Clinical trial results:
Estudio de fase II de la combinación de panitumumab con paclitaxel como tratamiento de primera línea de sujetos con cáncer de cabeza y cuello recurrente o metastásico. Estudio “VECTITAX”.

Summary

EudraCT number	2010-018898-37
Trial protocol	ES
Global end of trial date	23 September 2014
Results information	
Result version number	v1 (current)
This version publication date	08 February 2020
First version publication date	08 February 2020

Trial information

Trial identification	
Sponsor protocol code	TTCC-2009-03
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01264328
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	TTCC Grupo Español de Tratamiento de Tumores de Cabeza y Cuello
Sponsor organisation address	C/ Velázquez, 7 – 3º , Madrid, Spain, 28001
Public contact	General Manager, Carmen Montalbán, +34 676 154 172, ttccmanager@yahoo.com
Scientific contact	Dr Ricard Mesia Nin is the scientific contact point, Ricard Mesia Nin, +34 618 179 500,

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	02 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 September 2014
Global end of trial reached?	Yes
Global end of trial date	23 September 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of the combination of panitumumab and paclitaxel on objective response rate in first-line treatment of metastatic or recurrent squamous cell carcinoma of head and neck (SCCHN).

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki (Seoul 2008 version) and the local laws and regulations. The study was approved by the Institutional Review Board of the participant centers. All patients gave written informed consent. Patients could completely or partially withdraw study at any time for any reason without any disadvantage or prejudice.

The infusion was stopped in patients who experienced any serious reaction during the administration of panitumumab. Patients who experienced toxicities and needed to permanently discontinue the administration of panitumumab were withdrawn of treatment but continued a safety and survival follow-up.

Background therapy:

Not applicable.

Evidence for comparator:

Panitumumab, a fully human IgG2 anti-EGFR monoclonal antibody, has shown activity in preclinical models of SCCHN and promising activity in refractory SCCHN patients in a phase I clinical trial. Recently, our cooperative group also reported encouraging outcomes of anti-EGFR-paclitaxel combination in a phase II study. On the basis of this background, a phase II clinical trial (VECTITAX study) was designed with the objective of evaluating the activity and safety profile of panitumumab in combination with paclitaxel in patients with recurrent or metastatic SCCHN.

Actual start date of recruitment	09 March 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	29
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between March 2011 and May 2012, 40 patients were included in 12 centers in Spain (ITT population). One patient met two exclusion criteria (second active neoplasm and B-Hepatitis) and four lacked post-baseline response assessment. Therefore, the PP population comprised 35 patients.

Pre-assignment

Screening details:

Key inclusion criteria: adult patients with histologically/cytologically confirmed recurrent or metastatic SCCHN; ECOG performance status of 0–1; measurable disease according to RECIST 1.1 criteria; adequate hematologic, renal, hepatic and metabolic functions. Prior treatment with anti-EGFR agents was not allowed within 24 weeks prior to study.

Period 1

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

Blinding implementation details:

Not applicable.

Arms

Arm title	Panitumumab + paclitaxel

Arm description:

Patients received paclitaxel (80 mg/m2/week) and panitumumab (6 mg/kg/2 weeks) until disease progression or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	Panitumumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Panitumumab 6 mg/kg was administered every 2 weeks, in one hour the first day and in 30 min thereafter (if no infusional reaction was observed).

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 80 mg/m2 was weekly administered one hour after panitumumab in one hour infusion.

Number of subjects in period 1	Panitumumab + paclitaxel
Started	40
Completed	40

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	40	40	
Age categorical Units: Subjects			
Adults (18-64 years)	29	29	
From 65-84 years	11	11	
Age continuous Units: years			
median	60.8		
inter-quartile range (Q1-Q3)	56.3 to 68.3	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	35	35	
ECOG-PS			
Eastern Cooperative Oncology Group (ECOG) performance status (PS)			
Units: Subjects			
ECOG-PS = 0	9	9	
ECOG-PS = 1	31	31	
Tumor site			
Primary tumor location			
Units: Subjects			
Larynx	14	14	
Oropharynx	12	12	
Oral cavity	10	10	
Hypopharynx	4	4	
Squamous cell carcinoma			
Grade of squamous cell carcinoma at diagnosis			
Units: Subjects			
Grade I	7	7	
Grade II	13	13	
Grade III	9	9	
Unknown	10	10	
Undifferentiated	1	1	
Laterality			
Tumor laterality at diagnosis			
Units: Subjects			
Left	10	10	
Right	25	25	
Both	3	3	
Undetermined	2	2	
Prior treatment: surgery			
Number of prior surgeries per patient			

Units: Subjects			
0 (no surgery)	11	11	
1 surgery	17	17	
2 surgeries	6	6	
3 surgeries	5	5	
4 surgeries	1	1	
Prior treatment: chemotherapy			
Number of chemotherapies per patient			
Units: Subjects			
0 (no chemotherapy)	17	17	
1 chemotherapy	9	9	
2 or more chemotherapies	14	14	
Prior treatment: radiotherapy			
Number of radiotherapies per patient			
Units: Subjects			
0 (no radiotherapy)	6	6	
1 radiotherapy	24	24	
2 radiotherapies	5	5	
3 or more radiotherapies	5	5	
Metastatic disease Units: Subjects			
Yes	21	21	
No	1	1	
Not avaluable	18	18	
Locoregional recurrence Units: Subjects			
Yes	30	30	
No	1	1	
Not avaluable	9	9	

End points

End points reporting groups

Reporting group title	Panitumumab + paclitaxel

Reporting group description:

Patients received paclitaxel (80 mg/m2/week) and panitumumab (6 mg/kg/2 weeks) until disease progression or unacceptable toxicity.

