Clinical trial results:
PHASE II STUDY OF EVEROLIMUS IN PATIENTS WITH THYMOMA AND THYMIC CARCINOMA PREVIOUSLY TREATED WITH CHEMOTHERAPY

Summary

EudraCT number	2010-019683-37
Trial protocol	IT
Global end of trial date	05 May 2019

Results information

Result version number	v1 (current)
This version publication date	05 January 2020
First version publication date	05 January 2020

Trial information

Trial identification

Sponsor protocol code	ONC-2010-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ISTITUTO CLINICO HUMANITAS
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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	27 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 May 2019
Global end of trial reached?	Yes
Global end of trial date	05 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the activity of Everolimus in patients with advanced or recurrent thymoma or thymic carcinoma by the determination of disease control rate (DCR), considered as complete response (CR) plus partial response (PR) plus stable disease (SD).

Protection of trial subjects:

Therapies considered necessary for patients' well being were given at the discretion of the Investigator, i.e chronic treatment for concomitant medical conditions, as well as agents required for life-threatening medical problems.

Background therapy: -

Evidence for comparator:

Not Applicable

Actual start date of recruitment	17 February 2011
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	Italy: 51
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	43
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with pathologically confirmed, advanced (ie, unresectable or metastatic) thymoma (T) or thymic carcinoma (TC) were eligible after failure of at least one previous line of platinum-based chemotherapy. 51 patients were enrolled between 17 February 2011 and 21 October 2013. One patient decided to leave the study before starting the treatment.

Period 1

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

Arms

Arm title	Arm 1

Arm description:

All patients treated with everolimus 10 mg once daily.

Arm type	Experimental
Investigational medicinal product name	Everolimus
Investigational medicinal product code	RAD001
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Everolimus was orally administered at the dosage of 10 mg once daily. Each cycle was considered as 21 days of treatment.

Number of subjects in period 1[1]	Arm 1
Started	50
Completed	20
Not completed	30
Adverse event, serious fatal	7
Consent withdrawn by subject	2
Physician decision	1
Adverse event, non-fatal	11
Not reported	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: A total of 51 patients were initially enrolled but one patient decided to leave the study before starting the treatment. Then 50 patients were treated and considered in the analysis.

Baseline characteristics

Reporting groups	
Reporting group title	Arm 1
Reporting group description:	
All patients treated with everolimus 10 mg once daily.	

Reporting group values	Arm 1	Total	
Number of subjects	50	50	
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)	0	0	
Adults (18-64 years)	42	42	
From 65-84 years	8	8	
85 years and over	0	0	
Age continuous Units: years			
median	55		
full range (min-max)	36 to 80	-	
Gender categorical Units: Subjects			
Female	22	22	
Male	28	28	
ECOG PS Units: Subjects			
0-1	50	50	
=2	0	0	
Myastenia gravis Units: Subjects			
Yes	10	10	
No	40	40	
Histologic type Units: Subjects			
Thymoma	32	32	
Thymic carcinoma	18	18	
Stage of disease Units: Subjects			
Recurrent	9	9	
Metastatic	41	41	
No. of previous treatment lines Units: Subjects			
< or =2	33	33	

> or = 3	17	17	
Type of previous line before everolimus Units: Subjects			
Platinum-based chemotherapy	34	34	
Other chemotherapy	10	10	
Target therapy	6	6	
Best response to previous line before everolimus Units: Subjects			
CR (complete response)	2	2	
PR (partial response)	10	10	
SD (stable disease)	17	17	
PD (progressive disease)	11	11	
UK (unknown)	10	10	

End points

End points reporting groups

Reporting group title	Arm 1
Reporting group description:	
All patients treated with everolimus 10 mg once daily.	
Subject analysis set title	All patient treated with everolimus 10 mg once daily
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patient treated with everolimus 10 mg once daily	
Subject analysis set title	Responder patients
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients that showed completed or partial tumor response.	
Subject analysis set title	p4E-BP1 low intensity
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients with low intratumoral expression levels of 4E-BP1 (translational regulator eukaryotic factor).	
Subject analysis set title	p4E-BP1 high intensity
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patiients with high intratumoral expression levels of 4E-BP1 (translational regulator eukaryotic factor).	
Subject analysis set title	IGF-1R low intensity
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients with low intratumoral expression levels of IGF-1R (insulin-like growth farctor receptor).	
Subject analysis set title	IGF-1R high intensity
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patiients with high intratumoral expression levels of IGF-1R (insulin-like growth farctor receptor).	

Primary: Disease control rate (DCR)

End point title	Disease control rate (DCR)[1]
End point description:	
Disease control rate was considered as proportion of patients who achieved complete response (CR) plus partial response (PR) plus stable disease (SD) according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.	
End point type	Primary
End point timeframe:	
During the entire study	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A Disease Control Rate (CR, PR or SD) ≤40% was considered clinically irrelevant whereas a proportion ≥ 60% was assumed to be of potential interest. Exact binomial 95% confidence intervals were calculated.

End point values	All patient treated with everolimus 10 mg once daily			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: percent				
number (confidence interval 95%)	88 (75.7 to 95.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: median Progression Free Survival (mPFS)

End point title	median Progression Free Survival (mPFS)

End point description:

PSF is calculated as the time from start of treatment until disease progression or death from any cause. Patients alive without any evidence of progressive disease were censored on the date of the last visit.

End point type	Secondary

End point timeframe:

Time from start of treatment until disease progression or death, whichever comes first.

End point values	All patient treated with everolimus 10 mg once daily			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: Months				
median (confidence interval 95%)	10.1 (6.0 to 14.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) 1 year

End point title	Overall Survival (OS) 1 year

End point description:

OS was was evaluated from the date of treatment start until the date of death from any cause. Patients alive were censored at last contact date. It is here reported the 1 year OS rate (95% CI) .

End point type	Secondary

End point timeframe:

From the start of treatment until death.

End point values	All patient treated with everolimus 10 mg once daily			
Subject group type	Subject analysis set			
Number of subjects analysed	50			
Units: percent				
number (confidence interval 95%)	72 (57.4 to 82.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response

End point description:

Duration of response is the length of time that a tumor continues to respond to treatment without the cancer growing or spreading. Data are reported as median and range.

End point type	Secondary

End point timeframe:

From the first treatment to disease progression.

End point values	Responder patients			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: months				
median (full range (min-max))	7.1 (1.2 to 25.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Relationship between p4E-BP1 tumor biomarker intensity and Progression Free Survival rate at 1 year

End point title	Relationship between p4E-BP1 tumor biomarker intensity and Progression Free Survival rate at 1 year

End point description:

The percentage of patients progression free survival at 1 year from tretment start by biomarker expression.

End point type	Secondary

End point timeframe:

From the start of treatment to 1 year from the first treatment.

End point values	p4E-BP1 low intensity	p4E-BP1 high intensity		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	6		
Units: percent				
number (not applicable)				
p4E-BP1	72.3	16.7		

Statistical analyses

Statistical analysis title	Survival curve comparison

Statistical analysis description:

Survival based on biomarker distribution: 4E-BP1 (translational regulator eukaryotic factor)

Comparison groups	p4E-BP1 high intensity v p4E-BP1 low intensity
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.09
Method	Logrank

Notes:

[2] - Log-rank test

Secondary: Relationship between IGF-1R tumor biomarker intensity and Progression Free Survival rate at 1 year

End point title	Relationship between IGF-1R tumor biomarker intensity and Progression Free Survival rate at 1 year

End point description:

The percentage of patients progression free survival at 1 year from tretment start by biomarker expression.

End point type	Secondary

End point timeframe:

From the start of treatment to 1 year from the first treatment.

End point values	IGF-1R low intensity	IGF-1R high intensity		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	7		
Units: percent				
number (not applicable)				
IGF-1R	66.3	35.7		

Statistical analyses

Statistical analysis title	Survival Curve Comparison
Statistical analysis description: Survival based on biomarker distribution: IGF-1R (insulin-like growth factor receptor)	
Comparison groups	IGF-1R low intensity v IGF-1R high intensity
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.241
Method	Logrank

Secondary: Relationship between p4E-BP1 tumor biomarker intensity and Overal Survival rate at 2 years

End point title	Relationship between p4E-BP1 tumor biomarker intensity and Overal Survival rate at 2 years
End point description: The percentage of overall survival at 2 years from tretment start by biomarker expression.	
End point type	Secondary
End point timeframe: From the start of treatment to 2 years from the first treatment.	

End point values	p4E-BP1 low intensity	p4E-BP1 high intensity		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	20	6		
Units: percent				
number (not applicable)				
p4E-BP1	94.7	33.3		

Statistical analyses

Statistical analysis title	Survival Curve Comparison
Statistical analysis description: Survival based on biomarker distribution: 4E-BP1 (translational regulator eukaryotic factor).	
Comparison groups	p4E-BP1 low intensity v p4E-BP1 high intensity

Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank

Secondary: Relationship between IGF-1R tumor biomarker intensity and Overall Survival rate at 2 years

End point title	Relationship between IGF-1R tumor biomarker intensity and Overall Survival rate at 2 years

End point description:

Relationship between IGF-1R tumor biomarker intensity and Overall Survival rate at 2 years.

End point type	Secondary

End point timeframe:

From the start of treatment to 2 years from the first treatment.

End point values	IGF-1R low intensity	IGF-1R high intensity		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	17	7		
Units: percent				
number (not applicable)				
IGF-1R	84.4	57.1		

Statistical analyses

Statistical analysis title	Survival Curve Comparison

Statistical analysis description:

Survival based on biomarker distribution: IGF-1R (insulin-like growth factor receptor).

Comparison groups	IGF-1R low intensity v IGF-1R high intensity
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	Logrank

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the Informed Consent signature to 30 days after the last dose of treatment, or until every ongoing drug-related toxicities and serious AEs had resolved or the investigator assessed them as "chronic" or "stable" or patient started a new therapy.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	All patient treated

Reporting group description: -

Serious adverse events	All patient treated		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 50 (38.00%)		
number of deaths (all causes)	24		
number of deaths resulting from adverse events	10		
Investigations			
Blood calcium decreased			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Haemoglobin decreased			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oxygen saturation decreased			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 2		
Neoplasms benign, malignant and			

unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Fatigue			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oedema			

subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Oedema peripheral			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 2		

Pneumonitis				
subjects affected / exposed	2 / 50 (4.00%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 2			
Pulmonary embolism				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory acidosis				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory failure				
subjects affected / exposed	4 / 50 (8.00%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 4			
Infections and infestations				
Appendicitis				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 2			
Lung infection				
subjects affected / exposed	1 / 50 (2.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 50 (4.00%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	2 / 3			
Pneumonia influenzal				

subjects affected / exposed	2 / 50 (4.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Anorexia nervosa			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	All patient treated		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 50 (96.00%)		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	27 / 50 (54.00%)		
occurrences (all)	53		
Chest pain			
subjects affected / exposed	7 / 50 (14.00%)		
occurrences (all)	11		
Chills			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	6 / 50 (12.00%)		
occurrences (all)	8		
Mucosal inflammation			
subjects affected / exposed	23 / 50 (46.00%)		
occurrences (all)	51		
Oedema peripheral			
subjects affected / exposed	9 / 50 (18.00%)		
occurrences (all)	10		
Pyrexia			

subjects affected / exposed	18 / 50 (36.00%)		
occurrences (all)	51		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	16 / 50 (32.00%)		
occurrences (all)	35		
Dyspnoea			
subjects affected / exposed	16 / 50 (32.00%)		
occurrences (all)	22		
Epistaxis			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Pneumonitis			
subjects affected / exposed	8 / 50 (16.00%)		
occurrences (all)	11		
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	4		
Investigations			
Blood cholesterol increased			
subjects affected / exposed	8 / 50 (16.00%)		
occurrences (all)	9		
Blood glucose increased			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	9		
Blood triglycerides increased			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	7		
Gamma-glutamyltransferase increased			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	8		
Haemoglobin decreased			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	9		
Neutrophil count decreased			

subjects affected / exposed occurrences (all) Platelet count decreased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 10 4 / 50 (8.00%) 10 2 / 50 (4.00%) 2		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	2 / 50 (4.00%) 4		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	2 / 50 (4.00%) 2 7 / 50 (14.00%) 9 6 / 50 (12.00%) 23		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 4		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea	4 / 50 (8.00%) 7 8 / 50 (16.00%) 10 6 / 50 (12.00%) 7		

subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Haemorrhoids subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Stomatitis subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	14 / 50 (28.00%) 32 2 / 50 (4.00%) 4 4 / 50 (8.00%) 4 7 / 50 (14.00%) 10 17 / 50 (34.00%) 36 3 / 50 (6.00%) 3		
Skin and subcutaneous tissue disorders Nail disorder subjects affected / exposed occurrences (all) Palmar-plantar erythrodysaesthesia syndrome subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 2 / 50 (4.00%) 2 2 / 50 (4.00%) 2 4 / 50 (8.00%) 6 16 / 50 (32.00%) 21		
Renal and urinary disorders Polyuria subjects affected / exposed occurrences (all)	 2 / 50 (4.00%) 3		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	5 / 50 (10.00%)		
occurrences (all)	7		
Muscle spasms			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	4		
Musculoskeletal pain			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Myalgia			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	5 / 50 (10.00%)		
occurrences (all)	5		
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 50 (10.00%)		
occurrences (all)	6		
Cystitis			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	4		
Folliculitis			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	8 / 50 (16.00%)		
occurrences (all)	13		
Localised infection			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	4		
Nail infection			

subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	7		
Onychomycosis			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Oral herpes			
subjects affected / exposed	5 / 50 (10.00%)		
occurrences (all)	17		
Paronychia			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Pharyngitis			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Pneumonia			
subjects affected / exposed	5 / 50 (10.00%)		
occurrences (all)	6		
Rhinitis			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	4		
Tooth abscess			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Anorexia nervosa			
subjects affected / exposed	10 / 50 (20.00%)		
occurrences (all)	12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29240542