Clinical trial results:
A Multi-center, Randomized, Phase 3 Study of Sequential Pralatrexate Versus Observation in Patients with Previously Undiagnosed Peripheral T-cell Lymphoma Who Have Achieved an Objective Response Following Initial Treatment with CHOP-based Chemotherapy

Summary

EudraCT number	2010-022230-81
Trial protocol	GB CZ IE ES BE IT
Global end of trial date	07 May 2015

Results information

Result version number	v1 (current)
This version publication date	09 August 2019
First version publication date	09 August 2019

Trial information

Trial identification

Sponsor protocol code	PDX-0170

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01420679
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Allos Therapeutics, Inc
Sponsor organisation address	11080 Circle Point Road, Suite 200, Westminster, CO, United States, CO80020
Public contact	David Stanbury, David Stanbury, +44 (0) 1462424406, clinicaltrials@bionical-emas.com
Scientific contact	David Stanbury, David Stanbury, +44 (0) 1462424406, clinicaltrials@bionical-emas.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	13 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 March 2015
Global end of trial reached?	Yes
Global end of trial date	07 May 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Determine the efficacy of pralatrexate compared to observation when administered to patients with previously undiagnosed peripheral T-cell lymphoma (PTCL) who have achieved an objective response after completing at least 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP)-based treatment.

Protection of trial subjects:

Signed and dated informed consent was obtained from enrolled-subjects prior to study participation. All study-related procedures were conducted only after a signed and dated ICF by the subject has been received and is counter-signed by the study investigator.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	06 June 2011
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	United Kingdom: 9
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Australia: 4
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	Canada: 2
Worldwide total number of subjects	21
EEA total number of subjects	12

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	9
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The actual start date of the study was 04 Aug 2011 and the end date was 13 Mar 2015. The study was prematurely terminated. The study was a Phase 3 confirmatory study to demonstrate efficacy of pralatrexate as part of the accelerated approval of Folotyn in the USA.

Pre-assignment

Screening details:

Eligible subjects were consented and screened against the eligibility criteria and patients randomised in a 2:1 ratio to either pralatrexate or observation.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequential pralatrexate

Arm description:

Patients randomized to the pralatrexate treatment group were to receive pralatrexate as an intravenous (IV) push administered over a minimum of 30 seconds up to a maximum of 5 minutes via a patent free-flowing IV line containing normal saline (0.9% sodium chloride [NaCl]) weekly for 3 weeks (± 1 day at each time point) of a 4-week cycle. The initial dose of pralatrexate was 30 mg/m2, which based on protocol-defined criteria, may be reduced to 20 mg/m2 with potential further reductions to 15 and 10 mg/m2. Pralatrexate was continued to be administered until a criterion for study treatment discontinuation was met or up to a maximum of 2 years.

Arm type	Experimental
Investigational medicinal product name	Pralatrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

30 mg/m2 for 3 weeks of a 4week cycle

Arm title	Observation

Arm description:

Patients randomized to the Observation group were to remain under observation, attend clinic visits every 4 weeks,
and be contacted by a healthcare professional during week 2 of every 4-week period until a criterion for study
treatment discontinuation was met.

Arm type	Standard of care

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Sequential pralatrexate	Observation
Started	14	7
Completed	0	0
Not completed	14	7
Patient decision	1	-
AE	4	-
Disease progression	-	2
More than 28 d between doses of pralatrexate	1	-
Investigator decision	1	2
Other reasons	1	-
Sponsor decision	3	3
Development of PD	3	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description:

Group 1: Pralatrexate was administered via IV push over a minimum of 30 seconds up to a maximum of 5 minutes. One cycle is 4 weeks in duration consisting of weekly dosing at a starting dose of pralatrexate 30 mg/m2 for 3 weeks, followed by 1 week of rest. Dose reduction to 20 mg/m2 with further reductions to 15 and 10 mg/m2 were allowed for defined toxicity. Pralatrexate was administered into a patent free-flowing IV line containing normal saline (0.9% sodium chloride [NaCl]).
Group 2: Patients randomized to the Observation group were to remain under observation, attend clinic visits every 4 weeks, and be contacted by a healthcare professional during week 2 of every 4-week period until a criterion for study treatment discontinuation was met.

Reporting group values	Overall trial	Total	
Number of subjects	21	21	
Age categorical Units: Subjects			
Adults (18-64 years)	9	9	
From 65-84 years	12	12	
Gender categorical Units: Subjects			
Female	8	8	
Male	13	13	

End points

End points reporting groups

Reporting group title	Sequential pralatrexate

Reporting group description:

Patients randomized to the pralatrexate treatment group were to receive pralatrexate as an intravenous (IV) push administered over a minimum of 30 seconds up to a maximum of 5 minutes via a patent free-flowing IV line containing normal saline (0.9% sodium chloride [NaCl]) weekly for 3 weeks (± 1 day at each time point) of a 4-week cycle. The initial dose of pralatrexate was 30 mg/m2, which based on protocol-defined criteria, may be reduced to 20 mg/m2 with potential further reductions to 15 and 10 mg/m2. Pralatrexate was continued to be administered until a criterion for study treatment discontinuation was met or up to a maximum of 2 years.

Reporting group title	Observation

Reporting group description:

Patients randomized to the Observation group were to remain under observation, attend clinic visits every 4 weeks,
and be contacted by a healthcare professional during week 2 of every 4-week period until a criterion for study
treatment discontinuation was met.

Primary: Progression-free survival (PFS) and overall survival (OS)

End point title	Progression-free survival (PFS) and overall survival (OS)[1]

End point description:

No efficacy assessments and analysis was conducted. A full statistical analysis and report were not completed.

End point type	Primary

End point timeframe:

Number of days from randomisation to the date of objective documentation of PD or death, regardless of cause (date of PD or death - date of randomisation +1)

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: The study was prematurely terminated. No efficacy assessments and analysis was conducted. A full statistical analysis and report were not completed.

End point values	Sequential pralatrexate	Observation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Number of days				

Notes:

[2] - Study prematurely terminated

[3] - Study prematurely terminated

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response (complete response [CR] or partial response [PR]) to pralatrexate versus observation

End point title	Objective response (complete response [CR] or partial response [PR]) to pralatrexate versus observation

End point description:

No efficacy assessments and analysis was conducted. A full statistical analysis and report were not

completed.

End point type	Secondary

End point timeframe:

Measured from randomisation

End point values	Sequential pralatrexate	Observation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: Disappearance or regression of disease				

Notes:

[4] - Study prematurely terminated

[5] - Study prematurely terminated

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

04 Aug 2011 and 7 May 2015

Adverse event reporting additional description:

Safety was evaluated by assessment of physical examinations, clinical laboratory values, treatment-emergent AEs (all grades), SAEs, and discontinuations due to treatment-related AEs. Safety was assessed according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) scale, Version 4.03.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Pralatrexate Treatment Group

Reporting group description:

Patients randomized to the pralatrexate treatment group were to receive pralatrexate as an intravenous (IV) push administered over a minimum of 30 seconds up to a maximum of 5 minutes via a patent free-flowing IV line containing normal saline (0.9% sodium chloride [NaCl]) weekly for 3 weeks (± 1 day at each time point) of a 4- week cycle. The initial dose of pralatrexate was 30 mg/m2, which based on protocol-defined criteria, may be reduced to 20 mg/m2 with potential further reductions to 15 and 10 mg/m2. Pralatrexate was continued to be administered until a criterion for study treatment discontinuation was met or up to a maximum of 2 years.

Reporting group title	Observation Group

Reporting group description:

Patients randomized to the Observation group were to remain under observation, attend clinic visits every 4 weeks,and be contacted by a healthcare professional during week 2 of every 4-week period until a criterion for study treatment discontinuation was met.

Serious adverse events	Pralatrexate Treatment Group	Observation Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 14 (28.57%)	0 / 7 (0.00%)	
number of deaths (all causes)	3	1	
number of deaths resulting from adverse events	1	0	
Injury, poisoning and procedural complications			
Subdural hematoma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			

subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIIth nerve paralysis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			

subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pralatrexate Treatment Group	Observation Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	6 / 7 (85.71%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Varicose vein			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
Endodontic procedure			
subjects affected / exposed	0 / 14 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Stent removal			
subjects affected / exposed	0 / 14 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Chills			

subjects affected / exposed	0 / 14 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Face oedema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	6 / 14 (42.86%)	2 / 7 (28.57%)	
occurrences (all)	10	2	
Local swelling			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Malaise			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Mucosal inflammation			
subjects affected / exposed	4 / 14 (28.57%)	0 / 7 (0.00%)	
occurrences (all)	8	0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	3 / 14 (21.43%)	1 / 7 (14.29%)	
occurrences (all)	4	1	
Mucosal inflammation/Intermittant Mucositis of Mouth			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 14 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	5 / 14 (35.71%)	3 / 7 (42.86%)	
occurrences (all)	7	3	
Dysphonia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Dyspnoea			
subjects affected / exposed	2 / 14 (14.29%)	1 / 7 (14.29%)	
occurrences (all)	5	1	
Epistaxis			
subjects affected / exposed	5 / 14 (35.71%)	0 / 7 (0.00%)	
occurrences (all)	9	0	
Hiccups			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Nasal congestion			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Oropharyngeal pain			
subjects affected / exposed	2 / 14 (14.29%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Pleuritic pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	0 / 14 (0.00%)	2 / 7 (28.57%)	
occurrences (all)	0	2	
Sneezing			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Confusional state			

subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Hallucination			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Mental status changes			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 14 (21.43%)	0 / 7 (0.00%)	
occurrences (all)	7	0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Body temperature increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Weight increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			

