ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 06/13/2014

ClinicalTrials.gov ID: NCT00148798

Study Identification

Unique Protocol ID:	EMR 62202-046
Brief Title:	Study of Cisplatin/Vinorelbine +/- Cetuximab as First-line Treatment of Advanced Non Small Cell Lung Cancer (FLEX)
Official Title:	Open, Randomized, Controlled, Multicenter Phase III Study Comparing Cisplatin/Vinorelbine Plus Cetuximab Versus Cisplatin/ Vinorelbine as First-line Treatment for Patients With Epidermal Growth Factor Receptor Expressing (EGFR-expressing) Advanced NSCLC.
Secondary IDs:	

Study Status

Record Verification:	June 2014
Overall Status:	Completed
Study Start:	October 2004
Primary Completion:	July 2007 [Actual]
Study Completion:	May 2012 [Actual]

Sponsor/Collaborators

Sponsor:	Merck KGaA
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes

Applicable Trial?:	Section 801 Clinical Trial? No Delayed Posting? No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: EK Nr. 318/2004 Board Name: Ethik Komission der Medizinischen Universität Wien und des Allgemeinen Krankenhauses der Stadt Wien AKH Board Affiliation: Borschkegasse 8b/6, 1090 Wien, Austria Phone: +43 1 404 00 Email: ethik-kom@meduniwien.ac.at
Data Monitoring?:	Yes
Plan to Share Data?:	
Oversight Authorities:	Austria: Federal Ministry for Health and Women

Study Description

Brief Summary:	The purpose of this trial is to investigate the efficacy of cetuximab in combination with chemotherapy in comparison to chemotherapy alone in patients with advanced non small cell lung cancer who did not received prior chemotherapy. Overall survival will be taken as primary measure of efficacy.
Detailed Description:	

Conditions

Conditions:	Non Small Cell Lung Cancer (NSCLC)
Keywords:	Cetuximab Non small cell lung cancer Lung cancer Cisplatin/vinorelbine Monoclonal antibody Erbitux

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment

Number of Arms:	2
Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Efficacy Study
Enrollment:	1861 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Cetuximab plus chemotherapy cetuximab + cisplatin + vinorelbine	Drug: cetuximab + cisplatin + vinorelbine cetuximab given as an intravenous (i.v.) infusion every week (400mg/m^2 initial dose and 250mg/m^2 subsequent doses) until progressive disease (PD) + cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle.
Active Comparator: Chemotherapy alone cisplatin + vinorelbine alone	Drug: cisplatin + vinorelbine cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- Diagnosis of histologically or cytologically confirmed NSCLC, stage IIIb with documented malignant pleural effusion or stage IV
- Immunohistochemical evidence of EGFR expression on tumor tissue
- Presence of at least 1 bi-dimensionally measurable index lesion, whereby index lesions must not lie in an irradiated area

Exclusion Criteria:

- Previous exposure to monoclonal antibodies, signal transduction inhibitors or EGFR-targeting therapy
- Previous chemotherapy for NSCLC
- Documented or symptomatic brain metastasis

- Superior vena cava syndrome contra-indicating hydration
- Previous malignancy in the last 5 years except basal cell carcinoma of the skin or pre-invasive carcinoma of the cervix

Contacts/Locations

Study Officials: Robert Pirker, Professor
Study Principal Investigator
Universitätsklinik für Innere Medizin I, Wien

Locations: Austria
Research Site
Wien, Austria

Australia
Research Site
Adelaide, Australia

Research Site
Sydney, Australia

Research Site
Randwick, Australia

Research Site
Melbourne, Australia

Research Site
Wodonga, Australia

Belgium
Research Site
Bruxelles, Belgium

Research Site
Liège, Belgium

Research Site
Charleroi, Belgium

Bulgaria
Research Site
Sofia, Bulgaria

Research Site

Pleven, Bulgaria

Research Site
Veliko Tarnovo, Bulgaria

Research Site
Stara Zagora, Bulgaria

Brazil
Research Site
Porto Alegre, Brazil

Research Site
Sao Paulo, Brazil

Switzerland
Research Site
Bern, Switzerland

Research Site
Zürich, Switzerland

Research Site
Thun, Switzerland

Czech Republic
Research Site
Ostrava, Czech Republic

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Praha, Czech Republic

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Pilsen, Czech Republic

Research Site
Brno, Czech Republic

Germany
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Großhansdorf, Germany

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Gauting, Germany

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Göttingen, Germany

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Köln, Germany

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Essen, Germany

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München, Germany

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Wuppertal, Germany

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Magdeburg, Germany

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Augsburg, Germany

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Löwenstein, Germany

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Mainz, Germany

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Freiburg, Germany

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Berlin, Germany

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Halle-Dölau, Germany

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Stralsund, Germany

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Hamburg, Germany

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Heidelberg, Germany

Spain
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Madrid, Spain

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Pontevedra, Spain

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San Sebastian, Spain

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Barcelona, Spain

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Valencia, Spain

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Pamplona, Spain

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Santander, Spain

Research Site
Barakaldo (Bilbao), Spain

Research Site
Elche Alicante, Spain

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Terrassa, Spain

Research Site
Granollers, Spain

France
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Brest, France

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Grenoble, France

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Caen, France

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Strasbourg, France

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Poitiers, France

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Marseille, France

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Rennes, France

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Paris, France

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Rouen, France

Hungary
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Budapest, Hungary

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Zalegerzeg-Pózva, Hungary

Research Site
Nyiregyháza, Hungary

Research Site
Torokbalint, Hungary

Research Site
Székesfehérvár, Hungary

Research Site
Szombathely, Hungary

Hong Kong
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Honh Kong, Hong Kong

Italy
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Bologna, Italy

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Carpi, Italy

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Milano, Italy

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Treviglio, Italy

Research Site
Rome, Italy

Ireland
Research Site
Dublin, Ireland

Italy
Research Site
Rozzano-Milano, Italy

Mexico
Research Site
Mexico-City, Mexico

Research Site
Monterrey, Mexico

Netherlands
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Amsterdam, Netherlands

Research Site
Zwolle, Netherlands

Research Site
Nieuwegeln, Netherlands

Poland
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Warszawa, Poland

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Otwock, Poland

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Posnan, Poland

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Olsztyn, Poland

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Wroclaw, Poland

Research Site
Bydgoszcz, Poland

Argentina
Research Site
Buenos Aires, Argentina

Research Site
Cordoba, Argentina

Chile
Research Site
Santiago de Chile, Chile

Korea, Republic of
Research Site
Seoul, Korea, Republic of

Chile
Research Site
Antofagasta, Chile

Russian Federation
Research Site
Moscow, Russian Federation

Research Site
St. Petersburg, Russian Federation

Sweden
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Uppsala, Sweden

Research Site
Stockholm, Sweden

Singapore
Research Site
Singapore, Singapore

Slovakia
Research Site
Bratislava, Slovakia

Research Site
Banska Bystrica, Slovakia

Research Site
Nitra-Zobor, Slovakia

Research Site
Poprad, Slovakia

Taiwan
Research Site
Taipei, Tao Yuan County, Taiwan

Research Site
Taipei, Taiwan

Turkey
Research Site
Ankara, Turkey

United Kingdom
Research Site
London, United Kingdom

Research Site
Sutton, United Kingdom

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Edinburgh, United Kingdom

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Bristol, United Kingdom

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Wolverhampton, United Kingdom

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Newcastle upon Tyne, United Kingdom

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Leicester, United Kingdom

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Aberdeen, United Kingdom

Research Site
Poole, United Kingdom

Ukraine

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Dnipropetrovsk, Ukraine

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Kyiv, Ukraine

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Kharkiv, Ukraine

Research Site
Sumy, Ukraine

Research Site
Poltava, Ukraine

Research Site
Ternopol, Ukraine

Research Site
Uzhgorod, Ukraine

Research Site
Lviv, Ukraine

References

Citations: [Study Results] Pirker R, Pereira JR, Szczesna A, von Pawel J, Krzakowski M, Ramlau R, Vynnychenko I, Park K, Yu CT, Ganul V, Roh JK, Bajetta E, O'Byrne K, de Marinis F, Eberhardt W, Goddemeier T, Emig M, Gatzemeier U; FLEX Study Team. Cetuximab plus chemotherapy in patients with advanced non-small-cell lung cancer (FLEX): an open-label randomised phase III trial. Lancet. 2009 May 2;373(9674):1525-31. doi: 10.1016/S0140-6736(09)60569-9. PubMed 19410716

Links:

Study Data/Documents:

Participant Flow

Recruitment Details	First/last subject (informed consent): October 2004/January 2006. Clinical data cut-off: 18 July 2007. Last subject completed 16 May 2012. Subjects randomized at 155 centers; Asia/Australia: 21; Europe: 120; South America: 14.
Pre-Assignment Details	Enrolled: 1,861 after consent to epidermal growth factor receptor (EGFR) assessment; 603 excluded (mainly non-fulfillment of inclusion or exclusion criteria). 1,258 screened for eligibility after consent for study procedures; 143 excluded (mainly non-fulfillment of inclusion or exclusion criteria). 1,125 subjects randomized.

Reporting Groups

	Description
Cetuximab Plus Chemotherapy	cetuximab given as an intravenous (i.v.) infusion every week (400mg/m^2 initial dose and 250mg/m^2 subsequent doses) until progressive disease (PD) + cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.
Chemotherapy Alone	cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.

Overall Study

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
Started	557 [1]	568 [2]
Completed	557	568
Not Completed	0	0

[1] Intent To Treat (ITT) Population
[2] ITT Population

Baseline Characteristics

Reporting Groups

	Description
Cetuximab Plus Chemotherapy	cetuximab given as an intravenous (i.v.) infusion every week (400mg/m^2 initial dose and 250mg/m^2 subsequent doses) until progressive disease (PD) + cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.
Chemotherapy Alone	cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.

Baseline Measures

	Cetuximab Plus Chemotherapy	Chemotherapy Alone	Total
Number of Participants	557	568	1125
Age, Continuous [units: years] Median (Full Range)	59 (18 to 78)	60 (20 to 83)	59 (18 to 83)
Age, Customized [units: participants]			
<18 years	0	0	0
Between 18 and 65 years	385	389	774
>=65 years	172	179	351
Gender, Male/Female [units: participants]			
Female	172	163	335
Male	385	405	790
Region of Enrollment [units: participants]			
Australia	20	23	43
Hong Kong	2	2	4
Singapore	5	5	10
Korea, Republic of	28	26	54

	Cetuximab Plus Chemotherapy	Chemotherapy Alone	Total
Taiwan	21	22	43
Austria	9	7	16
Belgium	3	10	13
Bulgaria	12	12	24
Czech Republic	12	17	29
France	25	25	50
Germany	91	88	179
Hungary	21	23	44
Ireland	3	4	7
Netherlands	10	10	20
Poland	59	50	109
Portugal	3	0	3
Russian Federation	23	16	39
Slovakia	8	12	20
Spain	16	13	29
Sweden	6	3	9
Switzerland	10	6	16
Turkey	1	2	3
United Kingdom	23	21	44
Ukraine	56	71	127
Chile	10	16	26
Italy	18	23	41
Argentina	5	2	7
Mexico	9	8	17
Brazil	48	51	99

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Overall Survival Time (OS)
Measure Description	Time from randomization to death. Patients without event are censored at the last date known to be alive or at the clinical cut-off date, whatever is earlier.
Time Frame	Time from randomisation to death or last day known to be alive, reported between day of first patient randomised, Oct 2004, until cut-off date 18 Jul 2007
Safety Issue?	No

Analysis Population Description

ITT

Reporting Groups

	Description
Cetuximab Plus Chemotherapy	cetuximab given as an intravenous (i.v.) infusion every week (400mg/m^2 initial dose and 250mg/m^2 subsequent doses) until progressive disease (PD) + cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.
Chemotherapy Alone	cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.

Measured Values

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
Number of Participants Analyzed	557	568
Overall Survival Time (OS) [units: months] Median (95% Confidence Interval)	11.3 (9.4 to 12.4)	10.1 (9.1 to 10.9)

Statistical Analysis 1 for Overall Survival Time (OS)

Statistical Analysis Overview	Comparison Groups	Cetuximab Plus Chemotherapy, Chemotherapy Alone
	Comments	Primary efficacy analysis: To test equality of OS time between treatment groups, applying the two-sided stratified log-rank test (Stage IIIb vs IV, ECOG 0/1 vs 2) (α=5%).

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0441
	Comments	[Not specified]
	Method	Other [Stratified Log Rank]
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Progression-free Survival Time
Measure Description	Duration from randomization until radiological progression (based on modified World Health Organisation (WHO) criteria) or death due to any cause. Only deaths within 60 days of last tumor assessment are considered. Patients without event are censored on the date of last tumor assessment.
Time Frame	Time from randomization to disease progression, death or last tumor assessment, reported between day of first patient randomised, Oct 2004, until cut-off date 18 Jul 2007
Safety Issue?	No

Analysis Population Description

ITT

Reporting Groups

	Description
Cetuximab Plus Chemotherapy	cetuximab given as an intravenous (i.v.) infusion every week (400mg/m^2 initial dose and 250mg/m^2 subsequent doses) until progressive disease (PD) + cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.
Chemotherapy Alone	cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.

Measured Values

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
Number of Participants Analyzed	557	568
Progression-free Survival Time [units: months] Median (95% Confidence Interval)	4.8 (4.2 to 5.3)	4.8 (4.4 to 5.4)

Statistical Analysis 1 for Progression-free Survival Time

Statistical Analysis Overview	Comparison Groups	Cetuximab Plus Chemotherapy, Chemotherapy Alone
	Comments	To test equality of progression free survival time between treatment groups, applying the two-sided stratified log-rank test (α=5%).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3869
	Comments	[Not specified]
	Method	Other [Stratified Log Rank]
	Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Best Overall Response Rate
Measure Description	The best overall response rate is defined as the proportion of subjects having achieved confirmed Complete Response + Partial Response as the best overall response according to radiological assessments (based on modified WHO criteria).
Time Frame	Evaluations were performed every 6 weeks until progression, reported between day of first patient randomised, Oct 2004, until cut-off date 18 Jul 2007
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Cetuximab Plus Chemotherapy	cetuximab given as an intravenous (i.v.) infusion every week (400mg/m^2 initial dose and 250mg/m^2 subsequent doses) until progressive disease (PD) + cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.
Chemotherapy Alone	cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.

Measured Values

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
Number of Participants Analyzed	557	568
Best Overall Response Rate [units: percentage of participants] Number (95% Confidence Interval)	36.4 (32.4 to 40.6)	29.2 (25.5 to 33.2)

Statistical Analysis 1 for Best Overall Response Rate

Statistical Analysis Overview	Comparison Groups	Cetuximab Plus Chemotherapy, Chemotherapy Alone
	Comments	The best overall response rate was compared in the Cochran-Mantel-Haenszel test (two-sided with α=5%).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0101
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

4. Secondary Outcome Measure:

Measure Title	Disease Control Rate

Measure Description	The disease control rate is defined as the proportion of subjects having achieved confirmed Complete Response + Partial Response + Stable Disease as best overall response according to radiological assessments (based on modified WHO criteria).
Time Frame	Evaluations were performed every 6 weeks until progression, reported between day of first patient randomised, Oct 2004, until cut-off date 18 Jul 2007
Safety Issue?	No

Analysis Population Description

ITT

Reporting Groups

	Description
Cetuximab Plus Chemotherapy	cetuximab given as an intravenous (i.v.) infusion every week (400mg/m^2 initial dose and 250mg/m^2 subsequent doses) until progressive disease (PD) + cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.
Chemotherapy Alone	cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.

Measured Values

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
Number of Participants Analyzed	557	568
Disease Control Rate [units: percentage of participants] Number (95% Confidence Interval)	72.5 (68.6 to 76.2)	71.5 (67.6 to 75.2)

Statistical Analysis 1 for Disease Control Rate

Statistical Analysis Overview	Comparison Groups	Cetuximab Plus Chemotherapy, Chemotherapy Alone
	Comments	The disease control rate was compared in the Cochran-Mantel-Haenszel test (two-sided with α=5%).
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6801
	Comments	[Not specified]
	Method	Cochran-Mantel-Haenszel
	Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Quality of Life (QOL) Assessment European Organisation for the Research and Treatment of Cancer (EORTC) QLQ-C30 Global Health Status
Measure Description	Mean global health status scores (EORTC QLQ-C30) against time for each treatment group. Scores were derived from mutually exclusive sets of items, with scale scores ranging from 0 to 100 after a linear transformation. Higher scores indicate a better QoL.
Time Frame	at baseline, at cycle 3, at month 6, reported between day of first patient randomised, Oct 2004, until cut-off date 18 Jul 2007
Safety Issue?	No

Analysis Population Description

670 subjects completed (348 in the cetuximab + chemotherapy arm and 322 in the chemotherapy alone arm) at least 1 evaluable QLQ-C30 questionnaire and were included in the Evaluable population. Numbers at each timepoint were (Cetuximab + chemotherapy/Chemotherapy alone, respectively): baseline 278/274; cycle 3 184/153; 6 month 102/96

Reporting Groups

	Description
Cetuximab Plus Chemotherapy	cetuximab given as an intravenous (i.v.) infusion every week (400mg/m^2 initial dose and 250mg/m^2 subsequent doses) until progressive disease (PD) + cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.
Chemotherapy Alone	cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.

Measured Values

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
Number of Participants Analyzed	348	322

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
Quality of Life (QOL) Assessment European Organisation for the Research and Treatment of Cancer (EORTC) QLQ-C30 Global Health Status [units: scores on a scale] Least Squares Mean (Standard Error)		
At baseline	45.72 (2.164)	46.36 (2.138)
At cycle 3	48.33 (2.325)	51.55 (2.464)
At month 6	54.71 (2.729)	52.92 (2.787)

6. Secondary Outcome Measure:

Measure Title	Quality of Life Assessment (EORTC QLQ-C30) Social Functioning
Measure Description	Mean social functioning scores (EORTC QLQ-C30) against time for each treatment group. Scores were derived from mutually exclusive sets of items, with scale scores ranging from 0 to 100 after a linear transformation. Higher scores indicate a higher level of functioning.
Time Frame	at baseline, at cycle 3, at month 6, reported between day of first patient randomised, Oct 2004, until cut-off date 18 Jul 2007
Safety Issue?	No

Analysis Population Description

670 subjects completed (348 in the cetuximab + chemotherapy arm and 322 in the chemotherapy alone arm) at least 1 evaluable QLQ-C30 questionnaire and were included in the Evaluable population. Numbers at each timepoint were (Cetuximab + chemotherapy/Chemotherapy alone, respectively): baseline 280/275; cycle 3 185/153; 6 month 101/97

Reporting Groups

	Description
Cetuximab Plus Chemotherapy	cetuximab given as an intravenous (i.v.) infusion every week (400mg/m^2 initial dose and 250mg/m^2 subsequent doses) until progressive disease (PD) + cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.
Chemotherapy Alone	cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.

Measured Values

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
Number of Participants Analyzed	348	322
Quality of Life Assessment (EORTC QLQ-C30) Social Functioning [units: scores on a scale] Least Squares Mean (Standard Error)		
At baseline	66.17 (2.836)	64.73 (2.825)
At cycle 3	58.05 (2.995)	67.13 (3.138)
At month 6	67.36 (3.449)	66.47 (3.515)

7. Secondary Outcome Measure:

Measure Title	A Population Pharmacokinetic (PK) Analysis for Cetuximab in Non-Small Cell Lung Cancer (NSCLC) - Serum Cetuximab Concentrations
Measure Description	Population PK analysis was conducted using non-linear mixed effects modeling (NONMEM) software, integrating the PK data from this study and the Phase II study EMR 62 202-011.
Time Frame	Week 1, Day 1: baseline and end of infusion; Week 7, Day 43: within 12 h after cetuximab administration.
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Cetuximab Concentration at End of Infusion Week 1	
Cetuximab Concentration Before Infusion Week 7	

Measured Values

	Cetuximab Concentration at End of Infusion Week 1	Cetuximab Concentration Before Infusion Week 7
Number of Participants Analyzed	454	298

	Cetuximab Concentration at End of Infusion Week 1	Cetuximab Concentration Before Infusion Week 7
A Population Pharmacokinetic (PK) Analysis for Cetuximab in Non-Small Cell Lung Cancer (NSCLC) - Serum Cetuximab Concentrations [units: ug/mL] Mean (Standard Deviation)	223.1 (64.6)	51.5 (33.1)

8. Secondary Outcome Measure:

Measure Title	Safety - Number of Patients Experiencing Any Adverse Event
Measure Description	Please refer to Adverse Events section for further details
Time Frame	time from first dose up to 30 after last dose of study treatment, reported between day of first patient randomised, Oct 2004, until cut-off date 18 Jul 2007
Safety Issue?	Yes

Analysis Population Description

Safety Population

Reporting Groups

	Description
Cetuximab Plus Chemotherapy	cetuximab given as an intravenous (i.v.) infusion every week (400mg/m^2 initial dose and 250mg/m^2 subsequent doses) until progressive disease (PD) + cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.
Chemotherapy Alone	cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.

Measured Values

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
Number of Participants Analyzed	548	562
Safety - Number of Patients Experiencing Any Adverse Event [units: participants]	545	549

Reported Adverse Events

Time Frame	Time from first dose up to 30 days after the last dose of study treatment.
Additional Description	Treatment-emergent adverse events were defined as those with onset occurring at or after the first dosing day of study medication and up to 30 days after the last administration of any study drug or the clinical cut-off date.

Reporting Groups

	Description
Cetuximab Plus Chemotherapy	cetuximab given as an intravenous (i.v.) infusion every week (400mg/m^2 initial dose and 250mg/m^2 subsequent doses) until progressive disease (PD) + cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.
Chemotherapy Alone	cisplatin 80mg/m^2 i.v. infusion on day 1 of each 3-week cycle + vinorelbine 25mg/m^2 i.v. infusion on days 1 and 8 of each 3-week cycle. Safety population: includes all treated subjects.

Serious Adverse Events

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Total	325/548 (59.31%)	244/562 (43.42%)
Blood and lymphatic system disorders		
Anaemia [A] †	11/548 (2.01%)	12/562 (2.14%)
Febrile bone marrow aplasia [A] †	4/548 (0.73%)	0/562 (0%)
Febrile neutropenia [A] †	96/548 (17.52%)	67/562 (11.92%)
Granulocytopenia [A] †	2/548 (0.36%)	1/562 (0.18%)
Leukopenia [A] †	15/548 (2.74%)	8/562 (1.42%)
Neutropenia [A] †	47/548 (8.58%)	33/562 (5.87%)
Pancytopenia [A] †	2/548 (0.36%)	0/562 (0%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Cardiac disorders		
Acute myocardial infarction [A] †	4/548 (0.73%)	0/562 (0%)
Angina pectoris [A] †	0/548 (0%)	1/562 (0.18%)
Arrhythmia supraventricular [A] †	1/548 (0.18%)	0/562 (0%)
Atrial fibrillation [A] †	0/548 (0%)	4/562 (0.71%)
Cardiac arrest [A] †	0/548 (0%)	2/562 (0.36%)
Cardiac failure [A] †	1/548 (0.18%)	2/562 (0.36%)
Cardiac failure acute [A] †	2/548 (0.36%)	0/562 (0%)
Cardiac tamponade [A] †	1/548 (0.18%)	0/562 (0%)
Cardio-respiratory arrest [A] †	1/548 (0.18%)	0/562 (0%)
Cardiogenic shock [A] †	1/548 (0.18%)	0/562 (0%)
Cardiopulmonary failure [A] †	3/548 (0.55%)	3/562 (0.53%)
Left ventricular failure [A] †	2/548 (0.36%)	0/562 (0%)
Microvascular angina [A] †	1/548 (0.18%)	0/562 (0%)
Myocardial infarction [A] †	2/548 (0.36%)	1/562 (0.18%)
Myocardial ischaemia [A] †	1/548 (0.18%)	1/562 (0.18%)
Palpitations [A] †	1/548 (0.18%)	0/562 (0%)
Pericardial effusion [A] †	2/548 (0.36%)	2/562 (0.36%)
Right ventricular failure [A] †	0/548 (0%)	1/562 (0.18%)
Supraventricular tachycardia [A] †	0/548 (0%)	2/562 (0.36%)
Tachycardia [A] †	0/548 (0%)	1/562 (0.18%)
Tricuspid valve incompetence [A] †	0/548 (0%)	1/562 (0.18%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Ventricular fibrillation [A] †	1/548 (0.18%)	1/562 (0.18%)
Congenital, familial and genetic disorders		
Tracheo-oesophageal fistula [A] †	1/548 (0.18%)	0/562 (0%)
Ear and labyrinth disorders		
Deafness [A] †	0/548 (0%)	1/562 (0.18%)
Vertigo [A] †	0/548 (0%)	1/562 (0.18%)
Eye disorders		
Retinal detachment [A] †	1/548 (0.18%)	1/562 (0.18%)
Gastrointestinal disorders		
Abdominal distension [A] †	1/548 (0.18%)	0/562 (0%)
Abdominal pain [A] †	6/548 (1.09%)	8/562 (1.42%)
Abdominal pain upper [A] †	2/548 (0.36%)	1/562 (0.18%)
Anal ulcer [A] †	1/548 (0.18%)	0/562 (0%)
Colitis [A] †	1/548 (0.18%)	0/562 (0%)
Constipation [A] †	5/548 (0.91%)	6/562 (1.07%)
Diarrhoea [A] †	8/548 (1.46%)	5/562 (0.89%)
Dyspepsia [A] †	1/548 (0.18%)	0/562 (0%)
Dysphagia [A] †	2/548 (0.36%)	0/562 (0%)
Enteritis [A] †	1/548 (0.18%)	0/562 (0%)
Faecaloma [A] †	0/548 (0%)	1/562 (0.18%)
Gastric ulcer [A] †	1/548 (0.18%)	0/562 (0%)
Gastrointestinal haemorrhage [A] †	0/548 (0%)	2/562 (0.36%)
Haematemesis [A] †	2/548 (0.36%)	0/562 (0%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Ileus paralytic [A] †	1/548 (0.18%)	0/562 (0%)
Intestinal obstruction [A] †	1/548 (0.18%)	0/562 (0%)
Intestinal perforation [A] †	1/548 (0.18%)	0/562 (0%)
Melaena [A] †	0/548 (0%)	1/562 (0.18%)
Nausea [A] †	6/548 (1.09%)	5/562 (0.89%)
Odynophagia [A] †	1/548 (0.18%)	0/562 (0%)
Oesophagitis [A] †	3/548 (0.55%)	1/562 (0.18%)
Vomiting [A] †	16/548 (2.92%)	14/562 (2.49%)
General disorders		
Asthenia [A] †	4/548 (0.73%)	2/562 (0.36%)
Chest discomfort [A] †	0/548 (0%)	2/562 (0.36%)
Chest pain [A] †	7/548 (1.28%)	6/562 (1.07%)
Death [A] †	2/548 (0.36%)	0/562 (0%)
Drug interaction [A] †	1/548 (0.18%)	0/562 (0%)
Fatigue [A] †	5/548 (0.91%)	2/562 (0.36%)
Gait disturbance [A] †	0/548 (0%)	1/562 (0.18%)
General physical health deterioration [A] †	22/548 (4.01%)	4/562 (0.71%)
Injection site reaction [A] †	1/548 (0.18%)	0/562 (0%)
Malaise [A] †	1/548 (0.18%)	1/562 (0.18%)
Mucosal inflammation [A] †	2/548 (0.36%)	1/562 (0.18%)
Multi-organ failure [A] †	0/548 (0%)	1/562 (0.18%)
Oedema [A] †	1/548 (0.18%)	0/562 (0%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Pain [A] †	1/548 (0.18%)	1/562 (0.18%)
Performance status decreased [A] †	0/548 (0%)	1/562 (0.18%)
Pyrexia [A] †	16/548 (2.92%)	6/562 (1.07%)
Sudden death [A] †	2/548 (0.36%)	0/562 (0%)
Hepatobiliary disorders		
Hepatic pain [A] †	1/548 (0.18%)	0/562 (0%)
Hyperbilirubinaemia [A] †	2/548 (0.36%)	0/562 (0%)
Immune system disorders		
Anaphylactic reaction [A] †	3/548 (0.55%)	0/562 (0%)
Anaphylactic shock [A] †	2/548 (0.36%)	0/562 (0%)
Drug hypersensitivity [A] †	1/548 (0.18%)	0/562 (0%)
Hypersensitivity [A] †	5/548 (0.91%)	1/562 (0.18%)
Serum sickness [A] †	1/548 (0.18%)	0/562 (0%)
Infections and infestations		
Anal abscess [A] †	0/548 (0%)	1/562 (0.18%)
Bacteraemia [A] †	1/548 (0.18%)	0/562 (0%)
Bacterial sepsis [A] †	0/548 (0%)	1/562 (0.18%)
Brain abscess [A] †	1/548 (0.18%)	0/562 (0%)
Bronchitis [A] †	2/548 (0.36%)	2/562 (0.36%)
Bronchitis bacterial [A] †	1/548 (0.18%)	0/562 (0%)
Bronchopneumonia [A] †	1/548 (0.18%)	1/562 (0.18%)
Catheter related infection [A] †	3/548 (0.55%)	0/562 (0%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Cellulitis [A] †	4/548 (0.73%)	0/562 (0%)
Central line infection [A] †	1/548 (0.18%)	1/562 (0.18%)
Clostridial infection [A] †	0/548 (0%)	1/562 (0.18%)
Clostridium difficile colitis [A] †	1/548 (0.18%)	0/562 (0%)
Dengue fever [A] †	0/548 (0%)	1/562 (0.18%)
Diverticulitis [A] †	0/548 (0%)	1/562 (0.18%)
Febrile infection [A] †	2/548 (0.36%)	0/562 (0%)
Gangrene [A] †	1/548 (0.18%)	0/562 (0%)
Gastroenteritis [A] †	0/548 (0%)	1/562 (0.18%)
Infection [A] †	3/548 (0.55%)	1/562 (0.18%)
Laryngitis [A] †	1/548 (0.18%)	0/562 (0%)
Laryngotracheo bronchitis [A] †	1/548 (0.18%)	0/562 (0%)
Lobar pneumonia [A] †	1/548 (0.18%)	0/562 (0%)
Lower respiratory tract infection [A] †	4/548 (0.73%)	2/562 (0.36%)
Lung abscess [A] †	1/548 (0.18%)	1/562 (0.18%)
Lung infection [A] †	2/548 (0.36%)	1/562 (0.18%)
Nasopharyngitis [A] †	1/548 (0.18%)	0/562 (0%)
Neutropenic infection [A] †	9/548 (1.64%)	5/562 (0.89%)
Neutropenic sepsis [A] †	9/548 (1.64%)	5/562 (0.89%)
Parotitis [A] †	1/548 (0.18%)	0/562 (0%)
Peritonsillar abscess [A] †	0/548 (0%)	1/562 (0.18%)
Pharyngitis [A] †	1/548 (0.18%)	0/562 (0%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Pharyngotonsillitis [A] †	1/548 (0.18%)	0/562 (0%)
Pneumonia [A] †	19/548 (3.47%)	13/562 (2.31%)
Pneumonia necrotising [A] †	1/548 (0.18%)	0/562 (0%)
Pneumonia streptococcal [A] †	1/548 (0.18%)	0/562 (0%)
Postoperative wound infection [A] †	0/548 (0%)	1/562 (0.18%)
Pulmonary tuberculosis [A] †	1/548 (0.18%)	1/562 (0.18%)
Pyothorax [A] †	1/548 (0.18%)	0/562 (0%)
Respiratory tract infection [A] †	2/548 (0.36%)	2/562 (0.36%)
Sepsis [A] †	9/548 (1.64%)	3/562 (0.53%)
Septic shock [A] †	6/548 (1.09%)	0/562 (0%)
Staphylococcal infection [A] †	1/548 (0.18%)	0/562 (0%)
Staphylococcal sepsis [A] †	1/548 (0.18%)	0/562 (0%)
Urinary tract infection [A] †	1/548 (0.18%)	0/562 (0%)
Wound infection [A] †	1/548 (0.18%)	0/562 (0%)
Injury, poisoning and procedural complications		
Femoral neck fracture [A] †	1/548 (0.18%)	0/562 (0%)
Femur fracture [A] †	1/548 (0.18%)	0/562 (0%)
Lumbar vertebral fracture [A] †	2/548 (0.36%)	0/562 (0%)
Overdose [A] †	0/548 (0%)	1/562 (0.18%)
Investigations		
Aspiration bronchial [A] †	1/548 (0.18%)	0/562 (0%)
Blood creatinine increased [A] †	5/548 (0.91%)	4/562 (0.71%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Blood glucose abnormal [A] †	0/548 (0%)	1/562 (0.18%)
Blood potassium decreased [A] †	0/548 (0%)	1/562 (0.18%)
Blood urea increased [A] †	1/548 (0.18%)	0/562 (0%)
C-reactive protein increased [A] †	2/548 (0.36%)	0/562 (0%)
Karnofsky scale worsened [A] †	1/548 (0.18%)	0/562 (0%)
Neutrophil count decreased [A] †	1/548 (0.18%)	0/562 (0%)
Pulmonary arterial pressure increased [A] †	0/548 (0%)	1/562 (0.18%)
Weight decreased [A] †	0/548 (0%)	1/562 (0.18%)
White blood cell count decreased [A] †	2/548 (0.36%)	1/562 (0.18%)
Metabolism and nutrition disorders		
Anorexia [A] †	4/548 (0.73%)	2/562 (0.36%)
Dehydration [A] †	12/548 (2.19%)	9/562 (1.6%)
Diabetes mellitus [A] †	1/548 (0.18%)	0/562 (0%)
Fluid overload [A] †	0/548 (0%)	1/562 (0.18%)
Hypercreatininaemia [A] †	1/548 (0.18%)	0/562 (0%)
Hyperglycaemia [A] †	1/548 (0.18%)	0/562 (0%)
Hyperkalaemia [A] †	2/548 (0.36%)	0/562 (0%)
Hypocalcaemia [A] †	1/548 (0.18%)	0/562 (0%)
Hypoglycaemia [A] †	1/548 (0.18%)	0/562 (0%)
Hypokalaemia [A] †	4/548 (0.73%)	0/562 (0%)
Hypomagnesaemia [A] †	1/548 (0.18%)	0/562 (0%)
Hyponatraemia [A] †	2/548 (0.36%)	1/562 (0.18%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Metabolic acidosis [A] †	1/548 (0.18%)	0/562 (0%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	1/548 (0.18%)	0/562 (0%)
Back pain [A] †	2/548 (0.36%)	0/562 (0%)
Bone pain [A] †	0/548 (0%)	1/562 (0.18%)
Muscular weakness [A] †	0/548 (0%)	2/562 (0.36%)
Musculoskeletal pain [A] †	2/548 (0.36%)	1/562 (0.18%)
Neck pain [A] †	1/548 (0.18%)	0/562 (0%)
Pathological fracture [A] †	2/548 (0.36%)	0/562 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Malignant neoplasm progression [A] †	1/548 (0.18%)	0/562 (0%)
Metastases to heart [A] †	1/548 (0.18%)	0/562 (0%)
Metastases to meninges [A] †	1/548 (0.18%)	0/562 (0%)
Neoplasm progression [A] †	1/548 (0.18%)	0/562 (0%)
Testis cancer [A] †	1/548 (0.18%)	0/562 (0%)
Tumour pain [A] †	2/548 (0.36%)	0/562 (0%)
Nervous system disorders		
Altered state of consciousness [A] †	0/548 (0%)	1/562 (0.18%)
Cerebellar syndrome [A] †	0/548 (0%)	1/562 (0.18%)
Cerebral artery embolism [A] †	1/548 (0.18%)	0/562 (0%)
Cerebral haemorrhage [A] †	0/548 (0%)	2/562 (0.36%)
Cerebral infarction [A] †	0/548 (0%)	2/562 (0.36%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Cerebral ischaemia [A] †	3/548 (0.55%)	0/562 (0%)
Cerebrovascular accident [A] †	2/548 (0.36%)	5/562 (0.89%)
Cognitive disorder [A] †	1/548 (0.18%)	0/562 (0%)
Coma [A] †	1/548 (0.18%)	0/562 (0%)
Convulsion [A] †	3/548 (0.55%)	0/562 (0%)
Coordination abnormal [A] †	1/548 (0.18%)	1/562 (0.18%)
Depressed level of consciousness [A] †	0/548 (0%)	1/562 (0.18%)
Dizziness [A] †	2/548 (0.36%)	0/562 (0%)
Dysarthria [A] †	0/548 (0%)	1/562 (0.18%)
Embolic cerebral infarction [A] †	0/548 (0%)	1/562 (0.18%)
Epilepsy [A] †	0/548 (0%)	1/562 (0.18%)
Headache [A] †	1/548 (0.18%)	0/562 (0%)
Hemiparesis [A] †	0/548 (0%)	1/562 (0.18%)
Hemiplegia [A] †	1/548 (0.18%)	0/562 (0%)
Horner's syndrome [A] †	1/548 (0.18%)	0/562 (0%)
Monoparesis [A] †	1/548 (0.18%)	0/562 (0%)
Nervous system disorder [A] †	0/548 (0%)	1/562 (0.18%)
Neuralgia [A] †	1/548 (0.18%)	0/562 (0%)
Paraparesis [A] †	0/548 (0%)	2/562 (0.36%)
Paraplegia [A] †	0/548 (0%)	1/562 (0.18%)
Somnolence [A] †	1/548 (0.18%)	0/562 (0%)
Speech disorder [A] †	2/548 (0.36%)	0/562 (0%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Spinal cord compression [A] †	1/548 (0.18%)	1/562 (0.18%)
Syncope [A] †	1/548 (0.18%)	2/562 (0.36%)
Syncope vasovagal [A] †	1/548 (0.18%)	1/562 (0.18%)
Transverse sinus thrombosis [A] †	1/548 (0.18%)	0/562 (0%)
Psychiatric disorders		
Agitation [A] †	0/548 (0%)	1/562 (0.18%)
Confusional state [A] †	5/548 (0.91%)	4/562 (0.71%)
Depression [A] †	0/548 (0%)	1/562 (0.18%)
Hallucination [A] †	0/548 (0%)	1/562 (0.18%)
Mental disorder [A] †	0/548 (0%)	1/562 (0.18%)
Renal and urinary disorders		
Renal colic [A] †	1/548 (0.18%)	0/562 (0%)
Renal failure [A] †	6/548 (1.09%)	6/562 (1.07%)
Renal failure acute [A] †	1/548 (0.18%)	1/562 (0.18%)
Renal impairment [A] †	2/548 (0.36%)	0/562 (0%)
Respiratory, thoracic and mediastinal disorders		
Acute pulmonary oedema [A] †	1/548 (0.18%)	0/562 (0%)
Acute respiratory distress syndrome [A] †	1/548 (0.18%)	0/562 (0%)
Acute respiratory failure [A] †	0/548 (0%)	1/562 (0.18%)
Apnoea [A] †	2/548 (0.36%)	0/562 (0%)
Cough [A] †	0/548 (0%)	1/562 (0.18%)
Dyspnoea [A] †	18/548 (3.28%)	13/562 (2.31%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Haemoptysis [A] †	3/548 (0.55%)	6/562 (1.07%)
Hypoxia [A] †	0/548 (0%)	2/562 (0.36%)
Lung infiltration [A] †	1/548 (0.18%)	1/562 (0.18%)
Pleural effusion [A] †	2/548 (0.36%)	4/562 (0.71%)
Pneumonitis [A] †	1/548 (0.18%)	1/562 (0.18%)
Pneumothorax [A] †	1/548 (0.18%)	3/562 (0.53%)
Pulmonary embolism [A] †	20/548 (3.65%)	13/562 (2.31%)
Pulmonary haemorrhage [A] †	1/548 (0.18%)	2/562 (0.36%)
Pulmonary oedema [A] †	1/548 (0.18%)	2/562 (0.36%)
Respiratory distress [A] †	1/548 (0.18%)	0/562 (0%)
Respiratory failure [A] †	14/548 (2.55%)	9/562 (1.6%)
Respiratory tract haemorrhage [A] †	0/548 (0%)	1/562 (0.18%)
Skin and subcutaneous tissue disorders		
Erythema [A] †	1/548 (0.18%)	0/562 (0%)
Rash [A] †	4/548 (0.73%)	0/562 (0%)
Rash maculo-papular [A] †	1/548 (0.18%)	0/562 (0%)
Vascular disorders		
Arterial occlusive disease [A] †	0/548 (0%)	2/562 (0.36%)
Arterial thrombosis [A] †	1/548 (0.18%)	0/562 (0%)
Axillary vein thrombosis [A] †	1/548 (0.18%)	0/562 (0%)
Deep vein thrombosis [A] †	9/548 (1.64%)	3/562 (0.53%)
Embolism [A] †	0/548 (0%)	1/562 (0.18%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Haematoma [A] †	1/548 (0.18%)	0/562 (0%)
Hypertension [A] †	1/548 (0.18%)	1/562 (0.18%)
Hypertensive crisis [A] †	1/548 (0.18%)	1/562 (0.18%)
Hypotension [A] †	5/548 (0.91%)	0/562 (0%)
Iliac artery occlusion [A] †	1/548 (0.18%)	0/562 (0%)
Jugular vein thrombosis [A] †	0/548 (0%)	1/562 (0.18%)
Pelvic venous thrombosis [A] †	1/548 (0.18%)	0/562 (0%)
Peripheral ischaemia [A] †	1/548 (0.18%)	0/562 (0%)
Phlebitis [A] †	0/548 (0%)	2/562 (0.36%)
Shock [A] †	1/548 (0.18%)	0/562 (0%)
Superior vena caval occlusion [A] †	1/548 (0.18%)	2/562 (0.36%)
Thrombosis [A] †	2/548 (0.36%)	2/562 (0.36%)
Varicose vein [A] †	0/548 (0%)	1/562 (0.18%)
Vascular fragility [A] †	0/548 (0%)	1/562 (0.18%)
Vasculitis [A] †	1/548 (0.18%)	0/562 (0%)
Vena cava thrombosis [A] †	0/548 (0%)	1/562 (0.18%)
Venous thrombosis [A] †	1/548 (0.18%)	1/562 (0.18%)
Visceral arterial ischaemia [A] †	1/548 (0.18%)	0/562 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (Unspecified)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Total	532/548 (97.08%)	537/562 (95.55%)
Blood and lymphatic system disorders		
Anaemia [A] †	226/548 (41.24%)	264/562 (46.98%)
Febrile neutropenia [A] †	36/548 (6.57%)	32/562 (5.69%)
Leukopenia [A] †	176/548 (32.12%)	155/562 (27.58%)
Neutropenia [A] †	302/548 (55.11%)	324/562 (57.65%)
Thrombocytopenia [A] †	23/548 (4.2%)	30/562 (5.34%)
Ear and labyrinth disorders		
Tinnitus [A] †	49/548 (8.94%)	55/562 (9.79%)
Eye disorders		
Conjunctivitis [A] †	33/548 (6.02%)	6/562 (1.07%)
Gastrointestinal disorders		
Abdominal pain [A] †	72/548 (13.14%)	72/562 (12.81%)
Abdominal pain upper [A] †	45/548 (8.21%)	37/562 (6.58%)
Constipation [A] †	204/548 (37.23%)	189/562 (33.63%)
Diarrhoea [A] †	126/548 (22.99%)	103/562 (18.33%)
Dyspepsia [A] †	68/548 (12.41%)	55/562 (9.79%)
Dysphagia [A] †	31/548 (5.66%)	7/562 (1.25%)
Nausea [A] †	291/548 (53.1%)	303/562 (53.91%)
Stomatitis [A] †	85/548 (15.51%)	27/562 (4.8%)
Vomiting [A] †	214/548 (39.05%)	225/562 (40.04%)
General disorders		

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Asthenia [A] †	90/548 (16.42%)	96/562 (17.08%)
Chest pain [A] †	70/548 (12.77%)	70/562 (12.46%)
Chills [A] †	35/548 (6.39%)	19/562 (3.38%)
Fatigue [A] †	202/548 (36.86%)	181/562 (32.21%)
Injection site reaction [A] †	33/548 (6.02%)	29/562 (5.16%)
Mucosal inflammation [A] †	56/548 (10.22%)	23/562 (4.09%)
Oedema peripheral [A] †	29/548 (5.29%)	39/562 (6.94%)
Pyrexia [A] †	112/548 (20.44%)	80/562 (14.23%)
Infections and infestations		
Nasopharyngitis [A] †	37/548 (6.75%)	16/562 (2.85%)
Paronychia [A] †	46/548 (8.39%)	0/562 (0%)
Investigations		
Blood creatinine increased [A] †	47/548 (8.58%)	49/562 (8.72%)
Weight decreased [A] †	75/548 (13.69%)	50/562 (8.9%)
White blood cell count decreased [A] †	36/548 (6.57%)	26/562 (4.63%)
Metabolism and nutrition disorders		
Anorexia [A] †	208/548 (37.96%)	202/562 (35.94%)
Hypocalcaemia [A] †	31/548 (5.66%)	10/562 (1.78%)
Hypokalaemia [A] †	75/548 (13.69%)	49/562 (8.72%)
Hypomagnesaemia [A] †	54/548 (9.85%)	27/562 (4.8%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	30/548 (5.47%)	22/562 (3.91%)
Back pain [A] †	39/548 (7.12%)	44/562 (7.83%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Bone pain [A] †	29/548 (5.29%)	28/562 (4.98%)
Myalgia [A] †	39/548 (7.12%)	37/562 (6.58%)
Pain in extremity [A] †	53/548 (9.67%)	32/562 (5.69%)
Nervous system disorders		
Dizziness [A] †	82/548 (14.96%)	57/562 (10.14%)
Dysgeusia [A] †	31/548 (5.66%)	33/562 (5.87%)
Headache [A] †	79/548 (14.42%)	60/562 (10.68%)
Paraesthesia [A] †	40/548 (7.3%)	27/562 (4.8%)
Peripheral sensory neuropathy [A] †	49/548 (8.94%)	46/562 (8.19%)
Psychiatric disorders		
Insomnia [A] †	58/548 (10.58%)	49/562 (8.72%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	97/548 (17.7%)	80/562 (14.23%)
Dysphonia [A] †	33/548 (6.02%)	14/562 (2.49%)
Dyspnoea [A] †	101/548 (18.43%)	95/562 (16.9%)
Epistaxis [A] †	30/548 (5.47%)	15/562 (2.67%)
Haemoptysis [A] †	45/548 (8.21%)	24/562 (4.27%)
Pharyngolaryngeal pain [A] †	31/548 (5.66%)	20/562 (3.56%)
Skin and subcutaneous tissue disorders		
Acne [A] †	38/548 (6.93%)	2/562 (0.36%)
Alopecia [A] †	107/548 (19.53%)	107/562 (19.04%)
Dermatitis acneiform [A] †	75/548 (13.69%)	1/562 (0.18%)
Dry skin [A] †	76/548 (13.87%)	9/562 (1.6%)

	Cetuximab Plus Chemotherapy	Chemotherapy Alone
	Affected/At Risk (%)	Affected/At Risk (%)
Pruritus [A] †	64/548 (11.68%)	13/562 (2.31%)
Rash [A] †	249/548 (45.44%)	17/562 (3.02%)
Skin fissures [A] †	30/548 (5.47%)	0/562 (0%)
Vascular disorders		
Hypertension [A] †	40/548 (7.3%)	27/562 (4.8%)
Hypotension [A] †	39/548 (7.12%)	23/562 (4.09%)
Phlebitis [A] †	48/548 (8.76%)	44/562 (7.83%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (Unspecified)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

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