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

Subject analysis set description:

The intention-to-treat (ITT) population included all patients in the study who signed the informed consent form and received at least one dose of panitumumab.

Subject analysis set title	PP
Subject analysis set type	Per protocol

Subject analysis set description:

The per-protocol (PP) population is defined as the subset of patients of the ITT population who completed the study without any major protocol deviations.

Primary: Objective response rate (ORR)

End point title	Objective response rate (ORR)[1]

End point description:

Incidence of confirmed complete response (CR) or partial response (PR) during the treatment period according to RECIST v1.1 criteria in the intention-to-treat population (ITT).

End point type	Primary

End point timeframe:

Tumor assessments were planned to be performed every two months. Response confirmation was to be assessed not before 4 weeks after a partial or complete response, or before 6 weeks after a stable disease.

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: Data were summarized using descriptive statistics.

End point values	ITT	PP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40	35		
Units: Percentage of patients				
number (confidence interval 95%)				
Yes (CR+PR)	47.50 (32.02 to 62.98)	51.43 (34.87 to 67.99)		
No	52.50 (37.02 to 67.98)	48.57 (32.01 to 65.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best response

End point title	Best response

End point description:

End point type	Secondary

End point timeframe:

Tumor assessments were planned to be performed every two months. Response confirmation was to be assessed not before 4 weeks after a partial or complete response, or before 6 weeks after a stable disease.

End point values	ITT	PP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40	35		
Units: Percentage of patients				
arithmetic mean (confidence interval 95%)				
Complete response	15.00 (3.93 to 26.07)	17.14 (4.66 to 29.63)		
Partial response	32.50 (17.99 to 47.01)	34.29 (18.56 to 50.01)		
Stable disease	27.50 (13.66 to 41.34)	31.43 (16.05 to 46.81)		
Disease progression	15.00 (3.93 to 26.07)	17.14 (4.66 to 29.63)		
Non evaluable	10.00 (0.70 to 19.30)	0.00 (0.00 to 0.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate

End point title	Disease control rate

End point description:

Incidence of confirmed complete response (CR) or partial response (PR) or stable disease (SD) during the treatment period according to RECIST v1.1 criteria.

End point type	Secondary

End point timeframe:

Tumor assessments were planned to be performed every two months. Response confirmation was to be assessed not before 4 weeks after a partial or complete response, or before 6 weeks after a stable disease.

End point values	ITT	PP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	40	35		
Units: Percentage of patients				
number (confidence interval 95%)				
Yes (CR+PR+SD)	75.00 (61.58 to 88.42)	82.86 (70.37 to 95.34)		
No	25.00 (11.58 to 38.42)	17.14 (4.66 to 29.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response

End point title	Time to response

End point description:

Time to response is defined as the number of months between the date of the first treatment administration and the date of the first objective response confirmation.

End point type	Secondary

End point timeframe:

Until confirmed response (CR+PR). Calculated only for patients who presented objective response.

End point values	ITT	PP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19	18		
Units: months				
median (inter-quartile range (Q1-Q3))	4.0 (3.7 to 7.2)	3.9 (3.7 to 7.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response

End point description:

Time from the first response until disease progression or death due to disease progression (first that occurred).

End point type	Secondary

End point timeframe:

Until disease progression or death. Calculated only for patients who responded during the treatment period.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: months				
median (confidence interval 95%)	4.30 (2.83 to 6.64)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)

End point description:

Time from the inclusion date until confirmed disease progression or death (first that occurred).

End point type	Secondary

End point timeframe:

Until disease progression or end of the study.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: months				
median (confidence interval 95%)	7.46 (4.93 to 8.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Time from the inclusion date until death due to any cause.

End point type	Secondary

End point timeframe:

Until death

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: months				
median (confidence interval 95%)	9.86 (7.95 to 16.26)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events were reported.

