EU Clinical Trials Register

Clinical trial results:
Home Delivery of Pemetrexed as Maintenance Treatment in Patients Who Have Not Progressed after Induction Therapy for Advanced Nonsquamous Nonsmall Cell Lung Cancer: A Feasibility Study

Summary

EudraCT number	2011-000841-19
Trial protocol	SE GB
Global end of trial date	23 September 2013

Results information

Result version number	v1 (current)
This version publication date	16 July 2016
First version publication date	16 July 2016

Trial information

Trial identification

Sponsor protocol code	H3E-EW-S133

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01473563
WHO universal trial number (UTN)	-
Other trial identifiers	Trial ID: 14079, Trail Alias: H3E-EW-S133

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon - Fri 9 AM - 5PM EST, Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Available Mon - Fri 9 AM - 5PM EST, Eli Lilly and Company, 1 877-285-4559,

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	23 September 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the adherence rate to pemetrexed administered in a domiciliary setting.

Protection of trial subjects:

This study was conducted in accordance with International Code of Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 43
Country: Number of subjects enrolled	Sweden: 9
Worldwide total number of subjects	52
EEA total number of subjects	52

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)	24
From 65 to 84 years	28

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During screening, 5 patients failed to meet study eligibility criteria and 1 patient was not enrolled due to an Adverse Event (AE).

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	Study Treatment

Arm description:

Pemetrexed: 500 milligrams per meter squared (mg/m^2) administered as an intravenous (IV) infusion over approximately 10 minutes on Day 1 of each 21-day cycle until disease progression or the participant discontinued for any other reason. The first dose of maintenance therapy was administered at the hospital; thereafter, therapy was administered in the home setting by qualified oncology homecare nurses.

Arm type	Experimental
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	LY231514, Alimta, Pemetrexed disodium, Pemetrexed sodium hydrate
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

500 milligrams per square meter (mg/m^2) pemetrexed administered intravenously over approximately 10 minutes on Day 1 of a 21-day cycle. Maintenance therapy administered until disease progression or the participant is discontinued for any other reason. The first dose of maintenance therapy will be administered at the hospital; thereafter, therapy will be administered in the home setting by qualified oncology homecare nurses.

Number of subjects in period 1	Study Treatment
Started	52
Received at Least 1 Dose of Study Drug	52
Completed	51
Not completed	1
Lost to Follow-up post-treatment discontinuation	1

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description:

Pemetrexed: 500 mg/m^2 IV infusion over approximately 10 minutes on Day 1 of each 21-day cycle until disease progression or the participant discontinued for any other reason. The first dose of maintenance therapy was administered at the hospital; thereafter, therapy was administered in the home setting by qualified oncology homecare nurses.

Reporting group values	Overall Study	Total	
Number of subjects	52	52	
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
median	66		
full range (min-max)	27 to 82.5	-	
Gender categorical			
Units: Subjects			
Female	26	26	
Male	26	26	
Race/Ethnicity, Customized			
Units: Subjects			
White	48	48	
Black or African American	4	4	
Region of Enrollment			
Units: Subjects			
United Kingdom	43	43	
Sweden	9	9	
Eastern Cooperative Oncology Group (ECOG) Performance Status			
Classified participants according to their functional impairment. Scores could have ranged from 0 (Fully Active) to 5 (Death).			
Units: Subjects			
0: Fully Active	14	14	
1: Restricted	38	38	
Most Recent Pathological Diagnosis			
Units: Subjects			
Adenocarcinoma, Lung	48	48	
Adenocarcinoma, Mucinous, No Other Symptoms (NOS)	1	1	
Adenocarcinoma, Moderately Differentiated, Lung	1	1	
Carcinoma, Non-Small Cell, Lung NOS	2	2	
Basis for Most Recent Pathological Diagnosis			
Units: Subjects			
Cytological	10	10	

Histopathological	42	42	

Stage of Disease

Disease stage described using American Joint Committee on Cancer (AJCC). Stages ranged from I (cancer was small and had not spread to the lymph nodes) to IV (cancer spread throughout the body). Stage III (cancer had spread to nearby tissue or lymph nodes) was further differentiated based on regional lymph nodes: Stage IIIA (spread to nearby lymph nodes) and Stage IIIB (spread to distance lymph nodes). The participant with Stage IIIA disease was enrolled in study because investigator considered participant not eligible for curative treatment.

Units: Subjects			
Stage IIIB	3	3	
Stage IV	48	48	
Stage IIIA	1	1	

Prior Systemic Therapy

Prior systemic therapies include carboplatin and gemcitabine; carboplatin and pemetrexed; cisplatin and pemetrexed; platinum-based therapy and pemetrexed. Participants pre-exposed to cisplatin and carboplatin were considered to have platinum-based therapy.

Units: Subjects			
Carboplatin + Gemcitabine	9	9	
Carboplatin + Pemetrexed	19	19	
Cisplatin + Pemetrexed	20	20	
Platinum-Based Therapy + Pemetrexed	4	4	

Best Response to Prior Systemic Therapy

Best response to prior systemic therapy was defined using Response Evaluation Criteria In Solid Tumors [RECIST, version (v) 1.1] criteria. PR was having at least a 30% decrease in sum of longest diameter of target lesions; PD was having at least 20% increase in sum of longest diameter of target lesions and minimum 5 mm increase above nadir; SD was small changes that did not meet above criteria. Participant with PD (borderline tumor increase) was considered a protocol violation.

Units: Subjects			
Partial Response (PR)	25	25	
Stable Disease (SD)	26	26	
Progressive Disease (PD)	1	1	

End points

End points reporting groups

Reporting group title	Study Treatment

Reporting group description:

Pemetrexed: 500 milligrams per meter squared (mg/m^2) administered as an intravenous (IV) infusion over approximately 10 minutes on Day 1 of each 21-day cycle until disease progression or the participant discontinued for any other reason. The first dose of maintenance therapy was administered at the hospital; thereafter, therapy was administered in the home setting by qualified oncology homecare nurses.

Primary: Percentage of Participants Who Adhered to Treatment Administration at Home

End point title	Percentage of Participants Who Adhered to Treatment Administration at Home[1]

End point description:

Participants were considered adherent from the time of the first dose in Cycle 1 (hospital administration) until either the last day of the cycle when the participant reverted to pemetrexed hospital administration or the last day of the cycle when the participant discontinued study treatment or the study for reasons related to the home setting. The percentage of participants who adhered to treatment administration at home was estimated by a Kaplan-Meier survival analyses approach. Participants who died or discontinued the study and treatment without reverting to hospital administration were censored at the time of discontinuation.

End point type	Primary

End point timeframe:

Cycle 1, Day 1 through Cycle 19, Day 1 and Cycle 19, Day 1 (21 days/cycle)

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 statistics are used to represent rates of adherence to home delivery for each cycle based on the Kaplan-Meier approach and are expressed as proportions (percentage of participants) and reported with the corresponding 95% confidence intervals.

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Percentage of Participants				
number (confidence interval 95%)				
Cycle 1, Hospital Delivery	100 (100 to 100)			
Cycle 2, Home Delivery	98 (86.4 to 99.7)			
Cycle 3, Home Delivery	98 (86.4 to 99.7)			
Cycle 4, Home Delivery	98 (86.4 to 99.7)			
Cycle 5, Home Delivery	98 (86.4 to 99.7)			
Cycle 6, Home Delivery	98 (86.4 to 99.7)			

Cycle 7, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 8, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 9, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 10, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 11, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 12, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 13, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 14, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 15, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 16, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 17, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 18, Home Delivery	90.7 (61.7 to 98.1)				
Cycle 19, Home Delivery	90.7 (61.7 to 98.1)				

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the European Quality of Life Instrument (EQ-5D) Visual Analogue Scale (VAS)