Contusion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Foot fracture			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Skull fracture			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Subdural haematoma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Congenital, familial and genetic disorders			
Ichthyosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Sinus bradycardia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Carotid artery occlusion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	

Convulsion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Dysaesthesia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	3 / 14 (21.43%)	1 / 7 (14.29%)	
occurrences (all)	4	1	
Hypokinesia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Neuropathy peripheral			
subjects affected / exposed	4 / 14 (28.57%)	1 / 7 (14.29%)	
occurrences (all)	5	1	
Paraesthesia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Sciatica			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Viith nerve paralysis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Thrombocytopenia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	10	0	
Eye disorders			
Cataract			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Ocular hypertension			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Visual acuity reduced			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
subjects affected / exposed	3 / 14 (21.43%)	1 / 7 (14.29%)	
occurrences (all)	10	1	
Aphthous stomatitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	3 / 14 (21.43%)	1 / 7 (14.29%)	
occurrences (all)	5	1	
Diarrhoea			

subjects affected / exposed	6 / 14 (42.86%)	1 / 7 (14.29%)	
occurrences (all)	9	1	
Dry mouth			
subjects affected / exposed	3 / 14 (21.43%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Impaired gastric emptying			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Lip ulceration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	6 / 14 (42.86%)	1 / 7 (14.29%)	
occurrences (all)	12	1	
Oral dysaesthesia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Stomatitis			
subjects affected / exposed	5 / 14 (35.71%)	1 / 7 (14.29%)	
occurrences (all)	16	1	
Vomiting			
subjects affected / exposed	4 / 14 (28.57%)	0 / 7 (0.00%)	
occurrences (all)	7	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 7 (14.29%)	
occurrences (all)	1	1	

Blister			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	2 / 14 (14.29%)	2 / 7 (28.57%)	
occurrences (all)	2	2	
Eczema			
subjects affected / exposed	1 / 14 (7.14%)	1 / 7 (14.29%)	
occurrences (all)	1	2	
Erythema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Macule			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Melanosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Nail disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Night sweats			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Onychoclasis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Penile ulceration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Pigmentation disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	

Pruritus			
subjects affected / exposed	4 / 14 (28.57%)	1 / 7 (14.29%)	
occurrences (all)	5	1	
Pruritus generalised			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	3 / 14 (21.43%)	0 / 7 (0.00%)	
occurrences (all)	5	0	
Rash maculo-papular			
subjects affected / exposed	0 / 14 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Rash pruritic			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Skin hyperpigmentation			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Skin ulcer			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Hypotension			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 14 (7.14%)	1 / 7 (14.29%)	
occurrences (all)	2	1	
Nocturia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Urinary tract pain			

subjects affected / exposed	0 / 14 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 14 (42.86%)	1 / 7 (14.29%)	
occurrences (all)	7	1	
Back pain			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	4	0	
Flank pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	0 / 14 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 7 (14.29%)	
occurrences (all)	1	1	
Myalgia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	1 / 14 (7.14%)	1 / 7 (14.29%)	
occurrences (all)	3	1	
Infections and infestations			
Bronchitis viral			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Clostridium difficile colitis			

subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Diverticulitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Fungal infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Skin infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 14 (21.43%)	2 / 7 (28.57%)	
occurrences (all)	3	2	
Viral infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	3 / 14 (21.43%)	1 / 7 (14.29%)	
occurrences (all)	5	1	
Hyponatraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 7 (0.00%)	
occurrences (all)	3	0	
Decreased appetite/Anorexia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 7 (14.29%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 May 2011	Amendment 1: The substantial amendment consists of an amendment to the protocol - protocol v2.0 submitted The patient consent documentation (v2.0) and the EudraCT form (12 May 2011) were updated to reflect the changes made to the protocol. Substantial changes were made to the IMPD. - IMPD v5.3 submitted
14 November 2011	Amendment 2: Substantial amendment to the IB - Edition 7.0 submitted
03 February 2012	Amendment 3: Substantial amendment consisting of an amendment to the protocol (v2.1), an update to the IMPD (v5.3) EudraCT form updated to reflect the changes made to the protocol and additional sections populated with data required for EudraCT version 8

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
13 March 2015	The study was prematurely terminated. The study was a Phase 3 confirmatory study to demonstrate efficacy of pralatrexate as part of the accelerated approval of Folotyn in the USA. Spectrum has agreed with FDA to stop the current trial and initiate a new trial with a study design that supports FDA post market requirement.	-

Notes:

Limitations and caveats

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

The study was prematurely terminated. No efficacy assessments and analysis was conducted. A full statistical analysis and report were not completed.

Notes: