Clinical trial results:
Efficacy of medical treatment with SOM230 LAR in patients with primary inoperable thymoma and/or with local recurrent thymoma to reduce tumor size

Summary

EudraCT number	2010-019017-25
Trial protocol	DE
Global end of trial date	30 October 2015

Results information

Result version number	v1 (current)
This version publication date	10 March 2017
First version publication date	10 March 2017
Summary attachment (see zip file)	CSOM230CIC01T_CSR synopsis (2_CSOM230CIC01T_CSR synopsis_20161024.pdf)

Trial information

Trial identification

Sponsor protocol code	CSOM230CIC01T

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02021942
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Freistaat Bayern, represented by Universitaet Regensburg
Sponsor organisation address	Universitaetsstrasse 84, Regensburg, Germany, 93053
Public contact	Prof. Dr. Berthold Schalke, Klinik und Poliklinik fuer Neurologie der Universitaet Regensburg, 49 9419413010, berthold.schalke@medbo.de
Scientific contact	Prof. Dr. Berthold Schalke, Klinik und Poliklinik fuer Neurologie der Universitaet Regensburg, 49 9419413010, berthold.schalke@medbo.de

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	24 October 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 October 2015
Global end of trial reached?	Yes
Global end of trial date	30 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Tumor shrinkage from baseline to EOS

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial. Before implementing this study, the protocol, the proposed informed consent form and other information to subjects, were reviewed by a properly constituted Independent Ethics Committee.
The occurrence of adverse events was sought by non-directive questioning of the patient at each visit during the study. Adverse events also may have been detected when they were volunteered by the patient during or between visits or through physical examination, laboratory tests, or other assessments. Adverse event monitoring had to be continued for 4 weeks following the last dose of study drug.
SAEs were monitored continuously.

Background therapy:

Prednisolone may be have been added to the therapeutic regime according to the investigator's decision after the 8 week control examination if the therapeutic response was not adequate. Prednisolone had to be taken from the investigator’s stock.

Evidence for comparator:

-

Actual start date of recruitment	09 March 2012
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	Germany: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	13
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This monocentric trial was conducted in Regensburg, Germany. The patients were asked for study participation by the investigator.
Recruitment started March 2012 and ended July 2014. The study runtime was extended by one year due to delayed patient recruitment.

Pre-assignment

Screening details:

The study population consisted of 16 adult patients with inoperable thymoma. All patients screened have been enrolled.
For one patient initial diagnosis of thymoma could not be confirmed, but a squamous cell carcinoma was diagnosed later by the central pathologist.

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

Arm title	SOM230 LAR

Arm description:

SOM230 LAR in a dosage of 60 mg i.m. once every 4 weeks

Arm type	Experimental
Investigational medicinal product name	Pasireotide
Investigational medicinal product code	SOM230 LAR
Other name	Signifor LAR
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

60 mg i.m. once every 4 weeks

Number of subjects in period 1	SOM230 LAR
Started	16
Completed	16

Baseline characteristics

Reporting groups

Reporting group title	Overall Study (overall period)

Reporting group description: -

Reporting group values	Overall Study (overall period)	Total	
Number of subjects	16	16	
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)	13	13	
From 65-84 years	3	3	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	52.6		
standard deviation	± 12.7	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	9	9	
WHO tumor classification			
The histological classification of thymomas was based on the WHO classification (Rosai, 1999; Travis et al., 2004).			
Units: Subjects			
AB	1	1	
B1	1	1	
B2	6	6	
B3	8	8	
Staging of thymoma			
Staging of thymoma was performed by modified Masaoka (1981) staging system as proposed by Shimosato and Mukai (1994/1997).			
Units: Subjects			
Stage I	0	0	
Stage II	0	0	
Stage III	1	1	
Stage IVa	15	15	
Stage IVb	0	0	
Type of tumor biopsy Units: Subjects			
Fine needle biopsy	5	5	
Open biopsy	5	5	

Previous surgery	6	6	

Subject analysis sets	
Subject analysis set title	FAS Screening
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS Screening comprises 16 patients out of 16 patients. None of the enrolled patients was rejected from the primary analysis (ITT population).

Subject analysis set title	FAS EOS
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS EOS comprises 16 patients out of 16 patients. None of the enrolled patients was rejected from the primary analysis (ITT population).

Reporting group values	FAS Screening	FAS EOS	
Number of subjects	16	16	
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	±	±	
Gender categorical Units: Subjects			
Female Male			
WHO tumor classification			
The histological classification of thymomas was based on the WHO classification (Rosai, 1999; Travis et al., 2004).			
Units: Subjects			
AB B1 B2 B3	1 1 6 8	1 1 6 8	
Staging of thymoma			
Staging of thymoma was performed by modified Masaoka (1981) staging system as proposed by Shimosato and Mukai (1994/1997).			
Units: Subjects			
Stage I	0	0	

Stage II	0	0	
Stage III	1	1	
Stage IVa	15	15	
Stage IVb	0	0	
Type of tumor biopsy Units: Subjects			
Fine needle biopsy	5	5	
Open biopsy	5	5	
Previous surgery	6	6	

End points

End points reporting groups

Reporting group title	SOM230 LAR
Reporting group description:	
SOM230 LAR in a dosage of 60 mg i.m. once every 4 weeks	
Subject analysis set title	FAS Screening
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS Screening comprises 16 patients out of 16 patients. None of the enrolled patients was rejected from the primary analysis (ITT population).	
Subject analysis set title	FAS EOS
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS EOS comprises 16 patients out of 16 patients. None of the enrolled patients was rejected from the primary analysis (ITT population).	

Primary: Evaluation of tumor shrinkage from screening to EOS

End point title	Evaluation of tumor shrinkage from screening to EOS
End point description:	
Tumor shrinkage was assessed by MRI. Primary endpoint was to prove a decrease in tumor volume of 20% at EOS as compared to baseline which is considered as response. For each patient at each visit only one lesion was observed. No multiple lesions were observed. EOS is defined as 4 weeks after patient fulfils criteria for operability of thymoma or after SOM230 LAR treatment discontinuation [either during 6-month treatment/observation period or FU, respectively].	
End point type	Primary
End point timeframe:	
Screening to EOS	

End point values	SOM230 LAR	FAS Screening	FAS EOS	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	16	16	16	
Units: percent volume/volume				
arithmetic mean (standard deviation)	-37.38 (± 44.1)	100 (± 0)	-37.38 (± 44.1)	

Statistical analyses

Statistical analysis title	Primary analysis
Statistical analysis description:	
A response rate of lower than 0.05 is considered not to warrant further investigation of a drug, whereas a response rate of at least 0.3 is considered to warrant further investigation. Accordingly, the following hypothesis will be tested: H0: P <= 0.050 versus H1: P >= 0.300. 16 patients were required to decide whether the response proportion, P, is less than or equal to 0.050 or greater than or equal to 0.300.	
Comparison groups	SOM230 LAR v FAS Screening v FAS EOS

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	≤ 0.05
Method	Fleming's "one-sample multiple testing

Notes:

[1] - As this was a proof of concept study it was designed according to Fleming's "one-sample multiple testing procedure for phase II clinical trials" (Fleming, 1989).

Secondary: Evaluation of Tumor Resection Status

End point title	Evaluation of Tumor Resection Status

End point description:

To evaluate the resection status based on the categories R0, R1 and ≥ R2 at EOS.

EOS is defined as 4 weeks after patient fulfils criteria for operability of thymoma or after SOM230 LAR treatment discontinuation [either during 6-month treatment/observation period or FU, respectively].

End point type	Secondary

End point timeframe:

EOS

End point values	SOM230 LAR			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Number of participants				
Surgery performed with resection status R0	6			
Surgery performed with resection status R1	4			
No surgery performed	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of tumor operability

End point title	Evaluation of tumor operability

End point description:

Evaluation of tumor operability as assessed by the treating surgeon. In addition the response criteria (see primary endpoint) had to be fulfilled.

End point type	Secondary

End point timeframe:

EOS

EOS is defined as 4 weeks after patient fulfils criteria for operability of thymoma or after SOM230 LAR treatment discontinuation [either during 6-month treatment/observation period or FU, respectively].

End point values	SOM230 LAR			
Subject group type	Reporting group			
Number of subjects analysed	16[2]			
Units: Number of participants				
Tumor assesed as operable	11			
Tumor assesed as not operable	5			

Notes:

[2] - The tumors of 11 patients were operable. One of these patients decided not to undergo surgery.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Safety: Number of Participants With Adverse Events (AE) and Serious Adverse Events (SAE)

End point title	Safety: Number of Participants With Adverse Events (AE) and Serious Adverse Events (SAE)

End point description:

End point type	Other pre-specified

End point timeframe:

Screening to EOS.

End point values	SOM230 LAR			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Number of Participants				
Number of participants with AEs	16			
Number of participants with SAEs	7			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Assessment of Myasthenia Gravis (MG) status by determining Titin-antibody status

End point title	Assessment of Myasthenia Gravis (MG) status by determining Titin-antibody status

End point description:

MG severity status is assessed by determining change of Titin-antibody status from Screening to EOS.

End point type	Other pre-specified

End point timeframe:

Screening until EOS.

End point values	SOM230 LAR			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Titin-antibody status				
Missing data at baseline or EOS	8			
Change from negative to negative	4			
Change from negative to positive	0			
Change from positive to positive	2			
Change from positive to negative	2			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Assessment of Myasthenia Gravis (MG) Status by Measuring ACHR-antibody Concentrations

End point title	Assessment of Myasthenia Gravis (MG) Status by Measuring ACHR-antibody Concentrations

End point description:

MG severity status is assessed by Change of ACHR-antibody concentrations at Baseline and EOS.

End point type	Other pre-specified

End point timeframe:

Baseline until EOS.

End point values	SOM230 LAR			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: ACHR-antibody concentration				
Missing data at baseline or EOS	8			
ACHR-antibody level increased	1			
ACHR-antibody level decreased	4			
ACHR-antibody level constant	3			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Health Related Quality of Life

End point title	Health Related Quality of Life

End point description:

Health related quality of life information was collected at Baseline and EOS using SF-36 questionnaire. Questionnaires had to be completed by the patients. Patient reported answers were transformed into domain scores according to the guidelines provided by RAND/MOS.
For statistical analysis only paired values were considered, i.e. patients for which both data from Baseline and EOS was available.

End point type	Other pre-specified

End point timeframe:

Baseline and EOS.

End point values	SOM230 LAR			
Subject group type	Reporting group			
Number of subjects analysed	11[3]			
Units: Score				
arithmetic mean (standard deviation)				
Physical function (SCR)	58.6 (± 28.9)			
Physical function (EOS)	49.1 (± 25.6)			
Role limitations due to physical health (SCR)	31.8 (± 38.9)			
Role limitations due to physical health (EOS)	34.1 (± 45.1)			
Pain (SCR)	57.3 (± 28.8)			
Pain (EOS)	52.3 (± 35.7)			
General health (SCR)	53.2 (± 12.9)			
General health (EOS)	47.1 (± 14.5)			
Energy/Fatigue (SCR)	43.6 (± 15.5)			
Energy/Fatigue (EOS)	39.2 (± 21.3)			
Social functioning (SCR)	61.4 (± 27.6)			
Social functioning (EOS)	60.2 (± 30.5)			
Role limitations due to emotional problems (SCR)	63.6 (± 45.8)			
Role limitations due to emotional problems (EOS)	60.6 (± 44.3)			
Emotional well-being (SCR)	60.4 (± 18.7)			
Emotional well-being (EOS)	56.6 (± 20.9)			
Change in health (general) (SCR)	38.6 (± 20.5)			
Change in health (general) (EOS)	50 (± 15.8)			

Notes:

[3] - 5 out of 16 patients were excluded from Analysis due to missing EOS data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to EOS.

Adverse event reporting additional description:

An adverse event (AE) is the appearance or worsening of any undesirable sign, symptom, or medical condition occurring after starting the study drug even if the event is not considered to be related to study drug. Medical conditions/diseases present before starting study drug are only considered AE if they worsen after starting study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	SOM230 LAR

Reporting group description:

SOM230 LAR in a dosage of 60 mg i.m. once every 4 weeks

Serious adverse events	SOM230 LAR		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 16 (43.75%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastasis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumor pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Embolism venous			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Venous thrombosis limb			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	SOM230 LAR		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

Oedema peripheral subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Peripheral swelling subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Pyrexia subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Immune system disorders Immunodeficiency subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Dyspnoea subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Epistaxis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 2		
Haemoptysis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Laryngeal inflammation subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Investigations Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Gamma-glutamyltransferase increased			

subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Glycosylated haemoglobin increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Troponin increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Muscle strain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Eye disorders			

Cataract			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	4		
Abdominal pain upper			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Abnormal faeces			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	10 / 16 (62.50%)		
occurrences (all)	12		
Flatulence			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Haemorrhoids			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Oral dysaesthesia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Erythema			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Skin hyperpigmentation			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Renal and urinary disorders			
Glycosuria			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Endocrine disorders			
Cushing's syndrome			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Intervertebral disc protrusion			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Muscle spasms			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Neck pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Infections and infestations			
Bacterial infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		

Cystitis subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2		
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2		
Oral candidiasis subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Oral herpes subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Penile infection subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Skin infection subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2		
Vaginal infection subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Metabolism and nutrition disorders Diabetes mellitus subjects affected / exposed occurrences (all)	2 / 16 (12.50%) 2		
Gout subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Hyperglycaemia subjects affected / exposed occurrences (all)	4 / 16 (25.00%) 12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 September 2012	The protocol was amended once during the study. The main purpose of the amendment was to update the safety information for patients after new data about SOM230 were available (safety update only). The study protocol was amended to implement urgent safety communication from the pharmaceutical manufacturer of the study drug (Novartis Pharma). It was observed in other SOM230-studies that healthy subjects treated with SOM230 fulfilled criteria for Hy's Law (i.e., that patients treated with a specific drug suffer from certain abnormities of liver enzymes, resulting in a higher risk of hepatotoxicity). Thus, Hy's Law should be considered as prognostic indicator for a pure drug-induced liver injury. In addition, the sponsor's procedures and responsibilities of safety monitoring were described in more detail.

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.

Eval. of 3 intended secondary efficacy parameters was suspended due to scarcity of resources: Histopath. eval. of tumor samples, immunohistochem. eval. of tumor derived cells and eval. of changes in the subset composition of intratumorous T-cells

Notes: