Clinical trial results:
Open-Label, Multi-Center, Phase 2 Study of Anti-CCR4 Monoclonal Antibody KW 0761 (mogamulizumab) in Subjects with Previously Treated Peripheral T-cell Lymphoma (PTCL)

Summary

EudraCT number	2011-004151-39
Trial protocol	GB DE ES DK NL
Global end of trial date	22 July 2015

Results information

Result version number	v1 (current)
This version publication date	13 August 2016
First version publication date	13 August 2016

Trial information

Trial identification

Sponsor protocol code	0761-007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01611142
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Kyowa Hakko Kirin Pharma, Inc.
Sponsor organisation address	212 Carnegie Center, Suite 101, Princeton, United States, NJ 08540
Public contact	Clinical Trial Information, Kyowa Hakko Kirin Pharma, Inc., 001 6099191100, KKD.KW-0761@kyowakirin.com
Scientific contact	Clinical Trial Information, Kyowa Hakko Kirin Pharma, Inc., 001 6099191100, KKD.KW-0761@kyowakirin.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	Final
Date of interim/final analysis	16 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 July 2015
Global end of trial reached?	Yes
Global end of trial date	22 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the overall response rate of KW-0761 for the treatment of subjects with relapsed or refractory PTCL

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki, the International Conference on Harmonization (ICH) consolidated guideline E6 - Good Clinical Practice (GCP) and any applicable national and local laws and regulations. Subjects were provided with written and oral information about the study (aims, methods, anticipated benefits, potential hazards and insurance arrangements). No procedures were conducted until informed consent was provided. The protocol included wording for the treatment of skin rash and hypersensitivity-like reactions (wording regarding premedication prior to KW-0761 infusion was also included in the protocol).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 June 2012
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	Netherlands: 4
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Denmark: 2
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Italy: 4
Worldwide total number of subjects	38
EEA total number of subjects	38

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	23
From 65 to 84 years	14
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Recruitment opened in May 2012 and closed in October 2013.

Pre-assignment

Screening details:

All subjects were screened for eligibility to participate in the trial. Subjects that met all inclusion/exclusion criteria as per protocol, were eligible for entry into the study.A total of 59 subjects were screened of which 21 failed the screening process. 38 patients were therefore enrolled into the study.

Period 1

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

Arms

Arm title	Mogamulizumab (KW-0761)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Mogamulizumab (KW-0761)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1.0mg/kg over at least 1 hr on Days 1, 8, 15 and 22 of the first cycle and Days 1 and 15 of each subsequent 28-day cycle.

Number of subjects in period 1	Mogamulizumab (KW-0761)
Started	38
Completed	35
Not completed	3
Adverse event, non-fatal	1
Patient discretion	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	38	38	
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)	23	23	
From 65-84 years	15	15	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	57.7		
full range (min-max)	19 to 87	-	
Gender categorical Units: Subjects			
Female	15	15	
Male	23	23	

End points

End points reporting groups

Reporting group title	Mogamulizumab (KW-0761)

Reporting group description: -

Primary: Number of patients achieving overall response

End point title	Number of patients achieving overall response[1]

End point description:

End point type	Primary

End point timeframe:

Disease response was assessed every 8 weeks.

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: Descriptive analysis was ultilised for this primary endpoint.

End point values	Mogamulizumab (KW-0761)			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Participants	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patient achieving progression free survival

End point title	Number of patient achieving progression free survival

End point description:

End point type	Secondary

End point timeframe:

Disease response was assessed every 8 weeks.

End point values	Mogamulizumab (KW-0761)			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: participants	35			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (days)

End point title	Duration of Response (days)

End point description:

Four subjects had response durations of >1, 43, 77, >539 study days.

End point type	Secondary

End point timeframe:

Duration of response was measured from the time measurement criteria were met for CR/PR (whichever was first recorded) until the first date that PD or death was objectively documented.

End point values	Mogamulizumab (KW-0761)			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Days	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From pre-treatment visit until 90 days after the last dose.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15

Reporting groups

Reporting group title	Baseline

Reporting group description: -

Serious adverse events	Baseline		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 38 (47.37%)		
number of deaths (all causes)	16		
number of deaths resulting from adverse events	2		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Septic shock			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Cardiac disorders			
Stress cardiomyopathy			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac Failure			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebellar syndrome			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Asthenia			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise			

subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Xerosis			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Leukopenia			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			

subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	5 / 38 (13.16%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 38 (5.26%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Aspergillosis			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus infection			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Pneumocystis jiroveci pneumonia			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sialoadenitis			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oral infection			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 38 (2.63%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Baseline		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 38 (92.11%)		
Injury, poisoning and procedural complications			

Fall subjects affected / exposed occurrences (all) Infusion related reaction subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2 3 / 38 (7.89%) 3		
Vascular disorders Hypertension subjects affected / exposed occurrences (all) Hypotension subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 3 5 / 38 (13.16%) 7		
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Neuropathy peripheral subjects affected / exposed occurrences (all)	4 / 38 (10.53%) 4 3 / 38 (7.89%) 3 2 / 38 (5.26%) 3		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymphadenopathy subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	4 / 38 (10.53%) 6 2 / 38 (5.26%) 2 3 / 38 (7.89%) 3		

Thrombocytopenia subjects affected / exposed occurrences (all)	5 / 38 (13.16%) 5		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Chills subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 5 / 38 (13.16%) 5 3 / 38 (7.89%) 3 3 / 38 (7.89%) 3 4 / 38 (10.53%) 7 8 / 38 (21.05%) 11		
Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 2 / 38 (5.26%) 2 2 / 38 (5.26%) 2 7 / 38 (18.42%) 10 4 / 38 (10.53%) 6 5 / 38 (13.16%) 6		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	6 / 38 (15.79%) 6		
Dyspnoea subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 4		
Hypoxia subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		
Nasopharyngitis subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		
Pleural effusion subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		
Skin and subcutaneous tissue disorders Drug eruption subjects affected / exposed occurrences (all)	10 / 38 (26.32%) 18		
Night sweats subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		
Pruritus subjects affected / exposed occurrences (all)	7 / 38 (18.42%) 10		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 38 (10.53%) 5		
Back pain subjects affected / exposed occurrences (all)	3 / 38 (7.89%) 3		
Bone pain subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		
Infections and infestations			

Bronchitis subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 3		
Fungal infection subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		
Lower respiratory tract infection subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		
Sepsis subjects affected / exposed occurrences (all)	2 / 38 (5.26%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2012	• Added only CCR4-positive subjects and the most common PTCL subtypes who expressed the CCR4 target excluding those with indolent disease and/or lower CCR4 expression; • Excluded subjects with a history of moderate or severe psoriasis or with psoriasis associated with systemic symptoms or with a 1st degree relative with history of psoriasis that required medical intervention; • Allowed subjects with known bone marrow involvement to participate if their platelet count was ≥75,000 and allowed for laboratory retesting if the criteria for hematologic, hepatic, and renal function were not met; • Specified that safety surveillance would be performed on a regular basis by the Sponsor and independent therapeutic experts and extended the safety monitoring period from 30 to 90 days after the last dose of study medication; • The subject was required to use contraception for 3 months after the last dose of study drug; • Provided guidelines for documenting and treating a treatment-emergent skin rash; • Incorporated the mSWAT for subjects with skin disease with the IWG response criteria (definitions added) for assessment of global response; • Included the assessment of AEs from the time of informed consent rather than after the first dose of study drug; • Allowed subjects to continue monthly treatment with mogamulizumab, at the discretion of the investigator, beyond CR; • Updated the guidelines for the treatment of hypersensitivity-like reactions; • Allowed skin biopsies for CCR4 expression in subjects with skin disease.
16 April 2013	• To modify the Inclusion/Exclusion Criteria; • To increase the number of sites; • To specify the permissible dosing interval for mogamulizumab; • To allow subjects with PD in one disease compartment to continue treatment for a period of up to 8 weeks and allow additional time for the demonstration of an objective response; • To allow subjects who experienced a CR to continue to be treated for a period of 12 months or until progression, whichever occurred first; • To clarify the guidance for the treatment of hypersensitivity-like reactions; • To remove clinical laboratory assessments (i.e., CD4 and CD8 cell counts) not necessary for the conduct of this study. • To lengthen the Screening period; • To clarify the acceptable age of archived lymph node or skin biopsy sample (i.e., collected within 3 months Pretreatment) and to allocate a portion of the sample collected to test a second method of CCR4 analysis in order to establish compatibility between the tests; • To clarify that the SWAT must be performed for all subjects; • To clarify that certain body weight changes requires dose adjustment and to describe the storage conditions of the reconstituted drug product; • To specify that in this study, disease progression and lymphopenia should not be considered adverse events.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported