improvement	8	1		

Attachments (see zip file)	ITT population/N. and % of pts with JIA plus SFS clinical PP population/N. and % of pts with JIA plus SFS clinical

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
At weeks 1, 2, 4, 6, 8, 10, 12 (end of treatment) and FU1 and FU3	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups	
Reporting group title	IT2357 - safety population
Reporting group description:	
Safety population: all recruited patients who received at least one dose of the study medication.	

Serious adverse events	IT2357 - safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 17 (11.76%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Varicella			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	IT2357 - safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 17 (82.35%)		
Investigations			

Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Injury, poisoning and procedural complications Injury subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1 1 / 17 (5.88%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Enteritis subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1 1 / 17 (5.88%) 1 1 / 17 (5.88%) 6 1 / 17 (5.88%) 3		
Respiratory, thoracic and mediastinal disorders Atelectasis subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1 3 / 17 (17.65%) 3		
Skin and subcutaneous tissue disorders			

Dermatitis contact subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 1 / 17 (5.88%) 1 2 / 17 (11.76%) 3		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	 1 / 17 (5.88%) 1		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all) Nephrolithiasis subjects affected / exposed occurrences (all)	 1 / 17 (5.88%) 1 1 / 17 (5.88%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Arthritis subjects affected / exposed occurrences (all) Joint swelling subjects affected / exposed occurrences (all)	 1 / 17 (5.88%) 1 3 / 17 (17.65%) 3 1 / 17 (5.88%) 3		
Infections and infestations Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Otitis media	 2 / 17 (11.76%) 2 1 / 17 (5.88%) 1		

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Otitis media acute			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 April 2007	Reason for the amendment was that some protocol changes were necessary following the occurrence of two SUSARs during treatment with ITF2357 in patients affected by onco haematological malignancies. The two SUSARs were: - A fatal liver failure - QTc prolongation (QTc > 500 msec) with concomitant sinus bradycardia, low serum K and Mg. The following protocol changes were introduced: more restrictive inclusion/exclusion criteria related to virological aspects, excluding patients with on-going clinically relevant viral infections or with risk of developing severe viral infections treatment discontinuation in case of occurrence of severe viral or bacterial infections more restrictive inclusion/exclusion criteria related to cardiovascular aspects, excluding patients with additional risk factors for Torsade de Pointes and excluding use of concomitant medications with potential risk of Torsade de Pointes calculation of QTc interval as for Bazett's formula at each ECG recording and measurements of serum concentration of Mg and K treatment discontinuation in case of QTc prolongation and/or serum levels of Mg and K falling below the Lower Limit of Normal Laboratory Ranges during the treatment with ITF2357. In addition the following inclusion criteria were modified: basal Hb below 11 mg/dL and previous treatment with methotrexate not required any longer as inclusion criteria check for sufficient therapeutic response restricted to week 4 and 8, based on either SFS reduction of 2 points and/or JIA30 achievement calculation of items 5 to 10 of the SFS to be done in comparison vs. pre-treatment values instead of values measured in the previous visit.

Notes:

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.

No limitations or caveats are applicable to this summary of results.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/21538322