End point title	Change From Baseline in the European Quality of Life Instrument (EQ-5D) Visual Analogue Scale (VAS)

End point description:

The EQ-5D scale was used to provide an estimate of the health state utility in this population. The EQ-5D scale includes a 5-dimensional descriptive system that measures each of the health state attributes: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression according to a 3-point scale (no problem, some problems, and major problems) and a VAS that allows participants to rate their present health condition from 0 (worst imaginable health state) to 100 (best imaginable health state). The change from baseline in EQ-5D VAS is reported.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 2 and 4 (21 days/cycle) and 30 days post treatment discontinuation

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Cycle 2 (n=34)	3 (± 18.6)			

Cycle 4 (n=20)	7.7 (± 21.7)				
30 days post treatment discontinuation (n=22)	-0.9 (± 18.9)				

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the EQ-5D Index Score

End point title	Change From Baseline in the EQ-5D Index Score

End point description:

The EQ-5D scale was used to provide an estimate of the health state utility in this population. The EQ-5D scale includes a 5-dimensional descriptive system that measures each of the health state attributes: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression according to a 3-point scale (no problem, some problems, and major problems) and a VAS that allows participants to rate their present health condition from 0 (worst imaginable health state) to 100 (best imaginable health state). The change from baseline EQ-5D Index score is reported and the EQ-5D Index score was calculated by converting health state scores into a weighted health state index according to a United Kingdom population-based algorithm. The possible values for the EQ-5D Index score range from −0.59 (severe problems in all 5 dimensions) to 1.0 (no problem in any dimension), on a scale where 1 represents the best possible health state.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 2 and 4 (21 days/cycle) and 30 days post treatment discontinuation

End point values	Study Treatment				
Subject group type	Reporting group				
Number of subjects analysed	38				
Units: Units on a scale					
arithmetic mean (standard deviation)					
Cycle 2 (n=38)	0.03 (± 0.22)				
Cycle 4 (n=23)	0.08 (± 0.22)				
30 days post treatment discontinuation (n=26)	-0.9 (± 0.28)				

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Improvement Over Baseline in Individual Lung Cancer Symptoms Scale (LCSS) Item Scores

End point title	Maximum Improvement Over Baseline in Individual Lung Cancer Symptoms Scale (LCSS) Item Scores

End point description:

LCSS is a 9-item questionnaire; 6 items are symptom-specific measures for lung cancer (loss of appetite, fatigue, cough, dyspnea, hemoptysis, and pain), and 3 summation items describe overall symptomatic distress, interference with activity level, and overall quality of life during the past 24 hours.

Participant responses were measured using a VAS with 100-millimeter (mm) lines. Scores ranged from 0 mm (no symptoms and no impact on activities, quality of life) to 100 mm (symptoms as bad as they could be, impacting activities and quality of life).

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each cycle (up to Cycle 19, 21 days/cycle), and 30 days post treatment discontinuation

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Millimeter (mm)				
arithmetic mean (standard deviation)				
Loss of Appetite (n=43)	16.3 (± 22)			
Fatigue (n=43)	24.5 (± 27.2)			
Cough (n=41)	9.2 (± 19.7)			
Dyspnea (n=41)	17.2 (± 26.7)			
Hemoptysis (n=43)	0.4 (± 4.3)			
Pain (n=40)	11.8 (± 25.1)			
Overall Symptomatic Distress (n=43)	8.3 (± 22.3)			
Interference With Activity Level (n=43)	15.3 (± 25.1)			
Overall Quality of Life (n=41)	12.2 (± 23)			

Statistical analyses

No statistical analyses for this end point

Secondary: Participant Satisfaction: Chemotherapy at Hospital

End point title	Participant Satisfaction: Chemotherapy at Hospital

End point description:

Participants were asked to evaluate their hospital experiences in this study by answering 4 questions (Q). Q1: "What do you consider advantages of having chemotherapy at the hospital? Choose all that apply." Choices included: "Support from other patients", "Access to other medical specialists", "Access to more technical services", "Safer in case something goes wrong", and "Other". Q2: "What do you consider disadvantages of having chemotherapy at the hospital? Choose all that apply." Choices included: "Need to travel", "Having to wait for treatment", "Not having a personalized treatment", "Lack of privacy on the ward", and "Other". Q3: "How would you rate your overall satisfaction with chemotherapy at the hospital?" and Q4: "How would you rate your overall satisfaction with the nursing staff during chemotherapy at the hospital?" Choices for Q3 and Q4 included: "Very dissatisfied", "Somewhat dissatisfied", "Neither satisfied nor dissatisfied", "Somewhat satisfied", or "Very satisfied".

End point type	Secondary

End point timeframe:

The first evaluation completed at either Cycle 4, Day 1 (21 days/cycle) or 30 days post treatment discontinuation

End point values	Study Treatment				
Subject group type	Reporting group				
Number of subjects analysed	39				
Units: Participants					
number (not applicable)					
Q1, Support from other patients	8				
Q1, Access to other medical specialists	19				
Q1, Access to more technical services	12				
Q1, Safer in case something goes wrong	19				
Q1, Other	3				
Q2, Need to travel	36				
Q2, Having to wait for treatment	27				
Q2, Not having a personalized treatment	5				
Q2, Lack of privacy on the ward	7				
Q2, Other	1				
Q3, Very dissatisfied	0				
Q3, Somewhat dissatisfied	3				
Q3, Neither satisfied nor dissatisfied	3				
Q3, Somewhat satisfied	11				
Q3, Very satisfied	21				
Q4, Very dissatisfied	3				
Q4, Somewhat dissatisfied	0				
Q4, Neither satisfied nor dissatisfied	0				
Q4, Somewhat satisfied	3				
Q4, Very satisfied	32				

Statistical analyses

No statistical analyses for this end point

Secondary: Participant Satisfaction: Chemotherapy at Home

End point title	Participant Satisfaction: Chemotherapy at Home

End point description:

Participants were asked to evaluate their home treatment experiences in this study by answering 4 questions (Q). Q5: "What do you do consider advantages of having chemotherapy at home? Choose all that apply." Choices included: "No need to travel", "Not having to wait for treatment", "Personalized service", "More privacy", and "Other". Q6:"What do you consider disadvantages of having chemotherapy at home? Choose all that apply." Choices included: "Lack of other patients' support", "Extra burden for family/friends", "Safety concerns", "Need to rely on 1 medical specialist", and "Other". Q7: "How would you rate your overall satisfaction with chemotherapy at home?" Choices included: "Very dissatisfied", "Somewhat dissatisfied", "Neither satisfied nor dissatisfied", "Somewhat satisfied", or "Very satisfied".

End point type	Secondary

End point timeframe:

The first evaluation completed at either Cycle 4, Day 1 (21 days/cycle) or 30 days post treatment discontinuation

End point values	Study Treatment				
Subject group type	Reporting group				
Number of subjects analysed	39				
Units: Participants					
number (not applicable)					
Q5, No need to travel	37				
Q5, Not having to wait for treatment	27				
Q5, Personalized service	28				
Q5, More privacy	20				
Q5, Other	2				
Q6, Lack of other patients' support	5				
Q6, Extra burden for family/friends	1				
Q6, Safety concerns	4				
Q6, Need to rely on 1 medical specialist	7				
Q6, Other	19				
Q7, Very dissatisfied	1				
Q7, Somewhat dissatisfied	0				
Q7, Neither satisfied nor dissatisfied	2				
Q7, Somewhat satisfied	1				
Q7, Very Satisfied	30				

Statistical analyses

No statistical analyses for this end point

Secondary: Participant Satisfaction: Regarding the Study Nurse

End point title	Participant Satisfaction: Regarding the Study Nurse

End point description:

Participants were asked 7 questions (Q) about their study nurse for home treatment. Q8: "Was the nurse an easy person to talk to?", Q9: "When the nurse came, did you feel he/she had enough time to do the required things?", Q10: "Do you think the nurse had time to discuss things with you?", Q11: "Did you feel that the nurse knew enough about you and your illness?" Choices for Q8 through Q11 included: "Yes" or "No". Q12: "Were you able to get all the information you wanted about your illness or treatment?" Choices included: "Yes", "No", or "Uncertain". Q13: "Would you say that the nurse gave…" Choices included: "a lot of reassurance and support", "some reassurance and support", or "hardly any reassurance and support". Q14: "How would you rate your overall satisfaction with the nursing staff during chemotherapy at home?" Choices included: "Very dissatisfied", "Somewhat dissatisfied", "Neither satisfied nor dissatisfied", "Somewhat satisfied", or "Very satisfied".

End point type	Secondary

End point timeframe:

The first evaluation completed at either Cycle 4, Day 1 (21 days/cycle) or 30 days post treatment discontinuation

End point values	Study Treatment				
Subject group type	Reporting group				
Number of subjects analysed	38				
Units: Participants					
number (not applicable)					
Q8, Yes	37				
Q8, No	0				
Q9, Yes	36				
Q9, No	1				
Q10, Yes	37				
Q10, No	1				
Q11, Yes	36				
Q11, No	0				
Q12, Yes	34				
Q12, No	0				
Q12, Uncertain	3				
Q13, Hardly any reassurance and support	0				
Q13, Some reassurance and support	2				
Q13, A lot of reassurance and support	35				
Q14, Very dissatisfied	3				
Q14, Somewhat dissatisfied	0				
Q14, Neither satisfied nor dissatisfied	1				
Q14, Somewhat satisfied	1				
Q14, Very satisfied	33				

Statistical analyses

No statistical analyses for this end point

Secondary: Participant Satisfaction: Preferences Regarding Home and/or Hospital Treatment

End point title	Participant Satisfaction: Preferences Regarding Home and/or Hospital Treatment

End point description:

Participants were asked to evaluate their preferences regarding home and/or hospital treatment delivery in this study by answering 2 questions (Q). Q15: "Do you prefer having your chemotherapy at home or at the hospital, or are you indifferent?" Choices included: "Home", "Hospital", or "Indifferent". Q16: "Would you recommend having chemotherapy at home to someone else in your same situation?" Choices included: "Yes", "No", or "Not sure".

End point type	Secondary

End point timeframe:

The first evaluation completed at either Cycle 4, Day 1 (21 days/cycle) or 30 days post treatment discontinuation

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Participant				
number (not applicable)				
Q15, Home	33			
Q15, Hospital	0			
Q15, Indifferent	5			
Q16, Yes	37			
Q16, No	0			
Q16, Not sure	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Physician Satisfaction: Distant Management of Participant

End point title	Physician Satisfaction: Distant Management of Participant

End point description:

The physician was asked, "How would you rate your overall satisfaction with the distant management of the participant during chemotherapy at home?" Choices included: "Very dissatisfied", "Somewhat dissatisfied", "Neither satisfied nor dissatisfied", "Somewhat satisfied", or "Very satisfied".

End point type	Secondary

End point timeframe:

30 days post treatment discontinuation

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Investigators				
number (not applicable)				
Very Dissatisfied	2			
Somewhat Dissatisfied	1			
Neither Satisfied Nor Dissatisfied	0			
Somewhat Satisfied	8			
Very Satisfied	20			

Statistical analyses

No statistical analyses for this end point

Secondary: Resource Utilization: Number of Participants With an Unplanned Use of Healthcare Resources

End point title	Resource Utilization: Number of Participants With an Unplanned Use of Healthcare Resources

End point description:

The number of participants who had at least 1 unplanned use of health care resources [accident and emergency department (dept.), specialists [oncologist, pulmonologist, etcetera (etc.)], general practitioner (GP) or family doctor, or diagnostic procedures] during the study is reported

End point type	Secondary

End point timeframe:

Cycle 1, Day 1 through last day of cycle when participant reverted to hospital administration or discontinued (up to Cycle 19, 21 days/cycle)

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Participants				
number (not applicable)				
#Participants w/Unplanned Use-Healthcare Resource	29			

Statistical analyses

No statistical analyses for this end point

Secondary: Resource Utilization: Duration of Health Care Visits

End point title	Resource Utilization: Duration of Health Care Visits

End point description:

The duration of the health care visit in the home setting is reported. The visit started when the nurse arrived and included the entire treatment process. The visit ended when the nurse left the home setting. Due to the limited number of participants with evaluable data, results are reported for Cycles 2 through 4.

End point type	Secondary

End point timeframe:

Cycle 2, Day 1 through last day of cycle when participant reverted to hospital administration or discontinued (up to Cycle 4, 21 days/cycle)

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: Hours				
arithmetic mean (standard deviation)				
Cycle 2 (n=42)	1.67 (± 0.493)			
Cycle 3 (n=35)	1.66 (± 0.683)			
Cycle 4 (n=28)	1.57 (± 0.311)			

Statistical analyses

No statistical analyses for this end point

Secondary: Resource Utilization: Distances Traveled

End point title	Resource Utilization: Distances Traveled

End point description:

The distance traveled is reported by region (Great Britain and Sweden) and includes the distance traveled by the participant from his/her home to the hospital (Cycle 1) and other cycles where the homecare nurse traveled from the hospital to the participant's home. Due to the limited number of participants with evaluable data, results are reported for Cycles 1 through 4.

End point type	Secondary

End point timeframe:

Cycle 1, Day 1 through last day of cycle when participant reverted to hospital administration or discontinued (up to Cycle 4, 21 days/cycle

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: Kilometers (km)				
arithmetic mean (standard deviation)				
Cycle 1, Home to Hospital, Great Britain (n=25)	19.7 (± 23.39)			
Cycle 1, Home to Hospital, Sweden (n=7)	30.7 (± 23.08)			
Cycle 2, Hospital to Home, Great Britain (n=24	15.5 (± 13.12)			
Cycle 2, Hospital to Home, Sweden (n=7)	23.9 (± 23.93)			
Cycle 3, Hospital to Home, Great Britain (n=11)	23.8 (± 16.72)			
Cycle 3, Hospital to Home, Sweden (n=4)	17.5 (± 17.97)			
Cycle 4, Hospital to Home, Great Britain (n=7)	11.7 (± 8.75)			
Cycle 4, Hospital to Home, Sweden (n=2)	24.5 (± 27.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) at 6 Months

End point title	Overall Survival (OS) at 6 Months

End point description:

The percentage of participants who were alive at Month 6 was calculated as a cumulative percentage by Kaplan-Meier survival analyses approach. For participants not known to have died as of the cut-off date, OS was censored as the last contact date (known alive).

End point type	Secondary

End point timeframe:

Cycle 1, Day 1 to the date of death from any cause (up to Month 6)

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Percentage of Participants				
number (confidence interval 95%)				
Overall Survival (OS) at 6 Months	73 (58.1 to 82.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Failure (TTF)

End point title	Time to Treatment Failure (TTF)

End point description:

The time from the date of the first dose of study treatment (Cycle 1, Day 1) to the date of death from any cause, PD (clinical and objective), or discontinuation of pemetrexed due to toxicity. Response was defined using RECIST, v1.1 criteria. PD was defined as having at least a 20% increase in the sum of the longest diameter of target lesions and at a minimum 5 mm increase above nadir. TTF was censored at the date of the last visit for participants who did not discontinue pemetrexed, who were still alive, and who had not progressed.

End point type	Secondary

End point timeframe:

Cycle 1, Day 1 to first event (up to Cycle 19, 21 days/cycle)

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Months				
number (confidence interval 95%)				
Time to Treatment Failure (TTF)	3 (2.3 to 4.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Resource Utilization: Unplanned Health Care Visits, Consultations, and Diagnostic Services

End point title	Resource Utilization: Unplanned Health Care Visits, Consultations, and Diagnostic Services

End point description:

The unplanned use of any 1 of the following 4 resources is reported, as well as the unplanned use of each resource: accident and emergency dept., specialists (oncologist, pulmonologist etc.), GP or family doctor, and diagnostic procedures. Results are reported as the number of participants with an unplanned resource use (visit) for a specified number of times.

End point type	Secondary

End point timeframe:

Cycle 1, Day 1 through last day of cycle when participant reverted to hospital administration or discontinued (up to Cycle 19, 21 days/cycle)

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Participants				
number (not applicable)				
1 Unplanned Visit, Any Resource	8			
2 Unplanned Visits, Any Resource	6			
3 Unplanned Visits, Any Resource	5			
4 Unplanned Visits, Any Resource	2			
5 Unplanned Visits, Any Resource	3			
9 Unplanned Visits, Any Resource	1			
10 Unplanned Visits, Any Resource	1			
13 Unplanned Visits, Any Resource	1			
1 Unplanned Visit, Accident and Emergency Dept.	7			
2 Unplanned Visits, Accident and Emergency Dept	2			
3 Unplanned Visits, Accident and Emergency Dept.	2			
1 Unplanned Visit, Specialist	9			
2 Unplanned Visits, Specialist	3			
5 Unplanned Visits, Specialist	1			
1 Unplanned Visit, GP or Family Doctor	6			
2 Unplanned Visits, GP or Family Doctor	3			
3 Unplanned Visits, GP or Family Doctor	2			
4 Unplanned Visits, GP or Family Doctor	3			

1 Unplanned Visit, Diagnostic procedures	6				
2 Unplanned Visits, Diagnostic procedures	2				
3 Unplanned Visits, Diagnostic procedures	3				
4 Unplanned Visits, Diagnostic procedures	1				

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of Participants Who Had Treatment-Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), or Died

End point title	Number of Participants Who Had Treatment-Emergent Adverse Events (TEAEs), Serious Adverse Events (SAEs), or Died

End point description:

The number of participants who had at least 1 TEAE or serious TEAE (regardless of causality) is reported along with the number of participants who died (due to any cause) while on therapy or during treatment discontinuation follow-up (up to 6 months). TEAEs started on or after the date and time of first dose of study drug, or started prior to study drug but worsened after study drug started. Clinically significant events were defined as SAEs and other non-serious adverse events (AEs). A summary of SAEs and other non-serious AEs is located in the Reported Adverse Events module.

End point type	Other pre-specified

End point timeframe:

First dose of study drug (Cycle 1, Day 1) through study completion [up to Cycle 19 (21 days/cycle) or treatment discontinuation, plus up to 6 months post treatment discontinuation]

End point values	Study Treatment			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Participants				
number (not applicable)				
At least 1 TEAE	51			
At least 1 Serious TEAE	21			
Death, AE (fell, multiple injuries)	1			
Death, Study Drug Toxicity (atypical pneumonia)	1			
Death, Study Disease	26			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

H3E-EW-S133

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Pemetrexed 500 mg/m2

Reporting group description: -

Serious adverse events	Pemetrexed 500 mg/m2		
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 52 (44.23%)		
number of deaths (all causes)	28		
number of deaths resulting from adverse events	1		
General disorders and administration site conditions			
chest discomfort			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
chest pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
device occlusion			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Reproductive system and breast disorders			
pelvic pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
dysphonia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
dyspnoea			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
haemoptysis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
hypoxia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

pleural effusion			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
pulmonary fibrosis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
blood creatinine increased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
neutrophil count decreased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
humerus fracture			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
multiple injuries			

alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			
atrial flutter			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
cardiac arrest			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
headache			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
loss of consciousness			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
spinal cord compression			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
sensory loss				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
anaemia				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	2 / 52 (3.85%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
thrombocytopenia				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
constipation				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
nausea				
alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
vomiting				
alternative dictionary used: MedDRA 16.1				

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

stomatitis

alternative dictionary used: MedDRA 16.1

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Skin and subcutaneous tissue disorders

rash

alternative dictionary used: MedDRA 16.1

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Renal and urinary disorders

haematuria

alternative dictionary used: MedDRA 16.1

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

renal impairment

alternative dictionary used: MedDRA 16.1

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal and connective tissue disorders

back pain

alternative dictionary used: MedDRA 16.1

subjects affected / exposed	2 / 52 (3.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

muscular weakness

alternative dictionary used: MedDRA 16.1

subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Infections and infestations

bronchitis

alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

atypical pneumonia

alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			

lower respiratory tract infection

alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	3 / 52 (5.77%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			

influenza

alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	1 / 52 (1.92%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

pneumonia

alternative dictionary used: MedDRA 16.1				
subjects affected / exposed	2 / 52 (3.85%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			

sepsis

alternative dictionary used: MedDRA 16.1				

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pemetrexed 500 mg/m2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 52 (90.38%)		
Investigations			
blood creatinine increased			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	5		
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	5		
dysgeusia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
lethargy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	9 / 52 (17.31%)		
occurrences (all)	12		
headache			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	8 / 52 (15.38%)		
occurrences (all)	11		
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	12 / 52 (23.08%)		
occurrences (all)	14		
General disorders and administration site conditions			
chest pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
fatigue			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	20 / 52 (38.46%)		
occurrences (all)	31		
influenza like illness			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
oedema peripheral			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		
pyrexia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	7		
pain			
alternative dictionary used: MedDRA 16.1			

subjects affected / exposed	3 / 52 (5.77%)
occurrences (all)	3

Eye disorders	
lacrimation increased	
alternative dictionary used: MedDRA 16.1	
subjects affected / exposed	6 / 52 (11.54%)
occurrences (all)	6

Gastrointestinal disorders	
abdominal pain	
alternative dictionary used: MedDRA 16.1	
subjects affected / exposed	4 / 52 (7.69%)
occurrences (all)	4
diarrhoea	
alternative dictionary used: MedDRA 16.1	
subjects affected / exposed	3 / 52 (5.77%)
occurrences (all)	4
constipation	
alternative dictionary used: MedDRA 16.1	
subjects affected / exposed	8 / 52 (15.38%)
occurrences (all)	10
dyspepsia	
alternative dictionary used: MedDRA 16.1	
subjects affected / exposed	3 / 52 (5.77%)
occurrences (all)	4
nausea	
alternative dictionary used: MedDRA 16.1	
subjects affected / exposed	17 / 52 (32.69%)
occurrences (all)	24
stomatitis	
alternative dictionary used: MedDRA 16.1	
subjects affected / exposed	4 / 52 (7.69%)
occurrences (all)	4
vomiting	
alternative dictionary used: MedDRA 16.1	

subjects affected / exposed	6 / 52 (11.54%)		
occurrences (all)	8		
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	12 / 52 (23.08%)		
occurrences (all)	12		
dyspnoea			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	9 / 52 (17.31%)		
occurrences (all)	10		
oropharyngeal pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		
productive cough			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	7 / 52 (13.46%)		
occurrences (all)	7		
Skin and subcutaneous tissue disorders			
rash			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	5 / 52 (9.62%)		
occurrences (all)	8		
back pain			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	9 / 52 (17.31%)		
occurrences (all)	9		
joint swelling			
alternative dictionary used:			

MedDRA 16.1

subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		

Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		
lower respiratory tract infection			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	3		
upper respiratory tract infection			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	3 / 52 (5.77%)		
occurrences (all)	4		

Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 16.1			
subjects affected / exposed	9 / 52 (17.31%)		
occurrences (all)	10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol?   No

Interruptions (globally)

Were there any global interruptions to the trial?   No

Limitations and caveats

 None reported