Adverse event reporting additional description:

National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 3.0.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Safety population

Reporting group description: -

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 40 (40.00%)		
number of deaths (all causes)	35		
number of deaths resulting from adverse events	6		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Lacunar infarction			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	2 / 40 (5.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Diarrhoea				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Haemorrhoids				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary embolism				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			

Respiratory insufficiency			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumothorax			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Disorientation			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Cervicalgia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lung abscess			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			

subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Intervertebral discitis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 40 (100.00%)		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Hypotension			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
General disorders and administration site conditions			

Asthenia subjects affected / exposed occurrences (all)	33 / 40 (82.50%) 75		
Pain subjects affected / exposed occurrences (all)	6 / 40 (15.00%) 6		
Facial pain subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 3		
Application site eczema subjects affected / exposed occurrences (all)	5 / 40 (12.50%) 11		
Oedema peripheral subjects affected / exposed occurrences (all)	5 / 40 (12.50%) 5		
Mucosal inflammation subjects affected / exposed occurrences (all)	27 / 40 (67.50%) 51		
Pyrexia subjects affected / exposed occurrences (all)	8 / 40 (20.00%) 8		
Feeling hot subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Xerosis subjects affected / exposed occurrences (all)	12 / 40 (30.00%) 29		
Reproductive system and breast disorders Balanoposthitis subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 3		
Respiratory, thoracic and mediastinal disorders Nasal congestion subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Dysphonia			

subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Dyspnoea			
subjects affected / exposed	10 / 40 (25.00%)		
occurrences (all)	12		
Dyspnoea exertional			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Pulmonary embolism			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Rhinorrhoea			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Nasal dryness			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Cough			
subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	10		
Productive cough			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	8		
Psychiatric disorders			
Disorientation			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Insomnia			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Investigations			
Transaminases increased			

subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
Injury, poisoning and procedural complications			
Stoma site haemorrhage			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Injury			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	5		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Dysgeusia			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	7		
Dizziness			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Neuropathy peripheral			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	7		
Neurotoxicity			
subjects affected / exposed	14 / 40 (35.00%)		
occurrences (all)	37		
Paraesthesia			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	14		
Somnolence			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	11		
Leukopenia			

subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	6		
Neutropenia			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		
Febrile neutropenia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Eye disorders			
Ectropion			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Keratitis			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	4		
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	8		
Diarrhoea			
subjects affected / exposed	18 / 40 (45.00%)		
occurrences (all)	21		
Dysphagia			
subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	9		
Abdominal pain			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Oral pain			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
Abdominal pain upper			

subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Stomatitis			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	10		
Constipation			
subjects affected / exposed	13 / 40 (32.50%)		
occurrences (all)	18		
Rectal haemorrhage			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Haemorrhoids			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Salivary hypersecretion			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Nausea			
subjects affected / exposed	9 / 40 (22.50%)		
occurrences (all)	14		
Odynophagia			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	6		
Cheilitis			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Tongue ulceration			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	7 / 40 (17.50%)		
occurrences (all)	7		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	6		

Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Alopecia			
subjects affected / exposed	9 / 40 (22.50%)		
occurrences (all)	14		
Dermatitis			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	14		
Dermatitis acneiform			
subjects affected / exposed	14 / 40 (35.00%)		
occurrences (all)	67		
Nail dystrophy			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Eczema			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	10 / 40 (25.00%)		
occurrences (all)	23		
Rash			
subjects affected / exposed	26 / 40 (65.00%)		
occurrences (all)	111		
Skin striae			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	8		
Skin fissures			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	20		
Skin injury			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	7		
Onycholysis			

subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Dry skin			
subjects affected / exposed	17 / 40 (42.50%)		
occurrences (all)	23		
Pruritus			
subjects affected / exposed	15 / 40 (37.50%)		
occurrences (all)	23		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Skin toxicity			
subjects affected / exposed	8 / 40 (20.00%)		
occurrences (all)	13		
Nail toxicity			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	5		
Nail disorder			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	5		
Skin ulcer			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Cervicalgia			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	9		
Back pain			

subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	4		
Pain in jaw			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Pain in extremity			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Musculoskeletal pain			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	3		
Infections and infestations			
Oral candidiasis			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	4		
Cellulitis			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Conjunctivitis			
subjects affected / exposed	10 / 40 (25.00%)		
occurrences (all)	12		
Folliculitis			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	4		
Respiratory tract infection			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	6		
Localised infection			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Lung infection			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		

Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 5		
Pneumonia subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 4		
Paronychia subjects affected / exposed occurrences (all)	16 / 40 (40.00%) 29		
Superinfection subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	19 / 40 (47.50%) 32		
Hypocalcaemia subjects affected / exposed occurrences (all)	7 / 40 (17.50%) 23		
Hypokalaemia subjects affected / exposed occurrences (all)	3 / 40 (7.50%) 5		
Hypomagnesaemia subjects affected / exposed occurrences (all)	21 / 40 (52.50%) 72		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 April 2010	After reviewing the considerations of the Clinical Investigation Ethic Committees the suggested changes in the Protocol, the patient Information Sheet and the Informed Consent Form were performed, as well as in the pregnant partner data emission form, with the aim of improving the comprehension. Moreover, the parallel optional study of molecular predictive factors (appendix L in the study protocol) as well as the patient Information Sheet and the corresponding Informed Consent (Appendix M of the study protocol) were attached, being both of new development.

Notes:

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/27865372